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, 2016

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.)**
34 Crosby Drive, Suite 105 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, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting 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	☐

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, 2016, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $88 million. The number of shares outstanding of the registrant's class of common stock, as of March 1, 2017: 28,756,870

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2017 Annual Meeting of Shareholders, 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, 2016.

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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:

- the timing of and our ability to submit applications and obtain and maintain regulatory approvals for DEXTENZA, OTX-TP and our other product candidates, including the New Drug Application, or NDA, we resubmitted to the U.S. Food and Drug Administration, or FDA, for DEXTENZA for the treatment of post-surgical ocular pain and our planned and potential NDA supplements for DEXTENZA for the treatment of post-surgical inflammation and for the treatment of allergic conjunctivitis;

- our plans to develop and commercialize our product candidates based on our proprietary bioresorbable hydrogel technology platform;

- our ongoing and planned clinical trials, including our Phase 3 clinical trials of DEXTENZA for the treatment of allergic conjunctivitis, our Phase 2 clinical trial of DEXTENZA for dry eye disease and our Phase 3 clinical trials of OTX-TP for the treatment of glaucoma and ocular hypertension;

- 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 intravitreal depot with protein-based or small molecule drugs, including tyrosine kinase inhibitors, for the treatment of wet age-related macular degeneration 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 age-related macular degeneration, 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 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;
- our plans to raise additional capital, including through equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and marketing and distribution arrangements;
- the impact of government laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "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 development and commercialization of innovative therapies for diseases and conditions of the eye using our proprietary hydrogel platform technology. Our bioresorbable hydrogel-based drug product candidates are designed to provide extended delivery of therapeutic agents to the eye. Our lead product candidates are DEXTENZA (dexamethasone insert), for the treatment of post-surgical ocular inflammation and pain, allergic conjunctivitis and dry eye disease, and OTX-TP, for the treatment of glaucoma and ocular hypertension, which are extended-delivery, drug-eluting 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. Our intracanalicular inserts combine our hydrogel technology with U.S. Food and Drug Administration, or FDA, approved therapeutic agents with the goal of providing extended delivery of drug to the eye. We also have an intravitreal hydrogel depot which is in preclinical development for the treatment of diseases and conditions of the back of the eye, including wet age-related macular degeneration, or wet AMD. Our initial development efforts are focused on the use of our hydrogel depot in combination with anti-angiogenic drugs, such as protein-based anti-VEGF drugs or small molecule drugs, such as tyrosine kinase inhibitors, or TKIs. Our intravitreal depot is designed to be delivered via injection to release therapeutic agents, such as antibodies to vascular endothelial growth factor, or VEGF, over an extended period. We have entered into a collaboration, option and license with Regeneron Pharmaceuticals, Inc., or Regeneron, for the development and potential commercialization of products containing our extended-delivery hydrogel depot in combination with Regeneron's large molecule VEGF-targeting compounds, with the initial focus on the VEGF trap aflibercept, currently marketed under the brand name Eylea. In addition to our ongoing product development, we currently market our first 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

Our most advanced product candidate, DEXTENZA, incorporates the FDA-approved corticosteroid dexamethasone as an active pharmaceutical ingredient into a hydrogel-based drug-eluting insert for intracanalicular use. In September 2015, we submitted to the FDA a New Drug Application, or NDA, for DEXTENZA for the treatment of post-surgical ocular pain. On July 25, 2016, we announced that we had received a Complete Response Letter, or CRL, from the FDA regarding our NDA for DEXTENZA. In the CRL, the concerns raised by the FDA 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. The CRL did not identify any efficacy or safety concerns with respect to the clinical data provided in the NDA nor any need for additional clinical trials for the approval of the NDA. In November 2016, we received notice from the District Office accepting that our responses satisfactorily addressed the remaining corrective actions in the Form 483. We subsequently had communications with the FDA, including the District Office and offices within the Center for Drug Evaluation and Research, or CDER, including the Office of Process and Facilities, with regard to manufacturing issues and our plans for a resubmission to the NDA. On January 23, 2017, we announced that we had resubmitted our NDA. On February 22, 2017, we announced that the FDA accepted for review our NDA resubmission. The FDA determined that our NDA resubmission is a complete response and designated the NDA resubmission as a class 2, or major, review with a target action date under the Prescription Drug User Fee Act, or

PDUFA, of July 19, 2017. The FDA has not confirmed to us whether a re-inspection of our manufacturing facility will be required as part of its review, but such re-inspection may still be required. Adequate resolution of the Form 483 manufacturing deficiencies with the District Office is a prerequisite to the approval of the NDA for DEXTENZA, although the final decision as to the adequacy of our manufacturing processes is made by CDER, with input from the Office of Process and Facilities, as part of the NDA review process.

In March and April 2015, we reported topline results from two Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular inflammation and pain. The data from these two completed Phase 3 clinical trials and a prior Phase 2 clinical trial are being used to support our NDA for post-surgical ocular pain. In the first Phase 3 clinical trial, DEXTENZA met both primary efficacy endpoints, absence of pain in the study eye at day 8 and absence of inflammatory cells in the anterior chamber of the study eye 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. In November 2016, we reported topline results from a third Phase 3 clinical trial of DEXTENZA for the treatment of post-surgical ocular inflammation and pain. In this third 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. DEXTENZA also showed statistical significance for the secondary endpoints of this third Phase 3 clinical trial, including the absence of inflammatory cells and absence of pain at all measured time points except for day 2 for the absence of inflammatory cells and for the absence of anterior chamber flare, an indicator of inflammation, at all measured time points. Subject to 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.

DEXTENZA is also in Phase 3 clinical development for the treatment of allergic conjunctivitis. We announced topline results of our first Phase 3 clinical trial for allergic conjunctivitis in October 2015 and announced topline results of our second Phase 3 clinical trial for this indication in June 2016. We met the primary efficacy endpoint for ocular itching in the first Phase 3 trial but did not meet the primary efficacy endpoint for conjunctival redness in this trial. We did not meet the sole primary endpoint for ocular itching in the second Phase 3 trial. Certain post-hoc analyses of the second Phase 3 trial for DEXTENZA for the treatment of allergic conjunctivitis have led us to believe that a placebo insert which was present through the timepoints chosen as the primary efficacy endpoints may have enhanced the performance of the placebo. As such, we believe a fast-resorbing placebo insert may lessen the placebo response we observed in the completed second Phase 3 trial. 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 DEXTENZA as a potential therapy for allergic conjunctivitis. We have completed the design of a fast-resorbing placebo insert and plan to conduct a non-significant risk study in humans in the middle of 2017 with a clinical research organization comparing this insert to the insert used in our DEXTENZA trials. Depending on the results of this study, we may incorporate a more rapidly resorbing insert into the placebo arm of a future Phase 3 clinical trial. In the second Phase 3 clinical trial, as well as other DEXTENZA clinical trials completed to date regardless of indication, DEXTENZA has exhibited a strong safety profile and has been generally well-tolerated. There were no serious adverse events observed in the second Phase 3 clinical trial.

Finally, DEXTENZA is in Phase 2 clinical development for the treatment of dry eye disease. We announced topline results from an exploratory Phase 2 clinical trial for this indication in December 2015. We are assessing our plans for our dry eye program going forward and may focus future efforts on an intracanalicular insert other than a corticosteroid.

If we obtain FDA approval of our NDA for DEXTENZA for the treatment of post-surgical ocular pain on the new PDUFA action date, we expect to commercially launch this product in the United States in the first quarter of 2018. We expect to sell DEXTENZA in the United States through a direct sales force, although we plan to use a contract sales organization, or CSO, to initially hire and deploy this sales force. We will need additional financing to support this planned commercial launch of DEXTENZA. During the period of time between potential FDA approval and the commercial launch of DEXTENZA expected upon the potential approval of the pass-through reimbursement code, we intend to prepare for the commercialization process by conducting surgical demonstrations to key surgeons and educating them on the potential benefits of DEXTENZA, subject to the approval of the NDA. We expect to apply for a transitional pass-through reimbursement status code, or C code, from the Center for Medicare and Medicaid Services, or CMS, for DEXTENZA for the treatment of post-surgical ocular pain. We would expect pass-through reimbursement status to remain in effect for three years if we receive this pass-through status code. We have submitted an application to the CMS for a J code for DEXTENZA.

OTX-TP

Our second product candidate, OTX-TP, incorporates travoprost, which is an FDA-approved prostaglandin analogue in eye drop form that reduces elevated intraocular pressure, or IOP, as its active pharmaceutical ingredient, into a hydrogel-based drug-eluting intracanalicular insert. OTX-TP is being developed as a treatment for 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 each of the two Phase 3 trials to enroll approximately 550 patients at 50 sites in the United States. Based on discussions with the FDA, the 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 intraocular pressure, compared to the placebo and a clinically meaningful reduction of intraocular pressure prior to granting marketing approval.

Back-of-the-Eye Programs

In addition to DEXTENZA and OTX-TP, we are engaged in the preclinical development of our hydrogel depot 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 depot in combination with anti-angiogenic drugs, such as protein-based anti-VEGF drugs or small molecule drugs, such as tyrosine kinase inhibitors, or 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 intravitreal injection, 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.

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

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. Regeneron will be responsible for funding an initial preclinical tolerability study. We do not expect our funding requirements 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 initially through a network of ophthalmology-focused distributors. In early 2017, we terminated these distributors and hired a contract sales force of four representatives to sell ReSure Sealant. 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.

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, ReSure Sealant and our intravitreal depot. 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. Transparency Market Research, a provider of business information reports and services, estimates that the annual worldwide market for ophthalmic medications was $16 billion as of 2012 and is expected to increase to $21.6 billion by 2018.

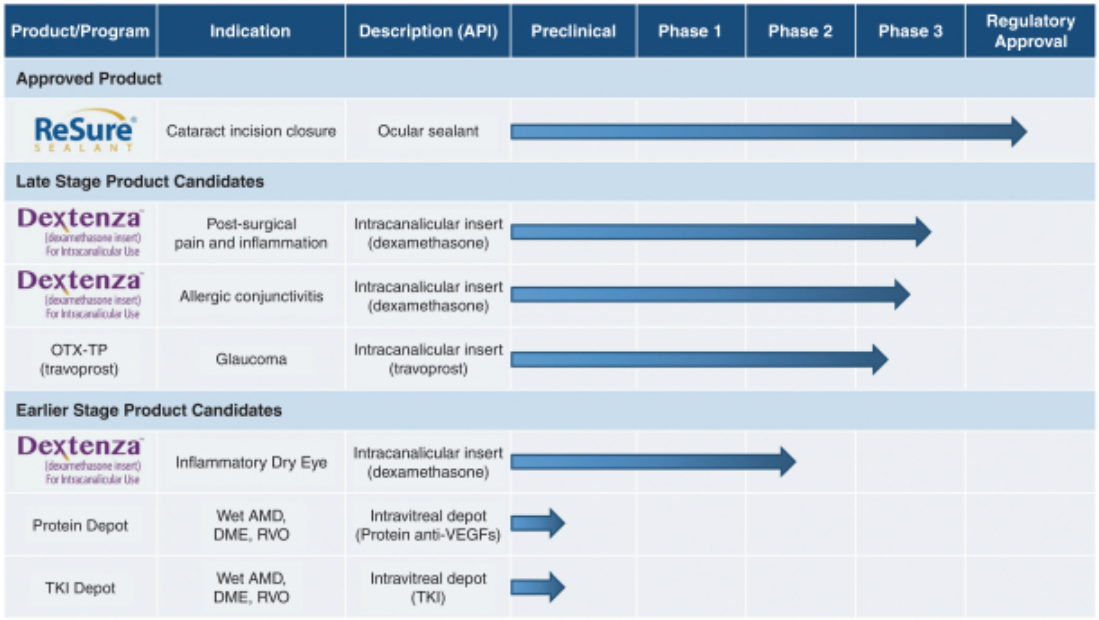
We have in-licensed all of the patent rights and a significant portion of the technology for ReSure Sealant and our hydrogel platform technology product candidates from Incept, LLC, or Incept, an intellectual property holding company. Amarpreet Sawhney, our President and Chief Executive Officer, is a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

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

Product Pipeline

The following table summarizes the status of our key product development programs and our marketed product. We hold worldwide exclusive commercial rights to the core technology underlying all of our products in development and have not granted commercial rights to any marketing partners other than the Option on commercial rights we

granted to Regeneron for the delivery of protein-based anti-VEGF drugs in our hydrogel depot for the treatment of retinal diseases.



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 combined with FDA-approved therapeutic agents to improve the delivery of these 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 to 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.

- *Rapidly 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 inflammation and pain and allergic conjunctivitis 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 pertaining to deficiencies in manufacturing process and controls identified during a facility inspection. We resubmitted our NDA in January 2017 and were notified in February 2017 that the resubmission has been designated as a class 2, or major, review with a target action date under PDUFA of July 19, 2017. In November 2016, we reported that we met both primary efficacy endpoints in a Phase 3 trial for DEXTENZA for the treatment of post-surgical ocular inflammation. We initiated the first of two Phase 3 trials of OTX-TP for the treatment of glaucoma and ocular hypertension in September 2016 and expect to initiate the second Phase 3 trial in the second half of 2017.

- *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. Subject to further advancing our DEXTENZA and OTX-TP clinical trials, we may allocate clinical development resources to additional clinical testing of our OTX-MP intracanalicular insert candidate, which incorporates the antibiotic moxifloxacin as an active pharmaceutical ingredient, for the treatment of ocular infections. 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.

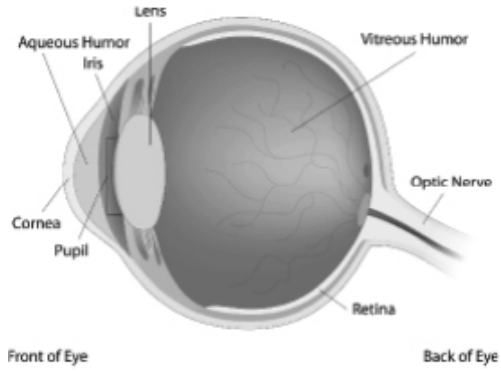
- *Pursue development of our intravitreal depot and other technologies for back-of-the-eye diseases and conditions*. We are developing a hydrogel-based drug delivery depot designed to release anti-angiogenic drugs, including anti-VEGF drugs, over a sustained period following administration by an intravitreal 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 depot 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 drug delivery depot could potentially provide a more consistent level of therapeutic agent compared with existing therapies. In 2015, sales of the most commonly prescribed anti-VEGF drugs approved for the treatment of wet AMD totaled approximately $4.2 billion in the United States. We have established in preclinical testing the compatibility of our technology with these compounds and observed sustained delivery over four to six months *in vivo* and initial evidence of tolerability of the drug-loaded hydrogel depot. We believe that results to date support the continuing preclinical development of this product candidate. In October 2016, we entered into the Collaboration Agreement, with Regeneron, for the development and potential commercialization of products containing our extended-delivery hydrogel depot 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 depot. 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 second half of 2017. We are also evaluating in early exploratory research additional opportunities beyond anti-VEGF drugs to utilize our hydrogel depot 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.

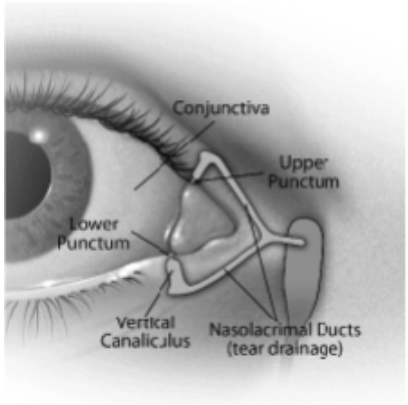
Eye Disease

The front of the human eye possesses focusing elements, consisting of the cornea on the surface of the eye, the lens and the aqueous humor, which is a transparent gelatinous fluid that fills the anterior and posterior chambers 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 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. 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 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 Inflammation and Pain

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

Post-Surgical Ocular Inflammation and Pain

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

further ocular complications, including pain, scarring and vision loss. Market Scope has estimated that approximately 5.6 million ocular surgeries were to be performed in the United States in 2016.

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 mast cell stabilizer or 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 and NSAIDs. Restasis is an ophthalmic formulation of the immune modulating drug cyclosporine. Restasis is a topical immunomodulator indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. 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 21.1 million prescriptions were filled in the United States in 2016 for anti-inflammatory drugs administered by eye drops for ocular diseases and conditions, resulting in sales of approximately $3.3 billion. These prescriptions consisted of approximately 9.1 million prescriptions and $774 million in sales for single-agent corticosteroids, 3.8 million prescriptions and $352 million in sales for NSAIDs, 4.8 million prescriptions and $289 million in sales for corticosteroid and antibiotic combination products and approximately 3.3 million prescriptions and $1.8 billion in sales of Restasis for dry eye disease. According to IMS Health data, approximately 7.2 million anti-allergy eye drop prescriptions were filled in the United States in 2016, resulting in sales of approximately $751 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure. The increased intraocular pressure associated with uncontrolled glaucoma results in degeneration of the optic nerve in the back of the eye. Once glaucoma develops, it is a chronic condition that requires life-long treatment. According to the Glaucoma Research Foundation, approximately 2.2 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 intraocular pressure, physicians typically initiate treatment by prescribing drugs administered as eye drops. These drugs either decrease fluid production or enhance fluid drainage. The classes of topical drugs used to treat glaucoma include prostaglandin analogs, or PGAs, beta-blockers, alpha-adrenergic agonists and carbonic anhydrase inhibitors. PGAs are the most widely prescribed class of drugs for glaucoma and are considered first-line glaucoma treatment. PGAs reduce intraocular pressure by enhancing the clearance and drainage of ocular fluid. The most frequently prescribed PGA is once-daily latanoprost, although travoprost, unoprostone and bimatoprost are also frequently used in the management of open-angle glaucoma. In cases where glaucoma is not easily managed by a drug regimen, surgical or laser treatments may be undertaken.

