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

o **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 001-36080

OPHTHOTECH CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	**20-8185347**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
One Penn Plaza, 19th Floor New York, NY	**10119**
(Address of principal executive offices)	(Zip Code)

(212) 845-8200
(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, $0.001 par value	The NASDAQ Stock Market LLC

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. o 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. o 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 o 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 o 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. o

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 o	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). o 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 $1,616.0 million, based on the closing price of the registrant's common stock on June 30, 2016.

The number of shares outstanding of the registrant's class of common stock, as of February 24, 2017: 35,808,442

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," "goals," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "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 potential benefits of our updated business plan and strategy to potentially expand our product pipeline;
- our ability to in-license or acquire additional products, product candidates or technologies to treat ophthalmic diseases and the timing, costs, conduct and outcome of preclinical development or clinical trials we undertake for these newly acquired assets;
- our expectations related to our use of available cash;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the timing, costs, conduct and outcome of our remaining Phase 3 clinical trial of Fovista® (pegpleranib) administered in combination with Eylea or Avastin for the treatment of wet age-related macular degeneration, or AMD, including statements regarding the timing and the availability of, and the costs to obtain, initial, top-line results from, and the completion of, such trial;
- the timing, costs, conduct and outcome of our clinical trials for Zimura® (avacincaptad pegol) for the treatment of patients with geographic atrophy, or GA, a form of dry AMD and, in combination with anti-VEGF drugs, for the treatment of wet AMD, including statements regarding the timing of the initiation of and completion of enrollment in such trials, and the costs to obtain and timing of receipt of initial results from, and the completion of, such trials;
- the timing of and our ability to obtain marketing approval of our product candidates, and the ability of our product candidates to meet existing or future regulatory standards;
- our ability to maintain a productive collaborative relationship with Novartis Pharma AG, including our ability to achieve remaining potential milestone payments under our agreement;
- the potential advantages of our product candidates;
- the rate and degree of potential market acceptance and clinical utility of our product candidates, if approved;
- our estimates regarding the potential market opportunity for our product candidates;
- the potential receipt of revenues from future sales of our product candidates, if approved;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for the manufacture of our product candidates;
- our intellectual property position;
- the impact of existing and new governmental laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and our stockholders 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. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and 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

We are a biopharmaceutical company specializing in the development of novel therapeutics to treat ophthalmic diseases, with a focus on diseases of the back of the eye. To date, our primary focus has been on developing therapeutics for age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina, known as the macula, that may result in blindness. Following our announcement in December 2016 that two of our three pivotal, Phase 3 clinical trials for Fovista® (pegpleranib), an anti-platelet derived growth factor, or PDGF, aptamer, in development for the treatment of wet AMD, failed to meet their primary endpoint, we initiated a plan to review our strategic alternatives in order to maximize shareholder value and implement an updated business plan. Without limiting any option, we plan to continue to focus on the development of product candidates for ophthalmic diseases, especially back of the eye disorders. We are actively exploring opportunities to obtain rights to additional products, product candidates and technologies to treat ophthalmic diseases. We are also currently continuing to develop our product candidate Zimura® (avacincaptad pegol), an inhibitor of complement factor C5, for the treatment of geographic atrophy, or GA, a form of dry AMD, and in combination with anti-VEGF drugs for the treatment of wet AMD, and are continuing our remaining Phase 3 Fovista clinical trial, OPH1004. We plan to reassess our existing Fovista and Zimura development programs throughout 2017 as the implementation of our updated business plan progresses and evolves, with the goal of aligning corporate resources in the context of a potentially broader product pipeline. We expect that our reassessment of our Fovista development program for the treatment of wet AMD will be primarily determined by the initial, top-line data from OPH1004 and that our reassessment of our Zimura development program may be particularly affected by the results of a competitor's Phase 3 clinical trial of a complement inhibitor being studied for the treatment of GA. Data from both our OPH1004 trial and our competitor's Phase 3 trial for the treatment of GA are expected during the second half of 2017. As a result of this reassessment, we may modify, expand or terminate some or all of our development programs or clinical trials at any time. We generally expect that we will not engage in internal early stage research and drug discovery and will thus avoid the related costs and risks of these activities.

In December 2016, we announced initial, top-line data from two pivotal clinical trials, which we refer to as OPH1002 and OPH1003, evaluating the safety and efficacy of 1.5mg of Fovista administered in combination with monthly 0.5mg Lucentis® (ranibizumab) anti-VEGF therapy compared to monthly Lucentis monotherapy for the treatment of wet AMD. The current standard of care for wet AMD is monotherapy targeting vascular endothelial growth factor, referred to as anti-VEGF therapy. The pre-specified primary endpoint of mean change in visual acuity at 12 months was not achieved for either OPH1002 or OPH1003. Moreover, we have not observed any clinically meaningful visual benefit when 1.5mg of Fovista was added to a monthly regimen of 0.5mg Lucentis therapy for any subgroup of patients that we have analyzed from the OPH1002 and OPH1003 trials, including subgroups based on baseline visual acuity, baseline lesion size or the baseline amount of the classic component of choroidal neovascularization, or CNV. Following the December 2016 data announcement, we subsequently stopped treating patients in, and terminated, both the OPH1002 and OPH1003 trials. OPH1004, our remaining Phase 3 clinical trial, which is evaluating the safety and efficacy of 1.5 mg of Fovista administered in combination with 2.0mg Eylea® (afilbercept) or 1.25mg Avastin® (bevacizumab) anti-VEGF therapy compared to Eylea or Avastin monotherapy for the treatment of wet AMD, remains ongoing, with initial, top-line data expected to be available during the second half of 2017. The failure of OPH1002 and OPH1003 to show any clinically meaningful visual benefit in adding 1.5mg of Fovista to a monthly regimen of 0.5mg of Lucentis and the recent failure of a competitor's Phase 2 trial investigating the combination of a PDGF inhibitor and a VEGF inhibitor, may be indicative of a low likelihood of success for OPH1004. In light of the data from the OPH1002 and OPH1003 trials, we have also stopped treating patients in our additional Phase 2 clinical trials that were

evaluating the potential additional benefits of Fovista administered in combination with anti-VEGF drugs in wet AMD patients, which we previously referred to collectively as the Fovista Expansion Studies.

There are two forms of AMD, dry AMD and wet AMD. Dry AMD can progress to wet AMD. Although dry AMD is the most common form of AMD, there are no therapies approved by the U.S. Food and Drug Administration or European Medicines Agency to treat this condition. We are currently developing our product candidate Zimura as a monotherapy for the treatment of GA, a form of dry AMD, as well as in combination with anti-VEGF drugs for the treatment of wet AMD. Zimura is an inhibitor of complement factor C5, a protein that is associated with complement mediated inflammation and cell damage, which we believe may be involved in the development and progression of dry AMD and wet AMD. We have completed a multicenter, uncontrolled, open-label Phase 1/2a clinical trial of Zimura monotherapy for the treatment of GA, a multicenter, uncontrolled, open-label, ascending dose and parallel group Phase 1/2a clinical trial of Zimura administered in combination with Lucentis for the treatment of wet AMD and a very small, uncontrolled, open-label Phase 2 clinical trial investigating Zimura's potential role when administered in combination with anti-VEGF drugs for the treatment of polypoidal choroidal vasculopathy, or PCV, which is a specific type of wet AMD, in patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF monotherapy fails. Currently, we have the following ongoing clinical trials for Zimura:

- *Zimura Phase 2a Wet AMD Study*. During the fourth quarter of 2015, we initiated an open-label Phase 2a clinical trial to evaluate Zimura's potential role when administered in combination with anti-VEGF therapy for the treatment of wet AMD in patients who do not respond adequately to treatment with anti-VEGF monotherapy. We plan to enroll up to approximately 60 patients in this trial, and may include patients with PCV. Recruitment of patients in this study is ongoing.

- *Zimura Phase 2/3 GA Study*. During the fourth quarter of 2015, we initiated a randomized, double-masked, controlled Phase 2/3 clinical trial to evaluate the safety and efficacy of Zimura monotherapy in patients with GA. Recruitment of patients in this study is ongoing.

We remain very early in the recruitment phase for both of our ongoing Zimura clinical trials.

In early 2017, we engaged a financial advisor and initiated a plan to review our strategic alternatives in order to maximize shareholder value following the failure of two of our three pivotal Fovista trials. Without limiting any option, the principal focus of this plan, based on our deep expertise and experience in ophthalmology, is to actively explore obtaining rights to additional products, product candidates and technologies to treat ophthalmic diseases, particularly those of the back of the eye. We are particularly interested in obtaining rights to product candidates for ocular indications with a high unmet medical need. We believe that with our expertise and experience in ophthalmology we are well positioned to explore and critically evaluate a variety of opportunities. We also believe that our focus on diseases of the eye and our experienced management team will make us an attractive collaborator or acquirer for companies seeking to out-license or sell rights to products, product candidates or technologies. As part of our updated business plan, we are also reviewing whether there is any scientific rationale for potentially developing our current product candidates, Fovista and Zimura, in one or more other ophthalmic indications where there is a high unmet need. As part of our strategic review, we may also consider other alternatives, including the acquisition of products, product candidates or technologies or other assets outside of ophthalmology, mergers or other transactions involving our company as a whole, collaboration transactions, or the license, sale or divestiture of some of our assets or technologies. We cannot be sure when or if this strategic review process will result in any type of transaction. As of December 31, 2016, we had $289.3 million in cash, cash equivalents, and marketable securities, of which approximately $100 million to $115 million is committed to the wind-down of OPH1002 and OPH1003 and the Fovista Expansion Studies, implementation of a previously announced reduction in personnel and related costs, cancellation fees related to manufacturing commitments, and obtaining initial, top-line data for the OPH1004 trial during the second half of 2017.

Eye Disease

Eye disease can be caused by many factors and can affect both the front and back of the eye. In its most extreme cases, eye disease can result in blindness. In the developed world, the major diseases that result in blindness are those affecting the retina, including AMD and diabetic retinopathy, and glaucoma. These diseases deprive patients of their sight and, as a result, their ability to live independently and perform daily activities. Any improvement in vision, or even a slowing of the rate of vision loss, has a tremendous impact on the quality of life of patients with impaired vision. There are also many other eye diseases, that may be less common but still have unmet medical need. We believe these other ophthalmic disease areas present several potential opportunities for ophthalmic drug development.

Age Related Macular Degeneration

AMD is a leading cause of vision loss in people over the age of 50 in the western world. There are two forms of AMD, dry AMD and wet AMD. According to AMD Alliance International, approximately 10 million people in the United States and 30 million people worldwide suffer from some form of AMD. AMD Alliance International estimates that dry AMD accounts for 85% to 90% of all AMD cases, while a study published in *Ophthalmology* in 2012 analyzing age and gender variations in AMD prevalence estimates that approximately 8 million people worldwide are affected by GA, a form of dry AMD. A study on the burden of AMD published in 2006 in the peer reviewed journal *Current Opinion in Ophthalmology*, estimated that 1,250,000 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. Based on U.S. Census Bureau data, we estimate that over the next two decades in the United States the number of people aged 55 or older is expected to increase by approximately 36% and the number of people aged 65 and older is expected to increase by approximately 69%. We expect that this increase in the number of elderly people will result in a significant increase in the number of cases of both dry AMD, including cases of GA, and wet AMD in the United States. In addition to having a devastating effect on patients, AMD also has a significant impact on the economy. According to a 2010 study sponsored by AMD Alliance International, the annual direct healthcare system costs of visual impairment worldwide due to AMD were estimated at approximately $255 billion.

Wet AMD

Wet AMD is preceded by dry AMD. In a subset of patients, dry AMD converts to wet AMD when new and abnormal blood vessels invade the retina. These abnormal new blood vessels originate beneath the retina, in a layer called the choroid, and invade into the overlying retinal layers. This abnormal new blood vessel growth is generally referred to as pathological angiogenesis. In the context of wet AMD, pathological angiogenesis is associated with both the development of neovascular cells and the accumulation of other cell types and altered tissue. The pathological neovascular tissue in wet AMD is called the choroidal neovascular complex or choroidal neovascularization. Choroidal neovascularization, or CNV, and adjacent and contiguous areas of blood and altered tissue are referred to as a lesion.

Abnormal new blood vessels tend to be fragile and often bleed and leak fluid into the macula, the central most portion of the retina responsible for central vision and color perception. Untreated, new blood vessel growth and associated leakage typically lead to retinal distortion and eventual retinal scarring, with irreversible destruction of the macula, resulting in loss of vision. This visual loss occurs rapidly with a progressive course. Approximately 90% of wet AMD cases involve subfoveal choroidal neovascularization, which is blood vessel growth directly under the central portion of the macula, known as the fovea. Our Phase 3 clinical program for Fovista enrolled patients with subfoveal wet AMD.

Wet AMD traditionally has been divided into subtypes based on the pattern of the abnormal new blood vessels using the diagnostic imaging technique fluorescein angiography or cross sectional location of the abnormal new blood vessels using the diagnostic imaging technique spectral domain optical coherence tomography, or SD-OCT. These subtypes form a continuous spectrum of pathological neovascularization based on whether the abnormal new blood vessels are well defined and delineated as determined by fluorescein angiography or whether they have invaded the retinal pigment epithelium, or RPE, layer of the retina. The RPE layer of the retina lies between the choroid and the neurosensory region of the retina. The term "classic" applies to the portion or component of the patient's abnormal new bloods vessels or neovascularization that is well defined by fluorescein angiography, with their location usually represented above the RPE. The term "occult" applies to the portion or component of the patient's abnormal new blood vessels that is poorly defined by fluorescein angiography, with their location usually represented below the RPE.

Abnormal new blood vessels are predominantly made up of two cell types, endothelial cells and pericytes. The endothelial cells line the inside of abnormal new blood vessels. Pericytes then intimately cover the outside of these blood vessels. Early in the process of abnormal new blood vessel formation, VEGF binds to a receptor on endothelial cells and causes endothelial cells to proliferate. The proliferating endothelial cells form new blood vessels. VEGF provides survival signals to

endothelial cells. VEGF also is one of the most potent inducers of blood vessel permeability, which causes the new blood vessels to leak.

PDGF binds to a receptor on pericytes. The binding of PDGF provides an important cell survival signal to pericytes. PDGF also recruits pericytes to the abnormal new blood vessel, where they mature and cover the endothelial cells. Pericytes locally supply the endothelial cells with growth and survival factors, including VEGF, and play a major role in endothelial cell survival. Pericytes also physically support and stabilize the abnormal new blood vessels. PDGF attracts pericytes, RPE cells and other cells, which are all involved in the formation of the choroidal neovascular complex.

The current standard of care for wet AMD is administration by intravitreal injection of anti-VEGF drugs as monotherapy. Anti-VEGF drugs prevent VEGF from binding to its natural receptor on endothelial cells in the abnormal new blood vessels, thereby inhibiting further abnormal new blood vessel growth and leakage associated with wet AMD. The FDA has approved the anti-VEGF drugs Lucentis, Eylea and Macugen for the treatment of wet AMD. The FDA also has approved photodynamic therapy with Visudyne (PDT) as a treatment of patients with wet AMD. In addition, although approved by the FDA as a cancer therapy, the anti-VEGF drug Avastin is used off-label to treat wet AMD. Lucentis is an antibody fragment derived from the same full length antibody from which Avastin was derived.

Fovista

Our product candidate Fovista is designed to target PDGF. We pursued development of Fovista based on a hypothesis that the administration of Fovista in combination with anti-VEGF drugs in patients with wet AMD may cause regression of neovascularization more effectively than anti-VEGF monotherapy, thereby potentially resulting in increased visual benefit for patients with wet AMD. However, in light of the failure of our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD to show a visual benefit from the addition of 1.5mg of Fovista to a monthly 0.5mg regimen of Lucentis therapy, the magnitude of such potential visual benefit, if any, remains to be demonstrated. Fovista is a pegylated aptamer, which means that polyethylene glycol is linked to a chemically-synthesized strand of nucleic acid. This pegylation increases the half-life of Fovista, which in turn increases the time that Fovista actively targets PDGF. In our Phase 3 clinical program, as well as our prior Phase 1 and Phase 2b clinical trials, Fovista was administered by intravitreal injection after a separate intravitreal injection of an anti-VEGF drug. Many other therapies used to treat serious retinal disorders, including Lucentis, Avastin and Eylea, also are administered by intravitreal injection.

Clinical Development of Fovista Combination Therapy for Wet AMD

Prior to commencing our pivotal, Phase 3 Fovista program in 2013, we completed a multicenter, uncontrolled, open-label, ascending dose Phase 1 clinical trial and a multicenter, randomized, controlled, double-masked Phase 2b clinical trial of Fovista administered in combination with Lucentis for the treatment of wet AMD. Our pivotal, Phase 3 Fovista clinical program consisted of three separate clinical trials, OPH1002, OPH1003 and OPH1004. All three of these Phase 3 clinical trials incorporated significant aspects from the design of our completed Phase 2b clinical trial. We enrolled a total of approximately 1,866 patients in more than 250 centers internationally across the three trials.

In December 2016, we announced initial, top-line data from OPH1002 and OPH1003, evaluating the safety and efficacy of 1.5mg of Fovista administered in combination with monthly 0.5mg Lucentis therapy compared to monthly 0.5mg Lucentis monotherapy for the treatment of wet AMD. The pre-specified primary endpoint of mean change in best-corrected visual acuity at 12 months was not achieved for either trial. Moreover, we have not observed any clinically meaningful visual benefit when 1.5mg of Fovista was added to a monthly regimen of 0.5mg Lucentis therapy for any subgroup of patients that we have analyzed from the OPH1002 and OPH1003 trials, including subgroups based on baseline visual acuity, baseline lesion size or the baseline amount of the classic component of CNV. Following the December 2016 data announcement, we subsequently stopped treating patients in, and terminated, both the OPH1002 and OPH1003 trials.

Our remaining Phase 3 clinical trial, OPH1004, evaluating the safety and efficacy of 1.5 mg of Fovista administered in combination with 2.0mg Eylea or 1.25mg Avastin compared to Eylea or Avastin monotherapy for the treatment of wet AMD remains ongoing. We expect initial, top-line data from the OPH1004 trial to be available during the second half of 2017. The failure of OPH1002 and OPH1003 to show any clinically meaningful visual benefit in adding 1.5mg of Fovista to a monthly regimen of 0.5mg of Lucentis and the recent failure of a competitor’s Phase 2 trial investigating the combination of a PDGF inhibitor and a VEGF inhibitor may be indicative of a low likelihood of success for OPH1004. In light of the data from the OPH1002 and OPH1003 trials, we have also stopped treating patients in our additional Phase 2 clinical trials that were evaluating the potential additional benefits of Fovista administered in combination with anti-VEGF drugs in wet AMD patients, which we previously referred to collectively as the Fovista Expansion Studies. In the event that we obtain favorable results from the OPH1004 trial, we expect that we would engage regulatory agencies, in particular the FDA and potentially, in

conjunction with Novartis, our ex-US commercialization partner for Fovista, the EMA, to seek such agencies' recommendations, if any, regarding future development in pursuit of potential marketing approval for Fovista. In all likelihood, even assuming favorable results from the OPH1004 trial, we will need to successfully complete an additional, confirmatory, pivotal trial in order to demonstrate the safety and efficacy of Fovista combination therapy for the treatment of wet AMD and obtain marketing approval.

Completed Phase 1 Clinical Trial of Fovista Combination Therapy for Wet AMD

In 2009, we completed a multicenter, uncontrolled, open-label, ascending dose Phase 1 clinical trial evaluating the safety and tolerability of Fovista administered in combination with Lucentis for the treatment of subfoveal wet AMD. We conducted our Phase 1 clinical trial in 23 patients at 11 centers in the United States. Fovista was generally well tolerated in this trial. Patients enrolled in our Phase 1 clinical trial were 50 years of age and older and newly diagnosed with subfoveal choroidal neovascularization secondary to AMD with some classic component as documented by fluorescein angiography. We enrolled patients with a range of baseline visual acuities. Visual acuity is measured as the number of letters, arranged in lines, that the patient can read on the Early Treatment Diabetic Retinopathy Study, or ETDRS, eye chart. Each line on the ETDRS eye chart has five letters. This is a well-established standardized chart of vision testing used in these types of trials. Normal visual acuity is commonly referred to as 20/20 vision. To qualify for enrollment in our Phase 1 clinical trial, the visual acuity in the patient's study eye had to be between 20/63 and 20/200. We enrolled patients with a wide range of lesion sizes and with a variety of other lesion characteristics.

Fovista administered in combination with Lucentis was generally well tolerated in our Phase 1 clinical trial. None of the patients experienced any dose limiting toxicities at any of the dose levels tested. We did not observe any evidence of drug related adverse events. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure. There were no adverse events related to Fovista or Lucentis, and no patients discontinued from the trial due to an adverse event. We did not observe any meaningful clinical immunologic reactions to Fovista.

Our Phase 1 clinical trial had a small sample size and a short follow up period. It was not designed to compare Fovista combination therapy to another therapy. However, we noted improvements in visual acuity and anatomical changes in the newly formed blood vessels of the eye that suggested the Fovista combination therapy was enhancing the visual outcome compared to results previously seen with anti-VEGF monotherapy.

Completed Phase 2b Clinical Trial of Fovista Combination Therapy for Wet AMD

In 2012, we completed a multicenter, randomized, controlled, double-masked Phase 2b clinical trial evaluating the safety and efficacy of Fovista administered in combination with Lucentis for the treatment of patients newly diagnosed with subfoveal wet AMD. We conducted this trial in 449 patients at approximately 69 centers in North America, South America, Europe and Israel. We made no meaningful changes to the inclusion and exclusion criteria in our Phase 2b clinical trial from those we used in our Phase 1 clinical trial.

The primary objective of this trial was to evaluate the effect of two different doses of Fovista administered in combination with Lucentis compared to Lucentis monotherapy. The primary efficacy endpoint of this trial was mean change in visual acuity from baseline at 24 weeks for Fovista and Lucentis combination therapy compared to Lucentis monotherapy. Prior to enrollment in the trial, we measured each patient's visual acuity to establish a baseline. Following assessment at baseline, visual acuity was measured at each subsequent four-week time point. We had diagnostic imaging techniques of fluorescein angiography and SD-OCT performed and assessed by an independent reading center at baseline and at week 24.

Secondary efficacy endpoints for this trial included the following:

- mean change in visual acuity in ETDRS letters from baseline at 12 weeks;
- proportion of patients in each treatment group gaining 15 or more ETDRS letters from baseline at 12 weeks;
- proportion of patients in each treatment group gaining 15 or more ETDRS letters from baseline at 24 weeks; and
- mean change in area of choroidal neovascularization from baseline at 24 weeks.

We randomly assigned patients in this trial to one of three treatment groups: 149 patients received intravitreal injections of 0.3 mg of Fovista following intravitreal injections of 0.5 mg of Lucentis; 152 patients received intravitreal injections of 1.5 mg of Fovista following intravitreal injections of 0.5 mg of Lucentis; and 148 patients in the control arm of the

trial received sham injections following intravitreal injections of 0.5 mg of Lucentis. Patients were treated and assessed once every four weeks for 24 weeks.

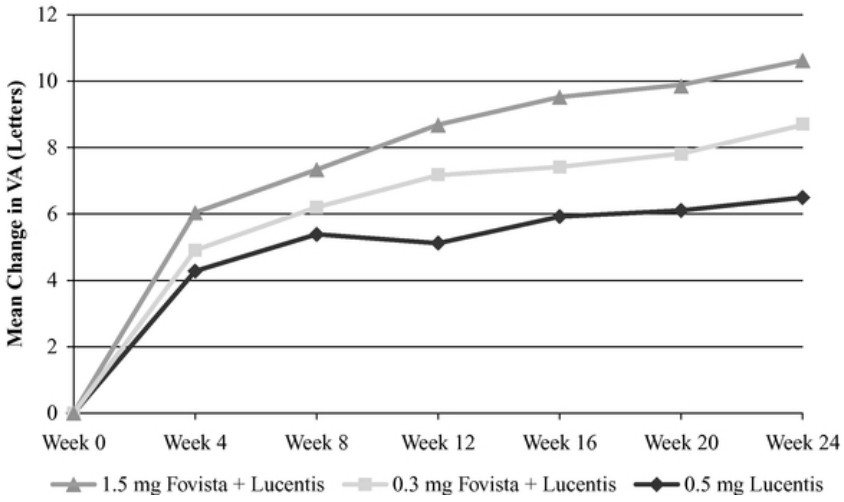
Measures of Mean Visual Acuity-Primary Efficacy Endpoint

Mean Change in Visual Acuity from Baseline at 24 Weeks. In this trial, the combination of 1.5 mg of Fovista and Lucentis demonstrated statistically significant superiority compared to Lucentis monotherapy based on the pre-specified primary endpoint of mean change in visual acuity from baseline at the 24 week time point. 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. However, when multiple doses of a drug are tested against a single control group, a more stringent statistical method that accounts for multiple comparisons must be applied. For this purpose, we used the Hochberg multiple comparison procedure. Under the Hochberg procedure, in order to demonstrate statistical significance for any particular dose, it is necessary to establish a p-value that meets a stricter standard than the conventional standard of 0.05 or less unless each dose is statistically significant with a p-value of 0.05 or less. In the case of our Phase 2b clinical trial, in which we evaluated two doses of Fovista administered in combination with Lucentis, the Hochberg procedure required a more stringent p-value of 0.025 or less to establish statistical significance for the comparison of the combination of 1.5 mg of Fovista and Lucentis to Lucentis monotherapy.

At 24 weeks, patients receiving the combination of 1.5 mg of Fovista and Lucentis gained a mean of 10.6 ETDRS letters compared to a mean of 6.5 ETDRS letters for patients receiving Lucentis monotherapy, representing a 62% comparative benefit from baseline, with a p-value of 0.019. This result was statistically significant. At 24 weeks, patients receiving the combination of 0.3 mg of Fovista and Lucentis gained a mean of 8.8 ETDRS letters. This result was not statistically significant, having a p-value greater than 0.05, compared to Lucentis monotherapy. We determined not to test the combination of 0.3 mg of Fovista and Lucentis compared to Lucentis monotherapy in our Phase 3 clinical program.

Patients treated with the combination of 1.5 mg of Fovista and Lucentis showed greater improvement in visual acuity from baseline compared to patients treated with Lucentis monotherapy at week four and at each subsequent four-week assessment. In addition, the relative magnitude of visual benefit favoring the combination of 1.5 mg of Fovista and Lucentis increased over the study period. The graph below sets forth the mean change in visual acuity from baseline for each treatment group over the course of the trial.

Mean Change in Visual Acuity (VA) from Baseline Over Time



Measures of Mean Visual Acuity-Secondary Endpoints

We evaluated measures of visual outcomes as secondary endpoints. Results from secondary endpoints are used to help interpret the primary result of the trial and to provide information for future research and clinical development. However, the statistical analysis plan for our Phase 2b clinical trial was not designed to establish and, as a result, we could not and did not

demonstrate, statistical significance with respect to these secondary endpoints. Accordingly, only descriptive analyses and trends for secondary endpoints are presented below.

Mean Change in Visual Acuity from Baseline at 12 Weeks. We observed differences on the secondary endpoint of mean change in visual acuity from baseline at the 12 week time point favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy. At 12 weeks, patients receiving the combination of 1.5 mg of Fovista and Lucentis gained a mean of 8.7 ETDRS letters compared to patients receiving Lucentis monotherapy who gained a mean of 5.1 ETDRS letters.

Proportion of Patients Gaining 15 or More Letters from Baseline at 12 Weeks and at 24 Weeks. We observed differences in the proportion of patients that showed improvement of 15 ETDRS letters, or three lines, or better in visual acuity favoring the combination of 1.5 mg of Fovista and Lucentis compared to Lucentis monotherapy both at 12 weeks and at 24 weeks of treatment.

The table below sets forth at 12 weeks and 24 weeks the number of patients in each treatment group and the percentage of patients in such treatment group who gained the specified number of lines in visual acuity and the percentage of patients whose final visual acuity improved to the specified level.

Proportion of Patients Gaining 15 or More ETDRS Letters

Arm	# (%) of Patients Gaining ≥ 15 letters at Week 12	# (%) of Patients Gaining ≥ 15 letters at Week 24
1.5 mg Fovista + Lucentis	48 (31.8)%	59 (39.1)%
0.3 mg Fovista + Lucentis	31 (21.1)%	49 (33.3)%
0.5 mg Lucentis	33 (22.4)%	50 (34.0)%

Measures of Anatomical Changes-Secondary Endpoint

We evaluated one measure of anatomical change as a secondary endpoint. The mean change in area of CNV from baseline at 24 weeks as determined by review of fluorescein angiograms was greater in patients treated with Lucentis monotherapy than in patients treated with the combination of 1.5 mg of Fovista and Lucentis. We believe that the inclusion of both larger and smaller CNV sizes in the single analysis of this secondary endpoint had the potential to create a distortion in the analysis of the mean change in area of CNV. This is because the average level of regression, as numerically measured, was approximately tenfold greater in a retrospective subgroup of patients with a large CNV size compared to the remaining subgroup of patients with a small CNV size. We believe that a treatment group with a greater number of patients with larger CNV sizes will show a markedly larger amount of regression on average. That was the case in our Phase 2b trial in which the Lucentis monotherapy group had a greater proportion of patients with large CNV sizes compared to the group treated with a combination of 1.5 mg of Fovista and Lucentis.

Safety

Fovista was generally well tolerated in the Phase 2b trial at both doses tested in combination with Lucentis. We did not observe any cases of infection inside the eye, or endophthalmitis. We observed one case of severe intraocular inflammation among the patients treated with 0.3 mg of Fovista in combination with Lucentis and no such cases among the patients treated with 1.5 mg of Fovista in combination with Lucentis. We did not observe any significant imbalances among treatment groups in the incidence of ocular adverse events or systemic adverse events, including cardiovascular events or stroke. The number of patients in our Phase 2b clinical trial with one or more serious systemic adverse events, the most common systemic serious adverse events in this trial organized by MedDRA system organ class, a standard method of reporting adverse events, and by antiplatelet trialists' collaboration events, a standard method of reporting cardiovascular adverse events, are set forth in the table below.

	Monotherapy Lucentis N = 148	0.3 mg Fovista + Lucentis N = 149	1.5 mg Fovista + Lucentis N = 152
Patients With One or More Systemic Serious Adverse Events	11 (7.4)%	13 (8.7)%	9 (5.9)%
MedDRA System Organ Class(1)			
Cardiac Disorders	2 (1.4)%	2 (1.3)%	2 (1.3)%
Gastrointestinal Disorders	1 (0.7)%	2 (1.3)%	3 (2.0)%
Infections	1 (0.7)%	2 (1.3)%	0 (0.0)%
Musculoskeletal Disorders	1 (0.7)%	0 (0.0)%	2 (1.3)%
Neoplasms	3 (2.0)%	3 (2.0)%	1 (0.7)%
Nervous System Disorders	3 (2.0)%	1 (0.7)%	0 (0.0)%
Respiratory Disorders	0 (0.0)%	3 (2.0)%	2 (1.3)%
Any Antiplatelet Trialists' Collaboration (APTC) Event			
Non-Fatal Myocardial Infarction	0 (0.0)%	0 (0.0)%	0 (0.0)%
Non-Fatal Stroke	2 (1.4)%	1 (0.7)%	0 (0.0)%
Vascular Death	1 (0.7)%	0 (0.0)%	0 (0.0)%

(1) Data are listed only for system organ classes with three or more events.

There was one serious adverse event in the study eye in each of the treatment groups. The serious adverse event was different among each of the treatment groups as shown in the table below.

	Monotherapy Lucentis N = 148	0.3 mg Fovista + Lucentis N = 149	1.5 mg Fovista + Lucentis N = 152
Ocular Serious Adverse Events	1 (0.7)%	1 (0.7)%	1 (0.7)%
Corneal Erosion	0 (0.0)%	0 (0.0)%	1 (0.7)%
Uveitis	0 (0.0)%	1 (0.7)%	0 (0.0)%
Visual Acuity Reduced	1 (0.7)%	0 (0.0)%	0 (0.0)%

The most common adverse events in the study eye are set forth in the table below.

Ocular Adverse Events Reported in Study Eye in 5% or More of Patients in Any Arm

	Monotherapy Lucentis N = 148	0.3 mg Fovista + Lucentis N = 149	1.5 mg Fovista + Lucentis N = 152
Patients with One or More Adverse Events	75 (50.7)%	79 (53.0)%	79 (52.0)%
Conjunctival hemorrhage	37 (25.0)%	34 (22.8)%	51 (33.6)%
Punctate keratitis	10 (6.8)%	19 (12.8)%	15 (9.9)%
Eye pain	8 (5.4)%	10 (6.7)%	13 (8.6)%
Conjunctival hyperemia	13 (8.8)%	9 (6.0)%	13 (8.6)%
Subretinal fibrosis	8 (5.4)%	6 (4.0)%	5 (3.3)%
Intraocular pressure increase	4 (2.7)%	8 (5.4)%	9 (5.9)%

Most of the common ocular adverse events in this trial were related to the intravitreal preparation and injection procedure and were not drug related. These intravitreal adverse events, as reflected in the table above, included conjunctival hemorrhage, punctate keratitis, eye pain and conjunctival hyperemia. Most adverse events of increased intraocular pressure occurred after injection, were transient, were related to the injection and were treated and resolved the same day. Mean intraocular pressure in each treatment group returned to pre-injection level at the next assessment, including at the end of the trial.

Phase 3 Clinical Program for Fovista Combination Therapy for Wet AMD

Our pivotal Phase 3 clinical program consists of three separate Phase 3 clinical trials to evaluate the safety and efficacy of 1.5 mg of Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD compared to anti-VEGF monotherapy. Two of these trials, OPH1002 and OPH1003, evaluated Fovista in combination with Lucentis compared to Lucentis monotherapy. The third trial, OPH1004, is evaluating Fovista in combination with Eylea or Avastin compared to Eylea or Avastin monotherapy.

OPH1002 and OPH1003 both investigated Fovista in combination with Lucentis compared to Lucentis monotherapy and were identical with respect to the trial design in the first year. Therefore, the databases from both OPH1002 and OPH1003 were unmasked and analyzed together, which allowed for the pooled analysis of certain relevant endpoints in accordance with the statistical analysis plan. In December 2016, we announced initial, top-line data from OPH1002 and OPH1003. The pre-specified primary endpoint of mean change in best-corrected visual acuity at 12 months was not achieved for either trial. We did not observe any clinically meaningful visual benefit in adding Fovista to Lucentis in any subgroup of patients, including any lesion type (CNV size). We subsequently stopped treating patients in both the OPH1002 and OPH1003 trials. Our remaining Phase 3 clinical trial, OPH1004, was fully enrolled in June 2016 and remains ongoing. We currently plan to continue OPH1004 at least until all patients reach the 12 month primary efficacy endpoint, as Fovista combination therapy was generally well tolerated through the 12 month time point in OPH1002 and OPH1003 and OPH1004 is investigating Fovista in combination with different anti-VEGF drugs than the anti-VEGF comparator for the two failed Lucentis trials. We expect initial, top-line data from the OPH1004 trial to be available during the second half of 2017. The failure of OPH1002 and OPH1003 to show any clinically meaningful visual benefit in adding 1.5mg of Fovista to a monthly regimen of 0.5mg of Lucentis and the recent failure of a competitor's Phase 2 trial investigating the combination of a PDGF inhibitor and a VEGF inhibitor may be indicative of a low likelihood of success for OPH1004. We plan to reassess our Fovista development program throughout 2017 as our updated business plan progresses and evolves, with the goal of aligning corporate resources relative to a potentially broader product pipeline. Our reassessment of Fovista for the treatment of wet AMD will be primarily determined by the initial, top-line data from OPH1004. As a result of this reassessment, we may modify, expand or terminate our Fovista development program at any time.

Phase 3 Trial Design

The primary efficacy endpoint in each of our Phase 3 clinical trials is mean change in best-corrected visual acuity from baseline at 12 months for Fovista and anti-VEGF combination therapy compared to anti-VEGF monotherapy. Prior to enrollment in the Phase 3 clinical trials, we measured each patient's visual acuity to establish a baseline. The protocols for each of these trials provide that patients be assessed monthly.

Secondary efficacy endpoints for our completed OPH1002 and OPH1003 Phase 3 clinical trials included the following:

- proportion of patients in each treatment group gaining 20 or more ETDRS letters from baseline at month 12;
- proportion of patients in each treatment group losing 5 or more ETDRS letters from baseline at month 12;
- proportion of patients in each treatment group achieving visual acuity of 20/25 or better at month 12; and
- proportion of patients with growth of choroidal neovascular lesion area from baseline to month 12 (as determined by fluorescein angiography).

Secondary efficacy endpoints for our ongoing OPH1004 Phase 3 clinical trial include the following:

- proportion of patients in each treatment group gaining 20 or more ETDRS letters from baseline at month 12;
- proportion of patients in each treatment group losing 5 or more ETDRS letters from baseline at month 12; and
- proportion of patients in each treatment group achieving visual acuity of 20/25 or better at month 12.

In each of OPH1002 and OPH1003, we randomly assigned patients to one of two treatment groups. Treatment for the two groups in each of these two trials was as follows:

- In the first group, 310 and 312 patients, respectively, for OPH1002 and OPH1003 received intravitreal injections of 1.5 mg of Fovista following intravitreal injections of 0.5 mg of Lucentis.
- In the second group, which served as the control arm for each trial, 309 and 314 patients, respectively, for OPH1002 and OPH1003, received sham injections following intravitreal injections of 0.5 mg of Lucentis.

In each of the OPH1002 and OPH1003 clinical trials, patients were treated monthly for the first 12 months. In OPH1002, for patients that were treated after month 12 (up to month 24), treatment was administered based on the stability of the patient's visual acuity, ophthalmic examination and imaging consistent with the EU label for Lucentis. In OPH1003, for patients that were treated after month 12 (up to month 24), patients were treated every other month and could be retreated during the intervening months in accordance with specific retreatment criteria set forth in the protocol for the trial based on visual acuity and imaging.

In the OPH1004 clinical trial, we randomly assigned patients to one of two treatment groups with approximately 311 patients in each group. Treatment for the two groups in this trial is as follows:

In the first group, patients are further randomized in a 1:1 ratio to receive intravitreal injections of one of the following treatments:

- 1.5 mg of Fovista following intravitreal injections of 1.25 mg of Avastin; or
- 1.5 mg of Fovista following intravitreal injections of 2.0 mg of Eylea.

In the second group, which serves as the control arm of the trial, patients are further randomized in a 1:1 ratio to receive one of the following treatments:

- sham injections following intravitreal injections of 1.25 mg of Avastin; or
- sham injections following intravitreal injections of 2.0 mg of Eylea.

The patients randomized to receive Avastin are treated monthly for the duration of the trial (up to 24 months) and the patients randomized to receive Eylea are treated every month for the first three months followed by every other month thereafter (up to 24 months).

We made no meaningful changes to the inclusion and exclusion criteria in these Phase 3 clinical trials from those we used in our Phase 2b clinical trial. However, we modified the methodology used to determine a patient's eligibility under certain of the inclusion and exclusion criteria for our Phase 3 clinical trials as compared to our Phase 2b clinical trial. For our Phase 2b trial, we assessed patient eligibility based on the fluorescein angiographic pattern of the choroidal neovascular membrane. Since the most commonly employed modality for imaging, diagnosing and managing neovascular AMD is currently SD-OCT, we modified the methodology to determine the patient's eligibility to participate in our Phase 3 program to include SD-OCT criteria. To ensure that uniform criteria were applied in characterizing patients' neovascular lesions, we engaged a centralized reading center to review the SD-OCT, fluorescein angiograms and fundus images of each patient's affected eye. Fundus images are photos of the back of the eye taken using a camera attached to a specialized, low-power microscope. These photos, which are often in color, show various elements of the back of the eye, including the retina, retinal vasculature, optic disc, macula and fovea. For our Phase 3 clinical trials, the reading center used all three of these imaging modalities, fluorescein angiography, SD-OCT and fundus images, to assess the eligibility of patients based on the presence of abnormal new blood vessels relative to the RPE at the time of enrollment. We believe that use of a centralized reading center and the latest imaging technologies has enabled us to confirm patient eligibility and properly classify neovascular characteristics and the associated leakage in an accurate and standardized manner prior to enrolling patients in the trial.

As was the case in both our Phase 1 clinical trial and our Phase 2b clinical trial, there is a 30-minute delay in the injection of Fovista after the anti-VEGF drug.

Data from OPH1002 and OPH1003

In the pooled analysis of results from OPH1002 and OPH1003 consisting of 1,245 treated patients, the combination of 1.5 mg of Fovista and Lucentis did not result in statistically significant benefit compared to Lucentis monotherapy based on the pre-specified primary endpoint of mean change in best-corrected visual acuity from baseline at the 12-month time point. In

these trials, a p-value of 0.05 or less represents statistical significance. Furthermore, there is no evidence to date from our analysis of the results from the OPH1002 and OPH1003 trials of any clinically meaningful benefit at any time point or in any subgroup of patients or any pattern with respect to the data suggestive of a potential drug effect by adding Fovista to Lucentis.

Measures of Mean Visual Acuity-Primary Efficacy Endpoint.

In the pooled analysis, patients receiving the combination of 1.5mg of Fovista and Lucentis gained a mean of 10.24 ETDRS letters at month 12 compared to a mean gain of 10.01 ETDRS letters for patients receiving Lucentis monotherapy, a resulting difference of 0.23 ETDRS letters. In OPH1002, consisting of 619 treated patients, patients receiving Fovista combination therapy gained a mean of 10.74 ETDRS letters at month 12, compared to a mean gain of 9.82 ETDRS letters in patients receiving Lucentis monotherapy, a resulting difference of 0.92 ETDRS letters, with a p-value of 0.44. In OPH1003, consisting of 626 treated patients, patients receiving Fovista combination therapy gained a mean of 9.91 ETDRS letters at month 12, compared to a mean gain of 10.36 ETDRS letters in patients receiving Lucentis monotherapy, a resulting difference of -0.44 ETDRS letters, with a p-value of 0.71. None of these results of the pre-specified primary efficacy analysis were statistically significant.

Measures of Mean Visual Acuity-Secondary Endpoints

We evaluated measures of visual outcomes as secondary endpoints. Results from secondary endpoints are used to help interpret the primary result of the trial and to provide information for future research and clinical development. As with our Phase 2b trial, the statistical analysis plan for our Phase 3 clinical trials was not designed to establish and, as a result, we could not and did not demonstrate, statistical significance with respect to these secondary endpoints. In addition, where the primary efficacy endpoint for a clinical trial has not been met, data regarding secondary endpoints are generally less relevant and are potentially uninterpretable.

Proportion of Patients Gaining 20 or More Letters from Baseline at 12 Months. In the pooled analysis of pre-specified secondary endpoints from both trials, 24.2% of patients receiving the combination of 1.5mg of Fovista and Lucentis gained 20 or more ETDRS letters from baseline at month 12, compared to 22.1% of patients receiving Lucentis monotherapy. In OPH1002, 25.9% of patients receiving Fovista combination therapy gained 20 or more ETDRS letters from baseline at month 12, compared to 20.0% of patients receiving Lucentis monotherapy. In OPH1003, 22.5% of patients receiving Fovista combination therapy gained 20 or more ETDRS letters from baseline at month 12, compared to 24.1% of patients receiving Lucentis monotherapy.

Proportion of Patients Losing 5 or More Letters from Baseline at 12 Months. In the pooled analysis, 12.1% of patients receiving the combination of 1.5mg of Fovista and Lucentis lost 5 or more ETDRS letters from baseline at month 12, compared to 11.2% of patients receiving Lucentis monotherapy. In OPH1002, 12.0% of patients receiving Fovista combination therapy lost 5 or more ETDRS letters at month 12, compared to 12.3% of patients receiving Lucentis monotherapy. In OPH1003, 12.2% of patients receiving Fovista combination therapy lost 5 or more ETDRS letters at month 12, compared to 10.2% of patients receiving Lucentis monotherapy.

Proportion of Patients Achieving Visual Acuity of 20/25 or Better at 12 Months. In the pooled analysis, 13.5% of patients receiving the combination of 1.5mg of Fovista and Lucentis achieved visual acuity of 20/25 or better at month 12, compared to 13.9% of patients receiving Lucentis monotherapy. In OPH1002, 13.6% of patients receiving Fovista combination therapy achieved visual acuity of 20/25 or better, compared to 13.2% of patients receiving Lucentis monotherapy. In OPH1003, 13.5% of patients receiving Fovista combination therapy achieved visual acuity of 20/25 or better, compared to 14.6% of patients receiving Lucentis monotherapy.

Measures of Anatomical Changes-Secondary Endpoint

We did not observe any difference in the proportion of patients with growth in choroidal neovascularization lesion area from baseline to month 12 as determined by review of fluorescein angiograms in patients treated with Fovista combination therapy as compared to patients treated with Lucentis monotherapy, in based on the treatment groups in either OPH1002 or OPH1003 or the pooled analysis.

Safety

Combination therapy consisting of 1.5mg of Fovista and 0.5mg of Lucentis and 0.5mg Lucentis monotherapy were each generally well tolerated in OPH1002 and OPH1003. We did not observe any clinically meaningful imbalances between the treatment groups in either trial or in the pooled analysis in the incidence of systemic adverse events, including arterial thromboembolic events.

Serious Systemic Adverse Events. The number of patients in each treatment group in OPH1002 and OPH1003, as well as the pooled analysis, with one or more serious systemic adverse events, for the most common serious systemic adverse events organized by MedDRA system organ class, and for the arterial thromboembolic events using Standardized MedDRA Queries, or SMQ, are set forth in the tables below. For the first table of serious systemic adverse events by MedDRA system organ class, data are listed only for serious systemic adverse events for system organ classes that occurred in 1% or more of patients in any of the treatment groups across the two trials.

	OPH1002		**OPH1003**		**OPH1002 + OPH1003**	
	1.5mg Fovista + 0.5mg Lucentis	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**
	N = 310	**N = 309**	**N = 312**	**N = 314**	**N = 622**	**N = 623**
Patients With One or More Serious Systemic Adverse Event	42 (13.55%)	34 (11%)	45 (14.42%)	46 (14.65%)	87 (13.99%)	80 (12.84%)
MedDRA System Organ Class (1)						
Infections and infestations	11 (3.55%)	10 (3.24%)	9 (2.88%)	8 (2.55%)	20 (3.22%)	18 (2.89%)
Cardiac disorders	11 (3.55%)	5 (1.62%)	5 (1.6%)	9 (2.87%)	16 (2.57%)	14 (2.25%)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	4 (1.29%)	6 (1.94%)	11 (3.53%)	10 (3.18%)	15 (2.41%)	16 (2.57%)
Injury, poisoning and procedural complications	2 (0.65%)	5 (1.62%)	7 (2.24%)	10 (3.18%)	9 (1.45%)	15 (2.41%)
Respiratory, thoracic and mediastinal disorders	5 (1.61%)	3 (0.97%)	4 (1.28%)	2 (0.64%)	9 (1.45%)	5 (0.8%)
Gastrointestinal disorders	6 (1.94%)	4 (1.29%)	2 (0.64%)	3 (0.96%)	8 (1.29%)	7 (1.12%)
Nervous system disorders	5 (1.61%)	6 (1.94%)	3 (0.96%)	3 (0.96%)	8 (1.29%)	9 (1.44%)
Vascular disorders	0 (0%)	6 (1.94%)	3 (0.96%)	1 (0.32%)	3 (0.48%)	7 (1.12%)

	OPH1002		**OPH1003**		**OPH1002 + OPH1003**	
	1.5mg Fovista + 0.5mg Lucentis	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**
	N = 310	**N = 309**	**N = 312**	**N = 314**	**N = 622**	**N = 623**
Patients With One or More Arterial Thromboembolic Events						
Standardized MedDRA Query						
Myocardial Infarction	3 (0.97%)	3 (0.97%)	0 (0%)	4 (1.27%)	3 (0.48%)	7 (1.12%)
Ischaemic CNS Vascular Conditions	3 (0.97%)	4 (1.29%)	4 (1.28%)	2 (0.64%)	7 (1.13%)	6 (0.96%)
Haemorrhagic CNS Vascular Conditions	2 (0.65%)	2 (0.65%)	1 (0.32%)	1 (0.32%)	3 (0.48%)	3 (0.48%)

CNS: Central Nervous System

Serious Ocular Adverse Events. The serious ocular adverse events observed in the study eye for each treatment group in OPH1002 and OPH1003, as well as the pooled analysis, are presented in the table below.

	OPH1002		OPH1003		OPH1002 + OPH1003	
	1.5mg Fovista + 0.5mg Lucentis	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**
	N = 310	**N = 309**	**N = 312**	**N = 314**	**N = 622**	**N = 623**
Patients With One or More Serious Ocular Adverse Event	5 (1.61%)	2 (0.65%)	10 (3.21%)	2 (0.64%)	15 (2.41%)	4 (0.64%)
Eye Disorders	3 (0.97%)	2 (0.65%)	5 (1.6%)	1 (0.32%)	8 (1.29%)	3 (0.48%)
Cataract	1 (0.32%)	0 (0%)	0 (0%)	0 (0%)	1 (0.16%)	0 (0%)
Retinal detachment	0 (0%)	0 (0%)	3 (0.96%)	0 (0%)	3 (0.48%)	0 (0%)
Macular hole	0 (0%)	1 (0.32%)	2 (0.64%)	0 (0%)	2 (0.32%)	1 (0.16%)
Cataract Subcapsular	1 (0.32%)	0 (0%)	0 (0%)	0 (0%)	1 (0.16%)	0 (0%)
Retinal pigment epithelial tear	0 (0%)	0 (0%)	1 (0.32%)	0 (0%)	1 (0.16%)	0 (0%)
Retinal tear	1 (0.32%)	0 (0%)	0 (0%)	0 (0%)	1 (0.16%)	0 (0%)
Vitreous hemorrhage	1 (0.32%)	0 (0%)	0 (0%)	1 (0.32%)	1 (0.16%)	1 (0.16%)
Visual acuity reduced	0 (0%)	1 (0.32%)	0 (0%)	0 (0%)	0 (0%)	1 (0.16%)
Infections and Infestations	2 (0.65%)	0 (0%)	6 (1.92%)	1 (0.32%)	8 (1.29%)	1 (0.16%)
Endophthalmitis	2 (0.65%)	0 (0%)	6 (1.92%)	1 (0.32%)	8 (1.29%)	1 (0.16%)
Injury, Poisoning and Procedural Complications	0 (0%)	0 (0%)	1 (0.32%)	0 (0%)	1 (0.16%)	0 (0%)
Cataract traumatic	0 (0%)	0 (0%)	1 (0.32%)	0 (0%)	1 (0.16%)	0 (0%)

The incidence of endophthalmitis per intravitreal injection was 2/6997 (0.029%) in the Fovista and Lucentis combination therapy group and 0.0% in the Lucentis monotherapy group during the first 12 months of treatment in OPH1002; 6/7006 (0.086%) in the Fovista and Lucentis combination therapy group and 1/3510 (0.029%) in the Lucentis monotherapy group during the first 12 months of OPH1003; and 8/14003 (0.057%) in the pooled Fovista and Lucentis combination therapy groups from the first 12 months of both OPH1002 and OPH1003 and 1/6944 (0.014%) in the pooled Lucentis monotherapy groups from the first 12 months of both OPH1002 and OPH1003. Although the incidence of endophthalmitis per intravitreal injection is higher in the pooled Fovista and Lucentis combination therapy groups as compared to the pooled Lucentis monotherapy groups, it is still within the range of the reported incidence of endophthalmitis associated with intravitreal injections in previously reported wet AMD clinical trials.

Ocular Adverse Events Reported in Study Eye in 5% or More of Patients in Any Treatment Group. The most common ocular adverse events observed in the study eye for each treatment group in OPH1002 and OPH1003, as well as the pooled analysis, are presented in the table below. Data are listed for study eye ocular adverse events that occurred in 5% or more of patients in any of the treatment groups across the two trials.

	OPH1002		OPH1003		OPH1002 + OPH1003	
	1.5mg Fovista + 0.5mg Lucentis	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**	**1.5mg Fovista + 0.5mg Lucentis**	**0.5mg Lucentis Monotherapy**
	N = 310	**N = 309**	**N = 312**	**N = 314**	**N = 622**	**N = 623**
Patients With One or More Ocular Adverse Event (1)	154 (49.68%)	140 (45.31%)	199 (63.78%)	162 (51.59%)	353 (56.75%)	302 (48.48%)
Eye Disorders	129 (41.61%)	121 (39.16%)	175 (56.09%)	150 (47.77%)	304 (48.87%)	271 (43.5%)
Conjunctival haemorrhage	60 (19.35%)	56 (18.12%)	74 (23.72%)	50 (15.92%)	134 (21.54%)	106 (17.01%)
Punctate keratitis	15 (4.84%)	18 (5.83%)	35 (11.22%)	40 (12.74%)	50 (8.04%)	58 (9.31%)
Eye pain	23 (7.42%)	26 (8.41%)	22 (7.05%)	21 (6.69%)	45 (7.23%)	47 (7.54%)
Conjunctival hyperaemia	15 (4.84%)	13 (4.21%)	24 (7.69%)	24 (7.64%)	39 (6.27%)	37 (5.94%)
Vitreous floaters	12 (3.87%)	6 (1.94%)	22 (7.05%)	12 (3.82%)	34 (5.47%)	18 (2.89%)
Eye irritation	5 (1.61%)	12 (3.88%)	18 (5.77%)	15 (4.78%)	23 (3.7%)	27 (4.33%)
Keratitis	2 (0.65%)	4 (1.29%)	18 (5.77%)	14 (4.46%)	20 (3.22%)	18 (2.89%)
Investigations	43 (13.87%)	30 (9.71%)	49 (15.71%)	25 (7.96%)	92 (14.79%)	55 (8.83%)
Intraocular pressure increased	43 (13.87%)	30 (9.71%)	49 (15.71%)	25 (7.96%)	92 (14.79%)	55 (8.83%)

Most of the commonly reported ocular adverse events in OPH1002 and OPH1003 were related to the intravitreal preparation and injection procedure and were not related to the study drugs. Of these most commonly reported ocular adverse events, conjunctival hemorrhage, increased intraocular pressure and vitreous floaters were reported in greater than 1% more patients in the pooled Fovista and Lucentis combination therapy groups than in the pooled Lucentis monotherapy groups. This result is not unexpected, as there were approximately twice as many intravitreal injections in the Fovista and Lucentis combination therapy groups compared to the Lucentis monotherapy groups. Most adverse events of increased intraocular pressure occurred after injection, were transient, related to the intravitreal injection procedure and resolved the same day. Mean intraocular pressure in each treatment group returned to near pre-injection levels at the next assessment, including at the end of the trial.

Fovista Expansion Studies in Wet AMD

In addition to our Phase 3 clinical program for Fovista, we undertook additional Phase 2 clinical trials to evaluate the potential additional benefits of Fovista administered in combination with anti-VEGF drugs in wet AMD patients. We refer to these trials as the Fovista Expansion Studies. Following our receipt and announcement of initial, top-line data from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we stopped treating patients in the Fovista Expansion Studies. The Fovista Expansion Studies included:

- *OPH1005 Fovista Anti-Fibrosis Study*. During the third quarter of 2014, we initiated an open-label Phase 2a clinical trial of 1.5 mg of Fovista administered in combination with either Lucentis, Eylea or Avastin, to study subretinal fibrosis in wet AMD patients. The trial did not have any pre-specified efficacy endpoints as it was uncontrolled, open-label Phase 2a study with broad patient eligibility criteria. We completed enrollment in this trial in May 2015 with a total of 101 patients enrolled. Patients were followed for up to a 24-month period prior to our determination in December 2016 to stop treating patients in the Fovista Expansion Studies.

- *OPH1006 Fovista Treatment Burden Reduction Study*. During the fourth quarter of 2014, we initiated an open-label Phase 2a clinical trial of 1.5 mg of Fovista administered in combination with anti-VEGF drugs (Lucentis, Eylea or Avastin) to investigate a different treatment regimen of Fovista combination therapy. We completed enrollment in this trial in October 2015 with a total of 64 patients enrolled. Patients in this trial were to be followed for up to a 24-month period prior to our determination in December 2016 to stop treating patients in the Fovista Expansion Studies.

- *OPH1007 Fovista in Combination with Avastin Discontinuous Regimen Study.* During the fourth quarter of 2015, we initiated a randomized, double-masked, controlled Phase 2b clinical trial to evaluate the safety and efficacy of a discontinuous, bimonthly regimen of 1.5 mg of Fovista administered in combination with Avastin during the maintenance phase of wet AMD treatment, compared to a discontinuous, bimonthly regimen of Avastin monotherapy. This trial was terminated prior to full enrollment.

- *OPH1008 Fovista Imaging Study*. During the fourth quarter of 2015, we initiated an open-label Phase 2a clinical trial to investigate the role of multi-modal imaging in assessing anatomic responses to various wet AMD treatment regimens of 1.5 mg of Fovista administered in combination with anti-VEGF drugs (Lucentis, Eylea or Avastin). This trial was terminated prior to full enrollment.

Fovista in Other Ophthalmic Diseases

We are supplying Fovista for a clinical trial conducted by the National Eye Institute for the treatment of Von Hippel-Lindau disease, or VHL. VHL is an inherited disease characterized by multiple benign and malignant tumors and cysts in the eye and other organs. Deficiency of the protein "pVHL" in multiple cell types is thought to cause VHL. In the eye, tumors consisting of blood cells called retinal capillary hemangiomas, or RCH, are the most common and earliest manifestation of VHL. These tumors cause significant retinal leakage and may lead to significant vision loss. Smaller lesions, located a significant distance from the central regions of the retina can be treated by laser or freezing via cryotherapy. However, larger and poorly situated lesions are usually untreatable or have poor visual prognoses. PDGF levels have been shown to be elevated in cells with deficiency of pVHL. Therefore, we believe that a combination of Fovista with an anti-VEGF drug may prove beneficial in RCH patients. VHL is rare, and we estimate that there are approximately 5,000 people with the disease in the United States. Recruitment is ongoing in this study.

Dry AMD

Dry AMD is a significant cause of moderate and severe loss of central vision, affecting vision in both eyes in most patients. Although dry AMD is the most common form of AMD, there are no therapies approved by the FDA or EMA to treat this condition. According to a 2011 publication from AMD Alliance International, approximately 30 million people worldwide have some form of AMD, with dry AMD accounting for 85% to 90% of these cases. A study published in *Ophthalmology* in 2012 analyzing age and gender variations in AMD prevalence estimates that approximately 8 million people worldwide are affected by a form of dry AMD known as GA.

Dry AMD is typically associated with yellow-white dots or deposits under the retina, known as drusen. Unlike in wet AMD, there is an absence of pathological neovascularization in dry AMD. The presence of drusen, in the absence of pathological neovascularization, is critical for making the diagnosis of dry AMD in patients over 50 years of age. GA, a form of dry AMD, can result in progressive and chronic degeneration of the retina characterized by variable thinning and dysfunction of retinal tissue.

The progression of visual outcomes for patients with dry AMD is variable. Most patients experience mild to moderate loss of visual function, manifesting in blurring of central vision in the affected eye, as a result of progressive degeneration of the light-sensitive photoreceptor elements in the macula. There are two settings in which visual loss from dry AMD may lead to severe vision loss:

- *Geographic Atrophy.* With severe and progressive macular degeneration, a readily identifiable pattern of severe degeneration called GA, forms, which consequently leads to profound and irreversible vision loss. GA is readily diagnosed by macular visualization using standard diagnostic instruments utilized by ophthalmologists. GA appears as abrupt and deep levels of macular tissue loss. It has sharp margins of characteristic degeneration compared to surrounding macular tissue, resulting in progressive and chronic degeneration of the retina characterized by variable thinning and dysfunction of retinal tissue.
- *Conversion to Wet AMD.* Dry AMD progresses to the wet form of the disease in approximately 10% - 15% of patients, leading to more rapid and further visual loss.

The Complement Cascade

The complement cascade consists of a series of proteins involved in the defense of a host body against infectious agents, or pathogens, and other foreign proteins. The complement cascade modulates a variety of immune and inflammatory responses to these pathogens and foreign proteins. Under normal circumstances, complement proteins, together with antibodies and white blood cells, act beneficially to protect the host body by removing the pathogens and foreign proteins, together with other cellular debris. The complement system is generally tightly regulated, achieving the proper balance of activation and inhibition depending on the host body's requirements. Poorly regulated or aberrant activation of the complement cascade, without a balanced or proportional inhibition of complement proteins, may result in the formation of inflammation-inducing proteins and molecules. These inflammation-inducing byproducts of the complement cascade have the potential to inflict damage to normal tissue known as immune or complement mediated damage.

Though the complement cascade can be activated through different pathways, these pathways eventually converge with the generation of an enzyme known as C3 convertase. C3 convertase cleaves, or separates, to form a protein called C3, which itself cleaves to from a molecule known as C3b. C3b is an important element of the body's immune response, as it binds to pathogens and makes them susceptible to destruction by white blood cells. Subsequent downstream reactions continue after the formation of C3b, with the eventual cleavage of another complement pathway protein known as C5. The cleavage of C5 results in the formation of other molecules known as terminal fragments, which are part of the terminal events of the complement pathway. One terminal fragment, known as C5a, is a potent mediator of inflammation and induces the release of VEGF from affected cells. The other terminal event is the generation of the membrane-attack complex, or MAC. The cellular response to the formation of MAC on affected cells can result in cell damage, cell death and the release of various angiogenic mediators, such as PDGF.

Complement-Mediated Pathology of AMD

Multiple published studies have implicated local inflammation resulting from poorly regulated or aberrant activation of the complement cascade in the development of both the dry and wet forms of AMD. For example, in third-party preclinical studies, analysis of both human and primate retinal drusen deposits, which are the hallmark of dry AMD, have been found to contain components of complement proteins. In addition, young patients, between the ages of 25 and 35, diagnosed with a kidney disease known as membranoproliferative glomerulonephritis have been observed to have developed retinal drusen deposits. The retinal drusen deposits are structurally and compositionally similar to those found in dry AMD patients.

