Filed Pursuant to Rule 424(b)(4)
Registration No.: 333-214836

4,000,000 Shares

Common stock

We are offering 4,000,000 shares of our common stock. Our common stock is listed on The NASDAQ Global Market under the symbol "CLSD." The last reported sale price of our common stock on The NASDAQ Global Market on December 8, 2016 was $11.53.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and are subject to reduced public company reporting requirements for this prospectus and our other filings.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk factors" beginning on page 16 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	$ 9.00	$36,000,000
Underwriting discount(1)	$ 0.54	$ 2,160,000
Proceeds, before expenses, to Clearside Biomedical, Inc.	$ 8.46	$33,840,000

(1) See "Underwriting" in this prospectus for a description of compensation payable to the underwriters.

The underwriters may also purchase up to an additional 600,000 shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus.

The underwriters expect to deliver the shares against payment in New York, New York on December 14, 2016.

Active book-running managers

J.P. Morgan **Cowen and Company**

Passive book-running manager

Stifel

Co-manager

Wedbush PacGrow

Prospectus dated December 9, 2016

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You should rely only on the information contained in this prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. We have not authorized anyone to provide you with information that is different from that contained in such prospectuses. We are offering to sell shares of our common stock, and seeking offers to buy shares of our common stock, only in jurisdictions where such offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

For investors outside of the United States: neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

Prospectus summary

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes thereto and the information set forth under the sections "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case included in this prospectus. Unless the context otherwise requires, we use the terms "Clearside," "company," "we," "us" and "our" in this prospectus to refer to Clearside Biomedical, Inc.

Overview of Clearside Biomedical

We are a late-stage clinical biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye. Our current product candidates focus on diseases affecting the retina, which is the tissue that lines the inside of the eye and is primarily responsible for vision, and the choroid, which is the layer adjacent to the retina that supplies the retina with blood, oxygen and nourishment. With our proprietary microinjector, drugs are injected into and spread within and through the suprachoroidal space, or SCS, which is the space located between the choroid and the outer protective layer of the eye known as the sclera. With the suprachoroidal injection, our product candidates are more directly administered to the retina and choroid as compared to other ocular drug administration techniques such as injections of drug into the vitreous, a jelly-like substance that occupies the central portion of the eye. Intravitreal injections rely on diffusion of drug outward from the vitreous to the retina and choroid. This diffusion can result in lower concentrations of drug in these targeted areas. At the same time, this diffusion can also result in drug spreading to unintended parts of the eye, where, for some drugs, it can cause significant side effects. We believe treatment of eye disease via suprachoroidal injection may provide a number of benefits, including lower frequency of necessary administration and faster onset of therapeutic effect. We hold the exclusive rights to develop and commercialize drugs for treatment via injection into the SCS. We estimate that there are nearly five million people in the United States diagnosed with our target indications and that worldwide annual sales of drugs to treat these indications were over $7 billion in 2015.

Our most advanced product candidates are based on commonly used ophthalmic drugs, which we believe will allow us to more efficiently and predictably pursue the regulatory approval of these product candidates under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act. Under Section 505(b)(2), if we can establish that reliance on the Food and Drug Administration's, or FDA's, previous findings of safety and effectiveness for an approved product is scientifically appropriate, or there is scientific literature to support the product's safety or effectiveness, or both, it may eliminate the need for us to conduct some of the preclinical studies or clinical trials for the new product candidate that might otherwise have been required.

Our current and planned development programs aim to restore or improve visual function primarily by reducing the macular edema associated with a number of diseases affecting the retina and choroid. Macular edema is the build-up of fluid that can cause abnormal swelling of the macula, the portion of the retina responsible for central vision and color perception. This swelling can rapidly result in deterioration of vision and can eventually lead to blindness. We are developing Zuprata, a proprietary, preservative-free formulation of the corticosteroid triamcinolone acetonide, or TA, for the treatment of macular edema associated with non-infectious uveitis, a condition that we estimate affects 350,000 patients in the United States. We have specifically designed Zuprata to be administered using our SCS Microinjector. We are currently enrolling patients with macular edema associated with non-infectious uveitis in a pivotal Phase 3 clinical trial. We expect

to enroll approximately 150 patients in this trial and to report preliminary results from the trial in late 2017 or early 2018. We believe, based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, that only one Phase 3 clinical trial will be required to support the potential filing of a New Drug Application, or NDA, with the FDA.

In the first quarter of 2016, we received data from a Phase 2 clinical trial in 22 patients with macular edema associated with non-infectious uveitis. Patients in this trial achieved a statistically significant (p=0.0017) mean change from baseline in retinal thickness at eight weeks, which was the primary endpoint of the trial, as well as statistically significant (p=0.0004) mean improvement from baseline in best corrected visual acuity, or BCVA, at eight weeks, a secondary endpoint. At four and eight weeks, the average reduction in retinal thickness was 135 and 164 microns, respectively, from a mean baseline of 526 microns, and the average improvement in BCVA was 7.7 and 9.2 letters, respectively, from a mean baseline of 60 letters. In our previously completed Phase 1/2 clinical trial, we observed a range of improvements in BCVA of between one and five lines on a standard eye chart, with each line of improvement corresponding to five letters. At the end of week 12, the average improvement in BCVA exceeded two lines, which is considered meaningful in standard clinical practice. At the end of week 26, four of the eight patients in the trial had still not required additional treatment. For those four patients, the average improvement in BCVA was nearly three lines at week 26.

We are also developing Zuprata along with an anti-VEGF agent for the treatment of macular edema associated with retinal vein occlusion, or RVO, a sight-threatening disorder resulting from the blockage of a retinal vein, that we estimate affects 2.2 million patients in the United States. We are exploring whether a suprachoroidal injection of Zuprata and a concomitant intravitreal injection of Eylea (aflibercept), an inhibitor of vascular endothelial growth factor, or VEGF, can provide improved visual acuity, reduced macular edema and reduced injection frequency as compared to administration of intravitreal Eylea alone. Corticosteroids and anti-VEGF agents have known advantages in treating RVO.

We have completed a Phase 2 clinical trial in 46 patients with macular edema associated with RVO. In this trial, 23 patients in the active arm initially received a single concomitant suprachoroidal injection of Zuprata and an intravitreal injection of Eylea and 23 patients in the control arm initially received only an intravitreal injection of Eylea. The objective of the trial was to determine whether patients receiving Zuprata together with Eylea could sustain improved visual acuity over the three months of the clinical trial while requiring fewer additional Eylea treatments than patients receiving intravitreal Eylea alone. Patients in each arm were evaluated at months one, two and three after the initial treatment using pre-specified criteria to determine if they continued to experience macular edema or reductions in visual acuity and therefore required additional Eylea treatments. The primary endpoint of the trial was met, with patients in the active arm requiring an aggregate of 60% fewer additional Eylea treatments than patients in the control arm over three months, a result that was statistically significant (p=0.013). In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant (p=0.003). In the same Phase 2 trial, patients in the active arm experienced greater improvement in visual acuity than those in the control arm, with patients in the active arm experiencing mean BCVA improvements at months one, two and three of 16, 20 and 19 letters, respectively, from a baseline of 49 letters, compared to improvements of 11, 12 and 11 letters, respectively, in the control arm, at the same time points and also from a baseline of 49 letters. Based on the results of this trial and after incorporating feedback from a recent end-of-Phase 2 meeting with the FDA, we intend to commence a Phase 3 clinical program in RVO in the first half of 2017.

We have recently expanded our Zuprata development programs to include another retinal vascular condition known as diabetic macular edema, or DME. DME is a common ocular complication of diabetes that results in

swelling in the macula and is the primary cause of vision loss associated with diabetes. In November 2016, we began enrolling patients with DME in a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal Zuprata, as well as suprachoroidal Zuprata alone, over a six-month evaluation period. We expect to enroll approximately 20 patients in this trial and to report preliminary results in the second half of 2017.

We are developing another product candidate, a proprietary injectable suspension formulation of the compound axitinib, to be administered suprachoroidally for the treatment of neovascular age-related macular degeneration, or wet AMD, a condition that we estimate affects 1.2 million patients in the United States. Axitinib has activities against both VEGF receptors and receptors of platelet derived growth factor, or PDGF. We believe that suprachoroidal injection of axitinib could be more effective than current treatments for wet AMD, which consist primarily of anti-VEGF agents injected intravitreally. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.

We are also working with third parties through collaborations and licenses to develop eye disease treatments using our proprietary SCS Microinjector and method of drug administration to the choroid and retina through the SCS. We are collaborating with Santen Pharmaceuticals, Ltd., or Santen, to develop compounds for suprachoroidal injection that are designed to treat DME, wet AMD and RVO. Additionally, we are collaborating with Santen to explore the potential benefits of suprachoroidal injection of compounds known to reduce intraocular pressure, or IOP, associated with glaucoma for a sustained period of time. All of these activities are currently in the preclinical development stage.

Our drug candidates, SCS Microinjector and method of drug administration into the SCS are protected by six issued U.S. patents, including one design patent, and 55 patent applications filed in the United States and major international markets, including the European Union, Canada, India, Japan, China and Australia. Our issued patents are broadly directed to methods of administering drugs of any type, including anti-inflammatory drugs, anti-VEGF drugs, and gene therapy, into the SCS by injection and are not scheduled to expire until 2027, 2029 and 2034, respectively. Our patent applications relate to suprachoroidal injection technology and methods, our current therapeutic drug candidates and formulations, various therapeutic uses, including treatment of specific indications such as macular edema associated with non-infectious uveitis and RVO, as well as wet AMD and DME, and administration of specific classes of drugs to the SCS, including anti-inflammatory drugs and anti-VEGF drugs. Our pending patent applications are not projected to expire until between 2027 and 2035.

If any of our product candidates are approved, we plan to build a specialized team of 30 to 40 sales and medical marketing support professionals to target the approximately 1,700 retinal specialists in the United States, and we may also pursue collaborations with third parties to commercialize any of our drugs approved for marketing outside the United States.

The members of our management team have held senior leadership positions at a number of pharmaceutical and biotechnology companies with approved ophthalmic drugs, including Alcon, Alimera Sciences and CIBA Vision. Members of our team have contributed to the development, regulatory approval and commercialization of several retinal products, such as Triesence, Iluvien and Nevanac.

The Clearside approach

We are developing drug candidates for back of the eye diseases to be administered to the retina and choroid through the SCS using our proprietary SCS Microinjector. We believe that our novel, patented approach of SCS drug administration may provide a number of potential benefits, including:

- *Improved bioavailability at the site of disease and faster onset of therapeutic effect.* In preclinical studies, we observed higher amounts of drug present in the retina and choroid following suprachoroidal injection, both at early time points and over the course of the experimental timeframe, as compared to the amounts of the same drug present over time in the retina and choroid following intravitreal administration. We believe this suggests that treatment using suprachoroidal injection of a drug may have a faster onset of therapeutic effect as compared to intravitreal administration, along with similar or better efficacy, in diseases such as uveitis, RVO, wet AMD and DME.
- *Similar efficacy profile with lower drug amounts required.* In a preclinical study in an animal model of uveitis, suprachoroidal injection of TA achieved similar efficacy results with only 10% of the drug amount commonly administered through intravitreal injection. We believe this suggests our approach may allow us to develop ocular therapies with similar efficacy, but with lower amounts of active drug, compared to current therapies.
- *Less frequent injections.* Current treatments for RVO require monthly intravitreal injections of anti-VEGF drugs, while current treatments for wet AMD require such injections as often as seven times per year. For RVO patients, we believe that a combination of a standard intravitreal injection of an anti-VEGF drug that addresses the vascular aspect of the disease, together with a suprachoroidal injection of Zuprata, which addresses the inflammatory aspect of RVO, may have efficacy similar to that of monthly intravitreal anti-VEGF injections but with a reduction in the frequency of treatment to once every 90 days. In wet AMD, we believe that more direct administration of drugs with anti-VEGF or dual anti-VEGF and anti-PDGF activity to the neovascularization in the choroid through suprachoroidal injection may substantially block the process of additional new vascular growth within the choroid before the vessels break into the retina and create further damage through leakage. If treatment through the SCS can block retinal damage before it occurs, we believe it could delay vision loss for a longer duration of time than the current standard intravitreal administration of anti-VEGF drugs and, accordingly, could require less frequent administration while providing at least the same levels of efficacy.
- *Enhanced safety profile.* Intravitreal injections result in drugs diffusing throughout the eye, including to the lens, iris and ciliary body at the front of the eye, which for some drugs, such as corticosteroids, has been associated with safety issues, such as cataract formation or exacerbation and elevated IOP levels, which can lead to glaucoma. Intravitreal administration of TA has been associated with cataracts and increases in IOP levels in 20% to 60% of patients. Because suprachoroidal injection of drugs in preclinical studies appeared to result in drug remaining mostly localized in the retina and choroid without substantial diffusion to the vitreous or the front portion of the eye, we believe suprachoroidal injection has the potential to reduce the incidence of these side effects. In our Phase 2 clinical trial in non-infectious uveitis, all 22 patients, who were all treated with a suprachoroidal injection of Zuprata, completed the full observation period and were evaluated for safety. There were no corticosteroid-related increases in IOP or treatment-related serious adverse events observed in this trial. None of the eight patients dosed in our Phase 1/2 clinical trial in non-infectious uveitis experienced cataracts, increased levels of IOP or other treatment-related serious adverse events over the course of 26 weeks following a single suprachoroidal injection of TA. In our Phase 2 clinical trial in RVO patients, there were no serious adverse events, and no adverse events that led to discontinuation of a patient in the trial.

- *Incorporated into standard medical practice.* If approved for marketing, our drugs will be packaged together with our SCS Microinjector for use by retinal specialists. The procedure for suprachoroidal injection with our SCS Microinjector is intended to be conducted in an in-office setting and is similar in terms of patient preparation and duration to the procedure for intravitreal injection, and we therefore expect our products, if they achieve regulatory approval, to be incorporated into retinal specialists' standard medical practice.

Strategy

Our goal is to be a leading biopharmaceutical company focused on the development and commercialization of therapeutics to treat blinding diseases of the eye, with a particular emphasis on diseases affecting the retina and the choroid. The key elements of our strategy are:

- *Advancing our most advanced product candidates to FDA approval under the Section 505(b)(2) NDA regulatory pathway.* Our most advanced product candidates utilize Zuprata, our proprietary formulation of TA, a corticosteroid that has been used for decades to treat ocular inflammatory conditions. We believe this approach will allow us to more efficiently and predictably pursue the regulatory approval of these product candidates under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. We are currently enrolling patients in a pivotal Phase 3 clinical trial of Zuprata for the treatment of macular edema associated with non-infectious uveitis and expect to report preliminary results from this trial in late 2017 or early 2018. Based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, we expect this trial to be the only pivotal clinical trial required to support a potential NDA filing for Zuprata in this indication. We have separately completed a 46-patient Phase 2 clinical trial with Zuprata injected into the SCS concomitantly with intravitreally injected Eylea for the treatment of macular edema associated with RVO. Based on the results of this trial and after incorporating feedback from the FDA, we intend to commence a Phase 3 clinical program with suprachoroidal Zuprata and intravitreal Eylea for the treatment of RVO in the first half of 2017.
- ***Advancing our DME development program.*** DME, like uveitis and RVO, is characterized by an inflammatory aspect. We are conducting a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal Zuprata, as well as suprachoroidal Zuprata alone, in patients with DME over a six-month evaluation period. We recently enrolled the first patient in this trial and expect to report preliminary results from this trial in the second half of 2017.
- *Advancing our wet AMD development program.* We are developing a proprietary suspension formulation of axitinib, a compound with dual anti-VEGF and anti-PDGF activity, for the treatment of wet AMD by injection into the SCS. We believe a single injection of a drug with dual anti-VEGF and anti-PDGF activity to the choroid and retina through the SCS may provide superior visual outcomes compared to intravitreal anti-VEGF treatment and could reduce the number of injections required to treat wet AMD. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.
- *Maximizing the commercial potential of our product candidates.* If we receive marketing approval for Zuprata, we plan to build a specialized team of 30 to 40 sales and medical marketing support professionals to target the approximately 1,700 retinal specialists in the United States. We expect that this sales force would be able to effectively sell more than one of our products, in the event that multiple product candidates are approved for marketing. We have retained the worldwide commercialization rights to all of our product candidates, except we have granted a third party the exclusive right to commercialize our product candidates in Russia and specified adjacent territories pursuant to a license agreement, as described later in this

prospectus. We may pursue additional collaborations with third parties to commercialize any of our drugs approved for marketing outside the United States, either through territorial licenses or distributor relationships.

- *Developing additional therapies through collaborations with third parties.* We plan to explore collaborations with third parties to develop suprachoroidally-injected treatments for eye diseases. These collaborations may take the form of in-licenses of the third parties' drugs or drug candidates for our own development for suprachoroidally-injected treatments, or out-licenses for third parties to use our intellectual property covering suprachoroidally-injected treatments as part of the development of their own drugs. For example, we are collaborating with Santen to develop compounds designed to treat macular edema and neovascularization associated with wet AMD, RVO and DME, as well as elevated IOP associated with glaucoma.
- *Maintaining and strengthening our intellectual property portfolio.* Our intellectual property strategy aims to control the commercialization of SCS access, with patents and patent applications covering suprachoroidal injection, novel formulations of drugs and microinjectors used to access the SCS, and methods of treatment of diseases through the SCS. Our current patents and patent applications provide us with exclusivity in the United States and major international markets, and are not projected to expire until between 2027 and 2035. We will seek to broaden the scope of and increase the geographic reach of our patent protection throughout the world.

Overview of our product candidates

The current development status of our product candidates is summarized in the chart below:

Proposed Indication	Product Candidate	Status and Upcoming Milestones
Macular edema Associated with non-infectious uveitis	Suprachoroidal injection of Zuprata	• Initiated ~150-patient single pivotal Phase 3 clinical trial, with preliminary results expected in late 2017 or early 2018
Macular edema Associated with RVO	Suprachoroidal injection of Zuprata together with intravitreal injection of anti-VEGF agent Eylea	• End-of-Phase 2 meeting held in October 2016 • Plan to commence enrollment of patients in Phase 3 clinical trial in first half of 2017
DME	Suprachoroidal injection of Zuprata alone or together with intravitreal injection of Eylea	• Initiated Phase 1/2 clinical trial • Plan to report data in second half of 2017
Wet AMD	Suprachoroidal injection of axitinib	• Plan to file IND application in the first half of 2017 to commence Phase 1/2 clinical trial

We have discussed our proposed development programs with the FDA for our uveitis and RVO programs, but we have not yet done so for our DME development program. For our wet AMD program, we have only held a pre-IND meeting with the FDA.

Zuprata for macular edema associated with non-infectious uveitis

The most common treatment for non-infectious uveitis, a condition characterized by inflammation of the choroid and surrounding tissues, involves the use of corticosteroids, such as TA. Zuprata is our formulation of TA, and TA is known to be effective in treating uveitis. We believe that our product candidate will be at least as effective as commonly used formulations of TA in treating all aspects of the disease, including the associated macular edema. If approved, Zuprata would be the first drug specifically indicated for macular edema associated with non-infectious uveitis. In November 2015, we enrolled the first patient in a pivotal Phase 3 clinical trial in which Zuprata is injected into the SCS with our SCS Microinjector. We intend to enroll approximately 150 patients with macular edema associated with non-infectious uveitis and expect to report preliminary results from this trial in late 2017 or early 2018. Based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, we believe this will be the only pivotal clinical trial necessary to support a potential 505(b)(2) NDA filing for Zuprata for macular edema associated with non-infectious uveitis.

We have completed a Phase 2 clinical trial in patients with macular edema associated with non-infectious uveitis to evaluate the safety and efficacy of Zuprata injected into the SCS with our SCS Microinjector. In this trial, we observed statistically significant improvement in both retinal thickness, the primary endpoint of the trial, and BCVA, a secondary endpoint. The 22 enrolled patients were randomized to receive a single suprachoroidal injection of one of two doses of Zuprata, with 17 patients receiving a 4.0 mg dose and five patients receiving a 0.8 mg dose. Patients returned for follow-up examinations between seven days and 11 days, at four weeks and at eight weeks following dosing. The patients who received the 4.0 mg dose of Zuprata were evaluated for change from baseline at eight weeks, the primary endpoint in this trial, and improvement in BCVA, a key secondary endpoint in this trial. At four and eight weeks, the average reduction in retinal thickness was 135 and 164 microns, with p-values of 0.0056 and 0.0017, respectively, from a mean baseline of 526 microns, and the average improvement in BCVA was 7.7 and 9.2 letters, with p-values of 0.0001 and 0.0004, respectively, from a mean baseline of 60 letters. These results all achieved statistical significance. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 or less represents statistical significance, meaning that there is a less than 1-in-20 likelihood that the observed results occurred by chance. All 22 patients completed the full observation period and Zuprata was generally well tolerated. There were no corticosteroid-related increases in IOP or treatment-related serious adverse events observed in this trial.

In our completed Phase 1/2 clinical trial, we evaluated the safety of suprachoroidal injection of Triesence, a TA formulation that is similar to Zuprata and has been approved by the FDA to treat non-infectious uveitis. While the trial was primarily a safety and tolerability study, we also assessed efficacy measures. Data from the eight patients enrolled in this trial indicated that suprachoroidal injection of the drug was generally well tolerated, with none of the eight patients having developed cataracts or experienced elevated IOP. At the end of week 12, the average improvement in BCVA exceeded two lines, which is considered in standard clinical practice to be a meaningful change. At the end of week 26, four of the eight patients in the trial had still not required additional treatment. For those four patients, the average improvement in BCVA was nearly three lines at week 26. Our preclinical studies suggest that suprachoroidal injection of TA may provide improved bioavailability of drug at the diseased retina and choroid, which may result in faster onset of therapeutic effect and a similar efficacy profile with lower drug amounts required. Our preclinical studies suggest the potential for suprachoroidal Zuprata to effectively treat uveitis for at least 90 days following a single suprachoroidal injection and our Phase 1/2 clinical trial observations potentially support a duration of action longer than 90 days since four of the eight patients in that trial did not require additional treatment over the 180-day observation period. Currently used ocular injections of TA are typically effective for approximately 90 days.

Zuprata along with intravitreal eylea for macular edema associated with retinal vein occlusion

We have completed a Phase 2 clinical trial for the treatment of macular edema associated with RVO, a sight-threatening disorder resulting from the blockage of a retinal vein. The current standard of care for RVO involves monthly intravitreal injections of an anti-VEGF drug, such as Lucentis (ranibizumab), Eylea (aflibercept) or off-label Avastin (bevacizumab). Corticosteroids are also indicated for the treatment of macular edema associated with RVO. In the Phase 2 trial, 23 patients in the active arm initially received a single suprachoroidal injection of Zuprata and an intravitreal injection of Eylea and 23 patients in the control arm initially received only an intravitreal injection of Eylea. The objective of the trial was to determine whether patients receiving Zuprata together with Eylea could maintain visual acuity improvements while requiring fewer additional Eylea treatments than patients receiving Eylea alone. Patients in each arm were evaluated at months one, two and three after the initial injection using specified criteria to determine if they continued to experience macular edema or reductions in visual acuity and therefore required additional Eylea treatments. The primary endpoint of the trial was met, with patients in the active arm requiring an aggregate of 60% fewer additional Eylea treatments than patients in the control arm over three months, a result that was statistically significant, with a p-value of 0.013. In addition, patients in the active arm experienced greater improvement in visual acuity than those in the control arm, with patients in the active arm experiencing mean BCVA improvements at months one, two and three of 16, 20 and 19 letters, respectively, from a baseline of 49 letters, compared to improvements of 11, 12 and 11 letters, respectively, in the control arm, at the same time points and also from a baseline of 49 letters. In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant, with a p-value of 0.003. Patients in the active arm also achieved mean levels of reduction in retinal thickness of approximately 450 microns after each of one, two and three months, from a baseline of 731 microns. Patients in the control arm achieved a mean reduction in retinal thickness of approximately 400 microns after one month, which reduction then declined to approximately 340 microns at months two and three, from a baseline of 728 microns. Normal retinal thickness on the instrument we used to measure retinal thickness is 270 microns, with a standard deviation of approximately 20 microns. This means that approximately 95% of the normal population has a retinal thickness of 310 microns or less, which is two standard deviations from the normal retinal thickness. There were no serious adverse events reported in the trial and the treatment was generally well tolerated.

Based on the results of our Phase 2 clinical trial, we believe that suprachoroidal injection of Zuprata, by addressing the inflammatory aspect of RVO, in combination with intravitreal anti-VEGF treatment, addressing the vascular aspect of RVO, may result in faster onset of therapeutic effect and may be able to improve visual acuity and reduce macular edema, compared to currently used intravitreal anti-VEGF treatment alone, while also potentially reducing the frequency of necessary anti-VEGF treatments from once every 30 days to once every 90 days. In addition, we believe that the side effect profile of suprachoroidal Zuprata with an intravitreal anti-VEGF agent will be similar to that of current intravitreal anti-VEGF treatments alone, because, based on preclinical data, suprachoroidal injections of Zuprata should allow the corticosteroid to remain substantially localized in the retina and choroid, potentially reducing side effects that are commonly observed with other routes of administration of corticosteroids.

We held an end-of-Phase 2 meeting with the FDA in October 2016. After incorporating feedback from the FDA, we intend to commence a Phase 3 clinical program in the first half of 2017.

Zuprata for diabetic macular edema

Our development program for DME is modeled on our approach for the treatment of RVO. We are conducting a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a single 4.0 mg dose of Zuprata, administered suprachoroidally, both alone and in combination with Eylea, in patients with DME over a six-month evaluation period. Efficacy endpoints will include changes in retinal thickness and BCVA. We plan to enroll 20 patients in this trial and expect to report preliminary results from this trial in the second half of 2017.

Axitinib for wet age-related macular degeneration

We are developing a proprietary suspension formulation of axitinib, a single molecule with dual anti-VEGF and anti-PDGF activity, for the treatment of wet AMD by injection into the SCS with our SCS Microinjector. Axitinib, also known by its brand name Inlyta, is currently marketed by Pfizer and is approved by the FDA for the treatment of advanced renal cell carcinoma, but not for any ophthalmology indications. Wet AMD is a condition that includes the abnormal formation and growth of new blood vessels in the choroid, their intrusion into the outer layers of the retina and the leakage of blood and fluid into the retina. The current standard of care for the treatment of wet AMD is intravitreal injection of anti-VEGF drugs as a standalone therapy, as often as seven times per year. Additionally, anti-PDGF molecules, when injected into the vitreous immediately following an anti-VEGF intravitreal injection, have shown clinical promise in Phase 1 and Phase 2 trials conducted by others in improving upon the visual acuity outcomes of the anti-VEGF agent alone. Because wet AMD manifests in the retina and choroid, we believe that suprachoroidal injection of drug more directly to the retina and choroid may result in faster onset of therapeutic effect as compared to intravitreal injection. We believe that suprachoroidal injection also has the potential to access the new blood vessels in the choroid before they intrude into the retina, which could reduce the necessary frequency of treatment, and reduce or prevent damage to the retina. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.

Future potential product candidates

We believe that our SCS-focused approach has the potential for application in treating other back of the eye diseases, and we intend to develop additional product candidates for suprachoroidal injection based on the results of our completed, current and planned clinical trials. In addition to uveitis, RVO, DME and wet AMD, there are a number of ophthalmic conditions affecting the retina and choroid with unmet medical need for which suprachoroidal injection of therapy may be beneficial. These indications include polypoidal choroidal vasculopathy, or PCV, a disorder resulting from the abnormal growth of new blood vessels in the choroid adjacent to the macula, and geographic atrophy, another advanced form of AMD.

Risks associated with our business

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are discussed more fully in the “Risk Factors” section of this prospectus. These risks include the following:

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

- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome, and we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- We rely, and expect to continue to rely, on third parties to conduct our clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.
- If the FDA does not conclude that our product candidates satisfy the requirements for the Section 505(b)(2) NDA regulatory approval pathway, or if the requirements under Section 505(b)(2) are not as we expect, the approval pathway for our product candidates will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.
- Our research and development efforts are focused on the development of product candidates for suprachoroidal injection, which is a novel approach to the treatment of eye diseases, and may fail to achieve and sustain market acceptance.
- If we are unable to establish sales, marketing and distribution capabilities for our product candidates, we may not be successful in commercializing those product candidates, if and when they are approved.
- If we are unable to obtain and maintain patent protection for our technology and product candidates, or if our licensors are unable to obtain and maintain patent protection for the technology or product candidates that we license from them, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be impaired.

Corporate information

We were incorporated under the laws of the State of Delaware in May 2011. Our principal executive offices are located at 1220 Old Alpharetta Road, Suite 300, Alpharetta, Georgia 30005 and our telephone number is (678) 270-3631. Our website address is *www.clearsidebio.com*. The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our common stock.

We have proprietary rights to a number of trademarks used in this prospectus which are important to our business, including Clearside®, SCS, Zuprata and the Clearside logo. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

Implications of being an emerging growth company

As a company with less than $1 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from some of the reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a non-binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the June 1, 2021, (b) in which we have total annual gross revenue of at least $1 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

The offering

Common stock offered by us	4,000,000 shares.
Common stock to be outstanding immediately after this offering	24,545,752 shares.
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase 600,000 additional shares of common stock.
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be $33.2 million. We anticipate that the majority of the net proceeds from this offering will be used to complete our pivotal Phase 3 clinical trial of suprachoroidal Zuprata for the treatment of macular edema associated with non-infectious uveitis, to initiate our Phase 3 clinical program of suprachoroidal Zuprata with an intravitreal anti-VEGF agent, Eylea, for the treatment of macular edema associated with RVO, to complete our ongoing Phase 1/2 clinical trial of Zuprata, alone or with Eylea, for the treatment of DME and to initiate and complete a planned Phase 1/2 clinical trial of axitinib for the treatment of wet AMD. The remaining proceeds will be used for the continued research and development of our earlier-stage programs, and for working capital and general corporate purposes. See “Use of Proceeds” for additional information.
Risk factors	You should read the “Risk Factors” section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
NASDAQ Global Market symbol	CLSD

The number of shares of our common stock that will be outstanding after this offering is based on 20,545,752 shares of common stock outstanding as of September 30, 2016, and excludes:

- 1,414,594 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2016, at a weighted average exercise price of $2.90 per share;
- 55,770 shares of our common stock issuable upon the exercise of warrants outstanding as of September 30, 2016 at a weighted average exercise price of $9.32 per share;
- 1,842,500 shares of our common stock reserved for future issuance under our equity incentive plans following this offering; and

- any additional shares that may be reserved for future issuance under our equity incentive plans as a result of automatic annual increases in the share reserves beginning on January 1, 2017.

Except as otherwise indicated herein, all information in this prospectus, including the number of shares that will be outstanding after this offering, assumes:

- no exercise of options or warrants outstanding as of September 30, 2016; and
- no exercise of the underwriters' option to purchase additional shares of common stock.

Summary financial data

The following tables set forth our summary financial data for the periods indicated. We have derived the following summary of our statement of operations data for the years ended December 31, 2014 and 2015 from our audited financial statements appearing elsewhere in this prospectus. We have derived the following summary of our statement of operations data for the nine months ended September 30, 2015 and 2016 and our balance sheet data as of September 30, 2016 from our unaudited interim financial statements appearing elsewhere in this prospectus.

The unaudited interim financial statements include all adjustments, consisting only of normal recurring adjustments, that we consider necessary for a fair presentation of our financial position and results of operations for these periods. Our historical results are not necessarily indicative of the results to be expected in the future, and our operating results for the nine months ended September 30, 2016 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 2016 or any other future period.

You should read this summary financial data together with the historical financial statements and related notes to those statements, as well as "Management's Discussion and Analysis of Financial Condition and Results of Operations," which are included elsewhere in this prospectus.

	Year Ended December 31,		Nine Months Ended September 30,	
	2014	2015	2015	2016
	(in thousands, except share and per share data)			
Statement of Operations Data:				
License revenue	$ —	$ —	$ —	$ 515
Operating expenses:				
Research and development	6,692	10,762	6,964	12,484
General and administrative	3,131	6,555	5,337	3,872
Total operating expenses	9,823	17,317	12,301	16,356
Loss from operations	(9,823)	(17,317)	(12,301)	(15,841)
Other income (expense):				
Interest expense	(371)	(330)	(174)	(432)
Interest income	5	8	6	77
Total other expense	(366)	(322)	(168)	(355)
Net loss	$ (10,189)	$ (17,639)	$ (12,469)	$ (16,196)
Net loss per share of common stock—basic and diluted	$ (5.86)	$ (7.54)	$ (5.59)	$ (1.54)
Weighted average shares outstanding—basic and diluted	1,738,660	2,338,950	2,231,830	10,502,459

The following table presents our summary balance sheet data as of September 30, 2016:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of 4,000,000 shares of common stock in this offering at the public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of September 30, 2016	
	Actual	As adjusted
	(in thousands)	
Balance Sheet Data:		
Cash and cash equivalents	$ 36,876	$ 70,116
Short-term investments	20,043	20,043
Total assets	57,771	91,011
Total liabilities	10,833	10,833
Total stockholders' equity	46,938	80,178

Risk factors

Investing in our common stock involves a high degree of risk. Before you invest in our common stock, you should carefully consider the following risks, as well as general economic and business risks, and all of the other information contained in this prospectus. Any of the following risks could have a material adverse effect on our business, operating results and financial condition and cause the trading price of our common stock to decline, which would cause you to lose all or part of your investment. When determining whether to invest, you should also refer to the other information contained in this prospectus, including our financial statements and the related notes thereto.

Risks related to our financial position and capital needs

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

We incurred net losses of $17.6 million and $16.2 million for the year ended December 31, 2015 and the nine months ended September 30, 2016, respectively.

We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We are still in the early stages of development of our product candidates, and we have not completed development of any drugs. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- conduct and complete our ongoing and planned clinical trials;
- initiate clinical trials of suprachoroidal axitinib for the treatment of wet AMD;
- seek to discover, research and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any drugs for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our drug development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval and manufacturing, marketing and selling any products for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we

are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in the initiation and completion of our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value 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 decline in our value could also cause you to lose all or part of your investment.

We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to delay, reduce or altogether cease our drug development programs or commercialization efforts.

We believe that our existing cash and cash equivalents, including the net proceeds from our recent initial public offering, or IPO, and this offering, as well as our borrowing availability under our credit facility, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 18 months. However, we will need to obtain substantial additional funding in connection with our continuing operations. Our future capital requirements will depend on many factors, including:

- the progress and results of our ongoing, planned and future clinical trial programs;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether cease our research and development programs 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.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements. We do not currently have any committed external source of funds other than our credit facility. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

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

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

We commenced active operations in 2012, and our operations to date have been largely focused on raising capital, identifying potential product candidates, broadening our expertise in the development of our product candidates, including our SCS Microinjector, and undertaking preclinical studies and conducting early clinical trials. We have not yet demonstrated an ability to successfully complete later-stage clinical trials, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

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

We may not be able to generate sufficient cash to service our indebtedness, which currently consists of our loan from Silicon Valley Bank and MidCap.

We have entered into an amended and restated loan and security agreement with Silicon Valley Bank and entities affiliated with MidCap Financial Services, which we refer to collectively as the Lenders, pursuant to which we have borrowed an aggregate of $8.0 million as of September 30, 2016. In the event that we produce clinical trial data sufficient to file an NDA for Zuprata for the treatment of uveitis, we will be able to draw an additional $7.0 million until December 31, 2017. Our obligations under the loan agreement are secured by substantially all

of our assets except for our intellectual property, and we may not encumber our intellectual property without the Lenders' prior written consent. The amended and restated loan agreement contains negative covenants restricting our activities, including limitations on dispositions, mergers or acquisitions, incurring indebtedness or liens, paying dividends or making investments and other specified business transactions. Our obligations under the loan agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition. We were in compliance with these covenants as of September 30, 2016. We may also enter into other debt agreements in the future which may contain similar or more restrictive terms.

Our ability to make scheduled monthly payments or to refinance our debt obligations depends on numerous factors, including the amount of our cash reserves and our actual and projected financial and operating performance. These amounts and our performance are subject to certain financial and business factors, as well as prevailing economic and competitive conditions, some of which may be beyond our control. We cannot assure you that we will maintain a level of cash reserves or cash flows from operating activities sufficient to permit us to pay the principal, premium, if any, and interest on our existing or future indebtedness. If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay capital expenditures, sell assets or operations, seek additional capital or restructure or refinance our indebtedness. We cannot assure you that we would be able to take any of these actions, or that these actions would permit us to meet our scheduled debt service obligations. Failure to comply with the conditions of the loan agreement could result in an event of default, which could result in an acceleration of amounts due under the loan agreement. We may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the Lenders could seek to enforce security interests in the collateral securing such indebtedness, which would harm our business.

Risks related to the development of our product candidates

Our research and development efforts are focused on the development of product candidates for treatment of eye diseases through suprachoroidal injection, which is a novel approach and may fail to achieve and sustain market acceptance.

Injecting drugs into the SCS is a novel approach for ophthalmic therapies, and there is no guarantee this approach will provide adequate patient benefit or be accepted by physicians, patients or third-party payors. We believe we are the first and only company developing drugs specifically for suprachoroidal injection for potential treatment of eye diseases. The scientific evidence to support the feasibility of developing drugs based on this approach is both preliminary and limited. Although our clinical trial results suggest that suprachoroidal injection of drugs, such as Zuprata, may be effective at treating back of the eye diseases, to date no company has developed a drug for suprachoroidal administration that has received marketing approval.

Additionally, we have limited clinical experience in suprachoroidal drug injection. Therefore, we cannot guarantee that suprachoroidal injection of drugs will prove in our ongoing and future clinical trials to be a safe or effective approach for treating back of the eye diseases in humans, nor can we ensure that we will achieve regulatory approval for our product candidates, even if our clinical trials are successful.

Even if we are able to achieve marketing approval for one of our product candidates, the novelty of suprachoroidal injection may make it difficult to demonstrate to physicians and third-party payors that suprachoroidal injection of our drugs is an appropriate approach for treating diseases such as non-infectious uveitis, RVO, DME and wet AMD and provides advantages compared to the current standards of care. Further, if we are not successful in conveying to physicians, patients and third-party payors that the administration of our drug candidates with our proprietary SCS Microinjector improves patient outcomes, we may experience reluctance, or refusal, on the part of physicians to order and use, and third-party payors to cover and provide

adequate payment for, our product candidates. Additionally, in some cases, our product candidates will complement the current standard of care, rather than serve as a replacement for the current standard of care. Therefore, we may encounter significant difficulty in gaining broad market acceptance by physicians, third-party payors and potential patients using Zuprata and our other product candidates.

All of our product candidates are in clinical or preclinical development. If we are unable to obtain regulatory approval for and commercialize our product candidates or if we experience significant delays in doing so, our business may be harmed.

Given our limited human experience with our clinical programs, the successful development of any of our product candidates is extremely uncertain, and we cannot guarantee that we will be successful in developing any of our product candidates. Further, the FDA may conclude that our clinical trials are not sufficient to support approval of our product candidates. For example, for our wet AMD program, the only clinical trial we have conducted to date is the Phase 1 exploratory trial of Avastin in Mexico. Although the exploratory trial was conducted in accordance with good clinical practices and had approval and oversight of the local institutional review board, the FDA could conclude that we may not rely on the results of the trial conducted in Mexico as part of our regulatory application seeking marketing approval for axitinib.

We have not completed the development of any product candidates, we currently generate no revenues from sales of any products and we may never be able to develop a marketable product. We have invested substantially all of our efforts and financial resources in the development of our proprietary SCS Microinjector for suprachoroidal injection of drugs and the identification of potential drug candidates using that technology. Our ability to generate revenue from our product candidates, which we do not expect will occur for several years, if ever, will depend heavily on their successful development and eventual commercialization. The success of those product candidates will depend on several factors, including the following:

- successful completion of preclinical studies and requisite clinical trials;
- performing preclinical studies and clinical trials in compliance with FDA requirements;
- receipt of marketing approvals from applicable regulatory authorities;
- ability to import sufficient quantity of product for trials or potential commercialization;
- obtaining marketing approvals with labeling for sufficiently broad patient populations and indications, without unduly restrictive distribution limitations or safety warnings, such as black box warnings or a risk evaluation and mitigation strategy, or REMS, program;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- launching commercial sales of products, if and when approved, whether alone or in collaboration with others;
- successful training of physicians in the proper use of our SCS Microinjector;
- our ability to market our products for use with our SCS Microinjector without a requirement from the FDA that we obtain a separate medical device authorization;
- acceptance of the therapies and of the concept of suprachoroidal injection of drugs, if and when approved, by physicians, patients and third-party payors;

- competing effectively with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of the drugs and our SCS Microinjector following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

The administration of Zuprata as a therapy together with an anti-VEGF drug for the treatment of macular edema associated with RVO is a novel approach and may fail to be successful.

We are developing Zuprata as a therapy to complement the current standard of care in the treatment of patients experiencing macular edema associated with RVO, with the goal of reducing current required monthly anti-VEGF injections to quarterly injections. The scientific evidence to support the potential efficacy of this treatment approach is limited to our phase 2 clinical trial results and, in addition based on third party clinical trials studying intravitreal injections of steroids in patients with RVO, which, although effective in reducing edema and improving visual outcomes, has been associated with side effects. While our clinical trial experience involving the suprachoroidal injection of triamcinolone acetonide suggests that these adverse side effects may be reduced using suprachoroidal injection, to date no other company has explored this specific concomitant treatment approach in clinical trials or preclinical studies.

Even if we are able to successfully develop, and achieve marketing approval of, Zuprata for the treatment of macular edema associated with RVO, it may be difficult to demonstrate to physicians and third-party payors that the administration of Zuprata concomitantly with anti-VEGF drugs, and the reduction in frequency of anti-VEGF treatments, is the appropriate approach for treating RVO and provides advantages over the current standard of care. Further, if we are not successful in conveying to physicians, patients and third-party payors that the administration of Zuprata concomitantly with anti-VEGF drugs improves patient outcomes, we may experience reluctance, or refusal, on the part of physicians to order and use, and third-party payors to pay for, Zuprata. Therefore, we may encounter significant difficulty in gaining broad market acceptance by physicians, third-party payors and potential patients using Zuprata for the treatment of macular edema associated with RVO.

We revised the design of our SCS Microinjector following early-stage clinical trials and do not yet have significant experience with our SCS Microinjector in humans.

In our preclinical studies and early clinical trials, we used several prototype iterations of the SCS Microinjector. We have since finalized the commercial design, which we used in our Phase 2 clinical trials of Zuprata for the treatment of macular edema associated with non-infectious uveitis and RVO and are using in our Phase 1/2 clinical trial of Zuprata for the treatment of DME. We also plan to use this revised microinjector in our other ongoing and planned clinical trials. Accordingly, in addition to the risks associated with drug development, we are also subject to the risks associated with developing the microinjector. For example, in our Phase 1/2 clinical trial of Zuprata for the treatment of macular edema associated with non-infectious uveitis, the needle of our earlier microinjector was not long enough to penetrate the scleras of two patients screened for the trial. If we encounter similar limitations with this design, or if it does not function properly in any way, we could be required to expend significant additional time and resources to redesign our microinjector, which would delay or compromise our drug development efforts. Additionally, our ability to successfully commercialize our

product candidates will depend on retinal specialists being comfortable with the design and functionality of our microinjector. If, for any reason, these specialists were unsatisfied with the form or function of our microinjector, it would harm the market acceptance and potential commercial success of our product candidates, if any, that receive marketing approval.