Market Data

According to IMS Health data, approximately 35.6 million prescriptions were filled in the United States in 2016 for drugs administered by eye drops for the treatment of glaucoma, resulting in sales of approximately $2.9 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 account for approximately half of the prescription volume in the glaucoma market. 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 19.1 million prescriptions were filled in the United States in 2016 for ophthalmic antibiotics administered by eye drops, resulting in sales of approximately $678 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 severe 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 intraocular pressure, 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 2014, sales of Lucentis and Eylea totaled approximately $3.5 billion in the United States.

Because eye drops are unable to carry effective drug concentrations to the back-of-the-eye, intravitreal injections are used to deliver medications to this location. However, the frequency of intravitreal injections 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 intraocular pressure, 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 2016 there were to be approximately 3.9 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 incisions that allow entry to the eye are the preferred 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 intraocular pressure fluctuates or as a result of the application of external pressure or manipulation. In addition, incisions that are left to self-seal are often associated with fluid leakage, which can sometimes result in complications. Complications from fluid leakage include the development of hypotony, or low intraocular pressure, 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 poor 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 and corneal distortion. 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 that can result from improper suture technique. 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

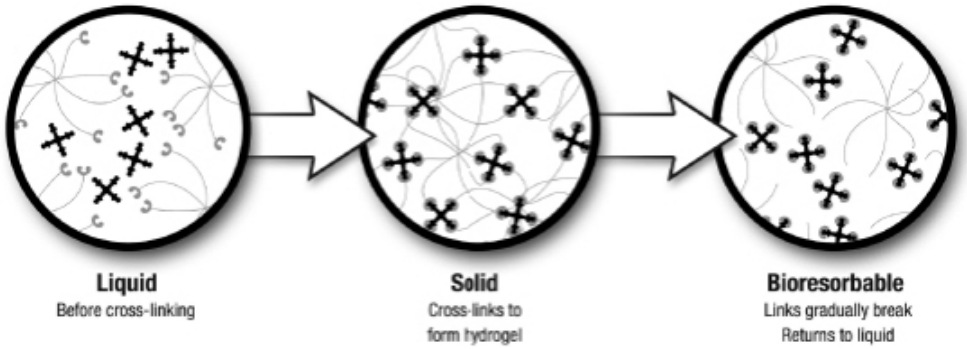
Our Hydrogel Technology Platform

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, ReSure Sealant and our intravitreal depot.

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

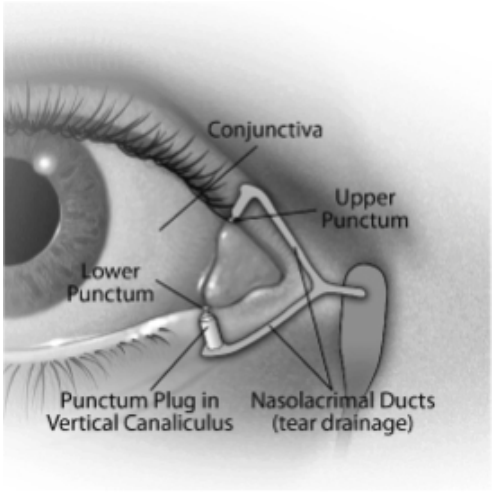
degradation rate. Our technology enables us to make hydrogels that can bioresorb over days, weeks or several months. The figure below depicts the formation and bioresorption of the hydrogel for ReSure Sealant.



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



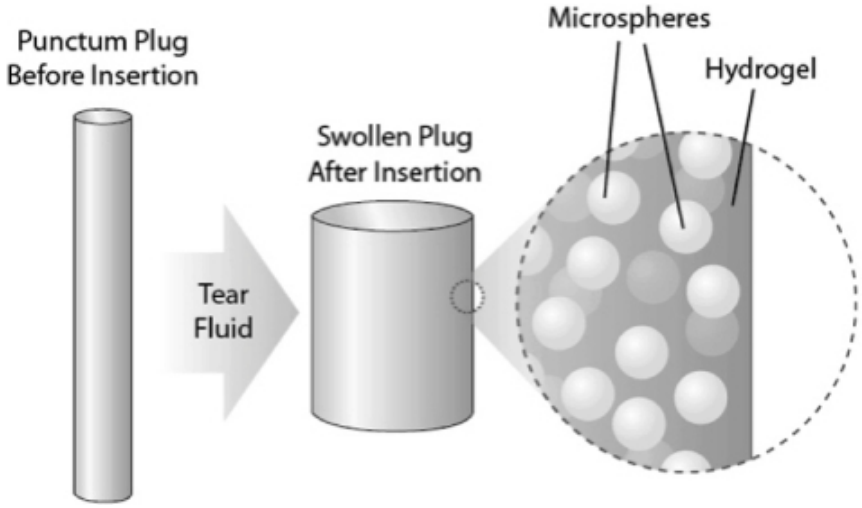
Our intracanalicular inserts utilize our proprietary hydrogel technology and are embedded with an active drug. Following insertion through the punctum, our inserts swell in tear fluid to fill the vertical canaliculus, which secures the inserts in place. We design our inserts to release drug in a sustained 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 easily remove an intracanalicular insert by a simple process of pushing the soft insert back through the punctum.

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

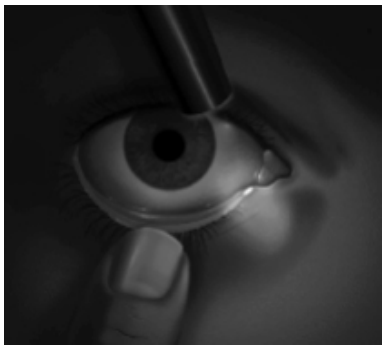
treatment. For chronic diseases, such as glaucoma, we have designed our intracanalicular inserts for repeat administration with extended dosing periods. We are concentrating our development efforts on intracanalicular inserts incorporating active pharmaceutical ingredients that are approved by the FDA 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, causing 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 intraocular pressure 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 Depot Injection for Back-of-the-Eye Diseases and Conditions

We are engaged in the preclinical development of our hydrogel depot 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 depot 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.

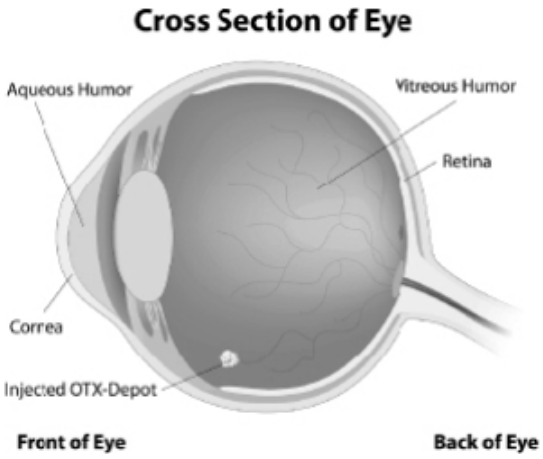
We are pursuing a multi-pronged strategy to seek to maximize the potential of this technology.

- We are evaluating an intravitreal depot 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 depot.

- We are also researching the delivery of small molecule TKIs from our hydrogel depot and have selected the TKI we plan to advance to an initial human clinical trial in the second half of 2017. 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 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.

Our intravitreal depot consists of a PEG-based hydrogel suspension, which contains embedded micronized protein particles of an anti-angiogenic compound. We designed the intravitreal depot 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 depot for delivery using ordinary syringes and fine gauge needles compatible with the current standard of care. Once in the vitreous humor, the hydrogel is designed to retain the anti-VEGF compound until it is 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 anti-VEGF compound release.

ReSure Sealant for Ocular Wound Closure

ReSure Sealant is our bioresorbable hydrogel product for wound closure following cataract surgery. This product received marketing approval from the FDA in January 2014. 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. 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. However, we 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. We do not expect to generate meaningful levels of revenue from the sale of ReSure in 2017.

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 inflammation and pain	Intracanalicular insert (Dexamethasone)	Phase 3	Two Phase 3 trials completed in the first quarter of 2015; NDA resubmission for ocular pain accepted in February 2017; FDA has established a target action date under PDUFA of July 19, 2017; third Phase 3 trial topline results reported for treatment of post-surgical ocular inflammation in November 2016
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
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
Anti-angiogenic hydrogel depot	Wet AMD	Injectable intravitreal hydrogel depot (protein-based and small molecule anti-angiogenic compounds)	Preclinical	Ongoing preclinical studies
OTX-TIC	Glaucoma and ocular hypertension	Intracameral injection (Travoprost)	Preclinical	Initiation of pilot study planned for second half of 2017

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 inflammation and pain, 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 this indication.

We selected dexamethasone as the active pharmaceutical ingredient for DEXTENZA because it:

- is approved by the FDA and has a long history of ophthalmic use;
- is available on a generic basis;
- is highly potent and is typically prescribed for prevention of ocular inflammation and pain following ocular surgery;
- is available from multiple qualified suppliers; and
- has physical properties that are well suited for incorporation within our 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 administration four to six times daily, 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 inflammation and pain as compared to eye drops and that a low dose amount may provide enhanced safety by eliminating spikes in intraocular pressure 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 intraocular pressure due to the high levels of drug, have limited its widespread adoption as a treatment for this condition. These spikes in intraocular pressure 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 inflammation and pain, allergic conjunctivitis and dry eye disease. Because DEXTENZA incorporates an active pharmaceutical

ingredient already approved by the FDA for the treatment of ocular inflammation and pain, we did not need to conduct Phase 1 clinical trials for this product candidate. 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 inflammation and pain. In the first Phase 3 clinical trial, DEXTENZA met both primary efficacy endpoints, absence of pain at day 8 and absence of inflammatory cells at day 14, with statistical significance. In the second Phase 3 clinical trial, DEXTENZA met the primary efficacy endpoint for absence of pain at day 8 with statistical significance but did not meet the primary efficacy endpoint for absence of inflammatory cells at day 14. We met with the FDA in April 2015 to discuss the path forward for seeking marketing approval of DEXTENZA for the treatment of post-surgical ocular inflammation and pain. In this pre-NDA clinical meeting, the FDA indicated that the existing data from our Phase 2 and two Phase 3 clinical trials are appropriate to support an NDA submission for DEXTENZA for a post-surgical ocular pain indication. The FDA further indicated that we would need additional data from a third Phase 3 clinical trial for the inflammation endpoint to support the potential labeling expansion of DEXTENZA's indications for use. We initiated a third Phase 3 clinical trial for DEXTENZA for the treatment of post-surgical ocular inflammation and pain in October 2015. In September 2015, we submitted to the FDA an NDA, for DEXTENZA for the treatment of post-surgical ocular pain. In July 2016, we received a CRL from the FDA pertaining to deficiencies in manufacturing process and controls identified during a facility inspection. We resubmitted our NDA to the FDA in January 2017 and were notified in February 2017 that the resubmission has been designated as a class 2, or major, review, with a target action date under PDUFA of July 19, 2017. In November 2016, we reported that we met both primary efficacy endpoints in a Phase 3 trial for DEXTENZA for the treatment of post-surgical ocular inflammation. 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 obtain FDA approval of our NDA for DEXTENZA for the treatment of post-surgical ocular pain on the new PDUFA action date, we expect to commercially launch DEXTENZA for post-surgical ocular pain in the United States in the first quarter of 2018. If we receive approval of the sNDA for post-surgical ocular inflammation, we would expect to expand the labeling to include this indication.

- In November 2014, we completed a Phase 2 clinical trial evaluating the safety and efficacy of DEXTENZA for the treatment of allergic conjunctivitis. Based upon the encouraging results of this Phase 2 clinical trial and a subsequent meeting with the FDA, we began enrollment for an initial Phase 3 clinical trial of DEXTENZA for this indication in June 2015. We announced topline results from this trial in October 2015. We initiated a second Phase 3 clinical trial of DEXTENZA for this indication in November 2015. We announced topline results for the second Phase 3 clinical trial in June 2016. We are planning to conduct a non-significant risk study of a rapidly resorbing intracanalicular insert and based on these results may initiate an additional Phase 3 clinical trial for this indication in the second half of 2017.

- 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 and may focus future efforts on an intracanalicular insert containing an immunosuppressant drug.

Clinical Trials for Post-Surgical Inflammation and Pain

Completed Phase 2 Clinical Trial

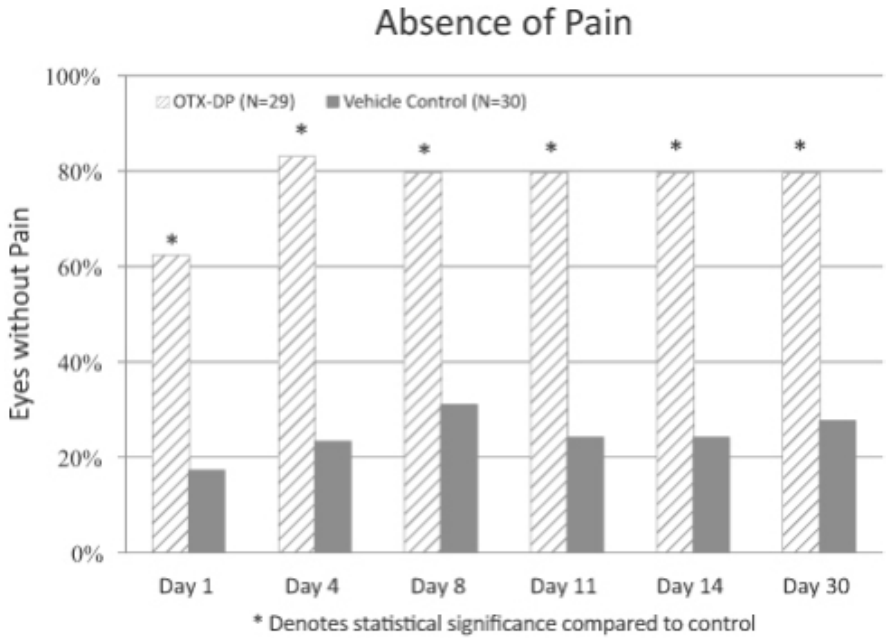
In 2013, we completed a prospective, randomized, parallel-arm, vehicle-controlled, multicenter, double-masked Phase 2 clinical trial evaluating the safety and efficacy of DEXTENZA for the treatment of ocular inflammation and pain following cataract surgery. We conducted this trial in 60 patients at four sites in the United States pursuant to an effective investigational new drug application, or 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.

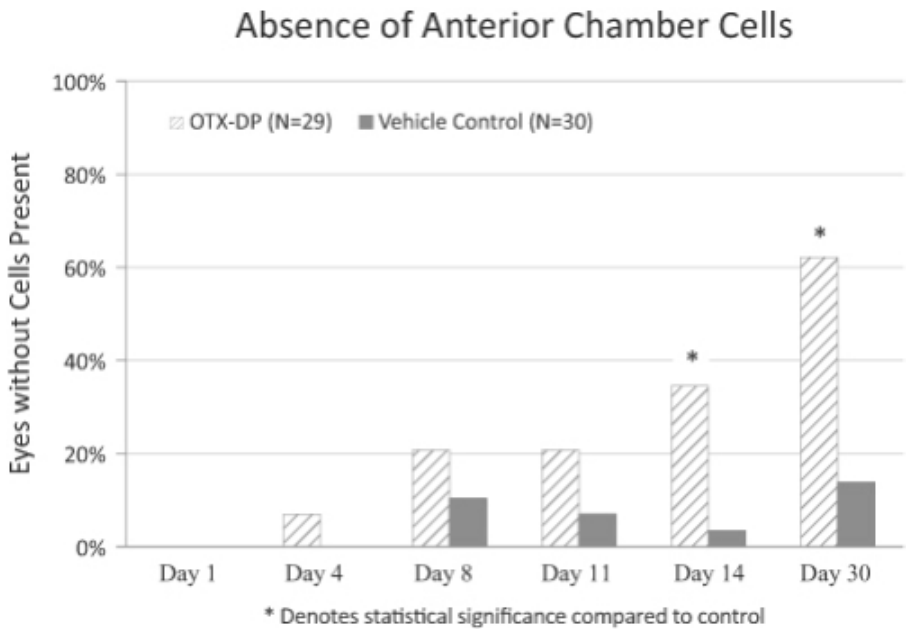
We enrolled patients in this trial who were at least 21 years of age undergoing unilateral clear corneal cataract surgery. We excluded patients from the trial if, among other reasons, they had intraocular inflammation or ocular pain in the study eye at screening or had glaucoma or ocular hypertension.