Complement activation is associated with membranoproliferative glomerulonephritis and may explain drusen formation in these patients, which would be otherwise unexpected in healthy subjects of a similar young age.

Inflammation is mediated by the presence of white blood cells. In third-party preclinical studies, choroidal neovascularization in animal subjects has been inhibited by the depletion of a specific white blood cell type known as monocytes. Similar effects on choroidal neovascularization have also been observed through the inhibition of other factors involved in inflammation. Furthermore, in the same preclinical retinal model, pharmacologic and genetic inhibition of C5a and MAC have inhibited neovascularization, suggesting that the inflammation responsible for choroidal neovascularization is complement mediated. In 2005, multiple studies published in the journal *Science* linked variations in the genetic sequence coding for specific complement regulatory proteins with a higher risk of developing both the dry and wet forms of AMD.

We believe one or more unidentified triggering events may lead to aberrant activation of the complement system in the macular region of AMD patients. Complement mediated inflammation, and in particular the excessive activation of C5, in the macular tissue may result in the accumulation of drusen, damage to retina cells and the release of angiogenic mediators, potentially resulting in the development of the dry and wet forms of AMD. Furthermore, data from multiple recently-published studies of complement mediated inflammation in human subjects who have developed wet AMD continues to support this strategy.

Zimura

We are developing our product candidate Zimura for the treatment of dry AMD and wet AMD. Zimura is designed to target and inhibit the complement protein C5. We believe Zimura binds to and inhibits C5 from cleaving into later stage proteins, or terminal fragments. By inhibiting the formation of complement system terminal fragments, Zimura may decrease complement mediated inflammation and the release of angiogenic mediators such as VEGF and/or PDGF, thereby providing the rationale as a potential therapy for patients with dry AMD and wet AMD. Zimura is a chemically synthesized, pegylated aptamer. Zimura is administered by intravitreal injection.

Clinical Development of Zimura

We have completed a Phase 1/2a clinical trial of Zimura monotherapy for the treatment of GA, a Phase 1/2a clinical trial of Zimura administered in combination with Lucentis for the treatment of wet AMD and a very small Phase 2 clinical trial investigating Zimura's potential role when administered in combination with anti-VEGF drugs for the treatment of polypoidal choroidal vasculopathy, or PCV, which is a specific type of wet AMD, in patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF monotherapy fails. During the fourth quarter of 2015, we initiated a Phase 2/3 clinical trial designed to evaluate the safety and efficacy of Zimura administered for the treatment of GA and an open-label Phase 2a clinical trial to evaluate Zimura’s potential role when administered in combination with anti-VEGF drugs for the treatment of wet AMD. We believe that, in wet AMD patients, Zimura may assist in inhibiting complement mediated inflammation which may improve visual outcomes, particularly when Zimura is administered in combination with an anti-VEGF drug. We plan to reassess our Zimura development program throughout 2017 as our updated business plan progresses and evolves. Our reassessment for Zimura may be particularly affected by the results of a competitor’s Phase 3 clinical trial of a complement inhibitor being studied for the treatment of GA, which are expected during the second half of 2017. As a result of this reassessment, we may modify, expand or terminate any of our Zimura development programs or clinical trials at any time.

Completed Phase 1/2a Clinical Trial of Zimura for Dry AMD

In 2011, we completed a multicenter, uncontrolled, open label Phase 1/2a clinical trial evaluating the safety and tolerability of Zimura administered as a monotherapy in patients with GA. We enrolled 47 patients in this trial. We randomly assigned patients in this trial to one of two dose groups. Patients received a total of five intravitreal injections of either 0.3 mg or 1.0 mg of Zimura over a 36-week treatment period. Patients received an intravitreal injection of Zimura at day 0, week 4, week 8, week 24 and week 36 of the trial, with a final follow-up visit at week 48. Zimura was generally well-tolerated in this trial. We did not observe any evidence of drug related adverse events. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure.

In addition, we performed assessments of visual acuity to detect any potential decrease in vision associated with intravitreal injections, the administered drug or natural progression of the disease if left untreated. We did not identify any drug related safety issues through measurements of visual acuity.

Our Phase 1/2a clinical trial was an uncontrolled study with a small sample size and was not powered to detect a difference between Zimura dose groups, or the efficacy of Zimura monotherapy, with statistical significance. The primary purpose of the study was to assess safety and tolerability. However, we observed a trend, in favor of the higher of two dose groups, of a relative reduction in the mean growth of the GA lesion area, as measured by an independent reading center, at 24 weeks. The mean growth from baseline in the GA lesion area during the first 24 weeks of the trial, when the injections were administered more regularly, was 1.00 mm^2 for the 24 patients receiving the 0.3 mg dose and 0.78 mm^2 for the 23 patients receiving the 1.0 mg dose. When the injections were administered on a reduced dosing schedule during the subsequent 24 weeks, this relative trend in reduced growth in GA lesion area was no longer present. We believe this apparent trend in reduction of growth in GA lesion area when Zimura was dosed more frequently, together with the relative loss of the benefit when Zimura was dosed less frequently, may suggest a possible drug effect. In addition, data from a third party targeting the complement pathway also exhibited a trend in reduction of GA growth with a pronounced effect in patients with a specific biomarker. Given the safety profile of Zimura to date when administered by intravitreal injection, what we believe is a strong preclinical rationale, the trend in the potential benefit that we observed in our Phase 1/2a clinical trial and results observed in studies from the third party targeting the complement pathway, we determined to move forward with a Phase 2/3 clinical trial evaluating Zimura in the treatment of dry AMD.

Phase 2/3 Clinical Trial of Zimura in Dry AMD

During the fourth quarter of 2015, we initiated a randomized, double-masked, controlled Phase 2/3 clinical trial to evaluate the safety and efficacy of Zimura monotherapy in patients with GA. Our initial plan was to enroll up to approximately 300 patients in the initial stage of the trial. During this stage, patients will be randomized into three groups, and will receive monthly injections of 1.0 mg of Zimura per eye, monthly injections of 2.0 mg of Zimura per eye or monthly sham injections as the control arm. At month 18, we plan to conduct an interim analysis to assess the safety and efficacy of Zimura compared to sham. Upon review of this interim analysis, a determination will be made whether to continue the trial and whether to expand the trial by enrolling additional patients. Patients in the trial will receive monthly injections for 24 months. Recruitment of patients in this trial is at a very early phase and is ongoing.

Completed Phase 1/2a Clinical Trial of Zimura for Wet AMD

In 2009, we completed a multicenter, uncontrolled, ascending dose and parallel group open label Phase 1/2a clinical trial evaluating the safety and tolerability of Zimura administered in combination with Lucentis for the treatment of wet AMD. We enrolled 60 patients in this trial. Zimura was generally well tolerated in this trial when tested in combination with Lucentis. None of the patients experienced any dose limiting toxicities at any of the dose levels tested. We observed only a single adverse event assessed by the investigators to be related to Zimura, mild subcapsular cataract in one patient in the group treated with 2.0 mg of Zimura. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure. One patient withdrew from the trial as a result of a serious adverse event of bacteremia unrelated to study drug or injection procedure, which resulted in a subsequent fatality. Systemic adverse events in this trial were not frequently reported. No systemic adverse events were assessed as drug related.

Our Phase 1/2a clinical trial was an uncontrolled study with a small sample size and was not powered to detect a difference between Zimura and Lucentis combination therapy and Lucentis monotherapy with any statistical significance. The primary purpose of the study was to assess safety and tolerability. However, in addition to our safety assessment, we performed assessments of visual acuity primarily as safety assessments to detect any decrease in vision associated with the intravitreal drug combination or the injection procedure. We did not identify any safety issues through measurements of visual acuity. In a subgroup of 43 patients who had not previously been treated with anti-VEGF drugs and who received six injections at doses of 0.3 mg, 1.0 mg or 2.0 mg of Zimura administered in combination with Lucentis, we observed a mean increase in visual acuity from baseline at all time points based on the number of ETDRS letters the patient can read. In a follow-up visit at week 24 of the trial, we noted improvements in mean visual acuity from baseline as follows: 13.6 letters for the 13 patients receiving the 0.3 mg dose, 11.7 letters for the 15 patients receiving the 1.0 mg dose and 15.3 letters for the 15 patients receiving the 2.0 mg dose. In this subgroup, 22 patients (51%) gained at least 15 letters, consisting of six patients (46%) in the 0.3 mg dose group, seven patients (47%) in the 1.0 mg dose group and nine patients (60%) in the 2.0 mg dose group.

Phase 2 Clinical Programs for Zimura for Wet AMD

In late 2014, we initiated a very small, uncontrolled, open-label, Phase 2a clinical trial to evaluate Zimura’s potential role when administered in combination with anti-VEGF drugs for the treatment of PCV, a specific type of wet AMD, in patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF monotherapy has failed, who we refer to as anti-VEGF resistant. Our analysis of the data from this trial has not revealed any safety concerns related to Zimura.

During the fourth quarter of 2015, we initiated an uncontrolled, open-label Phase 2a clinical trial to evaluate Zimura's potential role when administered in combination with anti-VEGF therapy for the treatment of wet AMD in patients who do not respond adequately to treatment with anti-VEGF monotherapy. We plan to enroll up to approximately 60 patients in this trial, and may include patients with PCV. Recruitment of patients in this trial is at a very early phase and is ongoing. This trial is an uncontrolled study with a small sample size and is not powered to detect a difference between Zimura and Lucentis combination therapy and Lucentis monotherapy with any statistical significance.

Option Agreement for Tivozanib

In November 2014, we entered into an exclusive research and option agreement with AVEO Pharmaceuticals to license tivozanib, a small molecule VEGF tyrosine kinase inhibitor, for the treatment of non-oncologic conditions of the eye. Under the terms of the agreement, we paid AVEO an upfront fee of $0.5 million for exclusive rights to investigate tivozanib's potency and potential as an ocular formulation. We terminated the option and research agreement in January 2017, prior to exercising our option.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. Although we rely and intend to continue to rely upon third-party contract manufacturers to produce our products and product candidates, we have recruited personnel with experience to manage the third-party contract manufacturers we engage to produce our product candidates. We do not have any long-term supply arrangements other than as described below.

Our current product candidates, Fovista and Zimura, are each chemically-synthesized aptamers. In pursuing our updated business plan, we could acquire or in-license a variety of types of product candidates, including small molecule drugs, protein drugs or biologics. Small molecule drugs are organic compounds of low molecular weight that are generally associated with ready availability of starting materials and ease of synthesis. In contrast, manufacturing for proteins and biologics is more complex, especially in large quantities. For example, biologic products must be made consistently and in substantial compliance with a clearly defined manufacturing process, and often must be manufactured under aseptic conditions.

The process for manufacturing Fovista and Zimura consists of chemical synthesis, purification, pegylation, further purification and finally freeze drying to form a powder, which is the active pharmaceutical ingredient, or API. Each of these steps involves a relatively common chemical engineering process. The chemical synthesis is similar to peptide manufacturing. In a separate process that follows the chemical synthesis, API for each of Fovista and Zimura is dissolved in a liquid solution that includes certain chemical buffers and then is placed into vials from which the intravitreal injection solution is drawn. This process of rendering the API into a liquid solution and placing it into vials is referred to as fill/finish services.

We currently rely upon a single third-party manufacturer, Agilent Technologies, Inc., or Agilent, to supply us with the chemically synthesized aptamers comprising the API for both Fovista and Zimura and a different, single third-party manufacturer, Ajinomoto Althea, Inc., or Althea, to provide fill/finish services for both Fovista and Zimura. We have entered into clinical and commercial supply agreements with Agilent with respect to Fovista. We have also entered into a clinical and commercial services agreement with Althea with respect to Fovista and Zimura. These agreements are described below. We currently obtain Zimura API from Agilent on a purchase order basis.

Fovista API Clinical Supply Agreement. In May 2014, we entered into a Clinical Manufacturing and Supply Agreement with Agilent pursuant to which Agilent has agreed to manufacture and supply to us, and we have agreed to purchase from Agilent, a specified percentage of our clinical requirements in specified jurisdictions of Fovista API. The clinical supply agreement has an initial five-year term, which is subject to automatic renewal absent termination by either party in accordance with the terms of the clinical supply agreement. We may terminate the clinical supply agreement or any statement of work thereunder upon 12 months' prior written notice to Agilent and Agilent may terminate the clinical supply agreement if we do not, over a specified period, purchase and take delivery from Agilent of a specified minimum quantity of API for Fovista. Each party also has the right to terminate the clinical supply agreement for other customary reasons such as material breach and bankruptcy. The clinical supply agreement contains provisions relating to compliance by Agilent with current Good Manufacturing Practices, cooperation by Agilent in connection with marketing applications for Fovista, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

Fovista API Commercial Supply Agreement. In September 2015, we entered into a Commercial Manufacturing and Supply Agreement with Agilent, pursuant to which Agilent has agreed to manufacture and supply to us, and we have agreed to purchase from Agilent, a specified percentage of our commercial requirements in all jurisdictions of Fovista API. The

commercial supply agreement has an initial term that runs for seven years from the date of our first commercial sale of Fovista, and which is subject to one two-year automatic renewal period, absent termination by either party in accordance with the terms of the commercial supply agreement. The commercial supply agreement provides for pricing for Fovista API structured on a tiered basis, with the price reduced as the volume of Fovista API ordered increases. We may cancel any purchase order under the commercial supply agreement at any time, subject to the payment of specified cancellation fees. We may terminate the commercial supply agreement with no financial penalty in the event that we cannot commercialize Fovista due to regulatory or other medical, scientific or legal reasons. Agilent may terminate the commercial supply agreement in the event that we do not, over a specified period, purchase and take delivery from Agilent of a specified minimum quantity of Fovista API. Each party also has the right to terminate the commercial supply agreement for other customary reasons such as material breach and bankruptcy. The commercial supply agreement contains provisions relating to compliance by Agilent with current Good Manufacturing Practices, cooperation by Agilent in connection with marketing applications for Fovista, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

In December 2016, following receipt of initial, top-line data from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we canceled all of our outstanding purchase orders with Agilent for the manufacture of Fovista API for commercial drug product. We have incurred substantial cancellation fees in connection with such canceled purchase orders, payment of which will be made in 2017 as we unwind our Fovista manufacturing commitments.

Althea Clinical and Commercial Services Agreement. In October , 2016, we and Ajinimoto Althea, Inc., or Althea, entered into a Clinical and Commercial Services Agreement, which we refer to as the Fill/Finish Services Agreement.

Pursuant to the Fill/Finish Services Agreement, Althea has agreed to provide clinical and commercial fill/finish services for Fovista and Zimura, as well as any future product candidates that we and Althea may mutually agree. The Fill/Finish Services Agreement has an initial term that will expire at the end of 2027, absent termination by either party in accordance with the terms of the Fill/Finish Services Agreement. The initial term of the Fill/Finish Services Agreement may be extended by mutual agreement of the parties. The amount payable by us to Althea under the Fill/Finish Services Agreement is based on the volume of finished drug product that we order, subject to periodic adjustments over the term of the Fill/Finish Services Agreement. In addition, in the event that we order a specified volume of product, Althea has agreed to supply biological or pharmaceutical drug products meeting certain parameters exclusively to us.

We may cancel any purchase order under the Fill/Finish Services Agreement at any time, subject to the payment of specified cancellation fees. We may terminate the Fill/Finish Services Agreement, without cause, as of any date following the third anniversary of the effective date upon six months' prior notice to Althea. Each party also has the right to terminate the Services Agreement for other customary reasons such as material breach and bankruptcy.

The Fill/Finish Services Agreement contains provisions relating to compliance by Althea with current Good Manufacturing Practices, cooperation by Althea in connection with marketing applications for our product candidates, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

In December 2016, following receipt of initial, top-line data from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we canceled all of our outstanding purchase orders with Althea for the fill and finish of Fovista commercial drug product. We incurred approximately $0.6 million in connection with such cancellations in relation to non-returnable materials procured by Althea in anticipation of fulfilling such purchase orders, payment of which will be made in 2017 as we unwind our Fovista manufacturing commitments.

Other Manufacturing Arrangements. Under a license, manufacturing and supply agreement with Nektar Therapeutics, or Nektar, described in more detail below under "-Acquisition, License and Collaboration Agreements-Nektar Therapeutics Manufacturing and Supply Agreement," we must purchase our entire clinical and commercial requirements for the polyethylene glycol, or PEG, reagent, which we use to make Fovista, exclusively from Nektar at an agreed price, which is subject to annual adjustment in accordance with changes in the producer price index, except under specified circumstances relating to Nektar's failure to supply, in which event Nektar has agreed to enable a third-party manufacturer to supply us. Under this agreement, Nektar has agreed to supply our entire clinical and commercial requirements for this PEG reagent, subject to certain forecasting and ordering requirements and other limitations, and has agreed to supply this PEG reagent only to us for the purpose of manufacturing a product produced by linking the active ingredient in Fovista to this PEG reagent by means of pegylation. The PEG reagent supplied by Nektar is proprietary to Nektar. We obtain a different PEG reagent used to make Zimura from a different third-party manufacturer on a purchase order basis.

In December 2016, following receipt of initial, top-line data from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we agreed with Nektar to purchase shipments of PEG reagent scheduled for delivery during the

first quarter of 2017 that Nektar had already commenced manufacturing. Nektar also agreed to cancel our remaining future commitments for the purchase of PEG reagent subject to our payment of a $2.2 million cancellation fee. We expect to make this payment in 2017 as we unwind our Fovista manufacturing commitments.

Sales and Marketing

We expect that our commercial strategy for any of our product candidates, including whether to retain commercial rights and market and sell the product candidate ourselves or to utilize collaboration, distribution or other marketing arrangements with third parties, will be determined based on a variety of factors, including the size and nature of the patient population, the disease area, the particular indication, the territory in which the product candidate may be marketed and the commercial potential for such product candidate. In addition, our commercial strategy will vary depending on whether the disease is typically treated by general ophthalmology practitioners, specialists, such as retinal specialists, or sub-specialists. For example, in the United States, retinal specialists perform most of the medical procedures involving diseases of the back of the eye. We believe that retinal specialists are sufficiently concentrated that we could effectively promote a product candidate approved for such an indication to these specialists with a targeted specialty sales and marketing group.

We have entered into a commercialization agreement with Novartis for Fovista pursuant to which we have granted to Novartis commercialization rights for Fovista outside of the United States in return for an upfront fee, milestones and royalties. See “Acquisition, License and Collaboration Agreements-Licensing and Commercialization Agreement with Novartis Pharma AG.” If successful in the development of Zimura, we would expect to utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Zimura in markets outside the United States.

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 or biosimilar drug companies. Many of our competitors have significantly greater financial and human resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. 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 enrollment for clinical trials, as well as in acquiring products, product candidates or other technologies that we may target to in-license or acquire in pursuit of our updated business plan.

Growth of our business through our updated business plan will be based on our selectively licensing or acquiring and then developing product candidates. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that address or seek to address unmet medical needs and creates value in ophthalmology. However, the acquisition and licensing of pharmaceutical products is a competitive area, and a number of more established companies, which have acknowledged strategies to license and acquire products, may have competitive advantages, as may emerging companies taking similar or different approaches to product acquisition. Established companies pursuing this strategy may have a competitive advantage over us due to their size, cash flows and institutional experience.

The key competitive factors affecting the success of our product candidates, if approved, are likely to be the respective drug’s efficacy, safety, method of administration, convenience, price, the level of generic competition and the availability of coverage and reimbursement from government and other third-party payors. The method of administration of Fovista and Zimura, intravitreal injection, is commonly used to administer ophthalmic drugs for the treatment of severe disease and is generally accepted by patients facing the prospect of severe visual loss or blindness. However, a therapy that offers a less invasive method of administration might have a competitive advantage over one administered by intravitreal injection, depending on the relative safety of the other method of administration.

The current standard of care for wet AMD is monotherapy administration of anti-VEGF drugs, principally Avastin, Lucentis and Eylea, which are well-established therapies and are widely accepted by physicians, patients and third-party payors. Physicians, patients and third-party payors may not accept the addition of Fovista or Zimura to their current treatment

regimens for a variety of potential reasons, including the incremental cost of our product, the burden to a patient or injecting physician of an additional intravitreal injection or the relative benefit offered by combination therapy with our product as compared to monotherapy treatment. A standalone therapy for wet AMD with demonstrated improved efficacy over currently marketed therapies in this indication and a favorable safety profile that does not involve VEGF or that does not require frequent or multiple intravitreal injections might pose a significant competitive threat to Fovista or Zimura.

Our commercial opportunity could be reduced or eliminated if one or more of our competitors develop and commercialize products that are more effective, safer, have fewer or less severe side effects, are more convenient to use or are less expensive than our product candidates. 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 relevant market.

There are a number of products in preclinical research and clinical development by third parties to treat wet AMD. Based on publicly available information, we are aware that Regeneron Pharmaceuticals, Ohr Pharmaceutical, Santen, Tyrogenex, Allergan, GrayBug and Somologic each have PDGF inhibitors in clinical or pre-clinical development for wet AMD. Several of these product candidates also inhibit VEGF or are administered directly with an anti-VEGF agent in a manner that could negatively impact demand for a separate intravitreal injection of an anti-PDGF agent such as Fovista. The most advanced of these product candidates is Regeneron’s, for which negative Phase 2 data was previously announced in December 2016 and additional data may be announced during 2017. Moreover, based on publicly available information, we are aware that several companies and research organizations are pursuing treatments targeting other molecular targets, potential gene therapy treatments and stem cell transplant treatments for the treatment of wet AMD. In addition, other companies are undertaking efforts to develop technologies to allow for a less frequent dosing schedule than the dosing schedule currently in use for standard of care anti-VEGF drugs.

There are a number of products in preclinical research and clinical development by third parties to treat dry AMD. In general, these product candidates can be categorized based on their proposed mechanisms of action. The mechanisms of action for these product candidates include inflammation suppression, such as complement system inhibitors and corticosteroids, visual cycle modulators, antioxidants and neuroprotectants, cell and gene therapies and vascular enhancers. Based on publicly available information, we are aware that Genentech, Novartis / MorphoSys, Apellis, Hemera Biosciences, Achillion, Ra Pharmaceuticals and Catalyst Biosciences each have complement inhibitors in development, the most advance of which is Genentech’s humanized Fab fragment targeting complement factor D, for which data from Phase 3 trials is expected during 2017. If Genentech's Phase 3 trials for its complement factor D product candidate are successful, it is likely that Genentech would obtain marketing approval for such product candidate several years in advance of when we could reasonably expect marketing approval for Zimura in GA, if at all. Moreover, based on publicly available information, we are aware that several other companies have announced development programs for the treatment of dry AMD targeting different mechanisms of action outside of the complement cascade.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our 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 seek to protect our proprietary position, among other methods and where patent protection is available, by filing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business, and by maintaining our issued patents. We also rely upon trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

Our patent portfolio includes the following:

- patents and patent applications owned by Ophthotech:
    - patents covering the treatment of wet AMD with a combination of Fovista and an anti-VEGF-A antibody or binding fragment thereof (such as Avastin or Lucentis), or the use of Fovista in the manufacture of a medicine for the treatment of wet AMD when administered with an anti-VEGF-A antibody or binding fragment thereof, which have issued in the United States, the European Union, Japan and certain other jurisdictions, and which are expected to expire in 2024; and patent applications covering the treatment of wet AMD with a combination of Fovista and an anti-VEGF-A antibody or binding fragment thereof or the use of Fovista in the manufacture of a medicine for the treatment of wet

AMD when administered with an anti-VEGF-A antibody or binding fragment thereof, which are pending in certain other jurisdictions, and which, if granted, are expected to expire in 2024;

- patent applications covering the treatment of wet AMD with a combination of Fovista and Eylea, or the use of Fovista in the manufacture of a medicine for the treatment of wet AMD when administered with Eylea, which are pending in the United States, the European Union, Japan and certain other jurisdictions, and which, if granted, are expected to expire in 2030;

- patents covering co-formulations of Fovista and an anti-VEGF-A antibody or binding fragment thereof, which have issued in the United States, Japan and certain other jurisdictions, and which are expected to expire in the United States in 2025 and elsewhere in 2024; and patent applications covering co-formulations of Fovista and an anti-VEGF-A antibody or binding fragment thereof, which are pending in the European Union and certain other jurisdictions, and which, if granted, are expected to expire in 2024;

- patents covering methods for treating AMD with a combination of Fovista and Macugen, which have issued in the United States, the European Union, Japan and certain other jurisdictions, and which are expected to expire in 2024; and patent applications covering methods for treating AMD with a combination of Fovista and Macugen, which are pending in certain other jurisdictions, and which, if granted, are expected to expire in 2024;

- patent applications covering co-formulations and other proprietary technology relating to Fovista, which are pending in the United States, the European Union, Japan and certain other jurisdictions, and which, if granted, are expected to expire in 2033;

- patent applications covering formulations and dosing regimens and other proprietary technology relating to Fovista, which are pending in the United States, the European Union, Japan and certain other jurisdictions, and which, if granted, are expected to expire in 2034;

- patent applications covering co-formulations and other proprietary technology relating to Zimura, which are pending in the United States, the European Union, Japan and certain other jurisdictions, and which, if granted, are expected to expire in 2034; and

- patent applications covering dosing regimens and methods for treating AMD and other proprietary technology relating to Fovista, which are pending in the United States and under the Patent Cooperation Treaty system, and which, if granted, are expected to expire in 2035; and

- patents and patent applications in-licensed from Archemix Corp., or Archemix:

  - composition-of-matter patents covering Fovista, which have issued in the European Union, Japan and certain other jurisdictions, and which are expected to expire in 2018;

  - composition-of-matter patents covering Zimura, which have issued in the United States, the European Union, Japan and certain other jurisdictions, and which are expected to expire in Japan in 2026 and elsewhere in 2025; and composition-of-matter patent applications covering Zimura, which are pending in certain other jurisdictions, and which, if granted, are expected to expire in 2025; and

  - patents covering the treatment of certain complement mediated disorders with Zimura, Zimura for use in a method of treating certain complement mediated disorders or a composition comprising Zimura for treating certain complement mediated disorders, which have issued in the United States, the European Union, Japan and certain other jurisdictions, and which are expected to expire in Japan and the United States in 2026 and elsewhere in 2025.

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 U.S. 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, upon 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 and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Acquisition, License and Collaboration Agreements

We are a party to several agreements under which we have in-licensed, acquired or out-licensed rights in certain patents, patent applications and other intellectual property. We entered into these agreements to acquire the intellectual property required to develop, manufacture and commercialize our product candidates. We also enter into these agreements to out-license intellectual property to our collaboration and research partners to assist in the development and, if approved, commercialization of our product candidates. These licenses impose certain license fee, royalty payment and diligence obligations on us. We expect to continue to enter into these types of license agreements in the future, particularly as we pursue our updated business plan to acquire or in-license additional products, product candidates or other technologies and expand our product pipeline. Our material acquisition, license and collaboration agreements are described below.

OSI (Eyetech) Divestiture Agreement

In July 2007, we entered into a divestiture agreement with OSI (Eyetech), Inc., or Eyetech, which agreement is now held by OSI Pharmaceuticals, LLC, or OSI Pharmaceuticals, a subsidiary of Astellas US LLC, under which we acquired specified technology, rights, and other assets owned or controlled by Eyetech relating to particular anti-PDGF aptamers, including Fovista, and assumed Eyetech's liabilities and obligations under specified agreements between Eyetech and Archemix, and between Eyetech and Nektar. These agreements with Archemix and Nektar, as subsequently amended, are described in more detail below.

We have agreed that we will not, alone or with any other party, research, develop or commercialize any compound, other than anti-PDGF products covered by the divestiture agreement, which solely and specifically binds to PDGF for its mode of action.

Financial Terms

In connection with the agreement, we paid Eyetech a $4.0 million upfront payment and issued Eyetech 3,000,000 shares of our junior series A preferred stock. We are obligated to pay OSI Pharmaceuticals additional one-time payments of $12.0 million in the aggregate upon marketing approval in the United States and the European Union, of a covered anti-PDGF product. We are obligated to pay OSI Pharmaceuticals a royalty at a low single-digit percentage of net sales of any covered anti-PDGF product we successfully commercialize. Our obligation to pay such royalties will expire on a product-by-product and country-by-country basis on the later of 10 years after the first commercial sale of each product in each country or the expiration of the last-to-expire valid claim of specified patents that cover the composition, manufacture or use of each product in each country.

Diligence Obligations

We are required to use commercially reasonable efforts to conduct the development and manufacture of a covered anti-PDGF product so as to obtain marketing approval and, thereafter, to commercialize a covered anti-PDGF product in the United States and in the European Union.

Term and Termination

The agreement, unless terminated earlier by us or by OSI Pharmaceuticals, will remain in effect until we no longer have any financial obligations to OSI Pharmaceuticals, after which the rights granted to us will become perpetual and fully paid-up. 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.

If we fail to use commercially reasonable efforts to meet our specified diligence obligations and fail to take specified steps after receiving written notice thereof from OSI Pharmaceuticals, then OSI Pharmaceuticals may terminate the agreement as to such countries with respect to which such failure has occurred, and upon such termination we will be obligated to grant, assign and transfer to OSI Pharmaceuticals specified rights and licenses related to our anti-PDGF aptamer technology and other related assets, and if we are manufacturing such anti-PDGF products at the time of such termination, may be obligated to provide transitional supply to OSI Pharmaceuticals of covered anti-PDGF products, for such countries.

Archemix License Agreements

In September 2011, we entered into two amended and restated exclusive license agreements with Archemix, one relating to anti-PDGF aptamers, which we refer to as the PDGF agreement, and the other relating to anti-C5 aptamers, which we refer to as the C5 agreement. The PDGF agreement superseded a 2004 agreement between Eyetech and Archemix that we assumed under the divestiture agreement described above. The C5 agreement superseded a July 2007 agreement between us and Archemix. Under these amended and restated agreements, we hold exclusive worldwide licenses (subject to certain pre-existing rights) under specified patents and technology owned or controlled by Archemix to develop, make, use, sell, offer for sale, distribute for sale, import and export pharmaceutical products comprised of or derived from any anti-PDGF aptamer or anti-C5 aptamer for the prevention, treatment, cure or control of human indications, diseases, disorders or conditions of the eye, adnexa of the eye, orbit and optic nerve, other than certain expressly excluded applications.

The licenses we received under these agreements include sublicenses to us of rights to specified technology, which we refer to as the SELEX technology, licensed by University License Equity Holdings, Inc., or ULEHI, to Gilead Sciences, Inc., or Gilead, and sublicensed by Gilead to Archemix, as well as sublicenses to us of rights to certain other technology licensed by Gilead to Archemix, including the composition-of-matter patents relating to Fovista. Our agreements with Archemix contemplate that our rights to these sublicensed technologies will survive termination of the license from ULEHI to Gilead as long as we are not in breach of the C5 agreement or PDGF agreement, as applicable, and will survive termination of the sublicense from Gilead to Archemix as long as such termination did not arise from our action or inaction, provided in each case that we agree to be bound to ULEHI or Gilead, as applicable, under the terms of our agreements with Archemix. However, if Archemix, its affiliates and all of Archemix's assignees and sublicensees, including us, cease to exercise reasonable efforts to develop commercial applications of products and services using the SELEX technology, then Archemix's rights to the SELEX technology may revert to Gilead or ULEHI, and we would lose our rights to the SELEX technology.

Financial Terms

In connection with these agreements, as amended, we paid Archemix aggregate upfront licensing fees of $1.0 million and issued to Archemix an aggregate of 2,000,000 shares of our series A-1 preferred stock and 500,000 shares of our series B-1 preferred stock. We have also paid Archemix an aggregate of $6.75 million in fees based on our achievement of specified clinical milestone events under these agreements.

Under the PDGF agreement, we are also obligated to make additional future payments to Archemix of up to an aggregate of $14.0 million if we achieve specified clinical and regulatory milestones with respect to Fovista, and up to an aggregate of $3.0 million if we achieve specified commercial milestones with respect to Fovista. Under the PDGF agreement, we also are obligated to make additional payments to Archemix of up to an aggregate of approximately $18.8 million if we achieve specified clinical and regulatory milestones with respect to each other anti-PDGF aptamer product that we may develop under the agreement, and up to an aggregate of $3.0 million if we achieve specified commercial milestones with respect to such other anti-PDGF aptamer product.

Under the C5 agreement, for each anti-C5 aptamer product that we may develop under the agreement, including Zimura, we are obligated to make additional payments to Archemix of up to an aggregate of $57.5 million if we achieve specified development, clinical and regulatory milestones, with $24.5 million of such payments relating to second and third indications, and, as to all anti-C5 products under the agreement collectively, up to an aggregate of $22.5 million if we achieve

specified commercial milestones. We are also obligated to pay Archemix a double-digit percentage of specified non-royalty payments we may receive from any sublicensee of our rights under the C5 agreement.

No royalties are payable to Archemix under either of the PDGF agreement or the C5 agreement.

Diligence Obligations

We are required to exercise commercially reasonable efforts in developing and commercializing at least one anti-PDGF aptamer product and at least one anti-C5 aptamer product and in undertaking investigations and actions required to obtain regulatory approvals necessary to market such products in the United States, the European Union, and Japan, and in such other markets where we determine that it is commercially reasonable to do so.

Term and Termination

Unless earlier terminated, the PDGF agreement will expire upon the later of 10 years after the first commercial sale in any country of the last licensed product and the expiration of the last-to-expire valid claim of the licensed patents that covers a licensed product.

Unless earlier terminated, the C5 agreement will expire upon the later of 12 years after the first commercial sale in any country of the last licensed product, the expiration of the last-to-expire valid claim of the licensed patents that covers a licensed product, and the date on which no further payments of sublicensing income are to be received by us.

Either we or Archemix may terminate each of the agreements if the other party materially breaches the applicable agreement and the breach remains uncured for a specified period. Archemix may also terminate each of the agreements, or may convert our exclusive licenses under the applicable agreement to non-exclusive licenses, if we challenge or assist a third party in challenging the validity or enforceability of any of the patents licensed under the applicable agreement. We may terminate each of the agreements at any time and for any or no reason effective at the end of a specified period following our written notice to Archemix of termination.

Nektar Therapeutics Manufacturing and Supply Agreement

In April 2012, February 2015 and April 2015, we amended a 2006 license, manufacturing and supply agreement between Eyetech and Nektar that we assumed under the Eyetech divestiture agreement described above. Under the agreement, as amended, Nektar has granted us the following licenses:

- an exclusive, worldwide license under specified patent rights and know-how owned or controlled by Nektar to make, have made, develop, use, import, offer for sale and sell particular products that are produced by linking the API in Fovista to a specified polyethylene glycol, or PEG, reagent by means of pegylation; and

- non-exclusive sublicenses of certain other patent rights controlled by Nektar.

Financial Terms

We have paid approximately $21.5 million and Eyetech previously paid approximately $0.3 million, to Nektar under the agreement. We are also obligated to pay Nektar additional specified amounts in relation to certain milestone events. Such specified milestone amounts that may be payable by us in the future include an aggregate of $6.5 million payable upon the achievement of specified clinical and regulatory milestones. In addition, a payment of $3.0 million will be triggered upon the achievement of a specified commercial sale milestone with respect to Fovista.

If we grant to any third-party commercialization rights to a licensed product under the agreement, we agreed to pay Nektar a low double-digit percentage of any upfront payment we receive from such third party, less certain milestone amounts we have paid to Nektar. In June 2014, we paid Nektar $19.8 million in connection with our entry into the Novartis Agreement.

We are also obligated to pay Nektar tiered royalties at low to mid single-digit percentages of net sales of any licensed product we successfully commercialize, with the royalty percentage determined by our level of licensed product sales, the extent of patent coverage for the licensed product and whether we have granted a third party commercialization rights to the licensed product. Our obligation to pay such royalties will expire on a licensed product-by-licensed product and country-by-country basis on the later of 10 years after first commercial sales of such licensed product in such country, and the expiration of the last-to-expire valid claim in the licensed patents that cover such licensed product in such country.

Exclusive Supply

Under the agreement, we must provide binding forecasts of requirements for the PEG reagent to Nektar and purchase our entire requirements for the PEG reagent, which we currently use to formulate Fovista, exclusively from Nektar at agreed prices based upon volume, which are subject to annual adjustment in accordance with changes in the producer price index, except under specified circumstances relating to Nektar's failure to supply, in which event Nektar has agreed to enable a third-party manufacturer to supply us.

Under the agreement, Nektar has agreed to supply our entire clinical and commercial requirements for this PEG reagent, subject to certain forecasting and ordering requirements and certain other limitations, and has agreed to supply this PEG reagent only to us for the purpose of manufacturing a product produced by linking the API in Fovista to this PEG reagent by means of pegylation.

Diligence Obligations

Under the terms of the agreement, if we fail to use commercially reasonable efforts to achieve the first commercial sale of Fovista in the United States or one of a specified group of other countries by June 30, 2018, which date Nektar and we may agree in good faith to extend in specified circumstances, Nektar may either terminate our license or convert our license for such country to a non-exclusive license. In addition, if we fail to use commercially reasonable efforts to develop Fovista and file and seek approval of NDAs on a schedule permitting us to make first commercial sales of Fovista in specified countries by June 30, 2019, do not make such first commercial sales of Fovista by such date, or thereafter fail to use commercially reasonable efforts to continue to commercialize and market Fovista in such countries, we will be in material breach of the agreement.

Term and Termination

The agreement, unless earlier terminated by us or Nektar, will expire upon the expiration of our obligation to pay royalties to Nektar on net sales of licensed products. We and Nektar each may terminate the agreement if the other party materially breaches the agreement and does not cure such breach within a specified cure period. We may terminate the agreement at any time, without cause, effective at the end of a specified period following our written notice to Nektar of termination, in which event we will be obligated to pay Nektar specified termination fees and reimburse Nektar for certain costs.

If we challenge the validity or enforceability of any Nektar licensed patent right, we must pay for the defense of such challenge if such challenge is not successful and our licenses under certain licensed patent rights will terminate.

Licensing and Commercialization Agreement with Novartis Pharma AG

In May 2014, we entered into a licensing and commercialization agreement with Novartis Pharma AG, which we refer to as the Novartis Agreement. Under the Novartis Agreement, we granted Novartis exclusive rights under specified patent rights, know-how and trademarks controlled by us to manufacture, from bulk API supplied by us, standalone Fovista products and products combining Fovista with an anti-VEGF drug to which Novartis has rights in a co-formulated product, for the treatment, prevention, cure or control of any human disease, disorder or condition of the eye, and to develop and commercialize those licensed products in all countries outside of the United States, which we refer to as the Novartis Territory. We agreed to use commercially reasonable efforts to complete our Phase 3 clinical program for Fovista and Novartis agreed to use commercially reasonable efforts to develop a standalone Fovista product and a co-formulated product containing Fovista and an anti-VEGF drug to which Novartis has rights, as well as a pre-filled syringe presentation of such products and to use commercially reasonable efforts, subject to obtaining marketing approval, to commercialize licensed products in the Novartis Territory in accordance with agreed development and marketing plans. Novartis has also granted us options, subject to specified limitations, and to the extent such rights are controlled by Novartis, to obtain exclusive rights from Novartis to develop and commercialize in the United States the co-formulated and pre-filled syringe products developed by Novartis. We and Novartis have each granted the other options, subject to specified limitations, to obtain access to study data from certain clinical trials of licensed products that we or Novartis may conduct, including for use by the other in regulatory filings in its territory. We have agreed to exclusively supply Novartis, and Novartis has agreed to exclusively purchase from us, its clinical and commercial requirements for the bulk API for Fovista for use in-licensed products in the Novartis Territory. We have agreed not to commercialize any product comprising Fovista or any other anti-PDGF product in the ophthalmic field in the Novartis Territory.

Novartis paid us a $200.0 million upfront fee upon execution of the Novartis Agreement. Novartis also paid us $50.0 million upon the achievement of each of two patient enrollment-based milestones, and $30.0 million upon the

achievement of a third, and final, enrollment-based milestone, for an aggregate of $130.0 million. Under the terms of the Novartis Agreement, Novartis is also obligated to pay us up to an aggregate of an additional $300.0 million upon achievement of specified regulatory milestones, including marketing approval and reimbursement approval in certain countries in the Novartis Territory, and up to an aggregate of an additional $400.0 million if Novartis achieves specified sales milestones in the Novartis Territory. Novartis is also obligated to pay us royalties with respect to standalone Fovista products and combination Fovista products that Novartis successfully commercializes. We will receive royalties at a mid-thirties percentage of net sales of standalone Fovista products and a royalty of approximately equal value for sales of combination Fovista products. Such royalties are subject to customary deductions, credits, and reductions for lack of patent coverage or market exclusivity. Novartis's obligation to pay such royalties will continue on a licensed product-by-licensed product and country-by-country basis until Novartis's last actual commercial sale of such licensed product in such country. We will continue to be responsible for royalties we owe to third parties on sales of Fovista products.

Novartis has agreed to pay our manufacturing costs for clinical supplies and our manufacturing costs plus a specified percentage margin for commercial supplies of the bulk API for Fovista that we supply to Novartis. If we or Novartis exercise our or its respective rights to obtain access to study data from clinical trials conducted by the other party, the party exercising the option will be obligated to pay the other party's associated past development costs and share with such other party any future associated development costs. If we exercise our option to obtain Novartis-controlled rights to develop, manufacture and commercialize any co-formulated Fovista product in the United States, we will be obligated to pay a specified percentage of Novartis's associated past development costs and share with Novartis any future associated development costs. Novartis and we will also need to negotiate and agree on financial and other terms that would apply to such rights. If we exercise our option to obtain Novartis-controlled rights to develop and commercialize a pre-filled syringe product in the United States, we will be obligated to either enter into a supply agreement with Novartis under which we will pay Novartis its manufacturing cost plus a specified percentage margin for supplies of Fovista products in pre-filled syringes that Novartis supplies to us, or obtain supplies of products in pre-filled syringes from a third party manufacturer and pay Novartis a low single-digit percentage of our net sales of such products.

We retained control over the design and execution of our Phase 3 clinical program for Fovista and remain responsible for funding the costs of that program, subject to Novartis's responsibility to provide Lucentis, an anti-VEGF drug to which Novartis has rights in the Novartis Territory, for use in Phase 2 and Phase 3 Fovista clinical trials in the Novartis Territory. Novartis will have control over, and will be responsible for the costs of, all other clinical trials that may be required to obtain marketing approvals in the Novartis Territory for licensed products under the agreement. Novartis is also responsible for costs associated with co-formulation development, pre-filled syringe development and other development costs in the Novartis Territory, but excluding regulatory filing fees in the European Union for the standalone Fovista product, for which we will be responsible.

The Novartis Agreement, unless earlier terminated by Novartis or us, will expire upon the expiration of Novartis's obligation to pay us royalties on net sales of licensed products. Novartis and we each may terminate the Novartis Agreement if the other party materially breaches the agreement and does not cure such breach within a specified cure period, if the other party experiences any specified insolvency event, if the other party challenges or assists a third party in challenging the validity or enforceability of certain patent rights controlled by the terminating party, or if the parties are prevented in any manner that materially adversely affects the progression of the development or commercialization of licensed products for a specified period as a result of specified governmental actions. Novartis may terminate the Novartis Agreement at any time without cause, or within a specified period after a change in control of us, as defined in the Novartis Agreement, or for specified safety reasons, effective at the end of a specified period following Novartis's written notice to us of Novartis's election to terminate the agreement. We may also terminate the agreement if Novartis determines to seek marketing approval of an alternative anti-PDGF product in the Novartis Territory as more fully described below. If we elect to terminate the Novartis Agreement because specified governmental actions prevent the parties from materially progressing the development or commercialization of licensed products as described above, we will be required to pay a substantial termination fee. Following any termination, all rights to Fovista that we granted to Novartis, including, without limitation, the right to commercialize standalone Fovista products in the Novartis Territory, will revert to us, Novartis will perform specified activities in connection with transitioning to us the rights and responsibilities for the continued development, manufacture and commercialization of the standalone Fovista product for countries in the Novartis Territory, and the parties will cooperate on an orderly wind down of development and commercialization activities for other licensed products in the Novartis Territory.

Novartis has agreed to specified limitations on its ability to in-license, acquire or commercialize any anti-PDGF product that does not contain Fovista, which we refer to as an Alternative Anti-PDGF Product, in the Novartis Territory and, to the extent Novartis develops, in-licenses or acquires such a product, to make such product available to us in the United States under specified option conditions. If we exercise our option, we will be obligated to make certain payments to Novartis, including specified milestone and royalty payments. The amounts of such payments will vary based on the product's stage of

clinical development at the time we exercise our option, whether the product is a standalone or combination product and whether Novartis exercises an option to co-promote such product in the United States. If Novartis determines to seek marketing approval of an Alternative Anti-PDGF Product in the Novartis Territory, we will, subject to specified limitations, have the option to terminate the Novartis Agreement, convert Novartis's exclusive licenses into non-exclusive licenses, or elect to receive a royalty on sales of such product by Novartis. If we elect to terminate the Novartis Agreement, Novartis will, subject to specified limitations, be required to pay to us certain payments based on achievement, with respect to such product, of the milestones that would have otherwise applied to licensed products under the Novartis Agreement.

The agreement contains standstill provisions pursuant to which Novartis agrees to certain restrictions relating to our voting securities until marketing approval for a standalone Fovista product is granted in either the United States or the European Union. The agreement contains indemnification and dispute resolution provisions that are customary for agreements of its kind.

During the fourth quarter of 2015, we were informed by Novartis that Genentech, Inc. a Roche wholly-owned subsidiary, elected to exercise its option to participate in the financial arrangements relating to Novartis' rights under the Novartis Agreement. Roche's option originated from a pre-existing agreement between Roche and Novartis. The ex-U.S. commercialization agreement between Novartis and us, including its financial terms, remains unchanged as a result of the exercise of the opt-in right. We continue to retain sole rights to Fovista in the United States.

Government Regulation and Product Approvals

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, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining marketing 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 in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

A product candidate must be approved by the FDA through an NDA. An applicant seeking approval to market and distribute a new drug 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 investigational new drug application, or 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 an NDA 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 the clinical data;

- payment of user fees and securing FDA approval of the NDA; 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

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, and the purity and stability of the drug substance, as well as *in vitro* and animal studies to assess the potential safety and activity of the drug 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 IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug 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 that is not the subject of an approved NDA. 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 and 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.

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

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.

Human Clinical Trials in Support of an NDA

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

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

- ***Phase 1.*** The drug is initially introduced into a small number of healthy human subjects or, in certain indications, 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 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.*** These clinical trials are commonly referred to as "pivotal" studies, which denotes a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. The drug 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, identify adverse effects, establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

- ***Phase 4.*** Post-approval studies may be required to be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the safety results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the 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 by the FDA

If clinical trials are successful, the next step in the drug development process is the preparation and submission to the FDA of an NDA. The NDA is the vehicle through which drug applicants formally propose that the FDA approve a new drug for marketing and sale in the United States for one or more indications. The NDA must contain a description of the manufacturing process and quality control methods, as well as results of preclinical tests, toxicology studies, clinical trials and proposed labeling, among other things. Every new drug must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee and the sponsor of an approved NDA is also subject to annual product and establishment user fees.

Following submission of an NDA, the FDA conducts a preliminary review of an NDA 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 an NDA 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. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has agreed to specified performance goals in the review process of NDAs. 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 drugs 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 PDUFA 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 NDA, 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 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, 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 an NME.

The FDA is required to refer an application for a novel drug 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

On the basis of the FDA's evaluation of the NDA 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.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations and Accelerated Approval

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation. The FDA may also approve certain products based on an accelerated basis.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and if the product demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

In 2012, Congress enacted the Food and Product Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely

advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

The FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case- by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Finally, the FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product 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 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. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

Post-Approval Requirements

Drugs 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, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs 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, or 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. Drugs 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.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are “abbreviated” because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, 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, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug...” Upon approval of an ANDA, the FDA indicates whether the generic product is “therapeutically equivalent” to the RLD in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. 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. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety, which is the molecule or ion responsible for the action of the drug substance, that has previously been approved by the FDA in any other NDA. In cases where such NCE 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.

505(b)(2) NDAs

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information

required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it 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, including clinical trials, to support the change from the previously approved RLD. The FDA may then approve the new product candidate for all, or some, of the label indications for which the RLD has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

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 or 505(b)(2) applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. 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 RLD'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 indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA 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 or the 505(b)(2) application 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 or 505(b)(2) application 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 applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Patent Term Restoration and Extension

A patent claiming a new drug product or its method of use may be eligible for a limited patent term extension, also known as patent term restoration, under the Hatch-Waxman Amendments, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. 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 extension 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 (PTO) reviews and approves the application for any patent term extension in consultation with the FDA.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act, 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 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 any 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.

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. Unless and until FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

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

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA for the drug and rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

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 increasing funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act, or PHSA, to reauthorize and expand funding for the NIH. The 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 the 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 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 the 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 the 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 Drugs in Europe and other Foreign Jurisdictions

In addition to regulations in the United States, a manufacturer is subject to a variety of regulations in foreign jurisdictions to the extent it chooses to sell any drug products in those foreign countries. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. To obtain regulatory approval of an investigational drug in the European Union, a manufacturer must submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, clinical trials are to be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Clinical Trial Approval in the European Union

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, an applicant must obtain approval from the competent national authority of the European Union Member State, or the EU Member State, in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than 28 May 2016. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Marketing Authorization

In the European Union, marketing authorizations for medicinal products may be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU Member States. The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. 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 written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a "major public health interest." Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as severely disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure provides for approval by one or more other concerned EU Member States of an assessment of an application for marketing authorization conducted by one EU Member State, known as the reference EU Member State. In accordance with this procedure, an applicant submits an application for marketing authorization to the reference EU Member State and the concerned EU Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States which, within 90 days of receipt, must decide whether to approve the assessment report and related materials.

If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States. In accordance with the mutual recognition procedure, the sponsor applies for national marketing authorization in one EU Member State. Upon receipt of this authorization the sponsor can then seek the recognition of this authorization by other EU Member States. Authorization in accordance with either of these procedures will result in authorization of the medicinal product only in the reference EU Member State and in the other concerned EU Member States.

A marketing authorization may be granted only to an applicant established in the European Union. Regulation No. 1901/2006 provides that, prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

Regulatory Data Exclusivity in the European Union

Innovative medicinal products authorized in the European Union on the basis of a full MAA (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, applicants for authorization of generic versions of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to ten years' of market exclusivity. During this ten year period no generic version of the medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals in the European Union

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU Member State. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU Member State with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

As in the United States, marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations.

The holder of an EU marketing authorization for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which detail requirements for conducting pharmacovigilance or the assessment and monitoring of the safety of medicinal products. These rules can impose on central marketing authorization holders for medicinal products the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies.

The manufacturing process for medicinal products in the European Union is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the European Union. Similarly, the distribution of medicinal products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States.

In the European Union, the advertising and promotion of products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the European Union. The applicable laws at the European Union level and in the individual EU Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. These laws may further limit or restrict the advertising and promotion of products to the general public and may also impose limitations on promotional activities with health care professionals.

Pediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the European Union, applicants must demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the Centralized Procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC.

Orphan Drug Designation and Exclusivity in the European Union

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of: (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and, in addition, a range of other benefits during the development and regulatory review process, including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of

available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. 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 are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

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 marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Government authorities and third-party payors, particularly Medicare, have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and encouraging the substitution of lower cost or generic products. Pricing pressures recently experienced by the pharmaceutical industry may be further exacerbated by legislative and policy changes under consideration by the Trump administration. For example, the new administration has expressed an interest in authorizing and/or directing the Center for Medicare & Medicaid Service or other agencies of the U.S. government to negotiate prices for drugs covered by Medicare directly with pharmaceutical companies. If this were to occur, especially for wet AMD drugs, where a large portion of the patient population is elderly and is therefore covered by Medicare, there could be significant downward pressure on prices charged, not only for patients covered by Medicare, but also for patients covered by private insurers who may follow the government's lead on price. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that 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 drug candidate to currently available therapies or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of 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 product or it may instead adopt a system of direct or indirect controls on the

profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. 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. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers 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, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, 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 civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or 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, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, 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 their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which 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 known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as 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, which may apply to healthcare items or services that are 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 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, Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act 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;

- established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- established 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. The Affordable Care Act 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 the Affordable Care Act 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.

With the new Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of some or all of the Affordable Care Act. 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 product candidates.

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 Affordable Care Act. 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 Affordable Care Act. Also in January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act 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 Affordable Care Act 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 Affordable Care Act provisions is highly uncertain in many respects, and it is possible that some of the Affordable Care Act provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with Affordable Care Act coverage expansion provisions.

Employees

As of January 31, 2017, we had 156 full-time employees, including a total of 20 employees with M.D. or Ph.D. degrees. Of our workforce, 116 employees are engaged in research and development. Following our receipt and announcement of initial, top-line data for our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD in December 2016, we determined to implement a reduction in personnel to focus on an updated business plan involving an expected workforce of approximately 30 employees. The reduction in personnel is expected to involve approximately 125 employees across our organization, including employees from nearly every department. We expect to substantially complete the reduction in personnel during the first and second quarters of 2017 as part of implementing our updated business plan. None of our employees are represented by labor unions or covered by collective bargaining agreements.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2007. Our principal executive offices are located at One Penn Plaza, 19th Floor, New York, NY 10119, and our telephone number is (212) 845-8200. Our Internet website is http://www.ophthotech.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 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 accessed 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 risks and uncertainties 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 Updated Business Plan, Financial Position and Need for Additional Capital

Following the failure of two of our three pivotal, Phase 3 trials of Fovista for the treatment of wet AMD, we are in the process of implementing a new, updated business plan that will continue to evolve as we evaluate new opportunities and await relevant clinical data. Our updated business plan may lead to one or more transactions that you do not agree with or that you do not perceive as favorable to your investment. In the event that we do not succeed in implementing some or all of our new business plan, the remaining assets in our company may not be sufficient to provide any return on our stockholders' investment.

We have invested a significant portion of our efforts and financial resources in the development of Fovista to be administered in combination with anti-VEGF drugs for the treatment of wet AMD, as well as the potential commercial launch of Fovista. In December 2016, we announced initial, top-line data from two pivotal, Phase 3 clinical trials, which we refer to as OPH1002 and OPH1003, evaluating the safety and efficacy of 1.5mg of Fovista administered in combination with monthly 0.5mg Lucentis® (ranibizumab) anti-VEGF therapy compared to monthly Lucentis monotherapy for the treatment of wet AMD. The pre-specified primary endpoint of mean change in visual acuity at 12 months was not achieved for either OPH1002 or OPH1003. Moreover, we have not observed any clinically meaningful visual benefit when 1.5mg of Fovista was added to a monthly regimen of 0.5mg Lucentis therapy for any subgroup of patients that we have analyzed from the OPH1002 and OPH1003 trials, including subgroups based on baseline visual acuity, baseline lesion size or the baseline amount of the classic component of choroidal neovascularization, or CNV. Following the December 2016 data announcement, we subsequently stopped treating patients in, and terminated, both the OPH1002 and OPH1003 trials. OPH1004, our remaining Phase 3 clinical trial, which is evaluating the safety and efficacy of 1.5 mg of Fovista administered in combination with 2.0mg Eylea® (afilbercept) or 1.25mg Avastin® (bevacizumab) anti-VEGF therapy compared to Eylea or Avastin monotherapy for the treatment of wet AMD, remains ongoing, with initial, top-line data expected to be available during the second half of 2017.

Following the failure of our pivotal OPH1002 and OPH1003 Fovista trials, we initiated a plan to review our strategic alternatives in order to maximize shareholder value and implement an updated business plan. This updated business plan requires us to be successful in a number of challenging, uncertain and risky activities, including identifying promising new assets for development that are available for acquisition or in-license, negotiating and executing an acquisition or in-license agreement on for one or more of those programs on favorable terms and designing and executing a clinical program for these any newly acquired product candidates, or for our existing product candidates, potentially in different indications than we have previously investigated. We may not be successful at one or more of the activities required for us to execute this new updated business plan. As part of our strategic review, we may also consider other alternatives, including the acquisition of products, product candidates or technologies or other assets outside of ophthalmology, mergers or other transactions involving our company as a whole, collaboration transactions, or the license, sale or divestiture of some of our assets our technologies. We cannot be sure when or if this strategic review process will result in any type of transaction. Even if we pursue a transaction, such transaction may not be consistent with our stockholders' expectations or may not ultimately be favorable for our stockholders, either in the shorter or longer term.

Until such time as we identify and acquire or in-license additional product candidates, initiate new development programs for our existing product candidates, or consummate an alternative strategic transaction involving our company, our growth prospects and the future value of our company will be substantially, if not completely, dependent on the progress of our ongoing clinical development programs for our current product candidates, Fovista and Zimura, together with the amount of our remaining available cash. The development of each of Fovista and Zimura is highly uncertain. We have very limited clinical data on the effects of Fovista when administered in combination with intravitreal injections of either Eylea or Avastin for the treatment of patients with wet AMD and are unable to predict whether the 12 month results from the OPH1004 trial will be at all favorable. In addition, there is a risk that patients will drop out of the OPH1004 trial based on the unfavorable results from OPH1002 and OPH1003, leaving us with too few patients to obtain clinically meaningful data. We currently expect initial, top-line data from the OPH1004 trial to be available during the second half of 2017. The failure of our pivotal OPH1002 and OPH1003 trials to show any clinically meaningful visual benefit in adding 1.5mg of Fovista to a monthly regimen of 0.5mg of Lucentis and the recent failure of a competitor's Phase 2 trial investigating the combination of a PDGF inhibitor and a VEGF

inhibitor may be indicative of a low likelihood of success for OPH1004. In addition, we have only very limited data from small, uncontrolled clinical trials regarding the safety and efficacy of Zimura for the treatment of GA or in combination with anti-VEGF drugs for the treatment of wet AMD. Our prior Zimura trials were not powered to demonstrate the efficacy of Zimura therapy with any statistical significance. We remain at the very early phase of enrollment in our two ongoing Zimura clinical trials and we cannot currently estimate when additional clinical data for Zimura from these or other trials will become available.

We plan to reassess our existing Fovista and Zimura development programs throughout 2017 as the implementation of our updated business plan progresses and evolves, with the goal of aligning corporate resources in the context of a potentially broader product pipeline. We expect that our reassessment of our Fovista development program for the treatment of wet AMD will be primarily determined by the initial, top-line data from OPH1004 and that our reassessment of our Zimura development program may be particularly affected by the results of a competitor's Phase 3 clinical trial of a complement inhibitor being studied for the treatment of GA. Data from both our OPH1004 trial and our competitor's Phase 3 trial for the treatment of GA are expected during the second half of 2017. As a result of this reassessment, we may modify, expand or terminate some or all of our development programs or clinical trials at any time.

We expect that our remaining cash balances will continue to decline as we pursue these development programs, pursue our updated business plan and until such time, if any, as we receive additional funding, and the value of our stockholders' investment may decline as a result.

Even if we receive positive data from OPH1004 in the second half of 2017, the prospects for Fovista combination therapy for the treatment of wet AMD may not be readily ascertainable and we would need to assess the financial, operational and regulatory implications of such an outcome. We may make further changes to our business plan once such data is available.

While we believe that there is a low likelihood of a positive data outcome for OPH1004, a positive data outcome may pose significant financial, operation and regulatory challenges. Even if such data are favorable, the regulatory path for the potential approval of Fovista combination therapy for the treatment of wet AMD would be highly uncertain. In such an event, we expect that we will be required to conduct one or more additional clinical trials to demonstrate the safety and efficacy of Fovista in combination with one or more anti-VEGF drugs for the treatment of wet AMD, unless we are able to agree with the FDA and similar regulatory authorities outside the United States on an alternative regulatory pathway for approval. The FDA and similar regulatory authorities outside the United States require two adequate and well controlled clinical trials demonstrating safety and effectiveness for marketing approval for an ophthalmic pharmaceutical product. Conducting another large Phase 3 study of Fovista combination therapy for the treatment of wet AMD would be expensive and time consuming and would require us to seek additional funding. Because we would have substantially completed our planned reduction in personnel involving approximately 80% of our workforce by the time we receive initial, top-line data from OPH1004, a positive outcome would require us to either hire additional employees or engage a large number of consultants or other vendors in order to successfully execute a large Phase 3 study. We would also need to make arrangements with our suppliers to restart activities for clinical and commercial manufacturing, supply, packaging and distribution of Fovista which could result in delays in commencing a Phase 3 study. Even if we do obtain favorable data from two adequate and well controlled clinical trials, the FDA or similar regulatory authorities outside the United States may not grant marketing approval for a product candidate if such regulatory authorities do not believe that the benefits offered by such product candidate are clinically meaningful or that such benefits outweigh the observed or potential risks, which they may conclude based on potentially inconsistent and conflicting data regarding the efficacy of Fovista combination therapy.

Even if we are able to obtain marketing approval for Fovista for use in combination with one or more anti-VEGF drugs, because Avastin is not approved for use in treating wet AMD, either in the United States or outside of the United States, regulatory authorities may not permit the product label for Fovista to include the use of Fovista in combination with Avastin. For example, we have had interactions regarding our planned application for marketing approval with the EMA's Committee for Medicinal Products for Human Use, or CHMP, which is the committee responsible for preparing opinions on questions concerning medicines for human use. The CHMP informed us that the final label for Fovista, if it receives marketing approval, may be required to specify the licensed anti-VEGF drugs that were studied in combination with Fovista; Avastin is not licensed for intravitreal use in the European Union.

Even with a positive result from OPH1004 or any other clinical trial we may conduct for Fovista in wet AMD and marketing approval, it likely would be difficult to estimate the size of the potential market for Fovista for the treatment of wet AMD and anticipate the level of market acceptance of Fovista in such market, as the failure of our pivotal, Phase 3 OPH1002 and OPH1003 trials of Fovista in combination with Lucentis and the failure of a competitor's Phase 2 trial of an anti-PDGF inhibitor administered in combination with an anti-VEGF agent have called into question PDGF as a target for treatment of wet

AMD. Furthermore, even with a positive data outcome, the inconsistent results from our Phase 3 Fovista program may adversely affect our ability to establish a price for Fovista to enable us to sell Fovista profitably, even if we obtain marketing approval. Moreover, it is possible that Novartis, our ex-U.S. commercialization partner for Fovista, may terminate the Fovista Licensing and Commercialization Agreement with us, either prior to or following our receipt of initial, top-line data from OPH1004, even if the data from the trial are positive. In this event, we would need to change our commercialization plans for Fovista outside the United States. For these and other reasons, the return on any further investment in developing Fovista in wet AMD following a favorable data outcome from OPH1004 may be highly uncertain.