We may not be successful in our efforts to build a pipeline of product candidates.

A key element of our strategy is to build a pipeline of product candidates for suprachoroidal injection and to progress these product candidates through clinical development for the treatment of a variety of diseases of the back of the eye. We may not be able to develop product candidates that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have significant side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval or achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which could significantly harm our financial position and adversely affect our stock price.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

The risk of failure for our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later 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, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, including failure to demonstrate statistical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators may issue a clinical hold, or regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not 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 or distribution restrictions or safety warnings, such as black box warnings or a REMS program;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our drug development costs may also increase if we experience delays in testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. For example, we began enrolling patients in our Phase 1/2 uveitis trial in July 2013 and intended to enroll approximately 10 patients in the trial, but we completed enrollment after dosing the eighth patient in July 2014. For our Phase 3 pivotal uveitis trial, we are seeking to enroll up to 150 patients. We have limited experience enrolling patients in our clinical trials, and cannot predict how successful we will be at enrolling patients in future clinical trials. In particular, because of the relatively low prevalence of patients with uveitis, we may encounter difficulties in identifying and enrolling our target number of patients in this trial on our expected timeframe. In addition, if we are not successful at enrolling patients in one clinical trial, it may affect when we are able to initiate our next clinical trial, which could result in

significant delays in our efforts to pursue regulatory approval of and commercialize our product candidates. In addition, some of our competitors have ongoing clinical trials to treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors. Patient enrollment is affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the availability of drugs approved to treat the diseases under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which could cause our value to decline and limit our ability to obtain additional financing.

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

If our product candidates are associated with side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the product candidate. In addition, in some cases, the FDA could issue a clinical hold to stop the study.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and management resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks related to our dependence on third parties

We expect to rely on third parties to conduct our clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or failing to comply with applicable regulatory requirements.

We have engaged contract research organizations, or CROs, for our ongoing and planned clinical trials. We also expect to engage CROs for any of our other product candidates that may progress to clinical development. We expect to rely on CROs, as well as other third parties, such as clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. Agreements with such third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would delay our drug development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will 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 regulatory standards, commonly referred to as good clinical practices, or 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 certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so by us or third parties can result in FDA refusal to approve applications based on the clinical data, enforcement actions, adverse publicity and civil and criminal sanctions.

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

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA of any NDA we submit. Any such delay or rejection could prevent us from commercializing Zuprata or our other product candidates.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure or regulatory noncompliance 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 Zuprata and our SCS Microinjector for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of Zuprata and our SCS Microinjector or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel. We currently procure the active pharmaceutical ingredient in Zuprata on a purchase order basis from a third-party manufacturer, and we anticipate entering

into commercial supply agreements with this or another manufacturer at a later date. In addition, we obtain each of the components of our SCS Microinjector on a purchase order basis from third-party suppliers. Some of our current suppliers are based outside of the United States. We expect to continue to rely on third parties as we proceed with preclinical and clinical testing using Zuprata with our SCS Microinjector, as well as for commercial manufacture, if any of our product candidates receives marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of Zuprata and our SCS Microinjector or such quantities at an acceptable cost or quality, which could delay, prevent or impair our ability to timely conduct our clinical trials or our other development or commercialization efforts.

We also expect to rely on third-party manufacturers or collaborators for the manufacture of commercial supply of any other product candidates for which we obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or collaborators or to do so on acceptable terms.

Even if we are able to establish agreements with third-party manufacturers or collaborators, reliance on third-party manufacturers or collaborators entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- 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.

Our product candidates, including our proprietary drug formulations packaged together with our SCS Microinjector, are drug/device combination products that will be regulated under the drug regulations of the Federal Food, Drug, and Cosmetic Act, or FDCA, based on their primary mode of action as drugs. Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations, regulations applicable to drug/device combination products, including applicable provisions of the FDA's drug cGMP regulations, device cGMP requirements embodied in the Quality System Regulation, or QSR, 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, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates.

Our product candidates that we may develop may compete with other drugs and devices for access to manufacturing facilities. There are a limited number of manufacturers that operate under the drug and device cGMP regulations applicable to our product candidates and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance or our SCS Microinjector. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our drugs and the components of our SCS Microinjector, we may incur added costs and delays in identifying and qualifying any such replacement. For example, the FDA could require supplemental data if a new supplier is relied upon for the active pharmaceutical ingredient used in our products. Any interruption or delay in the supply of components and materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand of our customers and cause them to cancel orders.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may compromise our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

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

We may seek third-party collaborators for the development and commercialization of our product candidates, particularly for the commercialization of any of our product candidates that are approved for marketing outside the United States or for product candidates targeted at larger indications in the United States such as wet AMD and DME. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We have entered into a collaboration with Santen to develop compounds that are designed to treat macular edema and neovascularization associated with wet AMD, RVO and DME, as well as elevated intraocular pressure, or IOP, associated with glaucoma. Under our collaboration with Santen, and if we enter into any future collaboration arrangements with any third parties, we will 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 will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized on terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to

product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

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

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies, such as our current collaboration with Santen, for the future development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under existing license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such 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 increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient

funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Risks related to the commercialization of our product candidates

If we are unable to establish sales, marketing and distribution capabilities for our product candidates, we may not be successful in commercializing those product candidates, if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical drugs or medical devices. To achieve commercial success for any product candidate for which we may obtain marketing approval in the United States, we will need to establish a sales and marketing organization. In the future, we expect to build a focused sales and marketing infrastructure to target the approximately 1,700 retinal specialists in the United States for any of our product candidates that receive marketing approval. There are risks involved with establishing our own sales, marketing and distribution capabilities. 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 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 drugs on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage compared to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and, instead, enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to sell, market and distribute any product candidates that we develop ourselves. 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 product candidates effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Even if any of our product candidates receives marketing approval, it 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.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Suprachoroidal injection of drugs is a novel approach and physicians, patients or third-party payors may be hesitant to deviate from or change the current standard of care. If our product candidates do not achieve an adequate level of market acceptance, we may not generate significant product revenue and we may not become profitable. The

degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- our ability to offer our drugs for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the willingness of the healthcare community and patients to adopt new technologies and our novel approach of suprachoroidal injection of drugs;
- the willingness of retinal specialists to expend the time necessary to receive proper training on injecting drugs into the SCS using our SCS Microinjector;
- the ability to manufacture our product in sufficient quantities and yields;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our drugs together with other medications.

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

The development and commercialization of new products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

With respect to Zuprata, we face competition from other commercially available forms of TA and other injectable and implantable corticosteroids. Bristol-Myers Squibb markets TA under the brand name Kenalog. Kenalog is indicated only for intramuscular or intraarticular injection, although it is commonly used off-label for intraocular inflammation. There are also a number of generic equivalents of Kenalog. In addition, Alcon's injectable TA, Triesence, is approved in the United States for the treatment of uveitis and other inflammatory conditions unresponsive to topical corticosteroids, although it is not indicated for the treatment of macular edema associated with uveitis or RVO or for the treatment of DME. Ozurdex, marketed by Allergan, is a bioerodable extended release implant that delivers the corticosteroid dexamethasone and is approved for the treatment of non-infectious uveitis affecting the back of the eye and RVO in both the United States and in the European Union, and recently received approval from the FDA to treat DME in adult patients who have an artificial lens implant or who are scheduled for cataract surgery. Bausch + Lomb markets Retisert, an intravitreal implant of the corticosteroid fluocinolone acetonide, for the treatment of non-infectious uveitis. Iluvien, marketed by Alimera Sciences, is a fluocinolone acetonide implant and is approved for the treatment of DME in both the United States and the European Union.

Our product candidates will also compete with anti-VEGF drugs, which are the current standard of care for RVO and wet AMD and have also been approved for DME. Genentech's products Lucentis and Avastin are both

anti-VEGF antibodies. Lucentis is currently approved in the United States and European Union for the treatment of wet AMD, macular edema associated with RVO and DME. Avastin is an anti-VEGF drug used by retinal specialists off-label in both the United States and in certain countries of the European Union in the treatment of numerous retinal diseases, but it is not indicated for ophthalmic use. Regeneron's anti-VEGF product, Eylea, is approved for the treatment of wet AMD, macular edema associated with RVO and DME in the United States. In the European Union, Eylea is approved for the treatment of wet AMD, DME and macular edema secondary to RVO.

Ophthotech's drug candidate, Fovista, an anti-PDGF agent, is in Phase 3 clinical trials as a potential treatment for wet AMD to be administered together with an anti-VEGF drug. We are also aware of several other drug candidates in earlier stages of development as potential treatments for the diseases that we intend to target.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product candidates that we may develop. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in product approval delays if a competitor obtains market exclusivity from the FDA or our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic drugs. For some of the indications that we are pursuing, drugs used off-label, such as Kenalog and Avastin, serve as a cheaper alternatives to our product candidates. Their lower prices could result in significant pricing pressure, even if our product candidates are otherwise viewed as a preferable therapy. Additional drugs may become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic drugs.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to commercialize any product candidates, our product candidates may be subject to unfavorable pricing regulations, third-party coverage and reimbursement policies or healthcare reform initiatives.

Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and adequate reimbursement for our product candidates will be available from government payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers, managed care plans and other third-party payors. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medical products they will pay for and establish reimbursement levels. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs and products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Inadequate reimbursement levels

may adversely affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our drugs may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement compared to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidates for which marketing approval is obtained.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. By way of example, the Medicare Prescription Drug Improvement and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs, including drugs currently on the market used by physicians to treat the clinical indications for which we are currently seeking FDA approval and likely our product candidates, if approved. As a result of this legislation and the expansion of federal coverage of drug products, there is additional pressure to contain and reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors. These cost reduction initiatives and other provisions of the MMA could decrease the coverage and reimbursement that we receive for any approved products, and could seriously harm our business.

Further, from time to time, typically on an annual basis, payment amounts are updated and revised by third-party payors. Because we expect that customers who use our product candidates, if approved, will be separately reimbursed for the procedure administering our products, these updates could directly impact the demand for our products. An example of payment updates is the Medicare program updates to physician payments, which is done on an annual basis using a prescribed statutory formula. In the past, when the application of the formula resulted in lower payment, Congress has passed interim legislation to prevent the reductions. However, the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, ended the use of the statutory formula, and provided for a 0.5% annual increase in payment rates under the Medicare Physician Fee Schedule through 2019, but no annual update from 2020 through 2025. MACRA also introduced a quality payment program under which individual providers with Medicare billings of $30,000 or 100 patient visits per year will be subject to certain incentives or penalties based on new program quality standards. The quality payment program has two tracks, one known as the merit based incentive payment system for providers in the fee-for service Medicare program, and the advanced alternative payment model for providers in specific care models, such as accountable care organizations. Payment adjustments for the Medicare quality payment program will begin in 2019. At this time it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program. In addition, the Medicare physician fee schedule has been adapted by some private payors into their plan-specific physician payment schedule. We cannot predict how pending and future healthcare legislation will impact our business, and any changes in coverage and reimbursement that further restricts coverage of our products or lowers reimbursement for procedures using our products could materially affect our business.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for coverage and reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent.

We believe that physicians who use our product candidates, if approved, will be reimbursed by third-party payors for both the suprachoroidal injection using our SCS Microinjector and for the drug itself. On July 1, 2016, the American Medical Association, or AMA, approved a new Category III Current Procedural Terminology, or CPT, code for the suprachoroidal injection of pharmacologic agents. Category III codes are a set of temporary codes maintained by the AMA for emerging technology, services and procedures. Payment for these services or procedures are based on the coverage policies of individual payors and Medicare administrative contractors. CPT code 0465T will become effective on January 1, 2017. We intend to seek a separate Healthcare Common Procedure Coding System, or HCPCS, code as maintained by CMS for the drug itself. We believe that separate CPT and HCPCS codes will help payors differentiate our drug candidates from other drugs currently on the market administered through intravitreal injections, although we can provide no assurance that CMS will approve the creation of a separate HCPCS code. Additionally, there is no guarantee that these billing codes or the payment amounts, if any, associated with such codes will not change in the future.

Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. However, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained at all. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved drugs that we develop could significantly harm our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues able to be generated 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.

There can be no assurance that our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication, that they will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available, or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably if they are approved for sale.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any drugs that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards paid to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any drugs that we may develop.

We currently hold $5.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $5.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks related to employee matters and managing our growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, research and development, clinical, financial and business development expertise of Daniel White, our Chief Executive Officer, Charlie Deignan, our Chief Financial Officer, and Glenn Noronha, our Chief Scientific Officer, as well as the other members of our scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

As of September 30, 2016, we had 23 full-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks related to our intellectual property

If we are unable to obtain and maintain patent protection for our technology and product candidates, or if our licensors are unable to obtain and maintain patent protection for the technology or product candidates that we license from them, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be impaired.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates. We and our licensors seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technology and product candidates.

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. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. For example, we do not control the prosecution of the patent applications licensed to us under the Emory/GT License described below. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

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 countries may not protect our rights to the same extent as the laws of the United States or visa-versa. 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 know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or product

candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and drugs. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. 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 United States patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and may also affect patent litigation. The United States Patent and Trademark Office 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 significantly harm our business and financial condition. In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our owned and licensed patents and patent applications.

Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs 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.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, and may not be of sufficient scope or strength to provide us with any commercial advantage. Our competitors may be able to design around our owned or licensed patents by developing similar or alternative technologies or drugs without infringing on our intellectual property rights.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, or limit the duration of the patent protection of our technology and drugs. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours, and our business will suffer.

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 our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming.

Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly, which would undermine our competitive position.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could significantly harm business.

Our commercial success depends upon our ability, and the ability of any collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. In particular, we are focused on developing product candidates based on widely used therapeutic agents, many of which are protected by proprietary rights of third parties, and we are developing proprietary formulations of these therapeutic agents specifically for suprachoroidal injection using our proprietary SCS Microinjector. For example, in our clinical program for wet AMD, we are developing a propriety formulation of axitinib to be administered by suprachoroidal injection, which we believe could be more effective than current treatments for wet AMD. Axitinib is currently marketed by Pfizer and was approved for the treatment of advanced renal cell carcinoma. Pfizer has Orange Book-listed as well as unlisted patents for axitinib that expire in 2020, without extension. Pfizer has also applied for Patent Term Extension under 35 U.S.C. § 156 that could extend the term of one listed patent to 2025 for the approved indication. Although we seek to develop our proprietary drug formulations that don't infringe the intellectual property rights of others, we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our drugs or other aspects of our technology, including interference or derivation proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our technology and drugs. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations.

Competing products may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit alleging our infringement of a competitor's patent, we could be prevented from marketing our products in one or more foreign countries. As a result, our ability to grow our business and compete in the market may be harmed.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be

negative, it could hurt the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

If we fail to comply with our obligations under our existing intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a license agreement with Emory University and Georgia Tech Research Corporation, or the Emory/GT License, and may enter into additional license agreements in the future. Our existing license agreement imposes, and we expect that future license agreements would impose, various diligence, milestone payment, royalty, insurance and other obligations on us. For example, under the Emory/GT License, we are required to use commercially reasonable efforts to develop and commercialize licensed products under the agreement and to satisfy other specified obligations, including the payment of license fees and minimum royalty payments. If we fail to comply with our obligations under our license agreements, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or to convert the license to a non-exclusive license, which could impair the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms. If our licensors under the Emory/GT License were to terminate their license agreement with us for any reason, we would lose access to critical technology related to our SCS Microinjector.

We may need to license additional intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

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 were previously employed at universities or other biotechnology or pharmaceutical companies. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We may also in the future be subject to claims that we have caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these potential claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may

be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A court could prohibit us from using technologies or features that are essential to our products, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and could be a distraction to management. In addition, any litigation or threat thereof may adversely affect our ability to hire employees or contract with independent service providers. Moreover, a loss of key personnel or their work product could hamper or prevent our ability to commercialize our products.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. Other than Zuprata, we have not yet selected trademarks for our product candidates or begun the process of applying to register trademarks for our product candidates. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for our product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. 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 of our product candidates and other legal compliance matters

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 will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, research, testing, manufacture, safety, efficacy, quality control, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, sale, distribution, import, export, and reporting of safety and other post-market information, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the European Medicines Agency, or EMA, and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates 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 on third-party CROs to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If any of our product candidates receives marketing approval, the accompanying label may limit its approved use, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and 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 is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

If the FDA does not conclude that our product candidates satisfy the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements under Section 505(b)(2) are not as we expect, the approval pathway for our product candidates will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

We intend to seek FDA approval through the Section 505(b)(2) regulatory pathway for Zuprata and may pursue that pathway for our other product candidates. Our product candidates, including our proprietary drug formulations packaged together with our SCS Microinjector, are drug/device combination products that will be regulated under the drug provisions of the FDCA, enabling us to submit NDAs for approval of our product candidates. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-

Waxman Amendments, added Section 505(b)(2) to the FDCA. Section 505(b)(2) 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 and for which the applicant has not obtained a right of reference.

If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as anticipated, we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for our product candidates, and complications and risks associated with our product candidates, would likely substantially increase. We may need to obtain additional funding, which could result in significant dilution to the ownership interests of our then existing stockholders to the extent we issue equity securities or convertible debt. We cannot assure you that we would be able to obtain such additional financing on terms acceptable to us, if at all. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway could result in competitive products reaching the market before our product candidates, which could impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization, or that a competitor would not obtain approval first, including subsequent market exclusivity from the FDA, thereby delaying potential approval of our product.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, some pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may be required to change its Section 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2).

The FDA may not approve our proposed trade name, Zuprata.

Although Zuprata, the trade name for our proprietary, preservative-free formulation of TA, has been registered with the U.S. Patent and Trademark Office, it must also be approved by the FDA. We are in the process of applying for conditional approval from the FDA for this trade name. The FDA conducts a rigorous review of proposed product names, and may reject a product name if it believes that the name inappropriately implies medical claims or if it poses the potential for confusion with other product names. If our trade name, Zuprata, is rejected, we will lose the benefit of any brand equity that may already have been developed for this product candidate, as well as the benefit of our existing trademark applications for this trade name. If the FDA does not approve the Zuprata trade name, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

Additional time may be required to obtain regulatory approval for our product candidates because they are combination products.

Our product candidates are drug/device combination products that require coordination within the FDA and similar foreign regulatory agencies for review of their device and drug components. Although the FDA and similar foreign regulatory agencies have systems in place for the review and approval of combination products such as ours, we may experience delays in the development and commercialization of our product candidates due to regulatory timing constraints and uncertainties in the product development and approval process. In addition, to date, the FDA has not requested a separate medical device authorization submission for our SCS Microinjector. However, the FDA may request a separate medical device authorization submission for our SCS Microinjector in the future, which could delay the development and commercialization of our product candidates.

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

In order to market and sell our products in the European Union and any other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, failure to obtain approval in one jurisdiction may impact our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

A variety of risks associated with marketing our product candidates internationally could affect our business.

We may seek regulatory approval for our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market with low or lower prices rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may compromise our ability to achieve or maintain profitability.

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

Any product candidate for which we 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, quality assurance 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 to the conditions of approval, including the requirement to implement a REMS, which could involve requirements for, among other things, a medication guide, special training for prescribers and dispensers, and patient registries. If any of our product candidates receives marketing approval, the accompanying label may limit its approved uses, which could limit sales of the product, or include a black box warning to highlight a specific health risk.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of products to ensure products are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our drugs for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our drugs, including device malfunctions, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have negative consequences, including:

- restrictions on such drugs, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- recall or withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- clinical holds;
- safety alerts;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our drugs;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European Union requirements regarding safety monitoring, or pharmacovigilance, and with requirements related to the development of drugs 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.

Even though we have received orphan drug designation in the European Union for our most advanced product candidate, Zuprata for the treatment of macular edema associated with non-infectious uveitis, we may not be able to obtain orphan drug marketing exclusivity for this product candidate.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. We have received orphan drug designation from the EMA for Zuprata for the treatment of macular edema associated with non-infectious uveitis, and we may seek orphan drug designation from the FDA or EMA for our future drug candidates. However, we do not plan to pursue orphan drug designation from the FDA for this product candidate.

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 this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. In addition, the period of market exclusivity may be reduced to six years if it can be demonstrated based on available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity. There is no guarantee that we will be able to obtain or maintain orphan exclusivity for Zuprata even if we receive marketing authorization for Zuprata in Europe.

Our employees, independent contractors, principal investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct or failure to comply with applicable regulatory requirements. Misconduct by employees and independent contractors, such as principal investigators, CROs, consultants, commercial partners and vendors, could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including, but not limited to, research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee and independent contractor misconduct could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in

regulatory sanctions and serious harm to our reputation. In addition, federal procurement laws impose substantial penalties for misconduct in connection with government contracts and require certain contractors to maintain a code of business ethics and conduct. It is not always possible to identify and deter employee and independent contractor misconduct, and any precautions we take to detect and prevent improper activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate.

Our current and future relationships with healthcare professionals, principal investigators, consultants, customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, physician payment transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to penalties.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we sell, market and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy and security regulation by the federal government and by the states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which 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, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws, including the federal False Claims Act, which impose 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, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the civil monetary penalties statute, which imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully

embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on "covered entities," including healthcare providers, health plans, and healthcare clearinghouses, as well as their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the Physician Payments Sunshine Act, created under Section 6002 of Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, and its implementing regulations, imposed annual reporting requirements for certain manufacturers of drugs, devices, biologicals and medical supplies for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties of up to an aggregate of $150,000 per year and up to an aggregate of $1.0 million per year for "knowing failures," for an aggregate potential annual liability of $1,150,000; and
- analogous state and foreign laws, such as state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or to adopt compliance programs as prescribed by state laws and regulations, or that otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report pricing and marketing information, payments and other transfers of value to physicians and other healthcare providers, or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Further, the Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the Affordable Care Act provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Efforts to ensure that our future business arrangements with third parties will comply with applicable healthcare laws and regulations may 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. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could significantly harm our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including future

collaborators, are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also affect our business.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we 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 ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, President Obama signed into law the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the Affordable Care Act of importance to our potential product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- a 2.3% medical device excise tax on certain transactions, including many U.S. sales of medical devices and drug and device combination products, which, under the Consolidated Appropriations Act, 2016, is suspended from January 1, 2016 to December 31, 2017, and, absent further legislative action, will be reinstated starting January 1, 2018;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- 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;
- 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 covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain

individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- the transparency reporting requirements under the federal Physician Payments Sunshine Act and its implementing regulations;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future, particularly in light of the pending change in administrations following the U.S. presidential election.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to the Bipartisan Budget Act of 2015, will stay in effect through 2025 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, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could negatively impact customers for our product candidates, if approved, and, accordingly, our financial operations. There has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

We expect that 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. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

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

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

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can

take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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

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

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

Risks related to this offering and ownership of our common stock

An active trading market for our common stock may not continue to develop or be sustained.

Prior to June 2, 2016, there was no public market for our common stock, and we cannot assure you that an active trading market will continue to develop or be sustained. If an active market for our common stock does not continue to develop or be sustained, it may be difficult for you to sell your shares without depressing the market price for your shares or to sell your shares at all.

The trading price of the shares of our common stock may be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has been and may continue to be volatile. Since our IPO, our common stock has traded at prices between $5.65 and $25.08 per share. The stock market in general and the market for biopharmaceutical 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, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- actual or anticipated variations in our operating results;

- changes in financial estimates by us or by any securities analysts who might cover our stock;
- conditions or trends in our industry;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- capital commitments;
- investors' general perception of us and our business;
- recruitment or departure of key personnel; and
- sales of our common stock, including sales by our directors and officers or specific stockholders.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. As a newly public company, we have only limited research coverage by equity research analysts. Equity research analysts may elect not to initiate or to continue to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. Even if we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

If you purchase shares of our common stock in this offering, you will suffer immediate dilution of your investment.

The public offering price of our common stock in this offering is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. Based on the public offering price of $9.00 per share, you will experience immediate dilution of $5.73 per share, representing the difference between our as adjusted net tangible book value per share after giving effect to this offering.

In addition, after this offering, we will have outstanding:

- stock options to purchase an aggregate of 1,414,594 shares of common stock at a weighted average exercise price of $2.90 per share; and

- warrants to purchase an aggregate of 55,770 shares of our common stock at a weighted average exercise price of $9.32 per share.

To the extent these outstanding options and warrants are exercised, there will be further dilution to investors in this offering.

The issuance of additional stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

Our certificate of incorporation authorizes us to issue up to 100,000,000 shares of common stock and up to 10,000,000 shares of preferred stock with such rights and preferences as may be determined by our board of directors. Subject to compliance with applicable rules and regulations, we may issue our shares of common stock or securities convertible into our common stock from time to time in connection with a financing, acquisition, investment, our stock incentive plans or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and cause the trading price of our common stock to decline.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to 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. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

Upon completion of this offering, based on the number of shares outstanding as of September 30, 2016, we will have 24,545,752 shares of common stock outstanding, assuming no exercise of outstanding options or warrants. Of these shares, approximately 9.5 million shares are, and the 4,000,000 shares sold in this offering will be, freely tradable. An additional 6.5 million shares are subject to a contractual lock-up with the underwriters for this offering for periods of up to 90 days following this offering. These shares can be sold, subject to any applicable volume limitations under federal securities laws, after the earlier of the expiration of, or release from, the lock-up period.

In addition, we filed a registration statement on Form S-8 registering the issuance of approximately 3.3 million shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. These registered shares will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements described above and, in the case of our affiliates, the restrictions of Rule 144.

Additionally, holders of an aggregate of approximately 9.6 million shares of our common stock, or their transferees, have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors are elected each year;
- stockholders are not entitled to remove directors other than by a 66 2/3% vote and only for cause;
- stockholders are not permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and

- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) ending December 31, 2021, which is the end of the fiscal year following the fifth anniversary of the completion of our recent IPO, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, the Sarbanes-Oxley Act and the rules and regulations of The NASDAQ Stock Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Commencing with our fiscal year ending December 31, 2017, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. To date, we have never been required to test our internal controls within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by The NASDAQ Stock Market, the Securities and Exchange Commission or other regulatory authorities.

We will have broad discretion in the use of proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not increase the value of your investment.

We have broad discretion over the use of proceeds from this offering. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. We anticipate that the majority of the net proceeds from this offering will be used to complete our pivotal Phase 3 clinical trial of suprachoroidal Zuprata for the treatment of macular edema associated with non-infectious uveitis, to initiate our Phase 3 clinical program of suprachoroidal Zuprata with an intravitreal anti-VEGF agent, Eylea, for the treatment of macular edema associated with RVO, to complete our ongoing Phase 1/2 clinical trial of Zuprata, alone or with Eylea, for the treatment of DME and to initiate and complete a planned Phase 1/2 clinical trial of axitinib for the treatment of wet AMD. The remaining proceeds will be used for the continued research and development of our earlier-stage programs, and for working capital and general corporate purposes. Our failure to apply the net proceeds from this offering effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these net proceeds. You will not have the opportunity to influence our decisions on how to use our net proceeds from this offering.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, our loan and security agreement with SVB and the entities affiliated with MidCap Financial Services currently prohibits us from paying dividends without the consent of the lenders under the agreement, and the terms of any future debt agreements may likewise preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

We plan to use potential future operating losses and our federal and state NOL carryforwards to offset future taxable income, if any. However, our ability to use existing NOL carryforwards could be limited as a result of issuances of equity securities.

As of December 31, 2015, we had approximately $36.6 million of federal and $44.9 million of state net operating loss, or NOL, carryforwards. If not utilized, these federal NOL carryforwards will begin to expire at various dates beginning in 2031, and these state NOL carryforwards will begin to expire at various dates beginning in 2027. To the extent we generate taxable income in the future, we plan to use our existing NOL carryforwards and future losses to offset income that would otherwise be taxable. However, under Section 382 of the U.S. Internal Revenue Code of 1986, as amended, as interpreted by the U.S. Internal Revenue Service, the amount of benefits from our NOL carryforwards may be impaired or limited if we incur a cumulative ownership change of more than 50% over a three-year period. The completion of this offering, our recent IPO, private placements and other transactions that have occurred, and future offerings of our securities may trigger, or may have already triggered, such an ownership change. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. We have not conducted an analysis as to whether such a change of ownership has occurred, but if such a change has occurred or occurs in the future, we will be limited regarding the amount of NOL carryforwards that can be utilized annually in the future to offset taxable income. Any such annual limitation may significantly reduce the value of our NOL carryforwards before they expire, which could result in greater tax liabilities than we would incur in the absence of such a limitation.

We have begun to incur increased costs and demands upon management as a result of being a public company.

As a public company listed in the United States, we have begun to incur significant additional legal, accounting and other costs. We estimate the additional costs we will incur as a result of being a public company to be approximately $1.5 million to $2.5 million annually. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and The NASDAQ Stock Market, may increase legal and financial compliance costs and make some activities more time consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities.

If, notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed. Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

Special note regarding forward-looking statements and industry data

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” but are also contained elsewhere in this prospectus. In some cases, you can identify forward-looking statements by the words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue” and “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

- our plans to develop and commercialize our product candidates;
- our ongoing and planned clinical trials for our product candidates;
- the timing of the availability of data from our clinical trials;
- the timing of our planned regulatory filings;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- our expectation that Zuprata, if approved, would be the first drug specifically indicated for macular edema associated with non-infectious uveitis;
- the clinical utility of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional drug candidates with significant commercial potential that are compatible with suprachoroidal injection and which are consistent with our commercial objectives; and
- our estimates regarding future revenues, expenses and needs for additional financing.

You should refer to the “Risk Factors” section of this prospectus for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding

that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

Use of proceeds

We estimate that the net proceeds from our issuance and sale of 4,000,000 shares of our common stock in this offering will be $33.2 million, or $38.3 million if the underwriters exercise their option to purchase additional shares in full, based upon the public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We anticipate that the majority of the net proceeds from this offering will be used to complete our pivotal Phase 3 clinical trial of suprachoroidal Zuprata for the treatment of macular edema associated with non-infectious uveitis, to initiate our Phase 3 clinical program of suprachoroidal Zuprata with an intravitreal anti-VEGF agent, Eylea, for the treatment of macular edema associated with RVO, to complete our ongoing Phase 1/2 clinical trial of Zuprata, alone or with Eylea, for the treatment of DME and to initiate and complete a planned Phase 1/2 clinical trial of axitinib for the treatment of wet AMD. The remainder may be used to fund continued research and development of our earlier-stage programs, including drug discovery for potential new applications for our suprachoroidal microinjection technology, and for working capital and other general corporate purposes.

In the ordinary course of our business, we expect to from time to time evaluate the acquisition of, investment in or in-license of complementary products, technologies or businesses, and we could use a portion of the net proceeds from this offering for such activities. We currently do not have any agreements, arrangements or commitments with respect to any potential acquisition, investment or license.

Based on the planned use of proceeds described above, we believe that the net proceeds from this offering and our current cash and cash equivalents will be sufficient to enable us to fund our operating expenses and capital expenditure requirements for at least the next 18 months. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. Predicting the cost necessary to develop product candidates can be difficult and we anticipate that we will need additional funds to complete our planned Phase 3 clinical program for Zuprata in RVO patients. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs.

Our management will have broad discretion in the application of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business. Pending these uses, we plan to invest these net proceeds in short-term, interest bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States. The goal with respect to the investment of these net proceeds is capital preservation and liquidity so that such funds are readily available to fund our operations.

Market price of common stock

Our common stock commenced trading on The NASDAQ Global Market under the symbol “CLSD” on June 2, 2016. The following table sets forth, for the periods indicated, the high and low reported sales prices of our common stock as reported on The NASDAQ Global Market:

	High	Low
2016		
Second quarter (from June 2, 2016)	$ 8.45	$ 6.67
Third quarter	$18.20	$ 5.65
Fourth quarter (through December 8, 2016)	$25.08	$11.27

As of December 5, 2016, there were 64 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities. The last reported sale price of our common stock on The NASDAQ Global Market on December 8, 2016 was $11.53 per share.

Dividend policy

We have never declared or paid any dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying cash dividends in the foreseeable future. Additionally, our ability to pay dividends on our common stock is limited by restrictions under the terms of the agreements governing our credit facility.

Capitalization

The following table sets forth our cash and cash equivalents, long-term debt and our capitalization as of September 30, 2016:

- on an actual basis; and
- on an as adjusted basis to give effect to our sale of 4,000,000 shares of common stock in this offering at the public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes appearing elsewhere in this prospectus.

	As of September 30, 2016	
	Actual	As adjusted
	(in thousands, except share and per share data)	
Cash and cash equivalents	$ 36,876	$ 70,116
Long-term debt, including current portion	$ 7,489	$ 7,489
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized and no shares issued and outstanding, actual and as adjusted	$ —	$ —
Common stock, $0.001 par value; 100,000,000 shares authorized and 20,545,752 shares issued and outstanding, actual; 100,000,000 shares authorized and 24,545,752 shares issued and outstanding, as adjusted	21	25
Additional paid-in capital	102,481	135,721
Accumulated deficit	(55,559)	(55,559)
Accumulated other comprehensive loss	(5)	(5)
Total stockholders' equity	46,938	80,178
Total capitalization	$ 54,427	$ 87,667

The number of shares of common stock outstanding in the table above does not include:

- 1,414,594 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2016, at a weighted average exercise price of $2.90 per share;
- 55,770 shares of our common stock issuable upon the exercise of warrants outstanding as of September 30, 2016 at a weighted average exercise price of $9.32 per share;
- 1,842,500 shares of our common stock reserved for future issuance under our equity incentive plans following this offering; and
- any additional shares that may be reserved for future issuance under our equity incentive plans as a result of automatic annual increases in the share reserves beginning on January 1, 2017.

Dilution

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share of our common stock immediately after this offering. Net tangible book value per share is determined by dividing our total tangible assets less total liabilities by the number of outstanding shares of our common stock.

As of September 30, 2016, our net tangible book value was $46.9 million, or $2.28 per share of common stock.

Investors participating in this offering will incur immediate and substantial dilution. After giving effect to the issuance and sale of 4,000,000 shares of our common stock in this offering at the public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2016 would have been $80.2 million, or $3.27 per share of common stock. This represents an immediate increase in the net tangible book value of $0.98 per share to existing stockholders, and an immediate dilution in the net tangible book value of $5.73 per share to investors purchasing shares of our common stock in this offering. The following table illustrates this per share dilution to new investors:

Public offering price per share		$9.00
Actual net tangible book value per share as of September 30, 2016	$2.28	
Increase in net tangible book value per share attributable to new investors participating in this offering	0.98	
As adjusted net tangible book value per share after this offering		3.27
Dilution per share to investors participating in this offering		$5.73

If the underwriters exercise their option in full to purchase 600,000 additional shares of common stock in this offering, the as adjusted net tangible book value per share after the offering would be $3.39 per share, the increase in the as adjusted net tangible book value per share to existing stockholders would be $1.11 per share and the dilution to new investors purchasing common stock in this offering would be $5.61 per share.

The shares of our common stock reserved for future issuance under our equity benefit plans may be subject to automatic annual increases in accordance with the terms of the plans. To the extent that options or warrants are exercised, new options or other equity awards are issued under our equity incentive plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

Selected financial data

The following tables set forth our selected financial data for the periods indicated. The following selected statement of operations data for the years ended December 31, 2014 and 2015 and the selected balance sheet data as of December 31, 2014 and 2015 are derived from our audited financial statements appearing elsewhere in this prospectus. The selected statement of operations data for the nine months ended September 30, 2015 and 2016 and the selected balance sheet data as of September 30, 2016 are derived from unaudited interim financial statements appearing elsewhere in this prospectus. The data should be read together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in conjunction with the financial statements, related notes, and other financial information included elsewhere in this prospectus.

The unaudited interim financial statements include all adjustments, consisting of normal recurring adjustments, that we consider necessary for a fair presentation of our financial position and results of operations for these periods. Our historical results are not necessarily indicative of the results to be expected in the future, and our operating results for the nine months ended September 30, 2016 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 2016 or any other future period.

	Year Ended December 31,		Nine Months Ended September 30,	
	2014	2015	2015	2016
	(in thousands, except share and per share data)			
Statement of Operations Data:				
License revenue	$ —	$ —	$ —	$ 515
Operating expenses:				
Research and development	6,692	10,762	6,964	12,484
General and administrative	3,131	6,555	5,337	3,872
Total operating expenses	9,823	17,317	12,301	16,356
Loss from operations	(9,823)	(17,317)	(12,301)	(15,841)
Other income (expense):				
Interest expense	(371)	(330)	(174)	(432)
Interest income	5	8	6	77
Total other expense	(366)	(322)	(168)	(355)
Net loss	$ (10,189)	$ (17,639)	$ (12,469)	$ (16,196)
Net loss per share of common stock—basic and diluted	$ (5.86)	$ (7.54)	$ (5.59)	$ (1.54)
Weighted average shares outstanding—basic and diluted	1,738,660	2,338,950	2,231,830	10,502,459

	As of December 31,		As of September 30,
	2014	2015	2016
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 8,269	$ 20,283	$ 36,876
Short-term investments	—	—	20,043
Total assets	10,299	21,055	57,771
Long-term debt (includes current portion)	—	5,976	7,489
Total liabilities	2,677	10,400	10,833
Total stockholders' (deficit) equity	(19,213)	(36,659)	46,938

Management's discussion and analysis of financial condition and results of operations

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes and other financial information included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" section of this prospectus 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 late-stage clinical biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye. Our current product candidates focus on diseases affecting the retina, which is the tissue that lines the inside of the eye and is primarily responsible for vision, and the choroid, especially diseases associated with macular edema, and are injected into the suprachoroidal space, or SCS, adjacent to the choroid, which is the layer adjacent to the retina that supplies the retina with blood, oxygen and nourishment. With our proprietary microinjector, drugs are injected into and spread within and through the suprachoroidal space, or SCS, which is the space located between the choroid and the outer protective layer of the eye known as the sclera. With the suprachoroidal injection, our product candidates are more directly administered to the retina and choroid as compared to other ocular drug administration techniques such as injections of drug into the vitreous, a jelly-like substance that occupies the central portion of the eye. Intravitreal injections rely on diffusion of drug outward from the vitreous to the retina and choroid. This diffusion can result in lower concentrations of drug in these targeted areas. At the same time, this diffusion can also result in drug spreading to unintended parts of the eye, where, for some drugs, it can cause significant side effects. We believe treatment of eye disease via suprachoroidal injection may provide a number of benefits, including lower frequency of necessary administration and faster onset of therapeutic effect. We hold the exclusive rights to develop and commercialize drugs for treatment via injection into the SCS.

Our most advanced product candidates are based on commonly used ophthalmic drugs, which we believe will allow us to more efficiently and predictably pursue the regulatory approval of these product candidates under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act. Under Section 505(b)(2), if we can establish that reliance on the Food and Drug Administration's, or FDA's, previous findings of safety and effectiveness for an approved product is scientifically appropriate, or there is scientific literature to support the product's safety or effectiveness, or both, it may eliminate the need for us to conduct some of the preclinical studies or clinical trials for the new product candidate that might otherwise have been required.

Our current and planned development programs aim to restore or improve visual function primarily by reducing the macular edema associated with a number of diseases affecting the retina and choroid. We are developing Zuprata, a proprietary, preservative-free formulation of the corticosteroid triamcinolone acetonide, or TA, for the treatment of macular edema associated with non-infectious uveitis. We are currently enrolling patients with macular edema associated with non-infectious uveitis in a pivotal Phase 3 clinical trial. We expect to enroll approximately 150 patients in this trial and to report preliminary results from the trial in late 2017 or early 2018. We believe, based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, that only one, Clearside-sponsored, Phase 3 clinical trial will be required to support the potential filing of a New Drug Application, or NDA, with the FDA.

We are also developing Zuprata along with an anti-VEGF agent for the treatment of macular edema associated with retinal vein occlusion, or RVO, a sight-threatening disorder resulting from the blockage of a retinal vein. We are exploring whether a suprachoroidal injection of Zuprata and a concomitant intravitreal injection of Eylea (aflibercept), an inhibitor of vascular endothelial growth factor, or VEGF, can provide improved visual acuity, reduced macular edema and reduced injection frequency as compared to administration of intravitreal Eylea alone.

We have completed a Phase 2 clinical trial in 46 patients with macular edema associated with RVO. In this trial, 23 patients in the active arm initially received a single concomitant suprachoroidal injection of Zuprata and an intravitreal injection of Eylea and 23 patients in the control arm initially received only an intravitreal injection of Eylea. The objective of the trial was to determine whether patients receiving Zuprata together with Eylea could sustain improved visual acuity over the three months of the clinical trial while requiring fewer additional Eylea treatments than patients receiving intravitreal Eylea alone. Based on the results of this trial and after incorporating feedback from a recent end-of-Phase 2 meeting with the FDA, we intend to commence a Phase 3 clinical program in RVO in the first half of 2017.

We have recently expanded our Zuprata development programs to include another retinal vascular condition known as diabetic macular edema, or DME. DME is a common ocular complication of diabetes that results in swelling in the macula and is the primary cause of vision loss associated with diabetes. In November 2016, we began enrolling patients with DME in a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal Zuprata, as well as suprachoroidal Zuprata alone, over a six-month evaluation period. We expect to enroll approximately 20 patients in this trial and to report preliminary results in the second half of 2017.

We are developing another product candidate, a proprietary injectable suspension formulation of the compound axitinib, to be administered suprachoroidally for the treatment of neovascular age-related macular degeneration, or wet AMD. Axitinib has activity against both VEGF receptors and receptors of platelet derived growth factor, or PDGF. We believe that suprachoroidal injection of axitinib could be more effective than current treatments for wet AMD, which consist primarily of anti-VEGF agents injected intravitreally. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.

If any of our product candidates are approved, we plan to commercialize them with a specialty team of 30 to 40 sales and medical marketing professionals to target the approximately 1,700 retinal specialists in the United States, and we may also pursue collaborations with third parties to commercialize any of our drugs approved for marketing outside the United States.

We have incurred net losses since our inception in May 2011. Our operations to date have been limited to organizing and staffing our company, raising capital, undertaking preclinical studies and other research and development initiatives and, beginning in 2013, conducting clinical trials of our most advanced drug candidates. To date, we have not generated any revenue, other than license revenue, and we have primarily financed our operations through our recent initial public offering, or IPO, private placement of our equity securities, issuance of convertible promissory notes and loan agreements. We have raised net cash proceeds of $51.4 million from the sale of common stock, $44.5 million from the sale of convertible preferred stock, $3.4 million from the sale of convertible promissory notes and $8.0 million from long-term loan agreements through September 30, 2016. As of September 30, 2016, we had an accumulated deficit of $55.6 million. We recorded net losses of $16.2 million and $17.6 million for the nine months ended September 30, 2016 and the year ended December 31, 2015, respectively. We anticipate that a substantial portion of our capital resources and efforts in the foreseeable future will be focused on completing the necessary development for and obtaining regulatory approval and preparing for potential commercialization of our product candidates.