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.

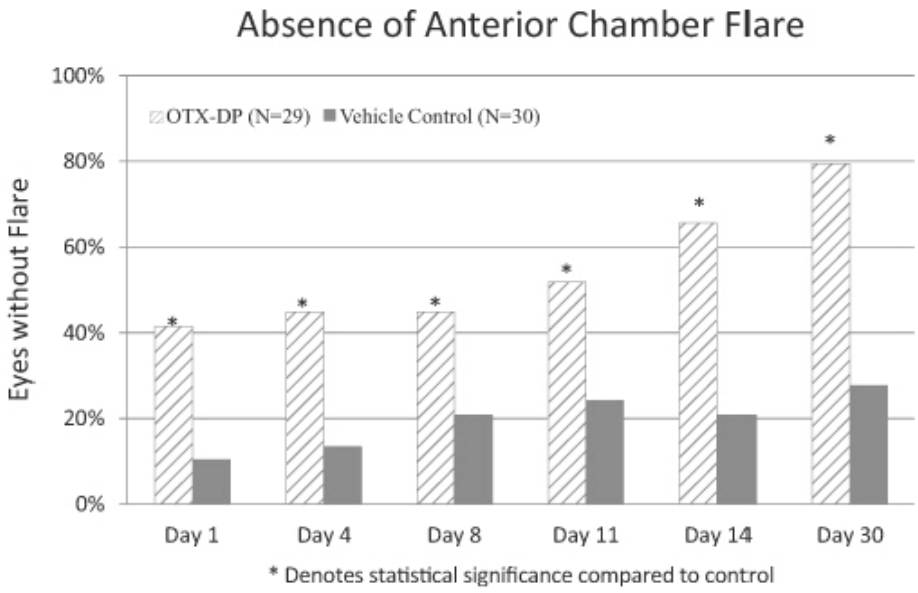


In this trial, DEXTENZA did not meet the primary efficacy endpoint with statistical significance for absence of cells in the anterior chamber compared to the vehicle control at day 8. However, there was a trend of improved absence

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 inflammation and pain following cataract surgery. We initiated the first of these Phase 3 clinical trials in February 2014 and the second trial in April 2014. Patient enrollment was completed in September 2014, and the topline efficacy data from these clinical trials was reported in March and April 2015. We initiated a third Phase 3 clinical trial in the October 2015. Patient enrollment in the third Phase 3 clinical trial was completed in May 2016 and the topline efficacy data was reported in November 2016.

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

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

We evaluated as secondary efficacy measures the level of flare, an indicator of inflammation in the anterior chamber of the study eye at each evaluation date until day 30 and absence of inflammatory cells in the anterior chamber of the study eye and absence of pain in the study eye at each evaluation date other than the day used for the primary efficacy measure until day 30. The secondary analyses on primary endpoints were intended to be exploratory assessments that can be used to support the results from the primary endpoints. If we obtain favorable results showing efficacy of DEXTENZA at earlier time points for absence of cells or absence of pain, we will consider seeking to expand the labeling for DEXTENZA as part of our NDA following any marketing approval that we may receive. 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 intraocular pressure, 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 pertaining to deficiencies in manufacturing process and controls identified during a facility inspection. We resubmitted our NDA to the FDA in January 2017 and were notified in February 2017 that the resubmission has been designated as a class 2, or major, review with a target action date under PDUFA of July 19, 2017. 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 obtain FDA approval of our NDA for DEXTENZA for the treatment of post-surgical ocular pain on the new PDUFA action date, we expect to commercially launch this product in the United States in the first quarter of 2018. If we receive 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 intraocular pressure, 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 intraocular pressure, 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 intraocular pressure, 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 intraocular pressure, 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 intraocular pressure 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 plan to conduct a non-significant risk study in humans to assess the potential efficacy effect of the placebo intracanalicular insert by comparing a rapidly resorbing insert against the placebo insert we used in the Phase 3 clinical trials. If we obtain favorable results in the non-significant risk study, we expect to conduct a third Phase 3 clinical trial, and 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 this third Phase 3 clinical trial, we plan to submit an sNDA to the FDA for DEXTENZA for the treatment of allergic conjunctivitis for only the ocular itching indication. We expect that we would submit this sNDA under Section 505(b)(2) of the FDCA. See "—Government Regulation—Section 505(b)(2) NDAs" for additional information. Based on discussions with the FDA, we expect to use safety results from our Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular inflammation and pain 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 BCVA, 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 prostaglandin analog 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.

Travoprost is a synthetic prostaglandin analog that reduces intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 ongoing 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 intraocular pressure, when compared to the placebo, as a primary efficacy endpoint, and a clinically meaningful reduction of intraocular pressure 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 intraocular pressure within a specified range and a specified minimum level of visual acuity in each eye. The trial protocol provided that if the participant's intraocular pressure 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:

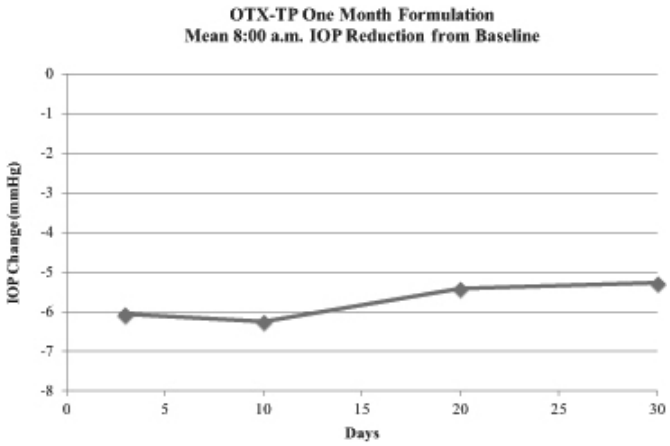
- mean intraocular pressure at 8:00 a.m. at each evaluation date as measured in millimeters of mercury, or mmHg;
- mean intraocular pressure at 10:00 a.m. and 4:00 p.m. at days 10, 20 and 30;
- change in mean intraocular pressure from baseline at each time point measured; and
- retention of the insert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

We assessed intraocular pressure at multiple time points on each evaluation date because intraocular pressure 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 intraocular pressure at baseline was included in the efficacy analysis.

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

We observed a clinically meaningful reduction in mean intraocular pressure over the 30 day trial period. For eyes that retained the insert, from a mean baseline intraocular pressure of 27.2 mmHg, the mean intraocular pressure during treatment was maintained at or below 22 mmHg at each evaluation date and time point. The mean reduction in intraocular pressure 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 intraocular pressure reduced risk of disease progression by approximately 50%. The results for change in mean intraocular pressure 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

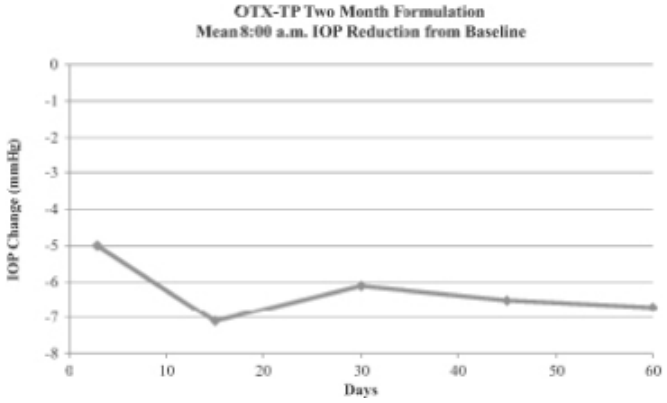
In 2012, we completed a prospective, single arm, open label pilot study evaluating the initial safety and efficacy of the two-month version of OTX-TP for the treatment of glaucoma and ocular hypertension. We conducted this trial in 20 patients, and in 36 eyes, at two sites in South Africa.

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 intraocular pressure, change in mean intraocular pressure 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 retained, 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 intraocular pressure 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 intraocular pressure over the 60 day trial period. For eyes that retained the insert, from a mean baseline intraocular pressure of 28.7 mmHg, the mean intraocular pressure during treatment was maintained at or below 22.0 mmHg beginning on day 15 and at all subsequent evaluation dates. The mean reduction in intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure from baseline on each evaluation date and at each time point;

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

- mean intraocular pressure 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 intraocular pressure 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 intraocular pressure at 8:00 a.m. at each evaluation date;
- mean intraocular pressure at 12:00 p.m. and 4:00 p.m. at days 30, 60 and 90;
- change in mean intraocular pressure 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 intraocular pressure at baseline was included in the primary efficacy analysis.

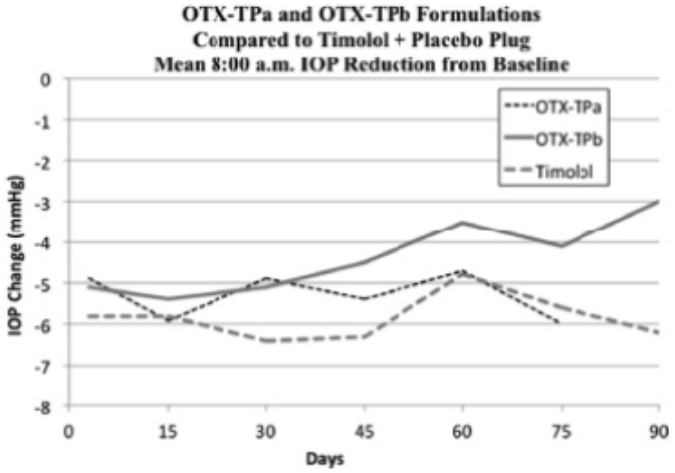
We evaluated safety in all patients at each study visit with an assessment of general eye conditions, including visual acuity, along with any adverse events.

Efficacy: In the timolol group, for eyes that retained the insert, from a mean baseline intraocular pressure of 26.1 mmHg, the mean intraocular pressure 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 intraocular pressure 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 intraocular pressure of 25.8 mmHg, the mean intraocular pressure 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 intraocular pressure 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 intraocular pressure of 26.4 mmHg, the mean intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure. The secondary efficacy endpoints in this trial were the difference between treatment groups in the mean change from baseline in average diurnal intraocular pressure at day 90, the difference between treatment groups in the mean change from baseline in intraocular pressure at each individual time point at day 60 and day 90, the difference between treatment groups in the mean change in average diurnal intraocular pressure and intraocular pressure 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 intraocular pressure and intraocular pressure 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 intraocular pressure 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. intraocular pressure 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 intraocular pressure and change in mean intraocular pressure from baseline at 8:00 a.m. at days 3, 15, 45 and 75; and

- mean intraocular pressure and change in mean intraocular pressure 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 intraocular pressure 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 intraocular pressure lowering effect of 3.3 mmHg compared to baseline, versus mean diurnal intraocular pressure 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 intraocular pressure lowering of 6.3 mmHg compared to baseline for the timolol group.

On day 60, the OTX-TP group experienced a mean intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure in the OTX-TP treatment group on day 60 was 21.81 mmHg. The mean diurnal intraocular pressure in the timolol treatment group on day 60 was 19.54 mmHg.

The mean diurnal intraocular pressure in the OTX-TP treatment group on day 90 was 21.53 mmHg. The mean diurnal intraocular pressure 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 intraocular pressure 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 intraocular pressure at day 30, 60 and 90 at all time points ranged from 18.9 mmHg to 20.7 mmHg. The mean reduction in intraocular pressure 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 intraocular pressure at day 30, 60 and 90 at all time points ranged from 21.0 mmHg to 22.3 mmHg. The mean reduction in intraocular pressure 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 intraocular pressure 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 intraocular pressure 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 intraocular pressure were 5.6 mmHg at day 30 and 5.4 mmHg at day 60 in this trial. We believe that the higher intraocular pressure 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 intraocular pressure 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 Intraocular Pressure (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 prostaglandin analogs. The compliance rate with prostaglandin analog 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 each of the two Phase 3 clinical trials for an exposure duration of three months in these pivotal clinical trials. A number of patients will be studied for up to 12 months for safety evaluations. In each of the two Phase 3 clinical trials, 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 intraocular pressure, when compared to the placebo, as a primary efficacy endpoint, and a clinically meaningful reduction of intraocular pressure in the absolute. The primary efficacy endpoint will be evaluated at 2, 6 and 12 weeks at 8 a.m., 10 a.m. and 4 p.m. at each of the three timepoints. We initiated the first Phase 3 clinical trial in September 2016 and expect to initiate the second Phase 3 clinical trial in the second half of 2017.

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

Intracameral Glaucoma (OTX-TIC) Product Candidate

We are conducting 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 insert 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 three to four months. Preclinical studies to date have demonstrated clinically meaningful intraocular pressure lowering and good pharmacokinetics in the aqueous humor. We expect to initiate a pilot clinical study outside the United States in the second half of 2017 to assess safety and obtain initial

efficacy data. The study is expected to be a prospective, single-center, randomized, double-masked, sham-controlled study to evaluate the safety, efficacy and tolerability of OTX-TIC compared to topical travoprost (eye drops) in up to 20 patients with open-angle glaucoma or ocular hypertension. If the results from this trial are promising, we plan to advance to a Phase 2 clinical development program in the United States.

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

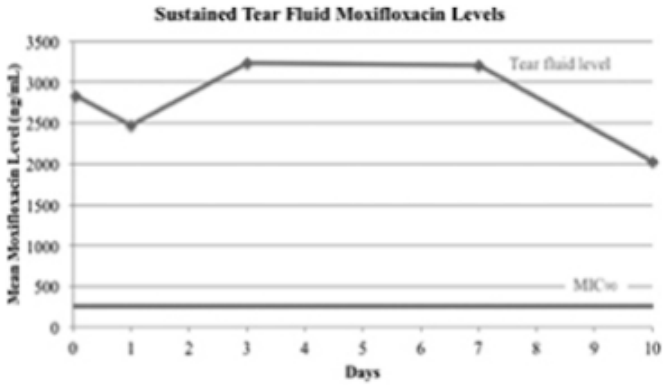
In 2010, we completed a prospective, single center, single arm, open label Phase 1 clinical trial evaluating the initial safety and pharmacokinetics of OTX-MP in post-cataract surgery patients. We conducted the trial in 10 patients at one site in Singapore.

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 Depot for the Treatment of Back-of-the-Eye Diseases

We are engaged in a preclinical development program of a sustained-release hydrogel depots 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 depot in combination with anti-angiogenic compounds, including anti-VEGF compounds, for the treatment of wet AMD. Our initial depots 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 depot, 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 depot.

- We are also researching the delivery of small molecule TKIs from our hydrogel depot and have selected the TKI we plan to advance to an initial human clinical trial in the second half of 2017. 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 depot has 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 depot. The injection of a bevacizumab formulation without our hydrogel depot 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 depot containing bevacizumab showed the same decrease of tissue concentration of bevacizumab in successively distant tissues. However, the injection of our hydrogel depot containing bevacizumab resulted in a sustained level of drug over the course of the 30 day study. Further, after injection our hydrogel depot 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 injection of our hydrogel depot containing bevacizumab exceeded those of bevacizumab injected without our hydrogel depot. 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 hydrogel depots 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 depot 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 depot 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. Upon market launch in the first quarter of 2014, we sold ReSure Sealant through a network of independent distributors across the United States. In early 2017, we terminated the distributors and hired a contract sales force of four representatives to sell ReSure Sealant. 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 ongoing post-approval study is designed to ascertain the incidence of endophthalmitis in patients treated with ReSure Sealant.

Pivotal Clinical Trial

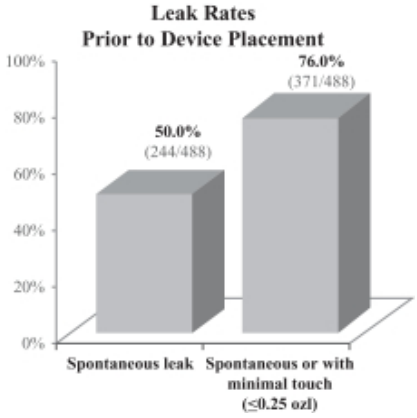
In 2013, we completed a prospective, randomized, parallel-arm, controlled, multicenter, subject-masked pivotal clinical trial evaluating the safety and effectiveness of ReSure Sealant. In this trial, we enrolled 488 patients at 24 sites across the United States. One patient was excluded prior to treatment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

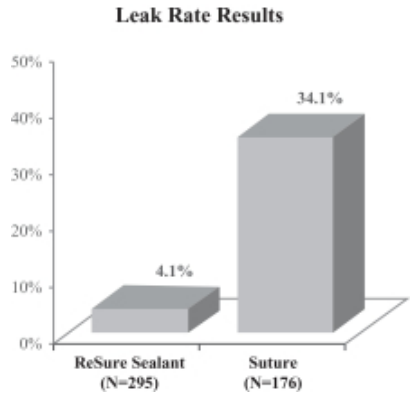
inferiority margin for the ReSure Sealant pivotal clinical trial was a percentage difference in leak rates between ReSure Sealant and sutures of 5%.

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. Upon the Advisory Committee's favorable recommendation, 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. We are required to provide periodic reports to the FDA on the progress of each post-approval study over the next four to five years.