Undertaking and pursuing the further development of Fovista in wet AMD may require that we divert resources away from, and may distract our management and other personnel from continuing to execute on, our plan to realign corporate resources toward a more broadly-diversified product pipeline. In such event, we may therefore abandon some or all of the initiatives that we undertake in pursuit of our updated business plan.

Our strategy of obtaining rights to products, product candidates or technologies for the treatment of a range of ophthalmic diseases through in-licenses and acquisitions may not be successful. Our failure to successfully acquire or in-license and develop additional product candidates would likely impair our ability to grow.

A major element of our strategy is to expand our product pipeline through opportunistically in-licensing or acquiring the rights to products, product candidates or technologies for the treatment of ophthalmic diseases. Because we expect generally that we will not engage directly in early stage research and drug discovery and because the development outlook for our current product candidates is highly uncertain, the future growth of our business likely will depend significantly on our ability to in-license or acquire the rights to approved products, additional product candidates or technologies. We may be unable, however, to in-license or acquire the rights to any such products, product candidates or technologies from third parties for several reasons. The success of this strategy depends partly upon our ability to identify, select and acquire or in-license promising product candidates and technologies. We may be unable to identify suitable products, product candidates or technologies within our area of focus. The process of proposing, negotiating and implementing a license or acquisition of a product candidate is lengthy and complex. The in-licensing and acquisition of pharmaceutical products is an area characterized by intense competition, and a number of companies (both more established and early stage biotechnology companies) are also pursuing strategies to in-license or acquire products, product candidates or technologies that we may consider attractive. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities, while earlier stage companies may be more aggressive or have a higher risk tolerance. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in-license or acquire the rights to the relevant product, product candidate or technology on terms that would allow us to make an appropriate return on our investment. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts or we may incorrectly judge the value or worth of an acquired or in-licensed product candidate or technology.

Further, any product candidate that we acquire would most likely require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate would not be shown to be sufficiently safe and effective for approval by regulatory authorities.

If we are unable to successfully obtain rights to suitable products, product candidates or technologies, our business, financial condition and prospects for growth could suffer. In addition, acquisitions and in-licensing arrangements for product candidates and technologies are inherently risky, and ultimately, if we do not complete an announced acquisition or license transaction or integrate an acquired or licensed product or technology successfully and in a timely manner, we may not realize the benefits of the acquisition or license to the extent anticipated and the perception of the effectiveness of our management team and our company may suffer in the marketplace. In addition, even if we are able to achieve the long-term benefits associated with our revised business plan, our expenses and short-term costs may increase materially and adversely affect our liquidity.

In addition, future acquisitions and in-licenses may entail numerous operational, financial and legal risks, including:

- exposure to known and unknown liabilities, including possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- higher than expected acquisition and integration costs;

- difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- inability to maintain uniform standards, controls, procedures and policies;
- restructuring charges related to eliminating redundancies or disposing of assets as part of any such combination;
- large write-offs and difficulties in assessing the relative percentages of in-process research and development expense that can be immediately written off as compare to the amount that must be amortized over the appropriate life of the asset;
- increased amortization expenses or, in the event that we write-down the value of acquired assets, impairment losses;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership;
- inability to retain personnel, key customers, distributors, vendors and other business partners integral to an in-licensed or acquired product candidate or technology;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges of an acquired or licensed product candidate or technology, including, without limitation, problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, revenue recognition or other accounting practices, partner disputes or issues and other legal and financial contingencies and known and unknown liabilities; and
- entry into indications or markets in which we have no or limited direct prior development or commercial experience and where competitors in such markets have stronger market positions.

If we are unable to successfully manage our acquisitions or other in-license transactions, our ability to develop new products and continue to expand and diversify our product pipeline may be limited.

We may not use our available cash and other sources of funding effectively as we pursue our updated business plan.

Our revised business plan may not be successful, or we may be unsuccessful in effectively executing our revised business plan, which, in either case, could result in the expenditure of our available cash and other sources of funding 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 have a material adverse effect on our business, 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 adequate income, if any, or that loses value. For example, as we implement our revised business plan, we could allocate our available capital resources to pursue a particular strategic opportunity or product candidate or technology that proves to be ineffective, or we could fail to allocate sufficient resources to strategic opportunities or product candidates or technologies that may be more profitable or for which there is a greater likelihood of success. If we fail to effectively allocate our available capital resources, we may not be able to achieve the goals in our revised business plan, and our financial condition and prospects for growth could suffer.

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 were incorporated and commenced active operations in 2007. Our operations to date have been focused on organizing and staffing our company, acquiring rights to product candidates, business planning, raising capital and developing Fovista, Zimura and other product candidates. We have not yet demonstrated our ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture at commercial scale, or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. 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, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. The failure of our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD has required us to

reevaluate our future development plans for our product candidates, as well as our business plan more broadly, and has significantly decreased the likelihood that we will commercialize Fovista or any other product in the near term. We may never be successful in developing or commercializing any of our product candidates. If successful in developing and obtaining marketing approval of one of our product candidates, we would need to transition from a company with a product development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We have incurred significant operating losses since our inception. We expect to continue to incur losses until such time, if ever, that we successfully commercialize our product candidates. We may never achieve or maintain profitability.

Since inception, we have experienced significant cash outflows in funding our operations. As of December 31, 2016, we had an accumulated deficit of $599.0 million. Our net loss was $193.4 million for the year ended December 31, 2016, and $105.7 million for the year ended December 31, 2015 and we expect to continue to incur significant operating losses for the foreseeable future. To date, we have not generated any revenues from product sales and have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, funds received under our royalty purchase and sale agreement with Novo A/S, which we refer to as the Novo Agreement, which we entered into in May 2013, our initial public offering, which we closed in September 2013, our follow-on public offering, which we closed in February 2014, and funds we received under the Novartis Agreement, which we entered into in May 2014.

We have devoted substantially all of our financial resources and efforts to the research and development of Fovista and Zimura and preparations for the potential commercial launch of Fovista, including manufacturing scale-up activities. We expect to continue to incur significant expenses and operating losses over the next few years as we implement our updated business plan and continue to and reassess our development plans for our existing product candidates. Our net losses may fluctuate significantly from quarter to quarter and year to year.

We currently have two product candidates, Fovista and Zimura, which are in clinical development. We expect to continue to incur significant research and development expenses as we wind-down the OPH1002 and OPH1003 trials and the Fovista Expansion Studies, continue the OPH1004 trial and pursue the development of Zimura for the treatment of GA and in combination with anti-VEGF drugs for the treatment of wet AMD, as we review whether there is any scientific rationale for potentially developing, or undertake development of, Fovista or Zimura in additional indications, and as we evaluate and potentially in-license or acquire, and undertake development of, additional product candidates. Furthermore, if we successfully develop and obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. For Fovista, our ex-U.S. commercialization partner Novartis is responsible for these commercialization expenses outside the United States. We are party to agreements, specifically a divestiture agreement with OSI (Eyetech), Inc., or Eyetech, which agreement is now held by OSI Pharmaceuticals, LLC, a subsidiary of Astellas US, LLC, and license agreements with Archemix Corp., or Archemix, and Nektar Therapeutics, or Nektar, that impose significant milestone payment obligations on us in connection with our achievement of specific clinical, regulatory and commercial milestones with respect to Fovista and Zimura. It is likely that any future in-licensing or acquisition agreements that we enter into with respect to additional products, product candidates or technologies would include similar obligations.

We expect that we will continue to incur significant expenses as we:

- in-license or acquire the rights to, and pursue the development of, other products, product candidates or technologies;
- complete the activities necessary to receive initial, top-line data from OPH1004 and wind down OPH1002, OPH1003 and the Fovista Expansion Studies and our Fovista contract manufacturing commitments;
- potentially undertake additional clinical development of Fovista in wet AMD if the initial, top-line data from OPH1004 is favorable or in other indications if we believe there is a sufficient scientific rationale to pursue such development;
- continue the clinical development of Zimura for the treatment of GA and in combination with anti-VEGF drugs for the treatment of wet AMD, or potentially in other indications if we believe there is a sufficient scientific rationale to pursue such development;
- complete our previously announced reduction in personnel;
- maintain, expand and protect our intellectual property portfolio;

- hire additional clinical, manufacturing, quality control, quality assurance and scientific personnel if we are successful in progressing the clinical development of any of our product candidates;

- seek marketing approval for any product candidates that successfully complete clinical trials; and

- expand our outsourced manufacturing activities, expand our commercial operations and establish sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any of our product candidates.

Our ability to become and remain profitable depends on our ability to generate revenue in excess of our expenses. Our ability to generate revenues from product sales is dependent on our obtaining marketing approval for and commercializing our product candidates or any product candidates we may in-license or acquire. We may be unsuccessful in our efforts to develop and commercialize product candidates or in our efforts to in-license or acquire additional product candidates. Even if we succeed in developing and commercializing one or more of our product candidates, we may never achieve sufficient sales revenue to achieve or maintain profitability. See "-Risks Related to Product Development and Commercialization" for a further discussion of the risks we face in successfully developing and commercializing our product candidates and achieving profitability.

We may require substantial, additional funding in order to achieve the goals in our revised business plan. 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.

As of December 31, 2016, we had cash, cash equivalents, and marketable securities of $289.3 million, of which approximately $100 million to $115 million is committed to the wind-down of OPH1002 and OPH1003 and the Fovista Expansion Studies, implementing a previously announced reduction in personnel and related costs, cancellation fees related to manufacturing commitments, and obtaining initial, top-line data during the second half of 2017 for the OPH1004 trial. We also had $394.2 million in total liabilities as of December 31, 2016, of which $335.0 million related to the Novo Agreement and deferred revenue associated with the Novartis Agreement, which we are required to show as liabilities on our balance sheets under generally accepted accounting principles but which, in the case of Novo, do not correspond to any contractual repayment obligation, or in the case of Novartis, are highly unlikely to be triggered.

We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our operations and capital expenditure requirements as currently planned for at least the next 12 months. This estimate does not reflect any additional expenditures resulting from the in-licensing or acquisition of additional product candidates or technologies or associated development that we may pursue as part of our revised business plan. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Our capital requirements will depend on several factors, including the success of our pursuit, by acquisition, in-licensing or otherwise, and subsequent development of additional product candidates or technologies, and the success of our ongoing development programs. We believe that it is likely that we will need additional funding in the event that we acquire or in-license one or more additional product candidates and undertake development. In addition, our expenses may exceed our expectations if we experience delays in enrollment or with the availability of drug supply for our clinical trials, if we experience any unforeseen issues in our ongoing clinical trials or if we further expand the scope of our clinical trials and programs. Our costs may also exceed our expectations for other reasons, for example, if we experience issues with manufacturing, process development, or if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or regulatory authorities in other jurisdictions to perform clinical or nonclinical trials or other studies in addition to those we currently expect to conduct. As a result, we may need or may seek to obtain additional funding in connection with our continuing operations prior than expected.

Our plan for the future development of Fovista and Zimura is highly uncertain. If the results from the OPH1004 trial are favorable and we determine to pursue further development of Fovista for use in combination with anti-VEGF drugs for the treatment of wet AMD, we would likely need to conduct one or more further pivotal, clinical trials for Fovista to support potential marketing approval, which would be time-consuming and expensive. Furthermore, to the extent we continue our Zimura development programs, we expect the clinical development for Zimura would continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete the clinical development of either Fovista or Zimura, complete process development and manufacturing scale-up and validation activities associated with Zimura and potentially seek marketing approval for Fovista and Zimura, or the nature, timing or costs of the efforts necessary to complete the development of any other product candidate we may develop.

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

- the extent to which we in-license or acquire rights to, and undertake development of products, product candidates or technologies;
- the amount of any upfront, milestone payments and other financial obligations associated with the in-license or acquisition of other product candidates;
- the scope, progress, results and costs of preclinical development and/or clinical trials for any other product candidates that we may acquire or in-license and develop;
- the scope, progress, costs and results of the OPH1004 trial and any additional clinical trials we undertake to obtain data sufficient to seek marketing approval for Fovista in wet AMD or any other indication;
- the scope, costs and results of our Zimura clinical programs, including our Zimura Phase 2/3 GA trial and our Zimura Phase 2a wet AMD trial, as well as any additional clinical trials we undertake to obtain data sufficient to seek marketing approval for Zimura in any indication (including a potential second Phase 3 trial for GA);
- if OPH1004 is positive, the costs and timing of restarting the manufacturing of commercial supply for Fovista;
- the costs and timing of process development and manufacturing scale-up and validation activities associated with Zimura;
- our ability to establish collaborations on favorable terms, if at all;
- the costs, timing and outcome of regulatory reviews of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending intellectual property-related claims;
- the timing, scope and cost of commercialization activities for any of our product candidates if we receive, or expect to receive, marketing approval for a product candidate; and
- subject to receipt of marketing approval, net revenue received from commercial sales of any of our product candidates, after milestone payments and royalty payments that we would be obligated to make.

Furthermore, following our receipt and announcement of initial, top-line results from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD in December 2016, we implemented a restructuring plan that included a reduction in personnel. This reduction in personnel is expected to involve approximately 80% of our workforce and will include employees from nearly every department. We may not be able to successfully implement the restructuring and we may not realize the planned or expected cost savings benefits, which could adversely affect our estimate of the period for which our cash, cash equivalents and marketable securities will be sufficient to fund our operations and capital expenditure requirements as currently planned.

We do not have any committed external source of funds other than the Novartis Agreement, and the remaining potential milestone payments under the Novartis Agreement are subject to our achievement of specified regulatory and commercial events related to Fovista, none of which are likely to be achieved given the data outcome of the OPH1002 and OPH1003 trials. Our future commercial revenues, if any, will be derived from sales of any of our product candidates that we are able to successfully develop, which, depending on the product, may not be available for several years, if at all. In addition, if approved, Fovista or Zimura or any product that we acquire or in-license or acquire may not achieve commercial success. If that is the case, we will need to obtain substantial additional financing to achieve our business objectives. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. In addition, a default under the Novo Agreement would permit Novo A/S to foreclose on the Fovista intellectual property.

Until such time, if ever, as we can generate substantial product revenues, we may need or may seek to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our existing stockholders' ownership interests would 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.

We are subject to diligence and other obligations under the Novo Agreement, including an obligation to use commercially reasonable efforts to develop, seek marketing approval for and commercialize Fovista. Our obligations under the Novo Agreement are secured by collateral, which includes certain intellectual property rights, including all of our intellectual property rights relating to Fovista and regulatory approvals, if any, of Fovista. If we fail to satisfy our diligence obligations or breach any other of our obligations under the Novo Agreement and fail to cure the breach within any applicable grace period, Novo A/S could declare an event of default. In such event, Novo A/S could seek to foreclose on the collateral securing our obligations. If Novo A/S successfully does so, we would lose our rights to develop and commercialize Fovista. Our obligations under the Novo Agreement and the pledge of our intellectual property rights in and regulatory approvals, if any, of Fovista as collateral under such agreement may limit our ability to obtain debt financing.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, products or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

We and certain of our current and former executive officers have been named as defendants in a lawsuit that could result in substantial costs and divert management's attention.

We and certain of our current and former executive officers have been named as defendants in a purported class action lawsuit initiated earlier this year that generally alleges that we and certain of our officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the prospects of our Phase 3 trials for Fovista in combination with anti-VEGF drugs for the treatment of wet AMD. The complaint seeks equitable and/or injunctive relief, unspecified damages, attorneys' fees, and other costs. We deny any allegations of wrongdoing and intend to vigorously defend against this lawsuit. We are unable, however, to predict the outcome of this matter at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business. Additional similar lawsuits might be filed.

Risks Related to Product Development and Commercialization

Companies in our industry face a wide range of challenging activities, each of which entails separate, and in many cases substantial, risk.

The long-term success of our company, and our ability to become profitable as a biopharmaceutical company will require us to be successful in a range of challenging activities, including:

- designing, conducting and completing clinical trials for our product candidates;
- obtaining favorable results from required clinical trials, including for each ophthalmic product candidate, favorable results from two adequate and well controlled pivotal clinical trials in the relevant indication;

- applying for and receiving marketing approvals from applicable regulatory authorities for the use of our product candidates;
- making arrangements with third-party manufacturers, receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities and ensuring adequate supply of drug product;
- establishing sales, marketing and distribution capabilities, either internally or through collaborations or other arrangements, to effectively market and sell our product candidates;
- achieving acceptance of the product candidate, if and when approved, by patients, the medical community and third-party payors;
- if our product candidates are approved, obtaining from governmental and third-party payors adequate coverage and reimbursement for our product candidates and, to the extent applicable, associated injection procedures conducted by treating physicians;
- effectively competing with other therapies, including the existing standard of care, and other forms of drug delivery;
- maintaining a continued acceptable safety profile of the product candidate during development and following approval;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting and enforcing our rights in our intellectual property portfolio; and
- complying with all applicable regulatory requirements, including FDA Good Clinical Practices, or GCP, Good Manufacturing Practices, or GMP, and standards, rules and regulations governing promotional and other marketing activities.

Each of these activities has associated risks, many of which are detailed below and throughout this "Risk Factors" section. We may never succeed in these activities and, even if we do, may never generate revenues from product sales that are significant enough to achieve commercial success and profitability. Our failure to be commercially successful and profitable would decrease 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 continue our operations. A decrease in the value of our company would also cause our stockholders to lose all or part of their investment.

Drug development is a highly uncertain undertaking. Our development efforts may be delayed for any number of reasons, in which case potential marketing approval or commercialization of our product candidates could be delayed or prevented.

Before obtaining approval from regulatory authorities for the sale of any product candidate, we must 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 clinical trials, and interim results of a clinical trial do not necessarily predict final results. 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.

We may experience numerous unforeseen events during drug development that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including the following:

- we may not be able to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical studies for any preclinical product candidates that we in-license or acquire;
- regulators or institutional review boards may not agree with our study design or 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 clinical research organizations or clinical trial sites;
- our contract research organizations or clinical trial sites may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we, through our clinical trial sites, may not be able to locate and enroll a sufficient number of eligible patients to participate in our clinical trials as required by the FDA or similar regulatory authorities outside the United States;
- 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, including GCPs, or a finding that the participants are being exposed to unacceptable health risks;
- there may be changes in regulatory requirements and guidance or we may have changes in trial design that require amending or submitting new clinical protocols;
- there may be changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- clinical trials of our product candidates may produce inconclusive or negative results, such as the results we observed in our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, 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 to demonstrate statistically significant results 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;
- 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, such as the anti-VEGF drugs we need to use in combination with Fovista and Zimura in our wet AMD trials, may become insufficient or inadequate or we may face delays in the manufacture and supply of such materials as a result our decision to transfer manufacturing between contract manufacturers or on account of interruptions in our supply chain, including in relation to the packaging and distribution or import / export of clinical materials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we contemplate, if we are unable to successfully complete clinical trials or of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

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

Despite our current development plans and ongoing efforts, we may not complete any of our ongoing clinical trials or any other clinical trial for our product candidates. Moreover, the timing of the completion of, and the availability of results from, clinical trials is difficult to predict. Furthermore, our development plans may change based on feedback we may receive from regulatory authorities throughout the development process. If we experience delays in testing or marketing approvals, our product development costs would increase. We do not know whether clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant 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 and may harm our business and results of operations.

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

If any of our product candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development of the compound.

Fovista administered in combination with Lucentis was generally well tolerated in our Phase 1 clinical trial and our Phase 2b clinical trial, as well as after one year of treatment in our pivotal OPH1002 and OPH1003 trials, based upon our preliminary analysis of safety data from these Phase 3 trials. There remains, however, the potential for patients receiving Fovista combination therapy to experience an increase in cumulative side effects resulting from two separate intravitreal injections and increased intraocular pressure, as compared to patients receiving monotherapy anti-VEGF treatment. We may observe an unfavorable safety and tolerability profile in the Fovista combination therapy arms of OPH1004 or any other clinical trial of Fovista that we may conduct, as compared to our prior Fovista clinical trials and monotherapy anti-VEGF trials, which may be reflected in an increase in adverse events and/or serious adverse event rates (either ocular, systemic or both) in patients receiving Fovista or Fovista combination therapy. For example, there may be, among others, an increase in the rates of intraocular infections, or endophthalmitis, intraocular pressure, glaucoma, retinal tears, cataracts, retinal detachment, intraocular inflammation, retinal and/or choroidal circulation compromise, cardiovascular disease such as myocardial infarctions, stroke, blood clots or emboli, or hospitalizations in patients who receive Fovista combination therapy.

In addition, we have very limited clinical and safety data with respect to the effects of Fovista administered in combination with intravitreal injections of either Eylea or Avastin. The safety results of our combination therapy trials, including OPH1004, are dependent, in part, on the safety and tolerability of the anti-VEGF drug(s) administered in combination with our product candidate. Avastin is not approved for the treatment of wet AMD, and according to some third party clinical trials, may be associated with a greater risk of serious adverse events or undesirable side effects as compared to Lucentis.

We have limited data regarding the safety, tolerability and efficacy of Zimura administered for the treatment of GA or administered in combination with anti-VEGF drugs for the treatment of wet AMD. Our clinical trials for Zimura will involve multiple intravitreal injections over an extended period of time and, as such, may involve risks regarding multiple and chronic intravitreal injections, similar to those described above for Fovista.

Our experience manufacturing our product candidates is limited. Manufacturing issues may arise that could cause delays in our development programs or increase costs. In addition, we may experience delays in regulatory approval of our product candidates if we do not satisfy applicable manufacturing regulatory requirements.

Our current product candidates, Fovista and Zimura, are each chemically-synthesized aptamers. In pursuing our updated business plan, we could acquire or in-license a variety of types of product candidates, including small molecule drugs, protein drugs or biologics. Small molecule drugs are organic compounds of low molecular weight that are generally associated with ready availability of starting materials and ease of synthesis. In contrast, manufacturing for proteins and biologics is more complex, especially in large quantities. For example, biologic products must be made consistently and in substantial compliance with a clearly defined manufacturing process, and often must be manufactured under aseptic conditions.

We do not have any internal manufacturing capabilities and likely would be dependent on outside contract manufacturers to manufacture any of the product candidates that we would acquire or in-license as part of pursuing our updated business plan. Manufacturing for these product candidates could be complicated or present novel technical challenges. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

We currently rely upon a single third-party manufacturer, Agilent Technologies, to supply us with the chemically synthesized aptamers comprising the API for both Fovista and Zimura and a different, single third-party manufacturer,

Ajinomoto Althea, to provide fill/finish services for both Fovista and Zimura. In order to obtain and maintain regulatory approval for Fovista or Zimura, our third-party manufacturers will be required to consistently produce the API used in Fovista or Zimura in commercial quantities and of specified quality and to execute fill/finish services on a repeated basis and document their ability to do so. If the third-party manufacturers are unable to satisfy this requirement, our business would be materially and adversely affected. During the third quarter of 2016, we completed the manufacture of validation batches of Fovista API produced at commercial scale. However, given the negative results from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we are not currently manufacturing clinical or commercial supplies of Fovista. If OPH1004 is positive, we would need to restart the process for commercial supply, including obtaining scheduling commitments from both Agilent and Althea which could prove challenging if these manufacturers are at or near capacity. To date, we have not yet scaled up the manufacturing process for Zimura beyond the scale used for developmental clinical batches, nor have we validated the manufacturing process.

These manufacturing processes and the facilities of our third-party manufacturers, including our third-party API manufacturer and our third-party fill/finish service provider, are subject to inspection and approval by the FDA, referred to as a pre-approval inspection, before we can commence the commercial sale of any approved product candidate, and thereafter on an ongoing basis. Our third-party API manufacturer has undergone only one pre-approval inspection by the FDA, and has not yet gone through a pre-approval inspection for Fovista or Zimura. Our third-party fill/finish service provider is subject to FDA inspection from time to time. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in delays in the approval of our applications for marketing approval in the event a recommendation to withhold is issued, as well as regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. Additionally, on October 22, 2014, the FDA issued its final guidance on the circumstances that constitute delaying, denying, limiting or refusing a drug inspection pursuant to Section 707 of the Food and Drug Administration Safety and Innovation Act of 2012. If any of our third-party manufacturers are found to have delayed, denied, limited or refused a drug inspection, our API or drug product could be deemed adulterated. Based on the severity of the regulatory action, our clinical or commercial supply of API or our fill/finish services could be interrupted or limited, which could have a material adverse effect on our business.

Some of the standards of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, which establishes basic guidelines and standards for drug development in the United States, the European Union, Japan and other countries, do not apply to oligonucleotides, including aptamers. As a result, there are no established generally accepted manufacturing or quality standards for the production of Fovista or Zimura. Even though the FDA has reviewed the quality standards for Fovista used in our Phase 3 clinical program, the FDA has the ability to modify these standards at any time and foreign regulatory agencies may impose differing quality standards and quality control on the manufacture of Fovista. The lack of uniform manufacturing and quality standards among regulatory agencies may delay regulatory approval of Fovista, Zimura or any future product candidate.

In addition, in order to manufacture and supply any of our product candidates on a commercial scale in the future, we will need to bolster our quality control and quality assurance capabilities, including by augmenting our manufacturing processes and adding personnel. We also may encounter problems hiring and retaining the experienced specialist scientific and manufacturing personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. As we or any manufacturer we engage scales up manufacturing of any approved product, we may encounter unexpected issues relating to the manufacturing processes or the quality, purity or stability of the product, and we may be required to refine or alter our manufacturing processes to address these issues. Resolving these issues could result in significant delays and may result in significantly increased costs. If we underestimate the demand for an approved product, given the long lead times required to manufacture our products, we could potentially face commercial drug product supply shortages. If we experience significant delays or other obstacles in producing any approved product at commercial scale, our ability to market and sell any approved products may be adversely affected and our business could suffer.

Any problems in our manufacturing process or our third-party contract manufacturers' facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in our manufacturing process or facilities also could restrict our ability to meet market demand for our products.

Even if any of our product candidates receives marketing approval, such product candidate 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 any of our products and product candidates may be smaller than we estimate.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current treatments for wet AMD, including Lucentis, Eylea and low cost, off-label use of Avastin, are well established in the medical community, and doctors may continue to rely upon these treatments without Fovista. If any of our product candidates, if approved, do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of Fovista, Zimura or any other product candidate that we may develop, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments, including the existing standard of care;
- any restrictions in the label on the use of our products in combination with other medications;
- any restrictions in the label on the use of our products by a subgroup of patients;
- restrictions in the label on of any for our combination therapy product candidates, such as Fovista or Zimura, limiting their use in combination with particular standard of care drugs, such as a particular anti-VEGF drug;
- our and any commercialization partner's ability to offer our products at competitive prices, particularly in light of the cost of any of our combination therapy product candidates in addition to the cost of the underlying standard of care drug;
- availability of third-party coverage and adequate reimbursement, particularly by Medicare given the target market for AMD indications for persons over age 55;
- increasing reimbursement pressures on treating physicians due to the formation of accountable care organizations and the shift away from traditional fee-for-service reimbursement models to reimbursement based on quality of care and patient outcomes;
- willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, particularly in light of the existing available standard of care;
- prevalence and severity of any side effects; and
- whether competing products or other alternatives are more convenient or easier to administer, including whether co-formulated alternatives, alternatives that can be co-administered in a single syringe or alternatives that offer a less invasive method of administration than intravitreal injection come to market.

In addition, the potential market opportunity for any product candidate is difficult to estimate precisely. Our estimates of the potential market opportunity for our product candidates include several key assumptions based on our expectations of the safety and effectiveness of the relevant product candidate, our industry knowledge, industry publications, market response to marketed AMD drugs, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions and any of these assumptions could prove to be inaccurate, and the actual market for such product candidates could be smaller than our estimates of our potential market opportunity.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of wet AMD, GA or other disease indications for which we may develop Fovista or Zimura. 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. Some of these

competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. We also will face similar competition with respect to any other products or product candidates that we may seek to develop or commercialize in the future for the treatment of wet AMD, GA or any other indication.

There are a number of products in preclinical research and clinical development by third parties to treat wet AMD. Based on publicly available information, we are aware that Regeneron Pharmaceuticals, Ohr Pharmaceutical, Santen, Tyrogenex, Allergan, GrayBug and Somologic each have PDGF inhibitors in clinical or pre-clinical development for wet AMD. Several of these product candidates also inhibit VEGF or are administered directly with an anti-VEGF agent in a manner that could negatively impact demand for a separate intravitreal injection of an anti-PDGF agent such as Fovista. The most advanced of these product candidates is Regeneron's, for which negative Phase 2 data was previously announced in December 2016 and additional data may be announced during 2017.

Moreover, based on publicly available information, we are aware that several companies and research organizations are pursuing treatments targeting other molecular targets, potential gene therapy treatments and stem cell transplant treatments for the treatment of wet AMD. In addition, other companies are undertaking efforts to develop technologies to allow for a less frequent dosing schedule than the dosing schedule currently in use for standard of care anti-VEGF drugs.

There are a number of products in preclinical research and clinical development by third parties to treat dry AMD. In general, these product candidates can be categorized based on their proposed mechanisms of action. The mechanisms of action for these product candidates include inflammation suppression, such as complement system inhibitors and corticosteroids, visual cycle modulators, antioxidants and neuroprotectants, cell and gene therapies and vascular enhancers. Based on publicly available information, we are aware that Genentech, Novartis / MorphoSys, Apellis, Hemera Biosciences, Achillion, Ra Pharmaceuticals and Catalyst Biosciences each have complement inhibitors in development, the most advance of which is Genentech's humanized Fab fragment targeting complement factor D, for which data from Phase 3 trials is expected during 2017. If Genentech's Phase 3 trials for its complement factor D product candidate are successful, it is likely that Genentech would obtain marketing approval for such product candidate several years in advance of when we could reasonably expect marketing approval for Zimura in GA, if at all. Moreover, based on publicly available information, we are aware that several other companies have announced development programs for the treatment of dry AMD targeting different mechanisms of action outside of the complement cascade.

Our commercial opportunity could be reduced or eliminated if one or more of our competitors develop and commercialize products that are more effective, safer, have fewer or less severe side effects, are more convenient to use or are less expensive than our product candidates. The commercial opportunity for Fovista or Zimura also could be reduced or eliminated if our competitors develop and commercialize products that reduce or eliminate the use of anti-VEGF drugs for the treatment of patients with wet AMD. 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 relevant market.

In addition, our ability to compete may be affected in many cases by insurers or other third-party payors, particularly Medicare, seeking to encourage the use of less expensive or more convenient products. We expect that if Fovista or Zimura is approved for combination therapy for the treatment of wet AMD, the cost of combination treatment would be higher than the cost of treatment of wet AMD with Lucentis, Eylea or particularly Avastin monotherapy. Insurers and other third-party payors may encourage the use of anti-VEGF drugs as monotherapy and discourage the use of Fovista in combination with these drugs. This could limit sales of Fovista.

Many of our competitors have significantly greater financial and human resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. 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 enrollment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our clinical development programs.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing any of our product candidates that we develop if and when any such product candidate is approved.

As a company, we have no experience in the sale, marketing or distribution of pharmaceutical products. We currently do not have any sales, marketing or distribution infrastructure. To achieve commercial success for any approved product, we

must either develop a sales, marketing and distribution organization or outsource those functions to third parties. We expect that our commercial strategy for any of our product candidates, including whether to retain commercial rights and market and sell the product candidate ourselves or to utilize collaboration, distribution or other marketing arrangements with third parties, would be determined based on a variety of factors, including the size and nature of the patient population, the disease area, the particular indication, the territory in which the product candidate may be marketed and the commercial potential for such product candidate. Pursuant to the Novartis Agreement, we have granted to Novartis the exclusive right to commercialize Fovista outside of the United States in consideration for royalties on any such sales. In addition, our commercial strategy would vary depending on whether the disease is typically treated by general ophthalmology practitioners, specialists, such as retinal specialists, or sub-specialists.

There are risks involved with establishing our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution 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.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to adequate numbers of physicians who may prescribe our products;
- the lack of complementary products to be offered by our 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 enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute ourselves any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable 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 sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we would not be successful in commercializing our product candidates.

If Fovista is successfully developed, which, again, we believe has a low likelihood following our receipt of initial, top-line data from two of our three pivotal clinical trials, and we do not maintain a productive collaborative relationship with Novartis, to whom we have granted exclusive commercialization rights for Fovista outside of the United States, or if Novartis is unable to meet its contractual obligations, we may be forced to focus our efforts internally to commercialize Fovista outside of the United States without the assistance of a commercialization partner or seek another commercialization partner, either of which would result in us incurring greater expenses and could cause a delay in market penetration while we expand our commercial operations or seek an alternative commercialization partner. Such costs may exceed the increased revenues we would receive from direct Fovista sales outside of the United States, at least in the near term. We would also be forced to declare a breach of the Novartis Agreement and seek a termination of the agreement which could result in an extended and uncertain dispute with Novartis, including arbitration or litigation, any of which would be costly.

Even if we are able to commercialize any of the product candidates that we may develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Health care reform is an issue of intense political focus, particularly in the United States. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals or in ways that could alter the mechanism by which pharmaceutical prices are negotiated or otherwise determined. 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 or negotiation 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 or any commercialization partner's 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. 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 and are widely accepted and prescribed or used by physicians.

Our ability and the ability of any commercialization partner, such as Novartis, our ex-U.S. commercialization partner for Fovista, to commercialize Fovista, Zimura or any other product candidate successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers 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 major trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors, particularly Medicare, have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and encouraging the substitution of lower cost or generic products. Pricing pressures recently experienced by the pharmaceutical industry may be further exacerbated by legislative and policy changes under consideration by the Trump administration. For example, the new Administration has expressed an interest in authorizing and/or directing the Center for Medicare & Medicaid Service or other agencies of the U.S. government to negotiate prices for drugs covered by Medicare directly with pharmaceutical companies. If this were to occur, especially for wet AMD drugs where a large portion of the patient population is over the age of 65 and is therefore covered by Medicare, there could be significant downward pressure on prices charged, not only for patients covered by Medicare, but also for patients covered by private insurers who may follow the government's lead on price. Moreover, increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for Fovista, Zimura or any other product that we commercialize or any commercialization partner commercializes on our behalf, and, even if these are available, the level of reimbursement may not be satisfactory.

Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician and because, in the case of Fovista, our drug will be administered in combination with other drugs that may carry high prices. In addition, physicians, patients and third-party payors may be sensitive to the addition of the cost of Fovista to the cost of treatment with anti-VEGF drugs. We or any commercialization partner may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies, including in the case of Fovista, relative to monotherapy with anti-VEGF drugs. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize Fovista, Zimura or any other product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. 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, a policy that President Trump has expressed interest in pursuing. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our and any commercialization partner's inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

The pricing of prescription pharmaceuticals is subject to governmental control outside of the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or a commercialization partner may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If

reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Product liability lawsuits against us or any commercialization partner could divert resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop or in-license.

We face an inherent risk of product liability exposure related to the testing of any product candidate that we develop in human clinical trials, and we and any commercialization partner will face an even greater risk if we commercially sell any products that we develop or in-license. Because our Phase 3 clinical program for Fovista and our Zimura wet AMD trial involves the administration of our product candidates in combination with anti-VEGF drugs, including off-label use by intravitreal injection of Avastin provided by us, we also face an inherent risk of product liability exposure related to the testing of such anti-VEGF drugs. If we become subject to or otherwise cannot successfully defend ourselves against claims that our product candidates, anti-VEGF drugs administered in combination with our product candidates or our 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 may develop or in-license;
- 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 may develop or in-license.

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 when and if we begin commercializing an approved product. 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. In addition, if Novartis or one of our other future commercialization or collaboration partners were to become subject to product liability claims or were unable to successfully defend themselves against such claims, any such commercialization or collaboration partners could be more likely to terminate such relationship with us and therefore substantially limit the commercial potential of our products.

Risks Related to Our Dependence on Third Parties

If we are not able to establish additional, future collaborations, we may have to alter our development and commercialization plans.

The development and potential commercialization of our product candidates is likely to require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology 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 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.

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 and generate product revenue.

We may enter into collaborations with third parties for the development or commercialization of our product candidates. If any of our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to commercialize our product candidates, either in the United States, or in markets outside the United States, such as the Novartis Agreement. We also may seek third-party collaborators for development and commercialization of other product candidates we may develop. 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. If we do enter into any additional arrangements with third parties in the future, we would likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements and our arrangement with Novartis for Fovista will depend on our collaborators' and Novartis's abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates, including our collaboration with Novartis, could pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, changes in product candidate priorities or available funding or changes in priorities as a result of a merger, acquisition or other corporate restructuring or transaction;
- 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;
- we could grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disagreements or disputes with collaborators, including disagreements or disputes over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of products or product candidates, might lead to additional responsibilities for us with respect to product candidates or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and be expensive;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights, may infringe the intellectual property rights of third parties, may misappropriate our trade secrets 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 litigation and potential liability; and

- collaborations may be terminated for the convenience of the collaborator, our breach of the terms of the collaboration or other reasons and, if terminated, we may need to raise additional capital to pursue further development or commercialization of the applicable product candidates.

For example, the Novartis Agreement is subject to early termination in the event of certain customary defaults, such as material breach of the agreement and bankruptcy. In addition, the agreement is subject to early termination by either us or Novartis if the other party challenges or assists a third party in challenging the validity or enforceability of certain patent rights controlled by the terminating party, or if the parties are prevented in any manner that materially adversely affects the progression of the development or commercialization of licensed products for a specified period as a result of specified governmental actions. Novartis may also terminate the agreement at any time without cause, or within a specified period after a change in control of us, as defined in the agreement, or for specified safety reasons, effective at the end of a specified period following Novartis's written notice to us of Novartis's election to terminate the agreement. We may also terminate the agreement if Novartis determines to seek marketing approval of an alternative anti-PDGF product outside the United States. If we do not maintain a productive collaborative relationship with Novartis or if Novartis is unable to meet its contractual obligations or if there is an early termination of the agreement as described above, we would be forced to either establish a commercial infrastructure outside of the United States so that we could undertake the commercialization efforts which had been theretofore undertaken by Novartis or we would need to seek an alternative partner. The establishment of a commercial infrastructure and assumption by us of commercialization activities outside of the United States would require substantial resources, financial and otherwise, and could result in us incurring greater expenses than the increase in revenues from our direct sales of Fovista. It could also cause a delay in market penetration while we expand our commercial operations. Seeking and obtaining an alternative commercial partner outside the United States could also adversely impact sales of Fovista and market penetration outside of the United States.

If a collaborator of ours, such as Novartis, were to be involved in a business combination or other transaction, the foregoing risks would be heightened, and the business combination or transaction may divert attention or resources or create competing priorities. The collaborator may delay or terminate our product development or commercialization program. If one of our collaborators, including Novartis, terminates its agreement with us, we could find it more difficult to attract new collaborators and the perception of our company in the business and financial communities could be adversely affected.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We rely upon third parties in conducting our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We have relied on third-party clinical research organizations, or CROs, in conducting our completed clinical trials of Fovista and Zimura. We expect to continue to rely upon third parties, such as CROs, clinical data management organizations, medical institutions (including reading centers) and clinical investigators, in conducting our clinical trials for our product candidates. We or these third parties may terminate their engagements with us at any time for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities could potentially be delayed and could potentially be very costly.

Our reliance on these third parties for clinical 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 GCPs 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 also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties 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 would not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and would not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also rely upon other third parties to store, package and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of both Fovista and Zimura for clinical trials and expect to continue to do so in connection with the potential commercialization of either product candidate and for clinical trials and commercialization of any other product candidates that we develop or may develop. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of Fovista or Zimura and have limited personnel with manufacturing experience. We currently rely upon and expect to continue to rely upon third-party contract manufacturers to manufacture preclinical and clinical supplies of product candidates we are developing or may develop and commercial supplies of products if and when approved for marketing by applicable regulatory authorities. Our current and anticipated future dependence upon others for the manufacture of the product candidates that we are developing or may develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. In addition, any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. Under the Novartis Agreement, we are responsible for supplying to Novartis Fovista API for clinical and commercial supply.

We currently rely exclusively upon a single third-party manufacturer to provide supplies of both Fovista API and Zimura API and a different single third-party manufacturer to provide fill/finish services for Fovista and Zimura. Although we have agreements in place with Agilent for the supply of Fovista API and with Althea for clinical and commercial fill/finish services, we do not currently have any contractual commitments for the supply of Zimura API . Additionally, given the negative results from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we are not currently manufacturing commercial supplies of Fovista. If OPH1004 is positive, we would need to restart the process for commercial supply, including obtaining scheduling commitments from both Agilent and Ajinomoto Althea which could prove challenging if these manufacturers are at or near capacity. We also do not currently have arrangements in place for redundant supply or a second source for API for Fovista or Zimura or for a redundant supply or a second source for fill/finish services. The prices for manufacturing activities that are not yet contractually committed may vary substantially over time and adversely affect our financial results. Furthermore, we and our contract manufacturers currently rely upon sole-source suppliers of certain raw materials and other specialized components of production used in the manufacture and fill/finish of each of Fovista and Zimura.

We currently rely exclusively upon Nektar to supply us with a proprietary polyethylene glycol, or PEG, reagent for Fovista under a manufacturing and supply agreement. PEG reagent is a chemical we use to modify the chemically synthesized aptamer in Fovista. The PEG reagent made by Nektar is proprietary to Nektar.

We obtain a different proprietary PEG reagent used to modify the chemically synthesized aptamer in Zimura from a different supplier on a purchase order basis. We do not currently have any contractual commitments for supply of the PEG reagent we use for Zimura.

If any of our third-party manufacturers fail to fulfill our purchase orders, or if any of these manufacturers should become unavailable to us for any reason, including as a result of capacity constraints, financial difficulties or insolvency, we believe that there are a limited number of potential replacement manufacturers, and we likely would incur added costs and delays in identifying or qualifying such replacements. We could also incur additional costs and delays in identifying or qualifying a replacement manufacturer for fill/finish services if our existing third-party fill/finish provider should become unavailable for any reason. We may be unable to establish agreements with such replacement manufacturers or fill/finish providers or to do so on acceptable terms.

Reliance on third-party manufacturers entails additional risks, including:

- our product candidates may compete with other product candidates and products for access to a limited number of suitable manufacturing facilities that operate under current good manufacturing practices, or cGMP, regulations;
- reliance on the third party for regulatory compliance, quality assurance and quality control;
- the possible breach of the manufacturing agreement by the third party;
- the possible breach of our supply obligations to Novartis;

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

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, 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 harm our business and results of operations.

We depend on licenses and sublicenses for development and commercialization rights to our product candidates and technologies. Termination of these rights or the failure by us or our licensees, including our commercialization or collaboration partners to comply with obligations under these or other agreements under which we obtain such rights or have obtained funding could materially harm our business and prevent us from developing or commercializing our products and product candidates.

We are party to various agreements, including a divestiture agreement with OSI Pharmaceuticals and license agreements with Archemix and Nektar that we depend on for rights to Fovista and Zimura. These agreements impose, and we expect to enter into additional licensing arrangements or other agreements with third parties that would impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our divestiture agreement with OSI Pharmaceuticals and our licensing agreement with Nektar, we are obligated to pay royalties on net product sales of Fovista or other product candidates or related technologies to the extent they are covered by the applicable agreement. Under our license agreements with Archemix and Nektar, we would not be able to avoid our payment obligations even if we believed a licensed patent right was invalid or unenforceable because the license agreements provide that our licenses to all licensed patent rights would terminate if we challenge the validity or enforceability of any licensed patent right.

We also have diligence and development obligations under our divestiture agreement with OSI Pharmaceuticals and our license agreements with Archemix and Nektar. Generally, these diligence obligations require us to use commercially reasonable efforts to develop, seek regulatory approval for and commercialize our products in the United States, the European Union and, in some cases, certain other specified countries. Although the Novartis Agreement provides that Novartis will be responsible for performing certain of these obligations with respect to specified countries for Fovista, we still remain directly liable under our agreements with OSI Pharmaceuticals, Archemix and Nektar. If we fail to comply with our obligations under current or future acquisition, license and funding agreements, or otherwise breach an acquisition, license or funding agreement as a result of our own actions or inaction or the actions or inactions of our commercialization or collaboration partners, our counterparties may have the right to terminate these agreements, in which event we might not have the rights or the financial resources to develop, manufacture or market any product that is covered by these agreements. Such a failure to comply or breach by us under any of these agreements could also lead to a breach by us of the Novartis Agreement. Our counterparties also may have the right to convert an exclusive license to non-exclusive in the territory in which we fail to satisfy our diligence obligations, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or restated agreements with less favorable terms, seek alternative sources of financing or cause us to lose our rights under these agreements, including our rights to Fovista, Zimura and other important intellectual property or technology. Any of the foregoing could prevent us from commercializing Fovista, Zimura or other product candidates we may develop, which could have a material adverse effect on our operating results and overall financial condition.

In addition to the generally applicable diligence obligations set forth above, we have specific obligations with respect to the licensing agreements described below:

- Under the terms of the agreement with OSI Pharmaceuticals under which we acquired certain rights to develop and commercialize Fovista, if we or our commercialization or collaborative partners fail to meet certain obligations, OSI Pharmaceuticals may terminate the agreement as to such countries with respect to which such failure has occurred, and upon such termination we will be obligated to grant, assign and transfer to OSI Pharmaceuticals specified rights and licenses related to our anti-PDGF aptamer technology and other related assets, and if we are manufacturing such anti-PDGF products at the time of such termination, may be obligated to provide transitional supply to OSI Pharmaceuticals of covered anti-PDGF products, for such countries.

- Under the terms of the amended license, manufacturing and supply agreement with Nektar, pursuant to which we obtained, among other licenses, an exclusive, worldwide license to make, develop, use, import, offer for sale and sell certain products that incorporate a specified PEG reagent linked with the active ingredient in Fovista, if we fail to use commercially reasonable efforts to achieve the first commercial sale of Fovista in the United States by June 30, 2018, we and Nektar may agree in good faith to extend such date in specified circumstances. If such date is not extended, Nektar may either terminate our license or convert our license for such country to a non-exclusive license. In addition, if we fail to use commercially reasonable efforts to develop Fovista and file and seek approval of new drug applications on a schedule permitting us to make first commercial sales of Fovista in specified countries by June 30, 2019, do not make such first commercial sales of Fovista by such date, or thereafter fail to use commercially reasonable efforts to continue to commercialize and market Fovista in such countries, we would be in material breach of the agreement and Nektar would have the right to terminate the agreement.

In addition to the above risks, certain of our intellectual property rights are sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. For example, the licenses from Archemix include sublicenses to us of rights to specified technology, which we refer to as the SELEX technology, licensed by University License Equity Holdings, Inc. to Gilead Sciences, Inc., or Gilead, and sublicensed by Gilead to Archemix, as well as other technology owned by Gilead and licensed to Archemix. In addition, the licenses we have obtained from Nektar include sublicenses of certain rights. Should our licensors or any of their upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize Fovista, Zimura and other product candidates may be materially harmed and could also lead to a breach by us of the Novartis Agreement. While the applicable agreements may contain contractual provisions that would in many instances protect our rights as a sublicensee in these circumstances, these provisions may not be enforceable and may not protect our rights in all instances. Further, we do not have the right to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and their upstream licensors, which may not be forthcoming. Our business could be materially adversely affected if we are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively.

Risks Related to Our Intellectual Property

The patent prosecution process is expensive and time-consuming, is highly uncertain and involves complex legal and factual questions. 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.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing in the United States and in certain foreign jurisdictions patent applications related to our novel technologies and product candidates that are important to our business.

The patent prosecution process is expensive and time-consuming, and we 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 addition, we may not pursue or obtain patent protection in all major markets. Moreover, in some circumstances, we do not have the right to control the preparation, filing or prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties or covering technology that a collaboration or commercialization partner may develop, the eventual commercialization of which could potentially entitle us to royalty payments. In some circumstances, our licensors have the right to enforce the licensed patents without our involvement or consent, or to decide not to enforce or to allow us to enforce the licensed patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights that we have licensed may be reduced or eliminated and our ability to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign jurisdictions may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. 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 be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Moreover, the U.S. Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, term, enforceability and commercial value of our patent rights are highly uncertain.

Our pending and future patent applications, and any collaboration or commercialization partner's 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 or their ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We or any collaboration or commercialization partner 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 or other countries may diminish the value of our or a collaboration or commercialization partner's patents or narrow the scope of our or their patent protection.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation and switch the U.S. patent system from a "first-to-invent" system to a "first-to-file" system. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. 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. 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, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. Based on available information, we believe that *inter partes* review proceedings, brought by financial investors who may be selling short the stock of the patent holder, are becoming more prevalent. 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 product candidates.

If we are unable to obtain and maintain patent protection for our technology and products during the period of their commercialization, or if the scope of the patent protection is not sufficiently broad, 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 adversely affected.

The last to expire of the U.S. patent rights covering the composition of matter of Fovista expired in early 2017, which is well in advance of any marketing approval we may ultimately receive for Fovista. We own an issued U.S. patent covering methods of treating wet AMD with Fovista in combination with Avastin or Lucentis, which is expected to expire in 2024. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent restoration term of up to five years as partial compensation for patent term effectively lost during product development and the FDA regulatory review process occurring after the issuance of a patent. We may be able to obtain a patent term extension for this U.S. patent. The European patent rights covering the composition of matter of Fovista are expected to expire in 2018. Such expiration date is before the date by which we expect Fovista to be commercialized in Europe. We own a granted European patent covering a combination of Fovista and Lucentis or Avastin for use in a method for treating wet AMD. This European patent is expected to expire in 2024. Similar to the patent term restoration available in the United States, the regulatory framework in the European Union and certain other foreign jurisdictions provides the opportunity to extend the term of a patent that covers an approved drug in certain circumstances. Notwithstanding the availability of patent term extension or restoration provisions, we may not be granted patent term extensions 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 applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term or scope of any such extension is less than we request, any period during which we have the right to exclusively market our product would be shorter than we would otherwise expect, and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

In addition to the patents described above, we also have filed patent applications in the United States covering a method of treating wet AMD in patients with Fovista in combination with Eylea and patent applications in Europe and Japan covering a combination of Fovista and Eylea for use in a method for treating wet AMD. We also have filed patent applications in the United States, Europe, Japan and elsewhere covering our formulation for Fovista. These patent applications are in the early stages of prosecution and may not result in patents being issued that protect the use of Fovista in combination with Eylea for treating wet AMD, that protect our formulation for Fovista or that effectively prevent others from commercializing competitive technologies and products. If a patent is granted following prosecution of any such application for the combination of Fovista and Eylea, the latest projected patent expiry, absent any patent term adjustment or extension or patent restoration, would be in 2030. If a patent is granted following prosecution of any such application for our formulation for Fovista, the latest projected patent expiry, absent any patent term adjustment or extension or patent restoration, would be in 2034.

Method-of-treatment patents are more difficult to enforce than composition-of-matter patents because of the risk of off-label sale or use of a drug for the patented method. 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. Off-label sales of other products having the same API as Fovista, Zimura or any other product candidates we may develop would limit our ability to generate revenue from the sale of Fovista, Zimura or such other product candidates, if approved for commercial sale. In addition, European patent law generally makes the issuance and enforcement of patents that cover methods of treatment of the human body difficult. Further, once the composition-of-matter patents relating to Fovista, Zimura or any other product candidate in a particular jurisdiction, if any, expire, competitors will be able to make, offer and sell products containing the same API as Fovista, Zimura or such other product candidate in that jurisdiction so long as these competitors do not infringe any other of our patents covering Fovista's or Zimura's composition of matter or method of use or manufacture, do not violate the terms of any marketing or data exclusivity that may be granted to us by regulatory authorities and obtain any necessary marketing approvals from applicable regulatory authorities. In such circumstances, we also may not be able to detect, prevent or prosecute off-label use of such competitors' products containing the same API as Fovista or Zimura in combination with any anti-VEGF drug, even if such use infringes any of our method-of-treatment patents.

The Hatch-Waxman Act also permits the manufacture, use, offer for sale, sale or importation of a patented invention other than a new animal drug or veterinary biological product, if the manufacture, use, offer for sale, sale or importation is solely for uses that are reasonably related to development of information that could be submitted to the FDA. For this reason, our competitors might be able under certain circumstances to perform activities within the scope of the U.S. patents that we own or under which we are licensed without infringing such patents. This might enable our competitors to develop during the lifetime of these patents drugs that compete with Fovista or Zimura, if approved.

The U.S. patent rights covering Zimura as a composition of matter are expected to expire in 2025. Such expiration date may be prior to the date by which we would be able to commercialize Zimura in the United States if we seek and obtain marketing approval. The U.S. patent rights covering methods of treating certain complement protein mediated disorders with Zimura are expected to expire in 2026. As a result, if we obtain marketing approval for Zimura, we may not be able to exclude competitors from commercializing products similar or identical to ours if such competitors do not use or promote our claimed methods of treatment or do use or promote our methods of treatment after our patents expire. Depending on potential delays in the regulatory review process for Zimura, we may be able to obtain a patent term extension for one of these patents in the United States, but we can provide no assurances that such an extension will be obtained.

Our issued patents may not be sufficient to provide us with a competitive advantage. For example, competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Even if our owned or licensed patent applications issue as patents, they may not issue with a scope broad enough to provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. We could also fail to take the required actions and pay the necessary governmental fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, term, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example,

if we receive marketing approval for our product candidates, other pharmaceutical companies may seek approval of generic versions of our products with the FDA or regulatory authorities in other jurisdictions. We may then be required to initiate proceedings against such companies in order to enforce our intellectual property rights. The risk of being involved in such proceedings is likely to increase if our products are commercially successful. In any such proceedings, the inventorship, ownership, scope, term, validity and enforceability of our patents may be challenged. These and other challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to prevent others from using or commercializing similar or identical technology and products or from launching generic versions of our products, or could limit the duration of the patent protection of our technology and products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for our product, which could have a material adverse effect on our business. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable. 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 or otherwise violating 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 and the ability of our collaboration and commercialization partners to develop, manufacture, market and sell our product candidates and products and use our proprietary technologies without infringing or otherwise violating the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We or our collaboration and commercialization partners may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, re-examination, post-grant review, *inter partes* review, opposition, cancellation or similar proceedings before the USPTO or its foreign counterparts. The risks of being involved in such litigation and proceedings may also increase as our or their product candidates near commercialization. Third parties may assert infringement claims against us or our collaboration or commercialization partners based on existing or future intellectual property rights. We or they may not be aware of all such intellectual property rights potentially relating to our product candidates and their manufacture and uses. Thus, we do not know with certainty that Fovista, Zimura or any other product candidate, or our intended commercialization thereof, does not and will not infringe or otherwise violate any third party's intellectual property.

If we are or one of our collaboration or commercialization partners is found to infringe or otherwise violate a third party's intellectual property rights, we or they could be required to obtain a license from such third party to continue developing and marketing our or their products and technology or to continue using a trademark. However, we or our collaboration and commercialization partners may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or they were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our collaboration and commercialization partners and could require us or them to make substantial licensing and royalty payments. We or our collaboration and commercialization partners 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 or other intellectual property right. A finding of infringement could prevent us or our collaboration and commercialization partners from commercializing our or their product candidates or force us or them to cease some of our business operations, which could materially harm our business. Claims that we or our collaboration and commercialization partners have misappropriated the

confidential information or trade secrets of third parties could expose us or them to similar liabilities and have a similar negative impact on our business.

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

Many of our employees and contractors were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or contractors have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or contractor'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 conception or 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 conceives or develops intellectual property that we regard as our own. Moreover, because we acquired rights to Fovista from Eyetech, Archemix and Nektar and rights to Zimura from Archemix, we must rely upon these parties' and their successors' practices, and those of their predecessors, with regard to the assignment of intellectual property therein. 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.

Intellectual property litigation could cause us to spend substantial resources and could 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 have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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 some of our technology and products, we also rely upon 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. We cannot guarantee that we have executed such agreements with each party that may have or have had access to our trade secrets. Moreover, because we acquired certain rights to Fovista from Eyetech, Archemix and Nektar, we must rely upon these parties' and their successors' practices, and those of their predecessors, with regard to the protection of Fovista-related trade secrets before we acquired them. Any party with whom we or they have executed a non-disclosure and confidentiality agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our proprietary information may also be obtained by third parties by other means, such as breaches of our physical or computer security systems.

Detecting the disclosure or misappropriation of a trade secret and 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 marketing 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 are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue would be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and by the EMA and comparable regulatory agencies in other countries.

In general, the FDA and similar regulatory authorities outside the United States require two adequate and well controlled clinical trials demonstrating safety and effectiveness for marketing approval for an ophthalmic pharmaceutical product. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market Fovista, Zimura or any other product candidate from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely upon third-party CROs and, in the case of Fovista, Novartis, to assist us in this process. Securing marketing approval requires obtaining positive safety and efficacy data from required clinical trials, as well as 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 efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authorities. The FDA or other regulatory authorities may determine that Fovista, Zimura or any other product candidate that we may develop is not effective, is only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. The FDA or other regulatory authority may limit the approval of Fovista or Zimura to use with only specified anti-VEGF drugs rather than with all anti-VEGF drugs. Such limitation could limit sales of Fovista or Zimura.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. 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. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are 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 ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Marketing approval of novel product candidates such as Fovista and Zimura manufactured using novel manufacturing processes can be more expensive and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical products, due to regulatory agencies' lack of experience with them. We believe that the FDA has only granted marketing approval for one aptamer product to date. This lack of experience may lengthen the regulatory review

process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we fail to obtain approval of Fovista, Zimura or any other product candidate that we develop, the commercial prospects for such product candidate may be harmed and our ability to generate revenues would be materially impaired.

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

In order to market and sell our product candidates in the European Union and many other jurisdictions, we or our third-party commercialization partners, including Novartis, our ex-U.S. commercialization partner for Fovista, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional preclinical or clinical 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 approved for sale in that country. We or our third-party commercialization partners, including Novartis, our ex-U.S. commercialization partner for Fovista, 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. We and our third-party commercialization partners may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

A fast track designation or grant of priority review status by the FDA may not actually lead to a faster development or regulatory review or approval process. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

In the United States, our lead product candidate, Fovista, received fast track designation and may be eligible for priority review status. If a drug is intended for the treatment of a serious or life-threatening disease or condition and the drug demonstrates the potential to address unmet medical needs for this disease or condition, the drug sponsor may apply for FDA fast track designation. If a drug offers major advances in treatment, the drug sponsor may apply for FDA priority review status. The FDA has broad discretion whether or not to grant fast track designation or priority review status, so even if we believe a particular product candidate is eligible for such designation or status the FDA could decide not to grant it. Even though Fovista has received fast track designation for the treatment of wet AMD and may be eligible for priority review status, we may not experience a faster development process, review or approval compared to conventional FDA procedures.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates would receive marketing approval.

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interactions and communications between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we or our third-party commercialization partners may be subject to penalties if we or our third-party commercialization partners fail to comply with regulatory requirements or if we or our third-party commercialization partners experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we or our commercialization partners obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control and quality assurance, complaints and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or may be subject to significant conditions of approval or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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 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;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- 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;
- injunctions or the imposition of civil or criminal penalties; and
- 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 and our commercialization partners' relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us and our commercialization partners to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates, including Fovista, for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us and our commercialization partners 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 and our commercialization partners market, sell and distribute any products for which we or they 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 drugs 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 drug 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 or our commercialization partners' operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us or them, we or they 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 or their 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 collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our and any commercialization partner's ability to generate revenue from, sell profitably or commercialize any product candidates 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 a commercialization partner receives for any approved product.

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 ACA. Among the provisions of the ACA 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 drugs 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 drugs 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 drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability 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 drug 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 drugs; and

- establishment of 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 ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, 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 ACA, 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 ACA. 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 ACA 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 ACA provisions is highly uncertain in many respects, and it is possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions.

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.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to

promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

If we or our third-party manufacturers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We and our third-party manufacturers 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 and flammable materials, including chemicals and biological materials, and produce hazardous waste products. 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 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 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 our 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 Our Operations

We are in the process of implementing a substantial reduction in personnel, which could disrupt our operations. In addition, we may experience difficulties in retaining key employees that we have identified for retention.

In December 2016, following our receipt and announcement of initial, top-line results from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we announced that we had determined to implement a reduction in personnel to focus on an updated business plan. This reduction in personnel is expected to involve approximately 80% of our workforce and will include personnel from nearly every department. We expect the reduction in personnel to be substantially complete during the first and second quarters of 2017. Although we are reducing our personnel substantially, we are continuing to function as a development company and need to continue all or nearly all of our prior business functions to support such development, including clinical operations, regulatory affairs, drug safety, data management, outsourced manufacturing and supply chain and quality assurance, as well as all of our general and administrative functions and public company infrastructure. Due to our limited financial resources and the inherent challenges associated with managing such a reduction in personnel, we may not be able to manage effectively the reduction in personnel and transition of operations to remaining employees. In addition, as part of implementing our reduction in personnel, we have issued notices of termination under our existing office leases, each of which now is scheduled to terminate in late 2017 or early 2018. It is possible that we may not be able to find suitable replacement office space for our remaining employees on acceptable terms, or at all, which could harm our operating results and/or materially disrupt our operations.

Notwithstanding the reduction in personnel, we remain highly dependent on David R. Guyer, M.D., our Chief Executive Officer, and Glenn P. Sblendorio, our President and Chief Financial Officer, as well as the other principal members of our management, scientific and clinical teams. We do not maintain "key person" insurance for any of our executives or other employees. Although we have entered into letter agreements with our executive officers, each of them and our non-executive employees may terminate their employment with us at any time. As a result, key employees that we expect to retain through specific dates to assist with transition activities may choose not to remain employees. In addition, we may experience difficulties in retaining key employees that we have identified for retention, given the change in prospects for our company as well as other challenges. 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 updated business strategy. Furthermore, replacing any such 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 marketing 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, if at all, 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 strategically attract or retain high quality personnel as we implement our new business plan, our ability to pursue our development strategy would be limited.