We expect to continue to incur significant and increasing operating losses at least for the next several years. We do not expect to generate product revenue unless and until we successfully complete necessary development for, and obtain regulatory approval for one or more of our product candidates. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials and our expenditures on other research and development activities. We anticipate that our expenses will increase substantially as we:

- complete our ongoing Phase 3 clinical trial for Zuprata for the treatment of macular edema associated with non-infectious uveitis and our ongoing Phase 1/2 clinical trial of Zuprata for the treatment of DME, as well as future clinical trials, as necessary;
- initiate our planned Phase 3 clinical program for Zuprata for the treatment of macular edema associated with RVO and our planned Phase 1/2 clinical trial of axitinib for the treatment of wet AMD, as well as future clinical trials for these programs, as necessary;
- seek to discover, research and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials and other developmental efforts necessary to seek such approvals;
- establish sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any product candidates for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our development and potential future commercialization efforts; and
- operate as a public company.

Components of operating results

Revenue

We have not generated any revenue from the sale of any drugs, and we do not expect to generate any revenue unless or until we obtain regulatory approval of and commercialize our product candidates. The only revenue we have derived, consisting primarily of $0.5 million in the first quarter of 2016, has been from up-front payments in connection with out-licensing our proprietary microinjection technology for suprachoroidal drug administration to third-party strategic collaborators. In 2014, we executed a license agreement with NovaMedica LLC, or NovaMedica, and in 2015, we executed a license agreement with Spark Therapeutics, Inc., or Spark. In connection with these agreements, we received up-front payments of $200,000 from NovaMedica and $500,000 from Spark. We deferred recognizing these payments through 2015. In the first quarter of 2016, we began recognizing revenue related to the NovaMedica payment and we recognized the entire payment from Spark.

Research and development

Since our inception, we have focused on our development programs. Research and development expenses consist primarily of costs incurred for the research and development of our preclinical and clinical product candidates, which include:

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense for research and development personnel;

- expenses incurred under agreements with contract research organizations, or CROs, as well as contract manufacturing organizations and consultants that conduct clinical trials and preclinical studies;
- costs associated with preclinical activities and development activities;
- costs associated with technology and intellectual property licenses;
- costs for our research and development facility; and
- depreciation expense for assets used in research and development activities.

We expense research and development costs to operations as incurred. The costs for some of our development activities, such as clinical trials, are recognized based on the terms of underlying agreements, as well as an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations and additional information provided to us by our vendors about their actual costs occurred.

Expenses related to activities, such as manufacturing and stability and toxicology studies, that are supportive of a product candidate itself, are classified as direct non-clinical costs. Expenses related to clinical trials and similar activities, including costs associated with CROs, are classified as direct clinical costs. Expenses related to activities that support more than one development program or activity, such as salaries, share-based compensation and depreciation, are not classified as direct clinical costs or non-clinical costs and are separately classified as unallocated.

For the nine months ended September 30, 2016, substantially all of our research and development expenses have been related to the non-clinical and clinical development of our product candidates. From inception through September 30, 2016, we have incurred $37.5 million in research and development expenses.

The following table shows our research and development expenses by development program and type of activity for the years ended December 31, 2014 and 2015, the nine months ended September 30, 2015 and 2016, and the period from May 26, 2011 (date of inception) to September 30, 2016.

	Year Ended December 31,		Nine Months Ended September 30,		Period from May 26, 2011 (Date of Inception) to September 30, 2016
	2014	2015	2015	2016	
	(in thousands)				
Zuprata (uveitis program):					
Direct non-clinical	$1,617	$ 722	$ 516	$ 1,579	$ 6,170
Direct clinical	828	3,155	1,135	3,747	7,903
Total	2,445	3,877	1,651	5,326	14,073
Axitinib (wet AMD program):					
Direct non-clinical	251	1,256	968	2,507	4,167
Direct clinical	6	3	—	—	176
Total	257	1,259	968	2,507	4,343
Zuprata (RVO program):					
Direct non-clinical	102	20	2	1	168
Direct clinical	633	1,442	1,051	1,582	3,657
Total	735	1,462	1,053	1,583	3,825
Unallocated	3,255	4,164	3,292	3,068	15,303
Total research and development expense	$6,692	$10,762	$ 6,964	$ 12,484	$ 37,544

Our expenses related to clinical trials are based on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for the services received and efforts expended under contracts with research institutions, consultants and CROs that conduct and manage clinical trials on our behalf. We generally accrue expenses related to clinical trials based on contracted amounts applied to the level of patient enrollment and activity according to the protocol. If future timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we would modify our estimates of accrued expenses accordingly on a prospective basis. Historically, any such modifications have not been material.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect our research and development expenses to increase over the next several years as we progress our product candidates through clinical development. However, it is difficult to determine with certainty the duration and completion costs of our current or future preclinical programs and clinical trials of our product candidates, or if, when or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors that include, but are not limited to, the following:

- number of trials required for approval and any requirement for extension trials;
- per patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up; and
- the efficacy and safety profiles of the product candidates.

In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. We will determine which programs to pursue and how much to fund each program in response to the scientific and clinical success of each product candidate, as well as an assessment of each candidate's commercial potential.

General and administrative

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in executive, finance and administrative functions. General and administrative costs include facility related costs not otherwise included in research and development expenses, professional fees for legal, patent, consulting, and accounting and audit services.

We anticipate that our general and administrative expenses will increase in the future to support our continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses.

Additionally, we anticipate increased costs associated with being a public company including expenses related to services associated with maintaining compliance with NASDAQ listing rules and SEC requirements, director and officer insurance, and investor and public relations costs.

Other income (expense)

Other income consists of interest income earned on our cash, cash equivalents and short-term investments. Interest income is not considered significant to our financial statements, but we expect our interest income to increase as we invest the net proceeds from our IPO pending their use in operations.

Other expense consists of interest accrued under promissory notes and the loan agreements and changes in the value of the stock purchase warrant liability described in the footnotes to our financial statements.

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 have been prepared in accordance with accounting principles generally accepted in the United States of America, or U.S. GAAP. The preparation of these financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the dates of the balance sheets and the reported amounts of expenses during the reporting periods. In accordance with U.S GAAP, we evaluate our estimates and judgments on an ongoing basis. Significant estimates include assumptions used in the determination of share-based compensation and some of our research and development expenses. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. While our significant accounting policies are more fully described in Note 2 to our financial statements appearing elsewhere in this prospectus, we believe the following are the critical accounting policies used in the preparation of our financial statements that require significant estimates and judgments.

Accrued expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable vendor personnel to identify 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 actual cost. 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. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued expenses include fees paid to CROs and investigative sites in connection with clinical trials.

We accrue our expenses related to clinical trials based on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct research activities or manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary

from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the level of effort varies from our estimate, we will adjust the accrual accordingly. If we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. Although we do not currently anticipate the future settlement of existing accruals to differ materially from our estimates, 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 for any period. There have been no material changes in estimates for the periods presented in our financial statements.

Fair value measurements

We record some of our financial assets and liabilities at fair value in accordance with the provisions of Accounting Standards Codification, or ASC, Topic 820 on fair value measurements. As defined in the guidance, fair value, defined as an exit price, represents the amount that would be received to sell an asset or pay to transfer a liability in an orderly transaction between market participants. As a result, fair value is a market-based approach that should be determined based on assumptions that market participants would use in pricing an asset or a liability. As a basis for considering these assumptions, the guidance defines a three-tier value hierarchy that prioritizes the inputs used in the valuation methodologies in measuring fair value.

- Level 1—Unadjusted quoted prices in active, accessible markets for identical assets or liabilities.
- Level 2—Other inputs that are directly or indirectly observable in the marketplace.
- Level 3—Unobservable inputs that are supported by little or no market activity.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

Our material financial instruments at December 31, 2014 and 2015 and September 30, 2016 consisted primarily of cash and cash equivalents, long-term debt and stock purchase warrant liabilities. The fair value of cash and cash equivalents, other current assets and accounts payable approximate their respective carrying values due to the short term nature of these instruments. The fair value of long-term debt approximates the carrying value due to variable interest rates that correspond to market rates. We have determined our short-term investments, comprised of certificates of deposit, corporate bonds and government bonds and agency obligations, to be Level 2 in the fair value hierarchy. The fair value was determined using a market approach, based on prices and other relevant information generated by market transactions involving similar assets. The short-term investments consist of investments with original maturity dates from date of acquisition of 90 to 365 days and are classified as available-for-sale. We have determined our stock purchase warrants liability to be Level 3 in the fair value hierarchy.

Share-based compensation

We recognize compensation costs related to stock options and restricted stock granted to employees, directors and consultants ratably over the requisite service period, which in most cases is the vesting period of the award for employees, based on the estimated fair value of the awards on the date of grant. Compensation expense for options granted to non-employees is determined as the fair value of consideration received or the fair value of the equity instruments issued, whichever is more reliably measured. The fair value of the awards granted to non-employees is re-measured each period until the related service is complete.

Share-based compensation expense was $0.4 million and $0.7 million for the years ended December 31, 2014 and 2015, respectively, and $0.5 million and $0.8 million for the nine months ended September 30, 2015 and 2016, respectively.

Significant factors, assumptions and methodologies used in determining fair value

Determining the appropriate fair value measurement of share-based awards requires the use of subjective assumptions. Prior to our initial public offering, or IPO, we conducted retrospective assessments and contemporaneous valuations of our common stock. The determination of the fair value measurement of options using the Black-Scholes option pricing model is affected by our estimated common stock fair values as well as assumptions regarding a number of other subjective variables. These other variables include the expected term of the options, our expected stock price volatility over the expected term of the options, stock option exercise and cancellation behaviors, risk-free interest rates and expected dividends.

We estimated the fair value of stock options at the grant date using the following assumptions:

- *Fair value of our common stock.* Prior to the IPO, no public market existed for our stock, and we estimated its fair value, as discussed in "—Pre-IPO Common Stock Valuations" below. For stock options granted after June 1, 2016, the date of our IPO, we estimate the fair value of our common stock by reference to the closing price of our common stock on The NASDAQ Global Market on the date of grant.
- *Volatility.* As we do not have a trading history for our common stock, we utilize data from a representative group of publicly traded companies to estimate expected stock price volatility. We selected representative companies from the pharmaceutical industry with similar characteristics to us, including stage of product development and therapeutic focus.
- *Expected term.* We used the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, as we do not have sufficient historical exercise and post-vesting termination data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees.
- *Risk-free rate.* The risk-free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected time to liquidity.
- *Forfeitures.* Forfeitures are estimated such that we only recognize expense for the shares expected to vest, and adjustments are made if actual forfeitures differ from those estimates. We have estimated our forfeiture rates to be zero for the periods presented in this prospectus.
- *Dividend yield.* We have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future.

The table below lists the weighted average assumptions utilized in the Black-Scholes option pricing model for the years ended December 31, 2014 and 2015 and the nine months ended September 30, 2016.

	Year Ended December 31,		Nine Months Ended September 30,	
	2014	2015	2015	2016
Expected term (years)	7.00	7.00	7.00	7.00
Expected stock price volatility	85.64%	86.63%	89.00%	94.49%
Risk-free interest rate	1.99%	2.09%	2.04%	1.40%
Dividend yield	0.00%	0.00%	0.00%	0.00%

The estimation of the number of stock awards that will ultimately vest requires judgment, and to the extent actual results or updated estimates differ from our current estimates, such amounts will be recorded as a cumulative adjustment in the period in which estimates are revised.

Pre-IPO common stock valuations

Prior to our IPO, our common stock valuations were determined by our board of directors in its sole discretion based on recommendations from management and, beginning in 2014, taking into account advice and assistance provided by a third-party valuation consultant engaged to assist us in connection with such valuations. The valuations of our common stock were determined utilizing guidelines outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

Our common stock valuations were performed using a hybrid method, which used market approaches to estimate our enterprise value. We selected the hybrid method based on the availability and the quality of information to develop the assumptions for the methodology. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more of the scenarios is calculated using an option-pricing method, or OPM. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. Under this method, the common stock value is based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available, as well as the rights of each class of stock. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the preferred stock liquidation preference at the time of a liquidity event, such as a strategic sale or merger.

In the hybrid method used in each of our third-party valuations, we considered several future event scenarios, including various OPM scenarios and IPO scenarios. The relative probability of each type of future event scenario was based on our analysis of market conditions at the time, including then-current IPO valuations of similarly situated companies and expectations as to the timing and likely prospects of the future event scenarios. To determine our enterprise values under the OPM scenarios, we used the OPM backsolve approach. To determine our enterprise values under the IPO scenarios, we used the guideline public company method under the market approach, which analyzed enterprise values at the IPO date of publicly traded biopharmaceutical companies. To derive the fair value of the common stock for each future event scenario under the hybrid method, the proceeds to the common stockholders were calculated based on the conversion rights and preferences of the preferred stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

There are significant judgments and estimates inherent in these valuations. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an initial public offering or other liquidity event and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per common share could have been significantly different.

Tax valuation allowance

We recorded deferred tax assets of $15.7 million, related to our net operating losses, as of December 31, 2015, which have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize

these tax benefits. We record a valuation allowance if it is more likely than not that a deferred tax asset will not be realized. We provided a full valuation allowance on our deferred tax assets that primarily consist of cumulative net operating losses, or NOLs, of $36.6 million for the period from our inception on May 26, 2011 to December 31, 2015. We incurred a net loss for tax purposes of $16.1 million for the year ended December 31, 2015. Due to our three-year cumulative loss position, history of operating losses and losses expected to be incurred in the foreseeable future, we considered it necessary to provide for a full valuation allowance against our net deferred tax assets.

Our deferred tax assets are primarily composed of federal and state tax NOL carryforwards. As of December 31, 2015, we had federal NOL carryforwards of $36.6 million and state NOL carryforwards of $44.9 million available to reduce future taxable income, if any. These federal NOL carryforwards will begin to expire at various dates starting in 2031. The state NOL carryforwards will begin to expire at various dates starting in 2027. In general, if we experience a greater than 50 percentage point aggregate change in ownership of specified significant stockholders over a three-year period, utilization of our pre-change NOL carryforwards will be subject to an annual limitation under Section 382 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and similar state laws. Such limitations may result in expiration of a portion of the NOL carryforwards before utilization and may be substantial. If we experience a Section 382 ownership change in connection with this offering or as a result of future changes in our stock ownership, some of which changes are outside our control, the tax benefits related to the NOL carryforwards may be further limited or lost.

Results of operations for the nine months ended September 30, 2015 and 2016

The following table sets forth our results of operations for the nine months ended September 30, 2015 and 2016.

	Nine Months Ended September 30,		Period-to-Period Change
	2015	2016	
	(in thousands)		
License revenue	$ —	$ 515	$ 515
Operating expenses:			
Research and development	6,964	12,484	5,520
General and administrative	5,337	3,872	(1,465)
Total operating expenses	12,301	16,356	4,055
Loss from operations	(12,301)	(15,841)	(3,540)
Other expense	(168)	(355)	(187)
Net loss	$(12,469)	$(16,196)	$ (3,727)

Revenue. In the nine months ended September 30, 2016, we recognized $0.5 million of revenue associated with our license agreement with NovaMedica and the license and collaboration agreement with Spark. We did not recognize any revenue in the nine months ended September 30, 2015.

Research and development. Research and development expense increased from $7.0 million for the nine months ended September 30, 2015 to $12.5 million for the nine months ended September 30, 2016, an increase of $5.5 million, or 79%. This increase was primarily attributable to a $3.1 million increase in costs related to the ongoing Phase 3 clinical for Zuprata for the treatment of macular edema associated with non-infectious uveitis, a $0.4 million increase in costs for the Phase 2 clinical trial for Zuprata in RVO patients, a $1.1 million increase in device manufacturing costs and a $0.4 million increase in costs associated with the pre-clinical studies of axitinib for wet AMD. We also incurred increased personnel and related costs of $0.1 million during the nine months ended September 30, 2016 as compared to the same period in 2015.

General and administrative. General and administrative expenses decreased by $1.5 million, or 27%, from $5.3 million for the nine months ended September 30, 2015 to $3.9 million for the nine months ended September 30, 2016. The decrease was primarily attributable to recognizing $1.9 million of expenses related to previously deferred offering costs in the 2015 period and a $0.2 million decrease in professional fees in the nine months ended September 30, 2016 compared to the prior year period. This was partially offset by an increase of $0.3 million of employee-related costs, a $0.1 million increase for marketing expenses and a $0.3 million increase in the costs of operating as a public company, including an increase in director and officer insurance premiums and non-employee director compensation in the nine months ended September 30, 2016.

Other expense. Other expense increased by $0.2 million in the nine months ended September 30, 2016, from $0.2 million to $0.4 million. This was primarily the result of an increase in the mark-to-market warrant liability and the acceleration of the final payment from the original loan agreement with SVB.

Results of operations for the years ended December 31, 2014 and 2015

The following table sets forth our results of operations for the years ended December 31, 2014 and 2015.

	Year Ended December 31,		Period-to-Period Change
	2014	2015	
	(in thousands)		
Operating expenses:			
Research and development	$ 6,692	$ 10,762	$ 4,070
General and administrative	3,131	6,555	3,424
Total operating expenses	9,823	17,317	7,494
Loss from operations	(9,823)	(17,317)	(7,494)
Other income (expense):			
Interest expense	(371)	(330)	41
Interest income	5	8	3
Total other expense	(366)	(322)	44
Net loss	$(10,189)	$(17,639)	$ (7,450)

Research and development. Research and development expense increased from $6.7 million for the year ended December 31, 2014 to $10.8 million for the year ended December 31, 2015, an increase of 61%. This was primarily attributable to a $0.8 million increase in costs related to the ongoing Phase 2 clinical trial and a $1.7 million increase for the initiation of the Phase 3 clinical trial for Zuprata for the treatment of macular edema associated with non-infectious uveitis, a $0.8 million increase in costs for the startup and ongoing costs of the Phase 2 clinical trial of Zuprata in RVO patients and a $1.0 million increase in costs for pre-clinical studies of axitinib for wet AMD. This increase was partially offset by a $0.7 million decrease in device development costs due to finalizing the commercial prototype during 2014. We also incurred increased personnel and related costs of $0.7 million during 2015 as compared to 2014.

General and administrative. General and administrative expenses increased by $3.4 million, from $3.1 million for the year ended December 31, 2014 to $6.6 million for the year ended December 31, 2015. The increase was primarily attributable to recognizing $1.9 million of expenses related to previously deferred offering costs, a $0.6 million increase in personnel costs, including share-based compensation, a $0.4 million increase in patent expenses and a $0.3 million increase in investor and public relations expenses.

Interest expense. Interest expense decreased from $0.4 million in the year ended December 31, 2014 to $0.3 million in the year ended December 31, 2015. The decrease was primarily related to the accelerated

amortization of debt discount related to the convertible promissory notes upon their conversion to Series B convertible preferred stock that occurred during 2014. This was offset by the amortization of the financing costs, and the accretion of the warrants and the final payment related to the loan agreements.

Liquidity and capital resources

Sources of liquidity

For the period from our inception on May 26, 2011 to September 30, 2016, we have used cumulative net cash in operating activities of $49.4 million and incurred cumulative net losses of $55.6 million. As of September 30, 2016, we had cash, cash equivalents and short-term investments of $56.9 million. We invest any cash in excess of our immediate requirements primarily with a view to liquidity and capital preservation. As of September 30, 2016, our funds were held in cash, money market funds, certificates of deposit, corporate bonds and government bonds and agency obligations.

On June 7, 2016, we closed our IPO in which we sold 7,200,000 shares of common stock at a public offering price of $7.00 per share, and on June 30, 2016, the underwriters exercised their option to purchase 948,843 additional shares. These issuances resulted in net proceeds of $51.4 million after deducting underwriting discounts and commissions and offering expenses.

Prior to our IPO, we funded operations primarily through the sale of convertible preferred stock, a long-term loan agreement and the issuance of convertible promissory notes. We raised net cash proceeds of $44.5 million from the sale of convertible preferred stock, $6.0 million from a long-term loan agreement and $3.4 million from the sale of convertible promissory notes through September 30, 2016.

On September 28, 2016, we entered into an amended and restated loan and security agreement, or the Loan Agreement, with Silicon Valley Bank, or SVB, and entities affiliated with MidCap Financial Services, which we refer to collectively with SVB as the Lenders. The Loan Agreement amended and restated in its entirety our prior loan and security agreement with Silicon Valley Bank. The Loan Agreement provides for new term loans of up to $15.0 million, with a floating interest rate equal to 7% plus the greater of (i) the 30-day U.S. LIBOR, reported in the Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, or (ii) 0.50%. We borrowed an initial tranche of $8.0 million on September 28, 2016, of which $5.3 million was used to repay all amounts outstanding under our prior loan agreement with SVB. The remaining $7.0 million will become available beginning on the later of (i) September 30, 2017 and (ii) the date on which the Lenders have received evidence, in form and substance reasonably satisfactory to them, that we have produced clinical trial data sufficient to file an NDA for Zuprata for the treatment of uveitis. Once the draw period for the remaining $7.0 million has commenced, we may draw funds at our discretion until the earlier of (i) December 31, 2017 and (ii) the occurrence of an event of default under the Loan Agreement. We are required to pay accrued interest only through December 31, 2017 on the outstanding amount, followed by 30 equal payments of principal and accrued interest. We have the option to prepay the outstanding balance of the term loans in full, subject to a prepayment fee of (i) 3% of the original principal amount of the aggregate term loans for any prepayment prior to September 28, 2017 or (ii) 2% of the original principal amount of the aggregate term loans for any prepayment between September 28, 2017 and May 31, 2020. A final payment of $0.5 million, or 6.50% of the aggregate borrowed amount, is due at maturity of the term loans on June 1, 2020, or upon the prepayment of the facility or the acceleration of amounts due under the facility as a result of an event of default.

The term loans under the Loan Agreement are secured by substantially all of our assets, except that the collateral does not include any of our intellectual property. However, pursuant to the terms of a negative pledge arrangement, we have agreed not to encumber any of our intellectual property.

In connection with the Loan Agreement, we issued warrants to the Lenders to purchase up to 29,796 shares of common stock at a price per share of $10.74. The warrants expire in September 2026, or earlier upon the occurrence of specified mergers or acquisitions of our company, and are immediately exercisable.

In connection with the prior loan agreement, we issued a warrant to SVB to purchase 25,974 shares of our common stock at an exercise price of $7.70 per share. Unless earlier exercised, the warrant will expire in April 2025.

Funding requirements

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, laboratory and related supplies, clinical costs, legal and other regulatory expenses and general overhead costs.

The successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of our product candidates, although we will require additional funding to complete our planned Phase 3 clinical program for Zuprata in RVO patients. We are also unable to predict when, if ever, material net cash inflows will commence from product sales. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- successful enrollment in, and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates; and
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that candidate.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements. We do not currently have any committed external source of funds other than under the Loan Agreement. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

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

We will also incur costs as a public company that we have not previously incurred or have previously incurred at lower rates, including but not limited to, increased costs and expenses for fees to members of our board of directors, increased personnel costs, increased directors and officers insurance premiums, audit and legal fees, investor relations fees and expenses for compliance with reporting requirements under the Exchange Act and rules implemented by the SEC and NASDAQ.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our cash flows from license revenue and existing cash and cash equivalents, including the net proceeds from our IPO and this offering, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 18 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress in these trials is uncertain.

Cash flows

The following is a summary of the net cash flows provided by (used in) our operating, investing and financing activities (in thousands):

	Year Ended December 31,		Nine Months Ended September 30,	
	2014	2015	2015	2016
Net cash (used in) provided by:				
Operating activities	$ (9,124)	$(13,902)	$ (10,073)	$ (16,253)
Investing activities	(140)	(28)	(4)	(20,068)
Financing activities	15,624	25,944	5,994	52,914
Net change in cash and cash equivalents	$ 6,360	$ 12,014	$ (4,083)	$ 16,593

During the nine months ended September 30, 2016 and 2015, our operating activities used net cash of $16.3 million and $10.1 million, respectively. The use of cash in each period primarily resulted from our net losses. The increase in net loss for the nine months ended September 30, 2016 as compared to the nine months ended September 30, 2015 was primarily attributable to higher research and development expenses.

During the nine months ended September 30, 2016, our net cash used by investing activities was $20.1 million. This was for purchase of short-term, available-for-sale investments including certificates of deposit, corporate bonds and government bonds and agency obligations. During the nine months ended September 30, 2015, we did not engage in any material investing activities.

During the nine months ended September 30, 2016 and 2015, our net cash provided by financing activities was $52.9 million and $6.0 million, respectively. The net cash provided by financing for the nine months ended September 30, 2016 was related primarily to $51.4 million received from our IPO, net of the underwriters' discounts and commissions and other offering expenses, and $7.9 million received from the Loan Agreement, partially offset by $6.3 million in payments of long-term debt, which includes the $5.3 million to repay all amounts owed under the prior loan agreement with SVB. The net cash provided by financing activities during the nine months ended September 30, 2015 was primarily due to amounts borrowed under that prior loan agreement.

During the years ended December 31, 2014 and 2015, our operating activities used net cash of $9.1 million and $13.9 million, respectively. The use of net cash in each period primarily resulted from our net losses. The increase in net loss for the year ended December 31, 2015 as compared to the year ended December 31, 2014 was primarily attributable to higher research and development expenses, increased personnel related costs and higher interest expenses. The other changes from operating activities were caused primarily by changes in our accounts payable and other accrued liabilities, share-based compensation and deferred offering costs. The net cash used in investing activities during the years ended December 31, 2014 and 2015 was comprised of the purchase of fixed assets. The net cash provided by financing activities during the year ended December 31, 2014 related primarily to $3.0 million received from the issuance of the bridge notes and $12.7 million from the sale of our Series B convertible preferred stock. The net cash provided by financing during the year ended December 31, 2015 was primarily due to $20.0 million from the sale of our Series C convertible preferred stock and our $6.0 million long-term debt agreement with Silicon Valley Bank.

Contractual obligations

The following table summarizes our significant contractual obligations as of September 30, 2016, all of which consisted of obligations under a lease for our corporate headquarters in Alpharetta, Georgia and obligations under the Loan Agreement.

	Payments due by period (in thousands)				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Operating lease obligations	$ 46	$ 46	$ —	$ —	$ —
Long-term debt obligations	8,520	—	8,520	—	—
Total	$8,566	$ 46	$ 8,520	$ —	$ —

Subsequent to September 30, 2016, we entered into a new office lease agreement for our corporate headquarters, under which we have agreed to lease approximately 20,000 square feet of space in Alpharetta, Georgia. We expect to move into this new space in the first half of 2017. Under this lease, we will pay an initial annual base rent of $421,740, or $35,145 per month, subject to an increase of 3% per year.

We have no material non-cancelable purchase commitments with contract manufactures or service providers, as we have generally contracted on a cancelable purchase order basis.

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 SEC rules.

Recent accounting pronouncements

In August 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update (“ASU”) 2016-15, *Statement of Cash Flows Classification of Certain Cash Receipts and Cash Payments*. The update addresses eight specific cash flow matters with the objective of reducing diversity in practice in how certain cash receipts and payments are classified in the statement of cash flows. The update is effective for annual periods beginning after December 15, 2017, and interim periods within the period. Early adoption is permitted. We are currently evaluating the impact the adoption of ASU 2016-15 will have on our financial statements and related disclosures.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718).* The new guidance simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. For public companies, the amendments in this standard are effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted. The effects of this standard on our financial statements and related disclosures are not expected to be material.

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

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 provides guidance about management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. The new standard is effective for the annual period ending after December 15, 2016 and for annual and interim periods thereafter, with early adoption permitted. We do not expect this accounting standard to have an impact on our financial statements and related disclosures.

In May 2014, FASB issued ASU 2014-09, *Revenue from Contracts with Customers*. Under ASU 2014-09, companies will be required to recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration (that is, payment) to which the company expects to be entitled in exchange for those goods or services. The new standard also will result in enhanced disclosures about revenue, provide guidance for transactions that were not previously addressed comprehensively (for example, service revenue and contract modifications) and modify guidance for multiple-element arrangements. In August 2015, the FASB issued ASU 2015-14, which deferred by one year the effective date of ASU 2014-09. The one year deferral of the effective date of this standard changes the effective date for us to January 1, 2018. Early adoption is permitted, but not before the original effective date. We are currently evaluating the effect this standard may have on our financial statements and related disclosures.

JOBS Act

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Section 107(b) of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Quantitative and qualitative disclosures about market risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of September 30, 2016 and December 31, 2015, we had cash and cash equivalents of $36.9 million and $20.3 million, respectively. We generally hold our cash in interest-bearing money market accounts. As of September 30, 2016, we had short-term investments of $20.0 million. The short-term investments include certificates of deposit, corporate bonds and government bonds and agency obligations. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash equivalents and short-term investments and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents and short-term investments.

We do not engage in any hedging activities against changes in interest rates. Our outstanding debt instruments carry a floating interest rate that is 7.0% plus the greater of (i) the 30-day U.S. LIBOR, reported in the Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, or (ii) 0.50%. We estimate that a one percentage point increase in the prime rate would have resulted in an $80,000 and $60,000 increase in interest expense for the nine months ended September 30, 2016 and the year ended December 31, 2015, respectively.

We do not have any foreign currency or other derivative financial instruments.

Business

Overview

We are a late-stage clinical biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye. Our current product candidates focus on diseases affecting the retina, which is the tissue that lines the inside of the eye and is primarily responsible for vision, and the choroid, especially diseases associated with macular edema, and are injected into the suprachoroidal space, or SCS, adjacent to the choroid, which is the layer adjacent to the retina that supplies the retina with blood, oxygen and nourishment. With our proprietary microinjector, drugs are injected into and spread within and through the suprachoroidal space, or SCS, which is the space located between the choroid and the outer protective layer of the eye known as the sclera. With the suprachoroidal injection, our product candidates are more directly administered to the retina and choroid as compared to other ocular drug administration techniques such as injections of drug into the vitreous, a jelly-like substance that occupies the central portion of the eye. Intravitreal injections rely on diffusion of drug outward from the vitreous to the retina and choroid. This diffusion can result in lower concentrations of drug in these targeted areas. At the same time, this diffusion can also result in drug spreading to unintended parts of the eye, where, for some drugs, it can cause significant side effects. We believe treatment of eye disease via suprachoroidal injection may provide a number of benefits, including lower frequency of necessary administration and faster onset of therapeutic effect. We hold the exclusive rights to develop and commercialize drugs for treatment via injection into the SCS. We estimate that there are nearly five million people in the United States diagnosed with our target indications and that worldwide annual sales of drugs to treat these indications were over $7 billion in 2015.

Our most advanced product candidates are based on commonly used ophthalmic drugs, which we believe will allow us to more efficiently and predictably pursue the regulatory approval of these product candidates under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act. Under Section 505(b)(2), if we can establish that reliance on the Food and Drug Administration's, or FDA's, previous findings of safety and effectiveness for an approved product is scientifically appropriate, or there is scientific literature to support the product's safety or effectiveness, or both, it may eliminate the need for us to conduct some of the preclinical studies or clinical trials for the new product candidate that might otherwise have been required.

Our current and planned development programs aim to restore or improve visual function primarily by reducing the macular edema associated with a number of diseases affecting the retina and choroid. Macular edema is the build-up of fluid that can cause abnormal swelling of the macula, the portion of the retina responsible for central vision and color perception. This swelling can rapidly result in deterioration of vision and can eventually lead to blindness. We are developing Zuprata, a proprietary, preservative-free formulation of the corticosteroid triamcinolone acetonide, or TA, for the treatment of macular edema associated with non-infectious uveitis, a condition that we estimate affects 350,000 patients in the United States. We have specifically designed Zuprata to be administered using our SCS Microinjector. We are currently enrolling patients with macular edema associated with non-infectious uveitis in a pivotal Phase 3 clinical trial. We expect to enroll approximately 150 patients in this trial and to report preliminary results from the trial in late 2017 or early 2018. We believe, based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, that only one, Clearside-sponsored, Phase 3 clinical trial will be required to support the potential filing of a New Drug Application, or NDA, with the FDA.

In the first quarter of 2016, we received data from a Phase 2 clinical trial in 22 patients with macular edema associated with non-infectious uveitis. Patients in this trial achieved a statistically significant (p=0.0017) mean change from baseline in retinal thickness at eight weeks, which was the primary endpoint of the trial, as well as statistically significant (p=0.0004) mean improvement from baseline in best corrected visual acuity, or BCVA, at eight weeks, a secondary endpoint. At four and eight weeks, the average reduction in retinal thickness was 135

and 164 microns, respectively, from a mean baseline of 526 microns, and the average improvement in BCVA was 7.7 and 9.2 letters, respectively, from a mean baseline of 60 letters. In our previously completed Phase 1/2 clinical trial, we observed a range of improvements in BCVA of between one and five lines on a standard eye chart, with each line of improvement corresponding to five letters. At the end of week 12, the average improvement in BCVA exceeded two lines, which is considered meaningful in standard clinical practice. At the end of week 26, four of the eight patients in the trial had still not required additional treatment. For those four patients, the average improvement in BCVA was nearly three lines at week 26.

We are also developing Zuprata along with an anti-VEGF agent for the treatment of macular edema associated with retinal vein occlusion, or RVO, a sight-threatening disorder resulting from the blockage of a retinal vein, that we estimate affects 2.2 million patients in the United States. We are exploring whether a suprachoroidal injection of Zuprata and a concomitant intravitreal injection of Eylea (aflibercept), an inhibitor of vascular endothelial growth factor, or VEGF, can provide improved visual acuity, reduced macular edema and reduced injection frequency as compared to administration of intravitreal Eylea alone. Corticosteroids and anti-VEGF agents have known advantages in treating RVO.

We have completed a Phase 2 clinical trial in 46 patients with macular edema associated with RVO. In this trial, 23 patients in the active arm initially received a concomitant suprachoroidal injection of Zuprata and intravitreal injection of Eylea and 23 patients in the control arm initially received only an intravitreal injection of Eylea. The objective of the trial was to determine whether patients receiving Zuprata together with Eylea could sustain improved visual acuity over the three months of the clinical trial while requiring fewer additional Eylea treatments than patients receiving intravitreal Eylea alone. Patients in each arm were evaluated at months one, two and three after the initial treatment using pre-specified criteria to determine if they continued to experience macular edema or reductions in visual acuity and therefore required additional Eylea treatments. The primary endpoint of the trial was met, with patients in the active arm requiring an aggregate of 60% fewer additional Eylea treatments than patients in the control arm over three months, a result that was statistically significant ($p=0.013$). In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant ($p=0.003$). In the same Phase 2 trial, patients in the active arm experienced greater improvement in visual acuity than those in the control arm, with patients in the active arm experiencing mean BCVA improvements at months one, two and three of 16, 20 and 19 letters, respectively, from a baseline of 49 letters, compared to improvements of 11, 12 and 11 letters, respectively, in the control arm, at the same time points and also from a baseline of 49 letters. Based on the results of this trial and after incorporating feedback from a recent end-of-Phase 2 meeting with the FDA, we intend to commence a Phase 3 clinical program in RVO in the first half of 2017.

We have recently expanded our Zuprata development programs to include another retinal vascular condition known as diabetic macular edema, or DME. DME is a common ocular complication of diabetes that results in swelling in the macula and is the primary cause of vision loss associated with diabetes. In November 2016, we began enrolling patients with DME in a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal Zuprata, as well as suprachoroidal Zuprata alone, over a six-month evaluation period. We expect to enroll approximately 20 patients in this trial and to report preliminary results in the second half of 2017.

We are developing another product candidate, a proprietary injectable suspension formulation of the compound axitinib, to be administered suprachoroidally for the treatment of neovascular age-related macular degeneration, or wet AMD, a condition that we estimate affects 1.2 million patients in the United States. Axitinib has activities against both VEGF receptors and receptors of platelet derived growth factor, or PDGF. We believe

that suprachoroidal injection of axitinib could be more effective than current treatments for wet AMD, which consist primarily of anti-VEGF agents injected intravitreally. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.

We are also working with third parties through collaborations and licenses to develop eye disease treatments using our proprietary SCS Microinjector and method of drug administration to the choroid and retina through the SCS. We are collaborating with Santen Pharmaceuticals, Ltd., or Santen, to develop compounds for suprachoroidal injection that are designed to treat DME, wet AMD and RVO. Additionally, we are collaborating with Santen to explore the potential benefits of suprachoroidal injection of compounds known to reduce intraocular pressure, or IOP, associated with glaucoma for a sustained period of time. All of these activities are currently in the preclinical development stage.

We believe administration of drug using our SCS Microinjector may provide improved bioavailability to the targeted retina and choroid, with drug remaining more localized and away from other parts of the eye, where the drug could cause side effects. Corticosteroids are effective both at treating the inflammatory aspect of ocular disease and at reducing macular edema, but when delivered intravitreally, they have been associated with significant side effects, such as cataract formation or exacerbation and elevated IOP, which can lead to glaucoma. Anti-VEGF drugs, while highly effective in reducing macular edema, require frequent administration, in some cases as often as monthly. We believe that our differentiated approach of injecting ocular drugs into the SCS may result in fewer side effects and improved bioavailability of drug at the diseased retina and choroid, as compared to intravitreal administration, a faster onset of therapeutic effect, a similar efficacy profile with lower drug amounts required, and longer duration of therapeutic effect with less frequent required injections. The procedure for suprachoroidal injection with our SCS Microinjector is conducted in an in-office setting and is similar in terms of patient preparation and duration to the procedure for intravitreal injection, and we therefore expect our products, if they achieve regulatory approval, to be incorporated into retinal specialists' standard medical practice.

We have completed a Phase 2 clinical trial of Zuprata in patients with non-infectious uveitis, a condition characterized by inflammation of the choroid and surrounding tissues not caused by an infectious agent. The most common treatment for non-infectious uveitis involves the use of corticosteroids or other immunosuppressive agents that are used systemically or locally. A commonly used corticosteroid is triamcinolone acetonide, or TA. We have specifically designed Zuprata, our proprietary, preservative-free formulation of TA, to be administered through our proprietary SCS Microinjector.

In our Phase 2 clinical trial, we observed statistically significant improvement in both retinal thickness, the primary endpoint of the trial, and BCVA, a secondary endpoint. The 22 enrolled patients were randomized to receive a single suprachoroidal injection of one of two doses of Zuprata, with 17 patients receiving a 4.0 mg dose and five patients receiving a 0.8 mg dose. Patients returned for follow-up examinations between seven days and 11 days, at four weeks and at eight weeks following dosing. The patients who received the 4.0 mg dose of Zuprata were evaluated for an average change in retinal thickness from baseline at eight weeks and improvement in BCVA. At four and eight weeks, the average reduction in retinal thickness was 135 and 164 microns, respectively, from a mean baseline of 526 microns, and the average improvement in BCVA was 7.7 and 9.2 letters, respectively, from a mean baseline of 60 letters. These results all achieved statistical significance. All 22 patients, who were all treated with a suprachoroidal injection of Zuprata, completed the full observation period and were evaluated for safety. There were no corticosteroid-related increases in IOP or treatment-related serious adverse events observed in this trial.

In our Phase 1/2 clinical trial, we evaluated the efficacy and safety of a suprachoroidal injection of Triesence, a TA formulation that is pharmaceutically equivalent to Zuprata and that has been approved by the FDA to treat

non-infectious uveitis. While the trial was primarily a safety and tolerability study, we also assessed efficacy measures, including BCVA improvement and reduction in retinal thickness, which is a common measure of macular edema. During the course of the trial, we observed a range of improvements in BCVA of between one and five lines on a standard eye chart with each line of improvement corresponding to five letters. At the end of week 12, the average improvement in BCVA exceeded two lines, which is considered meaningful in standard clinical practice. At the end of week 26, four of the eight patients in the trial had still not required additional treatment. For those four patients, the average improvement in BCVA was nearly three lines at week 26. At the end of weeks 12 and 26 of the trial, the average reduction in retinal thickness for patients was greater than 100 microns from their respective baselines, with a reduction of 50 microns being considered meaningful in standard clinical practice. In the trial, suprachoroidal injection of Triesence was generally well tolerated, with none of the eight dosed patients developing cataracts or experiencing elevated IOP through week 26.

Because our uveitis program uses our formulation of TA for the treatment of uveitis, and TA is known to be effective in treating uveitis, we believe that our product candidate will be at least as effective as commonly used formulations of TA for locally treating the disease, including the associated macular edema, with a reduced incidence of side effects, such as uncontrolled elevated IOP and cataracts. Our preclinical studies suggest that suprachoroidal injection of TA may provide improved bioavailability of drug at the diseased retina and choroid compared to other local intraocular or periocular administration methods, which may result in faster onset of therapeutic effect and a better efficacy profile with lower drug amounts required. Our preclinical ocular drug distribution studies suggest the potential for Zuprata to effectively treat uveitis for at least 90 days following a single suprachoroidal injection and the Phase 1/2 clinical trial observations potentially support a duration of action longer than 90 days since four of the eight patients did not require additional treatment over the 180-day observation period in that trial. Currently used ocular injections of TA are typically effective for approximately 90 days.

In November 2015, we enrolled the first patient in a pivotal Phase 3 clinical trial with Zuprata injected into the SCS. We intend to enroll approximately 150 patients with macular edema associated with non-infectious uveitis in this trial and expect to report data from this trial in late 2017 or early 2018. We believe, based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, that only one, Clearside-sponsored, Phase 3 clinical trial will be required to support the potential filing of a New Drug Application, or NDA, with the FDA. If approved, Zuprata would be the first drug specifically indicated for macular edema associated with non-infectious uveitis.

Under our RVO program, we have completed a Phase 2 clinical trial for the treatment of macular edema associated with RVO, a sight-threatening disorder resulting from the blockage of a retinal vein. We enrolled 46 patients in this trial. The current standard of care for RVO involves monthly intravitreal injections of an anti-VEGF drug, such as Lucentis (ranibizumab), Eylea (aflibercept) or Avastin (bevacizumab). Corticosteroids are also indicated for the treatment of macular edema associated with RVO.