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. 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. 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. In the first quarter of 2017, we terminated the independent distributors and started selling ReSure Sealant through a small team of in-house sales representatives calling on ambulatory service centers and hospitals. We continue to build a marketing 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. If we obtain FDA approval of our NDA for DEXTENZA for the treatment of post-surgical ocular pain on the new PDUFA action date, we expect to commercially launch this product in the United States in the first quarter of 2018. Subject to receiving approval for the pain indication pursuant to the initial 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. Within the United States, we plan to initially use a contract sales organization, or CSO, to hire and deploy a sales force dedicated to selling DEXTENZA and to hire our own sales management team. We expect to deploy 60 to 70 sales representatives at commercial launch through the CSO in addition to a team of reimbursement specialists. We will need additional financing to support this planned commercial launch of DEXTENZA. Over time, we may elect to selectively convert CSO sales representatives to direct employees. If OTX-TP is approved for marketing, we may use a combination of 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 depot 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 expect to initiate a Phase I clinical trial of our TKI product candidate in the second half of 2017. 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 insert and depot 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 multi-product 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. Once the leasehold improvements being made to this facility have been completed, we plan to seek FDA validation of this facility. We plan to maintain our existing manufacturing space and extend the operating lease beyond its current expiration date of June 2018.

We purchase active pharmaceutical ingredient drug substance from independent suppliers on a purchase order basis for incorporation into our drug insert and depot products. 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 maximum flexibility and rapid changeover 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 intracanalicular insert and intravitreal depot 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, 2017, we have licensed from Incept a total of 22 U.S. patents, ten U.S. patent applications and foreign counterparts of some of these patents and patent applications. Thirteen of the 22 licensed U.S. patents and three of the ten licensed U.S. patent applications cover the technology that underlies our intracanalicular insert product candidates, ReSure Sealant or our intravitreal depot.

Intracanalicular Insert Product Candidates

In the United States, we have licensed from Incept four patent families related to our intracanalicular insert product candidates, comprised of an aggregate of seven U.S. patents. The first patent family, which is licensed on an exclusive basis, is comprised of two U.S. patents that will expire in 2030 and covers composition and method claims specific to the drug delivery and design of the intracanalicular inserts. The second and third patent families, which are licensed on an exclusive basis, are comprised of three U.S. patents that will expire between 2018 and 2020 and cover the hydrogel composition of the intracanalicular inserts and methods of making and using hydrogel implants that swell in tissue tracts. The fourth patent family, which is licensed on a non-exclusive basis, is comprised of a U.S. patent that will expire in 2018 and a U.S. patent that will expire in 2029 that collectively covers the hydrogel composition of OTX-TP and OTX-MP and the process of making them in combination with certain drug release particles.

In the European Union and some other areas outside of the United States, we have licensed from Incept three patent families related to our intracanalicular insert product candidates, comprised of an aggregate of six patents and three patent applications. The first patent family, which is licensed on an exclusive basis, is comprised of one issued patent that will expire in 2028 that covers certain drug release features of the intracanalicular inserts in combination with their hydrogel composition. The second patent family, which is licensed on an exclusive basis, is comprised of three issued patents that expire in 2030 and three patent applications that, if granted, will expire in approximately 2030 and covers composition and method claims related to the drug delivery and design of the intracanalicular inserts, in combination with their hydrogel composition. The third patent family, which is licensed on a non-exclusive basis, is comprised of two patents that will expire in approximately 2019 that covers the hydrogel composition of the OTX-TP and OTX-MP intracanalicular inserts in combination with certain drug release particles.

ReSure Sealant

In the United States, we have exclusively licensed from Incept two patent families comprised of six U.S. patents related to ReSure Sealant. One U.S. patent that will expire in 2024 covers the process of making and using compositions of the hydrogel. A second U.S. patent that will expire in 2032 covers certain features of the ReSure Sealant package. A third U.S. patent that expires in 2019 covers the hydrogel composition. The remaining three U.S. patents, which expire between 2017 and 2019, cover compositions and methods of making or using the hydrogel, in combination with a visualization agent.

Outside of the United States, we have exclusively licensed only one patent in Canada that expires in 2019 that is directed to a medical kit for use with ReSure Sealant.

Intravitreal Depot

In the United States, we have exclusively licensed from Incept four patent families related to the intravitreal depot, comprised of an aggregate of two U.S. patents and three U.S. patent applications. The first patent family is comprised of a U.S. patent application that, if granted will expire in approximately 2027, and covers certain drug-release features of the hydrogel depot in combination with its hydrogel composition. The second patent family is comprised of one U.S. patent that will expire in 2033 and one U.S. application that, if granted, will expire in approximately 2032; these cover the process of making the hydrogel depot with its drug release features and the resultant compositions. The third patent family, comprised of a U.S. patent that expires in 2019, covers the hydrogel composition of the hydrogel depot. The fourth patent family, comprised of a U.S. patent application that, if granted, will expire in approximately 2036, is directed to a drug delivery vehicle and method.

In the European Union and some other areas outside of the United States, we have exclusively licensed from Incept three patent families related to the intravitreal depot. The first patent family is comprised of one patent and one patent application that if the application is granted, will expire in approximately 2027, and covers certain drug-release features of the hydrogel depot in combination with its hydrogel composition. The second patent family is directed to a hydrogel depot with its drug release features and the resultant compositions and is comprised of eight patent applications that, if granted, will expire in approximately 2032. The third patent family is directed to a drug delivery vehicle and method, and has one PCT application that is expected to serve as the basis for filings in multiple countries outside of the United States and, if granted, will expire in approximately 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 President and Chief Executive Officer, 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 containing the Company's sustained-release hydrogel depot 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.

Following the exercise of the Option, 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.

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. is conducting Phase 3 clinical development of IBI-10090, a biodegradable therapeutic for injection of dexamethasone into the anterior chamber of the eye to treat inflammation associated with cataract surgery.

Competitors of OTX-TP

Inotek Pharmaceuticals is in Phase 3 clinical development of an eye drop-based product candidate for the treatment of glaucoma and has designed their Phase 3 clinical trials as a superiority to a placebo control arm. Allergan, Inc. is conducting Phase 2 clinical development of Bimatoprost Sustained-Release, a biodegradable intraocular implant consisting of a PGA and a biodegradable polymer matrix to treat glaucoma. ForSight VISION5 is conducting 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 is conducting Phase 2 clinical development of an intracanalicular insert for the treatment of glaucoma. Invisia 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 Depot

Our intravitreal depot 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. In addition, Ophthotech Corporation is currently conducting Phase 3 clinical trials of Fovista, an anti-platelet-derived growth factor, or PDGF, product candidate to be administered in combination with anti-VEGF compounds for the treatment of wet AMD.

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, 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 regulates drugs under the FDCA and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. Biological products are subject to regulation by the FDA under the Public Health Service Act, or PHSA, 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 inflammation and pain 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 who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or IND so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial. 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 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 drug; 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 NDAs and BLAs is subject to an application user fee, which for federal fiscal year 2017 is $2,038,100. The sponsor of an approved NDA or BLA is also subject to annual product and establishment user fees, which for fiscal year 2017 are $97,750 per product and $512,200 per establishment. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses, an exception from the establishment fee when the establishment does not engage in manufacturing the drug during a particular fiscal year, and an exception from the product fee for a drug that is the same as another drug approved under an abbreviated pathway.

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 NDA 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. 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 NDA, 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 drug'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.

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.

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. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

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.

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.

Biosimilars

The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, or PPACA, 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. To date, four biosimilar products have been approved by FDA 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.

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.

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.

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 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.

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.

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.

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 PPACA, 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 PPACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of PPACA 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. PPACA 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 PPACA 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.

In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the PPACA. The Budget Resolution is not a law, although it is widely viewed as the first step toward the potential passage of legislation that would repeal certain aspects of the PPACA. Also in January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

The President and Congressional leaders have expressed particular interest in repealing certain PPACA provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. It is possible that these 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. The scope of potential future legislation to repeal and replace PPACA provisions is highly uncertain in many respects, and it is possible that some of the PPACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with PPACA coverage expansion provisions.

Employees

As of March 1, 2017, we had 118 full-time employees. Of these full-time employees, 86 employees are primarily engaged in research and development activities. In 2016, 2015, and 2014, we spent $27.1 million, $26.6 million, and $18.9 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 34 Crosby Drive, Suite 105, 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 $28.7 million for the year ended December 31, 2014, $39.7 million for the year ended December 31, 2015 and $44.7 million for the year ended December 31, 2016. As of December 31, 2016, we had an accumulated deficit of $173.9 million. Through December 31, 2016, 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 the first quarter of 2014, we began recognizing revenue from sales of ReSure Sealant, which was approved in January 2014 by the U.S. Food and Drug Administration, or FDA, to seal clear corneal incisions following cataract surgery. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials and, beginning in the first quarter of 2014, commercialization of ReSure Sealant. 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 that our expenses will increase substantially if and as we:

- continue to pursue the clinical development of our most advanced intracanalicular insert product candidates, DEXTENZA and OTX-TP;
- conduct joint research and development under our strategic collaboration with Regeneron Pharmaceuticals, Inc., or Regeneron, for the development and potential commercialization of products containing our extended-delivery hydrogel depot in combination with Regeneron's large molecule vascular endothelial growth factor, or 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 preclinical development activities associated with our back-of-the-eye 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. In the CRL, the concerns raised by the FDA pertain 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. On February 22, 2017, we announced that the FDA accepted for review our NDA resubmission. The FDA determined that our NDA resubmission is a complete response and designated the NDA resubmission as a class 2, or major, review with a target action date under the Prescription Drug User Fee Act, or PDUFA, of July 19, 2017. The FDA has not confirmed to us whether a re-inspection of our manufacturing facility will be required as part of its review, but such re-inspection may still be required. Adequate resolution of the Form 483 manufacturing deficiencies with the District Office is a prerequisite to the approval of the NDA for DEXTENZA, although the final decision as to the adequacy of our manufacturing processes is made by CDER, with input from the Office of Process and Facilities, as part of the NDA review process.

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, 2016, we had cash and cash equivalents and marketable securities of $68.1 million. Based on our current plans and forecasted expenses, we believe that our existing cash and cash equivalents and marketable securities will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into the second quarter of 2018. We will need to obtain additional capital to the support the planned commercial launch of DEXTENZA, subject to FDA approval. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities, including our current NDA for DEXTENZA;
- the level of product sales from any additional product 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 depot 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 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 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 do not expect to generate significant revenue from sales of any product for several years, if at all. Accordingly, we will need to obtain substantial additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or 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 a combination of revenue from sales of ReSure Sealant and potential payments under our collaboration with Regeneron, 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. In April 2014, we entered into a credit facility with Silicon Valley Bank , or SVB and MidCap Financial SBIC, LP, or MidCap. In December 2015, we amended this facility to increase the aggregate principal amount to $15.6 million and extend both the interest-only payment period and the maturity date. In

March 2017, we further amended this facility to increase the total commitment of $38.0 million, including $18.0 million of borrowings drawn at closing, and options on two additional tranches of $10.0 million, each contingent upon the achievement by us of regulatory and commercial milestones. The interest-only payment period was extended through February 1, 2018 and can be further extended upon the achievement of certain regulatory and commercial milestones. 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.

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 marketable securities 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 inflammation and pain, allergic conjunctivitis and dry eye disease 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 and expanding 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, 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 and our Phase 1 clinical trial of OTX-MP, were conducted with small patient populations, making it difficult to predict whether the favorable results that we observed in such studies will be repeated in larger and more advanced clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

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

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 inflammation and pain 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 2016, we received a CRL from the FDA regarding our NDA for DEXTENZA. In the CRL, the concerns raised by the FDA pertain to deficiencies in manufacturing process and controls 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 inflammation and pain 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 inflammation and pain, achieving statistically significant differences between the treatment group and the placebo group for the absence of inflammatory cells on day 14 and the absence of pain on day 8, respectively. Secondary analyses on the primary efficacy measures have also been completed. DEXTENZA achieved each of the secondary endpoints related to absence of inflammatory cells, absence of pain, and absence of anterior chamber flare with statistical significance compared to placebo at each of the pre-specified 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 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 obtain 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. In this trial, on day 60 at the 8:00 a.m. time point, the OTX-TP group experienced a mean intraocular pressure lowering effect of 4.7 mmHg, compared with intraocular pressure 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 intraocular pressure lowering effect of 5.1 mmHg, compared with an intraocular pressure 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 intraocular pressure 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 intraocular pressure, 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. The trial design will not have eye drops, placebo or active, administered in either the treatment or the placebo-controlled arm. However, results from our Phase 2 clinical trials may not necessarily predict a likelihood of achieving our primary endpoint in the Phase 3 clinical trials with statistical significance, including as a result of differences in trial design. If we do not achieve our primary endpoint in the Phase 3 clinical trials with statistical significance, 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. 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 following insertion and 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 sustained-release 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 Phase 3 trials 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 intend to conduct, 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 inflammation and pain following cataract surgery until after

approval of such product in adult populations for that indication. While the FDA ultimately approved our request, if the FDA had required us to conduct pediatric studies in advance of FDA approval in adult populations, we would have experienced significant delays in our ability to obtain marketing approval for DEXTENZA for 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.

Patient enrollment is affected by a variety of factors, 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.

Each of our two Phase 3 clinical trials of OTX-TP are expected to enroll an aggregate of approximately 550 patients at 50 sites in the United States and will be the largest clinical trials we will have conducted to date. Patients randomized into the placebo control arm will not receive any glaucoma medications during the course of the trials. Our inability to enroll a sufficient number of patients in the Phase 3 clinical trials 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 inflammation and pain following cataract surgery, there were two subjects that experienced serious adverse events in the DEXTENZA group in each trial, none of which were ocular in nature or considered by the investigator to be related to the study treatment. In our third Phase 3 clinical trial of DEXTENZA for the treatment of post-surgical ocular inflammation and pain, there were three subjects that experienced serious adverse events in the DEXTENZA group, one of which was ocular in nature and none of which were considered by the investigator to be related to the study treatment. There was one ocular serious adverse event in the vehicle control group in the three completed Phase 3 clinical trials, which was hypopyon, or inflammatory cells in the anterior chamber. In our earlier Phase 2 clinical trial of DEXTENZA for the same indication, there were three serious adverse events, none of which was considered by the investigator to be related to the study treatment. In the DEXTENZA group of this Phase 2 clinical trial of DEXTENZA, the only adverse event that occurred more than once for the same subject was reduced visual acuity, which occurred twice but was not considered by the investigator to be related to the study treatment.

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 eye 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 a hydrogel-based drug delivery depot designed to release therapeutic antibodies and small molecules such as tyrosine kinase inhibitors, or 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 depot 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. 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 and 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 multi-product facility located at our corporate headquarters 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, add manufacturing personnel and ensure that validated processes are consistently implemented in our facility. The upgrade and expansion of our facility will require additional regulatory approvals. In addition, it will be costly and time-consuming to expand our facility and recruit necessary additional personnel. If we are unable to expand our manufacturing 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 ongoing 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. The concerns raised in the CRL pertain to the deficiencies in manufacturing processes raised in the February Form 483 letter. On January 23, 2017, we announced that we had resubmitted our NDA. On February 22, 2017, we announced that the FDA accepted for review our NDA resubmission. The FDA determined that our NDA resubmission is a complete response and designated the NDA resubmission as a class 2, or major, review with a target action date under the Prescription Drug User Fee Act, or PDUFA, of July 19, 2017. The FDA has not confirmed to us whether a re-inspection of our manufacturing facility will be required as part of its review, but such re-inspection may still be required. Adequate resolution of the Form 483 manufacturing deficiencies with the District Office is a prerequisite to the approval of the NDA for DEXTENZA, although the final decision as to the adequacy of our manufacturing processes is made by CDER, with input from the Office of Process and Facilities, as part of the NDA review process.

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 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 the manufacturing facility at our corporate headquarters 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 a third party. Even if we could transfer manufacturing to a third party, the shift would likely be expensive and time-consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need FDA approval before selling any products manufactured at that facility. 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 inflammation and pain 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 may determine to build a direct sales force to sell DEXTENZA, if approved for marketing and may initially use a contract sales organization to staff a dedicated team of sales representatives. We may also consider co-promotional arrangements with larger ophthalmology companies. 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 depot in combination with Regeneron's large molecule VEGF-targeting compounds. Because we do not plan to determine whether to seek regulatory approval for any of our product candidates outside of the United States until after we receive 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.

Other companies have 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.

We expect to apply for a transitional pass-through reimbursement status, or C code, from the Centers for Medicare and Medicaid Services, or CMS for DEXTENZA for the treatment of post-surgical ocular pain, subject to the approval of the NDA resubmission we filed with the FDA for this indication. 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 depot 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 depot 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 depot 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. 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 depot product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our intravitreal depot product candidates. We may not be able to

seek and obtain a viable, alternative collaborator to partner 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 with protein based anti-VEGF compounds to explore the feasibility of delivering their drugs using our intravitreal depot. 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 intravitreal depot 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 inflammation and pain 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, Integra LifeSciences Holdings Corporation, or Integra, another licensee of Incept, has filed suit against HyperBranch Medical Technology, Inc. alleging infringement of several patents which we also license. This enforcement action could result in one or more of these patents which both we and Integra license being invalidated or rendered unenforceable. 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 four issued patents outside of the United States for two of our three intracanalicular insert product candidates, and two of these expire by 2019. We have two 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 extension 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. 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.