In connection with the reduction in personnel, we estimate that we will incur approximately $14.4 million of pre-tax charges during the first and second quarters of 2017, of which approximately $12.3 million is expected to result in future cash expenditures, representing a significant cost in relation to our remaining limited resources. Moreover, the reduction in personnel may divert our management's time and attention. Any inability to manage the reduction in personnel could delay the execution of our updated business plan or disrupt our operations.

If we fail to establish and maintain effective internal control over financial reporting, our ability to accurately report our financial results could be adversely affected.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements would not be prevented or detected on a timely basis. If any material weakness in our internal control over financial reporting is discovered or occurs in the future, our financial statements may contain material misstatements and we could be required to restate our financial results. As previously disclosed in July 2015, our management concluded that we experienced a material weakness in internal controls related to technical accounting expertise over the accounting for deferred tax assets and income tax accounting in general during certain prior financial reporting periods. The deficiency in the application of our controls relating to technical accounting expertise over the accounting for deferred tax assets and income tax accounting in general resulted in the audit committee of our board of directors concluding that the relevant financial statements should not be relied upon, and our subsequent restatement of the relevant financial statements.

During the year ended December 31, 2015, we took the following steps to remediate the identified material weakness: we added staffing within our finance department and engaged a nationally recognized accounting firm, in each case, with technical expertise in the area of tax accounting and financial reporting. Our management concluded that the identified material weakness in internal control over financial reporting was fully remediated as of December 31, 2015. Although we have remediated this deficiency in internal control over financial reporting, we cannot be certain that the remedial measures that we took in the past or other measures we take in the future, especially in light of our decreased size as a result of the implementation of our planned reduction in personnel, and the associated decrease in staffing in our accounting and finance areas, will ensure that we maintain adequate controls over our financial reporting going forward and, accordingly, additional material weaknesses could occur or be identified. Any additional material weaknesses or combination of deficiencies could materially and adversely affect our ability to provide timely and accurate financial information, and the current and future deficiencies may impact investors' confidence in our internal controls and our company, which could cause our stock price to decline.

Risks Related to Information Technology

We rely significantly upon information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

In the ordinary course of our business, we and our third-party contractors maintain sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential business information relating to our business and that of our clinical trial participants and business partners. In particular, we rely on contract research organizations and other third parties to store and manage information from our clinical trials, including our Fovista Phase 3 clinical program. The secure maintenance of this sensitive information is critical to our business and reputation. Despite the implementation of security measures, our internal computer systems and those of our third-party contractors are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. In particular, we believe that companies and other entities and individuals have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access to systems and information. These threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack. Cyber threats may be generic, or they may be custom-crafted against our information systems or those of our third-party contractors. For information stored with our third-party contractors, we rely upon, and the integrity and confidentiality of such information is dependent upon, the risk mitigation efforts such third-party contractors have in place. In the recent past, cyber-attacks have become more prevalent and much harder to detect and defend against. Our and our third-party contractors' respective network and storage applications may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. It is often difficult to anticipate or immediately detect such incidents and the damage caused by such incidents. System failures, data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. System failures or accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. A data security breach could also lead to public exposure of personal information of our clinical trial patients and others. Cyber-attacks could cause us to incur significant remediation costs, result in product development delays, disrupt key business operations and divert attention of management and key information technology resources. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate public disclosure of confidential or proprietary information, we could incur liability and our product research, development and commercialization efforts could be delayed.

Risks Related to Our Common Stock

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, 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 by-laws 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 the 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 certain provisions of our certificate of incorporation or by-laws.

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.

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

Our stock price may be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares of common stock at or above the price at which they purchased their shares. The market price for our common stock may be influenced by many factors, including:

- the success of products or technologies that compete with our product candidates, including results of clinical trials of product candidates of our competitors;
- results of clinical trials for our product candidates and the timing of the receipt of such results;
- the results of our efforts to in-license or acquire the rights to other products, product candidates and technologies for the treatment of ophthalmic diseases;
- political, 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 personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- 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;
- 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.

For example, following our announcement of initial, top-line results from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, the closing price of our common stock declined from $38.77 on December 9, 2016 to $5.29 on December 12, 2016. In addition, following the announcement by Regeneron on September 30, 2016 that its co-formulated anti-PDGF/Eylea product candidate failed to meet the primary endpoint of a Phase 2 clinical trial at 12 weeks, the closing price of our common stock declined from $54.12 on September 28, 2016 to $30.85 on November 3, 2016. Following periods of volatility in the market price of a company's stock, securities class-action litigation has often been instituted against

that company. We and certain of our current and former executive officers have been named as defendants in a purported class action lawsuit following our announcement of the initial, top-line results. See “Part II, Item 1-Legal Proceedings” and “-Risks Related to Our Updated Business Plan, Financial Position and Need for Additional Capital-We and certain of our current and former executive officers have been named as defendants in a lawsuit that could result in substantial costs and divert management’s attention.” This proceeding and other similar litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources, which could seriously harm our business.

If a significant portion of our total outstanding shares are sold into the market, the market price of our common stock could drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Moreover, we have filed registration statements on Form S-8 registering all shares of common stock that we may issue under our equity compensation plans. Once registered on Form S-8, shares underlying these equity awards can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates.

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

As a public company, we incur and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Select 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 have made some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish with our periodic Exchange Act reports a report by our management on our internal control over financial reporting. We are also required to include with our annual report an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we must 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 and engage outside consultants 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. There is a risk that our internal control over financial reporting may, in the future, be found to be ineffective under Section 404. Our identification of one or more material weaknesses 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 common 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 common 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 any future debt agreements may preclude us from paying dividends. 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 properties consist of office space in New York, New York and Princeton, New Jersey. We lease approximately 22,400 square feet of office space in New York, New York under a lease that terminates in January 2018. In Princeton, New Jersey, we lease approximately 35,200 square feet of office space for our primary Princeton location under a sublease that terminates in April 2018, and approximately 1,800 square feet of office space under a lease that expires in October 2017.

Item 3. Legal Proceedings

A purported class action lawsuit has been filed against us and certain of our current and former executive officers in the United States District Court for the Southern District of New York, captioned Frank Micholle et al. v. Ophthotech Corporation, et al., No. 1:17-cv-00210, filed on January 11, 2017. The complaint purports to be brought on behalf of shareholders who purchased our common stock between May 11, 2015 and December 12, 2016. The complaint generally alleges that we and certain of our officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the prospects of our Phase 3 trials for Fovista in combination with anti-VEGF drugs for the treatment of wet AMD. The complaint seeks equitable and/or injunctive relief, unspecified damages, attorneys' fees, and other costs. We deny any allegations of wrongdoing and intend to vigorously defend against this lawsuit. We are unable, however, to predict the outcome of this matter at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business.

Item 4. Mine Safety Disclosures

None.

PART II

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

Our common stock has been publicly traded on The NASDAQ Global Select Market under the symbol "OPHT" since September 25, 2013. The following table sets forth the high and low sale prices per share for our common stock on The NASDAQ Global Select Market for the periods indicated:

	Year ended December 31, 2016		Year ended December 31, 2015	
	High	Low	High	Low
Quarter ended March 31,	$ 74.07	$ 40.40	$ 58.29	$ 44.30
Quarter ended June 30,	$ 58.45	$ 41.84	$ 53.17	$ 44.55
Quarter ended September 30,	$ 65.03	$ 46.13	$ 72.51	$ 35.72
Quarter ended December 31,	$ 45.30	$ 4.82	$ 80.00	$ 37.45

Holders

As of January 31, 2017, there were approximately 112 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.

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

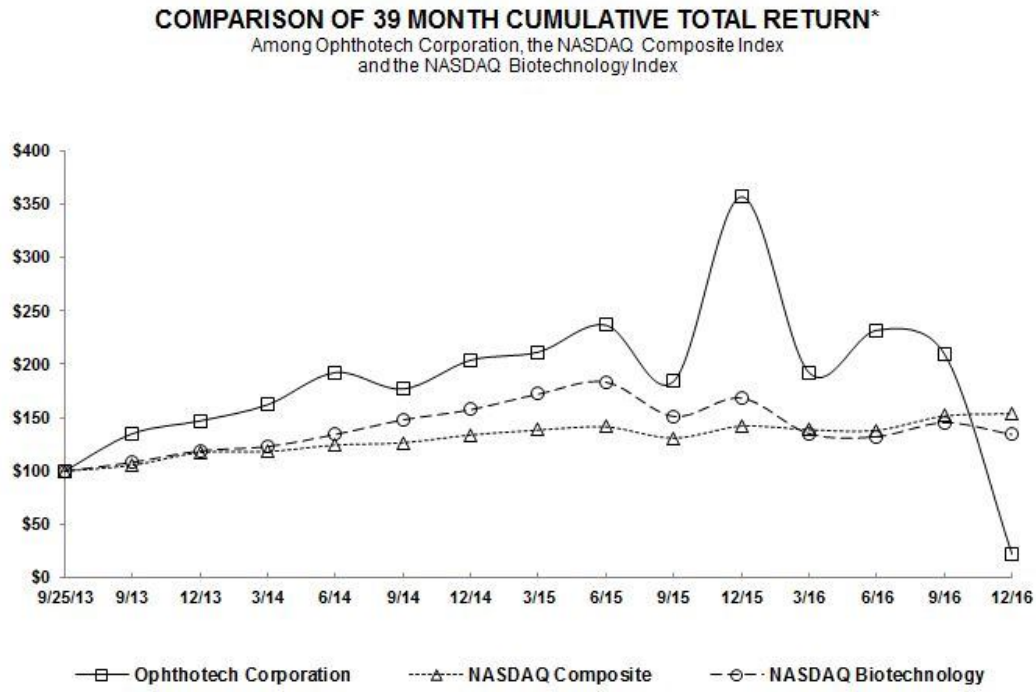
There were no issuances of equity securities that were not registered under the Securities Act of 1933, as amended, or the Securities Act, during the period covered by this Annual Report on Form 10-K.

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.

Stock Performance Graph

The following graph and chart compares the cumulative annual stockholder return on our common stock over the period commencing September 25, 2013 and ending on December 31, 2016, to that of the total return for the NASDAQ Composite Index and the NASDAQ Biotechnology Index, assuming an investment of $100 on August 31, 2013. In calculation cumulative total annual stockholder return, reinvestment of dividends, if any, is assumed. The indices are included for comparative purposes only. They do not necessarily reflect management's opinion that such indices are an appropriate measure of the relative performance of our common stock and are not intended to forecast or be indicative of future performance of our common stock. The following graph and related information shall not be deemed "soliciting material" or to be "filed: with the Securities and Exchange Commission, nor shall such information be incorporated by reference in any of our filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. We obtained information used on the graph from Research Data Group, Inc., a source we believe to be reliable.



* $100 invested on September 25, 2013 in stock or August 31, 2013 in index, including reinvestment of dividends.

	9/25/2013	9/30/2013	12/31/2013	3/31/2014	6/30/2014	9/30/2014	12/31/2014	3/31/2015
Ophthotech Corporation	$ 100.00	$ 135.05	$ 147.05	$ 162.16	$ 192.32	$ 176.95	$ 203.95	$ 211.50
NASDAQ Composite	100.00	105.46	117.13	118.23	124.11	126.29	133.19	137.78
NASDAQ Biotechnology	100.00	108.52	118.51	122.37	133.81	147.15	156.52	171.61

	6/30/2015	9/30/2015	12/31/2015	3/31/2016	6/30/2016	9/30/2016	12/31/2016
Ophthotech Corporation	$ 236.64	$ 184.18	$ 356.95	$ 192.14	$ 231.95	$ 209.68	$ 21.95
NASDAQ Composite	140.65	130.11	141.32	138.82	138.21	151.71	153.66
NASDAQ Biotechnology	181.93	149.90	166.10	135.14	132.26	145.41	134.22

Use of Proceeds from Registered Securities

On September 30, 2013, we closed our initial public offering of 8,740,000 shares of our common stock, including 1,140,000 shares of our common stock pursuant to the exercise by the underwriters of an over-allotment option, at a public offering price of $22.00 per share for an aggregate offering price of approximately $192.3 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-190643), which was declared effective by the SEC on September 24, 2013.

We received aggregate net proceeds from the offering of $175.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

As of December 31, 2016, we have used all of the $175.6 million in net proceeds from the offering as follows:

- approximately $136.9 million to fund certain costs of our Phase 3 clinical program for Fovista administered in combination with anti-VEGF drugs for the treatment of wet AMD, which costs consists of external research and development expenses and clinical development related employee expenses; and

- approximately $38.7 million for working capital and other general corporate purposes.

Other than payments related to executive officer and director compensation, all as described in our public filings, we have not used any of the net proceeds from the offering to make payments, directly or indirectly, to any director or officer of ours, or any of their associates, to any person owning 10 percent or more of our common stock or to any affiliate of ours.

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, 2014, 2013 and 2012 and the balance sheet data as of December 31, 2016, 2015, 2014, 2013 and 2012 from our audited financial statements, which have been audited by Ernst & Young LLP, an independent registered accounting firm. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our results for any interim period are not necessarily indicative of results to be expected for a full fiscal year.

	Years ended December 31,				
	2016	2015	2014	2013	2012
	(in thousands, except per share data)				
Statements of Operations Data:					
Collaboration revenue	$ 50,909	$ 51,505	$ 41,259	$ —	$ —
Operating expenses:					
Research and development	196,295	131,012	88,385	33,215	6,792
General and administrative	50,178	44,021	33,387	14,210	6,889
Total operating expenses	246,473	175,033	121,772	47,425	13,681
Loss from operations	(195,564)	(123,528)	(80,513)	(47,425)	(13,681)
Interest income (expense)	1,704	971	217	(1,454)	(507)
Loss on extinguishment of debt	—	—	—	(1,091)	—
Other income (expense)	34	53	—	(1,175)	(374)
Loss before income tax (benefit) provision	(193,826)	(122,504)	(80,296)	(51,145)	(14,562)
Income tax (benefit) provision	(406)	(16,787)	36,476	—	—
Net loss	(193,420)	(105,717)	(116,772)	(51,145)	(14,562)
Add: accretion of preferred stock dividends	—	—	—	(5,891)	(7,063)
Net loss attributable to common stockholders	$ (193,420)	$ (105,717)	$ (116,772)	$ (57,036)	$ (21,625)
Net loss per common share:					
Basic and diluted	$ (5.45)	$ (3.06)	$ (3.51)	$ (6.34)	$ (14.89)
Weighted average common shares outstanding:					
Basic and diluted	35,486	34,580	33,258	9,003	1,452

	As of December 31,				
	2016	2015	2014	2013	2012
	(in thousands)				
Balance sheets data:					
Cash, cash equivalents, and marketable securities	$ 289,278	$ 391,890	$ 463,560	$ 210,596	$ 4,304
Total assets	$ 299,630	$ 428,851	$ 479,786	$ 217,682	$ 4,879
Deferred revenue	$ 209,976	$ 213,066	$ 209,624	$ —	$ —
Royalty purchase liability	$ 125,000	$ 125,000	$ 125,000	$ 41,667	$ —
Total liabilities	$ 394,248	$ 368,904	$ 351,249	$ 47,962	$ 14,410
Additional paid-in capital	$ 504,517	$ 465,927	$ 428,390	$ 352,739	$ —
Accumulated deficit	$ (598,959)	$ (405,539)	$ (299,822)	$ (183,050)	$ (126,471)
Total stockholders' equity (deficit)	$ (94,618)	$ 59,947	$ 128,537	$ 169,720	$ (123,470)

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 specializing in the development of novel therapeutics to treat ophthalmic diseases, with a focus on diseases of the back of the eye. To date, our primary focus has been on developing therapeutics for age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina, known as the macula, that may result in blindness. Following our announcement in December 2016 that two of our three pivotal, Phase 3 clinical trials for Fovista® (pegpleranib), an anti-platelet derived growth factor, or PDGF, aptamer, in development for the treatment of wet AMD, failed to meet their primary endpoint, we initiated a plan to review our strategic alternatives in order to maximize shareholder value and implement an updated business plan. Without limiting any option, we plan to continue to focus on the development of product candidates for ophthalmic diseases, especially back of the eye disorders. We are actively exploring opportunities to obtain rights to additional products, product candidates and technologies to treat ophthalmic diseases. We are also currently continuing to develop our product candidate Zimura® (avacincaptad pegol), an inhibitor of complement factor C5, for the treatment of geographic atrophy, or GA, a form of dry AMD, and in combination with anti-VEGF drugs for the treatment of wet AMD, and are continuing our remaining Phase 3 Fovista clinical trial, OPH1004. We plan to reassess our existing Fovista and Zimura development programs throughout 2017 as the implementation of our updated business plan progresses and evolves, with the goal of aligning corporate resources in the context of a potentially broader product pipeline. We expect that our reassessment of our Fovista development program for the treatment of wet AMD will be primarily determined by the initial, top-line data from OPH1004 and that our reassessment of our Zimura development program may be particularly affected by the results of a competitor's Phase 3 clinical trial of a complement inhibitor being studied for the treatment of GA. Data from both our OPH1004 trial and our competitor's Phase 3 trial for the treatment of GA are expected during the second half of 2017. As a result of this reassessment, we may modify, expand or terminate some or all of our development programs or clinical trials at any time. We generally expect that we will not engage in internal early stage research and drug discovery and will thus avoid the related costs and risks of these activities.

In December 2016, we announced initial, top-line data from two pivotal clinical trials, which we refer to as OPH1002 and OPH1003, evaluating the safety and efficacy of 1.5mg of Fovista administered in combination with monthly 0.5mg Lucentis® (ranibizumab) anti-VEGF therapy compared to monthly Lucentis monotherapy for the treatment of wet AMD. The current standard of care for wet AMD is monotherapy targeting vascular endothelial growth factor, referred to as anti-VEGF therapy. The pre-specified primary endpoint of mean change in visual acuity at 12 months was not achieved for either OPH1002 or OPH1003. Moreover, we have not observed any clinically meaningful visual benefit when 1.5mg of Fovista was added to a monthly regimen of 0.5mg Lucentis therapy for any subgroup of patients that we have analyzed from the OPH1002 and OPH1003 trials, including subgroups based on baseline visual acuity, baseline lesion size or the baseline amount of the classic component of choroidal neovascularization, or CNV. Following the December 2016 data announcement, we

subsequently stopped treating patients in, and terminated, both the OPH1002 and OPH1003 trials. OPH1004, our remaining Phase 3 clinical trial, which is evaluating the safety and efficacy of 1.5 mg of Fovista administered in combination with 2.0mg Eylea® (afilbercept) or 1.25mg Avastin® (bevacizumab) anti-VEGF therapy compared to Eylea or Avastin monotherapy for the treatment of wet AMD, remains ongoing, with initial, top-line data expected to be available during the second half of 2017. The failure of OPH1002 and OPH1003 to show any clinically meaningful visual benefit in adding 1.5mg of Fovista to a monthly regimen of 0.5mg of Lucentis and the recent failure of a competitor's Phase 2 trial investigating the combination of a PDGF inhibitor and a VEGF inhibitor, may be indicative of a low likelihood of success for OPH1004. In light of the data from the OPH1002 and OPH1003 trials, we have also stopped treating patients in our additional Phase 2 clinical trials that were evaluating the potential additional benefits of Fovista administered in combination with anti-VEGF drugs in wet AMD patients, which we previously referred to collectively as the Fovista Expansion Studies.

There are two forms of AMD, dry AMD and wet AMD. Dry AMD can progress to wet AMD. Although dry AMD is the most common form of AMD, there are no therapies approved by the U.S. Food and Drug Administration or European Medicines Agency to treat this condition. We are currently developing our product candidate Zimura as a monotherapy for the treatment of GA, a form of dry AMD, as well as in combination with anti-VEGF drugs for the treatment of wet AMD. Zimura is an inhibitor of complement factor C5, a protein that is associated with complement mediated inflammation and cell damage, which we believe may be involved in the development and progression of dry AMD and wet AMD. We have completed a multicenter, uncontrolled, open-label Phase 1/2a clinical trial of Zimura monotherapy for the treatment of GA, a multicenter, uncontrolled, open-label, ascending dose and parallel group Phase 1/2a clinical trial of Zimura administered in combination with Lucentis for the treatment of wet AMD and a very small, uncontrolled, open-label Phase 2 clinical trial investigating Zimura's potential role when administered in combination with anti-VEGF drugs for the treatment of polypoidal choroidal vasculopathy, or PCV, which is a specific type of wet AMD, in patients who do not respond adequately to treatment with anti-VEGF monotherapy or for whom anti-VEGF monotherapy fails. Currently, we have the following ongoing clinical trials for Zimura:

- *Zimura Phase 2a Wet AMD Study*. During the fourth quarter of 2015, we initiated an open-label Phase 2a clinical trial to evaluate Zimura's potential role when administered in combination with anti-VEGF therapy for the treatment of wet AMD in patients who do not respond adequately to treatment with anti-VEGF monotherapy. We plan to enroll up to approximately 60 patients in this trial, and may include patients with PCV. Recruitment of patients in this study is ongoing.

- *Zimura Phase 2/3 GA Study*. During the fourth quarter of 2015, we initiated a randomized, double-masked, controlled Phase 2/3 clinical trial to evaluate the safety and efficacy of Zimura monotherapy in patients with GA. Recruitment of patients in this study is ongoing.

We remain very early in the recruitment phase for both of our ongoing Zimura clinical trials.

In early 2017, we engaged a financial advisor and initiated a plan to review our strategic alternatives in order to maximize shareholder value following the failure of two of our three pivotal Fovista trials. Without limiting any option, the principal focus of this plan, based on our deep expertise and experience in ophthalmology, is to actively explore obtaining rights to additional products, product candidates and technologies to treat ophthalmic diseases, particularly those of the back of the eye. We are particularly interested in obtaining rights to product candidates for ocular indications with a high unmet medical need. We believe that with our expertise and experience in ophthalmology we are well positioned to explore and critically evaluate a variety of opportunities. We also believe that our focus on diseases of the eye and our experienced management team will make us an attractive collaborator or acquirer for companies seeking to out-license or sell rights to products, product candidates or technologies. As part of our updated business plan, we are also reviewing whether there is any scientific rationale for potentially developing our current product candidates, Fovista and Zimura, in one or more other ophthalmic indications where there is a high unmet need. As part of our strategic review, we may also consider other alternatives, including the acquisition of products, product candidates or technologies or other assets outside of ophthalmology, mergers or other transactions involving our company as a whole, collaboration transactions, or the license, sale or divestiture of some of our assets or technologies. We cannot be sure when or if this strategic review process will result in any type of transaction. As of December 31, 2016, we had $289.3 million in cash, cash equivalents, and marketable securities, of which approximately $100 million to $115 million is committed to the wind-down of OPH1002 and OPH1003 and the Fovista Expansion Studies, implementation of a previously announced reduction in personnel and related costs, cancellation fees related to manufacturing commitments, and obtaining initial, top-line data for the OPH1004 trial during the second half of 2017.

Novartis Agreement

In May 2014, we entered into a licensing and commercialization agreement with Novartis Pharma AG, which we refer to as the Novartis Agreement. Under the Novartis Agreement, we granted Novartis exclusive rights under specified patent rights, know-how and trademarks controlled by us to manufacture, from bulk active pharmaceutical ingredient, or API, supplied by us, standalone Fovista products and products combining Fovista with an anti-VEGF drug to which Novartis has rights in a co-formulated product, for the treatment, prevention, cure or control of any human disease, disorder or condition of the eye, and to develop and commercialize those licensed products in all countries outside of the United States, which we refer to as the Novartis Territory. We agreed to use commercially reasonable efforts to complete our ongoing pivotal Phase 3 clinical program for Fovista and Novartis agreed to use commercially reasonable efforts to develop a standalone Fovista product and a co-formulated product containing Fovista and an anti-VEGF drug to which Novartis has rights, as well as a pre- filled syringe presentation of such products and to use commercially reasonable efforts, subject to obtaining marketing approval, to commercialize licensed products in the Novartis Territory in accordance with agreed development and marketing plans.

Novartis paid us a $200.0 million upfront fee upon execution of the Novartis Agreement. Novartis also paid us $50.0 million upon the achievement of each of two patient enrollment-based milestones, and $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate of $130.0 million. Under the terms of the Novartis Agreement, Novartis is also obligated to pay us up to an aggregate of an additional $300.0 million upon achievement of specified regulatory milestones, including marketing approval and reimbursement approval in certain countries in the Novartis Territory. In addition, Novartis has agreed to pay us up to an aggregate of an additional $400.0 million if Novartis achieves specified sales milestones in the Novartis Territory. Novartis also is obligated to pay us royalties with respect to standalone Fovista products and combination Fovista products that Novartis successfully commercializes. We will receive royalties at a mid-thirties percentage of net sales of standalone Fovista products and a royalty of approximately equal value for sales of combination Fovista products. Such royalties are subject to customary deductions, credits, and reductions for lack of patent coverage or market exclusivity. Novartis's obligation to pay such royalties will continue on a licensed product-by-licensed product and country-by-country basis until Novartis's last actual commercial sale of such licensed product in such country. We will continue to be responsible for royalties we owe to third parties on sales of Fovista products.

We retained control over the design and execution of our pivotal Phase 3 clinical program for Fovista and remain responsible for funding the costs of that program, subject to Novartis's responsibility to provide Lucentis, an anti-VEGF drug to which Novartis has rights in the Novartis Territory, for use in the Phase 3 trials already initiated and in other Phase 2 and Phase 3 clinical trials in the Novartis Territory initiated following the effective date of the Novartis Agreement. Novartis will have control over, and will be responsible for the costs of, all other clinical trials that may be required to obtain marketing approvals in the Novartis Territory for licensed products under the agreement. Novartis is also responsible for costs associated with co-formulation development, pre-filled syringe development and other development costs in the Novartis Territory, but excluding regulatory filing fees in the European Union for the standalone Fovista product, for which we will be responsible.

In November 2015, we were informed by Novartis that Genentech, Inc., a Roche wholly-owned subsidiary, elected to exercise its option to participate in the financial arrangements relating to Novartis' rights under the Novartis Agreement. Roche's option originated from a pre-existing agreement between Roche and Novartis. The ex-U.S. commercialization agreement between Ophthotech and Novartis and its financial terms remained unchanged as a result of the exercise of the opt- in right. We continue to retain sole rights to Fovista in the United States.

Overview of Funding History and Requirements

We were incorporated and commenced active operations in 2007. Our operations to date have been primarily limited to organizing and staffing our company, acquiring rights to product candidates, business planning, raising capital and developing Fovista and Zimura. We acquired our rights to Fovista from (OSI) Eyetech, Inc., or Eyetech, in July 2007. The acquisition included an assignment of license rights and obligations under an agreement with Archemix Corp. We have licensed rights to our product candidate Zimura from Archemix Corp. Since inception, we have incurred significant operating losses. As of December 31, 2016, we had an accumulated deficit of $599.0 million. Our net loss was $193.4 million for the year ended December 31, 2016, and $105.7 million for the year ended December 31, 2015, and we expect to continue to incur significant operating losses in 2017. We have not generated any revenues from product sales and have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, funding under our royalty purchase and sale agreement with Novo A/S, which we refer to as the Novo Agreement, our initial public

offering of common stock, which we closed in September 2013, our follow-on public offering of common stock, which we closed in February 2014, and funds we received under the Novartis Agreement. We received net proceeds from our initial public offering of $175.6 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. We received net proceeds from the follow-on public offering of $55.4 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. We have received $125.0 million of funding under the Novo Agreement, which constitutes the full amount of funding under that agreement. We also received an upfront payment of $200.0 million from Novartis upon the execution of the Novartis Agreement, $50.0 million upon the achievement of each of two patient enrollment-based milestones, and $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate of $130.0 million.

We expect to continue to incur research and development expenses as we wind down the OPH1002 and OPH1003 trials and the Fovista Expansion Studies, continue the OPH1004 trial, for which we expect initial, top-line data to be available during the second half of 2017, and as we continue our Zimura development programs. However, due to the terminations of the OPH1002 and OPH1003 trials and the Fovista Expansion Studies, we expect our overall research and development expenses to decrease significantly compared to prior years until such time as we undertake additional development programs, including in relation to additional product candidates we may in-license or acquire as we pursue our updated business plan. We plan to reassess our existing Fovista and Zimura development programs throughout 2017 as the implementation of our updated business plan progresses and evolves, with the goal of aligning corporate resources in the context of a potentially broader product pipeline. We expect that our reassessment of our Fovista development program for the treatment of wet AMD will be primarily determined by the initial, top-line data from OPH1004 and that our reassessment of our Zimura development program may be particularly affected by the results of a competitor's Phase 3 clinical trial of a complement inhibitor being studied for the treatment of GA. Data from both our OPH1004 trial and our competitor's Phase 3 trial for the treatment of GA are expected during the second half of 2017. As a result of this reassessment, we may modify, expand or terminate some or all of our development programs or clinical trials at any time. The outcome of these reassessments, as well as the progress of our plans to potentially acquire additional products, product candidates or technologies will determine whether and to what extent we will continue to incur research and development costs for each of our development programs going forward.

Our ability to become and remain profitable depends on our ability to generate revenue in excess of our expenses. We do not expect to generate significant product revenue unless, and until, we obtain marketing approval for, and commercialize, any of our product candidates, which may take several years. We may be unsuccessful in our efforts to develop and commercialize these product candidates. Even if we succeed in developing and commercializing one or more of our product candidates, we may never achieve sufficient sales revenue to achieve or maintain profitability. Our capital requirements will also depend on many other factors, including whether we are successful in our pursuit to acquire or in-license and subsequently develop additional product candidates or technologies. We may 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.

Financial Operations Overview

Revenue

Prior to 2014, we had not generated any revenue. In May 2014, we received an upfront payment of $200.0 million in connection with our entry into the Novartis Agreement, which has not been recorded as revenue due to certain contingencies associated with the payment. In each of September 2014 and March 2015, we achieved a $50.0 million enrollment-based milestone, and in June 2016, we achieved a $30.0 million enrollment-based milestone, for an aggregate total of $130.0 million, under the Novartis Agreement. We use the relative selling price method to allocate arrangement consideration to our performance obligations under the Novartis Agreement. Below is a summary of the components of our collaboration revenue for the years ended December 31, 2016, 2015 and 2014:

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
License revenue	$ 22,937	$ 38,083	$ 38,373
Research and development activity revenue	9,741	8,378	2,000
API transfer revenue	18,212	5,020	883
Joint operating committee revenue	19	24	3
Total collaboration revenue	$ 50,909	$ 51,505	$ 41,259

In the future, we may generate additional revenue from a combination of product sales and license fees, milestone payments, research and development activity-related payments, payments for manufactured material and royalties from our commercialization partners, such as Novartis for Fovista outside the United States. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of certain milestone and other payments, if any, that we may receive from Novartis and the amount and timing of payments that we receive upon the sale of our products, to the extent any are successfully commercialized. If we fail to complete the development of Fovista, Zimura or other product candidates we may develop, in a timely manner or obtain regulatory approval for them, our ability to generate future revenue and our results of operations and financial position, would be materially adversely affected.

Research and Development Expenses

Research and development expenses primarily consist of costs associated with the development and clinical testing and manufacturing of Fovista and Zimura, as well as costs associated with the preclinical development of other product candidates and formulations. Our research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, and other vendors and contract manufacturing organizations, or CMOs, for the production of API and drug product; and
- employee-related expenses, including salaries, benefits and share-based compensation expense.

Research and development expenses also include costs of acquired product licenses and related technology rights where there is no alternative future use, costs of prototypes used in research and development, consultant fees and amounts paid to collaborative partners.

All research and development expenses are charged to operations as incurred in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic, or ASC, 730, *Research and Development*. We account for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made. To date, the large majority of our research and development activity has been related to Fovista and Zimura. We do not currently utilize a formal time allocation system to capture expenses on a project-by-project basis because we record expenses by functional department. Accordingly, we do not allocate expenses to individual projects or product candidates, although we do allocate some portion of our research and development expenses by functional area and by compound, as shown below.

The following table summarizes our research and development expenses for the years ended December 31, 2016, 2015 and 2014:

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
Fovista	$ 129,661	$ 86,906	$ 66,095
Zimura	7,400	7,644	4,377
Personnel-related	26,700	15,830	9,514
Share-based compensation	21,380	16,608	7,594
Other	11,154	4,024	805
	$ 196,295	$ 131,012	$ 88,385

We expect to continue to incur research and development expenses as we wind down the OPH1002 and OPH1003 trials and the Fovista Expansion Studies, continue the OPH1004 trial, for which we expect initial, top-line data to be available during the second half of 2017, and as we continue our Zimura development programs. We expect that the research and development expense required for us to continue the OPH1004 trial through our receipt of initial, top-line data during the second half of 2017 will be between approximately $15 million and $20 million. However, due to the terminations of the OPH1002 and OPH1003 trials and the Fovista Expansion Studies, we expect our overall research and development expenses to decrease significantly compared to prior years until such time as we undertake additional development programs, including in relation to additional product candidates we may in-license or acquire as we pursue our updated business plan.

Our expenses may exceed our expectations if we experience delays, including with respect to the availability of drug product for our clinical trials, if we experience any unforeseen issue in our ongoing clinical trials or if we further expand the scope of our clinical trials and programs. Our costs may also exceed our expectations for other reasons, for example, if we experience issues with process development, the scale-up of manufacturing activities or activities to enable and qualify second source suppliers or if we decide to increase licensing or preclinical research and development activities.

Our plan for the future development of Fovista and Zimura is highly uncertain. If the results from the OPH1004 trial are favorable and we determine to pursue further development of Fovista for use in combination with anti-VEGF drugs for the treatment of wet AMD, we would likely need to conduct one or more further pivotal, clinical trials for Fovista to support potential marketing approval, which would be time-consuming and expensive. Furthermore, to the extent we continue our Zimura development programs, we expect the clinical development for Zimura would continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete the clinical development of either Fovista or Zimura, complete process development and manufacturing scale-up and validation activities associated with Zimura and potentially seek marketing approval for Fovista and Zimura, or the nature, timing or costs of the efforts necessary to complete the development of any other product candidate we may develop.

The successful development of our product candidates is highly uncertain. See "Risk Factors." This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our research and development activities;
- the potential benefits of our product candidates over other therapies;
- clinical trial results;
- the terms and timing of regulatory approvals;
- our ability, together with any commercialization partner's ability, to market, commercialize and achieve market acceptance for any of our product candidates; and
- our ability to successfully file, prosecute, defend and enforce patent claims and other intellectual property rights, together with associated expenses.

A change in the outcome of any of these variables with respect to the development of our product candidates could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

See the "Liquidity and Capital Resources" section on page 97 of this Annual Report on Form 10-K for more information regarding our current and future financial resources and our expectations regarding our research and development expenses and funding requirements.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including share-based compensation expense, in our executive, legal, finance, commercial and business development functions. Other general and administrative expenses include facility costs and professional fees for legal, patent, pre-launch commercialization

activities, travel expenses, consulting and accounting services.

We anticipate that our general and administrative expenses will decrease in future periods as a result of a reduction in personnel to focus on an updated business plan involving a total expected workforce of approximately 30 employees. We expect to substantially complete the reduction in personnel during the first and second quarters of 2017 as part of implementing our updated business plan.

Interest Income

Our cash, cash equivalents and marketable securities are invested primarily in money market funds, U.S. Treasury securities and investment-grade corporate debt securities, which generate a nominal amount of interest income.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities 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 accrued research and development expenses, revenue recognition, share-based compensation and income taxes described in greater detail below. We base our estimates on our limited 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.

Our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this Annual Report on Form 10-K. Of those policies, we believe that the following accounting policies are the most critical to aid our stockholders in fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. 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. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses are related to expenses incurred with respect to CROs, CMOs and other vendors in connection with research and development and manufacturing activities.

We base our expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to quotations and contracts with such vendors that conduct research and development and manufacturing activities 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 applicable research and development or manufacturing expense. In accruing service fees, we estimate the time period over which services will be performed 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 expense 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 could result in us reporting amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented.

Revenue Recognition—Collaboration Revenue

Prior to 2014, we had not generated any revenue. In May 2014, we received an upfront payment of $200.0 million in connection with our entry into the Novartis Agreement, which has not been recorded as revenue due to certain contingencies associated with the payment. In each of September 2014 and March 2015, we achieved a $50.0 million enrollment-based milestone, and in June 2016, we achieved a $30.0 million enrollment-based milestone, for an aggregate total of $130.0 million, under the Novartis Agreement. We use the relative selling price method to allocate arrangement consideration to our performance obligations under the Novartis Agreement. Below is a summary of the components of our collaboration revenue for the years ended December 31, 2016, 2015 and 2014:

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	(in thousands)		
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API transfer revenue	18,212	5,020	883
Joint operating committee revenue	19	24	3
Total collaboration revenue	$ 50,909	$ 51,505	$ 41,259

In the future, we may generate additional revenues from a combination of product sales and license fees, milestone payments, research and development activity-related payments, payments for manufactured material and royalties in connection with the Novartis Agreement. The terms of this agreement and other potential collaboration or commercialization agreements we may enter into generally contain multiple elements, or deliverables, which may include (i) licenses, or options to obtain licenses, to certain of our technology and products, (ii) research and development activities to be performed on behalf of the collaborative partner and (iii) in certain cases, services in connection with the manufacturing of preclinical, clinical or commercial material. Payments to us under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; milestone payments; payments for manufactured material; and royalties on future product sales.

When evaluating multiple element arrangements, we consider whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires 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. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

We determine the estimated selling price for deliverables within each agreement 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. Determining the best estimate of selling price for a deliverable requires significant judgment. We use BESP to estimate the selling price for licenses to our proprietary technology, since we often do not have VSOE or TPE of selling price for these deliverables. In those circumstances where we utilize BESP to determine the estimated selling price of a license to our proprietary technology, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate that is subject to the license. In validating our BESP, we evaluate whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration among multiple deliverables.

When management believes the license to our intellectual property and products has stand-alone value, we generally recognize revenue attributed to the license upon delivery. When management believes such a license does not have stand-alone value from the other deliverables to be provided in the arrangement, we generally recognize revenue attributed to the license on a straight-line basis over our contractual or estimated performance period, which is typically the term of our research and development obligations. If management cannot reasonably estimate when our performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development agreement. Such a change could have a material impact on the amount of revenue we record in future periods.

At the inception of arrangements that include 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 (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance, and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment.

We aggregate our milestones into three categories: (i) clinical and development milestones, (ii) regulatory milestones, and (iii) commercial milestones. Clinical and development milestones are typically achieved when a product candidate advances into a defined phase of clinical research or completes such phase or when a contractually specified clinical trial enrollment target is attained. Regulatory milestones are typically achieved upon acceptance of the submission of an application for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other regulatory authorities. Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount.

Revenues from clinical and development and regulatory milestone payments, if the milestones are deemed substantive and the milestone payments are nonrefundable, are recognized upon successful accomplishment of the milestones. With regard to the Novartis Agreement, we have concluded that the clinical and development milestones and certain reimbursement approval milestones are not substantive and that the marketing approval milestones are substantive. Milestone payments received that are not considered substantive are included in the allocable arrangement consideration and are recognized as revenue in proportion to the relative-selling price allocation established at the inception of the arrangement. Revenues from commercial milestone payments are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Royalty Purchase Liability

The proceeds from the financing we received under the Novo Agreement have been recorded as a liability on our Balance Sheet in accordance with ASC 730, *Research and Development*. Because there is a significant related party relationship between us and Novo A/S, we are treating our obligation to make royalty payments under the Novo Agreement as an implicit obligation to repay the funds advanced by Novo A/S, and thus have recorded the proceeds as a liability on our Balance Sheet. As we make royalty payments to Novo A/S in accordance with the Novo Agreement, we will reduce the liability balance. At the time that such royalty payments become probable and estimable, and if such amounts exceed the liability balance, we will impute interest accordingly on a prospective basis based on such estimates, which would result in a corresponding increase in the liability balance.

Share-Based Compensation

We account for all share-based compensation payments issued to employees, non-employee directors, and consultants by estimating the fair value of each equity award. Accordingly, share-based compensation expense is measured based on the estimated fair value of the awards on the date of grant, net of forfeitures. We recognize compensation expense for the portion of the award that is ultimately expected to vest over the period during which the recipient renders the required services to us on a straight-line basis. In accordance with authoritative guidance, we re-measure the fair value of consultant share-based awards as the awards vest, and recognize the resulting value, if any, as expense during the period the related services are rendered.

We apply the fair value recognition provisions of ASC 718, *Compensation—Stock Compensation*. Determining the amount of share-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. We recognize share-based compensation expense ratably over the requisite service period, which in most cases is the vesting period of the award. For grants containing performance-based vesting provisions, expense is recognized over the estimated achievement period. Calculating the fair value of share-based awards requires that we make highly subjective assumptions.

We use the Black-Scholes option pricing model to value our stock option awards and the options to purchase shares under our Employee Stock Purchase Plan (the "ESPP"). Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the expected term of our stock options, and the risk free interest rate for a period that approximates the expected term of our stock options and the expected dividend yield of our common stock. As a recent public company, we do not have sufficient history to estimate the volatility of our common stock price or the expected life of the options. We calculate expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants.

We use the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term of stock option grants to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention to pay cash dividends. The weighted-average assumptions used to estimate grant date fair value of stock options using the Black-Scholes option pricing model were as follows for the years ended December 31,

2016, 2015 and 2014:

	Years ended December 31,		
	2016	2015	2014
Expected common stock price volatility	71%	72%	82%
Risk-free interest rate	1.14% - 2.37%	1.35% - 2.24%	1.61% - 2.13%
Expected term of options (years)	6.1	6.2	6.2
Expected dividend yield	—	—	—

We estimate the fair value of restricted stock units, or RSUs, granted to employees using the closing market price of our common stock on the date of grant.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. We use historical data to estimate pre-vesting forfeitures and record share-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised.

Share-based compensation expense for equity grants to employees, non-employee directors and consultants was $31.7 million, $24.8 million and $13.0 million for the years ended December 31, 2016, 2015, and 2014, respectively. As of December 31, 2016, we had $42.5 million of total unrecognized share-based compensation expense, which we expect to recognize over a weighted-average remaining vesting period of approximately 2.5 years. We expect our share-based compensation expense for our equity awards to employees, non-employee directors and consultants to increase as a result of recognizing our existing unrecognized share-based compensation for awards that will vest and as we issue additional equity awards to attract and retain our employees.

For the years ended December 31, 2016, 2015 and 2014, we allocated share-based compensation as follows:

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
Research and development	$ 21,380	$ 16,608	$ 7,594
General and administrative	10,280	8,152	5,446
Total	$ 31,660	$ 24,760	$ 13,040

Income Taxes

In 2014, we received $83.3 million from Novo A/S under the Novo Agreement, which was reported as revenue for income tax purposes. Also in 2014, we received $200.0 million from Novartis upon execution of the Novartis Agreement, a portion of which was reported as revenue for income tax purposes. In addition, we received a milestone payment of $50.0 million in 2014 from Novartis which was reported as revenue for income tax purposes. As a result of these payments, and after taking into account the utilization of our federal and state net operating loss carry-forwards and utilization of our research and development tax credits, we reported taxable income for tax purposes in 2014. We made income tax payments of $40.2 million during the year ended December 31, 2014.

In 2015, we incurred losses for tax purposes. As of December 31, 2015, we had recorded net deferred tax assets of $23.1 million. We realized these net deferred tax assets in 2016 as a result of the carry back of our 2015 federal tax loss to the 2014 tax year. We have carried-forward our 2015 state tax losses due to various state restrictions on the use of carryback claims. We are projecting tax losses for 2016. The deferred tax assets associated with these losses incurred to date in 2016 have a full valuation allowance recorded against them, however, due to our history of losses and the lack of other positive evidence to support future taxable income against which these losses could be applied. See Note 8 to our financial statements in Part IV-Item 15 of this Annual Report on form 10-K for further information regarding our expectations with respect to our income tax provision.

Results of Operations

Comparison of Years Ended December 31, 2016 and 2015

	Years ended December 31,		Increase (Decrease)
	2016	2015	
	(in thousands)		
Statements of Operations Data:			
Collaboration revenue	$ 50,909	$ 51,505	$ (596)
Operating expenses:			
Research and development	196,295	131,012	65,283
General and administrative	50,178	44,021	6,157
Total operating expenses	246,473	175,033	71,440
Loss from operations	(195,564)	(123,528)	72,036
Interest income	1,704	971	733
Other income	34	53	(19)
Loss before income tax (benefit) provision	(193,826)	(122,504)	71,322
Income tax (benefit) provision	(406)	(16,787)	(16,381)
Net loss	$ (193,420)	$ (105,717)	$ 87,703

Collaboration Revenue

Collaboration revenue for the year ended December 31, 2016 was $50.9 million, a decrease of $0.6 million compared to $51.5 million for the year ended December 31, 2015. Using the relative selling price method, for the year ended December 31, 2016, we allocated $22.9 million to the license delivered to Novartis under the Novartis Agreement, $9.7 million to research and development activities performed under the Novartis Agreement, $18.2 million related to Fovista API we transferred to Novartis, and a de minimis amount of revenue associated with our joint operating committee participation obligation.

Collaboration revenue for the year ended December 31, 2015 was $51.5 million, of which $38.1 million was allocated to the license delivered to Novartis under the Novartis Agreement, $8.4 million was allocated to research and development activities performed under the Novartis Agreement, $5.0 million related to Fovista API we transferred to Novartis, and a de minimis amount of revenue associated with our joint operating committee participation obligation during the same period.

Research and Development Expenses

Our research and development expenses were $196.3 million for the year ended December 31, 2016, an increase of $65.3 million compared to $131.0 million for the year ended December 31, 2015. The increase in research and development expenses for the year ended December 31, 2016 was primarily due to a $42.8 million increase in costs associated with our Fovista program, including our Fovista Phase 3 clinical program and our Fovista Expansion Studies. The increased costs for our Fovista program included higher clinical trial costs relating to increased patient enrollment in the Fovista Phase 3 clinical trials and the Fovista Expansion Studies, the initiation of additional Fovista Expansion Studies, as well as higher manufacturing costs to support our clinical trials and for API validation activities, and certain costs related to the cancellation of Fovista API purchase orders following our receipt of initial, top-line data from OPH1002 and OPH1003 in December 2016. Also contributing to the overall increase was a $10.9 million increase to personnel expenses associated with additional research and development staffing and a $4.8 million increase to share-based compensation costs. In addition, costs related to professional services and consulting fees increased by $6.1 million.

General and Administrative Expenses

Our general and administrative expenses were $50.2 million for the year ended December 31, 2016, an increase of $6.2 million, compared to $44.0 million for the year ended December 31, 2015. The increase was primarily due to an increase in personnel expenses of $2.6 million, including $2.1 million in share-based compensation costs, an increase of $2.8 million in facility costs, as well as other costs to support the expansion of our operations, including our public company infrastructure, and the early stages of a commercial organization. Also contributing to the increase were increased costs for professional services and consulting fees of $0.8 million.

Interest Income

Interest income for the year ended December 31, 2016 was $1.7 million compared to interest income of $1.0 million for the year ended December 31, 2015. The increase in interest income earned during the year ended December 31, 2016 was the result of an increase in our average investment portfolio balances, and a change in the mix of our investment portfolio, which previously included only investments in U.S. Treasury securities and now includes investments in certain investment-grade corporate debt securities.

Income Tax (Benefit) Provision

During the year ended December 31, 2016, we recorded a benefit from income taxes of approximately $0.4 million, which related to unanticipated refunds received and the reduction in our valuation allowances to reflect the income tax associated with unrealized gains in our investment portfolio. During the year ended December 31, 2015, we recorded a benefit for income taxes of approximately $16.8 million, which related to our tax losses for tax year 2015 and our ability to carry these losses back to 2014 to recapture a portion of the federal income tax payments we paid in 2014.

Comparison of Years Ended December 31, 2015 and 2014

	Years ended December 31,		Increase (Decrease)
	2015	2014	
	(in thousands)		
Statements of Operations Data:			
Collaboration revenue	$ 51,505	$ 41,259	$ 10,246
Operating expenses:			
Research and development	131,012	88,385	42,627
General and administrative	44,021	33,387	10,634
Total operating expenses	175,033	121,772	53,261
Loss from operations	(123,528)	(80,513)	43,015
Interest income	971	217	754
Other income	53	—	53
Loss before income tax provision	(122,504)	(80,296)	42,208
Income tax (benefit) provision	(16,787)	36,476	(53,263)
Net loss	$ (105,717)	$ (116,772)	$ (11,055)

Collaboration Revenue

Collaboration revenue for the year ended December 31, 2015 was approximately $51.5 million. Using the relative selling price method, we allocated $38.1 million to the license delivered to Novartis under the Novartis Agreement, $8.4 million to research and development activities performed under the Novartis Agreement, $5.0 million related to the Fovista API we transferred to Novartis, and a de minimis amount of revenue associated with our joint operating committee participation obligation during the year ended December 31, 2015.

Collaboration revenue for the year ended December 31, 2014 was $41.3 million, of which $38.4 million was allocated to the license delivered to Novartis under the Novartis Agreement, $2.0 million was allocated to research and development activities performed under the Novartis Agreement and $0.9 million related to Fovista API we transferred to Novartis during the same period.

Research and Development Expenses

Our research and development expenses were $131.0 million for the year ended December 31, 2015, an increase of $42.6 million compared to $88.4 million for the year ended December 31, 2014. Research and development expenses for the year ended December 31, 2014 included a $19.8 million milestone payment we made in connection with our entry into the Novartis Agreement, which represented a significant portion of our research and development expenses for the year ended December 31, 2014. The increase in research and development expenses for the year ended December 31, 2015 was primarily due to a $40.6 million increase in costs associated with our Fovista program, including our Fovista Phase 3 clinical program and our Fovista Expansion Studies. The increased costs for our Fovista program included higher clinical trial costs relating to increased

patient enrollment in the Fovista Phase 3 clinical trials and the Fovista Expansion Studies, the initiation of additional Fovista Expansion Studies, as well as higher manufacturing costs to support our clinical trials and for API validation activities. In addition, costs for our Zimura program increased by approximately $3.3 million, with such increase primarily related to increased manufacturing and clinical trial costs. Also contributing to the overall increase was a $9.0 million increase to share-based compensation costs and a $6.3 million increase to personnel expenses associated with additional research and development staffing.

General and Administrative Expenses

Our general and administrative expenses for the year ended December 31, 2015 were $44.0 million, an increase of $10.6 million compared to $33.4 million for the year ended December 31, 2014. The increase was primarily due to an increase in personnel costs of $3.0 million, share-based compensation costs of $2.7 million, an increase of $1.4 million in facility costs, as well as other costs to support the expansion of our operations, including our public company infrastructure, and the early stages of a commercial organization. Also contributing to the increase were increased costs for pre-launch commercialization activities, professional services and consulting fees of $2.0 million.

Interest Income (Expense), Net

Net interest income for the year ended December 31, 2015 was $1.0 million compared to net interest expense of $0.2 million for the year ended December 31, 2014. The increase in interest income earned during the year ended December 31, 2015 was the result of a change in the mix of our investment portfolio, which previously included only investments in U.S. Treasury securities and starting in the third quarter of 2015 included investments in certain investment-grade corporate debt securities.

Other Income (Loss)

Other income for the year ended December 31, 2015 was $0.1 million. There was no other income (loss) recorded for the year ended December 31, 2014.

Income tax (benefit) provision

During the year ended December 31, 2015, we recorded a benefit from income taxes of approximately $16.8 million, which related to our expected tax losses for tax year 2015 and our ability to carry these losses back to 2014 to recapture a portion of the federal income tax payments we paid in 2014. During the year ended December 31, 2014, we recorded a provision for income taxes of approximately $36.5 million, which primarily related to taxable income that resulted from payments we received under the Novartis Agreement and the Novo Agreement in 2014.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, funding we received under the Novo Agreement, our initial public offering of common stock, which we closed in September 2013, our follow-on public offering of common stock, which we closed in February 2014, and funds we received under the Novartis Agreement. In September 2013, we issued and sold an aggregate of 8,740,000 shares of common stock in our initial public offering at a public offering price of $22.00 per share. We received net proceeds from the initial public offering of $175.6 million. In February 2014, we issued and sold 1,900,000 shares of common stock and selling shareholders sold 728,571 shares of common stock in a follow-on public offering at a public offering price of $31.50 per share. We received net proceeds of $55.4 million from the follow-on offering. The Novo Agreement, which is described in more detail below, provided for financing of up to $125.0 million in the aggregate in return for the sale to Novo A/S of royalty interests in worldwide sales of Fovista. We received an aggregate of $125.0 million from this financing in separate tranches in May 2013, January 2014 and November 2014, which constitutes the full amount of funding under the Novo Agreement. In May 2013, we issued and sold an aggregate of 6,666,667 shares of our series C preferred stock at a price per share of $2.50, for an aggregate purchase price of $16.7 million. In August 2013, we issued and sold an aggregate of 13,333,333 additional shares of our series C preferred stock to the same purchasers at a price per share of $2.50, for an aggregate purchase price of $33.3 million.

In May 2014, we received an upfront payment of $200.0 million upon execution of the Novartis Agreement in connection with the grant of a license for the rights to commercialize Fovista outside the United States. In each of November 2014 and April 2015 we received payments of $50.0 million upon the achievement of two patient enrollment-based milestones, and in August 2016, $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate total of $130.0 million. See “Licensing and Commercialization Agreement with Novartis Pharma AG” below for further information.

Cash Flows

As of December 31, 2016, we had cash, cash equivalents and marketable securities totaling $289.3 million and no debt. We primarily invest our cash, cash equivalents and marketable securities in U.S. Treasury securities, money market funds and certain investment-grade corporate debt securities.

The following table shows a summary of our cash flows for the years ended December 31, 2016, 2015 and 2014:

	Years ended December 31,		
	2016	2015	2014
	(in thousands)		
Net cash (used in) provided by:			
Operating Activities	$ (108,596)	$ (78,531)	$ 111,088
Investing Activities	13,731	247,803	(427,817)
Financing Activities	6,934	12,775	145,947
Net change in cash and cash equivalents	$ (87,931)	$ 182,047	$ (170,782)

Cash Flows from Operating Activities

Net cash used in operating activities for the year ended December 31, 2016 was $108.6 million and relates primarily to net cash used to fund our Fovista Phase 3 program, our Fovista expansion studies, Fovista manufacturing activities, as well as manufacturing and clinical trial costs for our Zimura program and expenditures related to general and administrative expenses.

Net cash used in operating activities for the year ended December 31, 2015 was $78.5 million and related primarily to net cash used to fund our Fovista Phase 3 program, our Fovista expansion studies, Fovista manufacturing activities, as well as manufacturing and clinical trial costs for our Zimura program and expenditures related to general and administrative expenses. These expenditures were offset by a $50.0 million enrollment-based milestone payment we received in connection with the Novartis Agreement in April 2015.

See "—Funding Requirements" below for a description of how we expect to use our cash for operating activities in future periods.

Cash Flows from Investing Activities

Net cash provided by investing activities for the year ended December 31, 2016 was $13.7 million and relates primarily to proceeds from the sale or maturity of marketable securities totaling $86.5 million offset by purchases of marketable securities totaling $72.2 million. Net cash provided by investing activities for the year ended December 31, 2015 was $247.8 million and relates primarily to proceeds from the sale or maturity of marketable securities totaling $662.0 million offset by purchases of marketable securities totaling $411.6 million and capital expenditures associated with the expansion of our office facilities in New York, New York and the relocation to a new office facility in Princeton, New Jersey.

Cash Flows from Financing Activities

Net cash provided by financing activities was $6.9 million for the year ended December 31, 2016 and $12.8 million for the year ended December 31, 2015 and consisted of proceeds from stock option exercises.

Funding Requirements

We currently have two product candidates, Fovista and Zimura, which are in clinical development. We expect to continue to incur significant research and development expenses as we wind-down the OPH1002 and OPH1003 trials and the Fovista Expansion Studies, continue the OPH1004 trial and pursue the development of Zimura for the treatment of GA and in combination with anti-VEGF drugs for the treatment of wet AMD, as we review whether there is any scientific rationale for potentially developing, or undertake development of, Fovista or Zimura in additional indications, and as we evaluate and potentially in-license or acquire, and undertake development of, additional product candidates. Furthermore, if we successfully develop and obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. For Fovista, our ex-U.S. commercialization partner Novartis is responsible for these commercialization expenses outside the United States. We are party to agreements, specifically a divestiture agreement with OSI (Eyetech), Inc., or Eyetech, which agreement is now held by OSI Pharmaceuticals, LLC, a subsidiary of Astellas US, LLC, and license agreements with Archemix Corp., or Archemix, and Nektar Therapeutics, or Nektar, that impose significant milestone payment obligations on us in connection with our achievement of specific clinical, regulatory and commercial milestones with respect to Fovista and Zimura. It is likely that any

future in-licensing or acquisition agreements that we enter into with respect to additional products, product candidates or technologies would include similar obligations.

We expect that we will continue to incur significant expenses as we:

- in-license or acquire the rights to, and pursue the development of, other products, product candidates or technologies;
- complete the activities necessary to receive initial, top-line data from OPH1004 and wind down OPH1002, OPH1003 and the Fovista Expansion Studies and our Fovista contract manufacturing commitments;
- potentially undertake additional clinical development of Fovista in wet AMD if the initial, top-line data from OPH1004 is favorable or in other indications if we believe there is a sufficient scientific rationale to pursue such development;
- continue the clinical development of Zimura for the treatment of GA and in combination with anti-VEGF drugs for the treatment of wet AMD, or potentially in other indications if we believe there is a sufficient scientific rationale to pursue such development;
- complete our previously announced reduction in personnel;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing, quality control, quality assurance and scientific personnel if we are successful in progressing the clinical development of any of our product candidates;
- seek marketing approval for any product candidates that successfully complete clinical trials; and
- expand our outsourced manufacturing activities, expand our commercial operations and establish sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any of our product candidates.

As of December 31, 2016, we had cash, cash equivalents, and marketable securities of $289.3 million, of which approximately $100 million to $115 million is committed to the wind-down of OPH1002 and OPH1003 and the Fovista Expansion Studies, implementing a previously announced reduction in personnel and related costs, cancellation fees related to manufacturing commitments, and obtaining initial, top-line data during the second half of 2017 for the OPH1004 trial. We also had $394.2 million in total liabilities as of December 31, 2016, of which $335.0 million related to the Novo Agreement and deferred revenue associated with the Novartis Agreement, which we are required to show as liabilities on our balance sheets under generally accepted accounting principles but which, in the case of Novo, do not correspond to any contractual repayment obligation, or in the case of Novartis, are highly unlikely to be triggered.

We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our operations and capital expenditure requirements as currently planned for at least the next 12 months. This estimate does not reflect any additional expenditures resulting from the in-licensing or acquisition of additional product candidates or technologies or associated development that we may pursue as part of our revised business plan. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Our capital requirements will depend on several factors, including the success of our pursuit, by acquisition, in-licensing or otherwise, and subsequent development of additional product candidates or technologies, and the success of our ongoing development programs. We believe that it is likely that we will need additional funding in the event that we acquire or in-license one or more additional product candidates and undertake development. In addition, our expenses may exceed our expectations if we experience delays in enrollment or with the availability of drug supply for our clinical trials, if we experience any unforeseen issues in our ongoing clinical trials or if we further expand the scope of our clinical trials and programs. Our costs may also exceed our expectations for other reasons, for example, if we experience issues with manufacturing, process development, or if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or regulatory authorities in other jurisdictions to perform clinical or nonclinical trials or other studies in addition to those we currently expect to conduct. As a result, we may need or may seek to obtain additional funding in connection with our continuing operations prior than expected.

Our plan for the future development of Fovista and Zimura, if any, is highly uncertain. If the results from the OPH1004 trial are favorable and we determine to pursue further development of Fovista for use in combination with anti-VEGF drugs for the treatment of wet AMD, we will likely need to conduct one or more further pivotal, clinical trials for Fovista to support potential marketing approval, which will be time-consuming and expensive. Furthermore, to the extent we continue our Zimura development programs, we expect the clinical development for Zimura would continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete the clinical development of either Fovista or Zimura, complete process development and manufacturing scale-up and validation activities associated with Zimura and potentially seek marketing approval for Fovista and Zimura, or the nature, timing or costs of the efforts necessary to complete the development of any other product candidate we may develop.

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

- the extent to which we in-license or acquire rights to, and undertake development of products, product candidates or technologies;
- the amount of any upfront, milestone payments and other financial obligations associated with the in-license or acquisition of other product candidates;
- the scope, progress, results and costs of preclinical development and/or clinical trials for any other product candidates that we may acquire or in-license and develop;
- the scope, progress, costs and results of the OPH1004 trial and any additional clinical trials we undertake to obtain data sufficient to seek marketing approval for Fovista in wet AMD or any other indication;
- the scope, costs and results of our Zimura clinical programs, including our Zimura Phase 2/3 GA trial and our Zimura Phase 2a wet AMD trial, as well as any additional clinical trials we undertake to obtain data sufficient to seek marketing approval for Zimura in any indication (including a potential second Phase 3 trial for GA);
- if OPH1004 is positive, the costs and timing of restarting the manufacturing of commercial supply for Fovista;
- the costs and timing of process development and manufacturing scale-up and validation activities associated with Zimura;
- our ability to establish collaborations on favorable terms, if at all;
- the costs, timing and outcome of regulatory reviews of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending intellectual property-related claims;
- the timing, scope and cost of commercialization activities for any of our product candidates if we receive, or expect to receive, marketing approval for a product candidate; and
- subject to receipt of marketing approval, net revenue received from commercial sales of any of our product candidates, after milestone payments and royalty payments that we would be obligated to make.

Furthermore, following our receipt and announcement of initial, top-line results from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD in December 2016, we implemented a restructuring plan that included a reduction in personnel. This reduction in personnel is expected to involve approximately 80% of our workforce and will include employees from nearly every department. We may not be able to successfully implement the restructuring and we may not realize the planned or expected cost savings benefits, which could adversely affect our estimate of the period for which our cash, cash equivalents and marketable securities will be sufficient to fund our operations and capital expenditure requirements as currently planned.