In the Phase 2 trial, 23 patients in the active arm initially received a single concomitant suprachoroidal injection of Zuprata and an intravitreal injection of Eylea and 23 patients in the control arm initially received only an intravitreal injection of Eylea. The objective of the trial was to determine whether patients receiving Zuprata together with Eylea could maintain visual acuity improvements while requiring fewer Eylea retreatments than patients receiving Eylea alone. Patients in each arm were evaluated at months one, two and three after the initial injection using specified criteria to determine if they continued to experience increase in macular edema or reductions in visual acuity and therefore required additional Eylea treatments. The primary endpoint of the trial was met, with patients in the active arm requiring an aggregate of 60% fewer additional Eylea treatments than patients in the control arm over three months, a result that was statistically significant. In addition, patients in the active arm experienced greater improvement in visual acuity than those in the control arm, with patients in the active arm experiencing mean BCVA improvements at months one, two and three of 16, 20 and

19 letters, respectively, from a baseline of 49 letters, compared to improvements of 11, 12 and 11 letters, respectively, in the control arm, at the same time points and also from a baseline of 49 letters. In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant, with a p-value of 0.003. Patients in the active arm also achieved mean levels of reduction in retinal thickness of approximately 450 microns after each of one, two and three months, from a baseline of 731 microns. Patients in the control arm achieved a mean reduction in retinal thickness of approximately 400 microns after one month, which then decreased to approximately 340 microns at months two and three, from a baseline of 728 microns. Normal retinal thickness on the instrument we used to measure retinal thickness is 270 microns, with a standard deviation of approximately 20 microns. This means that approximately 95% of the normal population has a retinal thickness of 310 microns or less, which is two standard deviations from the normal retinal thickness. In terms of safety results, there were no serious adverse events reported in the trial and the treatment was generally well tolerated. We believe that suprachoroidal injection of Zuprata, in combination with intravitreal anti-VEGF treatment, may provide the potential benefits of improved visual acuity, reduced macular edema and reduced injection frequency. In addition, we believe that the side effect profile of Zuprata will be similar to that of current intravitreal anti-VEGF treatments alone, because, based on preclinical data, suprachoroidal injections of Zuprata should allow the corticosteroid to remain substantially localized in the retina and choroid, potentially reducing side effects that are commonly observed with other routes of administration of corticosteroids.

Under our DME program, in November 2016, we began enrolling patients with DME in a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal Zuprata, as well as suprachoroidal Zuprata alone, over a six-month evaluation period. We expect to enroll approximately 20 patients in this trial and to report preliminary results in the second half of 2017.

Under our wet AMD program, we are developing a proprietary suspension formulation of axitinib, a single molecule with dual anti-VEGF and anti-PDGF activity, for injection into the SCS with our SCS Microinjector. Wet AMD is a condition involving the abnormal formation and growth of new blood vessels in the choroid, their intrusion into the outer layers of the retina and the leakage of blood and fluid into the retina. The current standard of care for the treatment of wet AMD is intravitreal injection of anti-VEGF drugs as a standalone therapy, as often as seven times per year. Additionally, anti-PDGF molecules, when injected into the vitreous immediately following an anti-VEGF intravitreal injection, have shown clinical promise in Phase 1 and Phase 2 trials conducted by others in improving upon the visual acuity outcomes of the anti-VEGF agent alone. Because wet AMD manifests in the retina and choroid, we believe that suprachoroidal injection of drug more directly to the retina and choroid may result in faster onset of therapeutic effect as compared to intravitreal injection. We believe that suprachoroidal injection also has the potential to access the new blood vessels in the choroid, which could reduce the necessary frequency of treatment, since damage to the retina may be preventable or reduced before these new blood vessels can intrude into the retina and cause damage. We plan to further study these effects in any future clinical trials that we conduct as part of our wet AMD program.

Our drug candidates, SCS Microinjector and method of drug administration into the SCS are protected by six issued U.S. patents, including one design patent, and 55 patent applications filed in the United States and major international markets, including the European Union, Canada, India, Japan, China and Australia. Our issued patents are broadly directed to methods of administering drugs of any type, including anti-inflammatory drugs, anti-VEGF drugs, and gene therapy, into the SCS by injection and are not scheduled to expire until 2027, 2029 and 2034, respectively. Our patent applications relate to suprachoroidal injection technology and methods, our current therapeutic drug candidates and formulations, various therapeutic uses, including treatment of specific indications such as macular edema associated with non-infectious uveitis and RVO, as well as wet AMD and

DME, and administration of specific classes of drugs to the SCS, including anti-inflammatory drugs and anti-VEGF drugs. Our pending patent applications are not projected to expire until between 2027 and 2035.

If any of our product candidates are approved, we plan to build a specialized team of 30 to 40 sales and medical marketing support professionals to target the approximately 1,700 retinal specialists in the United States, and we may also pursue collaborations with third parties to commercialize any of our drugs approved for marketing outside the United States.

The members of our management team have held senior leadership positions at a number of pharmaceutical and biotechnology companies with approved ophthalmic drugs, including Alcon, Alimera Sciences and CIBA Vision. Members of our team have contributed to the development, regulatory approval and commercialization of several retinal products, such as Triesence, Iluvien and Nevanac.

Strategy

Our goal is to be a leading biopharmaceutical company focused on the development and commercialization of therapeutics to treat blinding diseases of the eye, with a particular emphasis on diseases affecting the retina and the choroid. The key elements of our strategy are:

- *Advancing our most advanced product candidates to FDA approval under the Section 505(b)(2) NDA regulatory pathway.* Our most advanced product candidates utilize Zuprata, our proprietary formulation of TA, a corticosteroid that has been used for decades to treat ocular inflammatory conditions. We believe this approach will allow us to more efficiently and predictably pursue the regulatory approval of these product candidates under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. We are currently enrolling patients in a pivotal Phase 3 clinical trial of Zuprata for the treatment of macular edema associated with non-infectious uveitis and expect to report preliminary results from this trial in late 2017 or early 2018. Based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, we expect this trial to be the only pivotal clinical trial necessary to support a potential NDA filing for Zuprata in this indication. We have separately completed a 46-patient Phase 2 clinical trial with Zuprata injected into the SCS concomitantly with intravitreally injected Eylea for the treatment of macular edema associated with RVO. Based on the results of this trial and after incorporating feedback from the FDA, we intend to commence a Phase 3 clinical program with suprachoroidal Zuprata and intravitreal Eylea for the treatment of RVO in the first half of 2017.
- *Advancing our DME development program.* DME, like uveitis and RVO, is characterized by an inflammatory aspect. We are conducting a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal Zuprata, as well as suprachoroidal Zuprata alone, in patients with DME over a six-month evaluation period. We recently enrolled the first patient in this trial and expect to report preliminary results from this trial in the second half of 2017.
- *Advancing our wet AMD development program.* We are developing a proprietary suspension formulation of axitinib, a compound with dual anti-VEGF and anti-PDGF activity, for the treatment of wet AMD by injection into the SCS. We believe a single injection of a drug with dual anti-VEGF and anti-PDGF activity to the choroid and retina through the SCS may provide superior visual outcomes compared to intravitreal anti-VEGF treatment and could reduce the number of injections required to treat wet AMD. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.
- *Maximizing the commercial potential of our product candidates.* If we receive marketing approval for Zuprata, we plan to build a specialized team of 30 to 40 sales and medical marketing support professionals to target the approximately 1,700 retinal specialists in the United States. We expect that this sales force would be able to effectively sell more than one of our products, in the event that multiple product candidates are approved for marketing. We have retained the worldwide commercialization rights to all of our product

candidates, except we have granted a third party the exclusive right to commercialize our product candidates in Russia and specified adjacent territories pursuant to a license agreement, as described later in this prospectus. We may pursue additional collaborations with third parties to commercialize any of our drugs approved for marketing outside the United States, either through territorial licenses or distributor relationships.

- *Developing additional therapies through collaborations with third parties.* We plan to explore collaborations with third parties to develop suprachoroidally-injected treatments for eye diseases. These collaborations may take the form of in-licenses of the third parties' drugs or drug candidates for our own development for suprachoroidally-injected treatments, or out-licenses for third parties to use our intellectual property covering suprachoroidally-injected treatments as part of the development of their own drugs. For example, we are collaborating with Santen to develop compounds designed to treat macular edema and neovascularization associated with wet AMD, RVO and DME, as well as elevated IOP associated with glaucoma.
- *Maintaining and strengthening our intellectual property portfolio.* Our intellectual property strategy aims to control the commercialization of SCS access, with patents and patent applications covering suprachoroidal injection, novel formulations of drugs and microinjectors used to access the SCS, and methods of treatment of diseases through the SCS. Our current patents and patent applications provide us with exclusivity in the United States and major international markets, and are not projected to expire until between 2027 and 2035. We will seek to broaden the scope of and increase the geographic reach of our patent protection throughout the world.

The Clearside approach

We are developing drug candidates for the treatment of back of the eye diseases to be administered to the retina and choroid through the SCS using our proprietary SCS Microinjector. We believe that our novel approach to treatment of eye diseases, through patented suprachoroidal drug administration, may provide a number of potential benefits, including:

- *Improved bioavailability at the site of disease and faster onset of therapeutic effect.* In preclinical studies, we observed higher amounts of drug present in the retina and choroid following suprachoroidal injection, both at early time points and over the course of the experimental timeframe, as compared to the amounts of the same drug present over time in the retina and choroid following intravitreal administration. We believe this suggests that treatment using suprachoroidal injection of a drug may have a faster onset of therapeutic effect as compared to intravitreal administration, along with similar or better efficacy, in diseases such as uveitis, RVO, wet AMD and DME.
- *Similar efficacy profile with lower drug amounts required.* In a preclinical study in an animal model of uveitis, suprachoroidal injection of TA achieved similar efficacy results with only 10% of the drug amount commonly administered through intravitreal injection. We believe this suggests our approach may allow us to develop ocular therapies with similar efficacy, but with lower amounts of active drug, compared to current therapies.
- *Less frequent injections.* Current treatments for RVO require monthly intravitreal injections of anti-VEGF drugs, while current treatments for wet AMD require such injections as often as seven times per year. For RVO patients, we believe that a combination of a standard intravitreal injection of an anti-VEGF drug that addresses the vascular aspect of the disease, together with a suprachoroidal injection of Zuprata, which addresses the inflammatory aspect of RVO, may have efficacy similar to that of monthly intravitreal anti-VEGF injections but with a reduction in the frequency of treatment to once every 90 days. In wet AMD, we believe that more direct administration of drugs with anti-VEGF or dual anti-VEGF and anti-PDGF activity to

the neovascularization in the choroid through suprachoroidal injection may substantially block the process of additional new vascular growth within the choroid before the vessels break into the retina and create further damage through leakage. If treatment through the SCS can block retinal damage before it occurs, we believe it could delay vision loss for a longer duration of time than the current standard intravitreal administration of anti-VEGF drugs and, accordingly, could require less frequent administration while providing at least the same levels of efficacy.

- *Enhanced safety profile.* Intravitreal injections result in drugs diffusing throughout the eye, including to the lens, iris and ciliary body at the front of the eye, which for some drugs, such as corticosteroids, has been associated with safety issues, such as cataract formation or exacerbation and elevated IOP levels, which can lead to glaucoma. Intravitreal administration of TA has been associated with cataracts and increases in IOP levels in 20% to 60% of patients. Because suprachoroidal injection of drugs in preclinical studies appeared to result in drug remaining mostly localized in the retina and choroid without substantial diffusion to the vitreous or the front portion of the eye, we believe suprachoroidal injection has the potential to reduce the incidence of these side effects. In our Phase 2 clinical trial in non-infectious uveitis, all 22 patients, who were all treated with a suprachoroidal injection of Zuprata, completed the full observation period and were evaluated for safety. There were no corticosteroid-related increases in IOP or treatment-related serious adverse events observed in this trial. None of the eight patients dosed in our Phase 1/2 clinical trial in non-infectious uveitis experienced cataracts, increased levels of IOP or other treatment-related serious adverse events over the course of 26 weeks following a single suprachoroidal injection of TA. In our Phase 2 clinical trial in RVO patients, there were no serious adverse events, and no adverse events that led to discontinuation of a patient in the trial.
- *Incorporated into standard medical practice.* If approved for marketing, our drugs will be packaged together with our SCS Microinjector for use by retinal specialists. The procedure for suprachoroidal injection with our SCS Microinjector is intended to be conducted in an in-office setting and is similar in terms of patient preparation and duration to the procedure for intravitreal injection, and we therefore expect our products, if they achieve regulatory approval, to be incorporated into retinal specialists' standard medical practice.

The current development status of our product candidates is summarized in the chart below:

Proposed Indication	Product Candidate	Status and Upcoming Milestones
Macular edema Associated with non-infectious uveitis	Suprachoroidal injection of Zuprata	• Initiated ~150-patient single pivotal Phase 3 clinical trial, with preliminary results expected in late 2017 or early 2018
Macular edema Associated with RVO	Suprachoroidal injection of Zuprata together with intravitreal injection of anti-VEGF agent Eylea	• End-of-Phase 2 meeting held in October 2016 • Plan to commence enrollment of patients in Phase 3 clinical trial in first half of 2017
DME	Suprachoroidal injection of Zuprata alone or together with intravitreal injection of Eylea	• Initiated Phase 1/2 clinical trial • Plan to report data in second half of 2017
Wet AMD	Suprachoroidal injection of axitinib	• Plan to file IND application in the first half of 2017 to commence Phase 1/2 clinical trial

We have discussed our proposed development programs with the FDA for our uveitis and RVO programs, but we have not yet done so for our DME development program. For our wet AMD program, we have only held a pre-IND meeting with the FDA.

Zuprata for macular edema associated with non-infectious uveitis

The most common treatment for non-infectious uveitis, a condition characterized by inflammation of the choroid and surrounding tissues, involves the use of corticosteroids, such as TA. Zuprata is our formulation of TA, and TA is known to be effective in treating uveitis. We believe that our product candidate will be at least as effective as commonly used formulations of TA in treating all aspects of the disease, including the associated macular edema. If approved, Zuprata would be the first drug specifically indicated for macular edema associated with non-infectious uveitis. In November 2015, we enrolled the first patient in a pivotal Phase 3 clinical trial in which Zuprata is injected into the SCS with our SCS Microinjector. We intend to enroll approximately 150 patients with macular edema associated with non-infectious uveitis and expect to report preliminary results from this trial in late 2017 or early 2018. Based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, we believe this will be the only pivotal clinical trial necessary to support a potential 505(b)(2) NDA filing for Zuprata for macular edema associated with non-infectious uveitis.

We have completed a Phase 2 clinical trial for this indication that we conducted with Zuprata, the results of which are described below. We have also completed a Phase 1/2 clinical trial in eight uveitis patients. We believe that Zuprata will be at least as effective in treating uveitis, including the associated macular edema, as commonly used treatments with corticosteroids. However, we believe that it may provide improved bioavailability of drug at the diseased retina and choroid, which may result in faster onset of therapeutic effect, a similar efficacy profile with lower drug amounts required, and longer duration of therapeutic effect, potentially resulting in a reduced frequency of necessary injections. We also believe that Zuprata may result in fewer side effects compared to commonly used corticosteroid treatments.

Market opportunity for treatment of macular edema associated with non-infectious uveitis

Uveitis is one of the most frequent causes of blindness in the developed world. Based on prevalence data published in the journal *Ophthalmology* in 2004 and United States census data for 2010, we estimate approximately 350,000 individuals in the United States suffer from some form of uveitis. Typically diagnosed in individuals between the ages of 20 and 50, uveitis can occur in both eyes approximately two-thirds of the time and accounts for approximately 10% of cases of blindness in the United States. Uveitis can be either infectious or non-infectious, with non-infectious uveitis accounting for approximately 80% of all uveitis cases. Macular edema was reported in 33% of uveitis patients according to a study published in 2006 in the journal *Ophthalmology*.

Limitations of currently available therapies for macular edema associated with non-infectious uveitis

Although there are drugs approved for the treatment of non-infectious uveitis, there are currently no approved drugs that specifically target macular edema associated with non-infectious uveitis. Corticosteroids are the most commonly used treatments for non-infectious uveitis. Corticosteroids administered through eye drops, although used to treat some uveitis patients, are generally ineffective in treating patients with macular edema associated with non-infectious uveitis. Corticosteroids administered orally or systemically can be effective in treating patients with macular edema associated with non-infectious uveitis, but their use is associated with significant side effects. As a result of the shortcomings associated with these methods of administering corticosteroids, the most common method for treating macular edema associated with non-infectious uveitis is intravitreal injection or implant of a corticosteroid, such as TA, dexamethasone or fluocinolone acetonide.

Examples of intravitreal corticosteroid treatments include Ozurdex®, Retisert®, Kenalog® and Triesence. Ozurdex is a single-use biodegradable dexamethasone implant that has been approved by the FDA as a treatment for non-infectious uveitis affecting the back of the eye, but has been associated with increased IOP in 25% of patients and cataracts in 5% of patients following administration. Retisert, a non-biodegradable fluocinolone acetonide implant that requires surgical administration, has also been approved by the FDA as a treatment for non-infectious uveitis, but more than 75% of patients receiving Retisert require additional medications within three years of receiving Retisert therapy to effectively treat their uveitis, more than 35% of patients require surgical intervention in order to control increase in IOP levels, and nearly all patients develop cataracts and require cataract surgery following treatment.

Triesence and Kenalog are the main injectable formulations of TA that are used for the treatment of intraocular inflammatory conditions. Prescription of Kenalog is off-label because it has not been approved by the FDA to treat intraocular conditions. TA has been associated with increases in IOP or cataract formation or progression in 20% to 60% of patients when injected intravitreally.

Immunosuppressive agents are also sometimes used to control the inflammation associated with non-infectious uveitis, but due to their ability to systemically impair the body's immune system and their association with additional side effects, physicians are cautious in using these agents. Anti-VEGF therapies are also used to treat macular edema in a variety of diseases, but are generally not used in uveitis patients because they do not treat the inflammation inherent to uveitis or many of the other complications associated with uveitis.

Potential benefits of Zuprata in treating macular edema associated with non-infectious uveitis

If approved by the FDA, Zuprata would be the first treatment specifically indicated for macular edema associated with non-infectious uveitis. Because our uveitis program is based on Zuprata, our formulation of TA, a corticosteroid known to be effective in treating uveitis, we believe that our product candidate will be effective in treating the disease, including the associated macular edema, with a reduced incidence of side effects, such as uncontrolled, elevated IOP and cataracts. Our preclinical studies suggest that suprachoroidal injection of TA may provide improved bioavailability of drug at the retina and choroid, both at early time points and over the course of 12 weeks following treatment. We believe improved bioavailability could result in faster onset of therapeutic effect and a similar efficacy profile with lower drug amounts required. Our clinical observations from the Phase 1/2 trial suggest the potential for Zuprata to be effective at treating uveitis for at least 12 weeks following a single suprachoroidal injection, as four of the eight treated patients did not receive any additional therapy for at least 26 weeks following a single suprachoroidal injection of TA. Currently used intraocular injections of TA are typically effective for approximately 12 weeks. In contrast to intravitreal injections, based on our preclinical studies, we believe that suprachoroidal injection will allow the drug to remain more localized in the diseased retina and choroid. As a result of this localization, we believe that Zuprata may be effective in treating non-infectious uveitis, including the associated macular edema, without significant drug exposure to other eye tissues, thereby potentially reducing the incidence of side effects associated with commonly used corticosteroid treatments. We will evaluate this result in our future clinical trials in our uveitis program.

Our clinical and preclinical development

Based on our consultation with the FDA, we have conducted or are conducting the following clinical trial and preclinical studies, in each case using TA injected using a prototype of our SCS Microinjector, as part of our uveitis development program:

- an ongoing Phase 3 clinical trial in patients with macular edema associated with non-infectious uveitis evaluating suprachoroidal injection of Zuprata with our SCS Microinjector, from which we expect to report data in late 2017 or early 2018;

- a completed 22-patient Phase 2 clinical trial in patients with macular edema associated with non-infectious uveitis evaluating suprachoroidal injection of Zuprata with our SCS Microinjector;
- a completed Phase 1/2 clinical trial in non-infectious uveitis patients evaluating suprachoroidal injections of Triesence, a commercially available TA formulation, with our SCS Microinjector;
- a completed preclinical study comparing the pharmacokinetic effects of suprachoroidal and intravitreal injection of Triesence in rabbits;
- a completed preclinical study comparing the pharmacokinetic effects of suprachoroidal injection of Zuprata and Triesence in rabbits;
- a completed preclinical study evaluating the pharmacodynamic effects of suprachoroidal and intravitreal injection of Triesence in a pig model of uveitis; and
- completed preclinical studies evaluating the toxicology of single and repeated suprachoroidal injections of Zuprata and Triesence in rabbits.

Details of these clinical trials and preclinical studies are summarized below.

Pivotal Phase 3 clinical trial

Clinical Trial Design. In November 2015, we initiated a pivotal Phase 3 randomized, controlled, multi-center clinical trial in patients with macular edema associated with non-infectious uveitis and we expect to report data from this trial in late 2017 or early 2018. Based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, we believe that this trial will be the only pivotal clinical trial necessary to support a filing of a Section 505(b)(2) NDA for this indication.

We intend to conduct the trial at approximately 50 investigational sites and to enroll approximately 150 patients with macular edema associated with non-infectious uveitis, randomized either to a treatment arm consisting of approximately 90 patients or to a sham injection procedure arm consisting of approximately 60 patients. We expect to use a sham injection procedure as a comparator for Zuprata suprachoroidal treatment, as opposed to an active drug, because there are no approved therapies for macular edema associated with non-infectious uveitis against which to compare Zuprata. All of the patients in the treatment arm will receive a 4.0 mg dose of Zuprata injected into the SCS using our SCS Microinjector. In order to simulate an injection to maintain masking, the sham injection procedure will include all steps involved in the suprachoroidal injection procedure, except that a microinjector with a needleless hub will be used to apply pressure to the eye. Patients in each arm will receive their designated procedure at the beginning of the trial and a second procedure of the same type at week 12. All patients will be followed and evaluated for a period of six months following the initial procedure.

Endpoints. The primary efficacy outcome of the trial will be a visual acuity outcome, as we evaluate patients' changes in BCVA from baseline at week 24. Secondary efficacy outcomes will include additional measures of changes in BCVA and reductions in retinal thickness from baseline. Safety measures will be monitored over the 24-week observation period and will include the incidence of adverse events and serious adverse events, including cataracts and increases in IOP.

Phase 2 clinical trial

We have completed a Phase 2 multi-center, masked, randomized, internally controlled clinical trial designed to evaluate the safety and efficacy of a single 4.0 mg or a single 0.8 mg dose of Zuprata administered through the SCS. We are using and expect to use Zuprata in all ongoing and future clinical trials intended to support a 505(b)(2) NDA submission for the uveitis program.

Clinical Trial Design. We enrolled 22 patients at 14 sites in this trial. Eligibility criteria included males and non-pregnant females over the age of 18 with macular edema associated with non-infectious uveitis, with fluid in the retina and with retinal thickness above 310 microns and reading better than 20/400 in the study eye, which corresponds to 20 or more letters of BCVA. Patients were excluded if they had other ocular conditions in the study eye. Patients were randomized to receive a single suprachoroidal injection of one of two doses of Zuprata, with 17 patients receiving a 4.0 mg dose and five patients receiving a 0.8 mg dose. Patients returned for follow-up examinations between seven days and 11 days, at four weeks and at eight weeks following dosing.

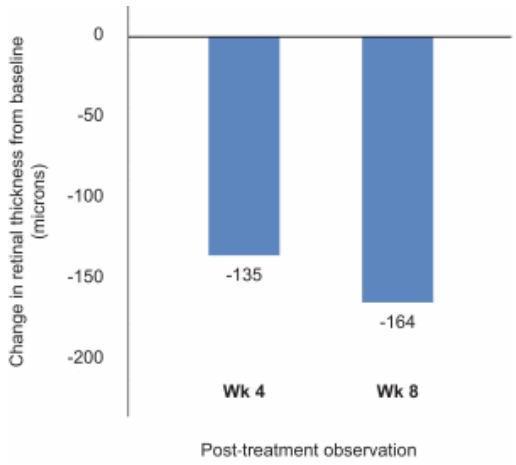
Patients enrolled in the trial ranged in age between 20 years and 83 years, with a median age of 53. Of the 22 patients enrolled, 12 were female and 10 were male; 18 were Caucasian and four were African-American.

Of the 17 patients in the 4.0 mg treatment group, two patients had anterior uveitis, meaning that the primary site of inflammation is the anterior chamber of the eye; five patients had intermediate uveitis, meaning that the primary site of inflammation is the ciliary body and the vitreous; one patient had posterior uveitis, meaning that the primary site of inflammation is the retina and choroid; and nine patients had pan-uveitis, meaning that the primary site of inflammation involves both the anterior and posterior regions.

Endpoints. The primary endpoint in this trial was mean change in retinal thickness from baseline at eight weeks following the suprachoroidal injection of the 4.0 mg dose of Zuprata. Secondary endpoints included evaluation of changes in BCVA. Only the 17 patients who received the 4.0 mg dose of Zuprata were evaluated for achievement of these endpoints. The efficacy data from the patients on the 0.8 mg dose is considered exploratory, and therefore was not considered in determining achievement of endpoints. We also evaluated safety endpoints in all 22 patients, including changes in IOP, in this trial.

Efficacy results—retinal thickness. Of the 17 patients who received the 4.0 mg dose of Zuprata, 16 were evaluated for changes in retinal thickness. At four and eight weeks, the average reduction in retinal thickness was 135 and 164 microns, respectively, with p-values of 0.0056 and 0.0017, respectively. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 or less represents statistical significance, meaning that there is a less than 1-in-20 likelihood that the observed results occurred by chance. These results are summarized in the chart below.

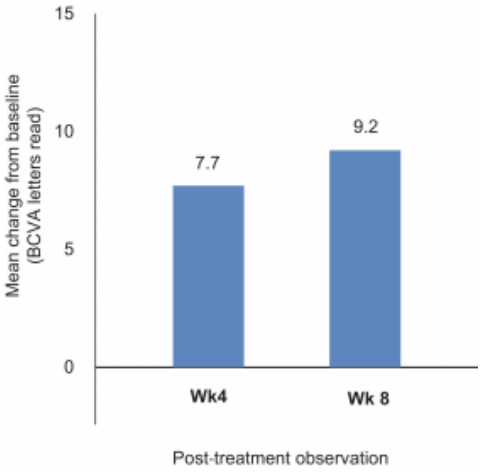
Mean reduction in retinal thickness



Of these 16 patients evaluated for changes in retinal thickness, nine patients achieved a reduction in retinal thickness to below 310 microns, which represents the maximum retinal thickness for approximately 95% of the population with normal retinas, at both week 4 and week 8. In addition, nine patients had reductions in thickness of at least 20% from their baseline levels at week 4, while 11 patients achieved this level of reduction at week 8.

Efficacy results—visual acuity. All 17 patients who received the 4.0 mg dose of Zuprata were evaluated for changes in BCVA, measured using the Early Treatment of Diabetic Retinopathy Study chart, or the ETDRS chart, a standard visual acuity measurement. At four and eight weeks, the average improvement in BCVA was 7.7 and 9.2 letters on the ETDRS chart, respectively, with p-values of 0.0001 and 0.0004, respectively. These results are summarized in the chart below.

Improvement in best corrected visual acuity



Of the 12 patients evaluated with worse than 20/40 vision, 92% of patients improved by at least five letters, 50% of patients improved by at least 10 letters, 33% of patients improved by at least 15 letters and 8% of patients improved by more than 25 letters.

In addition to the improvements in retinal thickness and visual acuity, we also observed improvements in other clinical signs of uveitis in the Phase 2 clinical trial. These included reductions in anterior chamber cells and reductions in anterior chamber flare, as well as improvements in the level of vitreous haze. In each case, the relevant severity scores decreased to zero or near zero or remained close to zero both for the overall average for all the patients as well as individually for a majority of the patients as measured by these markers of inflammation.

Safety results. All 22 patients completed the full observation period of the trial, and Zuprata was generally well tolerated. One patient experienced atrial fibrillation, a condition that resolved in one day. The principal investigator considered this serious adverse event to be unrelated to the treatment, an assessment that was reviewed and approved by an independent medical monitor. There were no serious adverse events related to study treatment and no corticosteroid-related increases in IOP observed in this trial and none of the patients experienced cataracts.

Phase 1/2 clinical trial

In February 2015, we completed a Phase 1/2 multi-center, open-label clinical trial designed to evaluate the safety and tolerability of a single injection of Triesence into the SCS in patients diagnosed with non-infectious uveitis. The trial was conducted under an IND we submitted to the FDA in December 2012 for the potential treatment of sympathetic ophthalmia, temporal arteritis, uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids. The IND was amended in March 2014 to update the specific treatment indication to be macular edema following non-infectious uveitis. The primary purpose of this trial was to demonstrate the overall safety of treating uveitis patients by injecting a commercially available formulation of TA into the SCS, rather than intravitreally.

Clinical trial design. We enrolled eight patients at three centers in this trial. Eligibility criteria included adult patients with non-infectious uveitis experiencing either macular edema or vitreous haze, another common complication of uveitis. We enrolled patients with either of these complications of uveitis in order to assess the safety and tolerability of suprachoroidal injection of TA and to determine whether suprachoroidal injection of TA could improve patient vision by reducing the effects of either of these conditions. Eligible patients had IOP levels of no greater than 22 millimeters of mercury, or mmHg, a common measure of pressure. Normal IOP levels are generally between 10 and 12 mmHg at the low end and 20 and 22 mmHg at the high end. IOP levels above 22 mmHg are considered to be elevated, increasing the patient's risk of developing glaucoma.

Each patient enrolled received a single suprachoroidal injection of 4.0 mg of Triesence, a common intravitreal dose of TA, at a location at the front of the eye similar to the location typically used for intravitreal injection. Patients returned for a follow-up examination on the day after the injection and then for eight additional evaluations at weeks 1, 2, 4, 8, 12, 16, 20 and 26 following the treatment. Patients could receive other treatment for non-infectious uveitis at any time during the trial with any accepted therapy, if the patient's condition deteriorated or if the treating physician otherwise determined it to be advisable. In the event a patient received other treatment, we continued to follow the patient for the duration of the trial for safety purposes, but, in accordance with the trial protocol, we no longer considered efficacy measures after the administration of other treatment as part of the evaluation of the suprachoroidal injection's effect on that patient.

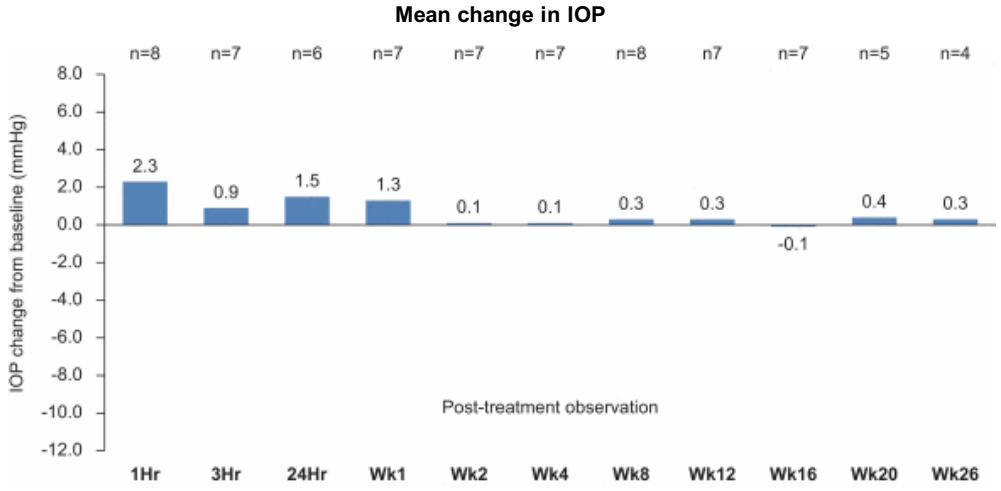
This Phase 1/2 clinical trial was not powered to show efficacy results with statistical significance. Statistical significance means that an effect is unlikely to have occurred by chance. Clinical trial results are considered statistically significant when the probability of the results occurring by chance, rather than from the efficacy of the product candidate, is sufficiently low. Since the trial was not powered to show results with statistical significance, the results from the trial may be attributable to chance and not to the clinical efficacy of TA. This trial design is typical of Phase 1 and some Phase 2 clinical trials, the principal purpose of which is to provide the basis for the design of larger, definitive trials with the inclusion of more patients to show statistical significance.

Endpoints. Our Phase 1/2 clinical trial was primarily a safety and tolerability study, although we also assessed efficacy measures. The main safety endpoint related to changes from baseline in IOP. We also assessed efficacy endpoints relating to changes in best-corrected visual acuity, or BCVA, and changes in retinal thickness, which is a common measurement of macular edema. BCVA is a common measurement of a patient's ability to see at distances. In this trial, BCVA was measured using a standard eye chart known as a Logarithm of the Minimum Angle of Resolution, or LogMAR, chart. A LogMAR chart has five letters per line, and improvement in BCVA of one line on the LogMAR chart corresponds to an improvement of 0.1 LogMAR units. A LogMAR score of zero corresponds to 20/20 vision, while a LogMAR score of 0.3 corresponds to 20/40 vision and a score of 0.6 corresponds to 20/80 vision.

Safety results. The chart below shows the mean change in IOP for the eight patients treated in the trial, as measured at different time points post-treatment. All eight patients completed the full 26-week observation

period. No patient experienced either a 10 mmHg increase in IOP from baseline or an absolute increase in IOP to a level above 30 mmHg. Such increases are generally considered meaningful in standard clinical practice and are often seen starting between six and 12 weeks after topical or intravitreal administration of steroid to the eye. For example, the prescribing information for the intravitreally administered corticosteroid, Ozurdex, notes that in clinical trials of over 300 patients, 28% of patients receiving Ozurdex experienced at least a 10 mmHg increase in IOP from baseline at a follow-up visit, and 33% of patients treated with Ozurdex experienced an increase in IOP to a level above 25 mmHg. Additionally, in our Phase 1/2 clinical trial, no patient required medication to lower increased IOP during the course of the trial.

The number of patients included in the results for each time point in the chart below, indicated with the notation "n=", varies because, at some time points up to week 4, one or two patients either missed a follow-up visit or a measurement was inadvertently skipped, resulting in only six or seven of the eight patients being measured. In addition, the number of patients included in the results for the time points in the chart below also varies because observations for the four patients who received other treatment for their non-infectious uveitis during the follow-up observation period of the trial are only included up to the point that these patients received such other treatment. One patient received additional treatment following the week 8 observation, two patients received additional treatment following the week 16 observation and a fourth patient received additional treatment following the week 20 observation.



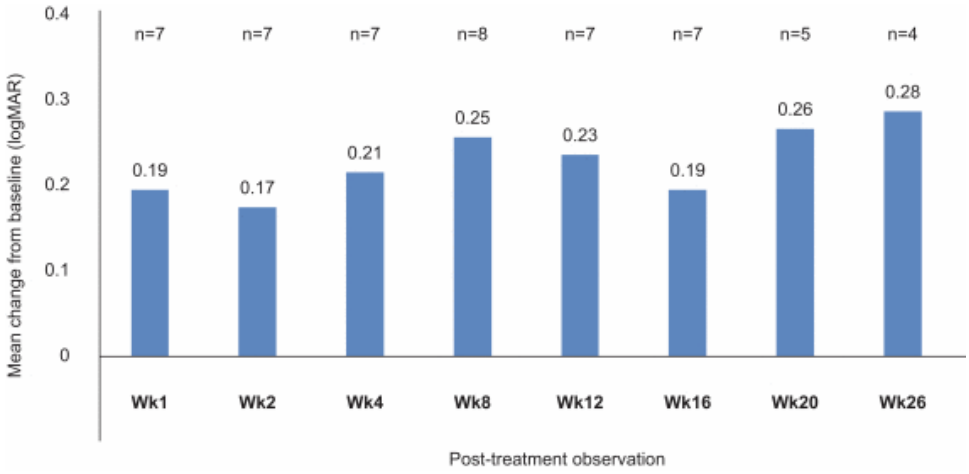
In addition to these IOP observations, the drug was generally well tolerated in this clinical trial. One patient with a history of pulmonary embolisms was hospitalized following a pulmonary embolism 10 weeks after treatment. The principal investigator considered this serious adverse event to be unrelated to the treatment, an assessment that was reviewed and approved by an independent medical monitor. The condition resolved after three days.

Efficacy results—visual acuity. In this trial, BCVA from baseline was measured at weeks 1, 2, 4, 8, 12, 16, 20 and 26 following treatment. Efficacy results were recorded until the patient required another treatment, after which the patient's BCVA was no longer measured in accordance with the trial protocol. Of the eight patients who received drug in this trial, one patient was given additional treatment following the week 8 observation, two patients were given additional treatment following the week 16 observation, and one patient was given additional treatment following the week 20 observation. The remaining four patients needed no additional treatment during the 26-week post-treatment observation period.

The chart below summarizes the mean improvement in BCVA observed at each evaluation time point in the trial, measured using a LogMAR chart. A LogMAR chart has five letters per line, and improvement in BCVA of one line on the LogMAR chart corresponds to an improvement of 0.1 LogMAR units. During the course of the trial, we observed a range of improvement in BCVA of between one and five lines (0.1 to 0.5 on the LogMAR chart). At the end of week 12, the average improvement in BCVA exceeded two lines, which is considered meaningful in standard clinical practice. At the end of week 26, four of the eight patients in the trial had still not required additional treatment. For those four patients, the average improvement in BCVA was nearly three lines at week 26.

As described above, the number of patients included in the results for the time points in the chart below varies because of missed follow-up visits and because observations for the four patients who received other treatment for their non-infectious uveitis during the follow-up observation period of the trial are only included up to the point that these patients received such other treatment.

Improvement in best corrected visual acuity
(0.1 LogMAR = one line)



The table below summarizes, for the patients at each time point who had not received other treatment, the number of patients who achieved improvements of at least two and three lines from their baseline measurements:

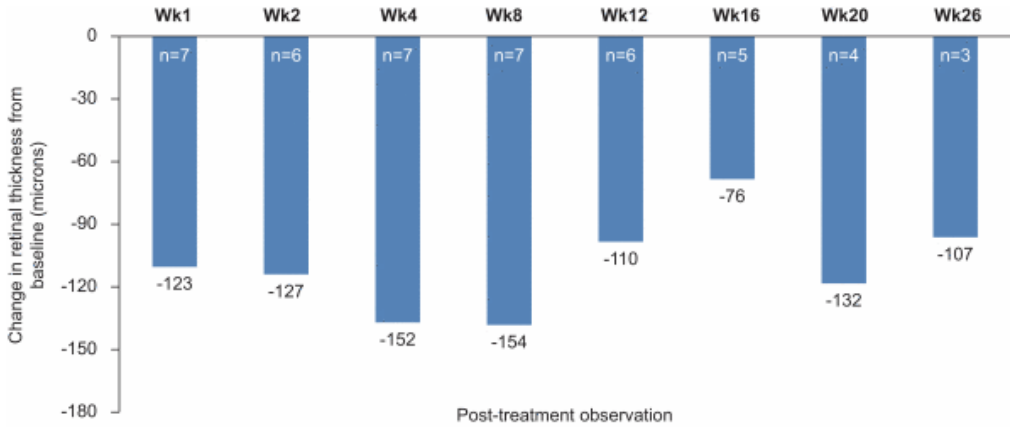
	Week 1 (n=7)	Week 2 (n=7)	Week 4 (n=7)	Week 8 (n=8)	Week 12 (n=7)	Week 16 (n=7)	Week 20 (n=5)	Week 26 (n=4)
□2 logMAR lines	3	3	5	6	5	4	4	4
□3 logMAR lines	2	2	2	5	3	3	2	2

Efficacy results—retinal thickness. Of the eight patients treated in the trial, seven were experiencing macular edema associated with their uveitis at the time of treatment and were therefore also evaluated for change in retinal thickness after the injection. A reduction in retinal thickness in patients with macular edema occurs with the removal of excess fluid from the retina, reflecting a reduction of the swelling of the macula and other parts of the retina, affected by the edema. The eighth patient was only experiencing vitreous haze associated with uveitis, an inflammatory symptom of uveitis where inflammatory cells cloud the vitreous, but in this case, the patient did not have macular edema, and change in retinal thickness is therefore not a relevant measurement for this patient.

The chart below summarizes the mean change in retinal thickness observed in the four patients that completed the 26-week post-observation period without other treatment. At weeks 12 and 26 of the trial, the average reduction in retinal thickness for patients was greater than 100 microns from their respective baselines.

In addition to the number of patients varying at each time point as a result of missing follow-up visits or skipped measurements, as described above under "—Safety Results," of the seven patients that were experiencing macular edema, the number of patients included in the results for the time points in the chart below also varies because efficacy observations for the two patients who received other treatment for their non-infectious uveitis during the follow-up observation period of the trial are only included up to the point that these patients received such other treatment.

Mean reduction in retinal thickness



We believe these results are encouraging because we observed consistent response after the suprachoroidal injection. It is important to note that the improvements in BCVA and reductions in retinal thickness were achieved only in a small patient population, with data from only eight patients, in an open-label setting, were not statistically significant and might not be replicated in larger-scale trials that we intend to conduct.

Preclinical study comparing the pharmacokinetic effects of suprachoroidal and intravitreal injection of Triesence in rabbits

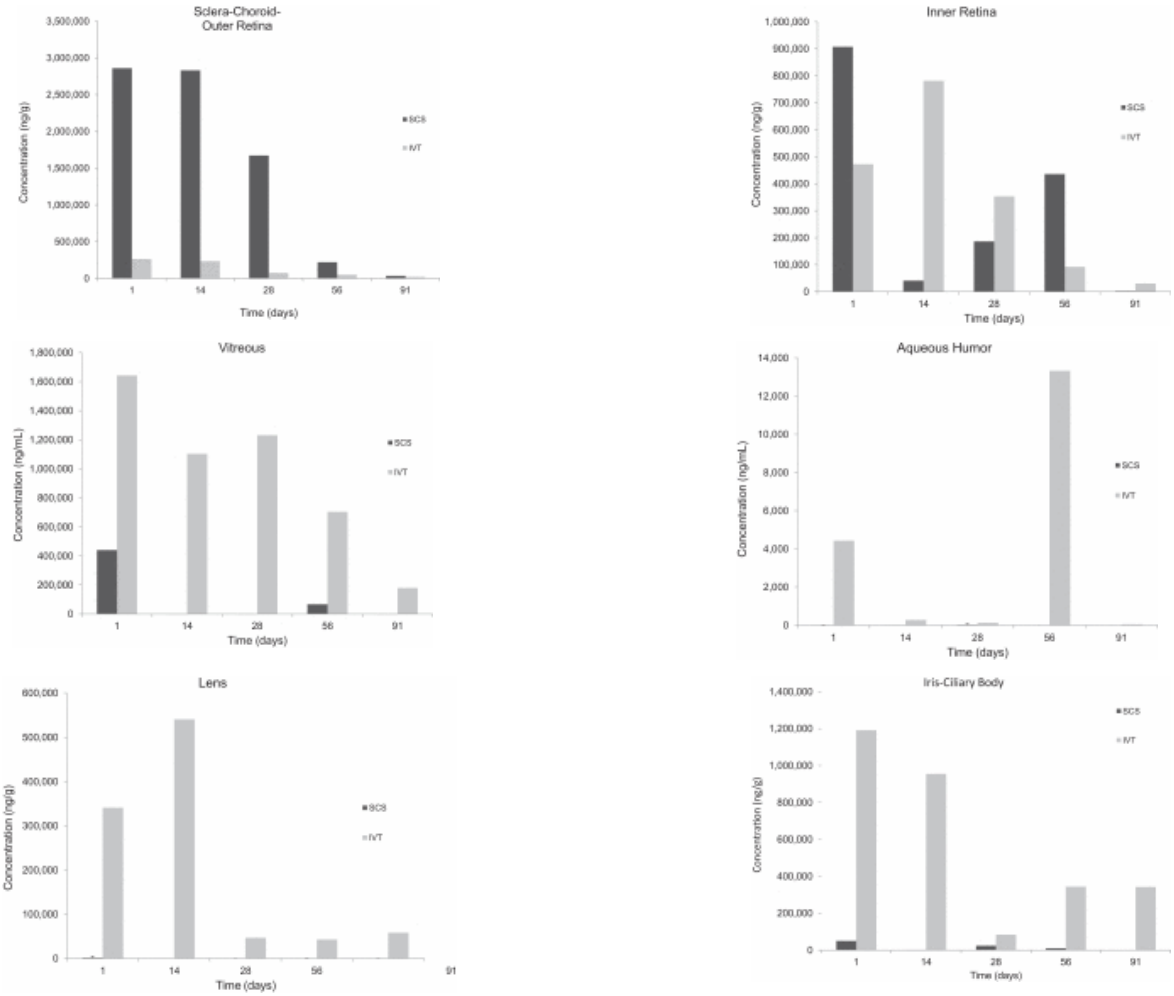
We conducted a preclinical study in rabbits to compare the pharmacokinetic results of suprachoroidal injections and intravitreal injections of Triesence, a commercially available TA formulation. Pharmacokinetics refers to the process by which a drug is distributed and metabolized in the body, which provides information on drug levels in specific tissues and how these levels change over time. To compare these results, we observed the relative distributions of Triesence in the different tissues and areas of the eye for each method of administration.