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.

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 the ongoing review 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.

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.

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.

Current and future legislation may increase the difficulty and cost for us and any current or future collaborators to obtain marketing approval of our other 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 other product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products 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 collaborators, may receive for any approved products.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- 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 of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- 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 product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new 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 products; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Other legislative changes have been proposed and adopted since the PPACA 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, due to subsequent legislation, will continue until 2025. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Moreover, the Medicare Access and CHIP Reauthorization Act of 2015, among other things, introduced the Quality Payment Program under which Medicare physicians will be required to either participate in an Advanced Alternative Payment Model, or AAPM, and assume some risk for patient outcomes, or participate in the Merit-Based Incentive Payment System, or MIPS, which will provide an incentive compensation structure that will rate physicians in part based on cost of services. 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.

We expect that the PPACA, 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. Pricing pressures recently experienced by the pharmaceutical industry may be further exacerbated by legislative and policy changes under consideration by the Trump administration.

In addition, with the new Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the PPACA. It remains to be seen, however, precisely what the new legislation will provide, when it will be enacted and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates. For example, the President and Congressional leaders have expressed particular interest in repealing certain PPACA provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. It is possible that these 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. The scope of potential future legislation to repeal and replace PPACA provisions is highly uncertain in many respects, and it is possible that some of the PPACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with PPACA coverage expansion provisions.

Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. 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 collaborators to more stringent product labeling and post-marketing testing and other requirements.

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

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

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

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

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

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

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

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

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

We, our collaborators and any third-party manufacturers we may engage in the future are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the

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

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

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

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

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 are highly dependent on the research and development, clinical and business development expertise of Amar Sawhney, Ph.D., our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We maintain "key person" insurance for Dr. Sawhney, but we do not have any such insurance for any of our other 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.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs, manufacturing, sales, marketing and

distribution. 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 June 2016, we entered into a lease agreement for new general office research and development and manufacturing space. We intend to relocate to this new space beginning in June 2017 as part of our expansion. We expect to incur significant expenses in renovating this facility and purchasing capital equipment. 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, including the move to, and buildout of, our new facility, or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock

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

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

This concentration of voting power may:

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

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

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

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

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

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

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

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 or if our commercial launch of ReSure Sealant is unsuccessful. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management's attention and resources.

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

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

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our stock incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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

We are an "emerging growth company," and 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 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 103,000 square feet of space. The lease for approximately 71,000 square feet of space expires in June 2027, the lease for approximately 20,000 square feet of space expires in 2018 and the lease for the remaining approximately 12,000 square feet of space expires in 2017.

Item 3. Legal Proceedings

We are not currently subject to any material legal proceedings.

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 sale prices per share for our common stock on the NASDAQ Global Market for the periods indicated:

2015	High	Low
First Quarter	$ 44.19	$ 19.55
Second Quarter	$ 42.78	$ 20.63
Third Quarter	$ 29.22	$ 13.36
Fourth Quarter	$ 17.34	$ 6.75
2016		
First Quarter	$ 10.19	$ 5.07
Second Quarter	$ 14.50	$ 4.63
Third Quarter	$ 8.23	$ 4.04
Fourth Quarter	$ 11.91	$ 4.82

Holders

As of March 1, 2017, there were approximately 40 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 2017 Annual Meeting of Shareholders 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, 2016 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

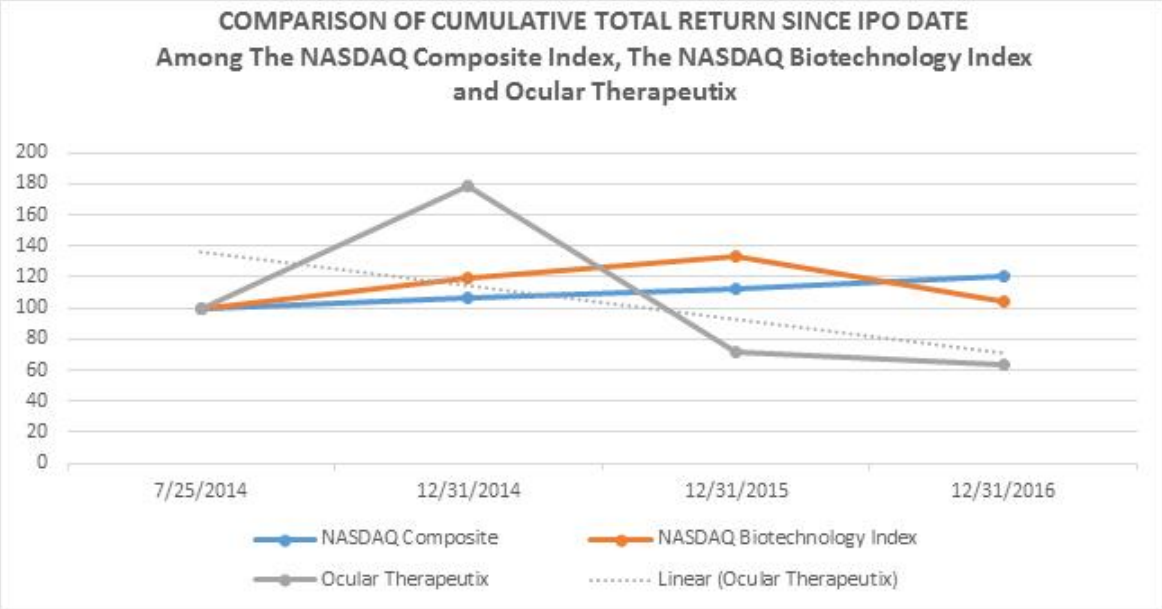
We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

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, 2016. 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, 2016, 2015, and 2014, and the balance sheet data as of December 31, 2016 and 2015 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, 2013 and 2012 and the balance sheet data as of December 31, 2014, 2013 and 2012 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,				
	2016	2015	2014	2013	2012
	(in thousands, except per share data)				
Statement of Operations Data:					
Revenue:					
Product revenue	$ 1,845	$ 1,354	$ 460	$ —	$ 10
Collaboration revenue	42	396	312	—	—
Total revenue	1,887	1,750	772	—	10
Costs and operating expenses:					
Cost of product revenue	443	319	91	—	7
Research and development	27,065	26,611	18,880	10,517	11,540
Selling and marketing	6,701	3,852	1,982	625	657
General and administrative	11,004	9,165	6,913	1,761	1,477
Total costs and operating expenses	45,213	39,947	27,866	12,903	13,681
Loss from operations	(43,326)	(38,197)	(27,094)	(12,903)	(13,671)
Other income (expense):					
Interest income	304	166	7	13	4
Interest expense	(1,680)	(1,724)	(1,119)	(441)	(377)
Other income (expense), net	(1)	7	(442)	14	(49)
Total other expense, net	(1,377)	(1,551)	(1,554)	(414)	(422)
Net loss	(44,703)	(39,748)	(28,648)	(13,317)	(14,093)
Accretion of redeemable convertible preferred stock to redemption value	—	—	(11)	(27)	(35)
Net loss attributable to common stockholders	$(44,703)	$(39,748)	$(28,659)	$(13,344)	$(14,128)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.80)	$ (1.71)	$ (2.69)	$ (5.11)	$ (5.60)
Weighted average common shares outstanding, basic and diluted	24,816	23,244	10,653	2,609	2,523

	As of December 31,				
	2016	2015	2014	2013	2012
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 68,145	$ 105,064	$ 74,828	$ 17,505	$ 23,854
Working capital	61,598	101,605	70,309	14,672	20,787
Total assets	74,939	110,306	78,193	19,146	25,285
Preferred stock warrant liability	—	—	—	254	268
Long-term debt, net of discount, including current portion	15,643	15,272	14,865	2,457	4,065
Redeemable convertible preferred stock	—	—	—	74,344	65,823
Total stockholders' equity (deficit)	52,008	89,588	58,696	(59,472)	(46,611)

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 development and commercialization of innovative therapies for diseases and conditions of the eye using our proprietary hydrogel platform technology. Our bioresorbable hydrogel-based drug product candidates are designed to provide extended delivery of therapeutic agents to the eye. Our lead product candidates are DEXTENZA (dexamethasone insert), for the treatment of post-surgical ocular inflammation and pain, allergic conjunctivitis and dry eye disease, and OTX-TP for the treatment of glaucoma and ocular hypertension, which are extended-delivery, drug-eluting 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. Our intracanalicular inserts combine our hydrogel technology with U.S. Food and Drug Administration, or FDA, approved therapeutic agents with the goal of providing extended delivery of drug to the eye. We also have an intravitreal hydrogel depot which is in preclinical development for the treatment of diseases and conditions of the back of the eye including wet age-related macular degeneration, or wet AMD. Our initial development efforts are focused on the use of our hydrogel depot in combination with anti-angiogenic drugs, such as protein-based anti-VEGF drugs or small molecule drugs, such as tyrosine kinase inhibitors, or TKIs. Our intravitreal depot is designed to be delivered via injection to release therapeutic agents, such as antibodies to vascular endothelial growth factor, or VEGF, over an extended period. We have entered into a collaboration, option and license with Regeneron Pharmaceuticals, Inc., or Regeneron, for the development and potential commercialization of products containing our extended-delivery hydrogel depot in combination with Regeneron's large molecule VEGF-targeting compounds, with the initial focus on the VEGF trap aflibercept, currently marketed under the brand name Eylea. In addition to our ongoing product development, we currently market our first 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

Our most advanced product candidate, DEXTENZA, incorporates the FDA-approved corticosteroid dexamethasone as an active pharmaceutical ingredient into a hydrogel-based drug-eluting insert for intracanalicular use. In September 2015, we submitted to the FDA a New Drug Application, or NDA, for DEXTENZA for the treatment of post-surgical ocular pain. On July 25, 2016, we announced that we had received a Complete Response Letter, or CRL, from the FDA regarding our NDA for DEXTENZA. On January 23, 2017, we announced that we had resubmitted our NDA. On February 22, 2017, we announced that the FDA accepted for review our NDA resubmission. The FDA determined that our NDA resubmission is a complete response and designated the NDA resubmission as a class 2, or major, review with a target action date under the Prescription Drug User Fee Act, or PDUFA, of July 19, 2017.

We have completed three Phase 3 clinical trials of DEXTENZA for the treatment of post-surgical ocular inflammation and pain. The data from 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 pursuant to our NDA, 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 is in Phase 2 clinical development for the treatment of dry eye disease. We announced topline results from an exploratory Phase 2 clinical trial for this indication in December 2015. We are assessing our plans for our dry eye program going forward and may focus future efforts on an intracanalicular insert containing an immunosuppressant drug.

OTX-TP

Our second product candidate, OTX-TP, incorporates travoprost, an FDA-approved prostaglandin analog that reduces elevated intraocular pressure, or IOP, as its active pharmaceutical ingredient, into a hydrogel-based drug-eluting intracanalicular insert. OTX-TP is being developed as a treatment for 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.

Back-of-the-Eye Programs

In addition to DEXTENZA and OTX-TP, we are engaged in the preclinical development of our hydrogel depot 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 depot in combination with anti-angiogenic drugs, such as protein-based anti-VEGF drugs or small molecule drugs, such as tyrosine kinase inhibitors, or 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.

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 containing our extended-delivery hydrogel depot 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. We granted Regeneron an option, or the Option, to enter into an exclusive, worldwide license under our intellectual property to develop and commercialize products containing our extended-delivery hydrogel depot in combination with Regeneron's large molecule VEGF-targeting compounds, or Licensed Products.

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. Regeneron will be responsible for funding an initial preclinical tolerability study. We do not expect our funding requirements 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.

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, initially through a network of ophthalmology-focused distributors. In early 2017, we terminated these distributors and hired a contract sales force of four representatives to sell ReSure Sealant. 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.

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 $44.7 million, $39.7 million and $28.6 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of $173.9 million.

Our total cost and operating expenses were $45.2 million, $39.9 million and $27.9 million for the years ended December 31, 2016, 2015 and 2014, respectively, including $6.0 million, $4.6 million and $5.0 million, respectively, in non-cash stock-based compensation expense and licensing and consulting fees paid in stock. We anticipate that our operating expenses will increase substantially as we 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 depot for the sustained delivery of protein-based or small molecule anti-angiogenic drugs, such as anti-VEGF drugs 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. We expect to continue to incur substantial additional expenses for product manufacturing, sales, marketing and distribution for our product candidates for which we obtain marketing approval.

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. As of February 28, 2017, we have sold 263,418 shares of common stock under the 2016 ATM Agreement at a weighted average exercise price of $8.87 per share resulting in net proceeds of approximately $2.0 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 $23.5 million after deducting underwriting discounts expenses. We believe that our existing cash and cash equivalents and marketable securities, will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into the second quarter of 2018. We will need to obtain additional capital to the support the planned commercial launch of DEXTENZA, subject to FDA approval. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

From our inception through December 31, 2016, 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 2017. 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.

In September 2013, we entered into a feasibility agreement with a biopharmaceutical company relating to our intravitreal drug delivery depot. Under this agreement, the biopharmaceutical company agreed to pay us up to $0.5 million under this feasibility study. In the event that the agreement was terminated in advance of the achievement of certain milestones, we would have been required to refund certain portions of the funding based on the actual work completed or milestones achieved as of the date of termination. In the fourth quarter of 2014, the Company completed the task related to the first milestone at which time the $0.3 million became non-refundable. The biopharmaceutical company has indicated that they will not proceed with the second phase of the agreement. The Company does not have any further obligations in connection with this agreement.

We entered into a feasibility agreement with a biotechnology company relating to our intravitreal drug delivery depot 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. Through December 31, 2016, the Company had recognized revenue of $0.5 million related to this agreement.

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, 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;
- expenses associated with preclinical development activities; and
- royalty and patent legal fees payable made under our licensing agreement with Incept, LLC, or Incept.

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,		
	2016	2015	2014
	(in thousands)		
ReSure Sealant	$ 236	$ 330	$ 40
DEXTENZA for post-surgical ocular inflammation and pain	2,686	2,058	2,151
DEXTENZA for allergic conjunctivitis	2,815	5,541	1,785
DEXTENZA for dry eye disease	101	662	—
OTX-TP for glaucoma and ocular hypertension	1,941	2,048	2,023
Unallocated expenses	19,286	15,972	12,881
Total research and development expenses	$27,065	$26,611	$18,880

We expect that our expenses will increase in connection with our ongoing activities. We estimate that in 2017, we will incur approximately $33.0 million to $35.0 million of research and development expenses, including costs related to clinical trials and other research and development activities. Of this amount, we estimate we will incur approximately $17.0 million to $19.0 million of external research and development expenses related to clinical trial and regulatory costs for our DEXTENZA and OTX-TP product candidates and approximately $15.0 million to $16.0 million of other research and development activities that we do not expect to track by program. We expect that our total costs to renovate our new facility, including research and development laboratories, manufacturing space and office space will be approximately $3.6 million, net of a landlord provided construction allowance of up to $2.8 million. In addition, we expect to purchase $2.0 million to $2.5 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 2017, as follows:

- approximately $2.0 million to $2.8 million for DEXTENZA for post-surgical ocular inflammation and pain;
- approximately $1.0 million to $1.2 million for DEXTENZA for allergic conjunctivitis;
- approximately $12.0 million to $15.0 million for OTX-TP for glaucoma and ocular hypertension; and
- approximately $0.9 million to $1.2 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. Through December 31, 2014, we incurred selling and marketing expenses in connection with our first-generation surgical sealant product. In addition, we invested in sales and marketing resources in anticipation of an earlier approval of our surgical sealant product in the United States than we ultimately received from the FDA, as a result of a change in designation from a 510(k) to a PMA regulatory path. During the years ended December 31, 2016, 2015 and 2014, we incurred selling and marketing expense in connection with ReSure Sealant, which we began commercializing in the first quarter of 2014.

We expect selling and marketing expenses to increase in preparation for the potential approval of our resubmitted NDA by the FDA and commercial launch of our DEXTENZA product candidate for the treatment of post-surgical ocular pain. We expect such expenses to further increase in preparation for the potential label expansion to include post-surgical ocular inflammation, subject to submission and approval of an NDA supplement.

Other Income (Expense)

Interest Income. Interest income consists primarily of interest income earned on cash and cash equivalents and marketable securities. In each of 2016, 2015, and 2014, our interest income has not been significant due to the low rates of interest being earned on our invested balances.

Interest Expense. Interest expense consists of interest expense on our debt. We borrowed $15.0 million in aggregate principal amount in April 2014. 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.

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 and 2016, 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,		
	2016	2015	2014
Risk-free interest rate	1.42 %	1.67 %	2.24 %
Expected term (in years)	6	6	6
Expected volatility	85 %	71 %	77 %
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.

Subsequent to the approval of ReSure Sealant in January 2014, we started to capitalize inventory of this product. We review our inventories for potential obsolescence.

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, 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
Cost 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 inflammation and pain	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 inflammation and pain 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 for ocular inflammation and pain 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 and 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 plan 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 and 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.