We do not have any committed external source of funds other than the Novartis Agreement, and the remaining potential milestone payments under the Novartis Agreement are subject to our achievement of specified regulatory and commercial events related to Fovista, none of which are likely to be achieved given the data outcome of the OPH1002 and OPH1003 trials. Our future commercial revenues, if any, will be derived from sales of any of our product candidates that we are able to successfully develop, which, depending on the product, may not be available for several years, if at all. In addition, if

approved, Fovista or Zimura or any product that we acquire or in-license or acquire may not achieve commercial success. If that is the case, we will need to obtain substantial additional financing to achieve our business objectives. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Until such time, if ever, as we can generate substantial product revenues, we may need or may seek to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements.

Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts.

In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our existing stockholders' ownership interests would be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect their 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. Our pledge of assets, including intellectual property rights, as collateral to secure our obligations under the Novo Agreement may limit our ability to obtain debt financing. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, products or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Licensing and Commercialization Agreement with Novartis Pharma AG

In May 2014, we entered into a licensing and commercialization agreement with Novartis Pharma AG, which we refer to as the Novartis Agreement. Under the Novartis Agreement, we granted Novartis exclusive rights under specified patent rights, know-how and trademarks controlled by us to manufacture, from bulk API supplied by us, standalone Fovista products and products combining Fovista with an anti-VEGF drug to which Novartis has rights in a co-formulated product, for the treatment, prevention, cure or control of any human disease, disorder or condition of the eye, and to develop and commercialize those licensed products in all countries outside of the United States, which we refer to as the Novartis Territory. We have agreed to use commercially reasonable efforts to complete our ongoing pivotal Phase 3 clinical program for Fovista and Novartis has agreed to use commercially reasonable efforts to develop a standalone Fovista product and a co-formulated product containing Fovista and an anti-VEGF drug to which Novartis has rights, as well as a pre-filled syringe presentation of such products and to use commercially reasonable efforts, subject to obtaining marketing approval, to commercialize licensed products in the Novartis Territory in accordance with agreed development and marketing plans. Novartis has also granted us options, subject to specified limitations, and to the extent such rights are controlled by Novartis, to obtain exclusive rights from Novartis to develop and commercialize in the United States the co-formulated and pre-filled syringe products developed by Novartis. We and Novartis have each granted the other options, subject to specified limitations, to obtain access to study data from certain clinical trials of licensed products that we or Novartis may conduct, including for use by the other in regulatory filings in its territory. We have agreed to exclusively supply Novartis, and Novartis has agreed to exclusively purchase from us, its clinical and commercial requirements for the bulk API for Fovista for use in-licensed products in the Novartis Territory. We have agreed not to commercialize any product comprising Fovista or any other anti-PDGF product in the ophthalmic field in the Novartis Territory.

Novartis paid us a $200.0 million upfront fee upon execution of the Novartis Agreement. Novartis also paid us $50.0 million upon the achievement of each of two patient enrollment-based milestones, and $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate of $130.0 million. Under the terms of the Novartis Agreement, Novartis is also obligated to pay us up to an aggregate of an additional $300.0 million upon achievement of specified regulatory milestones, including marketing approval and reimbursement approval in certain countries in the Novartis Territory, and up to an aggregate of an additional $400.0 million if Novartis achieves specified sales milestones in the Novartis Territory. Novartis is also obligated to pay us royalties with respect to standalone Fovista products and combination Fovista products that Novartis successfully commercializes. We will receive royalties at a mid-thirties percentage of net sales of standalone Fovista products and a royalty of approximately equal value for sales of combination Fovista products. Such royalties are subject to customary deductions, credits, and reductions for lack of patent coverage or

market exclusivity. Novartis's obligation to pay such royalties will continue on a licensed product-by-licensed product and country-by-country basis until Novartis's last actual commercial sale of such licensed product in such country. We will continue to be responsible for royalties we owe to third parties on sales of Fovista products.

Novartis has agreed to pay our manufacturing costs for clinical supplies and our manufacturing costs plus a specified percentage margin for commercial supplies of the bulk API for Fovista that we supply to Novartis. If we or Novartis exercise our or its respective rights to obtain access to study data from clinical trials conducted by the other party, the party exercising the option will be obligated to pay the other party's associated past development costs and share with such other party any future associated development costs. If we exercise our option to obtain Novartis-controlled rights to develop, manufacture and commercialize any co-formulated Fovista product in the United States, we will be obligated to pay a specified percentage of Novartis's associated past development costs and share with Novartis any future associated development costs. Novartis and we will also need to negotiate and agree on financial and other terms that would apply to such rights. If we exercise our option to obtain Novartis-controlled rights to develop and commercialize a pre-filled syringe product in the United States, we will be obligated to either enter into a supply agreement with Novartis under which we will pay Novartis its manufacturing cost plus a specified percentage margin for supplies of Fovista products in pre-filled syringes that Novartis supplies to us, or obtain supplies of products in pre-filled syringes from a third party manufacturer and pay Novartis a low single-digit percentage of our net sales of such products.

We have retained control over the design and execution of our pivotal Phase 3 clinical program for Fovista and remain responsible for funding the costs of that program, subject to Novartis's responsibility to provide Lucentis, an anti-VEGF drug to which Novartis has rights in the Novartis Territory, for use in the Phase 3 clinical trials already initiated and in other Phase 2 and Phase 3 clinical trials in the Novartis Territory initiated following the effective date of the Novartis Agreement. Novartis will have control over, and will be responsible for the costs of, all other clinical trials that may be required to obtain marketing approvals in the Novartis Territory for licensed products under the agreement. Novartis is also responsible for costs associated with co-formulation development, pre-filled syringe development and other development costs in the Novartis Territory, but excluding regulatory filing fees in the European Union for the standalone Fovista product, for which we will be responsible.

The Novartis Agreement, unless earlier terminated by Novartis or us, will expire upon the expiration of Novartis's obligation to pay us royalties on net sales of licensed products. Novartis and we each may terminate the Novartis Agreement if the other party materially breaches the agreement and does not cure such breach within a specified cure period, if the other party experiences any specified insolvency event, if the other party challenges or assists a third party in challenging the validity or enforceability of certain patent rights controlled by the terminating party, or if the parties are prevented in any manner that materially adversely affects the progression of the development or commercialization of licensed products for a specified period as a result of specified governmental actions. Novartis may terminate the Novartis Agreement at any time without cause, or within a specified period after a change in control of us, as defined in the Novartis Agreement, or for specified safety reasons, effective at the end of a specified period following Novartis's written notice to us of Novartis's election to terminate the agreement. We may also terminate the agreement if Novartis determines to seek marketing approval of an alternative anti-PDGF product in the Novartis Territory as more fully described below. If we elect to terminate the Novartis Agreement because specified governmental actions prevent the parties from materially progressing the development or commercialization of licensed products as described above, we will be required to pay a substantial termination fee. Following any termination, all rights to Fovista that we granted to Novartis, including, without limitation, the right to commercialize standalone Fovista products in the Novartis Territory, will revert to us, Novartis will perform specified activities in connection with transitioning to us the rights and responsibilities for the continued development, manufacture and commercialization of the standalone Fovista product for countries in the Novartis Territory, and the parties will cooperate on an orderly wind down of development and commercialization activities for other licensed products in the Novartis Territory.

Novartis has agreed to specified limitations on its ability to in-license, acquire or commercialize any anti-PDGF product that does not contain Fovista, which we refer to as an Alternative Anti-PDGF Product, in the Novartis Territory and, to the extent Novartis develops, in-licenses or acquires such a product, to make such product available to us in the United States under specified option conditions. If we exercise our option, we will be obligated to make certain payments to Novartis, including specified milestone and royalty payments. The amounts of such payments will vary based on the product's stage of clinical development at the time we exercise our option, whether the product is a standalone or combination product and whether Novartis exercises an option to co-promote such product in the United States. If Novartis determines to seek marketing approval of an Alternative Anti-PDGF Product in the Novartis Territory, we will, subject to specified limitations, have the option to terminate the Novartis Agreement, convert Novartis's exclusive licenses into non-exclusive licenses, or elect to receive a royalty on sales of such product by Novartis. If we elect to terminate the Novartis Agreement, Novartis will, subject to specified limitations, be required to pay to us certain payments based on achievement,

with respect to such product, of the milestones that would have otherwise applied to licensed products under the Novartis Agreement.

The agreement contains standstill provisions pursuant to which Novartis agrees to certain restrictions relating to our voting securities until marketing approval for a standalone Fovista product is granted in either the United States or the European Union. The agreement contains indemnification and dispute resolution provisions that are customary for agreements of its kind.

Manufacturing and Supply Agreements for API and Fill/Finish Services

Clinical API Supply Agreement with Agilent Technologies, Inc.

In May 2014, we entered into a Clinical Manufacturing and Supply Agreement with Agilent Technologies, Inc., or Agilent, pursuant to which Agilent has agreed to manufacture and supply to us, and we have agreed to purchase from Agilent, a specified percentage of our clinical requirements in specified jurisdictions of Fovista API. The clinical supply agreement has an initial five-year term, which is subject to automatic renewal absent termination by either party in accordance with the terms of the clinical supply agreement. The clinical supply agreement provides for pricing for Fovista API structured on a tiered basis with the price reduced as the volume ordered increases. We may terminate the clinical supply agreement or any statement of work thereunder upon 12 months' prior written notice to Agilent and Agilent may terminate the clinical supply agreement if we do not, over a specified period, purchase and take delivery from Agilent of a specified minimum quantity of API for Fovista. Each party also has the right to terminate the clinical supply agreement for other customary reasons such as material breach and bankruptcy. The clinical supply agreement contains provisions relating to compliance by Agilent with current Good Manufacturing Practices, cooperation by Agilent in connection with marketing applications for Fovista, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

Commercial API Supply Agreement with Agilent Technologies, Inc.

In September 2015, we entered into a Commercial Manufacturing and Supply Agreement with Agilent, pursuant to which Agilent has agreed to manufacture and supply to us, and we have agreed to purchase from Agilent, a specified percentage of our commercial requirements in all jurisdictions of Fovista API. The commercial supply agreement has an initial term that runs for seven years from the date of our first commercial sale of Fovista, and which is subject to one two-year automatic renewal period, absent termination by either party in accordance with the terms of the commercial supply agreement. The commercial supply agreement provides for pricing for Fovista API structured on a tiered basis, with the price reduced as the volume of Fovista API ordered increases. We may cancel any purchase order under the commercial supply agreement at any time, subject to the payment of specified cancellation fees. We may terminate the commercial supply agreement with no financial penalty in the event that we cannot commercialize Fovista due to regulatory or other medical, scientific or legal reasons. Agilent may terminate the commercial supply agreement in the event that we do not, over a specified period, purchase and take delivery from Agilent of a specified minimum quantity of Fovista API. Each party also has the right to terminate the commercial supply agreement for other customary reasons such as material breach and bankruptcy. The commercial supply agreement contains provisions relating to compliance by Agilent with current Good Manufacturing Practices, cooperation by Agilent in connection with marketing applications for Fovista, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

In December 2016, following receipt of initial, top-line data from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we canceled all of our outstanding purchase orders with Agilent for the manufacture of Fovista API for commercial drug product. We have incurred substantial cancellation fees in connection with such canceled purchase orders, payment of which will be made in 2017 as we unwind our Fovista manufacturing commitments.

Clinical and Commercial Services Agreement with Ajinimoto Althea, Inc.

In October 2016, we and Ajinimoto Althea, Inc., or Althea, entered into a Clinical and Commercial Services Agreement, which we refer to as the Fill/Finish Services Agreement. Pursuant to the Fill/Finish Services Agreement, Althea has agreed to provide clinical and commercial fill/finish services for Fovista and Zimura, as well as any future product candidates that we and Althea may mutually agree. The Fill/Finish Services Agreement has an initial term that will expire at the end of 2027, absent termination by either party in accordance with the terms of the Fill/Finish Services Agreement. The initial term of the Fill/Finish Services Agreement may be extended by mutual agreement of the parties. The amount payable by us to Althea under the Fill/Finish Services Agreement is based on the volume of finished drug product that we order, subject to periodic adjustments over the term of the Fill/Finish Services Agreement. In addition, in the event that we order a specified volume of product, Althea has agreed to supply biological or pharmaceutical drug products meeting certain

parameters exclusively to us. We may cancel any purchase order under the Fill/Finish Services Agreement at any time, subject to the payment of specified cancellation fees. We may terminate the Fill/Finish Services Agreement, without cause, as of any date following the third anniversary of the effective date upon six months' prior notice to Althea. Each party also has the right to terminate the Services Agreement for other customary reasons such as material breach and bankruptcy. The Fill/Finish Services Agreement contains provisions relating to compliance by Althea with current Good Manufacturing Practices, cooperation by Althea in connection with marketing applications for our product candidates, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

In December 2016, following receipt of initial, top-line data from our pivotal OPH1002 and OPH1003 Fovista trials for the treatment of wet AMD, we canceled all of our outstanding purchase orders with Althea for the fill and finish of Fovista commercial drug product. We incurred approximately $0.6 million in connection with such cancellations in relation to non-returnable materials procured by Althea in anticipation of fulfilling such purchase orders, payment of which will be made in 2017 as we unwind our Fovista manufacturing commitments.

Financing Agreement with Novo A/S

In May 2013, we entered into the Novo Agreement, pursuant to which we had the ability to obtain financing in three tranches in an amount of up to $125.0 million in return for the sale to Novo A/S of aggregate royalties of a mid-single-digit percentage on worldwide sales of Fovista, with the royalty percentage determined by the amount of funding provided by Novo A/S. The three tranches of financing, in which Novo A/S purchased three low single-digit royalty interests and paid us
$125.0 million in the aggregate, closed in May 2013, January 2014 and November 2014.

The royalty payment period begins on the commercial launch of Fovista and ends, on a country-by-country basis, on the latest to occur of the twelfth anniversary of the commercial launch of Fovista, the expiration of certain patent rights covering Fovista, and the expiration of regulatory exclusivity for Fovista, in each applicable country. Royalty payments will be payable quarterly in arrears during the royalty period. Our obligations under the Novo Agreement may also apply to certain other anti- platelet derived growth factor, or anti-PDGF, products we may develop.

We used a portion of the proceeds that we initially received under the Novo Agreement to repay in full an aggregate of $14.4 million of outstanding principal, interest and fees under our venture debt facility and used the remaining proceeds to support clinical development and regulatory activities for Fovista and for general corporate expenses.

The Novo Agreement requires the establishment by Novo A/S and us of a joint oversight committee in relation to the development of Fovista in the event that Novo A/S does not continue to have a representative on our board of directors. The Novo Agreement also contains customary representations and warranties, as well as certain covenants relating to the operation of our business, including covenants requiring us to use commercially reasonable efforts to continue our development of Fovista, to file, prosecute and maintain certain patent rights and, in our reasonable judgment, to pursue claims of infringement of our intellectual property rights. The Novo Agreement also places certain restrictions on our business, including restrictions on our ability to grant security interests in our intellectual property to third parties, to sell, transfer or out-license intellectual property, or to grant others rights to receive royalties on sales of Fovista and certain other products. We reimbursed Novo A/S for specified legal and other expenses and are required to provide Novo A/S with certain continuing information rights. We have agreed to indemnify Novo A/S and its representatives with respect to certain matters, including with respect to any third- party infringement or product liability claims relating to our products. Our obligations under the Novo agreement are secured by a lien on certain of our intellectual property and other rights related to Fovista and other anti-PDGF products we may develop.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2016:

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
	(in thousands)				
Operating Leases (1)	$ 4,565	$ 4,316	$ 249	$ —	$ —
Purchase Obligations (2)	44,263	44,263	—	—	—
Total (3)	$ 48,828	$ 48,579	$ 249	$ —	$ —

(1) In January 2017, we terminated our office leases in New York, NY and Princeton, NJ and made aggregate termination payments of approximately $2.1 million. The table above includes these termination payments, as well as our continuing rent obligations through February 2018.

(2) Purchase obligations represent our commitments under binding forecasts, and purchase orders (inclusive of cancellation fees), including those provided under our agreement with Nektar and our clinical and commercial supply agreements with Agilent. The actual amounts incurred will be determined based on the amount of goods purchased and the pricing then in effect under the applicable arrangement

(3) This table does not include (a) any milestone payments which may become payable to third parties under license agreements as the timing and likelihood of such payments are not known with certainty, (b) any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known, (c) anticipated expenditures under supply agreements for periods for which we are not yet bound under binding purchase orders, (d) contracts that are entered into in the ordinary course of business that are not material in the aggregate in any period presented above and (e) our royalty purchase liability of $125.0 million as of December 31, 2016, due to the fact that the royalty payment period, if any, is not known.

In addition to the amounts set forth in the table above, we may be required, under various agreements, to pay royalties and make milestone payments. In addition to the Novo Agreement, these agreements include the following:

- Under our divestiture agreement with OSI (Eyetech), Inc., which agreement is now held by OSI Pharmaceuticals, LLC., or OSI Pharmaceuticals, a subsidiary of Astellas US, LLC, for rights to particular anti-PDGF aptamers, including Fovista, we are obligated to pay to OSI Pharmaceuticals future one-time payments of $12.0 million in the aggregate upon marketing approval in the United States and the European Union of a covered anti-PDGF product. We also are obligated to pay to OSI Pharmaceuticals a royalty at a low single-digit percentage of net sales of any covered anti-PDGF product we successfully commercialize.

- Under a license agreement with Archemix Corp., or Archemix, with respect to pharmaceutical products comprised of or derived from any anti-PDGF aptamer, we are obligated to make future payments to Archemix of up to an aggregate of $14.0 million if we achieve specified clinical and regulatory milestones with respect to Fovista, up to an aggregate of $3.0 million if we achieve specified commercial milestones with respect to Fovista and, for each other anti-PDGF aptamer product that we may develop under the agreement, up to an aggregate of approximately $18.8 million if we achieve specified clinical and regulatory milestones and up to an aggregate of $3.0 million if we achieve specified commercial milestones. No royalties are payable to Archemix under this license agreement.

- Under a license agreement with Archemix with respect to pharmaceutical products comprised of or derived from anti- C5 aptamers, for each anti-C5 aptamer product that we may develop under the agreement, including Zimura, we are obligated to make future payments to Archemix of up to an aggregate of $57.5 million if we achieve specified development, clinical and regulatory milestones, and up to an aggregate of $22.5 million if we achieve specified commercial milestones. We are also obligated to pay Archemix a double-digit percentage of specified non-royalty payments we may receive from any sublicensee of our rights under this license agreement. No royalties are payable to Archemix under this license agreement.

- Under a license, manufacturing and supply agreement with Nektar Therapeutics, or Nektar, for specified pegylation reagents used to manufacture Fovista, we are obligated to make future payments to Nektar of up to an aggregate of $6.5 million if we achieve specified clinical and regulatory milestones, and an additional payment of $3.0 million if we achieve a specified commercial milestone with respect to Fovista. We are obligated to pay Nektar tiered royalties at low to mid-single-digit percentages of net sales of any licensed product we successfully commercialize, with the royalty percentage determined by our level of licensed product sales, the extent of patent coverage for the licensed product and whether we have granted a third party commercialization rights to the licensed product. In June 2014, we paid Nektar $19.8 million in connection with our entry into the Novartis Agreement.

We also have letter agreements with certain employees that require the funding of a specific level of payments, if certain events, such as a termination of employment in connection with a change in control or termination of employment by the employee for good reason or by us without cause, occur. For a description of these obligations, see our definitive proxy statement on Schedule 14A for our 2016 annual meeting of stockholders, as filed with the SEC on April 29, 2016.

In December 2016, we announced that we had determined to implement a reduction in personnel to focus on an updated business plan. In January 2017, our Board of Directors approved a plan to implement a reduction in personnel that is expected to involve approximately 80% of our workforce and is expected to be substantially complete during the first and second quarters of 2017. In connection with such reduction in personnel, we estimate that we will make future cash expenditures totaling approximately $12.3 million, which relate to expected severance and other employee costs.

In addition, in the course of normal business operations, we have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. Expenditures to CROs and CMOs represent significant costs in clinical development. Subject to required notice periods and our obligations under binding purchase orders, we can elect to discontinue the work under these agreements at any time. We could also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require upfront payments and even long-term commitments of cash.

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 under Securities and Exchange Commission rules.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $289.3 million as of December 31, 2016, consisting of cash, investments in money market funds certain investment-grade corporate debt securities, and direct investment in U.S. Treasury securities. 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 a significant portion of our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We contract with CROs and CMOs globally. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the U.S. dollar are recorded based on exchange rates at the time such transactions arise. As of December 31, 2016, substantially all of our total liabilities were denominated in the U.S. dollar.

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-27 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, as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended (the Exchange Act). Our internal control over financial reporting is a process designed by, or under the supervision of our Chief Executive Officer and our Chief Financial Officer, 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.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with 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 the original *Internal Control—Integrated Framework* updated in 2013. Based on that assessment, our management concluded that, as of December 31, 2016, our internal control over financial reporting was effective.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2016, has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders

Ophthotech Corporation

We have audited Ophthotech Corporation's internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Ophthotech Corporation's management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) 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 (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Ophthotech Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Ophthotech Corporation as of December 31, 2016 and 2015, and the related statements of operations, comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2016 of Ophthotech Corporation and our report dated February 28, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
MetroPark, New Jersey
February 28, 2017

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Directors and Executive Officers

The information required by this item will be set forth in our Proxy Statement for the 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 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 Ian Smith is an "audit committee financial expert" as defined by Item 407(d)(5) of Regulation S-K of the Exchange Act and Mr. Smith and the other members of our Audit Committee are "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 Accountant 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 and 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: February 28, 2017

OPHTHOTECH CORPORATION

By: /s/ DAVID R. GUYER

David R. Guyer, M.D.
Chief Executive Officer

Pursuant to the requirements of the Securities 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/ DAVID R. GUYER David R. Guyer, M.D.	Chief Executive Officer and Chairman of the Board of Directors (principal executive officer)	February 28, 2017
/s/ GLENN P. SBLENDORIO Glenn P. Sblendorio	President and Chief Financial Officer (principal financial and accounting officer)	February 28, 2017
/s/ AXEL BOLTE Axel Bolte	Director	February 28, 2017
/s/ THOMAS DYRBERG Thomas Dyrberg, M.D., D.M.Sc.	Director	February 28, 2017
/s/ DAVID E. REDLICK David E. Redlick	Director	February 28, 2017
/s/ MICHAEL ROSS Michael Ross, Ph.D.	Director	February 28, 2017
/s/ IAN SMITH Ian Smith	Director	February 28, 2017

OPHTHOTECH CORPORATION

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders

Ophthotech Corporation

We have audited the accompanying balance sheets of Ophthotech Corporation as of December 31, 2016 and 2015, and the related statements of operations, comprehensive loss, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2016. 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 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. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Ophthotech Corporation at 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 US generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Ophthotech Corporation's internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 28, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

MetroPark, New Jersey

February 28, 2017

Ophthotech Corporation

Balance Sheets

(in thousands, except share and per share data)

	December 31, 2016	December 31, 2015
Assets		
Current assets		
Cash and cash equivalents	$ 133,930	$ 221,861
Available for sale securities	155,348	74,731
Due from Novartis Pharma AG	3,531	4,389
Prepaid expenses and other current assets	3,078	5,504
Total current assets	295,887	306,485
Available for sale securities	—	95,298
Property and equipment, net	3,281	3,466
Deferred tax assets	—	23,113
Other assets	462	489
Total assets	$ 299,630	$ 428,851
Liabilities and Stockholders' Equity (Deficit)		
Current liabilities		
Accrued research and development expenses	$ 47,240	$ 18,820
Accounts payable and accrued expenses	12,032	12,018
Deferred revenue	6,646	6,667
Total current liabilities	65,918	37,505
Deferred revenue, long-term	203,330	206,399
Royalty purchase liability	125,000	125,000
Total liabilities	394,248	368,904
Stockholders' equity (deficit)		
Preferred stock—$0.001 par value, 5,000,000 shares authorized, no shares issued or outstanding	$ —	$ —
Common stock—$0.001 par value, 200,000,000 shares authorized, 35,733,276 and 35,196,567 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively	36	35
Additional paid-in capital	504,517	465,924
Accumulated deficit	(598,959)	(405,539)
Accumulated other comprehensive loss	(212)	(473)
Total stockholders' equity (deficit)	(94,618)	59,947
Total liabilities and stockholders' equity (deficit)	$ 299,630	$ 428,851

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

Ophthotech Corporation

Statements of Operations

(in thousands, except per share data)

	Years ended December 31,		
	2016	2015	2014
Collaboration revenue	$ 50,909	$ 51,505	$ 41,259
Operating expenses:			
Research and development	196,295	131,012	88,385
General and administrative	50,178	44,021	33,387
Total operating expenses	246,473	175,033	121,772
Loss from operations	(195,564)	(123,528)	(80,513)
Interest income	1,704	971	217
Other income	34	53	—
Loss before income tax (benefit) provision	(193,826)	(122,504)	(80,296)
Income tax (benefit) provision	(406)	(16,787)	36,476
Net loss	(193,420)	(105,717)	(116,772)
Net loss per common share:			
Basic and diluted	$ (5.45)	$ (3.06)	$ (3.51)
Weighted average common shares outstanding:			
Basic and diluted	35,486	34,580	33,258

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

Ophthotech Corporation

Statements of Comprehensive Loss

(in thousands)

	Years ended December 31,		
	2016	2015	2014
Net loss	$ (193,420)	$ (105,717)	$ (116,772)
Other comprehensive income (loss):			
Unrealized gain (loss) on available for sale securities, net of tax	261	(408)	(65)
Other comprehensive income (loss)	261	(408)	(65)
Comprehensive loss	$ (193,159)	$ (106,125)	$ (116,837)

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

Ophthotech Corporation

Statements of Stockholders' Equity (Deficit)

(in thousands)

	Junior Series A Preferred Stock		Common Stock		Additional paid-in capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
	Shares	Amount	Shares	Amount				
Balance at December 31, 2013	—	$ —	31,413	$ 31	$ 352,739	$ (183,050)	$ —	$ 169,720
Issuance of common stock under employee stock compensation plans and warrants	—	—	682	1	2,948	—	—	2,949
Issuance from follow-on public offering, net	—	—	1,900	2	55,407	—	—	55,409
Share-based compensation	—	—	—	—	13,040	—	—	13,040
Excess tax benefit from share-based compensation	—	—	—	—	4,256	—	—	4,256
Net loss	—	—	—	—	—	(116,772)	—	(116,772)
Unrealized loss on available for sale securities, net of tax	—	—	—	—	—	—	(65)	(65)
Balance at December 31, 2014	—	$ —	33,995	$ 34	$ 428,390	$ (299,822)	$ (65)	$ 128,537
Issuance of common stock under employee stock compensation plans and warrants	—	—	1,202	1	11,472	—	—	11,473
Share-based compensation	—	—	—	—	24,760	—	—	24,760
Excess tax benefit from share-based compensation	—	—	—	—	1,302	—	—	1,302
Net loss					—	(105,717)	—	(105,717)
Unrealized loss on available for sale securities, net of tax	—	—	—	—	—	—	(408)	(408)
Balance at December 31, 2015	—	$ —	35,197	$ 35	$ 465,924	$ (405,539)	$ (473)	$ 59,947
Issuance of common stock under employee stock compensation plans and warrants	—	—	536	1	6,933	—	—	6,934
Share-based compensation	—	—	—	—	31,660	—	—	31,660
Excess tax benefit from share-based compensation	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	(193,420)	—	(193,420)
Unrealized gain on available for sale securities, net of tax	—	—	—	—	—	—	261	261
Balance at December 31, 2016	—	$ —	35,733	$ 36	$ 504,517	$ (598,959)	$ (212)	$ (94,618)

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

Ophthotech Corporation

Statements of Cash Flows

(in thousands)

	Years ended December 31,		
	2016	2015	2014
Operating Activities			
Net loss	$ (193,420)	$ (105,717)	$ (116,772)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities			
Depreciation	757	698	127
Amortization of premium and discounts on investment securities	595	2,846	2,024
Gain on sale of marketable securities	—	(57)	—
Deferred income taxes	22,954	(17,341)	(214)
Share-based compensation	31,660	24,760	13,040
Excess tax benefits from share-based compensation	—	(1,302)	(4,256)
Changes in operating assets and liabilities:			
Due from Novartis Pharma AG	858	(3,429)	(960)
Prepaid expense and other current assets	2,426	3,308	(2,008)
Accrued interest receivable	203	155	280
Other assets	27	(107)	(127)
Accrued research and development expenses	28,420	10,902	5,433
Accounts payable and accrued expenses	14	3,311	4,897
Deferred revenue	(3,090)	3,442	209,624
Net cash (used in) provided by operating activities	(108,596)	(78,531)	111,088
Investing Activities			
Purchase of marketable securities	(72,197)	(411,565)	(597,762)
Sale of marketable securities	—	395,977	—
Maturities of marketable securities	86,500	266,000	171,600
Purchase of property and equipment	(572)	(2,615)	(1,655)
Proceeds from sale of assets	—	6	—
Net cash provided by (used in) investing activities	13,731	247,803	(427,817)
Financing Activities			
Proceeds from stock option/warrant exercises	6,934	11,473	2,949
Proceeds from follow-on public offering, net	—	—	55,409
Excess tax benefits from share-based compensation	—	1,302	4,256
Proceeds from royalty purchase agreement	—	—	83,333
Net cash provided by financing activities	6,934	12,775	145,947
Net change in cash and cash equivalents	(87,931)	182,047	(170,782)
Cash and cash equivalents			
Beginning of period	221,861	39,814	210,596
End of period	$ 133,930	$ 221,861	$ 39,814
Supplemental disclosure of cash paid			
Income taxes paid (received), net	$ (26,998)	$ 399	$ 40,159
Supplemental disclosures of non-cash information related to investing activities			
Change in unrealized gain (loss) on available for sale securities, net of tax	$ 261	$ (408)	$ (65)

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

1. Business

Description of Business and Organization

Ophthotech Corporation (the “Company” or “Ophthotech”) was incorporated on January 5, 2007, in Delaware. The Company is a biopharmaceutical company specializing in the development of novel therapeutics to treat ophthalmic diseases, with a focus on diseases of the back of the eye. To date, the Company's primary focus has been on developing therapeutics for age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina, known as the macula, that may result in blindness. Following the Company's announcement in December 2016 that two of its three pivotal, Phase 3 clinical trials for Fovista® (pegpleranib), an anti-platelet derived growth factor, or PDGF, aptamer, in development for the treatment of wet AMD, failed to meet their primary endpoint, the Company initiated a plan to review its strategic alternatives in order to maximize shareholder value and implement an updated business plan. Without limiting any option, the Company plans to continue to focus on the development of product candidates for ophthalmic diseases, especially back of the eye disorders. The Company is actively exploring opportunities to obtain rights to additional products, product candidates and technologies to treat ophthalmic diseases. The Company is also currently continuing to develop its product candidate Zimura® (avacincaptad pegol), an inhibitor of complement factor C5, for the treatment of geographic atrophy, or GA, a form of dry AMD, and in combination with anti-VEGF drugs for the treatment of wet AMD, and is continuing its remaining Phase 3 Fovista clinical trial, OPH1004. The Company plans to reassess its existing Fovista and Zimura development programs throughout 2017 as the implementation of its updated business plan progresses and evolves, with the goal of aligning corporate resources in the context of a potentially broader product pipeline. The Company expects that its reassessment of its Fovista development program for the treatment of wet AMD will be primarily determined by the initial, top-line data from OPH1004 and that its reassessment of its Zimura development program may be particularly affected by the results of a competitor’s Phase 3 clinical trial of a complement inhibitor being studied for the treatment of GA. Data from both the Company's OPH1004 trial and its competitor’s Phase 3 trial for the treatment of GA are expected during the second half of 2017. As a result of this reassessment, the Company may modify, expand or terminate some or all of its development programs or clinical trials at any time. The Company generally expects that it will not engage in internal early stage research and drug discovery and will thus avoid the related costs and risks of these activities.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Segment and geographic information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating and reporting segment.

Use of Estimates

The preparation of financial statements and related disclosures in conformity with GAAP requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes. The Company bases its estimates and judgments on historical experience and on various other assumptions that it believes are reasonable under the circumstances. The amounts of assets and liabilities reported in the Company's Balance Sheets and the amount of expenses reported for each of the periods presented are affected by estimates and assumptions, which are used for, but not limited to, accounting for research and development costs, revenue recognition, accounting for share-based compensation and accounting for income taxes. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of 90 days or less when purchased to be cash equivalents. The carrying amounts reported in the Balance Sheets for cash and cash equivalents are valued at cost, which approximates their fair value.

As of December 31, 2016, the Company had cash, cash equivalents and available for sale securities of approximately $289.3 million. The Company believes that its existing cash, cash equivalents and available-for-sale securities as of December 31, 2016 will be sufficient to fund its operations and capital expenditure requirements as currently planned for at least the next 12 months.

Available for Sale Securities

The Company considers securities with original maturities of greater than 90 days when purchased to be available for sale securities. Available for sale securities with original maturities of greater than one year are recorded as non-current assets. Available for sale securities are recorded at fair value and unrealized gains and losses are recorded within accumulated other comprehensive income (loss). The estimated fair value of the available for sale securities is determined based on quoted market prices or rates for similar instruments. In addition, the cost of debt securities in this category is adjusted for amortization of premium and accretion of discount to maturity. The Company evaluates securities with unrealized losses to determine whether such losses, if any, are other than temporary.

Revenue Recognition

Collaboration Revenue

Prior to 2014, the Company had not generated any revenue. In May 2014, the Company received an upfront payment of $200.0 million in connection with its licensing and commercialization agreement with Novartis Pharma AG, (the "Novartis Agreement"), which has not been recorded as revenue due to certain contingencies associated with the payment. In each of September 2014 and March 2015, the Company achieved a $50.0 million enrollment-based milestone, and in June 2016, the Company achieved a $30.0 million enrollment-based milestone, for an aggregate total of $130.0 million, under the Novartis Agreement. The Company uses the relative selling price method to allocate arrangement consideration to the Company's performance obligations under the Novartis Agreement. Below is a summary of the components of the Company's collaboration revenue for the years ended December 2016, 2015 and 2014:

	Years ended December 31,		
	2016	2015	2014
License revenue	$ 22,937	$ 38,083	$ 38,373
Research and development activity revenue	9,741	8,378	2,000
API transfer revenue	18,212	5,020	883
Joint operating committee revenue	19	24	3
Total collaboration revenue	$ 50,909	$ 51,505	$ 41,259

In the future, the Company may generate additional revenues from a combination of product sales and license fees, milestone payments, research and development activity-related payments, payments for manufactured material and royalties in connection with the Novartis Agreement. The terms of this agreement and other potential collaboration or commercialization agreements the Company may enter into generally contain multiple elements, or deliverables, which may include (i) licenses, or options to obtain licenses, to certain of the Company's technology and products, (ii) research and development activities to be performed on behalf of the collaborative partner, and (iii) in certain cases, services in connection with the manufacturing of preclinical, clinical and commercial material. Payments to the Company under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; milestone payments; payments for manufactured material; and royalties on future product sales.

When evaluating multiple element arrangements, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires 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. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables within each agreement 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. Determining the best estimate of selling price for a deliverable requires significant judgment. The Company uses BESP to estimate the selling price for licenses to the Company's proprietary technology, since the Company often does not have VSOE or TPE of selling price for these

deliverables. In those circumstances where the Company utilizes BESP to determine the estimated selling price of a license to the Company's proprietary technology, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate that is subject to the license. In validating the Company's BESP, the Company evaluates whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration among multiple deliverables.

When management believes the license to its intellectual property and products has stand-alone value, the Company generally recognizes revenue attributed to the license upon delivery. When management believes such a license does not have stand-alone value from the other deliverables to be provided in the arrangement, the Company generally recognizes revenue attributed to the license on a straight-line basis over the Company's contractual or estimated performance period, which is typically the term of the Company's research and development obligations. If management cannot reasonably estimate when the Company's performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

At the inception of arrangements that include 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 (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance, and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment.

The Company aggregates its milestones into three categories: (i) clinical and development milestones, (ii) regulatory milestones, and (iii) commercial milestones. Clinical and development milestones are typically achieved when a product candidate advances into a defined phase of clinical research or completes such phase or when a contractually specified clinical trial enrollment target is attained. Regulatory milestones are typically achieved upon acceptance of the submission of an application for marketing approval for a product candidate or upon approval to market the product candidate by the U.S. Food and Drug Administration (the "FDA") or other regulatory authorities. Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount.

Revenues from clinical and development and regulatory milestone payments, if the milestones are deemed substantive and the milestone payments are nonrefundable, are recognized upon successful accomplishment of the milestones. With regard to the Novartis Agreement, the Company has concluded that the clinical and development milestones and certain reimbursement milestones are not substantive and that the marketing approval milestones are substantive. Milestone payments received that are not considered substantive are included in the allocable arrangement consideration and are recognized as revenue in proportion to the relative-selling price allocation established at the inception of the arrangement. Revenues from commercial milestone payments are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Concentration of Credit Risk

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash and cash equivalents and available for sale securities. The Company maintains its cash in bank accounts, which generally exceed federally insured limits. The Company maintains its cash equivalents in investments in money market funds and, at times, in U.S. Treasury securities and investment-grade corporate debt securities with original maturities of 90 days or less.

The Company's available for sale securities are also invested in U.S. Treasury securities and investment-grade corporate debt securities. The Company believes it is not exposed to significant credit risk on its cash, cash equivalents and available for sale securities.

Concentration of Suppliers

The Company currently relies exclusively upon a single third-party manufacturer to provide supplies of the active pharmaceutical ingredient, or API, for both Fovista and Zimura. The Company also engages a single third-party manufacturer

to provide fill/finish services for clinical supplies of both Fovista and Zimura. In addition, the Company currently relies exclusively upon Nektar Therapeutics, or Nektar, to supply it with a proprietary polyethylene glycol, or PEG, reagent for Fovista under a manufacturing and supply agreement. PEG reagent is a chemical the Company uses to modify the chemically synthesized aptamer in Fovista. The PEG reagent made by Nektar is proprietary to Nektar. The Company obtains a different proprietary PEG reagent used to modify the chemically synthesized aptamer in Zimura from a different supplier on a purchase order basis. Furthermore, the Company and its contract manufacturers currently rely upon sole-source suppliers of certain raw materials and other specialized components of production used in the manufacture and fill/finish of each of Fovista and Zimura. If the Company's third-party manufacturers or fill/finish service providers should become unavailable to the Company for any reason, including as a result of capacity constraints, financial difficulties or insolvency, the Company believes that there are a limited number of potential replacement manufacturers, and the Company likely would incur added costs and delays in identifying or qualifying such replacements.

Foreign Currency Translation

The Company considers the U.S. dollar to be its functional currency. Expenses denominated in foreign currencies are translated at the exchange rate on the date the expense is incurred. The effect of exchange rate fluctuations on translating foreign currency assets and liabilities into U.S. dollars is included in the Statements of Operations. Foreign exchange transaction gains and losses are included in the results of operations and are not material in the Company's financial statements.

Financial Instruments

Cash equivalents and available for sale securities are reflected in the accompanying financial statements at fair value. The carrying amount of accounts payable and accrued expenses, including accrued research and development expenses, approximates fair value due to the short-term nature of those instruments.

Property and Equipment

Property and equipment, which consists mainly of manufacturing and clinical equipment, furniture and fixtures, computers, software, and other office equipment, and leasehold improvements, are carried at cost less accumulated depreciation. Depreciation is computed over the estimated useful lives of the respective assets, generally three to ten years, using the straight-line method.

Research and Development

Research and development expenses primarily consist of costs associated with the manufacturing, development and clinical testing of Fovista and Zimura as well as costs associated with the preclinical development of other product candidates and formulations. Research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as contract research organizations ("CROs") and other vendors and contract manufacturing organizations ("CMOs") for the production of drug substance and drug product; and
- employee-related expenses, including salaries, benefits and share-based compensation expense.

Research and development expenses also include costs of acquired product licenses and related technology rights where there is no alternative future use, costs of prototypes used in research and development, consultant fees and amounts paid to collaborative partners.

All research and development expenses are charged to operations as incurred in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic, or ASC, 730, *Research and Development*. The Company accounts for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made.

Income Taxes

The Company utilizes the liability method of accounting for deferred income taxes, as set forth in ASC 740, *Income Taxes*. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. The Company incurred U.S. federal net operating losses ("NOLs") in each year from its inception in 2007 through 2013 and utilized these NOLs in 2014. Additionally, the Company incurred a U.S. federal net operating loss in 2015 that has been carried back to 2014. Accordingly, all tax years since 2007 are subject to potential tax examination. In the second quarter of 2016, the Internal Revenue Service began an examination of the Company's 2014 corporate income tax return. To date, no findings or assessments have been received by the Company.

The Company also received notification from the New York State Department of Taxation and Finance of its intention to perform an audit of the Company's New York State income tax returns for the tax years 2013 and 2014. This audit is scheduled to commence during the second quarter of 2017.

Share-Based Compensation

The Company follows the provisions of ASC 718, *Compensation—Stock Compensation*, which requires the measurement and recognition of compensation expense for all share-based payment awards made to employees and non-employee directors, including employee stock options, restricted stock units (“RSUs”) and the option granted to employees to purchase shares under the 2016 Employee Stock Purchase Plan (the “ESPP”). Share-based compensation expense is based on the grant date fair value estimated in accordance with the provisions of ASC 718 and is generally recognized as an expense over the requisite service period, net of estimated forfeitures. For grants containing performance-based vesting provisions, expense is recognized over the estimated achievement period.

Stock Options

The Company estimates the fair value of stock options granted to employees and non-employee directors on the date of grant using the Black-Scholes option-pricing model. Due to the lack of trading history, the Company's computation of stock-price volatility is based on the volatility rates of comparable publicly held companies over a period equal to the expected term of the options granted by the Company. The Company's computation of expected term is determined using the "simplified" method, which is the midpoint between the vesting date and the end of the contractual term. The Company believes that it does not have sufficient reliable exercise data in order to justify the use of a method other than the "simplified" method of estimating the expected exercise term of employee stock option grants. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends to stockholders and has no current intentions to pay cash dividends. The risk-free interest rate is based on the zero-coupon U.S. Treasury yield at the date of grant for a term equivalent to the expected term of the option.

For stock options granted as consideration for services rendered by consultants, the Company recognizes expense in accordance with the requirements of ASC 505-50, *Equity Based Payments to Non-Employees*. Consultant stock option grants are recorded as an expense over the vesting period of the underlying stock options. At the end of each financial reporting period prior to vesting, the value of these options, as calculated using the Black-Scholes option-pricing model, will be re-measured using the fair value of the Company's common stock and the non-cash expense recognized during the period will be adjusted accordingly. Since the fair value of options granted to consultants is subject to change in the future, the amount of the future expense will include fair value re-measurements until the stock options are fully vested.

The weighted-average assumptions used to estimate grant date fair value of stock options using the Black-Scholes option pricing model were as follows for the years ended December 31, 2016, 2015 and 2014:

	Years ended December 31,		
	2016	2015	2014
Expected common stock price volatility	71%	72%	82%
Risk-free interest rate	1.14% - 2.37%	1.35% - 2.24%	1.61% - 2.13%
Expected term of options (years)	6.1	6.2	6.2
Expected dividend yield	—	—	—

RSUs

The Company estimates the fair value of RSUs granted to employees using the closing market price of the Company's common stock on the date of grant.

ESPP

In April 2016, the board of directors adopted the ESPP pursuant to which the Company may sell up to an aggregate of 1,000,000 shares of common stock. The ESPP was approved by the Company’s stockholders in June 2016. The ESPP is considered compensatory and the fair value of the discount and look back provision are estimated using the Black-Scholes option-pricing model and recognized over the six month withholding period prior to purchase.

Share-based compensation expense includes expenses related to stock options and RSUs granted to employees, non-employee directors and consultants, as well as the option granted to employees to purchase shares under the ESPP, all of which have been reported in the Company's Statements of Operations as follows:

	Years ended December 31,		
	2016	2015	2014
Research and development	$ 21,380	$ 16,608	$ 7,594
General and administrative	10,280	8,152	5,446
Total	$ 31,660	$ 24,760	$ 13,040

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-9, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-9"). ASU 2014-9 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. The FASB subsequently issued additional clarifying standards to address issues arising from implementation of the new revenue standard, including a one-year deferral of the effective date for the new revenue standard. Public companies should now apply the guidance in ASU 2014-9 to annual reporting periods beginning after December 15, 2017 and interim periods within those annual periods. Earlier application is permitted only as of annual reporting periods beginning after December 15, 2016, including interim periods within that annual period. Companies may use either a full retrospective or a modified retrospective approach to adopt ASU 2014-9. The Company has not yet completed its final review of the impact of this guidance, however the Company anticipates applying the modified retrospective method upon adoption of ASU 2014-9, effective January 1, 2018.

In August 2014, the FASB issued ASU 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, which defines management's responsibility to assess an entity's ability to continue as a going concern, and to provide related footnote disclosures if there is substantial doubt about its ability to continue as a going concern. The pronouncement is effective for annual and interim reporting periods ending after December 15, 2016 with early adoption permitted. The Company has adopted ASU 2014-15 effective December 31, 2016. The adoption of this guidance did not have a material impact on the Company's financial statements.

In November 2015, the FASB issued ASU 2015-17, *Income Taxes (Topic 740)*: *Balance Sheet Classification of Deferred Taxes*, which updated and simplified the presentation of deferred income taxes. Current GAAP requires an entity to separate deferred income tax assets and liabilities into current and non-current amounts in a classified statement of financial position. The requirement results in little or no benefit to users of financial statements because the classification does not generally align with the time period in which the recognized deferred tax amounts are expected to be recovered or settled. To simplify the presentation of deferred income taxes, the amendments in this update require that deferred tax assets and liabilities be classified as noncurrent in a classified statement of financial position. The current requirement that deferred tax assets and liabilities of a tax-paying component of an entity be offset and presented as a single amount is not affected by the amendments in this update. The amendments in this update are effective for financial statements issued for annual periods beginning after December 15, 2016 and interim periods within those annual periods. Earlier application is permitted as of the beginning of an interim or annual reporting period. The Company has adopted this standard retrospectively, effective December 31, 2015.

In February 2016, the FASB issued ASU No. 2016-2, Leases (Topic 842). Under the new guidance, lessees will be required to recognize the following for all leases (with the exception of short-term leases) at the commencement date: (1) A lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and (2) A right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. Under the new guidance, lessor accounting is largely unchanged. Certain targeted improvements were made to align, where necessary, lessor accounting with the lessee accounting model and Topic 606, *Revenue from Contracts with Customers*. The new lease guidance simplified the accounting for sale and leaseback transactions primarily because lessees must recognize lease assets and lease liabilities. Lessees will no longer be provided with a source of off-balance sheet financing. Public business entities should apply the amendments in ASU 2016-2 for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years (i.e., January 1, 2019, for a calendar year entity). Early application is permitted for all public business entities and all nonpublic business entities upon issuance. Lessees (for capital and operating

leases) and lessors (for sales-type, direct financing, and operating leases) must apply a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The modified retrospective approach would not require any transition accounting for leases that expired before the earliest comparative period presented. Lessees and lessors may not apply a full retrospective transition approach. 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 2016-9, *Compensation - Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*. The amendments are intended to improve the accounting for employee share-based payments and affect all organizations that issue share-based payment awards to their employees. Several aspects of the accounting for share-based payment award transactions are simplified, including: (*a*) income tax consequences; (*b*) classification of awards as either equity or liabilities; and (*c*) classification on the statement of cash flows. For public companies, the amendments are effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted in any interim or annual period. The Company early adopted ASU 2016-09 during the fourth quarter of 2016. Due to the Company's history of operating losses, the adoption did not result in changes to the Company's Net loss or Retained earnings and the classification of excess tax benefits on the statement of cash flows for prior periods have not been adjusted. In connection with the adoption of ASU 2016-9, the Company made a policy election to continue its methodology for the development and application of its forfeiture rate. On a prospective basis, effective the year ended December 31, 2016 the Company will record all excess tax benefits and deficiencies as income tax expense or benefit.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*, which clarifies the presentation of certain specific cash flow issues in the Statement of cash flows. For public companies, the amendments are effective for annual reporting periods beginning after December 15, 2017, and interim periods within those annual periods and early adoption is permitted. This new guidance is not expected to have a material impact on the Company’s Consolidated Financial Statements.

3. Net Loss Per Common Share

Basic and diluted net income (loss) per common share is determined by dividing net income (loss) by the weighted average common shares outstanding during the period. For the periods where there is a net loss, stock options and RSUs have been excluded from the calculation of diluted net loss per common share because their effect would be anti-dilutive. Therefore, the weighted average common shares used to calculate both basic and diluted net loss per common share would be the same. The following table sets forth the computation of basic and diluted net income (loss) per common share for the periods indicated:

	Years ended December 31,		
	2016	2015	2014
Basic and diluted net loss per common share calculation:			
Net loss	$ (193,420)	$ (105,717)	$ (116,772)
Weighted average common shares outstanding	35,486	34,580	33,258
Net loss per common share—basic and diluted	$ (5.45)	$ (3.06)	$ (3.51)

The following potentially dilutive securities have been excluded from the computations of diluted weighted average common shares outstanding for the periods presented, as they would be anti-dilutive:

	Years ended December 31,		
	2016	2015	2014
Stock options outstanding	3,359	3,009	3,680
Restricted stock units	721	288	37
Warrants	—	—	14
Total	4,080	3,297	3,731

4. Cash, Cash Equivalents and Available for Sale Securities

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at the date of purchase to be cash equivalents. Cash and cash equivalents included cash of $25.8 million and $5.5 million at December 31, 2016 and 2015, respectively. Cash and cash equivalents at December 31, 2016 and December 31, 2015 also included $108.1

million and $216.4 million, respectively, of investments in money market funds, U.S. Treasury securities and certain short-term investment-grade corporate debt securities with original maturities of 90 days or less.

The Company considers securities with original maturities of greater than 90 days at the date of purchase to be available for sale securities. The Company held available for sale securities with a fair value totaling $155.3 million and $170.0 million as of December 31, 2016 and 2015, respectively. These available for sale securities consisted of U.S. Treasury securities and investment-grade corporate debt securities. At December 31, 2016, the Company held available for sale securities of $155.3 million with maturities of less than one year. The Company did not hold any securities with maturities of greater than one year at December 31, 2016. The Company evaluates securities with unrealized losses, if any, to determine whether such losses are other than temporary. The Company has determined that there were no other than temporary losses in fair value of its investments as of December 31, 2016. The Company classifies these securities as available for sale, however, the Company does not currently intend to sell its investments and the Company believes it is more likely than not that the Company will recover the carrying value of these investments.

Available for sale securities, including carrying value and estimated fair values, are summarized as follows:

	As of December 31, 2016			
	Cost	Unrealized Gains	Unrealized Losses	Fair Value
U.S. Treasury securities	$ 120,288	$ 6	$ (33)	$ 120,261
Corporate debt securities	35,114	—	(27)	35,087
Total	$ 155,402	$ 6	$ (60)	$ 155,348

	As of December 31, 2015			
	Cost	Unrealized Gains	Unrealized Losses	Fair Value
U.S. Treasury securities	$ 130,507	$ —	$ (311)	$ 130,196
Corporate debt securities	39,995	—	(162)	39,833
Total	$ 170,502	$ —	$ (473)	$ 170,029

The Company's available for sale securities are reported at fair value on the Company's Balance Sheets. Unrealized gains (losses) are reported within accumulated other comprehensive income (loss) in the statements of comprehensive income (loss). The cost of securities sold and any realized gains/losses from the sale of available for sale securities are based on the specific identification method. The changes in accumulated other comprehensive income (loss) associated with the unrealized gain (loss) on available for sale securities for the years ended December 31, 2016 and December 31, 2015 were as follows:

	Years ended December 31,	
	2016	2015
Beginning balance	$ (473)	$ (65)
Current period changes in fair value before reclassifications, net of tax	261	(351)
Amounts reclassified from accumulated other comprehensive income (loss), net of tax	—	(57)
Total other comprehensive income (loss)	261	(408)
Ending balance	$ (212)	$ (473)

5. Licensing and Commercialization Agreement with Novartis Pharma AG

In May 2014, the Company entered into a licensing and commercialization agreement with Novartis Pharma AG ("Novartis", and such agreement, the "Novartis Agreement"). Under the Novartis Agreement, the Company granted Novartis exclusive rights under specified patent rights, know-how and trademarks controlled by the Company to manufacture, from bulk active pharmaceutical ingredient, or API, supplied by the Company, standalone Fovista products and products combining Fovista with an anti-VEGF drug to which Novartis has rights in a co-formulated product, for the treatment, prevention, cure or control of any human disease, disorder or condition of the eye, and to develop and commercialize those licensed products in all countries outside of the United States (the "Novartis Territory"). The Company has agreed to use commercially reasonable efforts to complete its ongoing pivotal Phase 3 clinical program for Fovista and Novartis has agreed to use commercially reasonable efforts to develop a standalone Fovista product and a co-formulated product containing Fovista and an anti-VEGF

drug to which Novartis has rights, as well as a pre-filled syringe presentation of such products and to use commercially reasonable efforts, subject to obtaining marketing approval, to commercialize licensed products in the Novartis Territory in accordance with agreed development and marketing plans. Novartis has also granted the Company options, subject to specified limitations, and to the extent such rights are controlled by Novartis, to obtain exclusive rights from Novartis to develop and commercialize in the United States the co-formulated and pre-filled syringe products developed by Novartis. The Company and Novartis have each granted the other options, subject to specified limitations, to obtain access to study data from certain clinical trials of licensed products that the Company or Novartis may conduct, including for use by the other in regulatory filings in its territory. The Company has agreed to exclusively supply Novartis, and Novartis has agreed to exclusively purchase from the Company, its clinical and commercial requirements for the bulk API for Fovista for use in licensed products in the Novartis Territory. The Company has agreed not to commercialize any product comprising Fovista or any other anti-PDGF product in the ophthalmic field in the Novartis Territory.

Novartis paid the Company a $200.0 million upfront fee upon execution of the Novartis Agreement. Novartis also paid the Company $50.0 million upon the achievement of each of two patient enrollment-based milestones, and $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate of $130.0 million. Under the terms of the Novartis Agreement, Novartis is also obligated to pay up to an aggregate of an additional $300.0 million upon achievement of specified regulatory milestones, including marketing approval and reimbursement approval in certain countries in the Novartis Territory. In addition, Novartis has agreed to pay the Company up to an aggregate of an additional $400.0 million if Novartis achieves specified sales milestones in the Novartis Territory. Novartis is also obligated to pay the Company royalties with respect to standalone Fovista products and combination Fovista products that Novartis successfully commercializes. The Company will receive royalties at a mid-thirties percentage of net sales of standalone Fovista products and a royalty of approximately equal value for sales of combination Fovista products. Such royalties are subject to customary deductions, credits, and reductions for lack of patent coverage or market exclusivity. Novartis's obligation to pay such royalties will continue on a licensed product-by-licensed product and country-by-country basis until Novartis's last actual commercial sale of such licensed product in such country. The Company will continue to be responsible for royalties it owes to third parties on sales of Fovista products.

Novartis has agreed to pay the Company’s manufacturing costs for clinical supplies and the Company’s manufacturing costs plus a specified percentage margin for commercial supplies of the bulk API for Fovista that the Company supplies to Novartis. If the Company or Novartis exercises each of their respective rights to obtain access to study data from clinical trials conducted by the other party, the party exercising the option will be obligated to pay the other party's associated past development costs and share with such other party any future associated development costs. If the Company exercises its option to obtain Novartis-controlled rights to develop, manufacture and commercialize any co-formulated Fovista product in the United States, the Company will be obligated to pay a specified percentage of Novartis's associated past development costs and share with Novartis any future associated development costs. The Company and Novartis will also need to negotiate and agree on financial and other terms that would apply to such rights. If the Company exercises its option to obtain Novartis-controlled rights to develop and commercialize a pre-filled syringe product in the United States, the Company will be obligated to either enter into a supply agreement with Novartis under which the Company will pay Novartis its manufacturing cost plus a specified percentage margin for supplies of Fovista products in pre-filled syringes that Novartis supplies to the Company, or obtain supplies of products in pre-filled syringes from a third party manufacturer and pay Novartis a low single-digit percentage of the Company's net sales of such products.

The Company has retained control over the design and execution of its pivotal Phase 3 clinical program for Fovista and remains responsible for funding the costs of that program, subject to Novartis's responsibility to provide Lucentis, an anti-VEGF drug to which Novartis has rights in the Novartis Territory, for use in the Phase 3 trials already initiated and in other Phase 2 and Phase 3 clinical trials in the Novartis Territory initiated following the effective date of the Novartis Agreement. Novartis will have control over, and will be responsible for the costs of, all other clinical trials that may be required to obtain marketing approvals in the Novartis Territory for licensed products under the agreement. Novartis is also responsible for costs associated with co-formulation development, pre-filled syringe development and other development costs in the Novartis Territory, excluding regulatory filing fees in the European Union for the standalone Fovista product, for which the Company will be responsible.

The Novartis Agreement, unless earlier terminated by the Company or Novartis, will expire upon the expiration of Novartis's obligation to pay the Company royalties on net sales of licensed products. The Company and Novartis each may terminate the Novartis Agreement if the other party materially breaches the agreement and does not cure such breach within a specified cure period, if the other party experiences any specified insolvency event, if the other party challenges or assists a third party in challenging the validity or enforceability of certain patent rights controlled by the terminating party, or if the parties are prevented in any manner that materially adversely affects the progression of the development or commercialization of licensed products for a specified period as a result of specified governmental actions. Novartis may terminate the Novartis Agreement at any time without cause, or within a specified period after a change in control of the Company, as defined in the

Novartis Agreement, or for specified safety reasons, effective at the end of a specified period following Novartis's written notice to the Company of Novartis's election to terminate the agreement. The Company may also terminate the agreement if Novartis determines to seek marketing approval of an alternative anti-PDGF product in the Novartis Territory as more fully described below. If the Company elects to terminate the Novartis Agreement because specified governmental actions prevent the parties from materially progressing the development or commercialization of licensed products as described above, the Company will be required to pay a substantial termination fee. Following any termination, all rights to Fovista that the Company granted to Novartis, including, without limitation, the right to commercialize standalone Fovista products in the Novartis Territory, will revert to the Company, Novartis will perform specified activities in connection with transitioning to the Company the rights and responsibilities for the continued development, manufacture and commercialization of the standalone Fovista product for countries in the Novartis Territory, and the parties will cooperate on an orderly wind down of development and commercialization activities for other licensed products in the Novartis Territory.

Novartis has agreed to specified limitations on its ability to in-license, acquire or commercialize any anti-PDGF product that does not contain Fovista (an "Alternative Anti-PDGF Product") in the Novartis Territory and, to the extent Novartis develops, in-licenses or acquires such a product, to make such product available to the Company in the United States under specified option conditions. If the Company exercises its option, the Company will be obligated to make certain payments to Novartis, including specified milestone and royalty payments. The amounts of such payments will vary based on the product's stage of clinical development at the time the Company exercises its option, whether the product is a standalone or combination product and whether Novartis exercises an option to co-promote such product in the United States. If Novartis determines to seek marketing approval of an Alternative Anti-PDGF Product in the Novartis Territory, the Company will, subject to specified limitations, have the option to terminate the Novartis Agreement, convert Novartis's exclusive licenses into non-exclusive licenses, or elect to receive a royalty on sales of such product by Novartis. If the Company elects to terminate the Novartis Agreement, Novartis will, subject to specified limitations, be required to pay to the Company, certain payments based on achievement, with respect to such product, of the milestones that would have otherwise applied to licensed products under the Novartis Agreement.

Activities under the Novartis Agreement were evaluated under ASC 605-25, *Revenue Recognition—Multiple Element Arrangements*("ASC 605-25") (as amended by ASU 2009-13, *Revenue Recognition* ("ASU 2009-13")) to determine if they represented a multiple element revenue arrangement. The Novartis Agreement includes the following deliverables: (1) an exclusive license to commercialize Fovista outside the United States (the "License Deliverable"); (2) the performance obligation to conduct research and development activities related to the Phase 3 Fovista clinical trials and certain Phase 2trials for Fovista (the "R&D Activity Deliverable"); (3) the performance obligation to supply API to Novartis for development and manufacturing purposes (the "Manufacturing Deliverable") and (4) the Company's obligation to participate on the joint operating committee established under the terms of the Novartis Agreement and related subcommittees (the "Joint Operating Committee Deliverable"). Novartis has the right, subject to certain approval rights of the Company, to sublicense the exclusive royalty-bearing license to commercialize Fovista in the Novartis Territory. The Company's obligation to provide access to clinical and regulatory information as part of the License Deliverable includes the obligation to provide access to all clinical data, regulatory filings, safety data and manufacturing data to Novartis which is necessary for the commercialization of Fovista in the Novartis Territory. The R&D Activity Deliverable includes the right and responsibility for the Company to conduct the Phase 3 Fovista clinical program and other studies of Fovista in the Novartis Territory which are necessary or desirable for regulatory approval or commercialization of Fovista. The Manufacturing Deliverable includes the obligation for the Company to supply API to Novartis for clinical purposes, for which Novartis has agreed to pay the Company’s manufacturing costs, and for commercial purposes, for which Novartis has agreed to pay the Company’s manufacturing costs plus a specified margin. The Joint Operating Committee Deliverable includes the obligation to participate in the Joint Operating Committee and related subcommittees at least through the first anniversary of regulatory approval in the European Union. All of these deliverables were deemed to have stand-alone value and to meet the criteria to be accounted for as separate units of accounting under ASC 605-25. Factors considered in this determination included, among other things, the subject of the licenses and the research and development and commercial capabilities of Novartis. Accordingly, each unit will be accounted for separately.