In this study, 50 rabbits received a single dose of 4.0 mg of Triesence on day 1 of the study injected either intravitreally or into the SCS. The rabbits were then observed for periods of up to 90 days and the concentration of TA in various parts of the eye was measured at days 14, 28, 56 and 91.

The tables below illustrate the results of this study. For each tissue type or area of the eye, the values shown represent the average concentration of drug observed in the rabbits at the particular measurement points

during the study, when comparing the two routes of injection. For clarity of presentation, the tables below include varying concentration scales.

Concentration of TA following either suprachoroidal injection (SCS) or intravitreal injection (IVT)



In the inner sclera, choroid and outer retina, significantly higher concentrations of TA injected into the SCS were present throughout the 91-day period as compared to TA injected intravitreally. The opposite was the case in the iris, ciliary body, lens and aqueous humor, all of which are located at the front of the eye, as well as in the vitreous, with each of these tissues showing higher levels of TA throughout the 91-day period when injected intravitreally as compared to its injection into the SCS. Only minimal levels of TA were present in the iris, ciliary body, lens and aqueous humor when injected into the SCS. Although there was variability in the relative concentrations in the inner retina, which is the part of the retina adjacent to the vitreous, at different time points, the concentrations were generally comparable across both administration methods. In this study, we also compared the drug levels in the blood plasma for each method of administration. Minimal levels of drug in the blood plasma were detected following each method of administration.

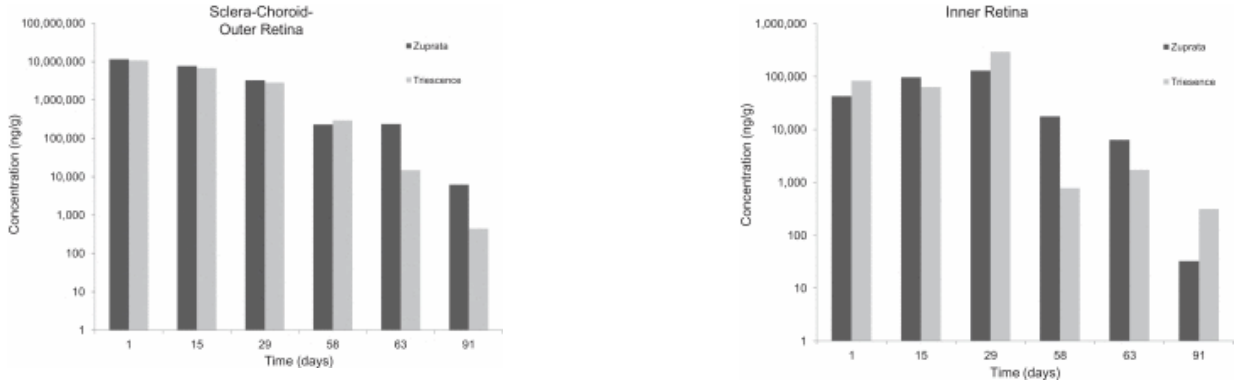
We believe these preclinical study results suggest that drugs administered through the SCS can remain substantially localized within the targeted retina and choroid, and away from other parts of the eye, where they could result in a higher incidence of side effects. We also believe these results suggest that suprachoroidal injection provides substantially better bioavailability for at least 90 days in the targeted retina and choroid than intravitreal injection. We intend to further evaluate this bioavailability data in future clinical trials before any potential submission of our marketing application to the FDA.

Preclinical study comparing the pharmacokinetic effects of suprachoroidal injection of Zuprata and Triesence in rabbits

In order to establish that Zuprata behaves in the same manner as Triesence despite the differences in formulation, we conducted a preclinical pharmacokinetic study in rabbits, comparing the pharmacokinetic profile of Zuprata with the profile of Triesence, each injected into the SCS. In the study, 25 rabbits received a single dose of 4.0 mg of either Zuprata or Triesence injected into the SCS on day 1. The rabbits were then observed for periods of up to 90 days and the resulting concentrations of each of the two TA formulations in various parts of the eye was measured at days 15, 29, 58, 63 and 91.

In this study, Zuprata and Triesence had comparable distributions throughout the eye over the 90-day period. As shown in the graphs below, both Zuprata and Triesence, administered through the SCS, remained present in the retina and choroid throughout the 90-day period following injection.

Concentration of either Zuprata or Triesence following suprachoroidal injection

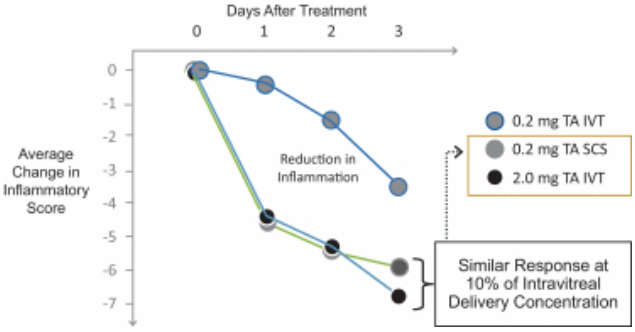


Preclinical study evaluating the pharmacodynamic effects of suprachoroidal and intravitreal injection of Triesence in a pig model of Uveitis

In this preclinical study, the results of which were published in the journal *Investigative Ophthalmology and Vision Science*, we studied the pharmacodynamics of Triesence injected into the SCS and injected intravitreally in a pig model of uveitis. Pharmacodynamics refers to the biochemical and physiological effects of a drug on the body. In this study, 20 pigs were assigned to one of three drug treatment arms: two intravitreal and one SCS. The intravitreal injections were with doses of either 0.2 mg or 2.0 mg of Triesence and the suprachoroidal injection was with a dose of 0.2 mg of Triesence. The pigs were observed for three days after injection to measure their average change in inflammatory score, as measured by an established scale for measuring inflammation in the eye, the modified McDonald-Shadduck grading system. After three days, both the 2.0 mg intravitreal and the 0.2 mg SCS doses were observed to be more effective at reducing uveitic inflammation than the 0.2 mg intravitreal injection. Additionally, the 0.2 mg SCS dose and 2.0 mg intravitreal dose achieved

similar reductions in inflammatory scores each day. Therefore, suprachoroidal injection of Triesence had a similar pharmacodynamic response to intravitreal injection at only 10% of the dose. The graph below illustrates these results.

Reduction in inflammation following either suprachoroidal or intravitreal injection of Triesence in a pig model of Uveitis



Preclinical studies evaluating the toxicology of suprachoroidal injection of Zuprata and Triesence in rabbits

We have conducted toxicology studies in rabbits in which both Zuprata and Triesence were well tolerated when injected into the SCS. In one study, 110 rabbits received a single suprachoroidal injection of either 3.2 mg or 5.2 mg of Triesence or of a vehicle control without active drug. The rabbits were then evaluated for the following 17 weeks. In the other study, 48 rabbits received an initial suprachoroidal injection of either 4.0 mg of Zuprata or of vehicle control and were then evaluated for the following 13 weeks. A subgroup of the 48 rabbits received a second suprachoroidal injection of Zuprata after the first 13 weeks and this subgroup was evaluated for an additional 13 weeks, resulting in a total observation period of 26 weeks. In both studies, the rabbits were observed for tolerability assessments as well as mortality and clinical observations, body weight and food and water consumption.

In these studies, all doses of Zuprata and Triesence were well-tolerated. In the study in which rabbits received Zuprata, a slight increase in IOP was observed. There were no other treatment-related or administration-related side effects, and in each case localization of TA in the back of the eye was observed, with minimal exposure in the front of the eye.

Additional studies

We will also be following patients from the Phase 3 trial in an extension trial to obtain additional information on the duration of action of Zuprata. In this extension trial, patients from the Phase 3 trial who have not received any other therapy will have the opportunity to be enrolled, and will receive no further treatments for their uveitis. Since the last treatment in the Phase 3 trial would have occurred at week 12 following the initial procedure, we expect to enroll patients starting at their week 24 exit visit and to follow eligible patients for an additional 24 weeks or until they receive additional treatment at the election of the physician.

We intend to enroll an additional 35 patients in a separate clinical trial in order to collect additional safety information to add to our overall safety database to reach the number required for our planned NDA submission. These additional patients will be evaluated over six months following dosing with Zuprata.

Regulatory approval pathway

If the results of our single pivotal Phase 3 clinical trial are favorable, we intend to seek regulatory approval of Zuprata for this indication by utilizing Section 505(b)(2) of the FDCA. As part of our NDA submission under Section 505(b)(2), we intend to rely on the results from all of our clinical trials, as well as the FDA's previous findings of safety and efficacy for TA and an analysis of available data from clinical literature.

We also intend to base any foreign marketing applications, in part, on data obtained through these trials.

Zuprata for macular edema associated with retinal vein occlusion

We are developing Zuprata for treatment of macular edema associated with RVO, a sight-threatening disorder resulting from the blockage of a retinal vein. In this program, we are using a suprachoroidal injection of Zuprata together with an intravitreal injection of the anti-VEGF drug, Eylea. We believe that we may provide a differentiated therapeutic benefit for RVO patients with our combination treatment that potentially couples the advantages of visual acuity gain and macular edema reduction along with a quarterly, rather than monthly, dosing schedule, compared to currently used intravitreal anti-VEGF injections alone.

We recently completed a 46-patient Phase 2 clinical trial with Zuprata injected into the SCS concomitantly with intravitreally injected Eylea for the treatment of macular edema associated with RVO. Based on feedback from a recent meeting with the FDA, we intend to commence a Phase 3 clinical program in the first half of 2017.

Market opportunity for treatment of RVO

RVO is a sight-threatening disorder resulting from a blockage of one of the veins carrying blood out of the retina. RVO is estimated to affect more than 16 million adults worldwide, according to a 2010 study published in the journal *Ophthalmology*, and we estimate RVO affects 2.2 million individuals in the United States. In RVO, the blockage of a retinal vein can lead to poor blood circulation, low oxygen, and sometimes inflammation. A blocked vein will leak its contents of blood and fluid. Bleeding within the retina and swelling from fluid can create macular edema.

Limitations of currently available therapies for macular edema associated with RVO

There are three primary treatments currently used for the treatment of RVO: intravitreal injections of anti-VEGF medications, intravitreal corticosteroid injections and laser surgery. The current standard treatment for macular edema associated with RVO involves intravitreal injections of anti-VEGF drugs, such as Lucentis, Eylea or Avastin. Lucentis and Eylea are indicated for monthly administration and Avastin is used in a similar fashion, but off-label. These monthly treatments are required throughout the course of the disease, which could last for years. Anti-VEGF drugs are effective in significantly improving vision in approximately 30% to 40% of patients with macular edema associated with RVO, and have limited side effects.

Corticosteroid treatment, specifically TA injected intravitreally, was previously evaluated in a series of randomized, multi-center clinical trials, called the SCORE studies, conducted by the National Eye Institute. For example, in the SCORE-CRVO study, approximately 26% of patients with macular edema associated with RVO had meaningful gains in visual acuity after one year with a dosing frequency of one intravitreal injection of TA every four months. However, several side effects were observed, including cataracts and elevated IOP. Because of these side effects, intravitreal administration of corticosteroids, such as TA, is not the preferred therapy, even though it has been observed to be effective in reducing macular edema associated with RVO. Another corticosteroid therapy, Ozurdex, an extended release dexamethasone implanted in the vitreous, has been approved by the FDA for the treatment of RVO, but has also been associated with increased IOP in 25% of patients and cataracts in 5% of patients.

Before the introduction of anti-VEGF drugs, laser surgery was the leading therapy for treating macular edema associated with RVO. Laser surgery can be used to help control bleeding and swelling, which can reduce the loss of sight, but cannot improve vision. Laser surgery, however, cannot be used long term because it permanently damages the retina.

Potential benefits of Zuprata in treating macular edema associated with RVO

In our RVO program, we are exploring the concomitant suprachoroidal injection of Zuprata and intravitreal injection of Eylea, a corticosteroid and an anti-VEGF agent, respectively, to provide the potential benefits of improved visual acuity, reduced macular edema and reduced injection frequency. Corticosteroids and anti-VEGF agents have known advantages in treating RVO. Based on the SCORE studies described above and our findings in our Phase 2 clinical trial and preclinical studies, we believe that each suprachoroidal injection of Zuprata may provide a duration of effect longer than anti-VEGF therapy alone, while also potentially reducing the frequency of necessary anti-VEGF treatments from once every 30 days to once every 90 days, due to the benefits of both corticosteroid and anti-VEGF treatment. In addition, we believe that the side effect profile of suprachoroidal Zuprata with an intravitreal anti-VEGF agent will be similar to that of current intravitreal anti-VEGF treatments alone, as based on preclinical data, suprachoroidal injections of Zuprata should allow the corticosteroid to remain substantially localized in the retina and choroid, potentially reducing side effects that are commonly observed with other routes of administration of corticosteroids. Combination therapy with a corticosteroid and an anti-VEGF agent has been shown to reduce treatment frequency to once every four months along with improved visual acuity outcomes based on a clinical trial conducted by a third party.

Clinical trials

We have completed a 46-patient Phase 2 clinical trial in which the goal was to demonstrate that patients treated with Zuprata injected into the SCS together with Eylea injected intravitreally require less frequent treatments than monotherapy of Eylea injected intravitreally. We enrolled 46 patients at 14 sites in the United States in this trial. All patients in the trial were randomized to receive one intravitreal injection of 2.0 mg of Eylea, in a total volume of 50 microliters, and a single suprachoroidal injection of 4.0 mg of Zuprata, in a total volume of 100 microliters, or one intravitreal injection of Eylea and a sham SCS procedure in the same visit. After randomization, patients were seen in the clinic once per month for three months. The 23 patients in each of the two treatment arms were evaluated for the need to receive additional intravitreal injections of Eylea alone at months one, two and three after the initial injection using specified criteria to determine if they continued to experience increases in macular edema or reductions in visual acuity, as determined by a masked, centralized reading center.

The primary objective of the trial was to evaluate the safety and efficacy of a single suprachoroidal injection of Zuprata together with the initial intravitreal injection of Eylea, compared to the control group initially receiving only an intravitreal Eylea injection. The primary efficacy endpoint in the trial was determining the number of follow-up Eylea treatments for which patients met the criteria, which we believe provides an indication of whether concomitant therapy provides any advantage to the patient in reducing the number of required Eylea treatments. Secondary efficacy endpoints included measures of change in BCVA and reductions in retinal thickness from baseline. The safety endpoints were the incidence of adverse events and serious adverse events, including increases in IOP.

For the primary endpoint, patients in the active arm, who initially received concomitant injections of Zuprata into the SCS and Eylea into the vitreous, met the criteria for an aggregate of nine intravitreal Eylea follow-up injections over three months, while patients in the control arm, who initially received only an intravitreal injection of Eylea, met the criteria for an aggregate of 23 intravitreal Eylea follow-up injections. These results

met the primary endpoint of the trial and were statistically significant, with a p-value of 0.013. In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant, with a p-value of 0.003.

For the BCVA secondary endpoint, patients in the active arm experienced greater improvement in visual acuity than those in the control arm, with patients in the active arm experiencing mean BCVA improvements at months one, two and three of 16, 20 and 19 letters, respectively, from a baseline of 49 letters, compared to improvements of 11, 12 and 11 letters, respectively, in the control arm, at the same time points and also from a baseline of 49 letters. The greater improvement in BCVA observed in the active arm, when compared to the control arm, of 4.7, 8.5 and 7.6 letters, was statistically significant at month two, but was not statistically significant at months one or three. For the retinal thickness endpoint, patients in the active arm had mean levels of reduction of approximately 450 microns after each of one, two and three months. Patients in the control arm achieved a mean reduction of approximately 400 microns after one month, which reduction then declined to approximately 340 microns at months two and three. The trial was not powered to show statistical significance on the secondary endpoints. There were no serious adverse events reported in the trial and the treatment was generally well tolerated.

Based on these results, we believe that the combination of a suprachoroidal injection of Zuprata and an intravitreal injection of Eylea may provide the benefits of improved visual acuity, reduced macular edema and reduced injection frequency.

We have also completed a GLP toxicology study in rabbits with a suprachoroidal injection of Zuprata together with an intravitreal injection of the anti-VEGF drug Eylea.

Phase 3 clinical program and regulatory approval pathway

We held an end-of-Phase 2 meeting with the FDA in the second half of 2016 to discuss the details of the regulatory approval pathway for Zuprata along with Eylea for the treatment of macular edema associated with RVO. Incorporating feedback from the FDA, we expect to be able to follow a 505(b)(2) NDA regulatory approval pathway and to initiate a Phase 3 clinical program in the first half of 2017 in order to support an NDA submission for Zuprata in macular edema associated with RVO. In pursuing the 505(b)(2) regulatory pathway, we intend to rely on the results from our RVO development program, the FDA's previous findings of safety and efficacy for TA, the FDA's previous findings of safety and efficacy for Eylea and peer-reviewed literature.

We intend to commence our first randomized, controlled, double-blind Phase 3 clinical trial with suprachoroidal Zuprata and intravitreal Eylea for the treatment of RVO in the first half of 2017. We intend to conduct this trial at approximately 150 investigational sites and to enroll approximately 460 patients with macular edema associated with RVO, randomized either to a treatment arm consisting of approximately 230 patients or a control arm consisting of approximately 230 patients. Patients in the treatment arm will receive suprachoroidal Zuprata together with intravitreal Eylea at the beginning of the trial, intravitreal Eylea alone at week 4, and suprachoroidal Zuprata together with intravitreal Eylea at weeks 12 and 24. Patients in the control arm will receive intravitreal Eylea alone at the beginning of the trial and follow-up treatments of intravitreal Eylea alone every four weeks through week 24. After 24 weeks, patients will be followed for approximately an additional six months. The primary objective of this trial will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at eight weeks after initial treatment.

Zuprata for diabetic macular edema

We are developing Zuprata, alone or with an anti-VEGF agent, for treatment for DME, a common ocular complication of diabetes that results in swelling in the macula and is the primary cause of vision loss associated with diabetes.

Market opportunity for treatment of DME

According to the U.S. Centers for Disease Control and Prevention, or CDC, the number of Americans diagnosed with diabetes has increased from approximately 7.7 million in 1994 to approximately 29.1 million in 2014. All patients with diabetes are at risk of developing some form of diabetic eye disease. DME accounts for a majority of vision loss in patients with diabetic eye disease. According to a study published in the journal *Diabetes Care* in 2003, patients with diabetes have a 10% risk of developing clinically significant DME over a 10-year period. A study published in the journal *Ophthalmology* in 2009 found that over a 25-year period, approximately 17% of diabetics studied were diagnosed with DME. We estimate approximately 1.1 million individuals in the United States suffer from DME.

Limitations of currently available therapies for DME

Currently, the only FDA-approved drugs for the treatment of DME are the anti-VEGF drugs Lucentis and Eylea and the intravitreal corticosteroid implants Ozurdex and Iluvien. Some retinal specialists also prescribe other anti-VEGF drugs for off-label use, such as Avastin, as well as corticosteroid therapies, primarily Kenalog and Triesence, and laser photocoagulation to treat DME. Laser photocoagulation is a procedure in which a laser is used to apply a burn or a pattern of burns to cauterize leaky blood vessels to reduce edema in the retina. Studies have shown that both anti-VEGF drugs and corticosteroids are effective in some DME patients. However, both anti-VEGF drugs and corticosteroids are limited by a need for multiple injections to maintain a therapeutic effect. This raises concerns, not only for patients, but also for caregivers who are affected by frequent doctor visits, as well as for healthcare providers who must monitor patients monthly. In addition, these therapies have safety concerns. Corticosteroids administered intravitreally have historically been associated with acceleration of cataract formation and significant increases in IOP, which may increase the risk of glaucoma, and monthly anti-VEGF treatments have been associated with increased risk of geographic atrophy. Laser photocoagulation can also have undesirable side effects, including partial loss of peripheral and night vision.

Clinical and preclinical development

Our development program for DME is modeled on our approach for the treatment of RVO. We are conducting a multi-center, open-label Phase 1/2 clinical trial to evaluate the safety and efficacy of administering a single 4.0 mg dose of Zuprata, administered suprachoroidally, both alone and in combination with Eylea, in patients with DME over a six-month evaluation period. We plan to enroll 20 patients in this trial. Efficacy endpoints will include changes in retinal thickness and BCVA. We recently enrolled the first patient in this trial. We expect to report data from this trial in the second half of 2017.

Axitinib for wet age-related macular degeneration

We are developing a proprietary suspension formulation of axitinib, a single molecule with dual anti-VEGF and anti-PDGF activity, for the treatment of wet AMD by injection into the SCS with our SCS Microinjector, which we believe could provide visual acuity benefits, macular edema reduction and potentially reduce the frequency of necessary treatments compared to the current standard of care. Wet AMD is a condition involving the abnormal formation and growth of new blood vessels in the choroid, their intrusion into the outer layers of the retina and

leakage of blood and fluid into the retina. Axitinib, also known by its brand name Inlyta, is currently marketed by Pfizer and is approved by the FDA for the treatment of advanced renal cell carcinoma, but not for any ophthalmology indications. We believe that developing a proprietary suspension formulation of axitinib to be administered by suprachoroidal injection could be more effective than current treatments for wet AMD. We believe that suprachoroidal injection of our proprietary formulation of axitinib could result in improvements in visual acuity compared to intravitreal injection of anti-VEGF drugs, while potentially reducing the frequency of necessary treatment. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.

Market opportunity for treatment of wet AMD

Wet AMD is a leading cause of severe vision loss and blindness in people over the age of 50 in the developed world. If untreated, the blood vessel growth and leakage associated with wet AMD can eventually lead to blindness. The majority of patients with wet AMD experience severe vision loss in the affected eye within approximately two years after diagnosis of the disease. According to a study published in 2004 in the journal *Ophthalmology*, approximately 1.2 million people in the United States suffer from wet AMD. Based on estimates from AMD Alliance International, a non-profit organization focused on AMD awareness, and census growth data, we estimate there are approximately 230,000 new cases of wet AMD each year in the United States. Because the risk of developing wet AMD increases with age, we expect that the overall aging of the population will result in a significant increase in the number of wet AMD cases, both in the United States and worldwide.

Limitations of currently available therapies for wet AMD

The current standard of care for the treatment of wet AMD is administration by intravitreal injection of anti-VEGF drugs as a standalone therapy. The anti-VEGF drugs most commonly used include Lucentis and Eylea, both of which have been approved by the FDA for the treatment of wet AMD, and Avastin, which is used off-label for the disease.

Because anti-VEGF therapies inhibit abnormal blood vessel growth and leakage, they are effective in reducing the macular edema associated with wet AMD. Anti-VEGF therapies have demonstrated the ability to prevent further visual loss in approximately 90% of treated patients. A retrospective study published in 2012 in the journal *Archives of Ophthalmology* concluded that the prevalence of both legal blindness and moderate visual impairment in patients two years after being diagnosed with wet AMD had decreased substantially following the introduction of anti-VEGF therapy. However, because anti-VEGF drugs do not appear to cause any regression of the underlying neovascularization associated with wet AMD, the current standard of care requires regular injections, typically as often as seven times per year, and therapy may be required indefinitely. Further, while anti-VEGF treatment is effective at preventing vision loss, only 30% of patients improve their visual acuity by 15 letters or more. Anti-VEGF treatments have been associated with subretinal fibrosis, or the formation of excess connective tissue under the retina, as well as retinal scarring in some patients, with 45% of patients experiencing scarring after two years of anti-VEGF therapy according to a 2014 study published by the American Academy of Ophthalmology. Additionally, monthly treatment with anti-VEGF agents have been associated with increased risk of geographic atrophy, according to a 2013 study published by the American Academy of Ophthalmology.

In addition to anti-VEGF therapies, anti-PDGF drugs are being developed as potential treatments for wet AMD. Because PDGF is a major factor in the formation and stabilization of blood vessel growth in the choroid, therapies inhibiting PDGF may also be effective in addressing the abnormal growth of new blood vessels associated with wet AMD. In clinical trials conducted by others, an intravitreal injection of a PDGF inhibitor together with an intravitreal injection of Lucentis improved visual acuity in approximately 60% of patients with

wet AMD compared to approximately 30% of patients receiving intravitreal injections of Lucentis alone. However, no anti-PDGF therapy has been approved by the FDA for the treatment of wet AMD, either alone or in combination with an anti-VEGF agent. Even if approved, we expect that anti-PDGF therapy would also require indefinite monthly injections.

Even though anti-VEGF and anti-PDGF therapies may be effective in treating wet AMD, intravitreal injection of these drugs relies on the process of diffusion of the drug from the vitreous outward to the retina and, eventually, the choroid, which results in lower bioavailability and the need for frequent retreatment.

Potential benefits of our proprietary suspension formulation of Axitinib

Axitinib has dual anti-VEGF and anti-PDGF activity. Based on prior clinical data from trials conducted by a third party, we believe that anti-PDGF properties together with anti-VEGF properties may provide superior visual outcomes to standalone anti-VEGF drugs. We believe that the suprachoroidal injection of drugs with anti-VEGF, or dual anti-VEGF and anti-PDGF, activity more directly to the neovascularization in the choroid through suprachoroidal injection could block the process of additional new vascular growth within the choroid before the vessels break into and create further damage through leakage into the retina. We believe that such suprachoroidal injection of treatment may, therefore, provide faster onset of therapeutic effect and delay vision loss for a longer duration of time than the current standard intravitreal administration and will require less frequent injections. We will test this hypothesis in any future clinical trials that we may conduct as part of our clinical development program for wet AMD.

Clinical and preclinical development

We have completed the following clinical trial and preclinical studies as part of our wet AMD development program:

- a completed Phase 1 clinical trial in wet AMD patients evaluating the safety and tolerability of suprachoroidal injection of Avastin, an anti-VEGF drug, with our SCS Microinjector;
- a completed preclinical efficacy study of suprachoroidal injection of a compound with dual anti-VEGF and anti-PDGF activity in a rabbit model of wet AMD;
- a completed preclinical efficacy study of suprachoroidal injection of Eylea in a rat model of wet AMD;
- a completed preclinical safety study of suprachoroidal injection of compounds with dual anti-VEGF and anti-PDGF activity; and
- a completed preclinical pharmacokinetic study to evaluate ocular distribution and duration of axitinib in a rabbit model.

Details of the trial and studies are summarized below.

Completed Phase 1 clinical trial with Avastin

In order to evaluate the safety and tolerability of suprachoroidal injection of Avastin, an anti-VEGF drug, in humans with our SCS Microinjector, we conducted a Phase 1, single-center, open-label clinical trial in 2012 at the Hospital of the Association to Prevent Blindness in Mexico. Because of its established safety profile and its prevalence as an off-label treatment for wet AMD, we selected Avastin as the therapy to be evaluated in this exploratory trial. Four patients with wet AMD were enrolled in the trial, each of whom was between the ages of 63 and 73. Each patient received a 2.5 mg dose of Avastin in a 100 microliter injection in one eye using a prototype of our SCS Microinjector. The trial was conducted in accordance with current U.S. good clinical practices.

Trial design. Eligibility criteria included adult patients with choroidal neovascularization associated with wet AMD that had previously responded to Avastin treatment, had retinal thickness in the study eye of between 275 and 600 microns in the central subfield, and had specified levels of visual acuity. In addition, patients could not have received any anti-VEGF treatment within 60 days of screening or have had any expectation of receiving such treatment during their participation in the study other than the single Avastin injection.

Once eligibility was established, each patient received a single suprachoroidal injection of Avastin and then returned for a follow-up examination on the day after the injection. Thereafter, patients returned for five additional evaluations at approximately weeks 1, 2, 3, 4 and 8 following the injection. No additional treatments were administered during the course of the trial.

Endpoints. The trial was primarily a safety and tolerability study. The safety endpoints included incidence, intensity and type of adverse events, as well as changes from baseline in IOP. We also measured efficacy endpoints, including change from baseline in BCVA letter score.

Safety results. *Suprachoroidal injection* of Avastin in the trial was observed to be generally well tolerated. No increases in IOP or serious or unexpected adverse events were reported in any of the patients. Two patients experienced hyperemia, or redness in the study eye, which was mild in severity, was determined to be unrelated to treatment in the trial and resolved within a day without other treatment.

Efficacy results. Two of the four patients achieved an improvement in BCVA letter score of at least 13 letters at the end of the eight-week trial following the suprachoroidal injection of Avastin. One of these patients improved by 16 letters within one day of treatment and maintained that level of improvement for the remainder of the trial. The second patient achieved an improvement of four letters by one week after treatment, which improved to 10 letters by week 3 after treatment and 13 letters by week 8. The other two patients in the trial maintained their BCVA letter score within four letters of their baseline at each measurement point in the trial. Overall, there was an average gain of nine letters in the four patients at the end of the eight-week observation period following the suprachoroidal injection of Avastin.

By comparison, in a trial conducted by the National Eye Institute, the Comparison of AMD Treatment Trial, or CATT, which was a Phase 3 randomized, masked, controlled, multi-center study, the efficacy of Avastin was compared to that of Lucentis, which has been approved by the FDA for the treatment of wet AMD. In the CATT trial, patients in the respective treatment arms received either monthly intravitreal injections of Lucentis or monthly intravitreal injections of Avastin over two years. After one year, patients receiving monthly Lucentis treatment experienced an average improvement in BCVA of 8.5 letters, while those receiving Avastin experienced an average improvement of 8.0 letters. After two years, the average improvement for the patients receiving Lucentis and Avastin was 8.8 letters and 7.8 letters, respectively.

Our Phase 1 trial was not designed to show any efficacy results with statistical significance and was conducted in an open-label, uncontrolled setting. While the data from this exploratory trial suggested potential improvement in visual acuity over eight weeks following suprachoroidal injection of Avastin, it is important to note that the results from this trial were observed in only four patients and might not be achieved by any other patient treated with a product candidate to be developed as part of our wet AMD program. Any later-stage trials intended to support an application for regulatory approval of a product candidate for this indication will need to show statistical significance in larger, well-controlled clinical trials.

Preclinical efficacy study of a compound with dual anti-VEGF and anti-PDGF activity in a rabbit model of wet AMD

We conducted a preclinical study assessing the effect on retinal leakage in a wet AMD rabbit model of a drug candidate with dual anti-VEGF and anti-PDGF activity administered by suprachoroidal injection. In this study, the treatment arm of three rabbits received a suprachoroidal injection of the drug and the control arm of three rabbits received a suprachoroidal injection of a vehicle without the active drug. After 28 days, retinal leakage was induced on the surface vessels of the inner retina in both arms and leakage was measured approximately two hours after this induction. The treatment arm showed 48% less retinal leakage than the vehicle arm. We believe this suggests that this dual anti-VEGF and anti-PDGF drug administered through the SCS may be effective in treating wet AMD by reducing leakage in the retina, and even in vessels in the inner retina, which is closest to the vitreous. We are continuing to evaluate this compound.

Preclinical efficacy study of suprachoroidal injection of Eylea in a rat model of wet AMD

We conducted a preclinical study to assess the effectiveness of suprachoroidal injection of Eylea, as compared to intravitreal injection, in reducing the lesion area in rats with choroidal neovascularization, in a well-established model of wet AMD in which laser burns are used to induce choroidal neovascularization. Rats were divided in groups and given either one 0.2 mg dose of Eylea by suprachoroidal injection, two separate 0.2 mg doses of Eylea by suprachoroidal injection, or suprachoroidal injections of saline. We measured the reduction in macular lesion area after 21 days and found that the lesion area reductions in the two groups receiving Eylea by suprachoroidal injection were comparable to historical data of lesion area reductions from intravitreal injections of Eylea at the 0.2 mg dosage level. We believe this suggests that administration of Eylea through suprachoroidal injection may be as effective as intravitreal administration in reducing leakage due to choroidal neovascularization in this rat model of wet AMD.

Preclinical safety study of suprachoroidal injection of compounds with dual anti-VEGF and anti-PDGF activity

We conducted a preclinical study assessing the safety of compounds with dual anti-VEGF and anti-PDGF activity administered by suprachoroidal injection. In this study, a total of 18 rabbits received a suprachoroidal injection of a number of compounds and were evaluated on days 1, 4 and 7. Overall, the compounds were well tolerated with only mild or transient ocular effects observed.

Preclinical pharmacokinetic study of ocular distribution and duration of Axitinib in rabbit model

We conducted a preclinical pharmacokinetic study to assess the rate at which axitinib distributes through the ocular tissues, in addition to the time-frame of such ocular distribution. In this study, we administered 4.0 mg of axitinib by suprachoroidal injection in both eyes of two rabbits. We measured the distribution and duration of the drug on days 1, 2, 4, 8, 15, 29, 61 and 91 following the injection. Key portions of the eye that were evaluated for levels of drug remaining were the sclera-choroid-retinal pigmented epithelium, or SCR, the neural retina and the vitreous. We also observed that, at 91 days, there was more than 60% of the original axitinib remaining in the SCR. There was also a significant amount of drug remaining in the neural retina. Based on calculations from the remaining amounts of drug, we believe the data suggest a possible half-life of axitinib of at least three months. We believe this duration of effect supports our belief that suprachoroidal administration of axitinib may require less frequent injections than the current standard intravitreal injections of anti-VEGF drugs.

Planned clinical development

Based on the results of our Phase 1 clinical trial in four wet AMD patients and our preclinical rabbit study, we believe that wet AMD may be effectively treated through suprachoroidal injection, and we will evaluate this hypothesis as part of any clinical development program. We have performed pharmacokinetic and toxicology

studies, as well as additional preclinical testing, to support an IND submission for our proprietary formulation of axitinib. We held a pre-IND meeting with the FDA in November 2016. We intend to submit an IND application in the first half of 2017 to commence a Phase 1/2 clinical trial of axitinib in wet AMD patients.

Future potential product candidates

We believe that our SCS-focused approach has the potential to become more broadly used for the treatment of other back of the eye diseases, and we intend to develop additional product candidates for suprachoroidal injection based on the results of our current and planned clinical trials. We will then seek to secure appropriate regulatory authorizations to begin additional clinical testing for any such product candidates. In addition to uveitis, RVO, DME and wet AMD, there are a number of ophthalmic conditions affecting the retina and choroid with unmet medical need for which suprachoroidal injection of therapy may be beneficial and for which we may seek marketing authorization, including:

- *Polypoidal choroidal vasculopathy*, or PCV, a disorder resulting from the abnormal growth of new blood vessels in the choroid adjacent to the macula. PCV is characterized by dilated and branching blood vessels in “polyp like” groups in the choroid that could lead to leakage;
- *Geographic atrophy*, an advanced form of AMD, is characterized by a loss of the layers of cells in the retina next to the choroid, eventually including the photoreceptor cells in the macula, leading to gradual irreversible loss of central vision and eventually blindness; and
- *Pseudophakic cystoid macular edema*, also known as Irvine-Gass syndrome, a common cause of visual impairment after cataract surgery.

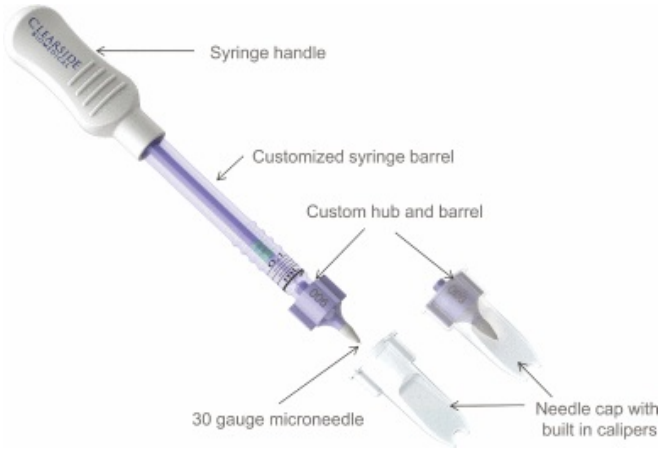
As part of our ongoing collaboration with Santen, we are evaluating the use of our SCS Microinjector to administer sustained-release formulations of known glaucoma drugs. Glaucoma is a progressive eye disease in which elevated levels of IOP are associated with damage to the optic nerve, which results in irreversible vision loss and potentially blindness. The National Eye Institute estimates that 2.7 million Americans suffered from glaucoma in 2010. Glaucoma is treated by the reduction of IOP, which has been shown to slow the progression of vision loss. Once glaucoma develops, it is a chronic condition that requires life-long treatment. The treatment of glaucoma, if successful, would be through the suprachoroidal administration of latanoprost or other drugs known to lower elevated IOP associated with glaucoma.

We are also evaluating the potential use of our SCS Microinjector to inject sustained-release formulations of other ocular therapies. We believe these formulations could include hydrogels, emulsions and liposomes, as well as treatments containing agents such as hyaluronic acid or micro- or nanoparticles.

The SCS Microinjector

Our drug candidates have been and will be specifically formulated to be injected with our SCS Microinjector into the SCS in order to spread around to the back of the eye. The single-use microinjector is intended to consistently inject drug into the SCS, in volumes similar to the amount of drug commonly used in an intravitreal injection. If approved for marketing by applicable regulatory authorities, the SCS Microinjector will be packaged with two 30-gauge hollow microneedles of varying lengths, each less than 1.2 millimeters, within a custom-designed hub that optimizes insertion and administration of drug into the eye. Based on our discussions with the FDA to date, we do not anticipate that the FDA will require a separate medical device authorization for the SCS Microinjector, but this could change during the course of its review of any marketing application that we may submit.

Our proprietary SCS Microinjector, shown below, can be used to inject a wide variety of drugs into the SCS.



The suprachoroidal injection is designed to be carried out perpendicular to the sclera, at a site similar to an intravitreal injection, under local anesthesia. Once the microneedle penetrates the sclera and reaches the SCS, the boundary between the sclera and the choroid, the open bevel of the needle releases the drug between these two layers. Once drug is injected into the SCS, it spreads within the SCS to the back of the eye, where diseases manifest. The preparation and injection will require minimal training for the administering retinal specialist and can be accomplished in an in-office setting.

Current intravitreal injections are performed in a procedure similar to that of suprachoroidal injections, except that the hypodermic needles and syringes used in intravitreal injection procedures are designed so that the needle penetrates through all of the layers of the eye and drug is injected into the vitreous cavity, where the precise spatial location of the needle is not as important as when injecting into the SCS. Intravitreal injections are typically performed using a needle that is approximately five millimeters in length, or four times the length of our microneedle. Using a needle of this length, the physician penetrates past the sclera, choroid and retina until reaching the vitreous and does not receive any tactile feedback as to when the needle had reached one of the layers between the sclera and the vitreous. By contrast, our SCS Microinjector is designed to enable the release of the drug into the SCS.

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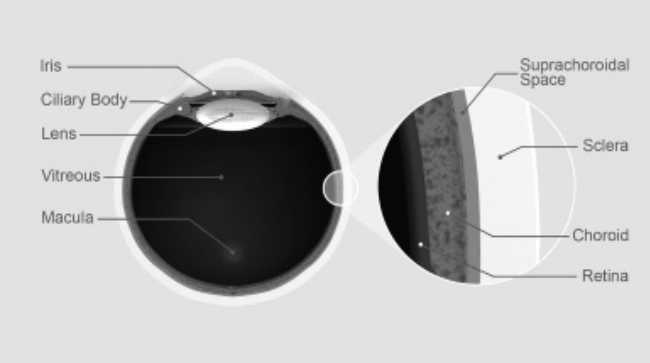
Background on eye disease

The human eye possesses focusing elements in the front, the cornea and lens, and a light-sensing element in the back, the retina. Light falls on the photoreceptors that are part of the retina, called rods and cones, and is converted into electrical energy, which travels via the optic nerve to the brain. The central portion of the retina is the macula, which is the region responsible for seeing color and the acute central vision necessary for activities such as reading, face recognition, watching television and driving. The brain processes the complex signals sent from the retina into vision. The following diagram illustrates the principal elements of the anatomy of a healthy eye, including a detailed cross-section of the back of the eye, which refers to the portion of the eye behind the lens.



Role of the choroid in retinal 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 either partial or total blindness. In the developed world, the major diseases that result in blindness are those affecting the retina. Millions of people live with varying degrees of irreversible vision loss because they have a degenerative eye disorder that affects the retina. In these conditions, the retina is damaged, affecting the retina's ability to send light signals to the brain. The choroid provides blood, oxygen and nourishment to the outer layers of the retina, but it is also thought to regulate retinal heat, to assist in the control of IOP and to absorb excess light so as to avoid reflection that can damage the retina.

The choroid can be subject to disorders that can lead to retinal damage and vision loss, including inflammatory disorders, vascular disorders and tumors. Our focus is on the first two categories of disorders. When the choroid and surrounding tissue become inflamed from an immune response, it can result in macular edema, or swelling in the macular region of the retina, which often results in distorted vision or even blindness. In addition, in the case of choroidal neovascularization, abnormal blood vessels forming from choroidal blood vessels may rupture and leak into the retina, also leading to macular edema.

Back of the eye diseases

Some of the more common diseases that originate or manifest in the retinal and choroidal areas of the eye include:

Uveitis

Uveitis is inflammation inside the eye and is classified anatomically as anterior, intermediate, posterior or pan-uveitis, according to the primary site of inflammation. Each of these categories, however, encompasses a

number of conditions that can be characterized further along other dimensions including: onset, duration, course and etiology. Prolonged or severe inflammation in the back of the eye associated with uveitis can result in the breakdown of cells at the interface of the retina and choroid, leading to the leakage and accumulation of fluid in the macular region of the retina. This fluid build-up can cause macular edema, which can rapidly result in distortion of vision, and eventually blindness, given the macula's critical role in vision. Approximately 30% of people with uveitis develop macular edema, which is the most frequent cause of visual impairment among patients with uveitis.