Comparison of the Years Ended December 31, 2015 and December 31, 2014

The following table summarizes our results of operations for the years ended December 31, 2015 and 2014:

	Year Ended December 31, 2015	2014	Increase (Decrease)
	(in thousands)		
Revenue:			
Product revenue	$ 1,354	$ 460	$ 894
Collaboration revenue	396	312	84
Total revenue	1,750	772	978
Costs and operating expenses:			
Cost of product revenue	319	91	228
Research and development	26,611	18,880	7,731
Selling and marketing	3,852	1,982	1,870
General and administrative	9,165	6,913	2,252
Total costs and operating expenses	39,947	27,866	12,081
Loss from operations	(38,197)	(27,094)	(11,103)
Other income (expense):			
Interest income	166	7	159
Interest expense	(1,724)	(1,119)	(605)
Other income (expense), net	7	(442)	449
Total other expense, net	(1,551)	(1,554)	3
Net loss	$(39,748)	$(28,648)	$(11,100)

Revenue

We generated $1.4 and $0.5 million of product revenue during the years ended December 31, 2015 and December 31, 2014, respectively, from sales of our ReSure Sealant product, for which we received FDA approval in January 2014. We generated $0.4 million and $0.3 million of revenue from our collaboration agreements in 2015 and 2014, respectively.

Research and Development Expenses

	Year Ended December 31, 2015	2014	Increase (Decrease)
	(in thousands)		
Direct research and development expenses by program:			
ReSure Sealant	$ 330	$ 40	$ 290
DEXTENZA for post-surgical ocular inflammation and pain	2,058	2,151	(93)
DEXTENZA for allergic conjunctivitis	5,541	1,785	3,756
DEXTENZA for dry eye disease	662	—	662
OTX-TP for glaucoma and ocular hypertension	2,048	2,023	25
Unallocated expenses:			
Personnel costs	9,345	5,828	3,517
All other costs	6,627	7,053	(426)
Total research and development expenses	$ 26,611	$ 18,880	$ 7,731

Research and development expenses were $26.6 million for the year ended December 31, 2015, compared to $18.9 million for the year ended December 31, 2014. The increase of $7.7 million was primarily due to an increase of $4.6 million in clinical trial and regulatory expenses and an increase of $3.1 million in unallocated expenses. Clinical trial and regulatory expenses increased for the year ended December 31, 2015, compared to the year ended December 31, 2014 primarily due to the timing of clinical trials being conducted for DEXTENZA product candidate for the treatment of allergic conjunctivitis and dry eye disease.

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 $2.1 million for our DEXTENZA product candidate for the treatment of post-surgical ocular inflammation and pain which was in Phase 3 clinical trials, $5.5 million for our DEXTENZA product candidate for the treatment of allergic conjunctivitis which was in Phase 3 clinical trials, $0.7 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 2b clinical trials. In comparison, for the year ended December 31, 2014, we incurred $6.0 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 2a clinical trials, $1.8 million for our DEXTENZA product candidate for the treatment of allergic conjunctivitis which was in Phase 2a clinical trials and $2.2 million for our DEXTENZA product candidate for the treatment of post-surgical ocular inflammation and pain which was in Phase 3 clinical trials. Unallocated research and development costs decreased $0.4 million for the year ended December 31, 2015, compared to the year ended December 31, 2014. In the year ended December 31, 2014, we recorded a one-time, non-cash expense of $1.7 million for a license fee paid in the form of stock which is included in the unallocated costs. In addition, unallocated personnel costs increased by $3.5 million, relating to additional hiring primarily in our clinical, regulatory and quality department and an increase in stock-based compensation expense.

Selling and Marketing Expenses

	Year Ended December 31, 2015	2014	Increase (Decrease)
	(in thousands)		
Personnel related (including stock-based compensation)	$ 1,508	$ 799	$ 709
Professional fees	1,625	852	773
Facility related and other	719	331	388
Total selling and marketing expenses	$ 3,852	$ 1,982	$ 1,870

Selling and marketing expenses were $3.9 million for the year ended December 31, 2015, compared to $2.0 million for the year ended December 31, 2014. The increase of $1.9 million was primarily due to an increase of $0.7 million in personnel costs relating to additional hiring and additional stock-based compensation expense, an increase of $0.8 million in professional fees including 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,		Increase
	2015	2014	(Decrease)
	(in thousands)		
Personnel related (including stock-based compensation)	$ 5,216	$ 4,469	$ 747
Professional fees	2,951	1,390	1,561
Facility related and other	998	1,054	(56)
Total general and administrative expenses	$ 9,165	$ 6,913	$ 2,252

General and administrative expenses were $9.2 million for the year ended December 31, 2015, compared to $6.9 million for the year ended December 31, 2014. The increase of $2.3 million was due to a $0.8 million increase in personnel related costs and an increase of $1.6 million in professional fees, partially offset by a decrease of $0.1 million in facility-related and other costs. Our personnel related costs increased due primarily to hiring in our general and administrative function. Professional fees increased primarily due to increased activities to support our operating as a public company for a full year.

Other Income (Expense), Net

Other expense, net was $1.6 million for the year ended December 31, 2015, compared to $1.6 million for the year ended December 31, 2014.

Liquidity and Capital Resources

Since inception, we have incurred significant operating losses. Our net losses were $44.7 million, $39.7 million and $28.7 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of $173.9 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, 2016, 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 263,418 shares of common stock under the 2016 ATM Agreement at a weighted average exercise price of $8.87 per share resulting in net proceeds of approximately $2.0 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 $23.5 million after deducting underwriting discounts expenses.

As of December 31, 2016, we had cash and cash equivalents and marketable securities of $68.1 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 commitment to $38.0 million including $18.0 million of borrowings drawn at closing, which was used primarily to pay-off outstanding balances as of the closing date, and options on two additional tranches of $10.0 million each contingent on the achievement of regulatory and commercial milestones for DEXTENZA. The interest-only payment period was extended through February 1, 2018 and there are provisions to further extend the interest-only period based on the achievement of certain milestones. See "—Contractual Obligations and Commitments" for additional information.

Cash Flows

As of December 31, 2016, we had cash and cash equivalents and marketable securities of $68.1 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

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

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Cash used in operating activities	$(34,001)	$(33,743)	$(20,496)
Cash provided by (used in) investing activities	35,568	(38,569)	(38,586)
Cash provided by financing activities	585	65,703	78,970
Net increase (decrease) in cash and cash equivalents	$ 2,152	$ (6,609)	$ 19,888

Operating activities. 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.

Net cash used in operating activities was $20.5 million for the year ended December 31, 2014, primarily resulting from our net loss of $28.6 million, partially offset by non-cash charges of $6.0 million and cash provided by changes in our operating assets and liabilities of $2.2 million. Our net loss was primarily attributed to research and development activities and our general and administrative expenses partially offset by $0.8 million of revenue in the period. Our net non-cash charges during the year ended December 31, 2014 primarily consisted of $2.4 million of licensing and consultant fees paid in common stock, $2.6 million of stock-based compensation expense and $0.5 million of depreciation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2014 consisted primarily of a $1.9 million increase in accrued expenses and deferred rent and a $0.5 million increase in accounts payable, which was due to the timing of vendor invoicing and payments, both partially offset by an increase in inventory of $0.1 million.

Investing activities. 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. Net cash used by investing activities for the year ended December 31, 2014 consisted of cash used to purchase property and equipment of $1.3 million and cash used to purchase marketable securities of $37.3 million. Purchases of property and equipment in 2014 consisted primarily of laboratory equipment, inclusive of building a clean room, which we commenced in 2013.

Financing activities. 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. Net cash provided by financing activities for 2014 was $79.0 million and consisted primarily of proceeds of $69.5 million, net of underwriters discount related to our IPO, and $14.9 million from our new credit facility, under which we borrowed $15.0 million in aggregate principal amount in April 2014, partially offset by the payment of issuance costs of $3.0 million in connection with our IPO and the repayment of $2.3 million of outstanding principal and other amounts due in connection with our termination of a prior credit facility and repayments of principal prior to our termination of the credit facility.

Funding Requirements

We expect our expenses to increase substantially 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 including DEXTENZA, subject to receiving FDA approval.

We anticipate that our expenses will increase substantially if and as we:

- continue to pursue the clinical development of our most advanced intracanalicular insert product candidates, DEXTENZA and OTX-TP;
- conduct joint research and development under our strategic collaboration with Regeneron for the development and potential commercialization of products containing our extended-delivery hydrogel depot 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 preclinical development activities associated with our back-of-the-eye 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 and marketable securities will enable us to fund our operating expenses, debt service obligations and capital expenditure requirements into the second quarter of 2018. We will need to obtain additional capital to support the planned commercial launch of DEXTENZA, subject to FDA approval. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

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

- the costs, timing and outcome of regulatory review of our product candidates by the FDA, the EMA or other regulatory authorities, including our current NDA for DEXTENZA;
- the level of product sales from any additional product 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 depot 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 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 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 a combination of revenue from sales of ReSure Sealant, 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 and amounts we may be able to draw under our amended credit facility upon the achievement of regulatory and commercial milestones. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your 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.

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, 2016, we had federal net operating loss carryforwards of $85.2 million, which begin to expire in 2026, and state net operating loss carryforwards of $73.9 million, which begin to expire in 2029. As of December 31, 2016, we also had federal research and development tax credit carryforwards of $4.1 million and state research and development tax credit carryforwards $2.1 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, 2016 and the effects such obligations are expected to have on our liquidity and cash flow in future periods:

	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
			(in thousands)		
Operating lease commitments	$ 14,373	$ 1,162	$ 2,696	$ 2,575	$ 7,940
Purchase commitments	3,416	2,185	1,231	—	—
New facility improvements, net	3,600	3,600	—	—	—
Manufacturing commitments	1,680	840	840	—	—
Debt obligations including interest	20,100	2,723	17,377	—	—
Total	$ 43,169	$10,510	$22,144	$ 2,575	$ 7,940

In the table above, we set forth our enforceable and legally binding obligations and future commitments at December 31, 2016, 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, 2016. 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 June 2017 and June 2018.

On June 17, 2016, we entered into a lease agreement for approximately 70,712 square feet of general office, research and development and manufacturing space. The lease expires on July 31, 2027. No base rent will be 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 intend to relocate our corporate headquarters to the new leased premises beginning in 2017 and expect to relocate all of our operations to the new leased premises by 2018. The lease agreement allows 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 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.

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 increase the total commitment to $38.0 million including $18.0 million of borrowings drawn at closing, which was used primarily to pay-off outstanding balances as of the closing date, and options on two additional tranches of $10.0 million each contingent upon on the achievement by us of regulatory and commercial milestones. The interest-only payment period was extended through February 1, 2018 and can be further extended upon the achievement of certain regulatory and commercial milestones. 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. We do not expect our funding requirements 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

In August 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40). ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern for a one year period subsequent to the date of issuance of its financial statements. An entity must provide certain disclosures if conditions or events raise substantial doubt about the entity's ability to continue as a going concern. The Company adopted ASU 2014-15 during the fourth quarter of 2016. Adoption did not require additional disclosures in the financial statements.

In May 2014, the FASB issued ASU 2014-09, "Revenue from Contracts with Customers (Topic 606)," or 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 requires 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. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. In August 2015, the FASB issued ASU 2015-14, "Deferral of the Effective Date", which amends ASU 2014-09. As a result, the effective date will be the first quarter of fiscal year 2018 with early adoption permitted in the first quarter of fiscal year 2017.

Subsequently, the FASB has issued the following standards related to ASU 2014-09: ASU 2016-08, "Revenue from Contracts with Customers (Topic 606), Principal versus Agent Considerations (Reporting Revenue Gross versus Net)," or ASU 2016-08; ASU 2016-10, "Revenue from Contracts with Customers (Topic 606), Identifying Performance Obligations and Licensing," or ASU 2016-10; ASU 2016-12, "Revenue from Contracts with Customers (Topic 606) Narrow-Scope Improvements and Practical Expedients," or ASU 2016-12; and ASU 2016-20, "Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers," or ASU 2016-20, which are intended to provide additional guidance and clarity to ASU 2014-09. The Company must adopt ASU 2016-08, ASU 2016-10, ASU 2016-12 and ASU 2016-20 along with ASU 2014-09, which we collectively refer to as the "New Revenue Standards.

The New Revenue Standards may be applied using one of two retrospective application methods: (1) a full retrospective approach for all periods presented, or (2) a modified retrospective approach that presents a cumulative effect as of the adoption date and additional required disclosures. We expect to adopt the New Revenue Standards in the first quarter of 2018 using the modified retrospective approach and are in the process of completing its initial analysis identifying the revenue streams that will be impacted by the adoption of this new standard and the impact to its financial statements and footnote disclosures.

In February 2016, the FASB issued ASU No. 2016-02, Leases (ASC 842), or ASU 2016-02. ASU 2016-02 requires lessees to recognize most leases on the balance sheet. This is expected to increase both reported assets and liabilities. The new lease standard does not substantially change lessor accounting. For public companies, the standard will be effective for the first interim reporting period within annual periods beginning after December 15, 2018, although early adoption is permitted. Lessees and lessors will be required to apply the new standard at the beginning of the earliest period presented in the financial statements in which they first apply the new guidance, using a modified retrospective transition method. The requirements of this standard include a significant increase in required disclosures. We are currently assessing the impact that adopting this new accounting guidance will have on our financial statements and footnote disclosures.

In March 2016, the FASB issued ASU No. 2016-09, Compensation – Stock Compensation, or 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 will be effective for the first interim period within annual reporting periods beginning after December 15, 2016. Early adoption is permitted. We are currently assessing the impact that adopting this new accounting guidance will have on our 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 add or 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, with early adoption permitted. We are currently assessing the potential impact of the adoption of ASU 2016-15 on our statement of cash flows.

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 effective date will be the first quarter of fiscal year 2018. We are currently assessing the impact that adopting this new accounting guidance will have on our financial statements and footnote disclosures.

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, 2016, we had cash and cash equivalents and marketable securities of $68.1 million, which consisted of money market funds, United States treasury notes and government agency notes. 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, 2016. 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, 2016, 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, 2016. 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, 2016, 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, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On March 7, 2017, we entered into a Second Amended and Restated Credit and Security Agreement, or the Amended Agreement, with MidCap Funding III Trust, or MidCap, Silicon Valley Bank, or SVB, and Flexpoint MCLS SPV LLC, or Flexpoint to amend that certain Credit and Security Agreement, dated as of April 17, 2014, as amended on December 3, 2015, by and among us; MidCap, as successor to MidCap Financial SBIC, LP; and SVB.

The Amended Agreement increased the principal amount of a secured term loan facility, which we refer to as the Credit Facility, from $15,600,000 to $38,000,000 including $18.0 million of borrowings drawn at closing, which was used primarily to pay-off outstanding balances as of the closing date, and options on two additional tranches of $10.0 million, each based on the achievement by us of regulatory and commercial milestones. The Amended Agreement also extended the interest-only payment period and permits the interest-only period to be further extended upon the achievement of certain regulatory and commercial milestones and extended the maturity date of the Credit Facility.

Pursuant to the Amended Agreement, the Company may make interest-only payments until February 1, 2018, which may be extended by us upon the achievement of certain regulatory and commercial milestones. The maturity date of the Credit Facility is December 1, 2020. Amounts borrowed under the Credit Facility incur interest at a LIBOR-base rate, subject to a minimum 1.00% floor, plus 7.25%.

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 2017 Annual Meeting of Shareholders 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 2017 Annual Meeting of Shareholders 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 2017 Annual Meeting of Shareholders 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 2017 Annual Meeting of Shareholders 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 2017 Annual Meeting of Shareholders 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 2017 Annual Meeting of Shareholders 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 2017 Annual Meeting of Shareholders 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 2017 Annual Meeting of Shareholders 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.

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 10, 2017

OCULAR THERAPEUTIX, INC.

By: /s/ W. Bradford Smith
W. Bradford Smith
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/ Amarpreet Sawhney, Ph.D. Amarpreet Sawhney, Ph.D.	Chairman of the Board of Directors, President and Chief Executive Officer (Principal Executive Officer)	March 10, 2017
/s/ W. Bradford Smith W. Bradford Smith	Chief Financial Officer (Principal Financial and Accounting Officer)	March 10, 2017
/s/ Jaswinder Chadha Jaswinder Chadha	Director	March 10, 2017
/s/ James Garvey James Garvey	Director	March 10, 2017
/s/ Jeffrey S. Heier, M.D. Jeffrey S. Heier, M.D.	Director	March 10, 2017
/s/ Richard L. Lindstrom, M.D. Richard L. Lindstrom, M.D.	Director	March 10, 2017
/s/ William James O'Shea William James O'Shea	Director	March 10, 2017
/s/ Bruce A. Peacock Bruce A. Peacock	Director	March 10, 2017
/s/ Charles Warden Charles Warden	Director	March 10, 2017

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.

In our opinion, the accompanying balance sheets and the related statements of operations and comprehensive loss, of changes in redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Ocular Therapeutix, Inc. as of December 31, 2016 and 2015, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2016 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 10, 2017

OCULAR THERAPEUTIX, INC.

BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 32,936	$ 30,784
Marketable securities	35,209	74,280
Accounts receivable	250	193
Inventory	113	134
Prepaid expenses and other current assets	1,390	1,592
Total current assets	69,898	106,983
Property and equipment, net	3,313	3,095
Restricted cash	1,728	228
Total assets	$ 74,939	$ 110,306
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,116	$ 1,957
Accrued expenses and deferred rent	4,635	3,379
Deferred revenue	—	42
Notes payable, net of discount, current	1,549	—
Total current liabilities	8,300	5,378
Deferred rent, long-term	537	68
Notes payable, net of discount, long-term	14,094	15,272
Total liabilities	22,931	20,718
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized at December 31, 2016 and 2015; no shares issued or outstanding at December 31, 2016 and 2015	—	—
Common stock, $0.0001 par value; 100,000,000 shares authorized at December 31, 2016 and 2015; 25,024,100 and 24,750,281 shares issued and outstanding at December 31, 2016 and 2015, respectively	3	2
Additional paid-in capital	225,889	218,830
Accumulated deficit	(173,879)	(129,176)
Accumulated other comprehensive loss	(5)	(68)
Total stockholders' equity	52,008	89,588
Total liabilities and stockholders' equity	$ 74,939	$ 110,306

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,		
	2016	2015	2014
Revenue:			
Product revenue	$ 1,845	$ 1,354	$ 460
Collaboration revenue	42	396	312
Total revenue	1,887	1,750	772
Costs and operating expenses:			
Cost of product revenue	443	319	91
Research and development	27,065	26,611	18,880
Selling and marketing	6,701	3,852	1,982
General and administrative	11,004	9,165	6,913
Total costs and operating expenses	45,213	39,947	27,866
Loss from operations	(43,326)	(38,197)	(27,094)
Other income (expense):			
Interest income	304	166	7
Interest expense	(1,680)	(1,724)	(1,119)
Other income (expense), net	(1)	7	(442)
Total other expense, net	(1,377)	(1,551)	(1,554)
Net loss	(44,703)	(39,748)	(28,648)
Accretion of redeemable convertible preferred stock to redemption value	—	—	(11)
Net loss attributable to common stockholders	$ (44,703)	$ (39,748)	$ (28,659)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.80)	$ (1.71)	$ (2.69)
Weighted average common shares outstanding, basic and diluted	24,816,348	23,244,162	10,652,865
Comprehensive loss:			
Net loss	$ (44,703)	$ (39,748)	$ (28,648)
Other comprehensive income (loss):			
Unrealized gain (loss) on marketable securities	63	(68)	—
Total other comprehensive income (loss)	63	(68)	—
Total comprehensive loss	$ (44,640)	$ (39,816)	$ (28,648)

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

OCULAR THERAPEUTIX, INC.

STATEMENTS OF CHANGES IN REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands, except share data)

	Series A, B, C, D and D-1 Redeemable Convertible 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, 2013	32,842,187	$ 74,344	2,676,648	$ —	$ 1,308	$ (60,780)	$ —	$ (59,472)
Issuance of common stock and restricted common stock	—	—	148,227	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	44,094	—	35	—	—	35
Issuance of common stock in connection with employee stock purchase plan	—	—	5,395	—	64	—	—	64
Issuance of common stock in payment of consultant fees	—	—	79,545	—	699	—	—	699
Issuance of common stock in payment of licensing fees	—	—	189,393	—	1,665	—	—	1,665
Accretion of redeemable convertible preferred stock to redemption value	—	11	—	—	(11)	—	—	(11)
Issuance of common stock upon initial public offering	—	—	5,750,000	1	69,517	—	—	69,518
Issuance costs	—	—	—	—	(3,113)	—	—	(3,113)
Conversion of preferred stock to common stock	(32,842,187)	(74,355)	12,440,205	1	74,354	—	—	74,355
Conversion of preferred stock warrants to common stock warrants	—	—	—	—	960	—	—	960
Stock-based compensation expense	—	—	—	—	2,644	—	—	2,644
Net loss	—	—	—	—	—	(28,648)	—	(28,648)
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	—	—	3,200,000	—	66,176	—	—	66,176
Issuance costs	—	—	—	—	(564)	—	—	(564)
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	—	—	102,077	1	871	—	—	872
Issuance costs	—	—	—	—	(245)	—	—	(245)
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

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

OCULAR THERAPEUTIX, INC.

STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2016	2015	2014
Cash flows from operating activities:			
Net loss	$ (44,703)	$ (39,748)	$ (28,648)
Adjustments to reconcile net loss to net cash used in operating activities			
Stock-based compensation expense	5,956	4,640	2,644
Licensing and consultant fees paid in common stock	—	—	2,364
Non-cash interest expense	371	166	103
Depreciation and amortization expense	881	754	547
Revaluation of preferred stock warrants	—	—	380
Loss on extinguishment of debt	—	—	57
(Gain)/loss on disposal of property and equipment	1,269	(3)	4
Purchase of premium on marketable securities	(37)	(338)	(133)
Amortization of premium on marketable securities	186	283	24
Changes in operating assets and liabilities:			
Accounts receivable from related party	—	—	19
Accounts receivable	(57)	136	(79)
Prepaid expenses and other current assets	924	(53)	(36)
Inventory	21	(1)	(133)
Accounts payable	(159)	348	507
Accrued expenses and deferred rent	1,389	219	1,946
Deferred revenue	(42)	(146)	(62)
Net cash used in operating activities	(34,001)	(33,743)	(20,496)
Cash flows from investing activities:			
Purchases of property and equipment	(1,919)	(1,778)	(1,260)
Proceeds from sale of property and equipment	2	7	—
Change in restricted cash	(1,500)	60	—
Purchases of marketable securities	(41,699)	(91,684)	(37,326)
Proceeds from maturities of marketable securities	80,684	54,826	—
Net cash provided by (used in) investing activities	35,568	(38,569)	(38,586)
Cash flows from financing activities:			
Proceeds from issuance of notes payable and preferred stock warrants	—	1,897	14,877
Proceeds from exercise of stock options	199	207	35
Proceeds from issuance of common stock pursuant to employee stock purchase plan	278	249	64
Proceeds from issuance of public offering, net	872	66,176	69,518
Payments of offering costs	(245)	(564)	(3,018)
Payments of insurance costs financed by a third-party	(519)	(762)	(233)
Repayment of notes payable	—	(1,500)	(2,273)
Net cash provided by financing activities	585	65,703	78,970
Net increase (decrease) in cash and cash equivalents	2,152	(6,609)	19,888
Cash and cash equivalents at beginning of period	30,784	37,393	17,505
Cash and cash equivalents at end of period	$ 32,936	$ 30,784	$ 37,393
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 1,301	$ 1,251	$ 844
Supplemental disclosure of non-cash investing and financing activities:			
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ —	$ 11
Conversion of redeemable convertible preferred stock to common stock	$ —	$ —	$ 74,354
Conversion of warrants for redeemable convertible preferred stock to warrants for common stock	$ —	$ —	$ 960
Additions to property and equipment included in accounts payable at balance sheet dates	$ 451	$ 293	$ 169
Insurance premium financed by a third party	$ 722	$ 706	$ 623
Initial public offering costs included in accounts payable	$ —	$ —	$ 95

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 development and commercialization of innovative therapies for diseases and conditions of the eye using its proprietary hydrogel platform technology. The Company's bioresorbable hydrogel-based product candidates are designed to provide sustained delivery of therapeutic agents to the eye. 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, 2016, 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 receiving FDA approval.

The Company has incurred losses and negative cash flows from operations since its inception. As of December 31, 2016, the Company had an accumulated deficit of approximately $174,000. The Company expects to continue to generate operating losses in the foreseeable future. The Company believes that its existing cash and cash equivalents and marketable securities, including net amounts raised under in January 2017 stock offering of approximately $23,500 in net proceeds (Note 18) and additional borrowings totaling approximately $2,400 from its March 2017 debt refinancing (Note 18) will enable it to fund its operating expenses, debt service obligations and capital expenditure requirements for at least 12 months from the issuance date of the financial statements. The Company will seek additional funding through public or private financings, debt financing and collaboration agreements. The Company has two additional $10,000 tranches of borrowing capacity under its credit facility, which are contingent upon achieving FDA approval and certain sales levels of DEXTENZA, respectively. The inability to access these funds or obtain other funding, as and when needed, would have a negative impact on the Company's financial condition and ability to pursue its business strategies. 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 if it were unable to access the additional borrowing capacity under the credit facility or obtain other financing.

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

On July 30, 2014, the Company completed an initial public offering ("IPO") of its common stock through the issuance and sale of 5,000,000 shares of its common stock at a public offering price of $13.00 per share, resulting in net proceeds of $57,337 after deducting underwriting discounts and other offering costs. Upon the closing of the IPO, all outstanding shares of the Company's redeemable convertible preferred stock were automatically converted into 12,440,205 shares of the Company's common stock and all outstanding warrants for the Company's redeemable convertible preferred stock were automatically converted into warrants for the Company's common stock. In August 2014, the underwriters of the Company's IPO exercised their over-allotment option to purchase an additional 750,000 shares of common stock at the initial public offering price of $13.00 per share, less underwriting discounts, resulting in additional net proceeds of $9,068 after deducting underwriting discounts (Note 10).

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 other offering expenses (Note 10).

In November 2016, the Company entered into an At-the-Market sales agreement, (the "2016 ATM Agreement") with Cantor Fitzgerald & Co., ("Cantor"), under which shares of 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 at a weighted average exercise price of $8.80 per share resulting in net proceeds of approximately $600 after underwriting discounts, commission and other offering expenses (Note 10). In January 2017, the Company sold 161,341 shares of common stock under the 2016 ATM Agreement at a weighted average exercise price of $8.91 per share resulting in net proceeds of approximately $1,400 after deducting underwriting discounts and commissions (Note 18).

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 $23,464 after deducting underwriting discounts, commissions and expenses (Note 18).

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,	
	2016	2015
Raw materials	$ 58	$ 75
Work-in-process	40	41
Finished goods	15	18
	$ 113	$ 134

Restricted Cash

As of December 31, 2016 and 2015, the Company held a certificate of deposit of $1,728 and $228, respectively, as security deposits for the lease of the Company's current and future 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, 2016 and 2015, the carrying value of the Company's outstanding notes payable (Note 7) approximates fair value of a level 2 reflecting interest rates currently available to the Company.

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, 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, 2015, marketable securities by security type consisted of:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
United States treasury notes	$ 44,587	$ —	$ (53)	$ 44,534
Agency bonds	29,761	—	(15)	29,746
Total	$ 74,348	$ —	$ (68)	$ 74,280

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 year ended December 31, 2016 comprehensive loss included a $63 unrealized gain on marketable securities. For the year ended December 31, 2015, comprehensive loss included a $68 unrealized loss on marketable securities. For the year ended December 31, 2014, there was no difference between net loss and comprehensive loss.

Net Income (Loss) Per Share

Prior to the closing of its IPO of common stock, the Company followed the two-class method when computing net income (loss) per share, as the Company had outstanding shares that met the definition of participating securities. The two-class method 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.

The Company's Redeemable Preferred Stock outstanding prior to the IPO, contractually entitled the holders of such shares to participate in dividends but did not contractually require the holders of such shares to participate in losses of the Company. Similarly, 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, 2016, 2015 and 2014.

Recently Issued and Adopted Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40). ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern for a one year period subsequent to the date of issuance of its financial statements. An entity must provide certain disclosures if conditions or events raise substantial doubt about the entity's ability to continue as a going concern. The Company adopted ASU 2014-15 during the fourth quarter of 2016. Adoption did not require additional disclosures in the Company's financial statements.

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 amends ASU 2014-09. As a result, the standard effective date will be in the first quarter of 2018 with early adoption permitted in the first quarter of 2017.

Subsequently, the FASB has issued the following standards related to ASU 2014-09: ASU 2016-08, "Revenue from Contracts with Customers (Topic 606), Principal versus Agent Considerations (Reporting Revenue Gross versus Net)," ("ASU 2016-08"); ASU 2016-10, "Revenue from Contracts with Customers (Topic 606), Identifying Performance Obligations and Licensing," ("ASU 2016-10"); ASU 2016-12, "Revenue from Contracts with Customers (Topic 606) Narrow-Scope Improvements and Practical Expedients," ("ASU 2016-12"); and ASU 2016-20, "Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers," ("ASU 2016-20"), which are intended to provide additional guidance and clarity to ASU 2014-09. The Company must adopt ASU 2016-08, ASU 2016-10, ASU 2016-12 and ASU 2016-20 along with ASU 2014-09 (collectively, the "New Revenue Standards").

The New Revenue Standards may be applied using one of two retrospective application methods: (1) a full retrospective approach for all periods presented, or (2) a modified retrospective approach that presents a cumulative effect as of the adoption date and additional required disclosures. The Company expects to adopt the New Revenue Standards in the first quarter of 2018 using the modified retrospective approach and is in the process of completing its

initial analysis identifying the revenue that will be impacted by the adoption of this new standard and the impact to 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. This is expected to increase both reported assets and liabilities. The new lease standard does not substantially change lessor accounting. For public companies, the standard will be effective for the first interim reporting period within annual periods beginning after December 15, 2018, although early adoption is permitted. Lessees and lessors will be required to apply the new standard at the beginning of the earliest period presented in the financial statements in which they first apply the new guidance, using a modified retrospective transition method. The requirements of this standard include a significant increase in required disclosures. The Company is currently assessing the impact that adopting this new accounting guidance will have on its financial statements and footnote disclosures.

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 will be effective for the first interim period within annual reporting periods beginning after December 15, 2016. Early adoption is permitted. The Company is currently assessing the impact that adopting this new accounting guidance 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, with early adoption permitted. The Company is currently assessing the potential impact of the adoption of ASU 2016-15 on its statement of cash flows.

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 effective date will be the first quarter of fiscal year 2018. The Company is currently assessing the impact that adopting this new accounting guidance will have on its financial statements and footnote disclosures.

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, 2016 and 2015 and indicate the level of the fair value hierarchy utilized to determine such fair value:

	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

	Fair Value Measurements as of December 31, 2015 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ —	$ 29,879	$ —	$ 29,879
Marketable securities:				
United States treasury notes	—	44,534	—	44,534
Agency bonds	—	29,746	—	29,746
Total	$ —	$ 104,159	$ —	$ 104,159

During the years ended December 31, 2016, 2015 and 2014, 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,	
	2016	2015
Equipment	$ 4,361	$ 3,359
Leasehold improvements	906	894
Furniture and fixtures	418	403
Software	89	54
Construction in progress	1,357	1,324
	7,131	6,034
Less: Accumulated depreciation	(3,818)	(2,939)
	$ 3,313	$ 3,095

Depreciation expense was $881, $754 and $547 for the years ended December 31, 2016, 2015 and 2014, respectively.

For the year ended December 31, 2016, the construction in progress is related to the build-out of the Company's new facility and equipment that will be used in that facility. For the years ended December 31, 2015 and 2014 the construction in progress is related to the build-out of an aseptic manufacturing suite clean room.

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,	
	2016	2015
Accrued payroll and related expenses	$ 2,146	$ 1,582
Accrued professional fees	1,018	471
Accrued research and development expenses	360	430
Accrued insurance	591	389
Accrued other	520	507
	$ 4,635	$ 3,379

6. Collaboration and Feasibility Agreements

The Company had a feasibility agreement with a biopharmaceutical company entered into in 2013. Under this agreement, the biopharmaceutical company agreed to pay up to $500 for completing certain tasks and achieving certain milestones. In the event that the agreement was terminated in advance of the completion of the tasks or achievement of

the milestones, the Company would have been required to refund portions of the amounts received, based on the actual work completed or milestones achieved as of the date of termination. In 2014, the Company completed the tasks related to the first milestone at which time $250 became non-refundable, therefore the Company recorded revenue of $250. The biopharmaceutical company has indicated that they will not proceed with the second phase of the agreement. The Company does not have any further obligations in connection with this agreement and no further payments will be received.

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 $42, $396 and $63 for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, the Company had no deferred revenue and no accounts receivable related to this agreement. As of December 31, 2015, the Company had deferred revenue of $42 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 containing the Company’s sustained-release hydrogel depot 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, or 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 to develop and commercialize products containing the Company’s sustained-release hydrogel depot in combination with Regeneron’s large molecule VEGF-targeting compounds (“Licensed Products”).

If the Option 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. 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 was fully drawn down. As part of the 2014 Credit Facility a previously

outstanding credit agreement issued in 2011 (the "2011 Credit Facility") was terminated. Additional capacity of $5,000 available to be drawn down under the 2014 Credit Facility was not drawn down and this additional capacity is no longer available to the Company. Promissory notes issued under the 2014 Credit Facility were to mature on April 1, 2018 and were collateralized by substantially all of the Company's personal property, other than its intellectual property. There were no financial covenants associated with the 2014 Credit Facility; however, there were 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 2014 Credit Facility were 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 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%.

The terms of the 2014 Credit Facility required that the existing outstanding borrowings be repaid. Accordingly, on April 17, 2014, the Company repaid $1,898 then due under the 2011 Credit Facility, consisting of $1,667 of principal, $6 of interest and $225 of a final payment. The Company accounted for the termination of the 2011 Credit Facility as an extinguishment in accordance with the guidance in ASC 470-50, Debt. The total amount of unamortized debt discount of $10 was reflected as a loss on extinguishment of debt and included in other expense within the statements of operations and comprehensive loss in 2014. Additionally, fees paid to the lenders that were allocated to the existing debt and treated as an extinguishment, inclusive of the value of warrants issued and debt issuance costs paid, totaling $47, were also reflected as a loss on extinguishment of debt included in other expense within the statements of operations and comprehensive loss in 2014.