Options are considered substantive if, at the inception of the arrangement, the Company is at risk as to whether the collaboration partner will choose to exercise the option. Factors that the Company considers in evaluating whether an option is substantive include the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the option, the cost to exercise the option and the likelihood that the option will be exercised. For arrangements under which an option is considered substantive, assuming the option is not priced at a significant and incremental discount, the Company does not consider the item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable arrangement consideration. Conversely, for arrangements under which an option is not considered substantive or if an option is priced at a significant and incremental discount, the Company would consider the item underlying the option to be a deliverable at the inception of the arrangement and a corresponding amount would be included in allocable arrangement consideration. All of the options included in the

Novartis Agreement have been determined to be substantive, and none of the options are priced at a significant and incremental discount.

The Novartis Agreement provides that, if the Company elects to terminate the Novartis Agreement because specified governmental actions prevent the parties from materially progressing the development or commercialization of licensed products as described above, the Company will be required to pay a substantial termination fee. The Company has concluded that this termination provision constitutes a contingent event that was unknown at the inception of the agreement. As such, the Company has recorded the $200.0 million upfront payment in deferred revenue, long-term until such time that the contingency related to this termination provision is resolved. The Company believes the enrollment-based milestones and certain reimbursement milestones that may be achieved under the Novartis Agreement do not meet the recognition criteria within the definition of a milestone included in ASU 2010-17, *Revenue Recognition—Milestone Method*, and therefore, payments received for the achievement of the enrollment milestones in excess of the termination fee will be included in the allocable arrangement consideration and allocated to the deliverables based upon BESP using the relative selling price method.

The Company believes the marketing approval milestones that may be achieved under the Novartis Agreement are consistent with the definition of a milestone included in ASU 2010-17, *Revenue Recognition—Milestone Method*, and, accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when the applicable milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone.

In May 2014, the Company received an upfront payment of $200.0 million in connection with its entry into the Novartis Agreement, which has not been recorded as revenue due to certain contingencies associated with the payment. In each of September 2014 and March 2015, the Company achieved a $50.0 million enrollment-based milestone, and in June 2016, the Company achieved a $30.0 million enrollment-based milestone, for an aggregate total of $130.0 million, under the Novartis Agreement. The Company uses the relative selling price method to allocate arrangement consideration to the Company's performance obligations under the Novartis Agreement. Below is a summary of the components of the Company's collaboration revenue for the years ended December 31, 2016, 2015, and 2014:

	Years ended December 31,		
	2016	2015	2014
License revenue	$ 22,937	$ 38,083	$ 38,373
Research and development activity revenue	9,741	8,378	2,000
API transfer revenue	18,212	5,020	883
Joint operating committee revenue	19	24	3
Total collaboration revenue	$ 50,909	$ 51,505	$ 41,259

As of December 31, 2016, the Company had recorded total deferred revenue of approximately $210.0 million, $200.0 million of which relates to the upfront payment, with the remaining $10.0 million primarily attributable to the Company’s on-going performance obligations under the R&D Activity Deliverable.

6. Financing Agreement with Novo A/S

In May 2013, the Company entered into a Purchase and Sale Agreement with Novo A/S, which is referred to as the Novo Agreement, pursuant to which the Company had the ability to obtain financing in three tranches in an amount of up to $125.0 million in return for the sale to Novo A/S of aggregate royalties of worldwide sales of (a) Fovista, (b) Fovista-Related Products, and (c) Other Products (each as defined in the Novo Agreement), calculated as mid-single digit percentages of net sales.

The Novo Agreement provided for up to three separate purchases for a purchase price of $41.7 million each, at a first, second and third closing, for an aggregate purchase price of $125.0 million. In each purchase, Novo A/S would acquire rights to a low single digit percentage of net sales. In each of May 2013, January 2014 and November 2014, the Company received cash payments of $41.7 million, or $125.0 million in the aggregate, and Novo A/S received, in the aggregate, a right to receive royalties on net sales of Fovista at a mid-single digit percentage.

The royalty payment period covered by the Novo Agreement begins on commercial launch and ends, on a product-by-product and country-by-country basis, on the latest to occur of (i) the 12th anniversary of the commercial launch, (ii) the expiration of certain patent rights and (iii) the expiration of the regulatory exclusivity for each product in each country.

Under the terms of the Novo Agreement, the Company is not required to reimburse or otherwise compensate Novo A/S through any means other than the agreed royalty entitlement. In addition, the Company does not, under the terms of the Novo Agreement, have the right or obligation to prepay Novo A/S in connection with a change of control of the Company or otherwise.

The $125.0 million in aggregate proceeds from the three financing tranches under the Novo Agreement represents the full funding available under the Novo Agreement, and has been recorded as a liability on the Company's Balance Sheet as of December 31, 2016, in accordance with ASC 730, *Research and Development*. Because there is a significant related party relationship between the Company and Novo A/S, the Company is treating its obligation to make royalty payments under the Novo Agreement as an implicit obligation to repay the funds advanced by Novo A/S. As the Company makes royalty payments in accordance with the Novo Agreement, it will reduce the liability balance. At the time that such royalty payments become probable and estimable, and if such amounts exceed the liability balance, the Company will impute interest accordingly on a prospective basis based on such estimates.

The Novo Agreement requires the establishment of a Joint Oversight Committee in the event that Novo A/S does not continue to have a representative on the Company's board of directors. The Joint Oversight Committee would have responsibilities that include "discussion and review" of all matters related to Fovista research, development, regulatory approval and commercialization, but there is no provision either implicit or explicit that gives the Joint Oversight Committee or its members decision-making authority.

7. Property and Equipment

Property and equipment as of December 31, 2016 and 2015 were as follows:

	Useful Life (Years)	December 31, 2016	December 31, 2015
Manufacturing and clinical equipment	7 - 10	$ 617	$ 617
Computer, software and other office equipment	5	1,711	944
Furniture and fixtures	7	774	738
Leasehold improvements	3 - 5	1,835	1,551
Construction-in-progress		—	515
		4,937	4,365
Accumulated depreciation		(1,656)	(899)
Property and equipment, net		$ 3,281	$ 3,466

For the years ended December 31, 2016, 2015 and 2014, depreciation expense was $757 thousand, $698 thousand and $127 thousand, respectively.

8. Income Taxes

The Company utilizes the liability method of accounting for deferred income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. A valuation allowance is established against deferred tax assets when, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company's policy is to record interest and penalties on uncertain tax positions as income tax expense.

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. A reconciliation of the statutory U.S. federal rate to the Company's effective tax rate is as follows:

	Years ended December 31,		
	2016	2015	2014
Percent of pre-tax income:			
U.S. federal statutory income tax rate	35.0 %	35.0 %	35.0 %
State taxes, net of federal benefit	2.8 %	7.4 %	6.8 %
Permanent items	(1.4)%	(0.5)%	2.3 %
Impact of state rate changes	(11.0)%	0.9 %	— %
Research and development credit	1.9 %	— %	— %
Other	1.1 %	— %	— %
Change in valuation allowance	(28.2)%	(29.1)%	(89.5)%
Effective income tax rate	0.2 %	13.7 %	(45.4)%

The components of income tax (benefit) expense are as follows:

	Years ended December 31,		
	2016	2015	2014
Current:			
Federal	$ (23,393)	$ 136	$ 29,505
State	21	91	11,440
Deferred:			
Federal	22,966	(17,014)	(4,469)
State	—	—	—
Income tax (benefit) expense	$ (406)	$ (16,787)	$ 36,476

Significant components of the Company's deferred tax assets (liabilities) for 2016 and 2015 consist of the following:

	As of December 31,	
	2016	2015
Deferred tax assets (liabilities)		
Deferred revenue	$ 125,634	$ 142,675
License and technology payments	10,532	13,150
Share-based compensation	16,494	11,427
Accrued expenses	530	743
Depreciation	(651)	(617)
Federal and state net operating loss carryforwards	75,177	26,065
Excess tax benefits related to share-based compensation	—	1,630
Research and development credits	3,720	—
Other	2,155	5
Deferred income tax assets	233,591	195,078
Valuation allowance	(233,591)	(171,965)
Net deferred tax assets	$ —	$ 23,113

In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible, and is impacted by the Company's ability to carry back losses to 2014, the only year in which the Company had taxable income. The Company incurred tax losses in 2016. The Company realized its net deferred tax assets recorded as of December 31, 2015 in 2016 as a result of the Company's carry back of its 2015 federal tax losses to 2014. The Company has carried forward its 2015 state tax losses due to various state restrictions on the use of carryback claims. The state NOLs are expected to begin to expire in 2027. Due to the Company's history of losses and lack of other positive evidence to support

taxable income after the 2014 tax year, the Company has recorded a valuation allowance against those remaining deferred tax assets that are not expected to be realized. As of December 31, 2016, the Company has federal NOLs carryforwards of approximately $187.4 million. These losses are due to expire in 2036.

For the years ended December 31, 2016 and 2015, the Company recorded a benefit from income taxes of $0.4 million and $16.8 million, respectively. The benefit from income taxes recorded in each period of 2016 and 2015 was based upon the Company's estimated federal and state income tax liability for those respective years.

For the year ended December 31, 2016, the Company recorded an income tax benefit of $0.4 million related to unanticipated refunds received and the reduction in its valuation allowances to reflect the income tax associated with unrealized gains on available for sale securities recorded in other comprehensive income (loss). A corresponding income tax provision was also recorded in other comprehensive income (loss).

Pursuant to ASC 740, *Income Taxes*, the Company routinely evaluates the likelihood of success if challenged on income tax positions claimed on its income tax returns. During the year ended December 31, 2016, the Company reduced certain deferred tax assets by $3.8 million and reduced the corresponding valuation allowance by an equivalent amount. These items have not been recognized in the financial statements and if disallowed by the tax authorities, would not result in an adjustment to the Company's effective tax rate, its balance sheet or its cash flow statements for the current year.

The Company's position with respect to uncertain tax positions is set forth below:

Opening balance	$	300
Gross amount of increases in unrecognized tax benefits during the period - current year provisions		—
Gross amount of increases in unrecognized tax benefits during the period - prior year provisions		3,828
Gross amount of increases in unrecognized tax benefits during the period - other		—
Decreases due to settlement with tax authorities during the period		—
Reduction of unrecognized tax benefits due to expiration of the state of limitations during the period		—
Closing Balance	$	4,128

As the Company is currently being audited by the Internal Revenue Service and also anticipates an audit by the New York State Department of Taxation and Finance to occur during 2017, an estimate of unrecognized tax benefits that may be realized over the next twelve months cannot be determined at this time.

The Company will continue to evaluate its ability to realize its deferred tax assets on a periodic basis and will adjust such amounts in light of changing facts and circumstances including, but not limited to, future projections of taxable income, tax legislation, rulings by relevant tax authorities, the progress of ongoing tax audits and the regulatory approval of products currently under development. Any additional changes to the valuation allowance recorded on deferred tax assets in the future would impact the Company's income taxes.

9. Operating Leases

The Company leases office space located in Princeton, New Jersey and New York, New York under operating lease arrangements. The lease for the Company's principal Princeton office space expires in February 2018, whereas the lease for the Company's New York office space expires in January 2018. Future minimum rental commitments under non-cancelable operating leases in effect as of December 31, 2016, are as follows:

2017	$	4,316
2018		249
Total	$	4,565

Rent expense is calculated on the straight-line basis and amounted to $3.0 million, $2.1 million and $1.0 million for the years ended December 31, 2016, 2015 and 2014, respectively. In January 2017, the Company terminated its office leases in New York, NY and Princeton, NJ and made aggregate termination payments of approximately $2.1 million. The table above includes these termination payments, as well as the Company's continuing rent obligations through February 2018.

10. Commitments and Contingencies

Under various agreements, the Company may be required to pay royalties and make milestone payments. These agreements include the following:

- Under the Company's divestiture agreement with OSI (Eyetech), Inc., which agreement is now held by OSI Pharmaceuticals, LLC., or OSI Pharmaceuticals, a subsidiary of Astellas US, LLC, for rights to particular anti-PDGF aptamers, including Fovista, the Company is obligated to pay to OSI Pharmaceuticals future one-time payments of $12.0 million in the aggregate upon marketing approval in the United States and the European Union of a covered anti-PDGF product. The Company is also obligated to pay to OSI Pharmaceuticals a royalty at a low single-digit percentage of net sales of any covered anti-PDGF product the Company successfully commercializes.

- Under a license agreement with Archemix Corp., or Archemix, with respect to pharmaceutical products comprised of or derived from any anti-PDGF aptamer, the Company is obligated to make future payments to Archemix of up to an aggregate of $14.0 million if the Company achieves specified clinical and regulatory milestones with respect to Fovista, up to an aggregate of $3.0 million if the Company achieves specified commercial milestones with respect to Fovista and, for each other anti-PDGF aptamer product that it may develop under the agreement, up to an aggregate of approximately $18.8 million if the Company achieves specified clinical and regulatory milestones and up to an aggregate of $3.0 million if the Company achieves specified commercial milestones. No royalties are payable to Archemix under this license agreement.

- Under a license agreement with Archemix with respect to pharmaceutical products comprised of or derived from anti-C5 aptamers, for each anti-C5 aptamer product that the Company may develop under the agreement, including Zimura, the Company is obligated to make future payments to Archemix of up to an aggregate of $57.5 million if the Company achieves specified development, clinical and regulatory milestones, and up to an aggregate of $22.5 million if the Company achieves specified commercial milestones. The Company is also obligated to pay Archemix a double-digit percentage of specified non-royalty payments the Company may receive from any sublicensee of the Company's rights under this license agreement. No royalties are payable to Archemix under this license agreement.

- Under a license, manufacturing and supply agreement with Nektar Therapeutics, or Nektar, for specified pegylation reagents used to manufacture Fovista, the Company is obligated to make future payments to Nektar of up to an aggregate of $6.5 million if the Company achieves specified clinical and regulatory milestones, and an additional payment of $3.0 million if the Company achieves a specified commercial milestone with respect to Fovista. The Company is obligated to pay Nektar tiered royalties at low to mid-single-digit percentages of net sales of any licensed product the Company successfully commercializes, with the royalty percentage determined by the Company's level of licensed product sales, the extent of patent coverage for the licensed product and whether the Company has granted a third-party commercialization rights to the licensed product. In June 2014, the Company paid Nektar $19.8 million in connection with its entry into the Novartis Agreement.

- Under the Novo Agreement, with respect to Fovista, the Company will be obligated to pay Novo A/S a mid-single-digit percentage royalty based on worldwide sales of Fovista. See "Note 6—Financing Agreement with Novo A/S" above for further information about Novo Agreement.

- Under an option agreement with AVEO Pharmaceuticals relating to tivozanib, the Company was obligated to make milestone payments of $2.0 million upon the submission of an Investigational New Drug Application to the FDA and $6.0 million upon the earlier of demonstration of proof of concept in humans and a specified date in January 2017, subject to any exercise by the Company of its right to terminate the option agreement. In January 2017, the Company provided notice of termination of the Agreement, effective April 3, 2017.

The Company also has letter agreements with certain employees that require the funding of a specific level of payments, if certain events, such as a termination of employment in connection with a change in control or termination of employment by the employee for good reason or by the Company without cause, occur. For a description of these obligations, see the Company’s definitive proxy statement on Schedule 14A for the Company’s 2016 annual meeting of stockholders, as filed with the SEC on April 29, 2016.

In addition, in the course of normal business operations, the Company has agreements with contract service providers to assist in the performance of the Company’s research and development and manufacturing activities. Expenditures to CROs and CMOs represent significant costs in clinical development. Subject to required notice periods and the Company’s obligations under binding purchase orders, the Company can elect to discontinue the work under these agreements at any time.

Legal Proceedings

A purported class action lawsuit has been filed against the Company and certain of its current and former executive officers in the United States District Court for the Southern District of New York, captioned Frank Micholle et al. v. Ophthotech Corporation, et al., No. 1:17-cv-00210, filed on January 11, 2017. The complaint purports to be brought on behalf of shareholders who purchased the Company's common stock between May 11, 2015 and December 12, 2016. The complaint generally alleges that the Company and certain of its officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the prospects of the Company's Phase 3 trials for Fovista in combination with anti-VEGF drugs for the treatment of wet AMD. The complaint seeks equitable and/or injunctive relief, unspecified damages, attorneys' fees, and other costs. The Company denies any allegations of wrongdoing and intend to vigorously defend against this lawsuit. The Company is unable, however, to predict the outcome of this matter at this time. Moreover, any conclusion of these matters in a manner adverse to the Company and for which it incurs substantial costs or damages not covered by the Company's directors' and officers' liability insurance would have a material adverse effect on its financial condition and business. In addition, the litigation could adversely impact the Company's reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to the Company's ability to grow its business, any of which could have a material adverse effect on the Company's business.

11. Stock Option and Compensation Plans

The Company adopted its 2007 Stock Incentive Plan (the "2007 Plan") for employees, non-employee directors and consultants for the purpose of advancing the interests of the Company's stockholders by enhancing its ability to attract, retain and motivate persons who are expected to make important contributions to the Company. The 2007 Plan provided for the granting of stock option awards, RSUs, and other stock-based and cash-based awards. Following the effectiveness of the 2013 Stock Incentive Plan described below in connection with the closing of the Company's initial public offering, the Company is no longer granting additional awards under the 2007 Plan.

In August 2013, the Company's board of directors adopted and the Company's stockholders approved the 2013 stock incentive plan (the "2013 Plan"), which became effective immediately prior to the closing of the Company's initial public offering. In June 2015, the Company's board of directors adopted a first amendment to the 2013 Plan. The 2013 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, RSUs, restricted stock awards and other stock-based awards. Upon the effectiveness of the 2013 Plan, the number of shares of the Company's common stock that were reserved for issuance under the 2013 Plan was the sum of (1) such number of shares (up to approximately 3,359,641 shares) as is equal to the sum of 739,317 shares (the number of shares of the common stock then available for issuance under the 2007 Plan), and such number of shares of the Company's common stock that are subject to outstanding awards under the 2007 Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right plus (2) an annual increase, to be added the first business day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until, and including, the fiscal year ending December 31, 2023, equal to the lowest of 2,542,372 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 fiscal year and an amount determined by its board of directors. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2013 Plan. However, incentive stock options may only be granted to employees of the Company.

In connection with the evergreen provisions of the 2013 Plan, the number of shares available for issuance under the 2013 Plan was increased by approximately 1,257,000 shares, effective as of January 1, 2014, by approximately 1,360,000 shares, effective as of January 1, 2015, and by approximately 1,408,000 shares, effective as of January 1, 2016. As of December 31, 2016, the Company had approximately 1,028,000 shares available for grant under the 2013 Plan. In connection with the evergreen provisions of the 2013 Plan, the number of shares available for issuance under the 2013 Plan was further increased by approximately 1,429,000 shares, effective as of January 1, 2017.

In April 2016, the board of directors adopted the ESPP pursuant to which the Company may sell up to an aggregate of 1,000,000 shares of common stock. The ESPP was approved by the Company's stockholders in June 2016. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each six month offering period during the term of the ESPP. The first offering period began in September 2016.

A summary of the stock option activity, weighted average exercise prices, options outstanding and exercisable as of December 31, 2016, 2015 and 2014 is as follows:

	Years ended December 31,					
	2016		2015		2014	
	Common Stock Options	Weighted Average Exercise Price	Common Stock Options	Weighted Average Exercise Price	Common Stock Options	Weighted Average Exercise Price
Outstanding, December 31, 2015	3,009	$ 30.43	3,680	$ 21.03	2,708	$ 9.41
Granted	972	$ 60.40	764	$ 47.31	1,744	$ 33.92
Exercised	(428)	$ 15.73	(1,133)	$ 10.31	(621)	$ 4.75
Expired or forfeited	(194)	$ 48.63	(302)	$ 34.09	(151)	$ 28.50
Outstanding, December 31, 2016	3,359	$ 39.92	3,009	$ 30.43	3,680	$ 21.03

	Years ended December 31,		
	2016	2015	2014
Options exercisable at December 31, 2016	1,531	955	993
Weighted average grant date fair value (per share) of options granted during the period	38.18	31.33	24.41

As of December 31, 2016, there were approximately 2,665,000 options outstanding, net of estimated forfeitures, that had vested or are expected to vest. The weighted-average exercise price of these options was $38.95 per option; the weighted-average remaining contractual life of these options was 7.5 years; and the aggregate intrinsic value of these options was approximately $0.3 million. A summary of the stock options outstanding and exercisable as of December 31, 2016 is as follows:

	December 31, 2016				
		Options Outstanding		Options Exercisable	
Range of Exercise Prices	Total Options Outstanding	Weighted Average Remaining Life (Years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$0.12-$10.03	193	5.3	$ 6.84	137	$ 5.52
$10.04-$20.00	273	6.5	$ 13.44	170	$ 13.48
$20.01-$30.00	154	6.8	$ 25.56	114	$ 25.53
$30.01-$40.00	1,087	6.7	$ 32.70	758	$ 32.97
$40.01-$55.00	1,125	8.6	$ 46.22	319	$ 45.49
$55.01-$73.22	527	9.0	$ 71.33	33	$ 69.08
	3,359	7.6	$ 39.92	1,531	$ 31.19
Aggregate Intrinsic Value	254			254	

Cash proceeds from, and the aggregate intrinsic value of, stock options exercised during the years ended December 31, 2016, 2015 and 2014, respectively, were as follows:

	Years ended December 31,		
	2016	2015	2014
Cash proceeds from options exercised	$ 6,934	$ 11,473	$ 2,949
Aggregate intrinsic value of options exercised	$ 14,439	$ 49,255	$ 21,646

In connection with stock option awards granted to employees, the Company recognized approximately $22.8 million, $15.5 million and $11.3 million in share-based compensation expense during the years ended December 31, 2016, 2015 and 2014, respectively, net of expected forfeitures. As of December 31, 2016, there were approximately $25.1 million of

unrecognized compensation costs, net of estimated forfeitures, related to stock option awards to granted employees, which are expected to be recognized over a remaining weighted average period of 2.3 years.

In connection with stock options awards granted to consultants, the Company recognized approximately $1.7 million, $4.1 million and $1.4 million in share-based compensation expense during the years ended December 31, 2016, 2015 and 2014, respectively, net of expected forfeitures. As of December 31, 2016, there were approximately $5.4 million of unrecognized compensation costs, net of estimated forfeitures, related to stock option awards granted to consultants, which are expected to be recognized over a remaining weighted average period of 2.5 years.

The following table presents a summary of the Company's outstanding shares of RSU awards granted as of December 31, 2016:

	Restricted Stock Units		Weighted Average Grant-Date Fair Value
Outstanding, December 31, 2015	288	$	44.54
Awarded	583	$	58.19
Vested	(109)	$	43.88
Forfeited	(41)	$	50.60
Outstanding, December 31, 2016	721	$	55.33

As of December 31, 2016, there were approximately 285,000 RSUs outstanding, net of estimated forfeitures, that are expected to vest. The weighted-average fair value of these RSUs was $56.07 per share; and the aggregate intrinsic value of these RSUs was approximately $1.4 million.

In connection with RSUs granted to employees, the Company recognized approximately $6.9 million, $5.2 million and $0.3 million in share-based compensation expense during the years ended December 31, 2016, 2015 and 2014, respectively, net of expected forfeitures. As of December 31, 2016, there was approximately $12.0 million of unrecognized compensation costs, net of estimated forfeitures, related to RSUs granted to employees, which are expected to be recognized over a remaining weighted average period of 2.9 years. The total fair value of the RSUs that vested during the year ended December 31, 2016 was $4.8 million.

In connection with the ESPP made available to employees, the Company recognized a de minimis amount of share-based compensation expense during the year ended December 31, 2016. The Company did not recognize any share-based compensation expense related to the ESPP during the years ended December 31, 2015 and 2014. As of December 31, 2016, there were approximately $0.1 million of unrecognized compensation costs, net of estimated forfeitures, related to the ESPP, which are expected to be recognized over 0.3 years.

12. Employee Benefit Plan

The Company maintains a defined contribution 401(k) plan available to employees. Employee contributions are voluntary and are determined on an individual basis, limited by the maximum amounts allowable under federal tax regulations. The Company's matching contributions to employees totaled approximately $0.8 million, $0.5 million and $0.2 million during the years ended December 31, 2016, 2015 and 2014, respectively.

13. Fair Value Measurements

ASC 820, *Fair Value Measurements and Disclosures*, defines fair value as the price that would be received to sell an asset, or paid to transfer a liability, in the principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value standard also establishes a three-level hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The Company reviews investments on a periodic basis for other than temporary impairments. This review is subjective as it requires management to evaluate whether an event or change in circumstances has occurred in the period that may have a significant adverse effect on the fair value of the investment. The Company uses the market approach to measure fair value for its financial assets. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets. The Company classifies its corporate debt securities within the fair value hierarchy as Level 2 assets, as it primarily utilizes quoted market prices or rates for similar instruments to value these securities.

The valuation hierarchy is based upon the transparency of inputs to the valuation of an asset or liability on the measurement date. The three levels are defined as follows:

- Level 1—inputs to the valuation methodology are quoted prices (unadjusted) for an identical asset or liability in an active market. The Company's Level 1 assets consist of investments in money market funds and U.S. Treasury securities.
- Level 2—inputs to the valuation methodology include quoted prices for a similar asset or liability in an active market or model-derived valuations in which all significant inputs are observable for substantially the full term of the asset or liability. The Company's Level 2 assets consist of investments in investment-grade corporate debt securities.
- Level 3—inputs to the valuation methodology are unobservable and significant to the fair value measurement of the asset or liability. The Company does not hold any assets that are measured using Level 3 inputs.

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2016:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 108,096	$ —	$ —
Investments in U.S. Treasury securities	$ 120,261	$ —	$ —
Investments in Corporate debt securities	$ —	$ 35,087	$ —

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2015:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 196,188	$ —	$ —
Investments in U.S. Treasury securities*	$ 150,387	$ —	$ —
Investments in Corporate debt securities	$ —	$ 39,833	$ —

* Investments in money market funds, U.S. Treasury securities and corporate debt securities with maturities less than 90 days are reflected in cash and cash equivalents in the accompanying Balance Sheets.

No transfer of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the years ended December 31, 2016 or December 31, 2015.

14. Selected Quarterly Financial Information (unaudited)

The following is a summary of the quarterly results of operations for the years ended December 31, 2016 and 2015:

	2016			
	March 31	June 30	September 30	December 31
Collaboration revenue	$ 15,721	$ 28,198	$ 1,668	$ 5,322
Research and development expenses	37,770	48,262	50,854	59,409
General and administrative expenses	14,696	10,489	12,024	12,968
Loss from operations	(36,745)	(30,553)	(61,210)	(67,055)
Net loss attributable to common stockholders	$ (36,301)	$ (29,945)	$ (60,891)	$ (66,283)
Basic and diluted loss per common share	$ (1.03)	$ (0.85)	$ (1.71)	$ (1.86)

	2015			
	March 31	June 30	September 30	December 31
Collaboration revenue	$ 41,678	$ 1,597	$ 3,448	$ 4,782
Research and development expenses	24,557	32,059	40,479	33,917
General and administrative expenses	9,584	11,959	10,412	12,066
Income (loss) from operations	7,537	(42,421)	(47,443)	(41,201)
Net income (loss) attributable to common stockholders	$ 6,636	$ (37,131)	$ (39,573)	$ (35,649)
Basic earnings (loss) per common share	$ 0.19	$ (1.08)	$ (1.14)	$ (1.02)
Diluted earnings (loss) per common share	$ 0.19	$ (1.08)	$ (1.14)	$ (1.02)

15. Subsequent Events

In December 2016, the Company announced that it had determined to implement a reduction in personnel to focus on an updated business plan. In January 2017, the Board of Directors approved a plan to implement a reduction in personnel is expected to involve approximately 80% of the Company's workforce and is expected to be substantially complete during the first and second quarters of 2017. In connection with such reduction in personnel, the Company estimates that it will incur approximately $14.4 million of pre-tax charges during the first and second quarters of 2017, of which approximately $13.8 million is expected to result in future cash expenditures. These pre-tax charges relate to (a) expected severance and other employee costs of approximately $12.3 million and (b) expected lease termination costs of approximately $2.1 million. The Company expects to realize estimated annualized cost savings from the reduction in personnel in the range of $25 million to $30 million starting in the third quarter of 2017.

EXHIBIT INDEX

Exhibit Number		Description of Exhibit	Form	Incorporated by Reference File Number	Incorporated by Reference Date of Filing	Exhibit Number	Filed Herewith
3.1		Restated Certificate of Incorporation of the Registrant	S-1/A	333-190643	9/9/2013	3.3	
3.2		Amended and Restated Bylaws of the Registrant	S-1/A	333-190643	9/9/2013	3.4	
4.1		Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-190643	9/9/2013	4.1	
10.1	+	Amended and Restated 2007 Stock Incentive Plan, as amended	S-1	333-190643	8/15/2013	10.1	
10.2	+	Form of Incentive Stock Option Agreement under Amended and Restated 2007 Stock Incentive Plan	S-1	333-190643	8/15/2013	10.2	
10.3	+	Form of Nonstatutory Stock Option Agreement under 2007	S-1	333-190643	8/15/2013	10.3	
10.4	+	2013 Stock Incentive Plan	10-K		3/2/2015	10.4	
10.5	+	Amendment No. 1 to Stock Incentive Plan, adopted June 4, 2015	10-Q		8/10/2015	10.1	
10.6	+	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-190643	9/9/2013	10.5	
10.7	+	Form of Nonqualified Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-190643	9/9/2013	10.6	
10.8	+	Form of Restricted Stock Unit Agreement under 2013 Stock Incentive Plan	10-K		3/2/2015	10.7	
10.9		Lease Agreement, dated as of September 30, 2007, between the Registrant and One Penn Plaza LLC, as the same has been supplemented by agreement dated March 12, 2013 and amended by the Amendment of Lease, dated as of August 30, 2013, Second Amendment to Lease, entered into on January 7, 2014, Third Amendment of Lease, dated as of April 18, 2014, and the Fourth Amendment of Lease, dated as of December 22, 2014	10-K		3/2/2015	10.8	
10.10		Sublease Agreement, dated April 7, 2015, by and between Otsuka America Pharmaceutical, Inc. and the Registrant	10-Q		8/10/2015	10.2	

Exhibit Number		Description of Exhibit	Incorporated by Reference				Filed Herewith
			Form	File Number	Date of Filing	Exhibit Number	
10.11		Lease Agreement with Carnegie 214 Associates Limited Partnership, dated as of October 25, 2013	S-1	333-193681	1/31/2014	10.8	
10.12		Office Lease Agreement, dated as of August 22, 2013, by and between the Registrant and PSN Partners, L.P.	S-1/A	333-190643	9/9/2013	10.17	
10.13	†	Divestiture Agreement, dated as of July 27, 2007, by and between the Registrant and (OSI) Eyetech, Inc.	S-1	333-190643	8/15/2013	10.9	
10.14	†	License, Manufacturing and Supply Agreement, dated as of September 30, 2006, by and between Nektar Therapeutics AL, Corporation and (OSI) Eyetech, Inc., as the same was assigned to the Registrant on July 27, 2007 and amended by Amendment No. 1 thereto, dated as of April 5, 2012, and supplemented by a letter agreement, dated as of June 20, 2013	S-1	333-190643	8/15/2013	10.10	
10.15	†	Amendment No. 2 to, Scope of Work #1 for, and Amendment No. 3 to License, Manufacturing and Supply Agreement, dated as of September 30, 2006, by and between Nektar Therapeutics AL, Corporation and (OSI) Eyetech, Inc., as the same was assigned to the Registrant on July 27, 2007 and amended by Amendment No. 1 thereto, dated as of April 5, 2012, and supplemented by a letter agreement, dated as of June 20, 2013.	10-Q		5/11/2015	10.1	
10.16	†	Amended and Restated Exclusive License Agreement, dated as of September 12, 2011, by and between the Registrant and Archemix Corp., as amended by Amendment No. 1 thereto dated December 20, 2011 and supplemented by a letter agreement, dated as of April 30, 2012	S-1	333-190643	8/15/2013	10.11	

Exhibit Number		Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
			Form	File Number	Date of Filing		
10.17	†	Amended and Restated Exclusive License Agreement, dated as of September 12, 2011, by and between the Registrant and Archemix Corp., as amended by Amendment No. 1 thereto, dated as of December 20, 2011	S-1	333-190643	8/15/2013	10.12	
10.18	†	Purchase and Sale Agreement, dated as of May 23, 2013, by and between the Registrant and Novo A/S	S-1	333-190643	8/15/2013	10.13	
10.19	†	Amendment No. 1 to the Purchase and Sale Agreement, dated as of May 23, 2013, by and between the Registrant and Novo A/S	10-K		3/2/2015	10.24	
10.20	†	Licensing and Commercialization Agreement by and between the Registrant and Novartis Pharma AG dated May 19, 2014	10-Q		8/6/2014	10.2	
10.21	†	Clinical Manufacturing and Supply Agreement by and between the Registrant and Agilent Technologies, Inc. dated May 2, 2014	10-Q		8/6/2014	10.1	
10.22	†	Amendment No. 1 to Clinical Manufacturing and Supply Agreement by and between the Registrant and Agilent Technologies, Inc. dated September 3, 2015	10-Q		11/5/2015	10.1	
10.23	†	Commercial Manufacturing and Supply Agreement by and between the Registrant and Agilent Technologies, Inc. dated September 3, 2015	10-Q		11/5/2015	10.2	
10.24	+	Offer of Employment between the Registrant and David Guyer	S-1/A	333-190643	9/9/2013	10.14	
10.25	+	Letter Agreement between the Registrant and David R. Guyer dated February 26, 2015, amending the Offer of Employment between the Registrant and David R. Guyer dated April 26, 2013	10-Q		5/11/2015	10.2	
10.26	+	Third Amended and Restated Employment Agreement between the Registrant and Samir C. Patel, dated May 1, 2015	10-Q		5/11/2015	10.3	

Exhibit Number		Description of Exhibit	Incorporated by Reference				Filed Herewith
			Form	File Number	Date of Filing	Exhibit Number	
10.27	+	Separation and Release of Claims Agreement between the Registrant and Samir C. Patel dated January 12, 2017					Yes
10.28	+	Consulting Agreement between the Registrant and Samir C. Patel dated January 12, 2017					Yes
10.29	+	Letter Agreement between the Registrant and Glenn P. Sblendorio, dated January 4, 2016	10-Q		5/9/2015	10.1	
10.30	+	Letter Agreement between the Registrant and Glenn P. Sblendorio, dated January 4, 2016	10-Q		5/9/2015	10.2	
10.31	+	Offer of Employment between the Registrant and Henric Bjarke, dated July 15, 2015	10-K		2/26/2016	10.31	
10.32	+	Letter Agreement between the Registrant and Henric Bjarke, dated July 15, 2015	10-K		2/26/2016	10.32	
10.33	+	Nonstatutory Stock Option Agreement between the Registrant and Henric Bjarke, dated August 31, 2015	10-K		2/26/2016	10.33	
10.34	+	Offer of Employment between the Registrant and Barbara A. Wood, dated October 21, 2013, revised October 22, 2013	10-K		2/26/2016	10.34	
10.35	+	Letter Agreement between the Registrant and Barbara A. Wood, dated February 20, 2015	10-Q		5/11/2015	10.6	
10.36	+	Form of Indemnification Agreement between the Registrant and each Director and Executive Officer	10-Q		8/5/2016	10.2	
10.37	+	2016 Employee Stock Purchase Plan	S-8	333-211916	6/8/2016	99.1	
10.38	*	Clinical and Commercial Services Agreement Between the Registrant and Ajinimoto Althea, Inc. dated October 31, 2016					Yes
23.1		Consent of Ernst & Young LLP					Yes
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.					Yes
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.					Yes
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.					Yes

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					Yes
101.INS	XBRL Instance Document.					Yes
101.SCH	XBRL Taxonomy Extension Schema Document.					Yes
101.CAL	XBRL Taxonomy Calculation Linkbase Document.					Yes
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.					Yes
101.LAB	XBRL Taxonomy Label Linkbase Document.					Yes
101.PRE	XBRL Taxonomy Presentation Linkbase Document.					Yes

† Confidential treatment has been granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

* Confidential treatment has been requested 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.

SEPARATION AND RELEASE OF CLAIMS AGREEMENT

This Separation and Release of Claims Agreement (the "Agreement") is made as of the Effective Date (as defined below) by and between Ophthotech Corporation (the "Company") and Samir Patel, M.D. ("Executive") (together, the "Parties").

WHEREAS, the Company and Executive are parties to the Third Amended and Restated Employment Agreement dated as of April 30, 2015 (the "Employment Agreement"), under which Executive currently serves as President of the Company;

WHEREAS, the Parties wish to establish terms for Executive's separation from employment with the Company; and

WHEREAS, the Parties agree that the payments, benefits and rights set forth in this Agreement and the consulting agreement attached to this Agreement as Attachment A (the "Consulting Agreement") shall be the exclusive payments, benefits and rights due Executive;

NOW, THEREFORE, in consideration of the mutual covenants and agreements contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1.**Separation Date; Post-Employment Consulting Arrangement** –

(a) Executive's effective date of separation from employment with the Company will be January 13, 2017 (the "Separation Date"). As of the Separation Date, the Employment Agreement will terminate and be of no further force or effect; provided, however, that Sections 7, 8 and 9 thereof shall, as amended by this Agreement, remain in full force and effect. Executive hereby resigns, as of the Separation Date, from his employment with the Company, as an officer of the Company and as a member of the Company's Board of Directors (the "Board"). Executive agrees to execute and deliver any documents reasonably necessary to effectuate such resignations, as requested by the Company. Executive shall be paid (x) in accordance with the Company's regular payroll practices, all unpaid base salary earned through the Separation Date, reimbursement of all unreimbursed business expenses incurred through the Separation Date and any accrued but unused vacation time in accordance with Company policy to which Executive was entitled through the Separation Date and (y) as of the date on which any other Company employees who are eligible to receive an annual bonus for 2016 receive such bonuses, any earned but unpaid annual bonus for 2016 (together, the "Accrued Benefits"). As of the Separation Date, all salary payments from the Company will cease and any benefits Executive had as of the Separation Date under Company-provided benefit plans, programs, or practices will terminate, except as required by federal or state law or as otherwise specifically set forth in this Agreement.

(b) Upon the Separation Date, the Company and Executive shall enter into the Consulting Agreement. During the Consultation Period (as such term is defined in the Consulting Agreement), any outstanding and unvested equity awards previously granted to Executive by the Company will continue to vest and be exercisable in accordance with the applicable equity plans and award agreements.

2.**Severance Benefits** – On the earlier to occur of the end of the Consultation Period (as such term is defined in the Consulting Agreement) and Executive's "separation from service" (as defined in

Exhibit I), and provided Executive (i) signs and returns this Agreement on or before January 24, 2017 and does not revoke his acceptance, (ii) timely enters into the Consulting Agreement, and (iii) signs and returns the Additional Release of Claims attached hereto as Attachment B (the "Additional Release") within five (5) business days following expiration or termination of the Consultation Period and does not revoke his acceptance, the Company will provide Executive with the following severance benefits in full satisfaction of the Company's severance obligations under the Employment Agreement and in further consideration of Executive's commitments and obligations set forth in this Agreement and the exhibits and attachments hereto (the "Severance Benefits"), subject to Exhibit I:

a. Salary Continuation – Commencing on the Company's first regularly scheduled payroll date that follows the Additional Release Effective Date (as defined in the Additional Release) (the "Payment Commencement Date"), the Company will, for a twelve (12) month period (the "Severance Period"), provide Executive with severance pay in the form of twelve equal monthly installments of $52,083.33, less all applicable taxes and withholdings.

b. Pro-Rata Bonus – On the Payment Commencement Date, the Company shall provide Executive with a pro-rata bonus payment of $14,469.18, which is equivalent to (x) sixty-five percent (65%) of Executive's annualized base salary as of the Separation Date, multiplied by (y) a fraction, the numerator of which is the number of days during calendar year 2017 during which Executive remained employed by the Company and the denominator of which is 365.

c. Group Health Insurance – Should Executive be eligible for and timely elect to continue receiving group health and/or dental insurance coverage under the law known as COBRA, the Company shall, until the earliest of (x) the last day of the Severance Period, (y) the date that Executive is no longer eligible for COBRA continuation coverage, and (z) the end of the calendar month in which Executive becomes eligible to receive group health insurance coverage under another employer's benefit plan (the "COBRA Contribution Period"), pay on Executive's behalf the employer share of premium for such coverage at the same rates as from time to time in effect for the Company's active workforce. Should Executive cease during the Severance Period to be eligible to continue receiving group health and/or dental insurance coverage under COBRA for reasons other than becoming enrolled in another group health plan (or should Executive have exhausted his COBRA coverage prior to the commencement of the Severance Period), the Company shall provide Executive with an additional monthly payment in an amount equal to the monthly employer premium paid during the final month of his COBRA continuation coverage until the earlier of (x) the last day of the Severance Period or (y) the end of the calendar month in which Executive becomes eligible to receive group health or dental insurance coverage under another employer's benefit plan(s), as applicable. For the avoidance of doubt, (i) the Company's assistance with health coverage costs shall in all events not extend beyond the Severance Period and (ii) to the extent Executive wishes to remain enrolled in COBRA following the expiration of the COBRA Contribution Period, all premium costs after the COBRA Contribution Period shall be paid by Executive on a monthly basis during the elected period of health insurance coverage under COBRA for as long as, and to the extent that, he remains eligible for and wishes to remain enrolled in COBRA continuation coverage.

d. Equity Exercise – Executive may exercise any stock options outstanding and vested as of the expiration or termination of the Consultation Period during the applicable period following the expiration or termination of the Consultation Period specified in, and otherwise in accordance with the terms of, the applicable option award agreements and equity plans under which any such outstanding stock options were awarded; provided further, however, that in no event may any stock option be exercised beyond the earlier of (x) the original maximum term specified in the applicable option award agreement, and (y) ten (10) years from the original grant date of such stock option.

Other than the Severance Benefits and Accrued Benefits, Executive will not be eligible for, nor shall he have a right to receive, any payments or benefits from the Company following the Separation Date or the expiration or termination of the Consultation Period, other than any payments or benefits he may be entitled to receive under the Consulting Agreement due through such date of expiration or termination (the "Remaining Fees"). For the avoidance of doubt, Executive will not be eligible to receive the Severance Benefits (or any payments or benefits from the Company other than the Remaining Fees and Accrued Benefits) if he fails to timely enter into this Agreement, the Consulting Agreement or the Additional Release.

3. **Release of Claims** – In exchange for the consideration set forth in this Agreement, which Executive acknowledges he would not otherwise be entitled to receive, Executive hereby fully, forever, irrevocably and unconditionally releases, remises and discharges the Company, its affiliates, subsidiaries, parent companies, predecessors, and successors, and all of their respective past and present officers, directors, stockholders, partners, members, employees, agents, representatives, plan administrators, attorneys, insurers and fiduciaries (each in their individual and corporate capacities) (collectively, the "Released Parties") from any and all claims, charges, complaints, demands, actions, causes of action, suits, rights, debts, sums of money, costs, accounts, reckonings, covenants, contracts, agreements, promises, doings, omissions, damages, executions, obligations, liabilities, and expenses (including attorneys' fees and costs), of every kind and nature that Executive ever had or now has against any or all of the Released Parties up to the date on which he signs this Agreement, whether known or unknown, including, but not limited to, any and all claims arising out of or relating to Executive's employment with, provision of consulting or other services to, separation or termination from, and/or ownership of securities of the Company, including, but not limited to, all claims under Title VII of the Civil Rights Act, the Americans With Disabilities Act, the Age Discrimination in Employment Act, the Genetic Information Nondiscrimination Act, the Family and Medical Leave Act, the Worker Adjustment and Retraining Notification Act, the Rehabilitation Act, Executive Order 11246, Executive Order 11141, the Fair Credit Reporting Act, and the Employee Retirement Income Security Act, all as amended; all claims arising out of the New York Human Rights Law, N.Y. Exec. Law § 290 et seq., the New York City Human Rights Law, N.Y.C. Admin. Code § 8-101 et seq., N.Y. Civ. Rights Law § 40-c et seq. (New York anti-discrimination law), N.Y. Lab. Law § 194 et seq. (New York equal pay law), N.Y. Lab. Law § 740 (New York whistleblower protection law), and N.Y. Lab. Law § 201-c (New York adoption leave law), all as amended; all claims arising out of the New Jersey Law Against Discrimination, N.J. Stat. Ann. § 10:5-1 et seq., the New Jersey Family Leave Act, N.J. Stat. Ann. § 34:11B-1 et seq., the New Jersey Conscientious Employee Protection Act, N.J. Stat. Ann. § 34:19-1 et seq., N.J. Stat. Ann. § 34:11-56.1 et seq. (New Jersey equal pay law), and the New Jersey "mini-WARN" Act **(**N.J.S.A. 34:21-1, et seq.), all as amended; all common law claims including, but not limited to, actions in defamation, intentional infliction of emotional distress, misrepresentation, fraud, wrongful discharge, and breach of contract (including, without limitation, all claims arising out of or related to the Employment Agreement);

all state and federal whistleblower claims to the maximum extent permitted by law; and any claim or damage arising out of Executive's employment with and/or separation from the Company (including a claim for retaliation) under any common law theory or any federal, state or local statute or ordinance not expressly referenced above; *provided, however, that nothing in this release of claims prevents Executive from filing a charge with, cooperating with, or participating in any investigation or proceeding before, the Equal Employment Opportunity Commission or a state fair employment practices agency (except that Executive acknowledges that he may not recover any monetary benefits in connection with any such charge, investigation, or proceeding, and Executive further waives any rights or claims to any payment, benefit, attorneys' fees or other remedial relief in connection with any such charge, investigation or proceeding).* Further, nothing herein shall prevent Executive from bringing claims to enforce this Agreement and/or the Consulting Agreement, or release (i) any rights Executive may have under the Company's certificate of incorporation, by-laws, insurance and/or any indemnification agreement between him and the Company (and/or otherwise under law) for indemnification and/or defense as an employee, officer or director of the Company for his service to the Company (recognizing that such indemnification and/or defense is not guaranteed by this Agreement and shall be governed by the instrument or law, if any, providing for such indemnification and/or defense), (ii) any rights Executive may have to vested equity ownership in the Company under the applicable equity plans and agreements, or (iii) any right to the Accrued Benefits.

4. **Non-Solicitation and Non-Competition Obligations** – Executive acknowledges and reaffirms his non-competition and non-solicitation obligations as set forth in Section 7 of the Employment Agreement (the "Restrictive Covenant Obligations"), which Restrictive Covenant Obligations survive his termination of employment and remain in full force and effect; provided, however, that in consideration of this Agreement and the Consulting Agreement, Executive acknowledges and agrees that (a) the duration of the Restrictive Covenant Obligations is amended hereby such that such Restrictive Covenant Obligations shall remain in effect during the Consultation Period and for a period of one (1) year thereafter, and (b) the definition of "Competitive" in Section 7(a)(ii) of the Employment Agreement is amended hereby such that a business will deemed "Competitive" with the Company if it satisfies such definition set forth in Section 7(a)(ii) as of the Separation Date or any date until and ending upon the termination of the Consultation Period.

5. **Non-Disclosure Obligations** – Executive acknowledges and reaffirms his obligation, except as otherwise permitted by Section 9 below, to keep confidential and not to use or disclose any and all non-public information concerning the Company or any of its subsidiaries that he acquired during the course of his employment with the Company, or may acquire during his service under the Consulting Agreement, including, but not limited to, any non-public information concerning the Company's or any of its subsidiaries' business, operations, products, programs, affairs, performance, personnel, technology, science, intellectual property, plans, strategies, approaches, prospects, financial condition or development related matters. Executive also acknowledges his continuing obligations with respect to confidential information and developments as set forth in the Invention and Non-Disclosure Agreement he executed on November 30, 2009 and that is referenced in Section 8 of the Employment Agreement (the "NDA"), which, as amended by the last sentence of this Section 5, survives his separation from employment with the Company and remains in full force and effect. Further, in consideration of this Agreement and the Consulting Agreement, Executive acknowledges and agrees that the NDA is amended hereby to apply to his Services for the Company during the Consultation Period, and all references in the NDA to "Employee" are amended hereby to refer as well to "Consultant" and all references to

"employment" therein are amended hereby to refer as well to "consulting services" (as set forth in the Consulting Agreement).

6. **Non-Disparagement** – Executive understands and agrees that, except as otherwise permitted by Section 9 below, he will not, in public or private, make any false, disparaging, negative, critical, adverse, derogatory or defamatory statements, whether orally or in writing, including online (including, without limitation, on any social media, networking, or employer review site) or otherwise, to any person or entity, including, but not limited to, any media outlet, industry group, key opinion leader, financial institution, research analyst or current or former employee, board member, consultant, shareholder, client or customer of the Company or any of its subsidiaries, regarding the Company, any of its subsidiaries or any of the other Released Parties, or regarding the Company's or any of its subsidiaries' business, operations, products, programs, affairs, performance, personnel, technology, science, intellectual property, plans, strategies, approaches, prospects, financial condition or development related matters. For the avoidance of doubt, the foregoing shall not prevent Executive from stating or repeating factual information with respect to the Company or its assets which is otherwise publicly available. The Company agrees that its Board members and its named executive officers (as determined pursuant to Item 402(a)(3) of Regulation S-K) will not, in public or private, make any false, disparaging, negative, critical, adverse, derogatory or defamatory statements, whether orally or in writing, including online (including, without limitation, on any social media, networking, or employer review site) or otherwise, to any person or entity, including, but not limited to, any media outlet, industry group, key opinion leader, financial institution, research analyst or current or former employee, board member, consultant, shareholder, client or customer of the Company or any of its subsidiaries, regarding Executive; provided, however, that nothing in this Section 6 shall restrict or otherwise limit such Board members or named executive officers from disclosing events or circumstances in such manner as they or the Company deem necessary to comply with or satisfy their or the Company's disclosure, reporting or other obligations under applicable law.

7. **Return of Company Property** – Executive confirms that he will, except as specifically instructed otherwise by the Company's Chief Executive Officer, return to the Company no later than January 19, 2017 all property of the Company, tangible or intangible, including but not limited to keys, files, records (and copies thereof), equipment (including, but not limited to, computer hardware, software and printers, wireless handheld devices, cellular phones, tablets, etc.), Company identification and any other Company-owned property in his possession or control and will leave intact all electronic Company documents, including but not limited to those that he developed or helped to develop during his employment or while performing services under the Consulting Agreement. Executive further agrees that he will, except as specifically instructed otherwise by the Company's Chief Executive Officer, cancel no later than January 19, 2017 all accounts for his benefit, if any, in the Company's name, including but not limited to, credit cards, telephone charge cards, cellular phone and/or wireless data accounts and computer accounts. Executive will provide a written and signed certification to the Company no later than January 19, 2017, that he has returned all property and cancelled all accounts as required in compliance with this Section 7.

8. **Confidentiality** – Executive understands and agrees that, except as otherwise permitted by Section 9 below, the contents of the negotiations and discussions resulting in this Agreement shall be maintained as confidential by Executive and his agents and representatives and shall not be disclosed except as otherwise agreed to in writing by the Company and except to his immediate

family, legal, financial and tax advisors, on the condition that any individuals so informed must hold the above information in strict confidence.

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

10. **Cooperation** – Executive agrees that, to the extent permitted by law, he shall, during the Consultation Period and for the longer of eighteen (18) months thereafter or the duration of any matter in which he and/or the Company are defendants or responding parties that is brought or is pending during such eighteen (18) month period, reasonably cooperate with the Company in the investigation, defense or prosecution of any claims or actions which already have been brought, are currently pending, or which may be brought in the future against the Company by a third party or by or on behalf of the Company against any third party, whether before a state or federal court, any state or federal government agency, or a mediator or arbitrator. Executive's reasonable cooperation in connection with such claims or actions shall include, but not be limited to, being available to meet with the Company's counsel, at reasonable times and locations designated by the Company, to investigate or prepare the Company's claims or defenses, to prepare for trial or discovery or an administrative hearing, mediation, arbitration or other proceeding, to provide any relevant information in his possession, and to act as a witness when requested by the Company. The Company will reimburse Executive for all reasonable and documented out of pocket costs that he incurs to comply with this paragraph. Executive further agrees that, to the extent permitted by law, he will notify the Company promptly in the event that he is served with a subpoena (other than a subpoena issued by a government agency), or in the event that he is asked to provide a third party (other than a government agency) with information concerning any actual or potential complaint or claim against the Company.

11. **Business Expenses; Final Compensation; Legal Fees** – Executive acknowledges that he has been reimbursed by the Company for all business expenses incurred in conjunction with the performance of his employment and that no other reimbursements are owed to him. Executive further acknowledges that he has received all compensation due to him from the Company, including, but not limited to, all wages, bonuses and accrued, unused vacation time, and that, other than pursuant to the Consulting Agreement, he is not eligible or entitled to receive any additional payments or consideration from the Company beyond that provided for in Section 2 of

this Agreement. Notwithstanding the foregoing, the Company will reimburse Executive for reasonable legal fees of up to $25,000 incurred by Executive in connection with Executive's review and negotiation of this Agreement and all exhibits and attachments hereto. Such reimbursement will be paid no later than thirty (30) days after Executive submits substantiation of having incurred the legal fees, which Executive must do within sixty (60) days after they are incurred.

12. **Amendment and Waiver** – This Agreement and the Additional Release shall be binding upon the Parties and may not be modified in any manner, except by an instrument in writing of concurrent or subsequent date signed by duly authorized representatives of the Parties. This Agreement and the Additional Release are binding upon and shall inure to the benefit of the Parties and their respective agents, assigns, heirs, executors/administrators/personal representatives, and successors. No delay or omission by the Company in exercising any right under this Agreement or the Additional Release shall operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion shall be effective only in that instance and shall not be construed as a bar to or waiver of any right on any other occasion.

13. **Validity** – Should any provision of this Agreement or the Additional Release be declared or be determined by any arbitrator acting pursuant to Section 18 below or court of competent jurisdiction to be illegal or invalid, the validity of the remaining parts, terms or provisions shall not be affected thereby and said illegal or invalid part, term or provision shall be deemed not to be a part of this Agreement or the Additional Release.

14. **Nature of Agreement –** Both Parties understand and agree that this Agreement is a separation agreement and does not constitute an admission of liability or wrongdoing on the part of the Company or Executive.

15. **Time for Consideration and Revocation –** Executive acknowledges that he was initially presented with this Agreement on January 2, 2017 (the "Receipt Date"). Executive understands that this Agreement shall be of no force or effect unless he signs and returns this Agreement on or before January 24, 2017, and does not revoke his acceptance in the subsequent seven (7) day period (the day immediately following expiration of such revocation period, the "Effective Date"). Executive further understands that he will not be eligible to receive the Severance Benefits unless he timely signs, returns, and does not revoke the Additional Release.

16. **Acknowledgments –** Executive acknowledges that he has been given at least twenty-one (21) days from the Receipt Date to consider this Agreement and the Additional Release (the "Consideration Period"), and that the Company is hereby advising him to consult with an attorney of his own choosing prior to signing this Agreement and the Additional Release. Executive further acknowledges and agrees that any changes made to this Agreement or any exhibits or attachments hereto following his initial receipt of this Agreement on the Receipt Date, whether material or immaterial, shall not re-start or affect in any manner the Consideration Period. Executive understands that he may revoke this Agreement and the Additional Release for a period of seven (7) days after he signs each respective agreement by notifying the Company in writing, and that neither agreement shall be effective or enforceable until the expiration of each respective seven (7) day revocation period. In the event the Executive executed this Agreement within less than twenty-one (21) days after the Receipt Date, he acknowledges that such decision was entirely voluntary and that he had the opportunity to consider this Agreement until the end of the twenty-one (21) day period. Executive understands and agrees that by entering into this

Agreement and the Additional Release he will be waiving any and all rights or claims he might have under the Age Discrimination in Employment Act, as amended by the Older Workers Benefit Protection Act, and that he has received consideration beyond that to which he was previously entitled.

17. **Voluntary Assent –** Executive affirms that no other promises or agreements of any kind have been made to or with Executive by any person or entity whatsoever to cause him to sign this Agreement or the Additional Release, and that he fully understands the meaning and intent of this Agreement and the Additional Release and that he has been represented by counsel of his own choosing. Executive further states and represents that he has carefully read this Agreement and the Additional Release, understands the contents herein, freely and voluntarily assents to all of the terms and conditions hereof, and signs his name of his own free act.

18. **Arbitration** – Any dispute between Executive and the Company relating in any way to this Agreement (including the Additional Release), the Consulting Agreement, Executive's ownership of any securities of the Company or Executive's relationship with the Company (including without limitation, Executive's service to the Company as a consultant or the termination thereof, or Executive's employment with the Company or separation therefrom), including, but not limited to (i) claims alleging unlawful discrimination, harassment, or retaliation on any basis protected by any applicable federal, state, or local law, (ii) claims for wages, bonuses, severance, employee benefits or other compensation, whether pursuant to contract or federal or state wage and hour laws, (iii) common law claims, including, but not limited to, tort claims, wrongful discharge claims, contract claims, defamation claims and unfair business practices claims, and (iv) any claim under any statute, law, or ordinance not expressly set forth above ("Arbitrable Claims") shall be resolved by binding arbitration before a neutral arbitrator as provided in this Section 18 (the "Arbitration"). For the avoidance of doubt, (1) either Party shall be entitled to elect to seek from a court injunctive relief, specific performance or a declaration of rights with respect to any claim relating to any dispute that could result in irreparable harm or loss to such Party and (2) Arbitrable Claims shall not include any claim for which a Party seeks from a court such injunctive relief, specific performance or a declaration of rights pursuant to clause (1) immediately above. Further, and for the avoidance of doubt, nothing herein prevents Executive from filing a charge with, cooperating with, or participating in any proceeding or investigation before the EEOC or a state fair employment practices agency (except that Executive acknowledges that he may not recover any monetary benefits in connection with any such charge, proceeding or investigation, and further waives any rights or claims to any payment, benefit, attorneys' fees or other remedial relief in connection with any such charge, proceeding or investigation); provided, however, that nothing in the immediately preceding parenthetical constitutes a waiver of any of Executive's rights or claims in connection with any arbitration proceeding hereunder. The Arbitration shall take place in New York, New York, unless otherwise agreed by Executive and the Company. The Arbitration shall be administered by the American Arbitration Association ("AAA") under its Employment Arbitration Rules and Mediation Procedures (the "Rules"), shall be final and binding upon Executive and the Company, and shall be the exclusive remedy for all claims covered by this arbitration provision. The Arbitration shall be presided over by a single arbitrator, who shall be selected by Executive and the Company in accordance with the AAA Rules and shall be experienced in employment law and/or securities law, as may be applicable. The arbitrator shall render an award and written opinion in the form typically rendered in employment arbitrations within the time provided in the Rules. The Company shall pay any filing fee and the fees and costs of the arbitrator; provided, however, that if Executive is the party initiating the Arbitration, Executive will pay an amount equivalent to the

filing fee that Executive would have paid to file a civil action or initiate a claim in a New York court of competent jurisdiction. Each Party shall pay for its own costs and attorneys' fees during the pendency of the Arbitration proceeding, but the arbitrator shall award reasonable attorneys' fees and costs to the prevailing party in the Arbitration. Either Executive or the Company may bring an action in court to compel arbitration under this Agreement or to enforce an arbitration award (an "Exempted Action"). Otherwise, neither Executive nor the Company shall initiate or prosecute any lawsuit or administrative action in any way related to any Arbitrable Claim. If any court or arbitrator finds that any term makes this arbitration provision unenforceable for any reason, the court or arbitrator shall have the power to modify such term (or if necessary delete such term) to the minimum extent necessary to make this arbitration provision enforceable to the fullest extent permitted by law. To the extent permitted by law and except as otherwise permitted by Section 9 above, the Parties shall keep confidential and shall not disclose any information relating to or the existence of any Arbitration under this Agreement. THE PARTIES HEREBY WAIVE ANY RIGHTS THEY MAY HAVE TO TRIAL BY JURY IN REGARD TO ARBITRABLE CLAIMS, INCLUDING WITHOUT LIMITATION ANY RIGHT TO TRIAL BY JURY AS TO THE MAKING, EXISTENCE, VALIDITY, OR ENFORCEABILITY OF THE AGREEMENT TO ARBITRATE.

19. **Governing Law** – This Agreement and the Additional Release shall be interpreted and construed by the laws of the State of New York, without regard to conflict of laws provisions. Each of the Company and Executive hereby irrevocably submits to and acknowledges and recognizes the exclusive jurisdiction and venue of the courts of the State of New York located in New York County, or if appropriate, the United States District Court for the Southern District of New York (which courts, for purposes of this Agreement and the Additional Release, are the only courts of competent jurisdiction), over any Exempted Action or claim that is not an Arbitrable Claim, and waives any objection to laying venue in any such action or proceeding in such courts, waives any objection that such courts are an inconvenient forum or do not have jurisdiction over either party, and agrees that service of process upon such party in any such action or proceeding shall be effective if such process is given as a notice in accordance with the terms of this Agreement.

20. **Entire Agreement** – This Agreement, including all exhibits and attachments hereto, contains and constitutes the entire understanding and agreement between the Parties hereto with respect to Executive's separation from the Company, severance benefits and the settlement of claims against the Company, and cancel all previous oral and written negotiations, agreements, commitments and writings in connection therewith; provided, however, that nothing in this Section 20 shall modify, cancel or supersede Executive's obligations set forth in Sections 4 and 5 above.

21. **Tax Acknowledgement** – In connection with the Severance Benefits provided to Executive pursuant to this Agreement and the Additional Release, the Company shall withhold and remit to the tax authorities the amounts required under applicable law, and Executive shall be responsible for all applicable taxes owed by him with respect to such Severance Benefits under applicable law. Executive acknowledges that he is not relying upon the advice or representation of the Company with respect to the tax treatment of any of the Severance Benefits set forth in this Agreement.

22. **Counterparts** – This Agreement may be executed in several counterparts, each of which shall be deemed to be an original, but all of which together will constitute one and the same Agreement. Facsimile and PDF signatures shall be deemed to be of equal force and effect as originals.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the Parties have set their hands and seals to this Agreement as of the date(s) written below.