Uveitis is one of the most frequent causes of blindness in the developed world. Based on prevalence data published in the journal *Ophthalmology* in 2004 and United States census data for 2010, we estimate approximately 350,000 individuals in the United States suffer from some form of uveitis. Uveitis can be either infectious, caused by an immune response to fight an infection inside the eye, or non-infectious. Non-infectious uveitis accounts for approximately 80% of all uveitis cases.

Uveitis is commonly treated with corticosteroids. Corticosteroids administered through eye drops, although used to treat some uveitis patients, are generally ineffective in treating patients with macular edema associated with non-infectious uveitis. Corticosteroids administered orally or systemically can be effective in treating patients with macular edema associated with non-infectious uveitis, but their long-term use is associated with significant side effects. As a result of the shortcomings associated with these methods of administering corticosteroids, the most common method for treating macular edema associated with non-infectious uveitis is intravitreal injection or implant of a corticosteroid, such as TA, dexamethasone or fluocinolone acetonide.

Retinal vein occlusion

RVO is a sight-threatening visual disorder resulting from a blockage of one of the veins carrying blood out of the retina. In RVO, the blockage of a retinal vein can lead to poor blood circulation, low oxygen, and sometimes inflammation in the area that is normally drained by the affected vein. A blocked vein will leak its contents of blood and fluid. This leakage within the retina and the consequential swelling from fluid can cause macular edema. Persistent inadequately treated macular edema associated with RVO can blur vision, cause significant loss in visual acuity and eventually lead to blindness. Macular edema is the most common cause of vision loss in people who suffer from RVO.

RVO is estimated to affect more than 16 million adults worldwide, according to a 2010 study published in the journal *Ophthalmology*. We estimate RVO affects 2.2 million individuals in the United States.

RVO can be treated and vision can be restored in most cases when treatment is administered relatively soon after initial diagnosis and aggressive treatment is obtained. One common method of reducing the macular edema associated with RVO is to use an anti-VEGF drug. Anti-VEGF drugs are effective in drying the leaking fluid and, therefore, they are useful in eye conditions where edema is a complication of the disease. An added challenge of RVO is inflammation that arises in response to the vascular damage and further contributes to the swelling by causing even more fluid to accumulate in the retina. Since inflammation also plays a role in vein occlusion, corticosteroids may provide an added advantage in the reduction of macular edema associated with RVO because they block the inflammatory pathways and also act to stabilize membranes.

Diabetic macular edema

DME is a complication of diabetic retinopathy, a disease affecting the blood vessels of the retina. Diabetic retinopathy results in multiple abnormalities in the retina, including retinal thickening, hemorrhages, impeded blood flow, excessive leakage of fluid from blood vessels and, in the final stages, abnormal blood vessel growth. When the blood vessel leakage causes swelling in the macula, it is referred to as DME. Poorly controlled blood

glucose levels, high blood pressure, abnormal kidney function causing fluid retention, high cholesterol levels and other general systemic factors are risk factors associated with DME. The principal symptom of DME is a severe loss of central vision.

According to the CDC, the number of Americans diagnosed with diabetes has increased from approximately 7.7 million in 1994 to approximately 29.1 million in 2014. According to a study published in the journal *Diabetes Care* in 2003, patients with diabetes have a 10% risk of developing clinically significant DME over a 10-year period. A study published in the journal *Ophthalmology* in 2009 found that over a 25-year period, approximately 17% of diabetics studied were diagnosed with DME. We estimate approximately 1.1 million individuals in the United States suffer from DME.

Currently, the only FDA-approved drugs for the treatment of DME are Iluvien, an injectable form of fluocinolone acetonide, the anti-VEGF drugs Lucentis and Eylea and the intravitreal corticosteroid implant Ozurdex. Some retinal specialists also prescribe other anti-VEGF drugs for off-label use, such as Avastin, as well as corticosteroid therapies, primarily Kenalog and Triesence, and laser photocoagulation to treat DME. Studies have shown that both anti-VEGF drugs and corticosteroids are effective in some DME patients. However, the early use of anti-VEGF drugs administered intravitreally is limited by a need for frequent injections to maintain a therapeutic effect and corticosteroids administered intravitreally have historically been associated with acceleration of cataract formation and significant increases in IOP, which may increase the risk of glaucoma. Laser photocoagulation can also have undesirable side effects, including partial loss of peripheral and night vision.

Age-related macular degeneration

AMD is a chronic, progressive disease of the macula that results in the loss of central vision. The most common symptoms are a central blurred or blank spot, distortion of objects or simply blurred vision. Peripheral vision usually remains intact. The disease typically affects patients initially in one eye, with a high likelihood of it occurring in the second eye over time. Because AMD is strongly correlated with aging, the disease may recur, notwithstanding treatment, as the aging process continues.

There are two forms of AMD, “dry” AMD and “wet” AMD. Dry AMD is the most common form, representing approximately 85% to 90% of all AMD cases. However, dry AMD cases can develop into wet AMD, and wet AMD accounts for 90% of the severe vision loss associated with advanced AMD.

Wet AMD occurs when new blood vessels in the choroid intrude into the retinal layers and leak fluid. The formation of these new blood vessels is referred to as choroidal neovascularization, since they arise from the capillaries in the choroid. Abnormal new blood vessels tend to be fragile and often bleed and leak fluid into the macula. Untreated, blood vessel growth and associated leakage typically lead to retinal distortion and eventual retinal damage and scarring, resulting in irreversible destruction of the macula and permanent loss of vision. This visual loss occurs rapidly with a progressive course.

According to a study published in 2004 in the journal *Ophthalmology*, approximately 1.2 million people in the United States suffer from wet AMD. Based on estimates from AMD Alliance International and census growth data, we estimate there are approximately 230,000 new cases of wet AMD each year in the United States. Because the risk of developing wet AMD increases with age, we expect that the overall aging of the population will result in a significant increase in the number of wet AMD cases, both in the United States and worldwide.

The current standard of care for the treatment of wet AMD is administration by intravitreal injection of anti-VEGF drugs as a standalone therapy. Because anti-VEGF therapies inhibit abnormal blood vessel growth and leakage, they are effective in reducing the macular edema associated with wet AMD. Anti-VEGF therapies are effective in reducing macular edema associated with wet AMD and have been shown to prevent visual loss in

over 90% of treated patients. They are also associated with improvements of 15 or more letters of visual acuity in approximately 30% of treated patients. However, anti-VEGF treatments have been associated with subretinal fibrosis, or the formation of excess connective tissue under the retina, as well as retinal scarring in some patients. In addition to anti-VEGF therapies, anti-PDGF drugs are being developed as potential treatments for wet AMD. Even though anti-VEGF and anti-PDGF therapies may be effective in treating wet AMD, intravitreal administration of these drugs requires frequent retreatment. Patients typically receive injections as often as seven times per year to manage this chronic disease.

Challenges of ophthalmic drug administration

Administration of drugs to treat back of the eye diseases is a significant issue in ophthalmology. Due to the effectiveness of the blood/eye barrier, it is difficult for oral or other systemically administered drugs to reach the eye in sufficient quantities to have a beneficial effect without adverse side effects to other parts of the body. It is also difficult to provide localized delivery of drug to the individual tissues of the eye through common eye drop or intravitreal injection techniques.

There is a need for more localized drug delivery to the back of the eye in a manner that is safe, effective and practical for long-term use. While there have been many attempts to administer drugs to the back of the eye, most do not achieve sufficient and consistent concentrations for the appropriate period of time. Currently, intravitreal injection remains as the standard for delivering drugs to the retina and choroid. We believe that our novel approach using suprachoroidal injection can address several of the shortcomings of current therapies.

Manufacturing

We do not have any manufacturing facilities. We utilize contract manufacturers to formulate and produce our drug candidates and to produce our SCS Microinjector used for our clinical trials. We procure the active pharmaceutical ingredient for our drugs from a third-party supplier. We expect to utilize third-party manufacturers to produce commercial quantities of our drugs and SCS Microinjector, if approved. We anticipate entering into commercial supply agreements with these or other manufacturers at a later date.

Commercialization

We intend to develop and, if approved by the FDA, to commercialize our product candidates in the United States, and we may enter into distribution or licensing arrangements for commercialization rights for other regions. Our management team, who will lead the commercialization of our lead product candidates, has substantial experience in sales and marketing based on their participation in the commercialization of ophthalmic drugs at large pharmaceutical companies including Alcon, Allergan, CIBA Vision and Novartis.

For marketing in the United States, we intend to build a specialty team of 30 to 40 sales and medical marketing professionals to target the approximately 1,700 retinal specialists in the United States.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. 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 candidate that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

With respect to Zuprata, we face competition from other commercially available forms of TA and other injectable and implantable corticosteroids. Bristol-Myers Squibb markets TA under the brand name Kenalog. Kenalog is indicated only for intramuscular or intraarticular injection, although it is used off-label for intraocular inflammation. There are also a number of generic equivalents of Kenalog. In addition, Alcon's injectable TA, Triesence, is approved in the United States for the treatment of uveitis and other inflammatory conditions unresponsive to topical corticosteroids, although it is not indicated for the treatment of macular edema associated with uveitis or RVO or DME. Ozurdex, marketed by Allergan, is a bioerodable extended release implant that delivers the corticosteroid dexamethasone and is approved for the treatment of non-infectious uveitis affecting the back of the eye and RVO in both the United States and in the European Union, and recently received approval from the FDA to treat DME. Bausch + Lomb markets Retisert, an intravitreal implant of the corticosteroid fluocinolone acetonide for the treatment of non-infectious uveitis. Iluvien, an injectable form of fluocinolone acetonide marketed by Alimera Sciences, has been approved in both the United States and the European Union for the treatment of DME.

Our product candidates will also compete with anti-VEGF drugs, which are the current standard of care for RVO, wet AMD and DME. Genentech's products Lucentis and Avastin are both anti-VEGF antibodies. Lucentis is currently approved in the United States and European Union for the treatment of wet AMD, macular edema following RVO, DME and diabetic retinopathy in patients with DME. Avastin is an anti-VEGF drug used off-label by retinal specialists in both the United States and in certain countries of the European Union in the treatment of numerous retinal diseases, but it is not indicated for ophthalmic use. In the United States, Regeneron's anti-VEGF product, Eylea, is approved for the treatment of wet AMD, macular edema following RVO and DME. In the European Union, Eylea is approved for the treatment of wet AMD, DME and macular edema secondary to RVO.

Ophthotech's drug candidate, Fovista, an anti-PDGF agent, is in Phase 3 clinical trials as a potential treatment for wet AMD to be administered together with an anti-VEGF drug. We are also aware of several other drug candidates in earlier stages of development as potential treatments for the diseases that we intend to target.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient recruitment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors may also obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or obtaining FDA market exclusivity, thereby delaying our product approvals. Competitors' patent protection could also potentially delay FDA approval of our product candidates for up to 30 months, and we will still be subject to potential patent litigation that might arise beyond the 30 months. The key competitive factors affecting the success of our product candidates, if approved for marketing, are likely to be their efficacy, safety, method of administration, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

Intellectual property

Our success depends in part on our ability to obtain and maintain patent and other intellectual property and proprietary protection for our technologies and methods of accessing the SCS, drug candidates and formulations as well as patent and other intellectual property and proprietary protection for novel applications, uses, and technological innovations related to our drug candidates, proprietary delivery devices and core technologies. We also rely on trade secrets, know-how, and continuing technological innovation to develop and maintain our proprietary position.

Patents and patent applications

Our patent estate, on a worldwide basis, includes six granted U.S. patents broadly directed to methods of administering drugs into the SCS by injection, including one design patent. In addition, our patent estate includes 17 patent applications pending in the United States, nine issued foreign patents, three pending international PCT applications and 55 patent applications pending in major international markets, including the European Union, Canada, India, Japan, China and Australia, relating to our SCS delivery technology, as well as the formulations of our current therapeutic drug candidates and delivery device. Of these patents and patent applications, we license four of the six issued U.S. patents, one pending U.S. application, four of the issued foreign patents, one of the pending international PCT applications and 12 foreign patent applications, each relating to methods of delivering drugs to the eye by microneedle administration, pursuant to a license agreement with Georgia Tech Research Corporation and Emory University that is described below. With respect to the in-licensed international PCT application, according to the terms of the license agreement, we advise Georgia Tech and Emory regarding the countries in which patent applications should be pursued. Subject to payment of required maintenance fees, annuities and other charges, our issued in-licensed U.S. patents are expected to expire between 2027 and 2029, without taking into account possible patent term adjustments or extensions. Applications relating to SCS delivery technology and methods, our current therapeutic drug candidates and formulations, various therapeutic uses, including treatment of specific indications such as macular edema associated with non-infectious uveitis and RVO, wet AMD as well as DME and improvement of specified clinical parameters, are expected to expire between 2027 and 2035, without taking into account possible patent term adjustments or extensions.

The term of individual patents depends on 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 extended 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.

Our product candidates are protected against genericization through several levels of patents, including the patented approach of administration into the SCS. In the case of Zuprata injected into the SCS, an applicant who files a paragraph 4 ANDA or 505(b)(2) NDA certifying they may circumvent our patents must also demonstrate comparability of the proposed drug, which we believe may require a clinical trial in macular edema associated with uveitis, against our product, unless a biowaiver is obtained.

Third-party patent filings

Numerous U.S. and foreign issued patents and patent applications owned by third parties exist in the fields in which we are developing products, including patents and applications related to surgical methods of accessing the SCS and certain formulations of TA. Because patent applications can take many years to issue, there may be applications unknown to us, which may later result in issued patents that our product candidates or proprietary technologies may infringe.

Under U.S. law, a person may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and nonobvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method.

License agreement with Emory and Georgia Tech

In July 2012, we entered into a license agreement with Emory University, or Emory, and the Georgia Tech Research Corporation, or GTRC, under which we received a worldwide exclusive license to specified patents relating to methods and devices for drug delivery using a microinjector. The field of the license covers all ophthalmic uses of the microinjector for mammals and birds. Under this license agreement, we have agreed to direct all prosecution of intellectual property to the licensors' patent counsel and have agreed to pay for all intellectual property expenses associated with the licensed patents.

Under this license agreement, we made an initial $30,000 upfront payment and a $35,000 milestone payment upon dosing of the first human patient in a clinical trial. This license agreement requires us to make a $75,000 milestone payment upon the occurrence of a specified event relating to the commercialization of a drug developed using the licensed patents. Beginning on the third anniversary of this license agreement, we will be obligated to pay an annual license maintenance fee of $25,000, which will continue until the first commercial sale of a product covered by the licensed patents. Additionally, we will owe a low single-digit royalty on any worldwide net product sales related to the licensed patents, with minimum annual royalties starting at $15,000 per year after commercialization. The minimum annual royalty increases each year after the first commercial sale, up to a maximum amount of $100,000 per year in the sixth calendar year and in subsequent years.

We are solely responsible for the development and commercialization of products related to the licensed patients. We are obligated to provide Emory and GTRC a written report detailing our activities related to the development and commercialization of products twice a year.

Royalties are calculated based on net sales of products covered by a patent licensed under the agreement, and are due on each such product sold as long as the patent covering that particular product is valid and unexpired. Unless otherwise terminated pursuant to its termination provisions, this license agreement will expire upon the expiration of the last to expire of the licensed patents. We have the right to terminate this license agreement at any time upon 60 days' written notice to Emory and GTRC. Emory and GTRC may also terminate this license agreement in the event of a material breach by us. This license agreement will immediately terminate if we challenge the validity or enforceability of any of the licensed patents in a court or other governmental agency of competent jurisdiction.

Research, option and license agreement with Spark

In April 2015, we entered into a research, option and license agreement with Spark Therapeutics, Inc., or Spark, under which we granted Spark the option to license exclusive rights to our SCS Microinjector technology and

related intellectual property for use in delivering gene therapies to the back of the eye. Under this agreement, we and Spark explored the feasibility of using our SCS Microinjector to deliver gene therapies to the choroid and the retina through the SCS for the treatment of several orphan diseases of the back of the eye.

Under the agreement, Spark made a $500,000 upfront payment to us. In February 2016, the initial study under the agreement was completed and Spark elected not to extend the arrangement or license the technology. Accordingly, the agreement expired in accordance with its terms.

Trademarks, trade secrets and know-how

Our trademark portfolio currently consists of one trademark registered in the European Union, one trademark registered in the European Union and New Zealand, and three pending U.S. trademark applications, as well as pending trademark applications in the European Union, Canada, Mexico, Brazil, Australia, China, India, Israel, Japan, New Zealand, Russia, Singapore, South Africa and South Korea. In addition to patent and trademark protection, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees, and consultants, and employees. These and other agreements, such as invention assignment agreements, grant us ownership of technologies that are developed through a relationship with a third party.

Government regulation

In the United States, the FDA regulates drug and device products under the FDCA and its implementing regulations. Our product candidates are subject to regulation as combination products, which means that they are composed of both a drug product and device product. If marketed individually, each component would be subject to different regulatory pathways and reviewed by different Centers within the FDA. A combination product, however, is assigned to a Center that will have primary jurisdiction over its regulation based on a determination of the combination product's primary mode of action, which is the single mode of action that provides the most important therapeutic action. In the case of our product candidates, the primary mode of action is attributable to the drug component of the product, which means that the FDA's Center for Drug Evaluation and Research has primary jurisdiction over the premarket development, review and approval of our product candidates. Accordingly, we plan to investigate our products through the IND framework and seek approval through the NDA pathway. Based on our discussions with the FDA to date, we do not anticipate that the FDA will require a separate medical device authorization for our SCS Microinjector, but this could change during the course of its review of any marketing application that we may submit.

The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements 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 imposition of a clinical hold, refusal by FDA to approve applications, withdrawal of an approval, import/export delays, issuance of warning letters and other types of enforcement 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 FDA and the Department of Justice or other governmental entities.

Drugs

The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are governed by extensive

regulation by governmental authorities in the United States and other countries. The FDA, under the Federal Food, Drug, and Cosmetic Act, or FDCA, regulates pharmaceutical products in the United States. The steps required before a drug may be approved for marketing in the United States generally include:

- preclinical laboratory tests and animal tests conducted under Good Laboratory Practices, or GLP;
- the submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product and conducted in accordance with Good Clinical Practices, or GCP;
- the submission to the FDA of an NDA;
- FDA acceptance, review and approval of the NDA, which might include an Advisory Committee review; and
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with current Good Manufacturing Practices, or cGMPs.

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. The FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Preclinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which must become effective before clinical trials may be commenced. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. The FDA may nevertheless initiate a clinical hold after the 30 days if, for example, significant public health risks arise.

Each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at each of the sites at which the trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Clinical trials are typically conducted in three sequential phases prior to approval, but the phases may overlap. These phases generally include the following:

Phase 1. Phase 1 clinical trials represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and pharmacodynamics.

Phase 2. Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the product candidate for specific indications, (2) determine dosage tolerance and optimal dosage and (3) identify possible adverse effects and safety risks.

Phase 3. If a product candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 clinical trials, the clinical trial program will be expanded to Phase 3 clinical trials to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical trial sites.

Phase 4 clinical trials may be conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved

under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in enforcement action or withdrawal of approval.

The results of preclinical studies and clinical trials, together with detailed information on the manufacture, composition and quality of the product, are submitted to the FDA in the form of an NDA, requesting approval to market the product. The application must be accompanied by a significant user fee payment, although waivers may be granted in limited cases. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

Review of application

Once an NDA has been accepted for filing, which occurs, if at all, 60 days after submission, the FDA sets a user fee goal date that informs the applicant of the specific date by which the FDA intends to complete its review. The Company will be required to pay a user fee to the FDA to review the NDA, unless it receives a waiver or qualifies for an exemption. This is typically 10 months from the date of submission for drugs that are not new molecular entities, such as our product candidates. The review process can be extended by FDA requests for additional information or clarification. The FDA reviews NDAs to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMPs to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA may inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and may also inspect clinical trial sites for integrity of the data supporting safety and efficacy. The device component of our products will also be subject to review as part of the NDA review process and its manufacturers subject to inspection for compliance with device cGMPs embodied in the Quality System Regulation, or QSR. During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS, and the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA could also require a special warning, known as a black box warning, to be included in the product label in order to highlight a particular safety risk. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA will issue either an approval of the NDA or a Complete Response Letter, detailing the deficiencies and information required for reconsideration of the application.

Post-approval requirements

Approved drugs that are manufactured or distributed in the United States are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product 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 and some manufacturing and supplier changes are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for products and the establishments at which such products are manufactured, as well as new application fees for certain supplemental applications.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to

further assess and monitor the product's safety and effectiveness after commercialization. The FDA may also require a REMS, which could involve requirements for, among other things, a medication guide, special training for prescribers and dispensers, and patient registries.

In addition, entities involved in the manufacture and distribution of approved devices or 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. The FDA has promulgated specific requirements for drug cGMPs, device cGMPs embodied in the QSR and combination product cGMPs that, for drug/device combination products, specify the requirements within the drug cGMPs and the QSR with which manufacturers must comply. 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 requirements 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 issue enforcement letters or withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Corrective action could delay product distribution and require significant time and financial expenditures. 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, 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 applications or supplements to approved applications, or suspension or revocation of product 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, including investigation by federal and state authorities.

The Hatch-Waxman amendments

Our regulatory strategy is to pursue development of our drugs for suprachoroidal delivery as Section 505(b)(2) NDAs under the FDCA. As an alternative path to FDA approval for modifications to formulations or uses of drugs previously approved by the FDA, 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. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which

the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This type of application permits reliance for such approvals on literature or on an FDA finding of safety, effectiveness or both for an approved drug product. As such, under Section 505(b)(2), the FDA may rely, for approval of an NDA, on data not developed by the applicant. Therefore, if we can satisfy the conditions required for a Section 505(b)(2) NDA submission, it may eliminate the need for us to conduct some of the preclinical studies or clinical trials for the new product candidate that might otherwise have been required, although the review time is not shortened. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved branded reference drug. The FDA may then approve the new product candidate for the new indication sought by the 505(b)(2) applicant.

Orange Book listing

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, known as the Orange Book. Any applicant who files an Abbreviated New Drug Application, or ANDA, seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify, for each patent listed in the Orange Book for the referenced drug, to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA, (2) such patent has expired, (3) the date on which such patent expires or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. The fourth certification described above is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. This section viii statement does not require notice to the patent holder or NDA owner. There might also be no relevant patent certification.

If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the applicant. Even if the 45 days expire, a patent infringement lawsuit can be brought and could delay market entry, but it would not extend the FDA-related 30-month stay of approval.

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 as described in further detail below.

Non-patent exclusivity

In addition to patent exclusivity, the holder of the NDA for the listed drug may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug.

A drug, including one approved under a 505(b)(2) application, may obtain a three-year period of non-patent market exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the

applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, the FDA can accept an application and begin the review process during the three-year exclusivity period. A 505(b)(2) NDA may also be subject to a five-year exclusivity period for a new chemical entity, whereby the FDA will not accept for filing, with limited exception, a product seeking to rely upon the FDA's findings of safety or effectiveness for such new chemical entity.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the United States, or in other limited cases. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan drugs are eligible for certain incentives, including tax credits for qualified clinical testing. In addition, an NDA for a product that has received orphan drug designation is not subject to a prescription drug user fee unless the application includes an indication other than the rare disease or condition for which the drug was designated.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same active moiety for the same indication for seven years, except in limited circumstances, such as another drug's showing of clinical superiority over the drug with orphan exclusivity. Competitors, however, may receive approval of different active moieties for the same indication or obtain approval for the same active moiety for a different indication. In addition, doctors may prescribe products for off-label uses and undermine our exclusivity. Orphan drug exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same active moiety for the same indication before we do, unless we are able to demonstrate that our product is clinically superior.

We do not plan to pursue orphan drug designation for Zuprata for the treatment of non-infectious uveitis in the United States. However, we may seek designation for other products in the future. We cannot guarantee that we will obtain orphan drug designation for any products in any jurisdiction. Even if we are able to obtain orphan drug designation for a product, we cannot be sure that such product will be approved, that we will be able to obtain orphan drug exclusivity upon approval, if ever, or that we will be able to maintain any exclusivity that is granted.

Foreign regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union and other geographies, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Federal and state fraud and abuse, data privacy and security and transparency laws

In addition to FDA restrictions on marketing and promotion of drugs and devices, other federal and state laws restrict our business practices. These laws include, without limitation, anti-kickback and false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the Anti-Kickback Statute has been violated.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Affordable Care Act to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. The civil False Claims Act also applies to false submissions that cause the government to be paid less than the amount to which it is entitled, such as a rebate. Intent to deceive is not required to establish liability under the civil False Claims Act. Several pharmaceutical, device and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-covered, uses.

The government may further prosecute conduct constituting a false claim under the criminal False Claims Act. The criminal False Claims Act prohibits the making or presenting of a claim to the government knowing such claim to be false, fictitious, or fraudulent and, unlike the civil False Claims Act, requires proof of intent to submit a false claim.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation

of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs.

Under HIPAA, the U.S. Department of Health and Human Services, or HHS, has issued regulations to protect the privacy and security of protected health information used or disclosed by covered entities including health care providers. HIPAA also regulates standardization of data content, codes and formats used in health care transactions and standardization of identifiers for health plans and providers. HIPAA, as amended by HITECH and its implementing regulations, including the omnibus final rule published on January 25, 2013, also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. Penalties for violations of HIPAA regulations include civil and criminal penalties. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that are applicable to our business. New laws governing privacy may be adopted in the future as well. Failure to comply with privacy requirements could result in civil or criminal penalties, which could have a materially adverse effect on our business.

Additionally, there has been a recent trend of increased federal and state regulation of payments and transfers of value provided to healthcare professionals and/or entities. On February 8, 2013, the Centers for Medicare & Medicaid Services, or CMS, released its final rule implementing the Physician Payments Sunshine Act that imposes annual reporting requirements on certain manufacturers of drugs, devices, biologicals and medical supplies for payments and other transfers of value provided by them, directly or indirectly, to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their family members. A manufacturer's failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in civil monetary penalties of up to an aggregate of $150,000 per year, and up to an aggregate of $1 million per year for "knowing failures." Any failure to comply could result in significant fines and penalties. Certain states also mandate implementation of commercial compliance programs, impose restrictions on pharmaceutical manufacturer and device manufacturer marketing practices or require tracking and reporting of gifts, compensation and other remuneration to particular types of healthcare professionals and entities.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such laws. The heightening compliance environment and the need to build and maintain robust and expandable systems to comply with different compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the health care laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal and civil and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs,

contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage and reimbursement

We believe that physicians who use our product candidates, if approved, will be reimbursed by third-party payors for both the suprachoroidal injection using our SCS Microinjector and for the drug itself. On July 1, 2016, the American Medical Association, or AMA, approved a new Category III Current Procedural Terminology, or CPT, code for the suprachoroidal injection of pharmacologic agents. Category III codes are a set of temporary codes maintained by the AMA for emerging technology, services and procedures. Payment for these services or procedures are based on the coverage policies of individual payors and Medicare administrative contractors. CPT code 0465T will become effective on January 1, 2017. We intend to seek a separate Healthcare Common Procedure Coding System, or HCPCS, code as maintained by CMS for the drug itself. We believe that separate CPT and HCPCS codes will help payors differentiate our drug candidates from other drugs currently on the market administered through intravitreal injections, although we can provide no assurance that CMS will approve the creation of a separate HCPCS code. Additionally, there is no guarantee that these billing codes or the payment amounts, if any, associated with such codes will not change in the future.

Our strategy will include efforts to engage physician societies and encourage third-party payors to establish coverage, coding and payment that will facilitate access to our product candidates and SCS Microinjector as we expand our commercialization efforts in the United States. Our success in these efforts depends in part on the extent to which governmental authorities, private health insurers and other third-party payors provide coverage for and establish adequate reimbursement levels for the procedures during which our product candidates are administered and for the drugs themselves. Failure by physicians, hospitals, ambulatory surgery centers, and other users of our products to obtain sufficient coverage and reimbursement from healthcare payors for the procedures administering our product candidates or for the product candidates themselves, or adverse changes in government and private third-party payors' policies would have a material adverse effect on our business, financial condition, results of operations and future growth prospects.

In the U.S., third-party payors continue to implement initiatives that restrict the use of certain technologies to those that meet certain clinical evidentiary requirements. Failure to obtain favorable coverage policies could have a material adverse effect on our business and operations.

In addition to uncertainties surrounding coverage policies, third-party payors from time to time update reimbursement amounts and also revise the methodologies used to determine reimbursement amounts. This includes annual updates to payments to ambulatory surgery centers, hospitals and physicians for the procedure performed administering our products, which could directly impact the demand for any of our product candidates that may be approved. An example of payment updates is the Medicare program updates to physician payments, which is done on an annual basis using a prescribed statutory formula. In the past, when the application of the formula resulted in lower payment, Congress has passed interim legislation to prevent the reductions. However, the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, ended the use of the statutory formula, and provided for a 0.5% annual increase in payment rates under the Medicare Physician Fee Schedule through 2019, but no annual update from 2020 through 2025. MACRA also introduced a quality payment program under which individual providers with Medicare billings of $30,000 or 100 patient visits per year will be subject to certain incentives or penalties based on new program quality standards. The

quality payment program has two tracks, one known as the merit based incentive payment system for providers in the fee-for service Medicare program, and the advanced alternative payment model for providers in specific care models, such as accountable care organizations. Payment adjustments for the Medicare quality payment program will begin in 2019. At this time it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program. Any changes in coverage and reimbursement that further restricts coverage of our products or lowers reimbursement for procedures using our products could materially affect our business.

Healthcare reform

Current and future legislative proposals to further reform healthcare or reduce healthcare costs may result in lower reimbursement for our products, or for the procedures associated with the use of our products, or limit coverage of our products. The cost containment measures that payors and providers are instituting and the effect of any healthcare reform initiative implemented in the future could significantly reduce our revenues from the sale of our products. However, we believe that the shift away from fee-for-service agreements to capitated payment models supports the value of our products, as we believe that our products reduce longitudinal resource utilization, which can be cost saving-for both payors and providers.

For example, implementation of the Affordable Care Act has the potential to substantially change healthcare financing and delivery by both governmental and private insurers, and significantly impact the pharmaceutical and medical device industries.

The Affordable Care Act imposed, among other things, a new federal excise tax on the sale of certain medical devices, established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents, 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, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, and provided incentives to programs that increase the federal government's comparative effectiveness research. In addition, the Affordable Care Act implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models. There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future particularly in light of the pending change in administrations following the U.S. presidential election.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to the Bipartisan Budget Act of 2015, will remain in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, 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. There has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for

their marketed products, which have resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressure.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

Employees

As of September 30, 2016, we had 23 full-time employees, all of whom are located in the United States. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Facilities

Our principal offices occupy approximately 8,800 square feet of leased office space in Alpharetta, Georgia, pursuant to a lease agreement that expires in March 2017. In November 2016, we signed a new office lease agreement to lease approximately 20,000 square feet of office space in Alpharetta, Georgia. We expect to relocate our corporate headquarters into this new space in the first half of 2017.

We believe that our current leased facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Legal proceedings

We are not currently a party to any material legal proceedings and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results or financial condition.

Management

Directors and executive officers

The following table sets forth information concerning our directors and executive officers, including their ages as of November 15, 2016:

Name	Age	Position
Executive Officers:		
Daniel H. White	49	President, Chief Executive Officer and Director
Charles A. Deignan	52	Chief Financial Officer
Glenn Noronha, Ph.D.	51	Chief Scientific Officer
Non-Management Directors:		
Christy L. Shaffer, Ph.D.	58	Chairman of the Board of Directors
Clay B. Thorp	48	Director
Evgeny Zaytsev, M.D.	48	Director
Gerald D. Cagle, Ph.D.	72	Director
William D. Humphries	50	Director
Derek Yoon	42	Director
Richard Croarkin	62	Director

Executive officers

Daniel H. White

Mr. White is the founder of our company and has served as our President and Chief Executive Officer and as a member of our board of directors since our inception in May 2011. From 2008 to 2011, Mr. White served as Executive Director, Global Corporate Development, for Stiefel Laboratories, Inc., a dermatology pharmaceutical company acquired by GlaxoSmithKline in 2009. From 2007 to 2008, he co-founded and served as President and Chief Executive Officer of Percept BioScience, Inc., a biotechnology company. In 2003, Mr. White co-founded, and until 2007 served as Vice President of Finance and Corporate Development of Alimera Sciences, Inc., a biopharmaceutical company focused on ophthalmology. Previously, he was Head of Business Development and Licensing for CIBA Vision, a Novartis company, and Director of Licensing and Business Development for AAIPharma. Mr. White holds an M.B.A. degree from Wake Forest University and a B.S. degree in Molecular Biology from Auburn University. Our board of directors believes that Mr. White's leadership of our company since its inception, extensive entrepreneurial experience, knowledge of our company as founder and experience with biotechnology companies prior to founding our company provides him with the qualifications and skills to serve as a director of our company.

Charles A. Deignan

Mr. Deignan has served as our Chief Financial Officer since January 2012. From 2009 to December 2011, Mr. Deignan was Vice President of Finance and Administration for Salutria Pharmaceuticals. Previously, from 1999 to 2009, Mr. Deignan served in a number of roles with AtheroGenics, Inc., a publicly held biopharmaceutical

company, including as its Vice President of Finance and Administration. Prior to that, he held management positions at AAIPharma, Inc. and Schering-Plough. Mr. Deignan received his B.S. degree in Business Administration from Boston University.

Glenn Noronha, Ph.D.

Dr. Noronha has served as our Executive Vice President, Research and Development since August 2013 and as our Chief Scientific Officer since August 2016. From August 2012 to May 2013, he served as Vice President, Research and Development at Sucampo Pharma Americas, LLC, a pharmaceutical company. From July 2011 to July 2012, Dr. Noronha was Chief Scientific Officer for JW Theriac, Inc., a pharmaceutical company focused on new drug research and development. From 2008 to July 2011, Dr. Noronha was Global Project Head for Retinal Development at Alcon Laboratories, Inc., a Novartis company. From 2002 to 2008, Dr. Noronha held several positions at TargeGen, Inc., a pharmaceutical company, including as co-lead for its ophthalmology programs. Previously, from 2000 to 2002, he was a research scientist and project leader for Medtronic MiniMed, Inc. Dr. Noronha received his Ph.D. degree from Loyola University of Chicago and was a post-doctoral fellow at the University of California at Irvine.

Non-management directors

Christy L. Shaffer, Ph.D.

Dr. Shaffer has served as a director of our company and as the chairman of our board of directors since January 2012. Since 2011, Dr. Shaffer has served as a Venture Partner with Hatteras Venture Partners, an investment firm, and as Managing Director of Hatteras Discovery, which invests in early-stage companies in the life sciences industry sector. From 1995 to March 2010, Dr. Shaffer served in increasing leadership positions at Inspire Pharmaceuticals, a publicly held biopharmaceutical company, beginning as the company's first full-time employee and Director of Clinical Operations and eventually being appointed as Chief Executive Officer and a director of the company in 1999, as its President in 2005 and a member of its Development Committee in 2009. Prior to Inspire, she was a clinical research scientist, international project leader and Associate Director of Pulmonary and Critical Care Medicine at Burroughs Wellcome Co. Dr. Shaffer currently serves in leadership roles on several non-profit boards, including as chair of the Morehead Planetarium and Science Center's advisory board, on the Board of Trustees for the Cystic Fibrosis Foundation, and as chair of the board of CFF Therapeutic, Inc. Dr. Shaffer is a receptor pharmacologist by training, earning her Ph.D. in Pharmacology from the University of Tennessee's Health Science Center in Memphis, Tennessee. She completed post-doctoral training at The Chicago Medical School as well as the University of North Carolina at Chapel Hill. In September 2008, the Securities and Exchange Commission approved a non-monetary settlement of its investigation relating to Inspire Pharmaceuticals' disclosures in its periodic reports relating to a clinical trial. The Commission also approved a settlement with Dr. Shaffer, as Inspire's President and Chief Executive Officer and a member of its board of directors, under which she consented to a cease and desist order against future violations of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder. The cease and desist order followed a finding by the Commission that three Quarterly Reports on Form 10-Q filed by Inspire included misleading disclosure about a clinical trial, specifically that the trial was described as "confirmatory" and "replicating" the efficacy found in an earlier trial. Dr. Shaffer did not admit or deny any findings in the order, and the order did not include any finding of any violation of any statute or regulation that involved any intentional wrongdoing or fraud, any monetary payments or other sanctions or otherwise affect Dr. Shaffer's future employment status, nor did it prohibit Dr. Shaffer from serving in any capacity on public company boards of directors. Our board of directors believes that Dr. Shaffer's clinical background as a scientist and her leadership experience as chief executive of a public company in the biopharmaceutical industry provides her with the qualifications and skills to serve as a director of our company.

Clay B. Thorp

Mr. Thorp has served as a director of our company since January 2012. In 2001, Mr. Thorp co-founded and has since served as General Partner of Hatteras Venture Partners, an investment firm, where he leads investments in a range of life science companies in the biopharmaceutical, medical device, diagnostics and research informatics sectors. Previously, he was instrumental in the founding of several life sciences companies, including serving as co-founder, Chief Executive Officer and Chairman of Synthematix, Inc., a chemistry informatics company that was acquired by Symyx Technologies in 2005, co-founder and former Chairman of PhaseBio Pharmaceuticals, Inc., co-founder and head of corporate development for Novalon Pharmaceutical Corporation, which was sold to Karo Bio in 2000, and co-founder and president of Xanthon, Inc., a bioinformatics company with electro-chemical detection technology for direct analysis of DNA, RNA and proteins. Mr. Thorp holds a Masters of Public Policy degree from Harvard University and a B.A. degree in Mathematics and History from the University of North Carolina at Chapel Hill. Our board of directors believes that Mr. Thorp's experience as an entrepreneur and an investor in life sciences companies provides him with the qualifications and skills to serve as a director of our company.

Evgeny Zaytsev, M.D.

Dr. Zaytsev has served as a director of our company since August 2014. Dr. Zaytsev has served as President, Chief Executive Officer and a managing partner of RMI Partners LLC since May 2013 and as the President and Chief Executive Officer of RMI Partners Inc. since November 2013. Dr. Zaytsev has also served as a general partner at Helix Ventures, which he co-founded to exclusively invest in novel therapeutic opportunities, since July 2009. Previously Dr. Zaytsev was a partner at Asset Management Company, one of the oldest venture firms in Silicon Valley, from 2002 to 2009. Dr. Zaytsev received his M.D. degree and Ph.D. degree from the Altai State Medical University and his M.B.A. degree from the Stanford Graduate School of Business. Our board of directors believes that Dr. Zaytsev's scientific background and experience as an investor in life sciences companies provides him with the qualifications and skills to serve as a director of our company.

Gerald D. Cagle, Ph.D.

Dr. Cagle has served on our board of directors since July 2013. Dr. Cagle has served as Chief Operating Officer at Cognoptix, Inc., a biotechnology company focused on the diagnosis of Alzheimer's disease, since December 2008. He also is Senior Advisor and Head of Business Development for GrayBug, LLC, a platform drug delivery company. Previously, Dr. Cagle served as Senior Vice President of Research & Development at Alcon Laboratories Inc. from 1997 to 2008, assuming the responsibility of Chief Scientific Officer in 2006. He currently serves on the board of directors of Aerie Pharmaceuticals, Inc., a publicly held biopharmaceutical company. Dr. Cagle has also served on the Wilmer Eye Institute Advisory Council and is a member of the ARVO Foundation Board of Governors. Dr. Cagle received his B.S. degree from Wayland College and earned M.S. and Ph.D. degrees from the University of North Texas. Our board of directors believes that Dr. Cagle's scientific background and experience provides him with the qualifications and skills to serve as a director of our company.

William D. Humphries

Mr. Humphries has served as a director of our company since January 2012. Mr. Humphries has served as President and Chief Executive Officer of the North American business of Merz, Inc., an affiliate of Merz Pharma Group, a specialty healthcare company, since March 2012. From 2006 to March 2012, he served in a number of leadership positions with Stiefel Laboratories, Inc., a dermatology pharmaceutical company, including as its Chief Commercial Officer and then as its President beginning in 2008. Stiefel was acquired by GlaxoSmithKline in 2009. After the acquisition, Mr. Humphries served as the President of Dermatology for Stiefel from 2009 until March

2012. Before Stiefel, Mr. Humphries served in executive roles in sales and marketing, business development, and international marketing for Allergan, Inc., concluding as vice president of its U.S. skincare business. Mr. Humphries currently serves on the board of Aclaris Therapeutics, Inc., a publicly traded company. Mr. Humphries has served on the board of ZARS Pharma, the GlaxoSmithKline Portfolio Investment Board and the GlaxoSmithKline Ophthalmology Board. Mr. Humphries received his M.B.A. degree from Pepperdine University and a B.A. degree from Bucknell University. Our board of directors believes that Mr. Humphries' experience as pharmaceutical company executive provides him with the qualifications and skills to serve as a director of our company.

Derek Yoon

Mr. Yoon has served as a director of our company since December 2015. Mr. Yoon has served as a Partner in the Boston, Massachusetts office of AJU IB Investment, a venture investment firm headquartered in Seoul, Korea, since January 2014. Prior to that, from April 2011 to December 2013, Mr. Yoon served as a Portfolio Manager, Healthcare Banking at RBS Citizens Bank. From July 2009 to May 2011, he served as a Research Associate at Berwind Private Equity. Before this, Mr. Yoon held a variety of positions in the investment banking industry. Mr. Yoon received his B.S. degree in Chemical Engineering from Yonsei University (Seoul, Korea), his M.B.A. degree from Babson College and his M.S.F. degree from Boston College. Our board of directors believes that Mr. Yoon's scientific and finance background and experience provide him with the qualifications and skills to serve as a director of our company.

Richard Croarkin

Mr. Croarkin has served as a director of our company since February 2016. From 2007 to 2010, Mr. Croarkin was the Senior Vice President, Chief Financial Officer, and Corporate Strategy Officer of Alcon, Inc., a public ophthalmic pharmaceutical and medical device company. From 2011 through early 2013, Mr. Croarkin served as the Chief Financial Officer of Nestlé Health Science, S.A., a division of Nestlé focused on medicalized nutrition solutions for chronic medical conditions. Mr. Croarkin retired in early 2013. Mr. Croarkin currently serves on the board of directors and audit committee of Aerie Pharmaceuticals, Inc., a public clinical stage pharmaceutical company. Mr. Croarkin also occasionally serves as a panelist on the NASDAQ Listing Qualifications Panel, a panel that adjudicates appeals by companies that have received notification of delisting by the NASDAQ. Mr. Croarkin received his B.A. in economics from Georgetown University and his M.B.A. degree in finance from the University of Connecticut. Our board of directors believes that Mr. Croarkin's financial background and healthcare experience provide him with the qualifications and skills to serve as a director of our company.

Board composition

Our board of directors currently consists of eight members. In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes with staggered three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Our directors are divided among the three classes as follows:

- Class I consists of Mr. White and Mr. Thorp, and their term will expire at our 2017 annual meeting of stockholders;
- Class II consists of Mr. Humphries, Mr. Croarkin and Dr. Cagle, and their term will expire at our 2018 annual meeting of stockholders; and
- Class III consists of Dr. Shaffer, Dr. Zaytsev and Mr. Yoon, and their term will expire at our 2019 annual meeting of stockholders.