In December 2015, the 2014 Credit Facility was amended (the "Amended 2014 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 2014 Credit Facility were $1,897. The Company is obligated to make monthly interest-only payments under the Amended 2014 Credit Facility until December 31, 2016 and, thereafter, are required to make monthly payments of principal and interest from January 1, 2017 through December 1, 2019. The interest rate under the Amended 2014 Credit Facility is unchanged at an annual rate of 8.25%. In addition, a final payment equal to 3.75% of amounts drawn under the Amended 2014 Credit Facility is due upon the new maturity date. There are no financial covenants associated with the Amended 2014 Credit Facility and the negative covenants remain unchanged. The Company accounted for the amendment of the Amended 2014 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 2014 Credit Facility is 10.6%.

As of December 31, 2016, the annual repayment requirements for the Amended 2014 Credit Facility, inclusive of the final payment of $585 due at expiration and after consideration of the 2017 refinancing discussed below, were as follows:

Year Ending December 31,	Principal	Interest and Final Payment	Total
2017	1,300	1,423	2,723
2018	5,294	1,339	6,633
2019	6,353	819	7,172
2020	2,653	919	3,572
	$15,600	$ 4,500	$20,100

In March 2017, the Company amended the terms of its debt with existing lenders and increased the total commitment to $38.0 million including borrowings of $18,000 drawn at closing, which was used primarily to pay-off outstanding balances as of the closing date, and options on two additional tranches of $10,000 each contingent upon the achievement by the Company of regulatory and commercial milestones related to DEXTENZA. (Note 18) 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 has 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 agreement.

8. Warrants

Upon the closing of the Company's IPO in July 2014, the Company's outstanding preferred stock warrants for the purchase of 236,836 shares of preferred stock were converted to warrants for the purchase of 89,708 shares of common stock at a weighted average exercise price of $6.32 per share. During the year ended December 31, 2016, no warrants were exercised. During the year ended December 31, 2015, warrants for 70,769 shares of common stock were exercised via net share settlement resulting in the issuance of 54,010 shares of common stock as a result of the exercise. Warrants for the purchase of 18,939 shares of common stock remain outstanding at December 31, 2016 at a weighted average exercise price of $7.92 per share and an expiration date of April 17, 2021.

9. Redeemable Convertible Preferred Stock

Prior to the Company's IPO, the Company had issued Series A, Series B, Series C, Series D and Series D-1 redeemable convertible preferred stock (collectively, the "Redeemable Preferred Stock"). The Redeemable Preferred Stock was classified outside of stockholders' equity (deficit) because the shares contained redemption features that were not solely within the control of the Company.

On July 10, 2014, the Company effected a 1-for-2.64 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of Redeemable Preferred Stock. Accordingly, all share and per share amounts for all periods presented in these financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios.

Upon the closing of the Company's IPO in July 2014, all outstanding shares of the Company's Redeemable Preferred Stock were converted into 12,440,205 shares of common stock.

10. Common Stock and Preferred Stock

On July 30, 2014, the Company adopted an amended and restated certificate of incorporation increasing the number of its authorized shares of its common stock to 100,000,000 shares. In conjunction with the IPO and the amended and restated certificate of incorporation, the Company is authorized to issue 5,000,000 shares of preferred stock, $0.0001 par value, all of which is undesignated.

On August 19, 2014, the Company completed the sale of an additional 750,000 shares of common stock at the initial public offering price of $13.00 per share to the underwriters of the Company's IPO pursuant to the exercise of their over-allotment option. The Company received additional net proceeds of $9,068 after deducting underwriting discounts and offering costs.

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 the 2016 ATM Agreement with Cantor, under which the Company may offer and sell its common stock having aggregate proceeds of up to $40,000 from time to time. During the fourth quarter of 2016, the Company sold 102,077 shares of common stock under the 2016 ATM Agreement at a weighted average exercise price of $8.80 per share resulting in net proceeds of approximately $600 after underwriting discounts, commission and other offering expenses.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders.

As of December 31, 2016, the Company had reserved 4,719,717 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 Option 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 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, 2016, the number of shares available for issuance under the 2014 Plan increased by 990,012. As of December 31, 2016, 1,346,083 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.

During the years ended December 31, 2016, 2015 and 2014, the Company granted options to purchase 1,147,025, 680,231 and 753,886 shares of common stock, respectively, to certain employees, consultants and directors. The vesting of most of these awards is time-based and the restrictions typically lapse over three to four years.

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, 2016, the number of shares available for issuance under the 2014 Plan increased by 123,752. During the years ended December 31, 2016, 2015 and 2014, 66,628, 20,916 and 5,395 shares, respectively were issued under the plan. As of December 31, 2016, 263,215 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. Prior to the Company's IPO in July 2014, the Company had been a private company and lacked company-specific historical and implied volatility information. Therefore, it 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, 2016, there were outstanding unvested service-based stock options held by nonemployees for the purchase of 5,985 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,		
	2016	2015	2014
Risk-free interest rate	1.42 %	1.67 %	2.24 %
Expected term (in years)	6	6	6
Expected volatility	85 %	71 %	77 %
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, 2015	2,115,519	$ 12.78	6.9	$ 5,897
Granted	1,147,025	6.42		
Exercised	(105,114)	1.90		
Forfeited	(65,950)	13.72		
Outstanding as of December 31, 2016	3,091,480	$ 10.77	7.3	$ 6,659
Options vested and expected to vest as of December 31, 2016	3,009,110	$ 10.74	7.2	$ 6,510
Options exercisable as of December 31, 2016	1,569,255	$ 9.80	6.0	$ 4,365

There was no restricted stock activity in 2016. 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 $575, $3,192 and $323 during the years ended December 31, 2016, 2015 and 2014, respectively.

The weighted average grant date fair value of stock options granted to employees and directors during the years ended December 31, 2016, 2015, 2014 was $4.52, $18.12 and $6.55 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, 2016, 2015 and 2014 was $0, $265, and $1,142, respectively.

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,		
	2016	2015	2014
Research and development	$ 1,900	$ 1,589	$ 397
Selling and marketing	490	340	68
General and administrative	3,566	2,711	2,179
	$ 5,956	$ 4,640	$ 2,644

As of December 31, 2016, the Company had an aggregate of $10,315 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 2.2 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, 2016, 2015 and 2014:

	Year Ended December 31,		
	2016	2015	2014
Numerator:			
Net loss	$ (44,703)	$ (39,748)	$ (28,648)
Accretion of redeemable convertible preferred stock to redemption value	—	—	(11)
Net loss attributable to common stockholders	$ (44,703)	$ (39,748)	$ (28,659)
Denominator:			
Weighted average common shares outstanding, basic and diluted	24,816,348	23,244,162	10,652,865
Net loss per share attributable to common stockholders, basic and diluted	$ (1.80)	$ (1.71)	$ (2.69)

The Company excluded the following common stock equivalents, outstanding as of December 31, 2016, 2015, and 2014, from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2016, 2015 and 2014 because they had an anti-dilutive impact due to the net loss attributable to common stockholders incurred for the periods.

	December 31,		
	2016	2015	2014
Options to purchase common stock	3,091,480	2,115,519	1,611,991
Non-vested restricted common stock	—	—	28,437
Warrants for the purchase of common stock	18,939	18,939	89,708
	3,110,419	2,134,458	1,730,136

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 June 2017, June 2018 and July 2027.

Future minimum lease payments for its operating leases as of December 31, 2016 are as follows:

Year Ending December 31,	
2017	$ 1,162
2018	1,461
2019	1,235
2020	1,270
2021	1,305
Thereafter	7,940
Total	$ 14,373

During the years ended December 31, 2016, 2015 and 2014, the Company recognized $1,084, $778 and $649, respectively, of rental expense, related to its office, laboratory and manufacturing space and office equipment.

On June 17, 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 will commence on February 1, 2017 and expire on July 31, 2027. No base rent will be 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 Company intends to relocate its corporate headquarters to the new leased premises beginning in 2017 and intends to relocate all of its operations to the new leased premises by 2018. 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.

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, 2016, royalties paid under this agreement related to product sales were $95.

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, 2016.

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, 2016, the Option has not been exercised and no payments have been made to Regeneron.

14. Income Taxes

During the years ended December 31, 2016, 2015 and 2014, the Company recorded no income tax benefits for the net operating losses incurred in each year or interim period, 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,		
	2016	2015	2014
Federal statutory income tax rate	(34.0)%	(34.0)%	(34.0)%
Federal and state research and development tax credit	(2.9)	(3.1)	(2.5)
State taxes, net of federal benefit	(4.8)	(2.0)	(4.6)
Stock-based compensation	1.4	1.2	1.6
Other	(0.6)	(0.2)	0.8
Change in deferred tax asset valuation allowance	40.9	38.1	38.7
Effective income tax rate	—%	—%	—%

Net deferred tax assets consisted of the following:

	December 31,	
	2016	2015
Net operating loss carryforwards	$ 31,960	$ 22,554
Research and development tax credit carryforwards	5,482	4,052
Capitalized start-up costs	1,723	1,915
Capitalized research and development expenses, net	26,943	21,357
Accrued expenses and other temporary differences	4,128	2,091
Total gross deferred tax assets	70,236	51,969
Valuation allowance	(70,236)	(51,969)
Net deferred tax assets	$ —	$ —

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2016, 2015 and 2014 related primarily to the increase in net operating loss carryforwards, capitalized research and development expenses and research and development tax credit carryforwards and were as follows:

	Year Ended December 31,		
	2016	2015	2014
Valuation allowance as of beginning of year	$ 51,969	$ 36,825	$ 25,776
Decreases recorded as benefit to income tax provision	—	—	—
Increases recorded to income tax provision	18,267	15,144	11,049
Valuation allowance as of end of year	$ 70,236	$ 51,969	$ 36,825

As of December 31, 2016, the Company had net operating loss carryforwards for federal and state income tax purposes of $85,246 and $73,876, respectively, which begin to expire in 2026 and 2029, respectively. Included in the federal and state net operating loss carryforwards are approximately $2,029 of deductions related to the exercise of stock options for which the tax benefit will be realized when it results in the reduction of cash income tax in accordance with ASC 718. As of December 31, 2016, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $4,085 and $2,116, 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, including the Company's history of cumulative net losses incurred since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2016 and 2015. Management reevaluates the positive and negative evidence at each reporting period.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2016 or 2015.

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,

2013 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.

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, 2016, 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. On February 12, 2014, the Company issued 189,393 shares of its common stock to Incept in connection with the expansion of the scope of the Incept License to include back-of-the eye technology held by Incept. The fair value of the shares of $1,665 as of the issuance date was recorded as research and development expense. Incept and certain owners of Incept participated in the Company's Series A, Series B and Series C preferred stock financing and have also been granted shares of common stock and redeemable convertible preferred stock of the Company. In addition, certain employees of the Company are shareholders of Incept. The Company's President and Chief Executive Officer is a general partner of Incept.

On February 12, 2014, the Company issued 79,545 shares of common stock to a former member of the Company's board of directors and current stockholder of Incept for consulting services rendered. The fair value of the shares of $699 as of the issuance date was recorded as general and administrative expense.

During the years ended December 31, 2016, 2015 and 2014, the Company invoiced Augmenix, Inc. ("Augmenix") $0, $4 and $82, respectively, for consulting and other services. During the years ended December 31, 2016, 2015 and 2014, Augmenix invoiced the Company $0, $0 and $27 for legal fees paid by Augmenix on behalf of the Company. Certain shareholders of Augmenix were holders of the Company's redeemable convertible preferred stock and common stock which is now entirely common stock. In addition, certain employees of the Company are shareholders of Augmenix. The Company's President and Chief Executive Officer 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 Chief Executive Officer, which grant was in lieu of $250 of the Chief Executive 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 Chief Executive 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 Service Agreement with Axtria, Inc. ("Axtria") in which Axtria will provide certain sales and marketing analytics to the Company. Jaswinder Chadha, co-founder and Chief Executive Officer of Axtria, is also a member of the Company's Board of Directors and is related to the Company's President and Chief Executive Officer. Through December 31, 2016, payments paid to Axtria under this agreement were $150 (Note 18).

The Company has engaged Wilmer Cutler Pickering Hale and Dorr LLP ("WilmerHale") to provide certain legal services to the Company. The Company's Chief Medical Officer 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 approximately $874 for the year ended December 31, 2016.

17. Selected Quarterly Financial Data (Unaudited)

	Three Months Ended							
	Dec. 31, 2016	Sept. 30, 2016	June 30, 2016	Mar 31, 2016	Dec. 31, 2015	Sept. 30, 2015	June 30, 2015	Mar 31, 2015
Statements of Operations Data:								
Product revenue	$ 511	$ 477	$ 441	$ 416	$ 394	$ 388	$ 334	$ 238
Collaboration revenue	—	—	—	42	42	41	125	188
Revenue	511	477	441	458	436	429	459	426
Loss from operations	(12,472)	(9,238)	(11,107)	(10,509)	(10,275)	(11,174)	(9,635)	(7,113)
Net loss	(12,822)	(9,596)	(11,445)	(10,840)	(10,637)	(11,524)	(10,009)	(7,578)
Net loss attributable to common stockholders	(12,822)	(9,596)	(11,445)	(10,840)	(10,637)	(11,524)	(10,009)	(7,578)
Basic and diluted net loss attributable to common stockholders per share	$ (0.52)	$ (0.39)	$ (0.46)	$ (0.44)	$ (0.43)	$ (0.47)	$ (0.45)	$ (0.35)

18. 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, 2017, the number of shares available for issuance under the 2014 Plan increased by 1,000,964.

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 ESPP increased by 125,121.

In January 2017, the Company sold 161,341 shares of common stock under the 2016 ATM Agreement at a weighted average exercise price of $8.91 per share resulting in net proceeds of approximately $1,400 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 $23,464 after deducting underwriting discounts, commissions and expenses.

In February 2017, the Company entered into statement of work totaling approximately $1,400 in which Axtria will provide data warehouse implementation, operations and maintenance support services to the Company. Jaswinder Chadha, co-founder and Chief Executive Officer of Axtria, is also a member of the Company's Board of Directors and is related to the Company's President and Chief Executive Officer (Note 16).

In March 2017, the Amended 2014 Credit Facility was amended (the "Amended 2017 Credit Facility") to increase the total commitment to $38,000, including $18,000 of borrowings drawn at closing, which was used primarily to pay-off outstanding balances as of the closing date, and options on two additional tranches of $10,000, each contingent upon the achievement by the Company of regulatory and commercial milestones related to DEXTENZA. The interest-only payment period was also extended through February 1, 2018 and there are provisions to further extend the interest-only period based on the achievement of certain milestones. Amounts borrowed under the 2017 Amended Credit Facility is at LIBOR base rate, subject to 1.00% floor, plus 7.25% with an indicative interest rate of 8.25% as of the closing date. In addition, a final payment equal to 3.5% of amounts drawn under the Amended 2017 Credit Facility is due upon the new

maturity date of December 1, 2020. There are no financial covenants associated with the Amended 2017 Credit Facility and the negative covenants remain unchanged.

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 24, 2014, by and between the Registrant and W. Bradford Smith	S-1/A	333-196932	7/11/2014	10.14	
10.14+	Employment Agreement, dated June 19, 2014, by and between the Registrant and James Fortune	S-1/A	333-196932	7/11/2014	10.15	
10.15+	Employment Agreement, dated July 3, 2014, by and between the Registrant and Eric Ankerud	S-1/A	333-196932	7/11/2014	10.16	
10.16	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	
10.17	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	
10.18	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	
10.19†	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	
10.20+	Employment Agreement, dated January 5, 2016, by and between the Registrant and Jonathan H. Talamo, M.D.	10-Q	001-36554	11/9/2016	10.2	
10.21+	Employment Agreement, dated October 10, 2016, by and between the Registrant and Andrew Hurley	10-Q	001-36554	11/9/2016	10.3	
10.21	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	
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

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	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.

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 and 333-210059) of Ocular Therapeutix, Inc. of our report dated March 10, 2017 relating to the financial statements, which appears in this Form 10-K.

/s/PricewaterhouseCoopers LLP
Boston, MA
March 10, 2017

Exhibit 31.1

CERTIFICATIONS

I, Amarpreet Sawhney, Ph.D., 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 10, 2017

By: /s/ Amarpreet Sawhney, Ph.D.
Amarpreet Sawhney, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, W. Bradford Smith, 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 10, 2017

By: /s/ W. Bradford Smith
W. Bradford Smith
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, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Amarpreet Sawhney, Ph.D., 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 10, 2017

By: /s/ Amarpreet Sawhney, Ph.D.
Amarpreet Sawhney, Ph.D.
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, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, W. Bradford Smith, 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 10, 2017

By: /s/ W. Bradford Smith
W. Bradford Smith
Chief Financial Officer
(Principal Financial and Accounting Officer)