OPHTHOTECH CORPORATION

By: /s/ David R. Guyer Date: January 12, 2017
Name: David R. Guyer
Title: CEO & Chairman of the Board

I hereby agree to the terms and conditions set forth above. I have been given at least twenty-one (21) days to consider this Agreement and I have chosen to execute this on the date below. I intend that this Agreement will become a binding agreement if I do not revoke my acceptance within seven (7) days. I further understand that the Severance Benefits are contingent upon my timely execution, return and non-revocation of the Additional Release.

Samir Patel, M.D.

/s/ Samir C. Patel Date: 1/12/2017

EXHIBIT I
Payment Subject to Section 409A

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

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

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

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

Each installment of the severance payments and benefits due under this Agreement that will be paid within the short-term deferral period (as defined in Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A; and

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

The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Exhibit I, "Company" shall include all persons with whom the Company would be considered a single employer as determined under Treasury Regulation Section 1.409A-1(h)(3).

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

Executive expressly acknowledges and agrees that the Company is not making any representations or warranties to him and shall have no liability to him or any other person with respect to payments made under this Agreement if any provisions of or payments under the Agreement are determined to constitute deferred compensation subject to Code Section 409A but not to satisfy the conditions of that section.

ATTACHMENT A

CONSULTING AGREEMENT

[filed as a separate Exhibit]

[*Attachment A to Separation and Release of Claims Agreement*]

ATTACHMENT B

ADDITIONAL RELEASE OF CLAIMS

This Additional Release of Claims (this "Additional Release") is made as of the date set forth opposite Executive's signature below, by and between the Company and Executive. Capitalized terms used but not defined herein have the meanings set forth in the Separation and Release of Claims Agreement (the "Separation Agreement") to which this Additional Release is attached.

WHEREAS, the Consultation Period has expired or terminated within the five (5) business days preceding execution of this Additional Release; and

WHEREAS, Executive is entering into this Additional Release in accordance with the terms and conditions set forth in Section 2 of the Separation Agreement.

NOW, THEREFORE, in consideration of the mutual covenants and agreements contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1. Release – In consideration of the Severance Benefits set forth in the Separation Agreement, which Executive acknowledges he would not otherwise be entitled to receive, Executive hereby fully, forever, irrevocably and unconditionally releases, remises and discharges the Company, its affiliates, subsidiaries, parent companies, predecessors, and successors, and all of their respective past and present officers, directors, stockholders, partners, members, employees, agents, representatives, plan administrators, attorneys, insurers and fiduciaries (each in their individual and corporate capacities) (collectively, the "Released Parties") from any and all claims, charges, complaints, demands, actions, causes of action, suits, rights, debts, sums of money, costs, accounts, reckonings, covenants, contracts, agreements, promises, doings, omissions, damages, executions, obligations, liabilities, and expenses (including attorneys' fees and costs), of every kind and nature that Executive ever had or now has against any or all of the Released Parties up to the date on which he signs this Additional Release, whether known or unknown, including, but not limited to, any and all claims arising out of or relating to Executive's employment with, provision of consulting or other services to, separation or termination from, and/or ownership of securities of the Company including, but not limited to, all claims under Title VII of the Civil Rights Act, the Americans With Disabilities Act, the Age Discrimination in Employment Act, the Genetic Information Nondiscrimination Act, the Family and Medical Leave Act, the Worker Adjustment and Retraining Notification Act, the Rehabilitation Act, Executive Order 11246, Executive Order 11141, the Fair Credit Reporting Act, and the Employee Retirement Income Security Act, all as amended; all claims arising out of the New York Human Rights Law, N.Y. Exec. Law § 290 et seq., the New York City Human Rights Law, N.Y.C. Admin. Code § 8-101 et seq., N.Y. Civ. Rights Law § 40-c et seq. (New York anti-discrimination law), N.Y. Lab. Law § 194 et seq. (New York equal pay law), N.Y. Lab. Law § 740 (New York whistleblower protection law), and N.Y. Lab. Law § 201-c (New York adoption leave law), all as amended; all claims arising out of the New Jersey Law Against Discrimination, N.J. Stat. Ann. § 10:5-1 et seq., the New Jersey Family Leave Act, N.J. Stat. Ann. § 34:11B-1 et seq., the New Jersey Conscientious Employee Protection Act, N.J. Stat. Ann. § 34:19-1 et seq., N.J. Stat. Ann. § 34:11-56.1 et seq. (New Jersey equal pay law), and the New Jersey "mini-WARN" Act **(**N.J.S.A. 34:21-1, et seq.), all as amended; all common law claims including, but not limited to, actions in defamation, intentional infliction of emotional distress, misrepresentation, fraud, wrongful discharge, and breach of contract (including, without limitation, all claims arising out of or related to the Consulting Agreement); all state and federal whistleblower claims to the maximum extent permitted by law; and any

claim or damage arising out of Executive's employment with and/or separation from the Company (including a claim for retaliation) under any common law theory or any federal, state or local statute or ordinance not expressly referenced above; *provided, however, that nothing in this release of claims prevents Executive from filing a charge with, cooperating with, or participating in any investigation or proceeding before, the Equal Employment Opportunity Commission or a state fair employment practices agency (except that Executive acknowledges that he may not recover any monetary benefits in connection with any such charge, investigation, or proceeding, and Executive further waives any rights or claims to any payment, benefit, attorneys' fees or other remedial relief in connection with any such charge, investigation or proceeding).* Further, nothing herein shall prevent Executive from bringing claims to enforce the Separation Agreement and/or the Consulting Agreement, or release (i) any rights Executive may have under the Company's certificate of incorporation, by-laws, insurance and/or any indemnification agreement between him and the Company (and/or otherwise under law) for indemnification and/or defense as an employee, officer or director of the Company for his service to the Company (recognizing that such indemnification and/or defense is not guaranteed by this Agreement and shall be governed by the instrument or law, if any, providing for such indemnification and/or defense), (ii) any rights Executive may have to vested equity ownership in the Company under the applicable equity plans and agreements, or (iii) any right to the Accrued Benefits.

2. **Return of Company Property** – Executive confirms that he has returned to the Company all property of the Company, tangible or intangible, including but not limited to keys, files, records (and copies thereof), equipment (including, but not limited to, computer hardware, software and printers, wireless handheld devices, cellular phones, tablets, etc.), Company identification and any other Company-owned property in his possession or control and that he has left intact all electronic Company documents, including but not limited to those that he developed or helped to develop during his employment or while performing services under the Consulting Agreement. Executive further agrees that he has canceled all accounts for his benefit, if any, in the Company's name, including but not limited to, credit cards, telephone charge cards, cellular phone and/or wireless data accounts and computer accounts.

3. **Acknowledgments** – Executive acknowledges that he has been given at least twenty-one (21) days to consider this Additional Release, and that the Company is hereby advising him to consult with an attorney of his own choosing prior to signing this Additional Release. Executive understands that he may revoke this Additional Release for a period of seven (7) days after he signs it by notifying the Company in writing, and the Additional Release shall not be effective or enforceable until the expiration of this seven (7) day revocation period (the day immediately following expiration of such revocation period, the "Additional Release Effective Date"). Executive understands and agrees that by entering into this Additional Release, he is waiving any and all rights or claims he might have under the Age Discrimination in Employment Act, as amended by the Older Workers Benefit Protection Act, and that he has received consideration beyond that to which he was previously entitled.

4. **Voluntary Assent** – Executive affirms that no other promises or agreements of any kind have been made to or with him by any person or entity whatsoever to cause him to sign this Additional Release, and that he fully understands the meaning and intent of this Additional Release. Executive states and represents that he has had an opportunity to fully discuss and review the terms of this Additional Release with an attorney. Executive further states and represents that he has carefully read this Additional Release, understands the contents herein, freely and voluntarily assents to all of the terms and conditions hereof, and signs his name of his own free act.

For the avoidance of double, this Additional Release supplements, and in no way limits, the Separation Agreement.

I hereby provide this Additional Release as of the current date and acknowledge that the execution of this Additional Release is in further consideration of the Severance Benefits, to which I acknowledge I would not be entitled if I did not sign this Additional Release. I intend that this Additional Release will become a binding agreement between me and the Company if I do not revoke my acceptance in seven (7) days.

Samir Patel, M.D.

_____ Date:_____

OPHTHOTECH CORPORATION

CONSULTING AGREEMENT

This Consulting Agreement (this "Agreement") is entered into as of January 13, 2017 (the "Effective Date") by and between Ophthotech Corporation (the "Company"), and Samir Patel, M.D. (the "Consultant").

WHEREAS, the Consultant has certain knowledge and expertise regarding the Company as a result of having served as its President; and

WHEREAS, the Company desires to have the benefit of the Consultant's knowledge and experience, and the Consultant desires to provide consulting services to the Company, all as hereinafter provided in this Agreement.

NOW, THEREFORE, in consideration of the promises and mutual agreements hereinafter set forth, the sufficiency of which are hereby acknowledged, the Company and the Consultant hereby agree as follows:

Section 1. Services.

(a) Services; Performance. The Consultant shall render to the Company the consulting services described in Exhibit A attached to this Agreement and any additional consulting services as mutually agreed to by the Consultant and the Company from time to time in writing (collectively, the "Services"). The Consultant shall perform, during regular business hours and such additional hours as may be reasonably required for satisfactory performance of the Services, such Services in a professional manner and consistent with the highest industry standards. The Consultant shall comply with all rules, procedures and standards promulgated from time to time by the Company with respect to the Consultant's access to and use of the Company's property, information, equipment and facilities in the course of the Consultant's provision of Services hereunder.

(b) Non-Exclusive. The parties agree that, at all times during the term of this Agreement, (i) the Company shall be free to obtain consulting and advisory services from any third party, and (ii) the Consultant shall be free to provide consulting and advisory services to any third party, so long as the provision of such services by the Consultant does not conflict with the Consultant's (x) provision of Services to the Company as described in Section 1(a), or (y) continuing obligations to the Company as detailed in the Separation and Release of Claims Agreement entered into by the parties concurrently with this Agreement and to which this Consulting Agreement is attached as Attachment A (the "Separation Agreement"), including the Consultant's ongoing Restrictive Covenant Obligations (as defined in the Separation Agreement and as amended thereby), and his continuing obligations under the Invention and Non-Disclosure Agreement executed by him on November 30, 2009 and amended by the Separation Agreement (the "NDA"). Further, the Consultant shall notify the Company immediately in writing if he begins service as a member of the board of directors or similar body of a company or other entity engaged in activities in the ophthalmology field or commences providing services of any kind to another person or entity engaged in activities in the ophthalmology field during the Consultation Period (as defined below), and in such notice identify such company, person or entity (including a description of its business), whether he has begun service as a member of the board of directors, and/or the nature of any other services he provides.

Section 2. Compensation and Reimbursement.

(a) Consulting Fees. As consideration for the performance of Services by the Consultant hereunder, the Company shall pay the Consultant during the Consultation Period consulting fees in the amount of $41,666.67 per month (the "Consulting Fees"), to be paid to the Consultant at the end of each month.

(b) Expense Reimbursement. The Company shall reimburse the Consultant for all reasonable out-of-pocket expenses incurred by the Consultant in connection with the performance of the Services under this Agreement, so long as they are approved in writing in advance by the Company.

(c) Health Insurance Payments. Should the Consultant be eligible for and elect to remain on the Company's group health and/or dental insurance plan(s) as an active enrollee, he shall be entitled to remain on such plan(s) through the end of the Consultation Period, and the Company shall contribute to the cost of the Consultant's group health and/or dental insurance plan(s) at the same rates as from time to time in effect for the Company's active workforce. If the Consultant is not or ceases to be eligible to remain on the Company's group health and/or dental insurance plan(s) and is eligible for and timely elects to continue receiving group health and/or dental insurance coverage under the law known as COBRA, the Company shall, through the earlier of (x) the end of the Consultation Period or (y) the date that the Consultant is no longer eligible for and enrolled in COBRA continuation coverage, continue to contribute on the Consultant's behalf the employer premium for such coverage at the same rates as from time to time in effect for the Company's active workforce. Should the Consultant cease during the Consultation Period to be eligible to continue receiving group health and/or dental insurance coverage under COBRA for reasons other than becoming enrolled in another group health plan, the Company shall provide the Consultant with an additional monthly payment for the duration of the Consultation Period in an amount equal to the monthly employer premium paid during the final month of his COBRA continuation coverage.

(d) Itemized Statements. At the end of any month in which the Consultant performs Services and incurs expenses in accordance with Section 2(b), the Consultant shall submit to the Company an itemized statement of the expenses incurred, including appropriate and reasonable documentation. The Company shall pay the Consultant the amount set forth on such itemized statement within forty-five (45) days after receipt.

(e) No Employee Benefits. The Consultant's relationship with the Company will be that of an independent contractor, and the Consultant shall not, in connection with this relationship, be entitled to any benefits, coverages or privileges, including without limitation social security, unemployment, workers compensation, pension payments, administrative support (other than as may be approved by the Company's Chief Executive Officer, Chief Financial Officer or Chief Operating Officer) or office space on the Company's premises, made available to employees of the Company.

Section 3. Term and Termination.

(a) Consultation Period. Subject to the terms and conditions hereinafter set forth, the term of this Agreement (the "Consultation Period") shall, provided the Consultant has timely entered into the Separation Agreement, commence on the Effective Date and continue until terminated as set forth in this Section 3(a) (and provided that the Consultation Period shall automatically terminate upon the death, physical incapacitation or mental incompetence of the Consultant). This Agreement may be terminated in the following manner: (i) by the Company at any time immediately upon written notice if the Consultant

has materially breached this Agreement or the Separation Agreement, followed by his failure to cure such material breach, if curable, after receiving from the Company notice of and a reasonable time (not to exceed fifteen (15) days) in which to cure such breach; (ii) by the Consultant at any time immediately upon written notice if the Company has materially breached this Agreement or the Separation Agreement, followed by its failure to cure such material breach, if curable, after receiving from the Consultant notice of and a reasonable time (not to exceed fifteen (15) days) in which to cure such breach; (iii) by the Consultant at any time, for any reason or no reason, upon not less than fifteen (15) days prior written notice to the Company; (iv) by the Company on or after the twelve (12)-month anniversary of the Effective Date, for any reason or no reason, upon not less than fifteen (15) days prior written notice to the Consultant; or (v) at any time upon the mutual written consent of the parties hereto.

(b) Effects of Termination. In the event of any termination under this Section 3, the Consultant shall be entitled only to the applicable pro rata portion of the Consulting Fees payable for the month in which termination occurs and expenses (including reimbursements and health insurance payments) incurred in accordance with Section 2(a), (b) and (c) prior to the effective date of such termination, and no further payments of any kind will be due under this Agreement.

Section 4. **Independent Contractor.** The Consultant is not as of the Effective Date, nor shall the Consultant be deemed to be at any time during the Consultation Period, an employee of the Company. The Consultant's status and relationship with the Company shall be that of an independent contractor and consultant. The Consultant is not authorized to assume or create any obligation or responsibility, express or implied, on behalf of, or in the name of, the Company or to bind the Company in any manner. Nothing herein shall create, expressly or by implication, a partnership, joint venture or other association between the parties. The Consultant shall be solely responsible for payment of all charges and taxes arising from the payments to be made to the Consultant under this Agreement and the Consultant agrees that the Company shall have no obligation or liability with respect to such charges and/or taxes.

Section 5. **Notice.** Any notice required or desired to be given shall be governed solely by this paragraph. Notice shall be deemed given only upon (a) mailing of any letter or instrument by overnight delivery with a reputable carrier or by registered mail, return receipt requested, postage prepaid by the sender, or (b) personal delivery.

If to the Consultant:
[redacted]

If to the Company:
Ophthotech Corporation
One Penn Plaza, 19th Floor
New York, NY 10119
Attn: Chief Executive Officer

From time to time, either party may, by written notice to the other in accordance with this Section 5, designate another address that shall thereupon become the effective address of such party for the purpose of this Section 5.

Section 6. **Miscellaneous.** This Agreement, together with the Separation Agreement and all exhibits and attachments hereto and thereto and the NDA, constitutes the entire understanding of the parties hereto with respect to the matters contained herein and supersedes all proposals and agreements, written or oral, and all other communications between the parties relating to the subject matter of this Agreement. For the avoidance of doubt, nothing herein supersedes the Separation Agreement (including the ongoing force and effect of the Restrictive Covenant Obligations) or the NDA. This Agreement shall be governed by and construed in accordance with the laws of the State of New York without regard to its conflict of laws

rules. The headings contained in this Agreement are for the convenience of the parties and are not to be construed as a substantive provision hereof. This Agreement may not be modified or amended except in writing signed or executed by the Consultant and the Company. In the event any provision of this Agreement is held to be unenforceable or invalid, such unenforceability or invalidity shall not affect any other provisions of this Agreement and such other provisions shall remain in full force and effect. If any provision of this Agreement is held to be excessively broad, it shall be reformed and construed by limiting and reducing it so as to be enforceable to the maximum extent permitted by law. This Agreement shall be binding upon, and inure to the benefit of, both parties hereto and their respective successors and assigns, including any corporation with or into which the Company may be merged or which may succeed to its assets or business; provided, however, that the responsibility for actual performance of the Services is personal to the Consultant and may not be assigned or delegated by the Consultant to any other person or entity. This Agreement may be executed in counterparts and by facsimile, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed as of the date first written above.

Samir Patel, M.D.

/s/ Samir C. Patel

OPHTHOTECH CORPORATION

By: /s/ David R. Guyer
Name: David R. Guyer
Title: CEO & Chairman of the Board

[*Signature Page to Consulting Agreement*]

Exhibit A

Description of Services

The Consultant shall, as directed by the Company's Chief Executive Officer, provide consulting and advisory services in areas which may include, without limitation, biopharmaceutical research and development, business development, clinical development, clinical trial site selection, strategy, research, regulatory matters, recruitment, data analysis and medical affairs.

CLINICAL AND COMMERCIAL SERVICES AGREEMENT

This **CLINICAL AND COMMERCIAL SERVICES AGREEMENT** (the ***"Agreement"***) is entered into as of the 31st day of October, 2016 (***"Effective Date"***) by and between **OPHTHOTECH CORPORATION**, a Delaware corporation, having its principal place of business at One Penn Plaza, Suite 1924, New York, NY 10119 (***"Client"***), and **AJINOMOTO ALTHEA, INC.**, a Delaware corporation, with a place of business located at 11040 Roselle Street, San Diego, CA 92121 (***"Althea"***);

WHEREAS, Client has Bulk Compound (capitalized terms are defined below) for filling and/or finishing;

WHEREAS, Althea has the expertise and the fill/finish facility suitable for the Production of Client Product; and

WHEREAS, Client wishes to have Althea perform such services, and Althea wishes to perform such services for Client.

NOW, THEREFORE, in consideration of the premises and the undertakings, terms, conditions and covenants set forth below, the parties hereto agree as follows:

1. DEFINITIONS.

1.1 "Acceptable Yield" shall have the meaning provided in Appendix E.

1.2 "Actual Yield" shall have the meaning provided in Appendix E.

1.3 "Affiliate" of a party hereto shall mean any entity that controls or is controlled by such party, or is under common control with such party. For purposes of this definition, an entity shall be deemed to control another entity if it owns or controls, directly or indirectly, at least 50% of the voting equity of such other entity (or other comparable interest for an entity other than a corporation).

1.4 "Agreement" shall have the meaning set forth in the Preamble.

1.5 "Althea" shall have the meaning set forth in the Preamble.

1.6 "Althea Indemnitee" shall have the meaning set forth in Section 17.1.

1.7 "Althea SOPs" shall mean Althea's Standard Operating Procedures, which will be in writing and customized on a product-specific basis, as necessary, for manufacture of Client Product. Client will review and approve in writing each Client Product-specific SOP prior to Production of Client Product and any subsequent revisions to these Client Product-specific SOPs. As part of any audit performed pursuant to this Agreement or the Quality Agreement, Client may also review other Althea SOPs that are applicable to Production (including all activities contemplated hereby) or any Non-Production Services.

1.8 "Althea's Project Intellectual Property" shall have the meaning set forth in Section 14.2.

1.9 "Bulk Compound" shall mean the active pharmaceutical ingredient of Client Product, in bulk form, supplied to Althea by Client.

1.10 "Cancellation" shall have the meaning set forth in Section 8.5.

1.11 "Certificate of Analysis" shall mean a certificate of analysis, signed by an authorized representative of Althea, that describes the testing methods applied to the Client Product in order to verify compliance with the Specifications, and the associated test results.

1.12 "Certificate of Compliance" shall mean the document prepared by Althea listing, for each Lot, the manufacturing date, unique Lot number and quantity of Bulk Compound in such Lot, certifying that such Lot was manufactured in accordance with the Production Standards and certifying, in accordance with the Quality Agreement, that all investigations of the cGMP manufacturing process or system are completed and approved.

1.13 "cGMP" shall mean applicable Good Manufacturing Practices for drugs pursuant to (i) the FDA rules and regulations, 21 CFR Parts 11, 210-211, 600 and 601, (ii) the U.S. Federal Food, Drug, and Cosmetic Act, as amended (21 USC 301 et seq.), (iii) the Commission Directive 2003/94/EEC of 08 October 2003, (iv) the EC Guide to Good Manufacturing Practice for Medicinal Licensed Products, including respective guidance documents, and the relevant current International Conference on Harmonization (ICH) guidance documents, and (v) any corresponding good manufacturing laws, rules or regulations of any agreed upon foreign jurisdiction, as they may be amended from time to time, *provided that* any such foreign jurisdiction good manufacturing requirements have been expressly agreed to in an SOW or other writing signed by Client and Althea.

1.14 "Claim" shall have the meaning set forth in Section 17.1.

1.15 "Client" shall have the meaning set forth in the Preamble.

1.16 "Client Indemnitee" shall have the meaning set forth in Section 17.2.

1.17 "Client Product" shall mean Client's pharmaceutical products and investigational compounds including Fovista® and Zimura® or such other compounds as the parties may agree in an SOW or DOS are subject to this Agreement as additional Client Products following the Effective Date pursuant to Section 3.7), in each case as specified in the Specifications, to be Produced by Althea in filled/finished dosage form. For the avoidance of doubt, Client Product includes such containers, enclosures and/or primary packaging of Client's pharmaceutical products as set forth in the relevant Specification.

1.18 "Client's Project Intellectual Property" shall have the meaning set forth in Section 14.2.

1.19 "Components" shall mean all components, including, without limitation, excipients and raw and other materials, used by Althea in Production of Client Product under this Agreement in accordance with the Specifications. Components are identified in the Specifications as Components supplied by Client or its vendors, including Bulk Compound (***"Client-Supplied Components"***) or Components supplied by Althea or its vendors ("***Althea-Supplied Components"***).

1.20 "Confidential Information" shall have the meaning set forth in Section 13.1.

1.21 "CRA" shall have the meaning set forth in Section 2.1.

1.22 "Deficiency Cure Product" shall have the meaning set forth in Section 5.5(b).

1.23 "Delay" shall have the meaning set forth in Section 8.5.

1.24 "Disclosing Party" shall have the meaning set forth in Section 13.1.

1.25 "Dispute" shall have the meaning set forth in Section 19.8.

1.26 "Effective Date" shall have the meaning set forth in the Preamble.

1.27 "Facility" shall mean either the Rota 150 Facility or the HSL Facility, or such other Althea cGMP manufacturing facility as is qualified and approved by Client after the Effective Date, in each case, as applicable.

1.28 "FDA" shall mean the United States Food and Drug Administration or any successor entity thereto.

1.29 "Force Majeure Event" shall have the meaning set forth in Section 11.1.

1.30 "Forecast" shall have the meaning set forth in Section 4.3.

1.31 "HSL Equipment" shall have the meaning set forth in the CRA.

1.32 "HSL Facility" shall mean Althea's facility to be located at 6173-6175 Lusk Boulevard, San Diego, CA 92121.

1.33 "Indemnitor" shall have the meaning set forth in Section 17.3.

1.34 "Initial Term" shall have the meaning set forth in Section 8.1.

1.35 "Invention" shall mean any creative work, invention, innovation, improvement, development, discovery, trade secret, method, know-how, process, technique or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which contained, and whether or not patentable or copyrightable.

1.36 "Intellectual Property" shall mean all rights, privileges and priorities provided under applicable international, national, federal, state or local law, rule, regulation, statute, ordinance, order, judgment, decree, permit, franchise, license, or other government restriction or requirement of any kind relating to intellectual property, whether registered or unregistered, in any country, including, without limitation: (a) all (i) patents and patent applications (including any patent that in the future may issue in connection therewith and all divisions, continuations, continuations-in-part, extensions, additions, registrations, confirmations, reexaminations, supplementary protection certificates, renewals or reissues thereto or thereof), (ii) copyrights and copyrightable works, including reports, software, databases and related items, (iii) trademarks, service marks, trade names, brand names, product names, corporate names, logos and trade dress, the goodwill of any business symbolized thereby, and all common-law rights relating thereto, (iv) confidential and/or proprietary information, Inventions, developments, techniques, materials, processes, compositions of matter or methods of use and trade secrets, and (v) any other intellectual property right which may subsist anywhere in the world, whether capable of grant, registration or not; and (b) all registrations, applications, recordings, rights of enforcement, rights of recovery based on past infringement and any and all claims of action related thereto and licenses or other similar agreements related to the foregoing.

1.37 "Latent Defect" shall have the meaning set forth in Section 5.3(a).

1.38 "Losses" shall have the meaning set forth in Section 17.1.

1.39 "Lot" shall mean a specific quantity of Client Product that (a) is intended to have uniform character and quality within specified limits and (b) is Produced in one continuous filling operation that is supported by an aseptic process.

1.40 "Master Batch Record" or "MBR" shall mean the formal set of written instructions for Production of a Client Product, approved and signed by both parties. The MBR shall be developed and maintained in Althea's standard format by Althea, using Client's master formula and technical support.

1.41 "Non-Conformity" shall have the meaning set forth in Section 5.3(a).

1.42 "Non-Production Fees" shall have the meaning set forth in Section 2.2.

1.43 "Non-Production Services" shall mean any non-Production services, e.g., storage, destruction, regulatory support and validation services, to be provided under this Agreement as set forth in an SOW, and shall exclude any services that are performed as part of a Purchase Order for the Production of Client Product.

1.44 "Order Change Fee" shall have the meaning set forth in Section 8.5.

1.45 "Permit" shall have the meaning set forth in Section 15.2(c).

1.46 "Person" shall mean any individual, partnership, corporation, limited liability company, unincorporated organization or association, any trust or any other business entity.

1.47 "Product Inventions" shall have the meaning set forth in Section 14.2.

1.48 "Production" or "Produce" shall mean all steps and activities to produce Client Product to be performed by Althea, as set forth in the MBR, the Specification and this Agreement, or in the applicable DOS or SOW, including, as stated in the DOS or SOW, the manufacturing, formulation, filling, packaging, inspection, labeling, testing (e.g., identification testing of Components, in process testing, release testing), biannual aseptic process validation, quality control and release.

1.49 "Production Process" shall mean the process for Producing the Client Product as set forth in the MBR.

1.50 "Production Standards" shall mean, collectively, the Specifications for the applicable Client Product and cGMP.

1.51 "Purchase Order" shall mean a written purchase order in the form attached hereto as Appendix F, to be delivered by Client to Althea for the Production of Client Product pursuant to this Agreement. For clarity, in the event of any conflict or ambiguity between this Agreement and any Purchase Order, the terms of this Agreement shall prevail.

1.52 "Purchase Price" shall have the meaning set forth in Appendix A.

1.53 "Quality Agreement" shall mean a written, mutually executed agreement between Althea and Client set forth in Appendix D that defines the quality roles and responsibilities of each party in connection with the Production of Client Product. For clarity, in the event of any conflict or ambiguity between this Agreement and the Quality Agreement, this Agreement shall prevail.

1.54 "Receiving Party" shall have the meaning set forth in Section 13.1.

1.55 "Regulations" shall have the meaning set forth in Section 9.6.

1.56 "Regulatory Authority" shall mean the FDA in the United States, and the equivalent authority in Europe or any other foreign jurisdiction; *provided that* Althea shall have no obligation to Produce Client Product in compliance with the requirements of any non-U.S., non-European Regulatory Authority, except as expressly agreed by the parties in an SOW or other mutually signed writing.

1.57 "Rejects" shall have the meaning set forth in Section 6.4.

1.58 "Released Executed Batch Record" shall mean the completed Batch Production Record (as defined in the Quality Agreement) and associated deviation reports, investigation reports, applicable certificates for Components and testing and Lot-specific Certificates of Analysis and Certificates of Compliance, created for each Lot of Client Product, in the standard form used by Althea and in compliance with the MBR. For the avoidance of doubt, the Released Executed Batch Record will, include a calculation of each of the Actual Yields listed on Appendix E and will not be considered complete if there are any open, unresolved deviations or investigations for the specific Lot(s).

1.59 "Renewal Term" shall have the meaning set forth in Section 8.1.

1.60 "Replacement Cost" shall have the meaning set forth in Section 5.4(c).

1.61 "Rota 150 Facility" means Althea's facility located at the campus centered at 11040 Roselle Street, San Diego CA 92121.

1.62 "Specifications" shall mean the applicable specifications for Client Product or Bulk Compound or other Components, as applicable, set forth in Appendix C, as such specifications may be amended from time to time in accordance with this Agreement.

1.63 "Statement of Work" or "SOW" or "DOS" shall mean a proposal, description of services or other written document(s) signed by both parties and made a part of this Agreement that set(s) forth the particular services required for Production and Non-Production Services to be provided by Althea under this Agreement, including, without limitation, the description of such services, deliverables and for Non-Production Services, fees (subject to Appendix A for storage fees), timelines, milestones, payment schedules and validation protocols and fees.

1.64 "Successful Validation" shall have the meaning given to such term in the CRA.

1.65 "Supply Deficiency" shall have the meaning set forth in Section 5.5(a).

1.66 "Supply Delay" shall have the meaning set forth in Section 5.5(a).

1.67 "**Supply Failure**" shall have the meaning set forth in Section 5.5(a).

1.68 "Term" shall have the meaning provided in Section 8.1.

1.69 "Term Trigger Date" shall have the meaning give to such term in the CRA.

1.70 "Theoretical Yield" shall have the meaning provided in Appendix E.

1.71 "Third Party" shall mean any Person who is not Althea or Client, or an Affiliate of Althea or Client.

1.72 "Vial" shall mean the vial specified in the Specifications.

1.73 "Yield" shall have the meaning provided in Appendix E.

1.74 "Yield Production Standard" shall have the meaning provided in Appendix E.

1.75 Interpretation; Headings. Each term used in any Exhibit to this Agreement and defined in this Agreement but not defined therein shall have the meaning set forth in this Agreement. Unless the context otherwise requires, (i) "**including**" means "including, without limitation" and (ii) words in the singular include the plural and words in the plural include the singular. A reference to any party to this Agreement or any other agreement or document shall include such party's successors and permitted assigns. A reference to any agreement or order shall include any amendment of such agreement or order from time to time in accordance with the terms hereof and thereof. A reference to any legislation, to any provision of any legislation or to any regulation issued thereunder shall include any amendment thereto, any modification or re-enactment thereof, any legislative provision or regulation substituted therefor and all regulations and statutory instruments issued thereunder or pursuant thereto. The headings contained in this Agreement are for convenience and reference only and do not form a part of this Agreement. Section, article and Exhibit references in this Agreement refer to sections or articles of, or exhibits to, this Agreement unless otherwise specified.

2. VALIDATION AND NON-PRODUCTION SERVICES.

2.1 Validation and other Non-Production Services. Althea shall qualify equipment and validate the Production Process (as applicable) according to the validation protocol(s) approved by both parties in advance in writing. Such validation protocol(s) and timeline shall be included in an SOW or in the Capacity Reservation Agreement between the parties of even date herewith ("***CRA***"). Althea shall perform validation and other Non-Production Services in a timely, professional and workmanlike manner consistent with industry standards and in accordance with this Agreement, the Quality Agreement, the applicable SOW and all Regulations applicable to such Services.

2.2 Non-Production Fees: The fees for any Non-Production Services provided by Althea hereunder (the ***"Non-Production Fees"***) shall be set forth in Appendix A or in an SOW.

2.3 Technical Contact. Each party will appoint a technical contact **(*"Technical Contact"*)** having primary responsibility for day-to-day interactions with the other party for the activities conducted hereunder. The parties may each specify a different Technical Contact for any Non-Production Services in the applicable SOW. Any change to a Technical Contact will be identified in writing to the other party. Each party will use reasonable efforts to provide the other party with at least [**] days prior written notice of any change in that party's Technical Contact. Unless otherwise set forth herein, all

communications between the parties regarding the conduct of activities performed hereunder will be addressed to the party's relevant Technical Contact.

3. PRODUCTION – GENERAL OBLIGATIONS

3.1 Documentation: The Master Batch Record shall be reviewed and approved by Althea and by Client in writing prior to commencement of Production. Any change to an approved Master Batch Record shall be reviewed and approved in a signed writing by Althea and by Client prior to said change being implemented. Each Lot of Client Product shall be Produced by using a true copy of the Master Batch Record. Each copy of the Master Batch Record for a Lot of Client Product shall be assigned a unique Lot number. Deviation(s) from the Master Batch Record must be documented as required by cGMP in the Released Executed Batch Record for each Lot. Althea shall provide Client with each Released Executed Batch Record in a form reasonably suitable for Client's submission to applicable Regulatory Authorities. The parties shall execute the Quality Agreement prior to or simultaneously with the execution of this Agreement or at a later time if mutually agreed by the parties, *provided that* such Quality Agreement shall be executed prior to commencement of Production under this Agreement.

3.2 Vendor and Supplier Audit and Certification: Client shall certify and audit all vendors and suppliers of Client-Supplied Components. Althea shall specify in the Specifications or obtain the prior written approval of Client for vendors and suppliers of Althea-Supplied Components. Althea shall certify and audit all vendors and suppliers of Althea-Supplied Components and shall provide reasonable access in accordance with Section 9.3 (Audits) to any information relevant to such certifications and/or audits to Client upon Client's request. Client may seek to audit Althea vendors and suppliers where Client reasonably believes that the Althea qualification process is insufficient and/or the Althea vendor or supplier qualification status is unsupported. Althea shall use its commercially reasonable efforts to facilitate any such audit.

3.3 Export Controls: Each party shall comply with applicable U.S. and other laws, rules and regulations that govern the import, export and re-export of Client Product, Components and other items relating to this Agreement, including the U.S. Export Administration Regulations, and shall obtain any required export and import authorizations. Althea shall not export any Bulk Compound or Client Product from the United States without Client's prior written approval. Client shall be the exporter of record for any Bulk Compound or Client Product shipped out of the United States, as Client remains the owner of the Bulk Compound or Client Product, as applicable. Client shall be responsible for ensuring that all shipments of Bulk Compound or Client Product exported from the United States are made in compliance with all applicable United States export laws and regulations and all applicable import laws and regulations into the country of deportation. Client shall be responsible for obtaining and paying for any licenses, clearances or other governmental authorization(s) necessary for such exportation from the United States. Client shall select and pay the freight forwarder who shall solely be Client's agent. Client and its freight forwarder shall be solely responsible for preparing and filing the shipper's export declaration and any other documentation required for the export.

3.4 Safety Data Sheet (SDS); Acceptable Materials: Client shall provide Althea a safety data sheet for Client-Supplied Components and Client Product. Althea shall conform to established safety practices and procedures set forth in any such safety data sheet and shall store and handle Client-Supplied Components and Client Product as required by the MBR, and all applicable laws and regulations. Althea is under no obligation to produce, nor shall Client ship or cause to be shipped to Althea without specific prior written approval, nor shall Althea produce or store in any facility or any fill/finish line or equipment used or intended to be used for Production hereunder any materials that: (a) contain a penicillin, cephalosporin, high-potent product, DEA controlled substance or radio label, (b) have

an occupational exposure limit of less than 1 µg/m^3 or (c) include substances that, under cGMP or industry standards (including 21 CFR Part 211.42(d)) may not share facilities or equipment with Client Product. Althea understands and agrees that the Bulk Compound may have unpredictable and unknown biological and/or chemical properties and should be used with caution and is not to be used for testing in or treatment of humans by Althea or for any purpose other than as provided herein. Althea shall immediately notify Client of any unusual health or environmental occurrence relating to Client Product, including, but not limited to, any claim or complaint by any employee of Althea or any of its Affiliates or Third Party contractors. Althea agrees to advise Client immediately of any safety or toxicity problems of which it becomes aware regarding the Client Product that are not already encompassed by the information contained in the Safety Data Sheet. Except as set forth in Article 6, the generation, collection, storage, handling, processing, disposal, transportation and movement of all hazardous materials and waste used or generated by Althea, as applicable, shall be the sole responsibility of Althea at its sole cost and expense.

3.5 Components: Client shall supply to Althea, at no cost (other than as provided for under Section 5.4(c) and (d)), Client-Supplied Components. As of the Effective Date, the only Client-Supplied Components are Bulk Compound and those Components previously purchased by Client under purchase orders issued prior to the Effective Date that are identified on Appendix A-1 (the "***Pre-Purchased Components***"), which are currently being stored by Althea. From and after the Effective Date, except as may otherwise be agreed between the parties in the SOW or DOS, Althea shall be responsible for procuring and providing all Components other than Bulk Compound (which shall always be supplied by Client); *provided* that (x) Althea shall first utilize the Pre-Purchased Components and provide a corresponding discount to the Purchase Price for any Production utilizing such Pre-Purchased Components, as set forth in more detail on Appendix A and (y) in the event that Client supplies or transfers to Althea any further Components (beyond the Bulk Compound and the Pre-Purchased Components), the Parties agree to make equitable adjustments to the Purchase Price (or otherwise provide for a credit to Client) for the Production of the applicable Lots for which such Components are provided. All Components procured and used by Althea for Production shall meet the Specifications for such Components set forth in the MBR. Althea shall not procure any Althea-Supplied Components on an exclusive basis or in a manner or on terms or conditions that would preclude Client or Client's other contract manufacturers from obtaining access to any such Components. Client shall supply any Client-Supplied Components for which it is responsible no later than [**] business days prior to the beginning of the Production of the relevant Lot(s) of Client Product. The parties may specify in the Specifications earlier dates by which Client shall supply Client-Supplied Components. Althea's use of Client-Supplied Components supplied by or on behalf of Client shall be limited to the Production of Client Product contemplated by this Agreement exclusively for Client.

(a) Within [**] business days of Althea's receipt of any Client Supplied Components, Althea shall conduct a visual inspection of such Client-Supplied Components, including the secondary packaging therefor, to determine quantities and whether such Client-Supplied Components have been compromised. In the event that such visual inspection indicates that the Client-Supplied Components have been compromised or quantities are incorrect, Althea shall notify Client of same within [**] business days. Within [**] business days of Althea's receipt of any Client-Supplied Components, Althea shall: (i) perform an identification test on the Client-Supplied Components and confirm the shipment quantity; (ii) conduct any other tests provided for in the Specifications or the MBR; and (iii) notify Client of any inaccuracies with respect to quantity or failure of such tests. In the event of the Client-Supplied Components had been compromised upon their arrival at Althea or in the event of a failure of the Client-Supplied Components to meet the quantity requirements or of any tests contemplated by this Section 3.5(a), Client shall supply to Althea replacement Client-Supplied Components. Prior to commencing Production using any Bulk Compound, Althea shall retrieve and retain (in partial consideration of the Production fees Ophthotech shall be liable to pay hereunder, and at no additional cost

to Ophthotech) retention samples of Bulk Compound as contemplated by 21 CFR 211.170(a). Althea will retain such samples for at least the minimum time periods required by 21 CFR 211.170(a).

(b) Client shall retain title to and, subject to the provisions of this Agreement (including, without limitation, Sections 5.4(c)), risk of loss for, the Client-Supplied Components delivered to Althea, including, without limitation, while they are at the Facility. Althea shall clearly identify all Client-Supplied Components in storage and in its books and records as goods belonging to Client. Client shall have access to the Client-Supplied Components as set forth in Sections 9.3 and 9.4. Client shall procure, at Client's cost, insurance covering damage or loss of Client Supplied Components during all times for which Client bears the risk of loss.

(c) Althea shall use first in first out and first expiry first out methods of usage of the Client-Supplied Components. Althea shall use its commercially reasonable efforts to obtain maximum yield of the Client Product from the Client-Supplied Components. Following [**] Production Lots on (i) the Rota 150 Facility, the parties shall agree on the Acceptable Yields for each of the Yields specified in Appendix E for such Facility and (ii) the HSL Facility, the parties shall agree on the Acceptable Yields for each of the Yields specified in Appendix E for such Facility. Althea shall promptly (but in any event within [**] Business Days) inform Client of any loss or damage to the Client-Supplied Components (over and above the acceptable yield loss rate) and promptly provide in writing all explanations and evidence. Remedies for the loss of Client-Supplied Components are set forth in Section 5.4(c).

(d) Althea shall maintain up-to-date records of all Client-Supplied Components and Client Product held in inventory or storage and, with respect to all Client-Supplied Components, shall provide to Client (i) as part of the Released Executed Batch Record, an accounting of all Client-Supplied Components used in the Production of the relevant Lot and (ii) through the JPC, during the [**] of each month, a complete and accurate list of all Client-Supplied Components held by it on the last day of the immediately preceding calendar month. Any such inventory list shall in particular specify the inventory balance of Client-Supplied Components at the relevant date and shall be accompanied by a report reconciling the quantities of the Client-Supplied Components provided to and held by Althea, the consumption of the Client-Supplied Components and the estimated yield losses in Production based on Actual Yields.

(e) In addition to the reports set forth in paragraph (d) above, Althea shall provide to Client the result of an inventory count to be carried out in accordance with Althea's usual year-end audit procedures, of all Client-Supplied Components and Client Product held by Althea as of a date prior to (and within [**] weeks) of [**] of each year, such count to be delivered promptly following the conclusion of such count (and in any event within [**] business days). Additional inventory counts may be conducted as agreed between the parties, including reasonable fees to Althea. Althea shall afford Ophthotech (and if reasonably requested by Ophthotech, a representative of Ophthotech's independent public accounting firm) a reasonable opportunity to be present during such counts. Althea shall be responsible for resolving, with Ophthotech's reasonable cooperation, all discrepancies (such as, for example, missing quantities) evidenced by such yearly inventory count. Each party shall pay for its own auditor's fees under this paragraph.

3.6 Subcontracting: Althea shall not subcontract or otherwise delegate, including, without limitation, to Affiliates or Third Parties, any portion of its obligations under this Agreement without Client's prior written approval and in accordance with the Quality Agreement; *provided* that approval shall not be required for individuals who are independent contractors performing ancillary services at Althea in the ordinary course of business. Althea shall ensure that such subcontractors and independent contractors are subject to relevant obligations consistent with Althea's obligations contained

in this Agreement and are properly qualified, including, in the case of independent contractors, through the use of appropriate background checks. Althea shall be responsible for any breach of this Agreement by any such subcontractor or independent contractor.

3.7 Other General Obligations: Althea shall (i) Produce Client Product only at the Facility and (ii) in a timely, professional and workmanlike manner consistent with industry standards and in accordance with this Agreement, the Quality Agreement, the Production Standards, the applicable Purchase Order and all Regulations applicable thereto. In the event Client proposes an additional Client Product for Production following the Effective Date, Althea will work with Client in good faith to establish and support Production Services with regards to such product hereunder, with any Non-Production Services in connection with such initiation to be performed by Althea at reasonable rates, all of which shall be agreed by the parties and effective when included in an SOW or DOS.

3.8 Exclusive Supply. Althea agrees that during any calendar year of the Term in which Ophthotech (a) (i) orders and pays for at least [**] vials of Client Product or (ii) orders and purchases at least [**]% of all its requirements for filling Fovista®, Zimura ® and such other Client Products as are added pursuant to Section 3.7 hereunder following the Effective Date, whichever is lower as between (i) and (ii), and (b) provided that Ophthotech is then in material compliance with all of its obligations hereunder, Althea and its Affiliates shall supply biological or pharmaceutical drug products (1) that are intended for ocular use and/or to treat diseases or conditions of the eye and (2) that include pegylated or unpegylated naturally or non-naturally occurring oligonucleotide that is intended to bind to and inhibit platelet-derived growth factor (PDGF) or its receptors (any such product meeting the requirements of both (1) and (2), a "***Competing Product***"), only to Client. The restrictions of this Section 3.8 with respect to Competing Products shall not apply to any Third Parties who are Althea customers (i.e. with existing production or contracts for production) as of the Effective Date. During any period prior to the Term Trigger Date that the Rota 150 is not available for commercial Production of Client Product or following the Term Trigger Date that the HSL Equipment is not available for commercial Production of Client Product, including during the pendency of a Force Majeure Event (as such term is defined in either the CRA or this Agreement), and for so long thereafter as Client has any open unfulfilled purchase orders with alternative fill/finish service providers issued during such period of unavailability, Client shall be excused from the requirements set forth in clause (a) of the first sentence of this Section 3.8 as a condition to the applicability of the restrictions imposed on Althea under this Section 3.8 with respect to Competing Products.

4. PRODUCTION – FORECASTS AND ORDERS

4.1 Quarterly Rolling Forecasts:

(a) Commencing with the first calendar quarter subsequent to the Effective Date, Client shall submit to Althea on a quarterly basis on or before the first business day of each calendar quarter a [**]-month rolling forecast that sets forth for each month the total quantity of Client Product(s) that Client expects to order from Althea and the expected Delivery Dates (the ***"Forecast"***). "***Delivery Date***" of Client Product or Lots means the date of delivery of the completed Released Executed Batch Record. The first [**] months of each Forecast (the "***Binding Portion***") shall be binding on Client (and Client shall submit or shall have submitted Purchase Orders consistent therewith), with the remaining periods covered by such Forecasts being non-binding. The non-binding portions of each Forecast submitted by Client shall be for planning purposes only.

(b) Subject to Section 4.1(c), each Forecast submitted by Client following January 1, 2018 shall cover [**] months, with the first [**] months being the Binding Portion.

(c) Each Forecast submitted following the Term Trigger Date (as defined in the CRA), shall cover [**] months, with the first [**] months being the Binding Portion.

4.2 Production for the Binding Portion of a Forecast (both quantities and delivery dates indicated on submitted Purchase Orders) may not be changed from the prior Forecast for the same periods, absent (a) mutual written agreement of the parties or (b) a rescheduling or Cancellation in compliance with sections 8.4 and 8.5 below. Changes to the non-binding portion of the Forecast shall be subject to section 4.3 below.

4.3 Amending Forecasts: Forecasts for any new period(s) not appearing in a prior Forecast shall be subject to Althea's acceptance, unless the amounts constitute Guaranteed HSL Capacity or priority Rota 150 capacity under the CRA (section 4.4) or as otherwise agreed in writing by Althea. The non-binding portion of a Forecast for quarters appearing in prior accepted Forecasts can be increased or reduced by Client from time to time, *provided* that the quantity difference may not be greater than [**]% versus the first accepted Forecast for that Client Product for the same quarter. Althea shall use commercially reasonable efforts to support any Client's need for increased volumes of Client Product should market conditions so require.

4.4 Purchase Order: Purchase Orders shall be submitted at least [**] months prior to the earliest Delivery Date specified therein. Each purchase order shall specify the number of Vials of Client Product ordered, the Delivery Date(s) for each Lot, the requested fill date(s) ("***Fill Date(s)***") for each Lot (which will be approximately [**] weeks prior to the applicable Delivery Date(s)) and the manner and address of delivery (or, if applicable, request for storage at Althea). Althea shall notify Client as to whether any Purchase Order has been accepted or rejected within [**] business days following Althea's receipt of such Purchase Order, *provided* that Althea may only reject a Purchase Order (a) that fails to comply with the requirements of the Forecast and this Agreement, or (b) due to force majeure under Article 11. Althea's failure to affirmatively reject a Purchase Order as permitted in the foregoing proviso within the [**]-business day period shall be deemed an acceptance of such Purchase Order. Althea and Client will confirm the scheduled Fill Date for each Lot of Client Product through the Purchase Order acceptance or otherwise through the JPC. In the event that Althea rejects a Purchase Order hereunder, Althea shall simultaneously notify Client in writing of the reasons why such order was rejected by Althea. Client may, at its option, submit a revised Purchase Order within [**]- business days of such rejection.

4.5 Prior Statements of Work, Quotations and Purchase Orders: Client and Althea acknowledge and agree that (a) services for incomplete lots of Client Products or other incomplete services in the Statements of Work (however designated) entered into prior to the Effective Date and identified in Appendix B, shall be governed by the terms and conditions of this Agreement and that such incomplete services performed under such Statements of Work shall be deemed to be services provided under this Agreement, (b) any references to Althea terms and conditions in such quotations or purchase orders as they relate to such incomplete services shall be deemed references to this Agreement and (c) the provisions of Section 14 shall apply to all statements of work, quotations or other proposals entered into by the parties prior to the Effective Date, whether or not such documents are identified on Appendix B.

5. PRODUCTION – RELEASE AND ACCEPTANCE

5.1 Released Executed Batch Record: Althea shall test, or cause to be tested by agreed upon third parties, as set forth in the MBR and in accordance with the Specifications or, in the case of clinical Production, the applicable SOW, each Lot of Client Product Produced pursuant to this Agreement before delivery of the Released Executed Batch Record to Client. The parties may agree that

parts of such testing be performed by Client or a qualified third party chosen by Client. The Certificate of Analysis and Released Executed Batch Record for each Lot Produced shall comply with the Quality Agreement.

5.2 Release: Althea shall send, or cause to be sent, all applicable certificates, including, without limitation, Certificates of Analysis and Certificates of Compliance, and the Released Executed Batch Record (with all opened deviations, investigations or other anomalous events related to such Lot having been resolved) together with any Client Product samples requested by Client to Client, or Client's designee, as soon as they become available with a target of not more than [**] weeks after the actual Fill Date for the applicable Lot, subject to reasonable resolution of issues by the applicable operating personnel of both parties or, if necessary, the Joint Project Committee defined under the CRA. Althea shall promptly, and in any event, within [**] business days, respond to any questions or requests for additional information that Client may have with respect to such Released Executed Batch Record and other relevant Lot documentation.

5.3 Acceptance, Non-Conforming Client Product; Latent Defects: Within [**] days after receipt by Client of the completed Released Executed Batch Record, and any requested Client Product samples and/or information required under the Quality Agreement, Client shall conduct such testing and/or inspection as it shall determine and either accept or reject the relevant Lot(s).

(a) If Client does not notify Althea within such [**]-day period (as it may be extended in accordance with this Section 5.3) that any Client Product does not conform to the Production Standards (a "***Non-Conformity***", and any such Client Product, "***Non-Conforming***") and reject such Lot, then Client shall be deemed to have accepted the Client Product as conforming, *provided that* Client may revoke acceptance of Client Product in the event of a Non-Conformity that (i) existed at the time of shipment by Althea under section 6.1 (ii) was not discoverable at the time of delivery by reasonable testing, inspection and review by Client, (iii) was caused solely by Althea's failure to Produce Client Product in accordance with cGMP or the MBR and (iv) Client gives notice thereof to Althea within [**] days of first learning of such non-conformity or defect, but in any event no later than [**] months from the date of shipment by Althea or [**] months following the Lot expiration date, whichever is earlier (a "***Latent Defect***").

(b) If Client believes any Client Product has a Non-Conformity or Latent Defect it shall provide Althea by telephone or email a detailed explanation of the Non-Conformity or Latent Defect. Within [**] business days of its receipt of such notice, Althea may investigate such alleged Non-Conformity or Latent Defect and shall notify Client of Althea's determination with respect to whether the Client Product is Non-Conforming or has a Latent Defect. If Althea agrees such Client Product is Non-Conforming or that such Client Product has a Latent Defect, Client shall have the remedies set forth in Section 5.4. If Althea disagrees with Client's determination that the Client Product is Non-Conforming or has a Latent Defect the parties shall follow the procedure set forth in paragraph 5.3(c) below.

(c) If the parties dispute whether Client Product is Non-Conforming or has a Latent Defect, the parties will follow the following procedures:

(i) The parties will establish the basis of the dispute in writing within [**] days of Althea's notice of determination in paragraph (b) above.

(ii) The parties will agree to the written description content and detail of the dispute by signing and dating the written dispute description.

(iii) The parties will appoint an independent third-party expert (which, in the case of an independent laboratory, must have qualified analytical methods to analyze Client Product) and may be [**] or another mutually agreeable third-party laboratory) (the "***Independent Expert***") to evaluate the dispute description document, as well as, if applicable, mutually acceptable samples of the Client Product.

(iv) The parties agree to accept as final and binding (absent manifest error) such Independent Expert's determination of whether or not a Non-Conformity or Latent Defect exists and the cause(s) thereof.

(v) Client and Althea shall share equally the costs of the Independent Expert.

(vi) The parties will use commercially reasonable efforts to obtain a decision from the Independent Expert as soon as reasonably practicable.

5.4 Remedies for Non-Conforming Client Product and Latent Defects:

(a) In the event Althea agrees that the Lot(s) of Client Product is Non-Conforming or has a Latent Defect or the Independent Lab determines under Section 5.3(c) that the Client Product is Non-Conforming due to the negligence of Althea and Client timely rejects the Lot (except for Latent Defects), then Althea, at Client's option and at Althea's expense, shall either (i) replace such Non-Conforming Client Product as soon as reasonably practicable but in no event later than [**] days (factoring in additional time for receipt of replacement Bulk Compound from Client, to the extent the same is called for given current inventory levels), (ii) except in the case of a Latent Defect, reprocess such Client Product, subject to mutually agreed reprocess plan, or (iii) except in the case of a Latent Defect, refund to Client any payments made by Client to Althea in respect of the relevant Lot(s) and cancel the remaining unpaid Purchase Price of such Client Product Production. In addition to the above remedies, the provisions of Sections 5.4(c) below shall apply to the cost of Client-Supplied Components and Bulk Compound used in the Production of any Non-Conforming Client Product or Client Product that has a Latent Defect. Upon failure of such replacement or rework of the same Lot(s) the matter shall be promptly escalated to the Joint Project Committee and the parties shall diligently and timely agree on a resolution and/or remedy. In addition, in the event any Non-Conformity causes a Supply Delay or in the event of a Latent Defect, Client shall have the remedies set forth in Section 5.5(c).

(b) In the event Althea does not agree that the Client Product is Non-Conforming or has a Latent Defect, and while the Independent Lab determination under Section 5.3(c) is pending, Client may submit a Purchase Order for immediate new Production of Client Product. Such Purchase Order shall be subject to Althea's acceptance, which shall not be unreasonably withheld, conditioned or delayed.

(c) Althea shall reimburse Client for the cost of any Client-Supplied Components (namely the direct, out-of-pocket and documented fees paid for their procurement, including, but not limited to, any transportation and insurance fees) (the "***Replacement Cost***") that (i) have been lost or cannot be used in the Production of Client Product as a result of an Althea Indemnitee's negligence or willful misconduct (including negligence or willful misconduct in complying with this Agreement, cGMP or the MBR) or (ii) have been used in the Production of Client Product that is Non-Conforming or has a Latent Defect as a result of an Althea Indemnitee's negligence or willful misconduct; provided that (x) Althea's obligation with respect to subclause (ii) of this sentence (A) shall only be effective from and after the completion of the process validation report for the Production of Client Product at the applicable Facility where Production occurs and (B) shall reflect only the amount of Client-Supplied Components

that have been lost over and above any applicable acceptable yield loss rate and (y) with respect to Bulk Compound that is subject to either subclause (i) or (ii) of this sentence, Althea shall file a claim under its professional liability insurance policy (or any other applicable insurance policy under which coverage may be claimed) for the Bulk Compound and Client shall be entitled to reimbursement by Althea of (1) the amount of any insurance proceeds received under such policy to cover the cost of such Bulk Compound plus (2) in the event that such proceeds do not cover the Replacement Cost for such Bulk Compound, subject to Article 16, up to [**]% of the Replacement Cost such Bulk Compound (but, when taken together with any amounts reimbursed under the foregoing clause (1), in an amount that does not exceed the Replacement Cost of such Bulk Compound) .

(d) In the event of a Latent Defect, Client shall have as its exclusive remedies, the remedies stated in Sections [**], as well as Section [**] in the event of the Termination of this Agreement pursuant to such Section.

(e) Client's rights and remedies under Sections 5.4, 5.5, 5.6, 6.3(d), and Articles 8, 10 and 17 and those remedies set forth in the Capacity Reservation Agreement, shall be Client's sole and exclusive remedies for failure to deliver conforming Client Product, including Supply Deficiencies, Supply Delays or Supply Failures, a Non-Conformity or Latent Defect.

5.5 Inability to Supply; Liquidated Damages and Second Source: Althea shall notify Client immediately upon becoming aware of an event that would render Althea unable to supply any quantity of Client Product under a Purchase Order or subject to the Binding Portion of a Forecast (other than Lot failures which shall be subject to Section 5.4). In such event, the parties shall use commercially reasonable efforts to agree on a remedy consistent with this Agreement; *provided, however*, that Client shall receive treatment proportionately no less favorable than any of Althea's other supply arrangements of similar products and quantities with respect to allocation of materials or capacity. For purposes of this section 5.5 (a) deliver(y) means completion of the relevant Production and deliver(y) of the completed Released Executed Batch Record and any samples due under Sections 5.1 through 5.3 above and (b) the terms of this Section do not apply to Latent Defects.

(a) A "***Supply Deficiency***" means Althea has due to its negligence or willful misconduct, failed to deliver the Client Product in accordance with the Yield Production Standard with respect to the applicable Lots by the date that is [**] business days following the scheduled Delivery Date. A "***Supply Delay***" means Althea has failed to cure a Supply Deficiency by delivering the full quantity of Client Product ordered within [**] days from a notice of Supply Deficiency from Ophthotech. A "***Supply Failure***" means in a [**]-month period Althea has failed to deliver at least [**] percent ([**]%) of the number of Lots ordered for delivery during such period. In connection with the foregoing, Althea shall not be responsible for delays due to lack of delivery of Client-Supplied Components or delays in reviews, approvals, information, documents or other items to be provided or performed by Client (assuming Althea has provided all relevant information and documentation, as required hereunder), and any such delays shall be excluded in determining the time periods set forth in this Section 5.5(a).

(b) Supply Deficiency: If there is a Supply Deficiency, then, as mutually agreed with Client, Althea shall, at Althea's cost, promptly take one or more of the following steps to remedy the Supply Deficiency: (i) increase the manufacturing time and the length of a manufacturing campaign at the Facility in order to Produce and deliver to Client additional Client Product that meet the requirements under this Agreement to remedy the Supply Deficiency ("***Deficiency Cure Product***"); (ii) make available and utilize the next reasonably available slot of manufacturing and production at the Facility (but in any event, within [**] days) to deliver to Client Deficiency Cure Product; (iii) coordinate and cooperate with Client to re-schedule Production and delivery of Client Product ordered hereunder in order to maximize

Althea's ability to Produce and deliver to Client Deficiency Cure Product while minimizing the disruption of manufacture at the Facility then in force and any contractual commitments to Third Party customers; and (iv) use commercially reasonable efforts to otherwise remedy the Supply Deficiency by utilizing and dedicating excess capacity not contractually committed to Third Party customers to Produce and deliver Deficiency Cure Product and to reserve such capacity for Client's requirements until the issues surrounding the Supply Deficiency have been remedied to Client's satisfaction. Althea shall bear any incremental cost of any such cure or attempted cure beyond the Purchase Price, including, but not limited to, any overtime labor costs Althea that may be required to increase Facility output to meet its requirements under this Section 5.5(b).

(c) Supply Delay; Liquidated Damages: The parties acknowledge and agree that Client's damages in the event of a Supply Delay will be substantial and difficult to calculate. If there is a Supply Delay, then Althea shall (i) use the measures described in items (i) through (iv) of Section 5.5(b) above to remedy such Supply Delay on a priority basis as soon as possible and (ii) credit (or in the event that Client does not have any unpaid balances owing under this Agreement, pay) to Client liquidated damages of [**]% of the Price for Production of the aggregate number of vials that are the subject of such Supply Delay (in the case of any vials to be delivered using Rota 150 Lot pricing, priced according to a pro rata calculation based on the number vials in question). In addition, for so long as a Supply Delay is continuing, Client shall be permitted, without penalty, to cancel, in whole or in part, any or all other open Purchase Orders for Production (i.e. those not subject to the remedies above) and to revise the Forecast accordingly. In the event Client cancels any open Purchase Orders that are subject to a Supply Delay, Althea shall promptly refund to Client all prepayments or other payments previously made by Client with respect to such Purchase Order.

(d) Supply Failure; Liquidated Damages: The parties acknowledge and agree that Client's damages in the event of a Supply Failure will be substantial and difficult to calculate. In the event a Supply Failure occurs, Althea shall credit (or in the event that Client does not have any unpaid balances owing under this Agreement, pay) to Client, as liquidated damages, [**] percent ([**]%) of the Price for Production of the aggregate number of vials that are the subject of such Supply Failure (in the case of any vials to be delivered using Rota 150 Lot pricing, priced according to a pro rata calculation based on the number of vials in question).

5.6 Yields; Reviews: The parties agree to negotiate in good faith an Acceptable Yield as set forth in Appendix E. The JPC shall periodically review and discuss the Theoretical Yields and Actual Yields achieved by Althea and other yield parameters as well as Supply Deficiency, Supply Delay and Supply Failure parameters with respect to Production performed hereunder based on historical experience and make adjustments as necessary to conform to such experience, subject to an appropriate amendment (with the written consent of both parties, such consent not to be unreasonably withheld, conditioned or delayed) to this Section 5.5 and/or Appendix E.

5.7 Alternative Supplier: Nothing in this Agreement shall prevent Client, at any time, from qualifying and/or establishing an alternate supplier to manufacture, fill/finish and supply Client Product. If Client desires to establish or qualify an alternate supplier, Althea shall, upon Client's request, reasonably assist Client for a reasonable period of time in such efforts, including, without limitation, providing reasonable technology, materials and information regarding Production of Client Product, subject to negotiation and execution of an SOW including reasonable fees for such services. Such fees shall be reduced if due to unresolved, repeated Lot failures due to Althea's negligence, or an unresolved inability to supply Client Product for a material period of time due to Althea's negligence.