Our amended and restated bylaws provide that the authorized number of directors may be changed only by resolution approved by a majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control.

Director independence

In January 2016, our board of directors reviewed the independence of the directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. As a result of this review, our board of directors has determined that Drs. Shaffer, Cagle and Zaytsev and Messrs. Humphries, Croarkin, Yoon and Thorp, representing seven of our eight directors, are "independent directors" as defined under NASDAQ rules.

Committees of the board of directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which has the composition and responsibilities described below. From time to time, the board may establish other committees to facilitate the management of our business.

Audit committee

Our audit committee reviews our internal accounting procedures and consults with and reviews the services provided by our independent registered public accountants. Our audit committee consists of three directors, Mr. Humphries, Mr. Croarkin and Mr. Yoon. Mr. Croarkin is the chairman of the audit committee and our board of directors has determined that Mr. Croarkin is an "audit committee financial expert" as defined by SEC rules and regulations. Our board of directors has determined that each of Mr. Humphries, Mr. Croarkin and Mr. Yoon are independent directors under NASDAQ listing rules and under Rule 10A-3 under the Exchange Act, as amended. We intend to continue to evaluate the requirements applicable to us and we intend to comply with the future requirements to the extent that they become applicable to our audit committee. The principal duties and responsibilities of our audit committee include:

- appointing and retaining an independent registered public accounting firm to serve as independent auditor to audit our financial statements, overseeing the independent auditor's work and determining the independent auditor's compensation;
- approving in advance all audit services and non-audit services to be provided to us by our independent auditor;
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding accounting, internal accounting controls, auditing or compliance matters, as well as for the confidential, anonymous submission by our employees of concerns regarding questionable accounting or auditing matters;
- reviewing and discussing with management and our independent auditor the results of the annual audit and the independent auditor's review of our quarterly financial statements; and
- conferring with management and our independent auditor about the scope, adequacy and effectiveness of our internal accounting controls, the objectivity of our financial reporting and our accounting policies and practices.

Compensation committee

Our compensation committee reviews and determines the compensation of all our executive officers. Our compensation committee consists of three directors, Dr. Cagle, Dr. Shaffer and Dr. Zaytsev, each of whom is a non-employee member of our board of directors as defined in Rule 16b-3 under the Exchange Act. Dr. Cagle is the chairman of the compensation committee. Our board of directors has determined that the composition of our compensation committee satisfies the applicable independence requirements under, and the functioning of our compensation committee complies with the applicable requirements of, stock exchange listing rules and SEC rules and regulations. We intend to continue to evaluate and intend to comply with all future requirements applicable to our compensation committee. The principal duties and responsibilities of our compensation committee include:

- establishing and approving, and making recommendations to the board of directors regarding, performance goals and objectives relevant to the compensation of our chief executive officer, evaluating the performance of our chief executive officer in light of those goals and objectives and setting, or recommending to the full board of directors for approval, the chief executive officer's compensation, including incentive-based and equity-based compensation, based on that evaluation;
- setting the compensation of our other executive officers, based in part on recommendations of the chief executive officer;
- exercising administrative authority under our stock plans and employee benefit plans;
- establishing policies and making recommendations to our board of directors regarding director compensation;
- reviewing and discussing with management the compensation discussion and analysis that we may be required from time to time to include in SEC filings; and
- preparing a compensation committee report on executive compensation as may be required from time to time to be included in our annual proxy statements or annual reports on Form 10-K filed with the SEC.

Nominating and corporate governance committee

The nominating and corporate governance committee consists of two directors, Dr. Shaffer and Dr. Cagle. Dr. Shaffer is the chairman of the nominating and corporate governance committee. Our board of directors has determined that the composition of our nominating and corporate governance committee satisfies the applicable independence requirements under, and the functioning of our nominating and corporate governance committee complies with the applicable requirements of, stock exchange listing standards and SEC rules and regulations. We will continue to evaluate and will comply with all future requirements applicable to our nominating and corporate governance committee. The nominating and corporate governance committee's responsibilities include:

- assessing the need for new directors and identifying individuals qualified to become directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- assessing individual director performance, participation and qualifications;
- developing and recommending to the board corporate governance principles;

- monitoring the effectiveness of the board and the quality of the relationship between management and the board; and
- overseeing an annual evaluation of the board's performance.

Code of Business Conduct and Ethics for employees, executive officers and directors

We have adopted a Code of Business Conduct and Ethics, or the Code of Conduct, applicable to all of our employees, executive officers and directors. The Code of Conduct is available on our website at *www.clearsidebio.com*. The nominating and corporate governance committee of our board of directors is responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for employees, executive officers and directors. We expect that any amendments to the Code of Conduct, or any waivers of its requirements, will be disclosed on our website.

Compensation committee interlocks and insider participation

None of our directors who currently serve as members of our compensation committee is, or has at any time during the past year been, one of our officers or employees. None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation committee of any other entity that has one or more executive officers serving on our board of directors or compensation committee.

Non-employee director compensation

Prior to our IPO, we did not historically pay cash retainers or other compensation with respect to service on our board of directors, except for reimbursement of direct expenses incurred in connection with attending meetings of the board or committees and the equity grants described below. In January 2012, we awarded an option to purchase 22,727 shares of our common stock to Mr. Humphries at an exercise price of $0.15 per share, which option was outstanding at December 31, 2015. In October 2013, we awarded an option to purchase 22,727 shares of our common stock to Mr. Humphries at an exercise price of $0.40 per share, which option was outstanding at December 31, 2015. As of December 31, 2015, these options were fully vested.

In June 2013, in connection with his appointment to our board of directors, we awarded an option to purchase 45,455 shares of our common stock to Dr. Cagle at an exercise price of $0.40 per share, which option was outstanding as of December 31, 2015. As of December 31, 2015, the option was vested as to 25,568 shares and the remaining 19,887 shares vest in equal quarterly installments through June 30, 2017 and are subject to full acceleration of vesting upon a change of control of our company. Other than Mr. Humphries and Dr. Cagle, none of our non-employee directors serving as of December 31, 2015 held any options to purchase our common stock.

In February 2016, in connection with Mr. Croarkin's appointment to the board, he was awarded an option to purchase 17,236 shares of common stock at an exercise price of $8.16 per share. The shares underlying this option vest in 36 equal monthly installments through January 31, 2019 and are subject to full acceleration of vesting upon a change of control of our company. This option was granted outside of our 2011 Stock Incentive Plan.

None of our non-employee directors received compensation for service on our board of directors during the year ended December 31, 2015 and, accordingly, we have not included a 2015 director compensation table. Mr. White, our President and Chief Executive Officer, is also a director but does not receive any additional compensation for his service as a director. Mr. White's compensation as an executive officer is set forth below under "Executive Compensation—Summary Compensation Table."

In January 2016, our board of directors approved a non-employee director compensation policy that became effective upon the completion of our IPO in June 2016. Under this director compensation policy, we pay each of our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of the board and of each committee receives an additional retainer for such service. These retainers are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors. The retainers paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	MEMBER ANNUAL SERVICE RETAINER	CHAIRMAN ADDITIONAL ANNUAL SERVICE RETAINER
Board of Directors	$ 35,000	$ 25,000
Audit Committee	7,500	7,500
Compensation Committee	5,000	5,000
Nominating and Corporate Governance Committee	3,000	2,000

We also continue to reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending our board of director and committee meetings.

In addition, under our director compensation policy, each new non-employee director elected to our board of directors after the completion of our IPO receives an option to purchase 17,235 shares of our common stock. The shares underlying such option will vest in 36 equal monthly installments, subject to the director's continuous service through each vesting date. Further, on the date of each annual meeting of stockholders held after the completion of our IPO, each non-employee director that continues to serve as a non-employee member on our board of directors following such meeting receives an option to purchase 8,618 shares of our common stock. The shares underlying each such option will vest in full on the earlier of the date immediately prior to the next annual meeting of stockholders or 12 months after the grant date, subject to the director's continuous service through the vesting date. The exercise price of these options will equal the fair market value of our common stock on the date of grant.

This policy is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Executive compensation

Our named executive officers for the year ended December 31, 2015 include our principal executive officer and our two other executive officers:

- Daniel H. White, our President and Chief Executive Officer;
- Charles A. Deignan, our Chief Financial Officer; and
- Glenn Noronha, Ph.D., our Chief Scientific Officer.

No other individuals served as executive officers of our company at any point during 2015.

Summary compensation table

The following table presents the compensation awarded to, earned by or paid to each of our named executive officers for the years ended December 31, 2014 and 2015.

Name and Principal Position	Year	Salary ($)(1)	Bonus ($)(2)	Option Awards ($)(3)	Non-Equity Incentive Plan Compensation ($)	Total ($)
Daniel H. White	2015	325,000	11,250	230,063	113,750	680,063
President and Chief Executive Officer	2014	263,294	12,424	387,500	37,576	700,794
Charles A. Deignan	2015	250,000	8,750	177,100	61,250	497,100
Chief Financial Officer	2014	203,090	6,040	155,000	24,161	388,291
Glenn Noronha, Ph.D.	2015	274,495	2,749	177,100	67,251	521,595
Chief Scientific Officer	2014	262,708	—	155,000	29,848	447,556

(1) Salary amounts represent actual amounts paid during the indicated year. See "—Narrative to Summary Compensation Table—Annual Base Salary" for a description of adjustments to base salaries made during the year.

(2) Represents the amount above the specified level of achievement under the annual bonus incentive plan. In 2014, the compensation committee exercised its discretion to award Mr. White and Mr. Deignan additional compensation in light of their roles in the achievement of corporate objectives outside of the scope of the stated objectives described below under "Narrative to Summary Compensation Table—Annual Bonus." In 2015, the compensation committee exercised its discretion to award Mr. White, Mr. Deignan and Dr. Noronha additional compensation in light of their roles in the achievement of corporate objectives outside of the scope of the stated objectives described below under "Narrative to Summary Compensation Table—Annual Bonus."

(3) The amounts reflect the full grant date fair value for awards granted during the indicated year. The grant date fair value was computed in accordance with ASC Topic 718, *Compensation—Stock Compensation*. Unlike the calculations contained in our financial statements, this calculation does not give effect to any estimate of forfeitures related to service-based vesting, but assumes that the executive will perform the requisite service for the award to vest in full. The assumptions we used in valuing options are described in note 11 to our financial statements included in this prospectus.

Narrative to summary compensation table

We review compensation annually for all employees, including our executives. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our company. We do not target a specific competitive position or a specific mix of compensation among base salary, bonus or long-term incentives.

The compensation committee of our board of directors has historically determined our executives' compensation. Our compensation committee typically reviews and discusses management's proposed compensation with the chief executive officer for all executives other than the chief executive officer. Based on

those discussions and its discretion, the compensation committee then recommends the compensation for each executive officer. Our compensation committee, without members of management present, discusses and ultimately approves the compensation of our executive officers. To date, our compensation committee has not engaged a compensation consultant or adopted a peer group of companies for purposes of determining executive compensation.

Annual base salary

Our named executive officers' base salaries are reviewed periodically by our board of directors, and adjustments may be made upon the recommendations of the compensation committee. In 2012, we entered into an employment agreement with Mr. White under which his annual base salary was established at $250,000. In February 2013, our compensation committee recommended, and our board of directors approved, an increase in Mr. White's annual base salary to $258,125. At the same time, our compensation committee recommended, and our board of directors approved, an increase in Mr. Deignan's base salary from $175,000 to $180,688. Dr. Noronha's annual base salary of $260,000 was approved by our board of directors in connection with the commencement of his employment with us in August 2013. In July 2014, our compensation committee recommended, and the board of directors approved, further increases in our named executive officers' salaries as follows: $268,450 for Mr. White, $215,722 for Mr. Deignan and $266,500 for Dr. Noronha. In November 2014, our compensation committee recommended, and in December 2014, our board of directors approved, further increases in our named executive officers' salaries effective January 1, 2015 as follows: $325,000 for Mr. White, $250,000 for Mr. Deignan and $274,495 for Dr. Noronha. In January 2016, our compensation committee approved further increases in our named executive officers' salaries, effective as of January 1, 2016, as follows: $334,750 for Mr. White, $257,500 for Mr. Deignan and $282,730 for Dr. Noronha.

Annual bonus

We seek to motivate and reward our executives for achievements relative to our corporate goals and expectations for each fiscal year. Each named executive officer has a target bonus opportunity, defined as a percentage of his annual salary. For 2014 and 2015, the target bonus was as follows:

	Target Bonus (% of Salary)	
Name	**2014**	**2015**
Daniel H. White	25	50
Charles A. Deignan	20	35
Glenn Noronha, Ph.D.	20	35

To reinforce the importance of integrated and collaborative leadership, our executives' bonuses have historically been solely based on company performance, and we did not include an individual performance component. In December 2014, our board of directors determined that the 2014 performance goals had been achieved at a 56% level in the aggregate. The bonuses paid to the named executive officers for 2014 performance at the 56% level are reflected in the "Non-Equity Incentive Plan Compensation" column of the Summary Compensation Table above. In January 2016, our compensation committee determined that the 2015 performance goals had been achieved at a 70% level in the aggregate. The bonuses paid to the named executive officers for 2015 performance at the 70% level are reflected in the "Non-Equity Incentive Plan Compensation" column of the Summary Compensation Table above.

Long-term incentives

Our 2011 Stock Incentive Plan authorized us to make grants to eligible recipients of non-qualified stock options, incentive stock options, restricted stock awards, restricted stock units and other stock-based awards. All of our awards under this plan have been in the form of stock options.

We typically grant stock options at the start of employment to each executive and our other employees. Through 2015, we have not maintained a practice of granting additional equity on an annual basis, but we have retained discretion to provide additional targeted grants in appropriate circumstances.

We award stock options on the date the compensation committee approves the grant. We set the option exercise price and grant date fair value based on our per-share valuation on the date of grant.

In December 2014, our compensation committee awarded options to Mr. White, Mr. Deignan and Dr. Noronha to purchase 113,636 shares, 45,455 shares and 45,455 shares of our common stock, respectively. Each of these options has an exercise price of $3.41 per share.

In December 2015, our compensation committee awarded options to Mr. White, Mr. Deignan and Dr. Noronha to purchase 41,334 shares, 31,818 shares and 31,818 shares of our common stock, respectively. Each of these options has an exercise price of $5.57 per share.

In July 2016, our compensation committee awarded options to Mr. White, Mr. Deignan and Dr. Noronha to purchase 60,000 shares, 30,000 shares and 30,000 shares of our common stock, respectively. Each of these options has an exercise price of $6.49 per share.

Employment arrangements and potential payments upon termination of employment

In September 2012, we entered into an employment agreement with Mr. White, under which he serves as our President and Chief Executive Officer. On January 1, 2015, we entered into an amended and restated employment agreement with Mr. White, under which he continues to serve as our President and Chief Executive Officer. On January 1, 2015, we also entered into employment agreements with Mr. Deignan and Dr. Noronha, pursuant to which they serve as our Chief Financial Officer and Chief Scientific Officer, respectively.

These employment agreements have one-year terms and are renewable for successive one-year terms unless either we or the executive officer gives notice of non-renewal at least 60 days prior to the end of the term. Pursuant to these employment agreements, Mr. White, Mr. Deignan and Dr. Noronha are eligible to receive severance benefits in specified circumstances.

In the event we terminate Mr. White without cause, he resigns for good reason or we elect not to renew his employment agreement, then, upon execution and effectiveness of a settlement agreement and release of claims in a form acceptable to us, Mr. White will be entitled to receive (a) an amount equal to 18 months of his annual base salary, less applicable deductions, payable in accordance with our normal payroll schedule, (b) reimbursement of the cost of health insurance premiums for 18 months or, if shorter, until he obtains reasonably comparable health insurance coverage and (c) each equity award held by him shall immediately vest and become exercisable to the extent the award would have vested had he remained employed by us for 18 months following the termination of the agreement.

If we or our successor terminates Mr. White without cause, he resigns for good reason or we elect not to renew his employment agreement within 12 months after a “change in control event” within the meaning of the regulations promulgated under Section 409A of the Internal Revenue Code, as amended, or the Code, in addition to the payments and benefits specified above, the equity awards held by Mr. White at the time of termination shall immediately vest and become exercisable until the earlier to occur of either the final exercise

date in the equity award or the end of the severance period. He shall also be entitled to receive 100% of the performance bonus earned by him in the most recent calendar year.

For the period of two years following January 1, 2015, to the extent that any payment, benefit or distribution by us or any of our affiliates to Mr. White pursuant to his employment agreement or any other agreement, plan or arrangement would constitute an “excess parachute payment” within the meaning of Section 280G of the Code and would be subject to the excise tax imposed under Section 4999 of the Code, Mr. White will be entitled to receive a “gross-up” payment equal to 36 months of his annual base salary. After such period, Mr. White will not be entitled to any such “gross up” and if all or a portion of the total payments to him would constitute an “excess parachute payment” within the meaning of 280G of the Code, he shall receive (a) an amount limited so that no portion shall fail to be deductible under Section 280G of the Code or (b) if the amount otherwise payable, under the employment agreement or otherwise, would be greater than the limited amount after paying the excise tax and any other taxes required, he shall receive the amount otherwise payable.

In the event we terminate Mr. Deignan without cause, he resigns for good reason or we elect not to renew his employment agreement, then, upon execution and effectiveness of a settlement agreement and release of claims in a form acceptable to us, Mr. Deignan will be entitled to receive (a) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with our normal payroll schedule, (b) reimbursement of the cost of health insurance premiums for 12 months or, if shorter, until he obtains reasonably comparable health insurance coverage and (c) each equity award held by him shall immediately vest and become exercisable to the extent the award would have vested had he remained employed by us for 12 months following the termination of the agreement.

If we or our successor terminates Mr. Deignan without cause, he resigns for good reason or we elect not to renew his employment agreement within 12 months after a “change in control event” within the meaning of the regulations promulgated under Section 409A of the Code, in addition to the payments and benefits specified above, the equity awards held by Mr. Deignan at the time of termination shall immediately vest and become exercisable until the earlier to occur of either the final exercise date in the equity award or the end of the severance period. He shall also be entitled to receive 67% of the performance bonus earned by him in the most recent calendar year.

For the period of two years following January 1, 2015, to the extent that any payment, benefit or distribution by us or any of our affiliates to Mr. Deignan pursuant to his employment agreement or any other agreement, plan or arrangement would constitute an “excess parachute payment” within the meaning of Section 280G of the Code and would be subject to the excise tax imposed under Section 4999 of the Code, Mr. Deignan will be entitled to receive a “gross-up” payment equal to 18 months of his annual base salary. After such period, Mr. Deignan will not be entitled to any such “gross up” and if all or a portion of the total payments to him would constitute an “excess parachute payment” within the meaning of 280G of the Code, he shall receive (a) an amount limited so that no portion shall fail to be deductible under Section 280G of the Code or (b) if the amount otherwise payable, under the employment agreement or otherwise, would be greater than the limited amount after paying the excise tax and any other taxes required, he shall receive the amount otherwise payable.

In the event we terminate Dr. Noronha without cause, he resigns for good reason or we elect not to renew his employment agreement, then, upon execution and effectiveness of a settlement agreement and release of claims in a form acceptable to us, Dr. Noronha will be entitled to receive (a) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with our normal payroll schedule, (b) reimbursement of the cost of health insurance premiums for 12 months or, if shorter, until he obtains reasonably comparable health insurance coverage and (c) each equity award held by him shall immediately vest and become exercisable to the extent the award would have vested had he remained employed by us for 12 months following the termination of the agreement.

If we or our successor terminates Dr. Noronha without cause, he resigns for good reason or we elect not to renew his employment agreement, in each case within 12 months after a "change in control event" within the meaning of the regulations promulgated under Section 409A of the Code, in addition to the payments and benefits specified above, the equity awards held by Dr. Noronha at the time of termination shall immediately vest and become exercisable until the earlier to occur of either the final exercise date in the equity award or the end of the severance period. He shall also be entitled to receive 67% of the performance bonus earned by him in the most recent calendar year.

For the period of two years following January 1, 2015, to the extent that any payment, benefit or distribution by us or any of our affiliates to Dr. Noronha pursuant to his employment agreement or any other agreement, plan or arrangement would constitute an "excess parachute payment" within the meaning of Section 280G of the Code and would be subject to the excise tax imposed under Section 4999 of the Code, Dr. Noronha will be entitled to receive a "gross-up" payment equal to 18 months of his annual base salary. After such period, Dr. Noronha will not be entitled to any such "gross up" and if all or a portion of the total payments to him would constitute an "excess parachute payment" within the meaning of 280G of the Code, he shall receive (a) an amount limited so that no portion shall fail to be deductible under Section 280G of the Code or (b) if the amount otherwise payable, under the employment agreement or otherwise, would be greater than the limited amount after paying the excise tax and any other taxes required, he shall receive the amount otherwise payable.

The following definitions have been adopted in Mr. White's, Mr. Deignan's and Dr. Noronha's employment agreements:

- "cause" means that our board of directors has determined that any of the following has occurred: (a) the material breach of the employment agreement, failure to diligently and properly perform his duties or failure to achieve the objectives specified by the board of directors, and such breach or failure has not been cured within 30 days after written notice thereof; (b) the misappropriation or unauthorized use of our property or breach of his agreements with us relating to confidentiality, intellectual property rights, non-competition or non-solicitation; (c) a material failure to comply with our policies or directives of our board of directors, and any such failure has not been cured within 30 days after written notice thereof, provided that the failure to comply with our policies related to harassment, unlawful discrimination, retaliation or workplace violence do not require notice or permit a cure period; (d) the use of illegal drugs or any illegal substance, or the use of alcohol in any manner that materially interferes with the performance of the executive officer's duties to the company; (e) a dishonest or illegal action by the executive officer, or any action determined to be detrimental to our interest and well-being, including harm to our reputation; (f) a failure to fully disclose any material conflict of interest that he may have in a transaction between us and a third party, which is materially detrimental to our interest and well-being; (g) any adverse action or omission by the executive officer which would be required to be disclosed under securities laws or which would limit our ability to sell securities or would disqualify us from an exemption otherwise available to us; and
- "good reason" means the existence of any of the following without the executive officer's prior consent: (a) any substantial reduction or diminution of his duties and responsibilities or salary; (b) any material breach of the employment agreement by us; or (c) a relocation of his place of employment by more than 50 miles from the location of our principal office, in each case after notice to us within 90 days following the initial existence of the event and after we have had the opportunity to but have not cured the event for 30 days following such notice, and the executive officer terminates his employment with us no later than two years after the initial existence of the event.

Outstanding equity awards at end of 2015

The following table provides information about outstanding stock options held by each of our executive officers at December 31, 2015. All of these options were granted under our 2011 Stock Incentive Plan.

	Option Awards				Stock Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($)(9)
Daniel H. White	39,996(1)	18,186(1)	0.40	02/28/2023		
	17,044(3)	17,047(3)	0.40	11/24/2023		
	28,409(4)	85,227(4)	3.41	12/18/2024		
	—	41,334(5)	5.57	12/02/2025		
Charles A. Deignan	16,248(1)	7,388(1)	0.40	02/28/2023	379(6)	2,391
	17,044(3)	17,047(3)	0.40	11/24/2023	3,977(7)	25,113
	11,364(4)	34,091(4)	3.41	12/18/2024	2,130(8)	13,452
	—	31,818(5)	5.57	12/02/2025		
Glenn Noronha, Ph.D.	33,141(2)	23,677(2)	0.40	08/06/2023		
	11,363(3)	11,365(3)	0.40	11/24/2023		
	11,364(4)	34,091(4)	3.41	12/18/2024		
	—	31,818(5)	5.57	12/02/2025		

(1) The shares underlying this option vested as to 25% of the shares on March 1, 2014, with the remainder vesting in 36 equal monthly installments thereafter, subject to the officer's continued service through each applicable vesting date. The option is subject to full acceleration of vesting following a change of control if the option is assumed or a substantially equivalent award is substituted, but the officer's employment is terminated without cause within 12 months following the change of control.

(2) The shares underlying this option vested as to 25% of the shares on August 1, 2014, with the remainder vesting in 36 equal monthly installments thereafter, subject to the officer's continued service through each applicable vesting date. The option is subject to full acceleration of vesting (a) upon a change of control if the option is not assumed or a substantially equivalent award is not substituted by the acquiring or succeeding entity or (b) following a change of control if the option is assumed or a substantially equivalent award is substituted, but the officer's employment is terminated without cause within 12 months following the change of control.

(3) The shares underlying this option vested as to 25% of the shares on December 13, 2014, with the remainder vesting in 36 equal monthly installments thereafter, subject to the officer's continued service through each applicable vesting date. The option is subject to full acceleration of vesting (a) upon a change of control if the option is not assumed or a substantially equivalent award is not substituted by the acquiring or succeeding entity or (b) following a change of control if the option is assumed or a substantially equivalent award is substituted, but the officer's employment is terminated without cause or for good reason within 12 months following the change of control.

(4) The shares underlying this option vested as to 25% of the shares on December 19, 2015, with the remainder vesting in 36 equal monthly installments thereafter, subject to the officer's continued service through each applicable vesting date. The option is subject to full acceleration of vesting (a) upon a change of control if the option is not assumed or a substantially equivalent award is not substituted by the acquiring or succeeding entity or (b) following a change of control if the option is assumed or a substantially equivalent award is substituted, but the officer's employment is terminated without cause or for good reason within 12 months following the change of control.

(5) The shares underlying this option vested as to 25% of the shares on December 2, 2016, with the remainder vesting in 36 equal monthly installments thereafter, subject to the officer's continued service through each applicable vesting date. The option is subject to full acceleration of vesting (a) upon a change of control if the option is not assumed or a substantially equivalent award is not substituted by the acquiring or succeeding entity or (b) following a change of control if the option is assumed or a substantially equivalent award is substituted, but the officer's employment is terminated without cause or for good reason within 12 months following the change of control.

(6) These restricted shares vested in equal monthly installments through January 31, 2016.

(7) These restricted shares vested in equal monthly installments through July 1, 2016. These restricted shares are subject to full acceleration of vesting (a) upon a change of control if the option is not assumed or a substantially equivalent award is not substituted by the acquiring or succeeding entity or (b) following a change of control if the option is assumed or a substantially equivalent award is substituted, but the officer's employment is terminated without cause or for good reason within 12 months following the change of control.

(8) These restricted shares vested in equal monthly installments through September 30, 2016. These restricted shares are subject to full acceleration of vesting (a) upon a change of control if the option is not assumed or a substantially equivalent award is not substituted by the

acquiring or succeeding entity or (b) following a change of control if the option is assumed or a substantially equivalent award is substituted, but the officer's employment is terminated without cause or for good reason within 12 months following the change of control.

(9) Based on a retrospective fair value assessment we performed in December 2015 in which we concluded that the fair value of our common stock on December 2, 2015 was $6.31 per share.

Stock option exercises and stock vested during 2015

The following table shows information regarding stock awards vested during the year ended December 31, 2015 with respect to our named executive officers.

	Stock Awards	
Name	Number of Shares Acquired on Vesting (#)	Value Realized on Vesting ($)
Charles A. Deignan	14,203(1)	75,724(2)

(1) Mr. Deignan acquired shares of stock pursuant to the early exercise of stock options, which stock was subject to a right of repurchase in favor of us. The number of shares acquired on vesting represents the number of such shares for which our rights of repurchase lapsed during the year.

(2) Represents the difference between the estimated value of the shares for which our repurchase right lapsed and the exercise price of $0.15 per share paid by Mr. Deignan in respect of such shares upon the early exercise of the options. For shares vested from January through March of 2015, the assumed value of such shares was $3.41 per share, the valuation of our common stock as of September 30, 2014. For shares vested from April through November of 2015, the assumed value of such shares was $6.16 per share, the valuation of our common stock as of March 31, 2015. For shares vested in December 2015, the assumed value of such shares was $6.31 per share, the valuation of our common stock as of December 2, 2015 as determined by a retrospective fair value assessment we performed in December 2015.

Health and welfare benefits

We maintain a defined contribution employee retirement plan for our employees. Our 401(k) plan is intended to qualify as a tax-qualified plan under Section 401 of the Internal Revenue Code so that contributions to our 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan. Our 401(k) plan provides that each participant may contribute a portion of his or her pre-tax compensation, up to a statutory limit, which was $17,500 for 2014 and is $18,000 for 2015 and 2016. Participants who are at least 50 years old can also make "catch-up" contributions, which in 2014 was up to an additional $5,500 above the statutory limit and in 2015 and 2016 an additional $6,000 above the statutory limit. Under our 401(k) plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan's trustee, subject to participants' ability to give investment directions by following specified procedures. We do not currently make discretionary contributions or matching contributions to our 401(k) plan.

Except for the benefits described above under "Narrative to Summary Compensation Table—Other Compensation," we do not provide perquisites or personal benefits to our named executive officers. We do, however, pay the premiums for medical, dental and term life insurance for all of our employees, including our named executive officers.

Equity incentive plans

2016 equity incentive plan

Our board of directors has adopted, and our stockholders approved, our 2016 Equity Incentive Plan, or our 2016 plan, which became effective on June 1, 2016 upon the pricing of our IPO. Our 2016 plan provides for the grant of incentive stock options within the meaning of Section 422 of the Code to our employees and our parent and subsidiary corporations' employees, and for the grant of nonstatutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of stock

compensation to our employees, including officers, consultants and directors. Our 2016 plan also provides for the grant of performance cash awards to our employees, consultants and directors.

Authorized shares

The maximum number of shares of our common stock that may be issued under our 2016 plan is 1,818,182 shares. The number of shares of our common stock reserved for issuance under our 2016 plan will automatically increase on January 1 of each year, for a period of not more than 10 years, from January 1, 2017 continuing through January 1, 2026, by 4.0% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by our board of directors. The maximum number of shares that may be issued pursuant to the exercise of incentive stock options under the 2016 plan is 27,272,727.

Shares issued under our 2016 plan may be authorized but unissued or reacquired shares of our common stock. Shares subject to stock awards granted under our 2016 plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, will not reduce the number of shares available for issuance under our 2016 plan. Additionally, shares issued pursuant to stock awards under our 2016 plan that we repurchase or that are forfeited, as well as shares reacquired by us as consideration for the exercise or purchase price of a stock award or to satisfy tax withholding obligations related to a stock award, will become available for future grant under our 2016 plan.

Administration

Our board of directors, or a duly authorized committee thereof, has the authority to administer our 2016 plan. Our board of directors has delegated its authority to administer our 2016 plan to our compensation committee under the terms of the compensation committee's charter. Our board of directors may also delegate to one or more of our officers the authority to (i) designate employees other than officers to receive specified stock awards and (ii) determine the number of shares of our common stock to be subject to such stock awards. Subject to the terms of our 2016 plan, the administrator has the authority to determine the terms of awards, including recipients, the exercise price or strike price of stock awards, if any, the number of shares subject to each stock award, the fair market value of a share of our common stock, the vesting schedule applicable to the awards, together with any vesting acceleration, the form of consideration, if any, payable upon exercise or settlement of the stock award and the terms and conditions of the award agreements for use under our 2016 plan.

The administrator has the power to modify outstanding awards under our 2016 plan. Subject to the terms of our 2016 plan, the administrator has the authority to reprice any outstanding option or stock appreciation right, cancel and re-grant any outstanding option or stock appreciation right in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

Section 162(m) limits

No participant may be granted stock awards covering more than 2,727,273 shares of our common stock under our 2016 plan during any calendar year pursuant to stock options, stock appreciation rights and other stock awards whose value is determined by reference to an increase over an exercise price or strike price of at least 100% of the fair market value of our common stock on the date of grant. Additionally, no participant may be granted in a calendar year a performance stock award covering more than 2,727,273 shares of our common stock or a performance cash award having a maximum value in excess of $2,000,000 under our 2016 plan.

These limitations enable us to grant awards that will be exempt from the $1,000,000 limitation on the income tax deductibility of compensation paid per covered executive officer imposed by Section 162(m) of the Code.

Performance awards

Our 2016 plan permits the grant of performance-based stock and cash awards that may qualify as performance-based compensation that is not subject to the $1,000,000 limitation on the income tax deductibility of compensation paid per covered executive officer imposed by Section 162(m) of the Code. To enable us to grant performance-based awards that will qualify, our compensation committee can structure such awards so that the stock or cash will be issued or paid pursuant to such award only following the achievement of specified pre-established performance goals during a designated performance period.

Corporate transactions

Our 2016 plan provides that in the event of a specified corporate transaction, including without limitation a consolidation, merger, or similar transaction involving our company, the sale, lease or other disposition of all or substantially all of the assets of our company or the consolidated assets of our company and our subsidiaries, or a sale or disposition of at least 50% of the outstanding capital stock of our company, the administrator will determine how to treat each outstanding stock award. The administrator may:

- arrange for the assumption, continuation or substitution of a stock award by a successor corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation;
- accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;
- cancel the stock award to the extent not vested or not exercised prior to the effective time of the corporate transaction, in exchange for no consideration;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase right held by us; or
- cancel the stock award prior to the transaction in exchange for a cash payment, which may be reduced by the exercise price payable in connection with the stock award.

The administrator is not obligated to treat all stock awards or portions of stock awards, even those that are of the same type, in the same manner. The administrator may take different actions with respect to the vested and unvested portions of a stock award.

Change in control

The administrator may provide, in an individual award agreement or in any other written agreement between us and the participant, that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change in control. In the absence of such a provision, no such acceleration of the stock award will occur.

Plan amendment or termination

Our board has the authority to amend, suspend, or terminate our 2016 plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. No incentive stock options may be granted after the tenth anniversary of the effective date of our 2016 plan.

2011 stock incentive plan

Our board of directors adopted, and our stockholders approved, the 2011 Stock Incentive Plan, or the 2011 plan, in November 2011. Our 2011 plan was amended by our board of directors and our stockholders in December 2011. Our 2011 plan provided for the grant of incentive stock options within the meaning of Section 422 of the Code to our employees, and for the grant of nonstatutory stock options, restricted stock awards, restricted stock units and other stock-based awards to our officers, directors, employees, consultants and advisers.

Authorized shares

As of September 30, 2016, there were 1,239,858 shares of our common stock reserved for issuance under our 2011 plan. As of September 30, 2016, 257,270 shares of our common stock have been issued upon the exercise of options granted under our 2011 plan and options to purchase 1,239,858 shares of our common stock were outstanding at a weighted average exercise price of $2.35 per share. Following the completion of our IPO, no further options or stock awards may be granted under our 2011 plan, but all outstanding stock awards continue to be governed by their existing terms.

Administration

Our board of directors, or a committee thereof appointed by our board of directors, administers our 2011 plan and the option and stock awards granted under it. Our board of directors delegated its authority to administer our 2011 plan to our compensation committee.

Corporate transactions

Our 2011 plan provides that, in the event of a specified change of control transaction, including without limitation a dissolution, merger, consolidation or reorganization of our company with one or more other entities in which our company is not the surviving entity, a sale of substantially all of the assets of our company, or any transaction which results in the disposition of at least a majority of the voting power or value of the securities of our company, the board may take any one or more of the following actions with respect to awards other than restricted stock awards:

- the assumption or substitution of the options by a successor corporation;
- the termination of the options immediately prior to the change of control transaction;
- provide that the options become exercisable, realizable or derivable, or that restrictions applicable to options shall lapse;
- the purchase of outstanding options for an amount of cash that could have been received upon the exercise of the options or the conversion of the options into a right to receive liquidation proceeds; or
- any combination of the foregoing.

With respect to restricted stock awards, upon the occurrence of a change of control transaction involving the liquidation or dissolution of our company, all restrictions and conditions on all restricted stock awards then outstanding shall automatically be deemed terminated or satisfied. With respect to a change of control transaction not involving the liquidation or dissolution of our company, all of our repurchase or other rights under each outstanding restricted stock award shall inure to the benefit of our successor.

2016 Employee Stock Purchase Plan

Our board of directors has adopted, and our stockholders approved, our 2016 Employee Stock Purchase Plan, or our 2016 ESPP, which became effective on June 1, 2016 upon the pricing of our IPO. To date, we have not granted any purchase rights under the 2016 ESPP, although our compensation committee has approved an offering period under the 2016 ESPP to commence on January 1, 2017.

The maximum number of shares of our common stock that may be issued under our 2016 ESPP is 181,818 shares. Additionally, the number of shares of our common stock reserved for issuance under our 2016 ESPP will automatically increase on January 1 of each year, beginning on January 1 of the year after the completion of this offering and ending on and including January 1, 2026, by the lesser of (i) 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year or (ii) 454,545 shares of common stock; provided, however, our board of directors may act prior to the first day of any calendar year to provide that there will be no January 1 increase in the share reserve for such calendar year or that the increase in the share reserve for such calendar year will be a lesser number of shares of common stock. Shares subject to purchase rights granted under our 2016 ESPP that terminate without having been exercised in full will not reduce the number of shares available for issuance under our 2016 ESPP.

Our board of directors, or a duly authorized committee thereof, will administer our 2016 ESPP. Our board of directors has delegated its authority to administer our 2016 ESPP to our compensation committee under the terms of the compensation committee's charter.

Employees, including executive officers, of ours or any of our designated affiliates may have to satisfy one or more of the following service requirements before participating in our 2016 ESPP, as determined by the administrator: (i) customary employment with us or one of our affiliates for more than 20 hours per week and more than five months per calendar year; or (ii) continuous employment with us or one of our affiliates for a minimum period of time, not to exceed two years, prior to the first date of an offering. An employee may not be granted rights to purchase stock under our 2016 ESPP if such employee (i) immediately after the grant would own stock possessing 5% or more of the total combined voting power or value of all classes of our common stock, or (ii) holds rights to purchase stock under our 2016 ESPP that would accrue at a rate that exceeds $25,000 worth of our stock for each calendar year that the rights remain outstanding.

A component of our 2016 ESPP is intended to qualify as an employee stock purchase plan under Section 423 of the Code and the provisions of this component will be construed in a manner that is consistent with the requirements of Section 423 of the Code. In addition, the 2016 ESPP authorizes the grant of options to purchase shares of our common stock that do not meet the requirements of Section 423 of the Code because of deviations necessary to permit participation in the 2016 ESPP by employees who are foreign nationals or employed outside of the United States while complying with applicable foreign laws. Any such options must be granted pursuant to rules, procedures or subplans adopted by our board designed to achieve these objectives for eligible employees and our company. The administrator may specify offerings with a duration of not more than 27 months, and may specify one or more shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for the employees who are participating in the offering. The administrator, in its discretion, will determine the terms of offerings under our 2016 ESPP.

Our 2016 ESPP permits participants to purchase shares of our common stock through payroll deductions up to 15% of their earnings. Unless otherwise determined by the administrator, the purchase price of the shares will be 85% of the lower of the fair market value of our common stock on the first day of an offering or on the date of purchase. Participants may end their participation at any time during an offering and will be paid their accrued contributions that have not yet been used to purchase shares. Participation ends automatically upon termination of employment with us.

A participant may not transfer purchase rights under our 2016 ESPP other than by will, the laws of descent and distribution or as otherwise provided under our 2016 ESPP.

In the event of a specified corporate transaction, such as a merger or change in control of our company, a successor corporation may assume, continue or substitute each outstanding purchase right. If the successor corporation does not assume, continue or substitute for the outstanding purchase rights, the offering in progress will be shortened and a new exercise date will be set. The participants' purchase rights will be exercised on the new exercise date and such purchase rights will terminate immediately thereafter.

Our board of directors has the authority to amend, suspend or terminate our 2016 ESPP, at any time and for any reason. Our 2016 ESPP will remain in effect until terminated by our board of directors in accordance with the terms of the 2016 ESPP.

Limitations on liability and indemnification matters

Our amended and restated certificate of incorporation contains provisions that limit the liability of our current and former directors for monetary damages to the fullest extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to the corporation or its stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

This limitation of liability does not apply to liabilities arising under federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we are required to indemnify our directors to the fullest extent permitted by Delaware law. Our amended and restated bylaws also provide that, upon satisfaction of certain conditions, we are required to advance expenses incurred by a director in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under the provisions of Delaware law. Our amended and restated bylaws also provide our board of directors with discretion to indemnify our officers and employees when determined appropriate by the board. We have entered into and expect to continue to enter into agreements to indemnify our directors, and we also expect to enter into agreements to indemnify our officers, as determined by the board of directors. With certain exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors. We also maintain customary directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement

and damage awards against directors and officers as required by these indemnification provisions. At present, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought and we are not aware of any threatened litigation that may result in claims for indemnification.

Rule 10b5-1 sales plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy.

Certain relationships and related party transactions

The following is a description of transactions since January 1, 2013 to which we have been a participant in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or any members of their immediate family, had or will have a direct or indirect material interest, other than compensation arrangements which are described under "Executive Compensation."

Participation in initial public offering

In our initial public offering, or IPO, certain of our 5% stockholders and their affiliates purchased an aggregate of 1,136,896 shares of our common stock. Each of those purchases was made through the underwriters at the initial public offering price of $7.00 per share. The following table sets forth the aggregate number of shares of our common stock that these 5% stockholders and their affiliates purchased in our initial public offering:

Purchaser	Shares of Common Stock
Entities affiliated with Hatteras Venture Partners(1)	785,714
Entities affiliated with GRA Venture Fund(2)	165,468
Santen Pharmaceuticals Co., Ltd.	142,857
RMI Investments S.a.r.l.	42,857

(1) Consists of 414,286 shares, 264,286 shares, 98,223 shares and 8,919 shares purchased by Hatteras Venture Partners IV, SBIC LP, Hatteras Venture Partners IV, LP, Hatteras Venture Partners III, LP and Hatteras Venture Affiliates III, LP, respectively.

(2) Consists of 138,228 shares and 27,240 shares purchased by GRA Venture Fund, LLC and GRA Venture Fund (T.E.), LLC, respectively.

Sales of Series A-1 convertible preferred stock

In January 2013, we sold an aggregate of 4,356,931 shares of our Series A-1 convertible preferred stock at a price of $1.8132 per share for an aggregate price of $7.9 million, 3,860,573 shares of which were sold to entities affiliated with members of our board of directors and holders of more than 5% of our voting securities. Each share of Series A-1 convertible preferred stock converted into 0.454545 shares of common stock upon the closing of our IPO. The table below summarizes these sales.

Purchaser	Shares of Series A-1 Convertible Preferred Stock Purchased	Aggregate Purchase Price
Entities affiliated with Hatteras Venture Partners(1)	1,654,531	$ 2,999,996
Entities affiliated with GRA Venture Fund(2)	275,754	499,997
Santen Pharmaceutical Co., Ltd.	1,930,288	3,499,998
Total	3,860,573	$ 6,999,991

(1) Consists of 631,997 shares purchased by Hatteras Venture Partners III, LP, 57,391 shares purchased by Hatteras Venture Affiliates III, LP, 689,388 shares purchased by Hatteras Venture Partners IV SBIC, LP and 275,755 shares purchased by Hatteras NC Fund, LP.