6. PRODUCTION – DELIVERY & STORAGE

6.1 Delivery Terms: Within [**] days of Client's receipt of the Released Executed Batch Records under section 5.2, Client shall provide shipping or storage instructions for the applicable Client Product. Subject to Section 6.3(b) below, Althea shall not ship Client Product unless and until Client has accepted (or has been deemed to have accepted) such Client Product pursuant to Section 5.3 and has authorized such shipment in writing (which may be by email). Althea shall ship or store all Client Product in accordance with this Agreement and any consistent storage or shipping instructions provided in Client's Purchase Order. Regardless of location or contemplated or actual further processing of Client Product Lot(s), title to and risk of loss for Client Product shall pass to Client following acceptance (or deemed acceptance) of such Client Product in accordance with Section 5.3 or upon earlier delivery by Althea to Client's courier, upon Client's instructions. All shipments of Client Product shall be shipped FCA (INCOTERMS 2010) Althea's Facility, at Client's expense. Client shall procure and maintain, at its cost, insurance covering damage or loss of Client Product at all times during which Client has title to and risk of loss for such Client Product. Althea shall not be entitled to deliver partial shipments of Client Product unless expressly authorized by Client in writing.

6.2 Storing, Packaging & Shipping Specifications: Storage, packaging (including external package labeling) and shipping specifications for Client-Supplied Components and Client Product, including temperature requirements and temperature monitoring instructions, shall be set forth in the Specifications.

6.3 Storage and Handling:

(a) Althea shall store and handle all Components (other than Bulk Compound, which is subject to the following sentence) under appropriate cGMP conditions and in accordance with any temperature, humidity, light and cleanliness specifications accompanying such Components. Althea shall store and handle Bulk Compound and Client Product in accordance with the Specifications and under appropriate cGMP conditions. In addition to the foregoing, Althea shall store and handle all Client-Supplied Components and Client Product so as to prevent the commingling of same with Althea's own inventories and supplies, or those held by Althea for third parties.

(b) So long as Client has open, unfulfilled Purchase Orders or binding forecasted Production: (i) Storage of Client-Supplied Components prior to scheduled Production and for [**] days following passage of title and risk of loss of Client Product under section 6.1 above shall be without additional charge and (ii) unshipped Client Product shall also be stored for the same [**]-day period without additional charge. Thereafter, or in the event that Client does not have any open, unfulfilled Purchase Orders, storage fees shall apply as set forth below. Unless otherwise instructed by Client, Althea shall retain remaining Client-Supplied Components and Client equipment related to a Lot after cessation or interruption of its Production. A storage fee may be assessed for such retained Client-Supplied Components or equipment beginning [**] days after cessation or interruption of the Production in the event that Client does not have any open, unfulfilled Purchase Orders or binding Forecasted Production.

(c) Storage fees for Client Product and Client-Supplied Components, to the extent applicable under Section 6.3(b), shall be at the price set forth in Appendix A. Storage may be at Althea's Facility or such other facilities (including, potentially, those of Althea's qualified subcontractors') that Client has approved in writing. If Althea is storing Client-Supplied Components and Client does not have any open, unfulfilled Purchase Orders or binding Forecasted Production, Althea may destroy such items at Client's expense, upon [**] days' notice of intent to destroy and opportunity to take delivery prior to

the scheduled shipment for destruction (it being understood that Althea shall not so destroy any Client-Supplied Components in the event that Client submits a Purchase Order.

(d) Althea shall reimburse Client for the Replacement Cost of any Client Product, including, any Purchase Price paid hereunder) stored by Althea following acceptance (or deemed acceptance) by Client that is lost or cannot be used as a result of an Althea Indemnitee's gross negligence or willful misconduct (including gross negligence or willful misconduct in complying with this Agreement or cGMP); provided that Althea shall file a claim under its professional liability insurance policy (or any other applicable insurance policy under which coverage may be claimed) for the Client Product and Client shall be entitled to reimbursement by Althea of (1) the amount of any insurance proceeds received under such policy to cover the cost of such Client Product plus (2) in the event that such proceeds do not cover Client's out-of-pocket procurement costs for such Client Product, up to [**]% of Client's out-of-pocket procurement costs of such Client Product (but, when taken together with any amounts reimbursed under the foregoing clause (1), in an amount that does not exceed Client's out-of-pocket procurement costs of such Client Product) subject to Article 16.

6.4 Rejects. Client Product which is Non-Conforming or tailings following Production ("***Rejects***") shall be stored by Althea for a reasonable period of time pending Released Executed Batch Record review and disposition in accordance with such review and the timeline set forth in section 5.3. Unless otherwise agreed in writing, disposition shall be by destruction performed by Althea, the costs of which are included in the Purchase Price; *provided* that Client shall be separately responsible for the costs associated with Althea destroying any Client Product that meets the Production Standard. No storage of Rejects by Althea beyond what is described above shall be required unless (a) Client's remedies under Section 5.4 so require or (b) the parties so agree in writing prior to the start of Production. The parties shall agree in writing in advance of Production of any alternative disposition instructions for Rejects, including any labeling and special conditions, which shall be incorporated into the Master Batch Record. Such instructions shall comply with cGMP and any other applicable laws and regulations. Client warrants that Rejects that are retained by Client shall only be used in accordance with applicable law and regulations. If Althea disposes of Rejects, Althea shall dispose of such Rejects in accordance with disposition instructions agreed with Client, or, in the absence of such instructions, in accordance with Althea SOPs and applicable law.

7. PAYMENT TERMS FOR PRODUCTION.

7.1 Payment for Production:

(a) Fees for Production of a Lot of Client Product shall be invoiced as follows : (i) [**]% on or after the actual Fill Date and (ii) [**] percent ([**]%) upon Althea's delivery of Released Executed Lot Records. Client shall pay all invoices for undisputed amounts by wire in accordance with the instructions below within [**] days of the invoice date. No tax or other withholding shall be made from payments due hereunder. Any payment due under this Agreement not received within the times noted above shall bear interest at the lesser of (i) the maximum rate permitted by law, and (ii) [**]% per month on the outstanding balance compounded monthly, including any disputed amounts ultimately due Althea.

Althea's wire instructions are as follows:

Bank Name: [**]
Address: [**]

Account #: [**]
SWIFT #: [**]
Routing #: [**]

7.2 Price Increases: The Purchase Price shall not, until January 1, 2018, increase from the prices set out in Appendix A. Thereafter Althea may reasonably increase the Purchase Price on an annual basis by providing notice of the same to Client on or before [**] of each calendar year, with new pricing to take effect for Production under any Purchase Order received by Althea following such notice (but not before January 1, 2018) *provided* that (a) for notices that may be given in 2017 through 2021, the increase shall not exceed [**]% annually and (b) thereafter the annual increase shall not exceed [**], except in each case, in the event of extraordinary circumstances (such as labor shortages, or extraordinary labor, facility or utility costs or cost increases including Components cost increases, in which case Althea shall provide written justification for such price increase and the parties shall meet and confer and negotiate Althea's requested price increase in good faith. The foregoing notwithstanding, within [**] days of the Term Trigger Date, Althea may request and upon such request Client agrees to meet, confer and negotiate in good faith an adjustment to the pricing and/or price constraint for Production using the HSL Equipment to reasonably compensate Althea in relation to its actual operating costs to Produce Client Product using the HSL Equipment.

8. TERM AND TERMINATION.

8.1 Term: Subject to any extension of the Initial Expiration Date pursuant to Section 11.1(b), this Agreement shall commence on the Effective Date and will expire on the earlier of (a) the eighth (8^{th}) anniversary of the Term Trigger Date (as such term is defined in the CRA); or (b) December 31, 2027 (such expiration date, the "***Initial Expiration Date***" and the initial term provided for in this sentence being referred to as the "***Initial Term***") unless sooner terminated pursuant to Section 8.2 herein. At either party's request, Althea and Client shall meet and negotiate in good faith an extension term for this Agreement, subject to a mutually signed amendment for any renewal term (together with the Initial Term, the "***Term***"). Two years prior to the end of the Initial Term (or any renewal term), at either party's request, Althea and Ophthotech shall meet and negotiate in good faith any requested extension of this Agreement and the CRA. Upon such request and provided that Client has materially satisfied all of its obligations under this Agreement and the CRA and Client has not terminated the CRA, until the date that is [**] prior to the end of the Initial Term, Althea shall not offer the capacity previously reserved for Client under the CRA (and any associated Production hereunder) to any other customer without having first offered such capacity (and associated Production) to Client on terms (including pricing) that are at least as favorable as those in effect hereunder at the time including permitted price increases.

8.2 Termination: This Agreement may be terminated upon the occurrence of any of the following events:

(a) Termination for Breach: Either party may terminate this Agreement upon the material breach (which shall include, but not be limited to, any breach of payment terms) of any provision of this Agreement by the other party if such breach is not cured by the breaching party within [**] days after receipt by the breaching party of written notice of such breach, or such additional time reasonably necessary to cure such breach as agreed by the parties *provided that* the breaching party has commenced a cure within the [**]-day period and is diligently pursuing completion of such cure. In the event that Client terminates this Agreement pursuant to this Section 8.2(a) as a result of Latent Defect(s) constituting a material breach of this Agreement by Althea, Ophthotech shall be entitled to a refund of any payments made by Client to Althea in respect of the relevant Lot(s) for which the Latent Defects contributed to such

breach, in lieu of replacement of such Lots, but in addition to any other amounts owed by Althea pursuant to the terms hereof.

(b) Termination for Financial Matters: This Agreement may be terminated immediately by either party by giving the other party written notice thereof in the event such other party, makes a general assignment for the benefit of its creditors, or proceedings of a case are commenced in any court of competent jurisdiction by or against such party seeking (i) such party's reorganization, liquidation, dissolution, arrangement or winding up, or the composition or readjustment of its debts, (ii) the appointment of a receiver or trustee for or over such party's property, or (iii) similar relief in respect of such party under any law relating to bankruptcy, insolvency, reorganization, winding up or composition or adjustment of debt, and such proceedings shall continue undismissed, or an order with respect to the foregoing shall be entered and continue unstayed, for a period of more than [**] days.

(c) Termination for Convenience: Client shall have the right to terminate this Agreement, without cause, with such termination to be effective as of any date following the third anniversary of the Effective Date, with six (6) months prior written notice to Althea. Client shall have the right to terminate an SOW, without cause, in accordance with the terms of the applicable SOW, subject to any applicable payments and fees set forth below.

8.3 Obligations in Connection with a Termination: In the event of a termination of this Agreement by Client pursuant to Section 8.2(a), 8.2(b) or 8.2(d) Althea shall co-operate, and cause its Affiliates and contractors to co-operate, in good faith with Client to bring about a smooth and orderly transition to a new supplier(s) of the Production of Client Product as set forth in section 5.7. In the event of a termination of this Agreement by Althea, Althea shall reasonably cooperate with Client in the return of any stored Client Product or Client-Supplied Components (and, at Client's option, any other Components for which Client may be financially responsible under Section 8.4), including, the provision of continuing storage for a reasonable period, at least [**] days of which following the effective date of such termination shall be without charge to Client, *provided that* Althea shall not have any such obligations if it has terminated this Agreement under sections 8.2(a) or 8.2(b) until Client has paid all amounts due hereunder and prepaid any storage charges that may apply for additional storage time under this sentence.

8.4 Payments on Cancellation; Expense Reimbursement:

In the event of a cancellation by Client of the Production or in the event of termination of an SOW or this Agreement, except in the event of a termination by Client pursuant to Section 8.2(a) or 8.2(d) or as a result of a Supply Delay, Client shall reimburse Althea for:

(a) all reasonable wind-down costs, costs of Althea-Supplied Components purchased by Althea in support of the binding portion of the most recent Forecast prior to termination and are not cancelable, returnable or otherwise usable by Althea, together with any restocking and shipping costs for those materials or supplies that are returnable;

(b) all work-in-process with respect to the Client Product commenced by Althea, and

(c) all completed Client Product Production (at the Purchase Price).

8.5 Payments on Cancellation/Delay; Short-Notice Fees:

Following the submission of a binding Purchase Order, until the date that is [**] days prior to the scheduled Fill Date, Client may request, and Althea agrees to use its commercially reasonable efforts, to reschedule such Production services to a later date within [**] days of the originally scheduled Fill Date. In the event of a cancellation as described in Section 8.4 or Production delay or rescheduling by Client of any Production under an issued Purchase Order (collectively "***Cancelled***" or a "***Cancellation***"), Client shall in addition to the reimbursements above pay Althea a ***Cancellation Fee**** based on the Binding Portion of the Production that was delayed or Cancelled as follows:

Days Notice Prior to Delivery Date	Cancellation Fee*
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]

*The Cancellation Fee shall be calculated as (a) the listed percentage of the Purchase Price for Production of the cancelled or delayed portion minus (b) the cost of any Althea-Supplied Components for Production of the cancelled or delayed portion that can be returned to the supplier for credit/refund or used in subsequent Production for Client or for similar services for another Althea customer.

provided that: (x) in the event Client gives notice at the time of Cancellation that it wishes to reschedule the Production and Althea, using its commercially reasonable efforts, (i) is able to use the Facility and dates reserved hereunder for Cancelled Production for substantially equivalent activities for other customer(s) (with ratable adjustments being made based on the number of shifts and/or days of replacement customer activities), and (ii) a new Production start date is available, then the Cancellation Fee shall be reduced to [**]% of the Cancellation Fee otherwise due and (y) amounts due under sections 8.4 and 8.5 shall not collectively exceed [**]% of the Purchase Price for the relevant Lots.

8.6 Special Circumstances. Notwithstanding anything to the contrary contained herein, in the event that, following the Term Trigger Date, the HSL Equipment and HSL Facility become unavailable for Production of Client Product for more than [**] days, Client shall be permitted to cancel or adjust any open Purchase Order for Production of Lots not yet commenced upon notice to Althea, or at Client's option, revise the Forecast accordingly, in each case, without any obligation to pay any fee to Althea pursuant the foregoing Section 8.5. In the event Client cancels any open Purchase Orders pursuant to the foregoing, Althea shall promptly refund or, to the extent Client has unpaid invoices or remaining unfulfilled Purchase Orders, credit to Client all prepayments previously made by Client with respect to such Purchase Order for Production of Lots not yet commenced. For the avoidance of doubt, Althea's procurement, receipt or testing of Components shall not constitute the commencement of Production for purposes hereof.

8.7 Survival: The provisions of Sections 4.5, 5.3, 5.4, 7.1, 8.3, 8.4, 8.5, 9.2 and Articles 10, 13, 14, 15, 16, 17, 18 and 19 hereof shall survive expiration or termination of this Agreement.

9. PRODUCTION RECORDS, AUDIT AND COMPLIANCE.

9.1 Manufacturing Compliance: Althea shall follow the procedures set forth in the Quality Agreement with respect to any inspection, audit or visit conducted (or proposed to be conducted) at a Facility by any Regulatory Authority.

9.2 Records: Any books and records relating to the receipt, Production, storage, handling or testing of Client Product and Components shall be maintained under this Agreement by Althea in accordance with applicable laws, rules, regulations, this Agreement and the Quality Agreement. Althea shall maintain shipping records with respect to Client Product supplied hereunder that contain all of the appropriate information as specified in cGMP.

9.3 Audits: Client shall have the audit and inspection rights, including "for cause" audit and inspection rights, provided for in the Quality Agreement. Althea will support each Client audit (including by providing necessary staffing) and provide relevant information regarding Client Product, Components, Production or the Facilities in connection therewith. Each party shall bear its expenses relating to any audit or inspection conducted by Client; *provided* that Althea and Client may agree to a different arrangement with respect to costs and expenses in connection with any audit or inspection that is not "for cause" and that is in excess of the number of routine audits agreed to in the Quality Agreement ([**] for not more than [**] days; provided that any such audit may be extended to the degree reasonably necessary to the extent there is an unreasonable delay by Althea in providing information requested by Client during such audit). In connection with the foregoing, Althea shall use commercially reasonable efforts to support additional Client audits (or additional time for Client audits) at reasonable rates upon reasonable request by Client. Any Client audit or inspection may be performed by Client or, in each case upon written agreement with Althea including appropriate confidentiality terms, its agents and may include representatives of Client's customers, distributors and/or licensees.

9.4 Observation by Client: Client shall be afforded the opportunity, at Client's sole cost and expense, during normal business hours at mutually agreeable times and upon reasonable notice to Althea, to visit the Facility during Production to ensure that the Production complies with the Production Standards. Any such visits Client visits will be conducted in accordance with the Quality Agreement. While in attendance at the Facility, Client agrees to comply with all Althea policies and Althea SOPs applicable to visitation of the Facility as provided by Althea to Client prior to or during such attendance. Such visits shall not interfere with Althea's operations. In the event of a non-conforming or defective Client Product delivery or a regulatory notice to Althea related to Production, Client shall have the for-cause audit and inspection rights described in the preceding paragraph.

9.5 Regulatory Support: Althea agrees to provide reasonable regulatory assistance as requested by Client to support existing, pending or new Client Product registrations and marketing approvals with a Regulatory Authority which assistance shall be subject to the relevant Non-Production Fees. The foregoing assistance rendered by Althea shall be mutually agreed in an SOW and may include, without limitation: (i) assisting Client in completing and submitting changes to any regulatory submissions related to Client Product; (ii) cooperation in connection with pre-approval inspections carried out by governmental authorities; and (iii) providing information to Client that may be required by a relevant governmental authority to support Client Product, including, without limitation, the manufacturing and exportation related thereto.

9.6 Regulatory Compliance: Each party shall comply in all material respects with applicable laws, rules and regulations (***"Regulations"***) in the conduct of its activities under this Agreement. Althea shall ensure that the Production Process and Althea's and its contractors' facilities (including the Facilities), utilities, equipment, procedures and personnel are qualified and validated to perform Althea's obligations under this Agreement, and Althea shall maintain the relevant portions of its operations and the relevant equipment at each Facility in a state of cGMP compliance. Althea shall be solely responsible for all contact with Regulatory Authorities with respect thereto, *provided that* Althea shall give Client a reasonable opportunity, where feasible, to comment on any correspondence with Regulatory Authorities which would reasonably be expected to have a material impact on the Production

of Client Product. Client shall be responsible for compliance with all Regulations as they apply specifically to Client Product, including the Client-Supplied Components, specific approval to manufacture Client Product at the Facility and the use, labeling and sale of Client Product, which responsibility shall include, without limitation, all contact with Regulatory Authorities regarding the foregoing.

10. CLIENT PRODUCT RECALLS.

If either party becomes aware of information about Client Product that has been shipped by Althea hereunder, indicating that it may be Non-Conforming, have a Latent Defect or that there is potential adulteration, misbranding and/or any potential issues regarding the safety or effectiveness of Client Product, it shall within [**] hours provide notice to that effect to the other party. Client shall initiate an investigation and assessment of such circumstances and shall promptly notify Althea of its findings and any proposed course of action. The parties shall promptly meet to discuss such circumstances and to consider appropriate courses of action. Client shall bear all costs associated with any recall, market withdrawal or similar action regarding Client Product (a "***Recall***") unless such Recall is caused by a Latent Defect, in which case Althea shall reimburse Client for its reasonable, documented, out of pocket costs of such Recall, provided that the reimbursement for such Recall(s) shall not exceed $[**] per Recall notice or series of related notices.

11. FORCE MAJEURE; SAFETY STOCK; RISK MANAGEMENT.

11.1 Force Majeure Events:

(a) Failure or delay of either party to perform under this Agreement shall not subject such party to any liability to the other if such failure or delay is caused by acts of God, acts of terrorism, fire, explosion, flood, drought, war, riot, sabotage, embargo, strikes or other labor trouble (other than, in the case of Althea, failure to hire and train, and ensure adequate staffing of to perform Production or Non-Production Services), compliance with any order or regulation of any government entity, or by any extraordinary cause beyond the reasonable control of the affected party, whether or not foreseeable (each a "***Force Majeure Event***"), *provided that* written notice of such event is promptly given to the other party. In the case of a force majeure event affecting Production activities by Althea, the parties shall use commercially reasonable efforts to arrange for the Production of Client Product through subcontracting or other means as appropriate to provide Client Product that conforms to the Production Standards and other requirements of this Agreement. The responsibility for any differential in the cost for such Production shall be mutually agreed upon by the parties. However, if Althea is unable to provide a solution for the Production of Client Product reasonably acceptable to Client and begin implementation of that solution within sixty (60) days of the commencement of such force majeure event and complete such solution within a commercially reasonable time, Client may terminate this Agreement or any Purchase Order upon notice to Althea, or at Client's option, revise the Forecast accordingly. In the event Client cancels any open Purchase Orders pursuant to the foregoing, Althea shall promptly refund to Client all prepayments previously made by Client with respect to such Purchase Order for Production of Lots not reasonably expected to be released by Althea within such commercially reasonable time.

(b) In the event a Force Majeure Event occurs with respect to Althea that impacts the availability of the HSL Facility or HSL Equipment, the Initial Expiration Date shall be extended for any period of time during which the HSL Facility or the HSL Equipment is unavailable for Production of Client Products.

11.2 Safety Stock: Althea shall at its own risk and expense, obtain and maintain ready access to no less than [**] months' supply of Althea-Supplied Components necessary for the uninterrupted Production and supply of Client Product based on the then-current Forecast. Such ready access shall, at a minimum, be adequate to cover up to a minimum of [**] vials during any calendar year. Althea shall obtain corresponding supply guarantees from its suppliers and other contractors, including an obligation of such suppliers and contractors to notify Althea of their intention to cease production of such Components by providing at least [**] months prior written notice to Client. Client shall purchase or reimburse Althea's costs for any such Althea-Supplied Components purchased by Althea for the binding portion of any Forecast that are unusable due to changes for which Client is responsible under Article 12.

11.3 Risk Management: To ensure continuous supply of Client Product and in connection with diligent risk management practices, within [**] days of the Effective Date, the parties via the Joint Project Committee shall develop and agree in writing to a risk management plan, which plan shall be consistent with prevailing industry standards and shall include, without limitation, a Components inventory strategy. The risk management plan shall detail strategies for quick responses to and recovery from a range of potential disruptive events regarding the Production and supply of Client Product. The parties shall use their commercially reasonable efforts to implement the risk management plan, and shall evaluate its implementation of the risk management plan on a regular basis and shall communicate promptly to the other party any issues arising relating to risk management in relation to either Facility or Production of Client Product. Nothing contained in the risk management plan or communicated in connection therewith shall relieve a party from any liability under this Agreement.

12. CHANGES IN PRODUCTION AND CLIENT PRODUCT.

12.1 Changes in Production and Client Product: The parties agree that no change to Client Product, Specifications, Facility, Production Process, Client Product specific SOPs, Components, MBR, Non-Production Services or other matters affecting the Production of Client Product, shall be made without the prior written agreement of both parties; *provided* that the foregoing shall not limit Client's ability to make changes to the Bulk Compound that would not affect Production and *provided further* that Client gives Althea notice of such changes prior to submitting Purchase Orders covering use of changed Bulk Product) (it being understood that, Althea agrees to use its commercially reasonable efforts to support a change to the Bulk Compound on shorter notice if at all practical). Each party agrees to notify the other party promptly of any regulatory or other requested changes. Any such change shall be subject to the agreed upon change management process as set forth in the Quality Agreement and the prior mutual agreement of the parties with respect to the costs and expenses associated with the agreed upon change, *provided that* the costs of any changes (a) requested by Client or (b) required by Regulations and relating specifically to Client Product shall be the responsibility of Client.

13. CONFIDENTIALITY.

13.1 Confidentiality: For purposes of this Agreement, ***"Confidential Information"*** means all non-public information provided by or on behalf of one party (the ***"Disclosing Party"***) to the other party in connection with this Agreement including, without limitation, all data, inventions and information developed in or as a result of the performance of this Agreement, whether in oral, written, graphic or electronic form. Without limiting the generality of the foregoing, all Inventions and Intellectual Property of either party shall be deemed the "Confidential Information" of such party. Each party agrees, with respect to any Confidential Information disclosed to such party (the ***"Receiving Party"***) by the Disclosing Party hereunder: (a) to use such Confidential Information only for the purposes set forth in this Agreement; (b) to receive, maintain and hold the Confidential Information in strict confidence and to use the same methods and degree of care (but at least reasonable care) to prevent disclosure of such

Confidential Information as it uses to prevent disclosure of its own proprietary and Confidential Information and to protect against its dissemination to unauthorized parties; (c) not to disclose, or authorize or permit the disclosure of any Confidential Information to any third party without the prior written consent of the Disclosing Party; and (d) except as needed to fulfill its obligations hereunder, to return or destroy any Confidential Information to the Disclosing Party at the request of the Disclosing Party and to retain no copies or reproductions thereof, except that the Receiving Party may retain (subject to the confidentiality obligations and use restrictions provided for herein) a single archival copy of the Confidential Information for the sole purpose of determining the scope of obligations incurred under this Agreement.

13.2 Exceptions: The Receiving Party shall not be obligated to treat information as Confidential Information of the Disclosing Party if the Receiving Party can show by competent tangible evidence that such information: (a) was already known to the Receiving Party without any obligations of confidentiality prior to receipt from the Disclosing Party; (b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party; (c) became generally available to the public or otherwise part of the public domain after its disclosure, other than through any act or omission of the Receiving Party in breach of any obligation of confidentiality; (d) was disclosed to the Receiving Party, by a third party who was not under any obligation, direct or indirect, to Disclosing Party with respect to confidentiality or non-use; or (e) was independently discovered or developed by the Receiving Party without the use of or reference to the Disclosing Party's Confidential Information.

13.3 Authorized Disclosure: Notwithstanding Section 13.1, the Receiving Party may disclose Confidential Information, without violating its obligations under this Article 13, to the extent the disclosure is required by a valid order of a court or other governmental body having jurisdiction, applicable securities laws and regulations or the rules and regulations of any securities exchange, or applicable law or regulation, including regarding submission to a Regulatory Authority by Client in connection with the issuance or maintenance of marketing approvals for Client Product; *provided, however,* that the Receiving Party, if permitted and practicable, gives reasonable prior written notice to the Disclosing Party of such required disclosure in order to allow Disclosing Party, at its option and expense, to seek a protective or other order preventing or limiting the disclosure. The Receiving Party will limit access to the Confidential Information of the Disclosing Party to only those of the Receiving Party's employees, contractors or professional advisors having a need to know and who are bound by written or statutory obligations of confidentiality and non-use consistent with those set forth herein. Notwithstanding the foregoing, Althea shall be permitted to disclose Client Product information to third party developmental and analytical service providers who have a need to know such information in connection with performance of Althea's obligations hereunder, *provided that* such providers shall be subject to written confidentiality agreements consistent with this Article 13. Receiving Party may disclose the terms of this Agreement to such party's Affiliates, investors or potential investors, sublicensees under section 14.7, acquirers, or merger candidates, *provided that* they are not competitors of the Disclosing Party, and are bound by written obligations of confidentiality and non-use consistent with those set forth herein.

13.4 Injunctive Relief: The parties expressly acknowledge and agree that any breach or threatened breach of this Article 13 may cause immediate and irreparable harm to the Disclosing Party which may not be adequately compensated by damages. Each party therefore agrees that in the event of such breach or threatened breach and in addition to any remedies available at law, the Disclosing Party shall have the right to seek equitable and injunctive relief in connection with such a breach or threatened breach.

13.5 Public Announcements: Neither party shall publicize or make any announcement concerning this Agreement or the other party which includes the identity, name(s), or other trademarks of the other party or its Confidential Information or the identity of Client Product or the financial terms of this Agreement without the other party's prior written consent; *provided, however, that* either party may disclose the terms of this Agreement insofar as required to comply with applicable securities laws or regulations (including applicable securities exchange rules), *provided further that* in the case of such compliance disclosures the party proposing to make such disclosure notifies the other party reasonably in advance of such disclosure and cooperates to minimize the scope and content of such disclosure. The failure of a party to respond in writing to a publication or disclosure proposal from the other party within [**] business days of such party's receipt of such publication shall be deemed as such party's approval of such publication or disclosure as received by such party. Each party agrees that it shall cooperate fully and in a timely manner with the other with respect to any disclosures to the Securities and Exchange Commission and any other governmental or regulatory agencies, including, without limitation, requests for confidential treatment of Confidential Information of either party included in any such disclosure.

13.6 Duration of Confidentiality: All obligations of confidentiality and non-use imposed upon the parties under this Agreement shall expire [**] years after the Initial Term or renewal term of this Agreement during which the Confidential Information was disclosed; *provided, however,* that Confidential Information that constitutes the trade secrets of a party if expressly labeled as such by the Disclosing Party at the time of disclosure shall be kept confidential indefinitely, subject to the limitations set forth in Sections 13.2 and 13.3.

14. INVENTIONS; INTELLECTUAL PROPERTY.

14.1 Existing Intellectual Property: Except as the parties may otherwise expressly agree in writing, each party shall continue to own its existing patents, trademarks, copyrights, trade secrets and other Intellectual Property, without conferring any interests therein on the other party. Without limiting the generality of the preceding sentence, Client shall retain all right, title and interest arising under the United States Patent Act, the United States Trademark Act, the United States Copyright Act and all other applicable laws, rules and regulations in and to all Client Product, Client-Supplied Components, Labeling and trademarks associated therewith. Neither Althea nor any third party shall acquire any right, title or interest in such Intellectual Property by virtue of this Agreement or otherwise, except to the extent expressly provided herein.

14.2 Individually-Owned Inventions: Except as the parties may otherwise agree in writing, all Inventions that are conceived, reduced to practice, or created solely or jointly by a party in the course of performing its obligations under this Agreement and that (a) pertain specifically to the Client Product or Bulk Compound, including, without limitation, that are specific to the manufacture or reconstitution of Client Product and Bulk Compound, or (b) are derived from or incorporate Client's Confidential Information (collectively, "***Product Inventions***") shall be solely owned and subject to use and exploitation by Client, and Althea hereby assigns all right, title and interest in such Product Inventions and Intellectual Property therein to Client. Althea agrees to execute such assignments and other documents, to cause its employees and contractors to execute such assignments and other documents, and to take such other actions as may be reasonably requested by Client, at Client's expense, from time to time in order to effect to the ownership provisions of this Section 14.2. With respect to Inventions that are conceived, reduced to practice, or created by a party in the course of performing its obligations under this Agreement and are not Product Inventions, the following terms of ownership shall apply: Client shall solely own all such Inventions made solely by employees and/or contractors of Client (the "***Client's Project Intellectual Property***"); and Althea shall solely own such Inventions made solely by employees and/or contractors of Althea (the "***Althea's Project Intellectual Property***").

14.3 Jointly-Owned Inventions: All Inventions that are conceived, reduced to practice, or created jointly by the parties and/or their respective agents in the course of the performance of this Agreement and that are not Product Inventions, Client's Project Intellectual Property or Althea's Project Intellectual Property shall be owned jointly by the parties. Subject to any licenses granted herein, each party shall have full rights to exploit such Inventions for its own business purposes without any obligation or duty of accounting to the other. The parties shall share equally in the cost of mutually agreed patent filings with respect to all such jointly owned Inventions. The decision to file for patent coverage on jointly-owned Inventions shall be mutually agreed upon, and the parties shall select a mutually acceptable patent counsel to file and prosecute patent applications based on such joint Inventions, *provided that* if either party declines to participate in, or share the costs of, such prosecution or payment of maintenance fees for jointly-owned Inventions, it shall assign its interest therein promptly to the other party.

14.4 Invention Disclosure: Each party shall notify the other party in writing promptly, but in no event later than [**] days after it receives any invention disclosure or other notice, of any Invention conceived, reduced to practice or created by or on behalf of such party in the course of the performance of this Agreement to which the other party may have any right, title, or interest in, together with a description of such Invention that is sufficiently detailed to permit to determine the patentability of such Invention.

14.5 Handling of Patents: Subject to Section 14.3, the party owning any Invention shall have the worldwide right to control the drafting, filing, prosecution and maintenance of patents covering the Inventions, including, without limitation, decisions about the countries in which to file patent applications. Patent costs associated with the patent activities described in this Section shall be borne by the sole owner. Each party will cooperate with the other party in the filing and prosecution of patent applications. Such cooperation will include, but not be limited to, furnishing supporting data and affidavits for the prosecution of patent applications and completing and signing forms needed for the prosecution, assignment and maintenance of patent applications.

14.6 Confidentiality of Inventions: Inventions and any disclosure of information by one party to the other under the provisions of this Article 14 shall be subject to the provisions of Article 13. It shall be the responsibility of the party preparing a patent application to obtain the written permission of the other party to use or disclose the other party's Confidential Information in the patent application before the application is filed and for other disclosures made during the prosecution of the patent application, such permission not to be unreasonably withheld, conditioned or delayed.

14.7 License Grants:

(a) License to Althea: During the Term, Client hereby grants to Althea a fully paid, non-exclusive license, without the right to sublicense, under any and all of Client's Intellectual Property, including, without limitation, Product Inventions and Client's Project Intellectual Property, that is necessary for Althea to perform its obligations under this Agreement, for the sole and limited purpose of Althea performing its obligations under this Agreement exclusively for Client.

(b) Licenses to Client: Althea hereby grants to Client an irrevocable, fully paid, royalty-free, perpetual, transferable, assignable, worldwide, exclusive license, with the right to grant and authorize sublicenses, under any Althea Project Intellectual Property and any Intellectual Property Althea owns jointly with Client, to the extent necessary for the sole and limited purpose of manufacturing, having manufactured, modifying, having modified, using, having used, selling, having sold, offering to sell, having offered to sell, importing, having imported, exporting, having exported and otherwise disposing or having disposed of Client Product, *provided that* such license shall be void upon any

termination hereof for cause by Althea under sections 8.2 (a) or (b), or any material breach of the provisions hereof that survive termination or expiration of the Agreement by Client or its sublicensees. In connection with the license granted in this Section 14.7(b), Althea agrees to provide reasonable support for technology transfer to Client and any third party designated by Client as set forth in section 5.7.

14.8 Third Party Intellectual Property Claims:

(a) If either party learns of any infringement or threatened infringement by a third party of a party's Intellectual Property relating to this Agreement, such party shall promptly notify the other party in writing and shall provide such other party with available evidence of such infringement.

(b) If a Third Party asserts that any Intellectual Property owned or controlled by it is infringed by the Production Process or Components, or the Non-Production Services or Intellectual Property provided by or on behalf of a party, excluding any information, instructions or materials supplied by the other party, and the first party has breached its warranty under sections 15.2(d) or 15.3(b) as applicable, such first party shall as the other party's sole and exclusive remedies: indemnify and hold the other party and its Indemnitees harmless and defend any such action, or at such first party's option, take action to remediate the same, including (i) replacing, re-performing or modifying its services, information, instructions or materials so as to be non-infringing by a mechanism or service equivalent in basic functionality and performance; (ii) obtaining an appropriate license from such third party; or (iii) opposing that allegation; and all losses, damages, liabilities, expenses and costs, including reasonable legal expenses and attorneys' fees, associated with any cause of action, and the conduct of the cause of action shall be borne and conducted by such indemnifying party; under the terms of section 17.3. The parties shall cooperate to obtain any such license(s) under (ii) above and to any other third party Intellectual Property that the parties jointly determine are necessary or desirable. Any such license shall only be entered into if both parties give their prior written consent.

14.9 No Other Rights: Except as otherwise expressly provided herein, nothing contained in this Agreement shall be construed or interpreted, either expressly or by implication, estoppel or otherwise, as: (a) a grant, transfer or other conveyance by either party to the other of any right, title, license or other interest of any kind in any of its Inventions or other Intellectual Property, (b) creating an obligation on the part of either party to make any such grant, transfer or other conveyance or (c) requiring either party to participate with the other party in any cooperative development program or project of any kind or to continue with any such program or project.

15. REPRESENTATIONS, WARRANTIES AND COVENANTS.

15.1 Mutual Representations and Warranties: Each party hereby represents and warrants to the other party that (a) such party is duly organized, validly existing, and in good standing under the laws of the jurisdiction of its establishment or incorporation, (b) such party has taken all action necessary to authorize it to enter into this Agreement and perform its obligations under this Agreement, (c) this Agreement constitutes the legal, valid and binding obligation of such party, and (d) neither the execution of this Agreement nor the performance of such party's obligations hereunder conflicts with, results in a breach of, or constitutes a default under any provision of the organizational documents of such party, or of any law, rule, regulation, authorization or approval of any government entity, or of any agreement to which it is a party or by which it is bound.

15.2 Althea Representations, Warranties and Covenants: Althea represents, warrants and covenants that:

(a) Subject to the limitations of Section 5.4(e) and Article 16 , all Client Product shall (i) be Produced at the Facility in compliance with the Production Standards;

(b) Client Product delivered to Client shall be delivered to Client with good and valid title, (i) free and clear of all third-party claims, liens, encumbrances, security interests and similar third party rights and (ii) once paid for by Client in accordance with the terms hereof, free and clear of all claims, liens, encumbrances and security interests;

(c) it has obtained (or will obtain prior to Producing Client Product), and shall remain in compliance with during the Term, all permits, licenses and other authorizations (the ***"Permits"***) that are required under federal, state and local laws, rules and regulations generally applicable to each Facility and to the manufacturing and fill/finish services of the type to be performed under this Agreement; *provided, however,* Althea shall have no obligation to obtain Permits specific to Client Product or Bulk Compound or relating to the sale, marketing, distribution or use of Bulk Compound or Client Product or with respect to the Labeling of Client Product;

(d) to Althea's knowledge, the Production Process and Althea-Supplied Components, and the Non-Production Services supplied by or on behalf of Althea (i) do not violate or infringe upon any Intellectual Property or other right held by any third party and (ii) do not include or incorporate any third party Intellectual Property; and Althea has not incorporated any Althea Intellectual Property (other than Althea Project Intellectual Property and Intellectual Property that Althea owns jointly with Client) into the Production Process, Althea-Supplied Components or Non-Production Services and shall not knowingly incorporate into such Production Process, Althea-Supplied Components or Non-Production Services any Althea Intellectual Property (other than Althea Project Intellectual Property or Intellectual Property that Althea owns jointly with Client) or any third party Intellectual Property without first obtaining Client's written approval and ensuring that Althea provides or has a license that permits it to do so together with the right to grant sublicenses to such third party Intellectual Property to Client, and the licenses granted by Althea to Client under this Agreement shall include if applicable such third party Intellectual Property; and

(e) neither Althea, nor any employee, personnel or contractor of Althea who will perform services under this Agreement, has been suspended, debarred or subject to temporary denial of approval, and to the best of its knowledge, is not under consideration to be suspended, debarred or subject to temporary denial of approval, by the FDA or any other governmental or regulatory authority from working in or providing services, directly or indirectly, to any applicant for approval of a drug product or any pharmaceutical or biotechnology company under the Generic Drug Enforcement Act of 1992 or any other similar law or regulation in any other jurisdiction.

15.3 Client Representations, Warranties and Covenants: Client represents, warrants and covenants that, as of the Effective Date, (a) it has the right to give Althea any Client-Supplied Components and information provided by Client hereunder, and that Althea has the right to use such Client-Supplied Components and information for the Production of Client Product for Client in accordance with the Specifications, and (b) Client has no knowledge of any Intellectual Property that would be infringed or misappropriated by the contemplated use of Client-Supplied Components or Althea's Production of Client Product for Client in accordance with the Specifications. Client further warrants that the Bulk Compound provided to Althea hereunder conforms to its Specifications.

15.4 Disclaimer of Representations and Warranties: EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR WARRANTY OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION,

ANY IMPLIED WARRANTY OF NON-INFRINGEMENT, MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Without limiting the foregoing, Althea makes no representation or warranty, and Client expressly waives all claims against all Althea Indemnitees arising out of or in connection with any claims relating to the stability, efficacy, safety, or toxicity of any Client Product Produced in accordance with the Product Standards.

The representations, warranties and covenants set forth in this Article 15 are for the benefit of the other party only. There are no third-party beneficiaries to this Agreement or any of its representations or warranties.

16. LIMITATION OF LIABILITY.

16.1 Limitation of Liability: EXCEPT IN CONNECTION WITH (I) THIRD PARTY CLAIMS UNDER ARTICLE 17 OR 14.8(B); (II) A BREACH OF ARTICLE 13; UNDER NO CIRCUMSTANCES SHALL EITHER PARTY BE LIABLE TO THE OTHER PARTY HEREUNDER FOR LOSS OF USE OR PROFITS, COLLATERAL, SPECIAL, CONSEQUENTIAL, PUNITIVE, INCIDENTAL OR INDIRECT DAMAGES, LOSSES OR EXPENSES, INCLUDING BUT NOT LIMITED TO COST OF COVER, IN CONNECTION WITH OR BY REASON OF THE PRODUCTION AND DELIVERY OF CLIENT PRODUCT UNDER THIS AGREEMENT WHETHER SUCH CLAIMS ARE FOUNDED IN TORT OR CONTRACT.

EXCEPT IN CONNECTION WITH (I) THIRD PARTY CLAIMS UNDER ARTICLE 17 OR SECTION 14.8(B), (II) A BREACH OF ARTICLE 13, OR ARTICLE 10, IN NO EVENT SHALL ALTHEA'S AGGREGATE LIABILITY WITH RESPECT TO ANY CLAIM (OR SERIES OF RELATED CLAIMS) MADE WITH RESPECT TO ANY [**] MONTH PERIOD EXCEED (A) THE FEES PAID BY CLIENT TO ALTHEA FOR PRODUCTION AND NON-PRODUCTION SERVICES (EXCLUDING ALTHEA'S ACTUAL COSTS FOR ALTHEA-SUPPLIED COMPONENTS) DURING THE [**] MONTHS PRECEDING THE FIRST EVENT GIVING RISE TO THE CLAIM OR SERIES OF CLAIMS (SUCH NUMBER BEING CALCULATED WITH RESPECT TO (1) THE INITIAL 12-MONTH PERIOD FOLLOWING THE EFFECTIVE DATE, WITH A FLOOR AS THOUGH A MINIMUM OF [**] VIALS OF CLIENT PRODUCT HAD BEEN PRODUCED DURING SUCH [**]-MONTH PERIOD AND (2) AS OF ANY TIME THERAFTER, WITH A FLOOR AS THOUGH A MINIMUM OF [**] VIALS OF CLIENT PRODUCT HAD BEEN PRODUCED DURING THE RELEVANT 12-MONTH PERIOD PLUS (B) DURING THE INITIAL TERM HEREOF ONE-EIGHTH OF THE AGGREGATE RESERVATION FEE PAID TO THE DATE OF SUCH FIRST EVENT BY CLIENT UNDER THE CRA. THIS LIMITATION SHALL APPLY NOTWITHSTANDING ANY FAILURE OF ESSENTIAL PURPOSE OF ANY LIMITED REMEDY. IN NO EVENT WILL ALTHEA BE RESPONSIBLE FOR REPLACING ANY COMPONENTS OR MATERIALS SUPPLIED BY CLIENT, EXCEPT AS EXPRESSLY SET FORTH HEREIN.

TO THE EXTENT ALTHEA PAYS ANY AMOUNTS UNDER SUBCLAUSE (B) OF THE FIRST SENTENCE OF THE IMMEDIATELY PRECEDING PARAGRAPH, THE LIMITATION ON ALTHEA'S AGGREGATE LIABILITY UNDER THE CRA SHALL BE REDUCED ACCORDINGLY.

17. INDEMNIFICATION.

17.1 Client Indemnification: Client hereby agrees to save, defend, indemnify and hold harmless Althea and its Affiliates and their respective directors, officers and employees (each, an "***Althea Indemnitee***") from and against any and all losses, damages, liabilities, expenses and costs, including reasonable legal expenses and attorneys' fees (***"Losses"***), to which any Althea Indemnitee may become subject as a result of any claim, demand, action or proceeding by any Third Party including, without

limitation, property damage, death or personal injury of Third Parties (a ***"Claim"***) against an Althea Indemnitee to the extent arising or resulting, directly or indirectly, from (a) Client's storage, promotion, labeling, marketing, distribution, use or sale of Client Product, (b) Client's or its contractors' or licensees' negligence or willful misconduct, or (c) Client's breach of this Agreement, including, without limitation, any representations, warranties or covenants herein, except to the extent any such Loss(es) are within any of the matters indemnified by Althea in Section 17.2 below.

17.2 Althea Indemnification: Althea hereby agrees to save, defend, indemnify and hold harmless Client and its Affiliates and their respective directors, officers and employees (each, a ***"Client Indemnitee"***) from and against any and all Losses to which any Client Indemnitee may become subject as a result of any Claim to the extent arising or resulting, directly or indirectly, from (a) an Althea Indemnitee's or Althea's suppliers' or other contractors' negligence or willful misconduct, or (b) the breach of this Agreement by Althea, including, without limitation, any representations, warranties or covenants herein, except to the extent any such Loss(es) are caused by or are within any of the matters indemnified by Client in Section 17.1 above.

17.3 Indemnitee Obligations: A party that makes a claim for indemnification under this Article 17 shall promptly notify the other party (the ***"Indemnitor"***) in writing of any action, claim or other matter in respect of which such party, intends to claim such indemnification; *provided*, *however,* that failure to provide such notice within a reasonable period of time shall not relieve the Indemnitor of any of its obligations hereunder except to the extent the Indemnitor is prejudiced by such failure. The indemnified party shall permit the Indemnitor, at its discretion, to settle any such action, claim or other matter, and the indemnified party agrees to the complete control of such defense or settlement by the Indemnitor. Notwithstanding the foregoing, the Indemnitor shall not enter into any settlement that (a) would adversely affect the indemnified party's rights, or impose any obligations on the indemnified party in addition to those set forth herein, in each case other than customary mutual general releases or (b) contains a finding or admission of a violation of law by the indemnified person or a violation of the rights of any person or wrongdoing by the indemnified person. No such action, claim or other matter shall be settled without the prior written consent of the Indemnitor, which shall not be unreasonably withheld, conditioned or delayed. The indemnified party shall, at the Indemnitor's expense, reasonably cooperate with the Indemnitor and its legal representatives in the investigation and defense of any action, claim or other matter covered by the indemnification obligations of this Article 17. The indemnified party shall have the right, but not the obligation, to be represented in such defense by counsel of its own selection and at its own expense.

18. INSURANCE.

18.1 Insurance: Each party shall procure and maintain, from the date that Althea first receives Bulk Compound for Production of Client Product ordered hereunder, through the date that is one (1) year after the expiration date of all Client Product Produced under this Agreement, commercial general liability insurance, including, without limitation, products and, in the case of Althea, professional liability coverage (the ***"Insurance"***). The Insurance, which shall be with an insurance carrier reasonably acceptable to the other party (the ***"Insured Party"***), shall cover amounts not less than (a) with respect to Althea's liability policies, $[**] combined single limit coverage, (b) with respect to Client's transit and storage insurance policy, $[**] combined single limit coverage and (c) with respect to Client's products liability coverage, $[**] combined single limit coverage (provided that such coverage for Client shall only be required to be in an amount of $[**] combined single limit coverage until such time as the first commercial sale of Client Product by Client). The Insured Party shall be named as an additional insured on the Insurance and the party procuring the Insurance shall promptly deliver a certificate of Insurance and endorsement of additional insured to the Insured Party evidencing such coverage. If the party fails to

furnish such certificates or endorsements, or if at any time during the Term the Insured Party is notified of the cancellation or lapse of the Insurance, and the party procuring the Insurance fails to rectify the same within [**] days after notice from the Insured Party, the Insured Party, at its option, may terminate this Agreement. Any deductible and/or self-insurance retention shall be the sole responsibility of the party procuring the Insurance.

19. GENERAL PROVISIONS.

19.1 Notices: Any notice to be given under this Agreement must be in writing and delivered either in person, by certified mail (postage prepaid) requiring return receipt, or by overnight courier to the party to be notified at its address given below, or at any address such party designates by prior written notice to the other. Notice shall be deemed sufficiently given for all purposes upon the delivery thereof at the address designated in accordance with this paragraph.

If to Client: Ophthotech Corporation
One Penn Plaza, Suite 1924
New York, NY 10119
Attn: Legal Department

Telephone: (212) 845-8200

If to Althea: Ajinomoto Althea, Inc.
11040 Roselle Street
San Diego, CA 92121
Attn: Senior Vice President, Operations

Telephone: (858) 882-0123

19.2 Entire Agreement; Amendment: The parties hereto acknowledge that this Agreement and the attachments or Appendices, together with the CRA and any incomplete SOWs as set forth in section 4.6, set forth the entire agreement and understanding of the parties and supersedes all prior written or oral agreements or understandings with respect to the subject matter hereof. No modification of any of the terms of this Agreement, or of any attachments or Appendices, shall be deemed to be valid unless in writing and signed by an authorized officer of both parties hereto. No course of dealing or usage of trade shall be used to modify the terms and conditions herein.

19.3 Waiver: None of the provisions of this Agreement shall be considered waived by any party hereto unless such waiver is agreed to, in writing, by authorized officer(s) of the waiving party. The failure of a party to insist upon strict conformance to any of the terms and conditions hereof, or failure or delay to exercise any rights provided herein or by law shall not be deemed a waiver of any rights of any party hereto.

19.4 Assignment: This Agreement may not be assigned or transferred by either party, including, without limitation, by operation of law, without the prior written consent of the other, which consent shall not be unreasonably withheld or delayed; *provided, however,* that either party may assign this Agreement, including, without limitation, by operation of law, without the other party's consent to an Affiliate or in connection with the transfer or sale of all or substantially all of the business of such party to which this Agreement relates, whether by merger, sale of stock, sale of assets or otherwise, *provided*

further that if such assignment is to an Affiliate, the assigning party shall be jointly responsible for Affiliate's obligations hereunder. Any attempted assignment of this Agreement not in compliance with this Section 19.4 shall be null and void. No assignment shall relieve either party of the performance of any accrued obligation that such party may then have under this Agreement. This Agreement shall inure to the benefit of and be binding upon each party signatory hereto, its successors and permitted assigns, and Affiliates.

19.5 Taxes: Subject to the final two sentences of this Section 19.5, Client shall bear the cost of all national, state, municipal or other sales, use, excise, import, franchise, value added, personal property or other similar taxes, assessments or tariffs assessed upon or levied against the Production or sale of Client Product pursuant to this Agreement or the sale or distribution of Client Product by Client (or at Client's sole expense, defend against the imposition of such taxes and expenses). Althea shall notify Client of any such taxes that any governmental authority is seeking to collect from Althea, and Client may assume the defense thereof in Althea's name, if necessary, and Althea agrees to fully cooperate in such defense to the extent of the capacity of Althea, at Client's expense. Althea shall pay all national, state, municipal or other taxes on the income resulting from the sale by Althea of the Client Product to Client under this Agreement, including, but not limited to, gross income, adjusted gross income, supplemental net income, gross receipts, excess profit taxes, or other similar taxes. Furthermore, each party shall be responsible for its employment and property taxes.

19.6 Independent Contractor: Althea shall act as an independent contractor for Client in providing the services required hereunder and neither party shall be considered an agent or employer of, or joint venture with, the other party or its employees. Unless otherwise provided herein to the contrary, Althea shall furnish all expertise, labor, supervision, machining and equipment necessary for performance hereunder and shall obtain and maintain all building and other permits and licenses required by public authorities.

19.7 Governing Law; Limitations: This Agreement is made under and shall be construed in accordance with the laws of the State of Delaware without giving effect to that jurisdiction's choice of law rules. Each party submits to the exclusive jurisdiction of the courts sitting in Delaware. The United Nations Convention on Contracts for the International Sale of Goods shall not apply to this Agreement or to transactions processed under this Agreement.

19.8 Dispute Resolution: Prior to initiating any court, administrative or other action on a claim, dispute, demand or assertion related to this Agreement or the services hereunder (collectively, a "***Dispute***"), the claimant shall give notice to the other party, detailing the nature of the Dispute and the facts relevant thereto and the parties shall in good faith attempt to resolve such Dispute. No court, administrative or other action shall be filed or otherwise initiated until the parties have exhausted good faith settlement attempts by first, direct negotiation and second, mediation by a mutually-agreeable professional mediator under the appropriate Mediation Procedures of the American Arbitration Association. The site of the mediation shall be Chicago, IL. The costs of mediation shall be borne equally by the parties. This Section shall not prevent either party from seeking injunctive relief. EACH PARTY HEREBY IRREVOCABLY WAIVES ALL RIGHT TO A TRIAL BY JURY IN ANY ACTION, PROCEEDING, CLAIM OR COUNTERCLAIM ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE SERVICES CONTEMPLATED HEREBY.

19.9 Attorney's Fees: Subject to Section 19.8, the successful party in any litigation or other dispute resolution proceeding to enforce the terms and conditions of this Agreement shall be entitled to recover from the other party reasonable attorney's fees and related costs involved in connection with such litigation or dispute resolution proceeding.

19.10 Compliance with Laws: Each party shall comply with all applicable laws and regulations governing the performance of such party's obligations under this Agreement.

19.11 Severability: In the event that any one or more of the provisions contained herein, or the application thereof in any circumstances, is held invalid, illegal or unenforceable in any respect for any reason, the parties shall negotiate in good faith with a view to the substitution therefor of a suitable and equitable provision in order to carry out, so far as may be valid and enforceable, the intent and purpose of such invalid provision; *provided*, *however*, that the validity, legality and enforceability of any such provision in every other respect and of the remaining provisions contained herein shall not be in any way impaired thereby, it being intended that all of the rights and privileges of the parties hereto shall be enforceable to the fullest extent permitted by law.

19.12 Hierarchy of Documents: Unless otherwise specifically agreed to by the parties, in the event of any conflict between the terms of this Agreement and its Appendices, and a Purchase Order or an SOW, the order of precedence is as follows: (i) the terms of this Agreement; (ii) its Appendices; (iii) any SOW(s) (iv) Purchase Orders.

19.13 No offset. Client shall not have the right to setoff any disputed amounts owed by Althea to Client under any other agreement or arrangement.

19.14 Counterparts: This Agreement may be executed in counterparts each of which, when executed and delivered, shall be original, but all such counterparts shall constitute one and the same document. The parties agree that signatures transmitted via portable document format (PDF) shall be deemed originals until originals replace such copies.

[signature page follows]

IN WITNESS WHEREOF, the parties hereto have each caused this Agreement to be executed by their duly-authorized representatives as of the Effective Date above.

OPHTHOTECH CORPORATION		**AJINOMOTO ALTHEA, INC.**	
By:	/s/ Glenn Sblendorio	By:	/s/ J. David Enloe Jr.
Name:	Glenn Sblendorio	Name:	J. David Enloe Jr.
Title:	EVP & CFO	Title:	President & CEO

APPENDIX A

INITIAL PURCHASE PRICE AND NON-PRODUCTION SERVICE FEES

Subject to Article 7 of the Agreement, the following are the not-to-exceed initial purchase prices for Production of Client Product ("***Purchase Price***") *provided that* the Purchase Price includes the Production services, all Components (other than Bulk Compound, with a credit to be reflected for any Pre-Purchased Components), analytical, in-process and release testing specified in the Specifications and MBR, batch documentation packets, shipping preparation, annual product maintenance fees and project management, but excludes Non-Production Services such as validation activities and drug product shipping fees. Except as provided below, all Non-Production Services shall be set forth in an SOW.

For Client Product Produced on the Rota 150 prior to Successful Validation of the HSL Equipment: $[**] per Lot with a target Lot size of [**] vials per Lot, such amount to be reduced by the cost of any Pre-Purchased Components that are used in Production.

For Client Product Produced following Successful Validation of the HSL Equipment with a minimum target Lot size of [**] units of Production within a [**] hour shift (but no less than [**] vials per Lot ordered): $[**] per vial filled and visually inspected. For clarity, Client will pay for the number of conforming vials produced (including testing and other samples), regardless of the target Lot size, but subject to the remedies set forth in Article 5.

Fees for storage, to the extent applicable under Section 6.3(b), shall be $[**] for each month (adjusted ratably) of storage per palette of stored materials.

Non-Production Fees for any other Non-Production Services shall be set forth in the applicable SOW.

APPENDIX A-1

PRE-PURCHASED COMPONENTS

- Ophthotech Purchase Order number 01-0415, dated July 1, 2015

APPENDIX B

LIST OF PRIOR STATEMENTS OF WORK, QUOTATIONS AND PURCHASE ORDERS

1. Ophthotech PO #000787 dated September 13, 2016 for Fovista Price Per Unit Agreement for Rota 150 Filling Line for 2017 Production of [**] Lots of Fovista

APPENDIX C

SPECIFICATIONS

Note: The Specifications appearing below are current as of September 30, 2016. Any changes to these Specifications will be handled through the change control process in accordance with this Agreement and the Quality Agreement and approved by Ophthotech. Those approved changes will replace the Specifications set forth herein as of the time of this Agreement's execution.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 28 pages were omitted. [**]

APPENDIX D

QUALITY AGREEMENT

[In revision by the parties.

See 2014 Quality Agreement pending such revisions.]

APPENDIX E

PRODUCTION YIELDS FOLLOWING PROCESS VALIDATION

[NTD: Parties to discuss how to incorporate these measures into the Batch Record.]

As contemplated by 21 CFR 210.3 (definition of "actual yield", "theoretical yield" and "percentage of theoretical yield"), following completion of [**] commercial Lot of a Client Product at each of the Rota 150 Facility and the HSL Facility (as defined in the CRA), as applicable, the parties shall establish the "***Theoretical Yield***" and "***Acceptable Yield***" (and corresponding acceptable yield loss rates) for each of the following yields ("***Yields***") for the Production of such Client Product for each such Facility*:

- **Stage 1 Bulk Compound formulation pre filtration –** Actual yield is based on (volume of product * concentration divided by theoretical yield) * 100%. Theoretical yield is based on Bulk Compound used to formulate solution, water content purity and concentration/volume.

- **Stage 2 Filtered drug product solution** – Actual yield is based on weight of product in bag (total minus tare) divided by theoretical * 100%. Theoretical yield = actual yield from stage 1 minus known filter loss.

- **Stage 3 Filling yield** – Number of vials filled during Production (including available for testing, retains, and visual inspection) * (average mass per vial) divided by (mass of filtered product in bag – (mass of prime, calibration, and weight check vials + mass of hold up)) x 100%

- **Stage 4 Acceptable vials** – Number of final acceptable vials divided by theoretical yield x 100%. Theoretical yield = actual vials from Stage 3 minus vials taken for stability and testing.

The Acceptable Yield established by the parties will be based on batch performance history, and the range of acceptable loss, as compared to the Theoretical Yield, which will not be unreasonably large. For each Production run, Althea shall calculate the actual yield for each of the foregoing Yields (the "***Actual Yields***"), in each case, achieved during Production. In the event that any Actual Yields in the aggregate for all Lots Produced over any [**] month period, or [**] Lots, whichever is greater, is less than [**]% of the aggregate Acceptable Yield for such Lots (the "***Yield Production Standard***"), the parties shall investigate, in accordance with the Quality Agreement, the factors contributing to such shortfall, and Althea shall take all reasonable steps to mitigate against any further shortfalls in future Production Yields.

*For clarity yield parameters for each Facility will be established after (a) up to [**] PPQ lots and (b) [**] commercial lots are completed, in each case, at such Facility.

APPENDIX F

FORM OF PURCHASE ORDER

OPHTHOTECH

Purchase Order

PO #:
PO Date:
Contact:
Dept & Cost Cen
Item:
Budget:

To:

Invoice:

Ophthotech Corp.
One University Square Dr. Suite 280
Princeton, NJ 08540

Accounts.payable@ophthotech.com
Tel: 609-606-6330
Fax: 609-452-7435

Invoices submitted against this PO will be paid within 30 days of receipt. Please supply and deliver the goods or services below as described in the quote:

Item	Quantity	Description	Unit Price	Total Price
			Subtotal	
			Tax	
			Total	

1. Please send two copies of your invoice.
2. Enter this order in accordance with the prices, terms, delivery dates, and specifications listed above.
3. Please notify us immediately if you are unable to ship/deliver as specified.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-211916) pertaining to the 2016 Employee Stock Purchase Plan of Ophthotech Corporation effective June 8, 2016,

(2) Registration Statement (Form S-8 No. 333-208893) pertaining to the 2013 Stock Incentive Plan and Inducement Stock Option Grant of Ophthotech Corporation, effective January 6, 2016,

(3) Registration Statement (Form S-8 No. 333-202438) pertaining to the 2013 Stock Incentive Plan and inducement stock options of Ophthotech Corporation, effective March 2, 2015,

(4) Registration Statement (Form S-8 No. 333-193694) pertaining to the 2013 Stock Incentive Plan of Ophthotech Corporation, effective January 31, 2014,

(5) Registration Statement (Form S-8 No. 333-191767) pertaining to the 2013 Stock Incentive Plan and Amended and Restated 2007 Stock Incentive Plan of Ophthotech Corporation, effective October 16, 2013,

of our reports dated February 28, 2017, with respect to the financial statements of Ophthotech Corporation, and the effectiveness of internal control over financial reporting of Ophthotech Corporation included in this Annual Report (Form 10-K) of Ophthotech Corporation for the year ended December 31, 2016.

/s/ Ernst & Young LLP

MetroPark, New Jersey

February 28, 2017

Exhibit 31.1

CERTIFICATIONS

I, David R. Guyer, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2016 of Ophthotech Corporation;

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: February 28, 2017

By: /s/ DAVID R. GUYER

David R. Guyer, M.D.

Chief Executive Officer

(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Glenn P. Sblendorio, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2016 of Ophthotech Corporation;

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: February 28, 2017

By: /s/ GLENN P. SBLENDORIO

Glenn P. Sblendorio
President and Chief Financial Officer
(Principal Financial 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 Ophthotech Corporation (the "Company") for the fiscal year ended December 31, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David R. Guyer, M.D., Chief Executive Officer of the Company, hereby certifies, pursuant to Rule 13a-14(b) and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 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: February 28, 2017

By: /s/DAVID R. GUYER

David R. Guyer, M.D.
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 Ophthotech Corporation (the "Company") for the fiscal year ended December 31, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Glenn P. Sblendorio, Chief Financial Officer of the Company, hereby certifies, pursuant to Rule 13a-14(b) and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 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: February 28, 2017

By: /s/ GLENN P. SBLENDORIO

Glenn P. Sblendorio
President and Chief Financial Officer
(Principal Financial Officer)