(2) Consists of 174,226 shares purchased by GRA Venture Fund, LLC and 101,528 shares purchased by GRA Venture Fund (T.E.), LLC.

Unsecured 7% convertible promissory notes

In April and May 2014, we issued an aggregate principal amount of $3.0 million of unsecured 7% convertible promissory notes, or the bridge notes, and warrants to purchase an aggregate of 112,802 shares of our common stock at an exercise price of $0.02 per share. We issued an aggregate principal amount of $2,196,993 of our bridge notes and warrants to purchase up to 82,613 shares of our common stock to holders of more than 5% of our voting securities, members of our board of directors and our officers. The table below summarizes these issuances.

Name	Principal Amount of Unsecured Convertible Notes	Common Stock Warrants
Entities affiliated with Hatteras Venture Partners(1)	$ 1,154,496	43,413
Entities affiliated with GRA Venture Fund(2)	499,997	18,801
Santen Pharmaceutical Co., Ltd.	500,000	18,801
Daniel H. White	17,500	658
Charles A. Deignan	12,500	470
Gerald D. Cagle, Ph.D.	12,500	470
Total	$ 2,196,993	82,613

(1) Consists of bridge notes and warrants issued to Hatteras Venture Partners III, LP.

(2) Consists of a principal amount of $315,911 of our bridge notes and warrants to purchase 14,101 shares of our common stock issued to GRA Venture Fund, LLC, and a principal amount of $184,086 of our bridge notes and warrants to purchase 4,700 shares of our common stock issued to GRA Venture Fund (T.E.), LLC.

All principal and interest under the bridge notes was converted into shares of our Series B convertible preferred stock in connection with our August 2014 financing described below.

Sales of Series B convertible preferred stock

In August 2014, we issued an aggregate of 6,009,202 shares of our Series B convertible preferred stock at a price of $2.69783 per share for an aggregate price of $16.2 million, 4,302,359 shares of which were sold to entities affiliated with members of our board of directors, our officers and holders of more than 5% of our voting securities. In some cases, some or all of the purchase price for these shares took the form of conversion of principal and interest under outstanding bridge notes held by the respective investors. In connection with this financing, we also issued warrants to purchase an aggregate of 780,415 shares of common stock at an exercise price of $0.02 per share, which became exercisable in February 2015. Of these warrants issued, warrants to purchase an aggregate of 558,748 shares of common stock were issued to entities affiliated with members of our board of directors, our officers and holders of more than 5% of our voting securities. All of the warrants issued in connection with this financing were exercised in May 2015. Each share of Series B convertible preferred stock converted into 0.454545 shares of common stock upon the closing of our IPO. The table below summarizes the issuances of shares of Series B convertible preferred stock and warrants to purchase common stock to entities affiliated with members of our board of directors, our officers and holders of more than 5% of our voting securities.

Purchaser	Shares of Series B Convertible Preferred Stock Purchased	Warrants to Purchase Common Stock Issued	Aggregate Purchase Price	
			Cash	Note Conversion
Entities affiliated with Hatteras Venture Partners(1)	865,881	112,452	$1,154,492	$ 1,181,508
Entities affiliated with GRA Venture Fund(2)	434,937	56,485	499,994	673,394
Santen Pharmaceutical Co., Ltd.	375,004	48,702	499,998	511,699
RMI Investments(3)	2,594,677	336,973	6,999,997	—
Daniel H. White	13,110	1,702	17,499	17,871
Charles A. Deignan	9,375	1,217	12,500	12,792
Gerald D. Cagle	9,375	1,217	12,500	12,792
Total	4,302,359	558,748	$9,196,980	$ 2,410,056

(1) Consists of (i) 396,920 shares of Series B convertible preferred stock and a warrant to purchase 51,548 shares of common stock issued to Hatteras Venture Partners III, LP, (ii) 36,020 shares of Series B convertible preferred stock and a warrant to purchase 4,678 shares of common stock issued to Hatteras Venture Affiliates III, LP and (iii) 432,941 shares of Series B convertible preferred stock and a warrant to purchase 56,226 shares of common stock issued to Hatteras Venture Partners IV SBIC, LP.

(2) Consists of (i) 236,711 shares of Series B convertible preferred stock and a warrant to purchase 30,742 shares of common stock issued to GRA Venture Fund, LLC, (ii) 137,935 shares of Series B convertible preferred stock and a warrant to purchase 17,914 shares of common stock issued to GRA Venture Fund (T.E.), LLC and (iii) 60,291 shares of Series B convertible preferred stock and a warrant to purchase 7,830 shares of common stock issued to Georgia Research Alliance, Inc.

(3) Entities affiliated with RMI Investments, or RMI, are holders of more than 5% of our voting securities and Evgeny Zaytsev, M.D. is affiliated with RMI Investments and is a member of our board of directors.

Sales of Series C convertible preferred stock

In November and December 2015, we issued an aggregate of 5,274,674 shares of our Series C convertible preferred stock at a price of $3.7917 per share for an aggregate price of $20.0 million, 1,902,158 shares of which were sold to entities affiliated with members of our board of directors and holders of more than 5% of our voting securities. The table below summarizes the issuances of shares of Series C convertible preferred stock to entities affiliated with members of our board of directors and holders of more than 5% of our voting securities. Each share of Series C convertible preferred stock converted into approximately 0.4814 shares of common stock upon the completion of our IPO.

Purchaser	Shares of Series C Convertible Preferred Stock Purchased	Aggregate Purchase Price
Entities Affiliated with Hatteras Venture Partners(1)	675,795	$2,562,412
Entities Affiliated with GRA Venture Fund(2)	171,427	650,000
AJU Life Science Overseas Expansion Platform Fund(3)	1,054,936	4,000,000
Total	1,902,158	$7,212,412

(1) Consists of (i) 309,768 shares of Series C convertible preferred stock issued to Hatteras Venture Partners III, LP, (ii) 28,130 shares of Series C convertible preferred stock issued to Hatteras Venture Affiliates III, LP and (iii) 337,897 shares of Series C convertible preferred stock issued to Hatteras Venture Partners IV SBIC, LP.

(2) Consists of (i) 143,120 shares of Series C convertible preferred stock issued to GRA Venture Fund, LLC and (ii) 28,307 shares of Series C convertible preferred stock issued to GRA Venture Fund (T.E.), LLC.

(3) Derek Yoon, a member of our board of directors, is a Partner of AJU IB Investment, which is affiliated with AJU Life Science Overseas Expansion Platform Fund.

NovaMedica license agreement

In August 2014, we entered into a license agreement with NovaMedica LLC, or NovaMedica. Under this agreement, we granted to NovaMedica the exclusive right in Russia and specified adjacent territories to use our intellectual property to develop and commercialize products involving the use of TA as the sole active pharmaceutical ingredient for administration in the SCS. In connection with this license, NovaMedica made an upfront payment to us of $200,000. In addition, NovaMedica has agreed to make royalty payments equal to the amount of any royalties we owe to Emory or GTRC pursuant to the Emory/GTRC License Agreement as a result of NovaMedica's sales of products and services covered by the license granted to NovaMedica, up to a maximum of a low single-digit percentage of net sales of such products or services by NovaMedica. NovaMedica has also agreed to make milestone payments, totaling $12.7 million in the aggregate, upon the achievement of specified development and commercial milestones. NovaMedica is jointly owned by Rusnano MedInvest LLC, or Rusnano MedInvest, and Domain Russia Investments Limited. RMI, which beneficially owns more than 5% of our voting securities, is a wholly owned subsidiary of Rusnano MedInvest.

The term of the NovaMedica license agreement will expire upon the expiration of the last-to-expire valid claim within the patents licensed to NovaMedica pursuant to the agreement. Either we or NovaMedica may terminate the agreement upon written notice in the event of the other party's material breach that is not cured within 20 business days of receiving written notice requesting a cure of a payment breach, and within 60 business days of receiving written notice requesting a cure in the case of all other breaches. Each party also has the right to terminate in the event of the other party's bankruptcy or insolvency. We may terminate the agreement immediately upon written notice in the event that NovaMedica commences or participates in any action challenging the validity or enforceability of the patents licensed to NovaMedica under the agreement.

Santen research collaboration

In January 2013, we entered into a collaboration agreement with Santen, which beneficially owns more than 5% of our common stock. Under this agreement, we and Santen agreed to conduct feasibility studies to identify compounds for further development. Each party to the agreement bears its own costs, except that some of the costs we may incur are limited to a maximum amount. We and Santen amended our collaboration agreement in April 2014, April 2015 and March 2016 to expand the scope of our collaboration and to extend the duration of Santen's option rights with respect to products we develop together under the agreement. We incurred research and development costs under this agreement of $162,000 during the year ended December 31, 2013, $98,000 during the year ended December 31, 2014, $145,000 during the year ended December 31, 2015 and $124,000 and $85,000 during the nine months ended September 30, 2015 and 2016, respectively.

Investor rights agreement

We have entered into an investor rights agreement, as amended, with our preferred stockholders, including entities affiliated with Hatteras, GRA and RMI, each of which beneficially own more than 5% of our common stock, as well as certain of our directors and executive officers, pursuant to which we have granted rights to register the resale of their shares. The provisions of this agreement other than those relating to registration rights terminated upon the completion of our IPO in June 2016. For more information regarding the registration rights provided in this agreement, please refer to the section titled "Description of Capital Stock—Registration Rights."

Voting agreement

We entered into a voting agreement, as amended, with some of our stockholders, including entities affiliated with Hatteras, GRA and RMI, as well as certain of our directors and executive officers. The voting agreement, among other things, provided for the voting of shares with respect to the constituency of our board of directors. The voting agreement terminated upon the completion of our IPO in June 2016.

Stock sale agreement

We entered into a stock sale agreement, as amended, with some of our stockholders, including entities affiliated with Hatteras, GRA and RMI, as well as certain of our directors and executive officers. The stock sale agreement, among other things:

- granted our investors and our founders rights of first refusal and co-sale with respect to proposed transfers of our securities by specified stockholders;
- granted us rights of first refusal with respect to proposed transfers of our securities by specified stockholders; and
- provided for the voting of shares with respect to specified transactions approved by a majority of holders of our outstanding convertible preferred stock.

The stock sale agreement terminated upon the completion of our IPO in June 2016.

Indemnification agreements

Our amended and restated certificate of incorporation contains provisions limiting the liability of directors, and our amended and restated bylaws provides that we will indemnify each of our directors to the fullest extent permitted under Delaware law. Our amended and restated certificate of incorporation and amended and restated bylaws also provide our board of directors with discretion to indemnify our officers and employees when determined appropriate by the board.

In addition, we have entered into an indemnification agreement with each of our directors. For more information regarding these agreements, see “Executive Compensation—Limitations on Liability and Indemnification Matters.”

Related person transaction policy

In connection with our IPO, we adopted a related person transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. For purposes of our policy only, a related person transaction is a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were or will be participants in which the amount involved exceeds $120,000. Transactions involving compensation for services provided to us as an employee or director are not covered by this policy. A related person is any executive officer, director or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our audit committee, or, if audit committee approval would be

inappropriate, to another independent body of our board of directors, for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer and, to the extent feasible, significant stockholder to enable us to identify any existing or potential related-person transactions and to effectuate the terms of the policy. In addition, under our Code of Business Conduct and Ethics, our employees and directors will have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest. In considering related person transactions, our audit committee, or other independent body of our board of directors, will take into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director's independence in the event that the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify or reject a related person transaction, our audit committee, or other independent body of our board of directors, must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our stockholders, as our audit committee, or other independent body of our board of directors, determines in the good faith exercise of its discretion.

Principal stockholders

The following table sets forth the beneficial ownership of our common stock as of November 15, 2016 for:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of our named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

The percentage ownership information shown in the column titled “Before Offering” in the table is based upon 20,568,180 shares of common stock outstanding as of November 15, 2016. The percentage ownership information shown in the column titled “After Offering” in the table is based upon 24,568,180 shares of our common stock outstanding after this offering, assuming no exercise of outstanding options or warrants and no exercise of the underwriters’ option to purchase up to 600,000 additional shares of common stock.

We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of common stock issuable pursuant to the exercise of stock options or warrants that are exercisable on or before January 14, 2017, which is 60 days after November 15, 2016. These shares are deemed to be outstanding and beneficially owned by the person holding those options or warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. This table is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G if any filed with the SEC. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the stockholders named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned.

Except as otherwise noted below, the address for persons listed in the table is c/o Clearside Biomedical, Inc., 1220 Old Alpharetta Road, Suite 300, Alpharetta, Georgia 30005.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
Principal stockholders:			
Entities affiliated with Hatteras Venture Partners(1)	4,262,819	20.7%	17.4%
Entities affiliated with Wellington Management Group(2)	2,087,448	10.1	8.5
Entities affiliated with Cormorant Global Healthcare(3)	1,988,208	9.7	8.1
RMI Investments(4)	1,558,024	7.6	6.3
Entities affiliated with Rock Springs Capital(5)	1,300,000	6.3	5.3
Santen Pharmaceutical Co., Ltd(6)	1,258,044	6.1	5.1
Executive officers and directors:			
Daniel H. White(7)	797,464	3.8	3.2
Charles A. Deignan(8)	199,839	1.0	*
Glenn Noronha, Ph.D.(9)	97,384	*	*
Christy L. Shaffer, Ph.D.	—	—	—
Clay B. Thorp(1)	4,262,819	20.7	17.4
William D. Humphries(9)	45,454	*	*
Gerald D. Cagle, Ph.D.(10)	45,713	*	*
Evgeny Zaytsev, M.D.	—	—	—
Derek Yoon	—	—	—
Richard Croarkin(9)	5,266	*	*
All current directors and executive officers as a group (10 persons)(11)	5,453,939	25.8	21.7

* Represents beneficial ownership of less than 1%.

(1) This information has been obtained from a Schedule 13D filed on June 17, 2016 by entities and individuals associated with Hatteras Venture Partners. Shares beneficially owned prior to this offering consist of (i) 2,090,170 shares of common stock held by Hatteras Venture Partners IV SBIC, LP ("HVP IV SBIC"), (ii) 1,634,603 shares of common stock held by Hatteras Venture Partners III, LP ("HVP III"), (iii) 264,286 shares of common stock held by Hatteras Venture Partners IV, LP ("HVP IV"), (iv) 148,417 shares of common stock held by Hatteras Venture Affiliates III, LP ("HVA III") and (v) 125,343 shares held by Hatteras NC Fund, LP ("Hatteras Fund"). Hatteras Venture Advisors III, LLC ("HVA III Advisors") is the general partner of HVP III and HVA III. Hatteras Venture Advisors IV SBIC, LP ("HVA SBIC Advisors") is the general partner of HVP IV SBIC. Hatteras Venture Advisors IV, LP ("HVA IV Advisors") is the general partner of HVP IV and Hatteras Fund. The shares held by HVP III, HVA III, HVP IV SBIC, HVP IV and Hatteras Fund are indirectly held by the individual managing members of the general partners, HVA III Advisors, HVA BIC Advisors and HVA IV Advisors, respectively, (collectively, the "GP Managing Members"). The GP Managing Members are John Crumpler, Clay Thorp, Ken Lee, Douglas Reed and Robert Ingram. The GP Managing Members may share voting and dispositive power over the securities directly held by HVP III, HVA III, HVP IV SBIC, HVP IV and Hatteras Fund. The principal business address of these persons and entities is 280 S. Mangum Street, Suite 350 Durham, North Carolina 27701.

(2) This information has been obtained from a Schedule 13G filed on July 11, 2016 by entities associated with Wellington Management Group, LLP ("WMG"). WMG, Wellington Group Holdings LLP ("WGH"), Wellington Investment Advisors Holdings LLP ("WIAH"), Wellington Management Company and ("WMC" and together with WMG, WGH and WIAH, the "Wellington Entities") share voting and dispositive power over the securities listed in the table. The principal business address of the Wellington Entities is 280 Congress Street, Boston, Massachusetts 02210.

(3) This information has been obtained from a Schedule 13G filed on June 13, 2016 by entities and an individual associated with Cormorant Global Healthcare Master Fund, LP ("CGHMF"). Cormorant Asset Management, LLC ("CAM") and Bihua Chen ("Chen") share voting and dispositive power with respect to 1,988,208 listed in the table. The securities reported in the table for CAM represent 1,658,151 shares which are beneficially owned by CGHMF and 330,057 shares which are beneficially owned by a managed account (the "Account"). CGH GP serves as the general partner of CGHMF, and CAM serves as the investment manager to both CGHMF and the Account. Chen serves as the managing member of CGH GP and CAM. The principal business address of these entities and Chen is 200 Clarendon Street, 52nd Floor, Boston, Massachusetts 02116.

(4) The shares directly held by RMI are indirectly held by RusnanoMedInvest, the parent company of RMI. RMI Partners LLC is the management company for RusnanoMedInvest. The CEO of RMI Partners LLC is Vladimir Gurdus. RusnanoMedInvest, RMI Partners LLC and Mr. Gurdus may be deemed to have shared voting and dispositive power over, and be deemed indirect beneficial owners of, the shares directly held by RMI. The principal business address of RMI is Business-Center 29/22, Capital Tower 1st Brestskaya Street, Moscow, 12 125047.

(5) This information has been obtained from a Schedule 13G filed on June 10, 2016 by Rock Springs Capital Management LP ("RSC Management") and Rock Springs Capital Master Fund LP ("RSC Fund" and together with RSC Management, the "RSC Entities"). The RSC Entities share voting and dispositive power over the securities reported in this table. The principal business address of RSC Management is 650 South Exeter, Suite 1070, Baltimore, Maryland 21202, and the principal business address of RSC Fund is c/o Intertrust Corporate Services (Cayman) Limited, 190 Elgin Avenue, George Town, Grand Cayman KY1-9005, Cayman Islands.

(6) The principal business address of Santen is 9-19 Shimoshinjo 3-chome, Higashiyodogawa-ku, Osaka 533-8651, Japan.

(7) Consists of (i) 530,817 shares held by Mr. White directly, (ii) 40,909 shares held by the White Family Trust, for which Mr. White's wife serves as trustee, (iii) 2,333 shares held for the benefit of Mr. White's children under the Georgia Uniform Transfers to Minors Act, for which Mr. White serves as custodian and (iv) 223,405 shares underlying options that are exercisable and vested within 60 days of November 15, 2016.

(8) Consists of 62,759 shares held by Mr. Deignan directly and 137,080 shares underlying options that are exercisable and vested within 60 days of November 15, 2016.

(9) Consists of shares underlying options that are exercisable and vested within 60 days of November 15, 2016.

(10) Consists of 5,941 shares held by Mr. Cagle directly and 39,772 shares underlying options that are exercisable and vested within 60 days of November 15, 2016.

(11) Consists of 4,905,578 shares of common stock and 548,361 shares underlying options that are exercisable and vested within 60 days of November 15, 2016.

Description of capital stock

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries. You should also refer to the amended and restated certificate of incorporation and the amended and restated bylaws, which are incorporated by reference as exhibits to the registration statement of which this prospectus is part.

General

Our amended and restated certificate of incorporation authorizes us to issue up to 100,000,000 shares of common stock, $0.001 par value per share, and 10,000,000 shares of preferred stock, $0.001 par value per share, all of which shares of preferred stock will be undesignated. Our board of directors may establish the rights and preferences of the preferred stock from time to time.

Common stock

Voting rights

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Under our amended and restated certificate of incorporation and amended and restated bylaws, our stockholders do not have cumulative voting rights. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. As of September 30, 2016, we had outstanding 20,545,752 shares of common stock, held of record by 63 stockholders. We believe the number of beneficial owners of our common stock at that date was substantially greater.

Dividends

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared from time to time by the board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Rights and preferences

Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Preferred stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of

shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of us and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock on the rights of holders of common stock until the board of directors determines the specific rights attached to that preferred stock.

There are no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options

As of September 30, 2016, under our 2011 plan and our 2016 plan, options to purchase an aggregate of 1,414,594 shares of common stock were outstanding. For additional information regarding the terms of this plan, see “Executive Compensation—Equity Incentive Plans.” We have also granted options to purchase 17,236 shares of common stock outside our 2011 plan.

Warrants

In April 2015, in connection with a loan agreement, we issued a warrant to the lenders to purchase up to 57,143 shares of Series B preferred stock at a price per share of $3.50. The term of the warrant extends until 10 years from the grant date and the warrant is exercisable at any time during that 10-year period. The warrant was automatically converted into a warrant to purchase 25,974 shares of common stock at an exercise price of $7.70 upon the closing of our IPO in June 2016.

In September 2016, in connection with an amended and restated loan and security agreement, we issued warrants to the lenders to purchase up to 29,796 shares of common stock at a price per share of $10.74. The warrants expire in September 2026, or earlier upon the occurrence of specified mergers or acquisitions of the Company, and are immediately exercisable.

Registration rights

We and some of our stockholders who held shares of our convertible preferred stock prior to our IPO have entered into an investor rights agreement. The registration rights provisions of this agreement currently provide some of those holders with demand and piggyback registration rights with respect to the shares of our common stock held by them. Approximately 9.6 million shares of common stock are entitled to these registration rights. However, pursuant to the lock-up agreements entered into in connection with this offering, holders of approximately 60% of the registrable securities have agreed not to exercise such registration rights for at least 90 days from the date of this prospectus.

Demand registration rights

The holders of at least 40% of the shares held by parties to the investor rights agreement in the aggregate have the right to demand that we file up to two Form S-1 registration statements, as long as the anticipated

aggregate offering price, net of underwriting discounts and commissions, would exceed $10.0 million. These registration rights are subject to specified conditions and limitations, including the right of the underwriters, if any, to limit the number of shares included in any such registration under specified circumstances. Upon such a request, we are required to effect the registration as soon as reasonably possible.

Piggyback registration rights

If we propose to register any of our securities under the Securities Act either for our own account or for the account of other stockholders, the parties to the investor rights agreement will each be entitled to notice of the registration and will be entitled to include their shares of common stock in the registration statement. These piggyback registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under specified circumstances. All piggyback registration rights have been waived in connection with this offering.

Registration on Form S-3

At any time after we become eligible to file a registration statement on Form S-3, the holders of at least 20% of the shares held by parties to the investor rights agreement will be entitled to have their shares registered by us on a Form S-3 registration statement at our expense, provided that such requested registration has an anticipated aggregate offering price, net of underwriting discounts and commissions, of at least $1.0 million and subject to other specified conditions and limitations.

Expenses of registration

We will pay all expenses relating to any demand, piggyback or Form S-3 registration, other than underwriting discounts and commissions, subject to specified conditions and limitations.

Termination of registration rights

The registration rights granted under the investor rights agreement will terminate upon the earliest to occur of (i) June 1, 2021, which is the fifth anniversary of the completion of our IPO or (ii) the closing of a liquidating event.

Anti-takeover provisions

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a "business combination" to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an "interested stockholder" as an entity or person who, together with the person's affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

Certificate of incorporation and bylaws

Our amended and restated certificate of incorporation, or our restated certificate, provides for our board of directors to be divided into three classes with staggered three-year terms. Only one class of directors is elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, stockholders holding a majority of the shares of common stock outstanding are able to elect all of our directors. Our restated certificate and our amended and restated bylaws, or our restated bylaws, also provide that directors may be removed by the stockholders only for cause upon the vote of 66 2/3% or more of our outstanding common stock. Furthermore, the authorized number of directors may be changed only by resolution of the board of directors, and vacancies and newly created directorships on the board of directors may, except as otherwise required by law or determined by the board, only be filled by a majority vote of the directors then serving on the board, even though less than a quorum.

Our restated certificate and restated bylaws also provide that all stockholder actions must be effected at a duly called meeting of stockholders and eliminated the right of stockholders to act by written consent without a meeting. Our restated bylaws also provides that only our chairman of the board, chief executive officer or the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors may call a special meeting of stockholders.

Our restated bylaws also provides that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide timely advance notice in writing, and specify requirements as to the form and content of a stockholder's notice.

Our restated certificate and restated bylaws provide that the stockholders cannot amend many of the provisions described above except by a vote of 66 2/3% or more of our outstanding common stock.

The combination of these provisions will make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Since

our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

Choice of forum

Our restated certificate provides that the Court of Chancery of the State of Delaware will be the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our restated certificate, or our amended and restated bylaws; or
- any action asserting a claim against us that is governed by the internal affairs doctrine.

The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our restated certificate to be inapplicable or unenforceable in such action.

Transfer agent and registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company. The transfer agent's address is 6201 15th Avenue, Brooklyn, NY 11219.

NASDAQ Global Market listing

Our common stock is listed on The NASDAQ Global Market under the trading symbol "CLSD."

Shares eligible for future sale

Based on the number of shares outstanding as of September 30, 2016, upon completion of this offering, 24,545,752 shares of common stock will be outstanding, assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options or warrants. All of the shares of common stock sold in our IPO and in this offering will be freely tradable without restrictions or further registration under the Securities Act, except for any shares sold to our "affiliates," as that term is defined under Rule 144 under the Securities Act. The remaining 12,396,909 shares of common stock held by existing stockholders are "restricted securities," as that term is defined in Rule 144 under the Securities Act. Restricted securities may be sold in the public market only if registered or if their resale qualifies for exemption from registration described below under Rule 144 promulgated under the Securities Act. Of these remaining shares, approximately 6.5 million shares will be eligible for sale in the public market upon expiration of lock-up agreements up to 90 days after the date of this prospectus, subject in certain circumstances to the volume, manner of sale and other limitations under Rule 144.

Rule 144

In general, persons who have beneficially owned restricted shares of our common stock for at least six months, and any affiliate of the company who owns either restricted or unrestricted shares of our common stock, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

Non-affiliates

Any person who is not deemed to have been one of our affiliates at the time of, or at any time during the three months preceding, a sale may sell an unlimited number of restricted securities under Rule 144 if:

- the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;
- we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

Any person who is not deemed to have been an affiliate of ours at the time of, or at any time during the three months preceding, a sale and has held the restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, will be entitled to sell an unlimited number of restricted securities without regard to the length of time we have been subject to Exchange Act periodic reporting or whether we are current in our Exchange Act reporting.

Affiliates

Persons seeking to sell restricted securities who are our affiliates at the time of, or any time during the three months preceding, a sale, would be subject to the restrictions described above. They are also subject to additional restrictions, by which such person would be required to comply with the manner of sale and notice provisions of Rule 144 and would be entitled to sell within any three-month period only that number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares of our common stock then outstanding, which will equal 245,458 shares immediately after the completion of this offering based on the number of shares outstanding as of September 30, 2016; or

- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Additionally, persons who are our affiliates at the time of, or any time during the three months preceding, a sale may sell unrestricted securities under the requirements of Rule 144 described above, without regard to the six month holding period of Rule 144, which does not apply to sales of unrestricted securities.

Form S-8 registration statements

We have filed with the SEC a registration statement on Form S-8 under the Securities Act to register the shares of our common stock that are issuable pursuant to our 2011 plan, 2016 plan and 2016 ESPP. This registration statement was effective immediately upon filing. Shares covered by this registration statement are eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described below and Rule 144 limitations applicable to affiliates.

Lock-up agreements

In connection with this offering, we, all of our officers and directors and some of our stockholders owning in the aggregate approximately 6.5 million shares of our common stock, have entered into lock-up agreements with the underwriters or otherwise agreed, subject to certain exceptions, that we and they will not, directly or indirectly, offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale, or otherwise dispose of or hedge any of our shares of common stock, any options or warrants to purchase shares of our common stock, or any securities convertible into, or exchangeable for or that represent the right to receive shares of our common stock, without the prior written consent of the representatives of the underwriters for periods of up to 90 days from the date of this prospectus.

Registration rights

Upon completion of this offering, the holders of approximately 2.9 million shares of our common stock will be entitled to specified rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See “Description of Capital Stock—Registration Rights” for additional information.

Material U.S. federal income tax consequences to non-U.S. holders

The following is a general discussion of the material U.S. federal income tax considerations applicable to non-U.S. holders with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. All prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock. In general, a non-U.S. holder means a beneficial owner of our common stock (other than a partnership or an entity or arrangement treated as a partnership for U.S. federal income tax purposes) that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or an entity treated as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if (1) a U.S. court can exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing U.S. Treasury Regulations promulgated thereunder, published administrative rulings and judicial decisions, all as in effect as of the date of this prospectus. These laws are subject to change and to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus.

We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment). This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances, nor does it address any aspects of U.S. federal taxes other than income taxes (except to the limited extent set forth below), or U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder, nor does it address any alternative minimum tax or Medicare contribution tax consequences, and does not address the special tax rules applicable to particular non-U.S. holders, such as holders that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below), corporations that accumulate earnings to avoid U.S. federal income tax, tax-exempt organizations, banks, financial institutions, insurance companies, brokers, dealers or traders in securities, commodities or currencies, tax-qualified retirement plans, holders who hold or receive our common stock pursuant to the exercise of employee stock options or otherwise as compensation, holders holding our common stock as part of a hedge, straddle or other risk reduction strategy, conversion transaction or other integrated investment, holders deemed to sell our common stock under the constructive sale provisions of the Code, controlled foreign corporations, passive foreign investment companies and certain former U.S. citizens or long-term residents.

In addition, this discussion does not address the tax treatment of partnerships (or entities or arrangements that are treated as partnerships for U.S. federal income tax purposes) or persons that hold their common stock through such partnerships. If a partnership, including any entity or arrangement treated as a partnership for U.S. federal income tax purposes, holds shares of our common stock, the U.S. federal income tax treatment of a partner in such partnership will generally depend upon the status of the partner and the activities of the partnership. Such partners and partnerships should consult their tax advisors regarding the tax consequences of the purchase, ownership and disposition of our common stock.

There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling with respect to the U.S. federal income tax consequences to a non-U.S. holder of the purchase, ownership or disposition of our common stock.

Distributions on our common stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's adjusted tax basis in the common stock. Any remaining excess will be treated as capital gain from the sale or exchange of such common stock, subject to the tax treatment described below in "Gain on Sale, Exchange or Other Disposition of Our Common Stock." Any such distribution will also be subject to the discussion below under the heading "Foreign Accounts."

Dividends paid to a non-U.S. holder will generally be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

Gain on sale, exchange or other disposition of our common stock

Subject to the discussion below regarding backup withholding and foreign accounts, in general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other disposition of shares of our common stock unless:

- the gain is effectively connected with a U.S. trade or business of the non-U.S. holder and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained in the United States by such non-U.S. holder, in which case the non-U.S. holder generally will be taxed at the

graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;

- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States); or
- our common stock constitutes a U.S. real property interest because we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation." Even if we are or become a U.S. real property holding corporation, provided that our common stock is regularly traded on an established securities market, our common stock will be treated as a U.S. real property interest only with respect to a non-U.S. holder that holds more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. In such case, such non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

U.S. federal estate tax

Shares of our common stock that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the dividends on our common stock paid to such holder and the tax withheld, if any, with respect to such dividends. Non-U.S. holders will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to the U.S. withholding tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner

similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder may be allowed as a credit against the non-U.S. holder's U.S. federal income tax liability, if any, and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

Foreign accounts

The Code generally imposes a U.S. federal withholding tax of 30% on dividends and the gross proceeds of a disposition of our common stock paid to a "foreign financial institution" (as specifically defined for this purpose), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing this withholding tax may be subject to different rules. A U.S. federal withholding tax of 30% also applies to dividends and the gross proceeds of a disposition of our common stock paid to a non-financial foreign entity, unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding substantial direct and indirect U.S. owners of the entity. The withholding provisions described above generally apply to dividends on our common stock and will apply with respect to gross proceeds of a sale or other disposition of our common stock on or after January 1, 2019. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC and Cowen and Company, LLC are acting as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	1,900,000
Cowen and Company, LLC	1,220,000
Stifel, Nicolaus & Company, Incorporated	600,000
Wedbush Securities, Inc.	280,000
Total	4,000,000

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares of common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $0.324 per share. After the initial public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters have an option to buy up to an additional 600,000 of shares of common stock from us. The underwriters have 30 days from the date of this prospectus to exercise this option. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $0.54 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	Without option exercise	With full option exercise
Per share	$ 0.54	$ 0.54
Total	$ 2,160,000	$ 2,484,000

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $600,000. We have agreed to reimburse the underwriters for up to $30,000 for expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc. The underwriters have agreed to reimburse us for up to approximately $200,000 of our expenses in connection with the offering.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We, our officers and directors and some of our stockholders have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer to sell, contract to sell, effect any short sale, pledge, transfer, establish a “put equivalent position” within the meaning of Rule 16a-l(h) under the Exchange Act;
- otherwise dispose of, or enter into any swap, hedge or similar arrangement that transfers, in whole or in part, the economic risk of ownership of, any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially;
- make any demand for, or exercise any right with respect to, the registration under the Securities Act of the offer and sale of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock; or
- publicly announce any intention to do any of the foregoing;

for periods of up to 90 days after the date of this prospectus without the prior written consent of the representatives.

Subject to limited exceptions described below, the lock-up restrictions terminate after the close of trading of the common stock on and including the 90th day after the date of this prospectus. The representatives may, in their sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements.

The restrictions described above to do not apply to:

- transfers of shares of our common stock or any security convertible into or exercisable or exchangeable for shares of our common stock (i) as a bona fide gift, or gifts, (ii) to an immediate family member or a trust for the direct or indirect benefit of the lock-up signatory or such immediate family member of the lock-up signatory or (iii) by will or intestacy;
- transactions relating to shares of our common stock or other securities acquired in the open market after the completion of this offering;
- if the lock-up signatory is a corporation, limited partnership, trust or other business entity, transfers of shares of our common stock to (i) another corporation, member, partner, trust or other business entity that is a direct or indirect affiliate (as defined in Rule 405 promulgated under the Securities Act) of the lock-up signatory or (ii) as part of a pro rata distribution or transfer by the lock-up signatory to its stockholders, members, partners, beneficiaries or other equity holders provided however, that any such transfer or distribution shall not involve a disposition for value;
- transfers to us in connection with the “cashless” exercise of options to purchase shares of our common stock pursuant to employee benefit plans disclosed in this prospectus;
- transfers in connection with the “net exercise” of warrants held by the lock-up signatory;
- transfers to us to satisfy tax withholding obligations in connection with the vesting or exercise of equity incentive awards under our employee benefit plans after the completion of this offering;

- transfers to us in connection with the repurchase of shares of our common stock issued pursuant to employee benefit plans disclosed in this prospectus upon the termination of service pursuant to an existing company right;
- transfers, sales, tenders or other dispositions of shares of our common stock, or any securities convertible into or exercisable or exchangeable for our common stock, occurring after the consummation of this offering, pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders of our capital stock that would result in the disposition of not less than a majority of the outstanding shares of our voting securities, provided that in the event that the tender offer, merger, consolidation or other such transaction is not completed, our common stock and any security convertible into or exchangeable for our common stock shall remain subject to the same restrictions;
- transfers pursuant to operation of law, including pursuant to a domestic order or negotiated divorce settlement;
- any issuance by us of shares of our common stock or securities convertible or exercisable or exchangeable for shares of our common stock pursuant to the exercise or conversion of warrants, options, or other convertible or exchangeable securities, in each case outstanding as of the date of this prospectus, provided that the underlying shares received shall continue to be subject to these restrictions;
- the establishment of a trading plan that complies with Rule 10b5-1 under the Exchange Act; provided, however, that (i) the restrictions shall apply in full force to sales or other dispositions pursuant to such Rule 10b5-1 plan during the 90-day lock-up period described above and (ii) no public announcement or disclosure of entry into such Rule 10b5-1 plan is made or required to be made; and
- with respect to certain stockholders affiliated with our directors, sales of 555,456 shares of our common stock pursuant to trading plans that comply with Rule 10b5-1 under the Exchange Act;

provided, however, that in the case of any transfer or distribution pursuant to the first, third and ninth clauses above, each donee, distributee recipient or transferee shall sign and deliver a lock-up agreement substantially in the form of the lock-up agreements described above; and in the case of any transfer or distribution pursuant to the first (except for sub-clause (iii)), second, third, fourth, fifth and sixth clauses above, no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of our common stock, shall be required or shall be voluntarily made during the lock-up period.

Except as set forth in the twelfth clause above, there are no existing agreements between the underwriters and any of our stockholders who have executed a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Our common stock is listed on The NASDAQ Capital Market under the symbol “CLSD.”

In connection with this offering, the underwriters may engage in stabilizing transactions, which involve making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involve the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to

purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discounts and commissions received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The NASDAQ Global Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The NASDAQ Global Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

United Kingdom

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). The securities are only available to, and any invitation, offer or agreement to subscribe for, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), from and including the date on which the European Union Prospectus Directive (the "EU Prospectus Directive") was implemented in that Relevant Member State (the "Relevant Implementation Date") an offer of securities described in this prospectus may not be made to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the EU Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of securities described in this prospectus may be made to the public in that Relevant Member State at any time:

- to any legal entity which is a qualified investor as defined under the EU Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the EU Prospectus Directive); or
- in any other circumstances falling within Article 3(2) of the EU Prospectus Directive, provided that no such offer of securities described in this prospectus shall result in a requirement for the publication by us of a prospectus pursuant to Article 3 of the EU Prospectus Directive.

For the purposes of this provision, the expression an "offer of securities to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the EU Prospectus Directive in that Member State. The expression "EU Prospectus Directive" means Directive 2003/71/EC (and any amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Canada

The common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Switzerland

The securities offered by this prospectus may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, us, the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA ("FINMA"), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Dubai International Financial Centre ("DIFC")

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority ("DFSA"). This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

United Arab Emirates

The securities offered by this prospectus have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing

the issue, offering and sale of securities. Further, prospectus supplement does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Australia

This prospectus:

- does not constitute a disclosure document under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the "Corporations Act");
- has not been, and will not be, lodged with the Australian Securities and Investments Commission ("ASIC"), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document under Chapter 6D.2 of the Corporations Act; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, or Exempt Investors, available under section 708 of the Corporations Act.

The securities offered by this prospectus may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the securities may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any securities may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the securities, you represent and warrant to us that you are an Exempt Investor.

As any offer of securities under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the securities you undertake to us that you will not, for a period of 12 months from the date of issue of the securities, offer, transfer, assign or otherwise alienate those securities to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Japan

The securities offered by this prospectus have not been and will not be registered under the Financial Instruments and Exchange Act. Accordingly, the securities may not be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan.

Hong Kong

The securities offered by this prospectus have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance

(Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Warning

The contents of this document have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than:

- to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA");
- to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA; or
- otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Bermuda

The securities offered by this prospectus may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

Saudi Arabia

This prospectus may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority ("CMA") pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended (the "CMA Regulations"). The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

British Virgin Islands

The securities are not being, and may not be offered to the public or to any person in the British Virgin Islands for purchase or subscription by or on behalf of us. The securities may be offered to companies incorporated under the BVI Business Companies Act, 2004 (British Virgin Islands),"BVI Companies"), but only where the offer will be made to, and received by, the relevant BVI Company entirely outside of the British Virgin Islands.

This prospectus has not been, and will not be, registered with the Financial Services Commission of the British Virgin Islands. No registered prospectus has been or will be prepared in respect of the securities for the purposes of the Securities and Investment Business Act, 2010 ("SIBA") or the Public Issuers Code of the British Virgin Islands.

The securities may be offered to persons located in the British Virgin Islands who are "qualified investors" for the purposes of SIBA. Qualified investors include (i) certain entities which are regulated by the Financial Services Commission in the British Virgin Islands, including banks, insurance companies, licensees under SIBA and public, professional and private mutual funds; (ii) a company, any securities of which are listed on a recognised exchange; and (iii) persons defined as "professional investors" under SIBA, which is any person (a) whose ordinary business involves, whether for that person's own account or the account of others, the acquisition or disposal of property of the same kind as the property, or a substantial part of our property; or (b) who has signed a declaration that he, whether individually or jointly with his spouse, has net worth in excess of US$1,000,000 and that he consents to being treated as a professional investor.

China

This prospectus does not constitute a public offer of the securities offered by this prospectus, whether by sale or subscription, in the People's Republic of China (the "PRC"). The securities are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the securities without obtaining all prior PRC's governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this document are required by the issuer and its representatives to observe these restrictions.

Korea

The securities have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder (the "FSCMA"), and the securities have been and will be offered in Korea as a private placement under the FSCMA. None of the securities may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder (the "FETL"). The securities have not been listed on any of securities exchanges in the world including, without limitation, the Korea Exchange in Korea. Furthermore, the purchaser of the securities shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the securities. By the purchase of the securities, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the securities pursuant to the applicable laws and regulations of Korea.

Malaysia

No prospectus or other offering material or document in connection with the offer and sale of the securities has been or will be registered with the Securities Commission of Malaysia ("Commission") for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Malaysia other than (i) a closed end fund approved by the Commission; (ii) a holder of a Capital Markets Services Licence; (iii) a person who acquires the securities, as principal, if the offer is on terms that the securities may only be acquired at a consideration of not less than RM250,000 (or its equivalent in foreign currencies) for each transaction; (iv) an individual whose total net personal assets or total net joint assets with his or her spouse exceeds RM3 million (or its equivalent in foreign currencies), excluding the value of the primary residence of the individual; (v) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign currencies) per annum in the preceding twelve months; (vi) an individual who, jointly with his or her spouse, has a gross annual income of RM400,000 (or its equivalent in foreign currencies), per annum in the preceding twelve months; (vii) a corporation with total net assets exceeding RM10 million (or its equivalent in a foreign currencies) based on the last audited accounts; (viii) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies); (ix) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010; (x) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010; and (xi) any other person as may be specified by the Commission; provided that, in the each of the preceding categories (i) to (xi), the distribution of the securities is made by a holder of a Capital Markets Services Licence who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus is subject to Malaysian laws. This prospectus does not constitute and may not be used for the purpose of public offering or an issue, offer for subscription or purchase, invitation to subscribe for or purchase any securities requiring the registration of a prospectus with the Commission under the Capital Markets and Services Act 2007.

Taiwan

The securities have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities

and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the securities in Taiwan.

South Africa

Due to restrictions under the securities laws of South Africa, the securities are not offered, and the Offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions applies:

- the offer, transfer, sale, renunciation or delivery is to duly registered banks, mutual banks, financial services provider, financial institution, the Public Investment Corporation (in each case registered as such in South Africa), a person who deals with securities in their ordinary course of business, or a wholly owned subsidiary of a bank, mutual bank, authorized services provider or financial institution, acting as agent in the capacity of an authorized portfolio manager for a pension fund (duly registered in South Africa), or as manager for a collective investment scheme (registered in South Africa); or
- the contemplated acquisition cost of the securities, for any single addressee acting as principal is equal to or greater than R1,000,000.

This document does not, nor is it intended to, constitute an "*offer to the public*" (as that term is defined in the South African Companies Act, 2008 (the "SA Companies Act") and does not, nor is it intended to, constitute a prospectus prepared and registered under the SA Companies Act. This document is not an "*offer to the public*" and must not be acted on or relied on by persons who do not fall within Section 96(1)(a) of the SA Companies Act (such persons being referred to as "relevant persons"). Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

A South African resident person or company or any non-South African company which is a subsidiary of a South African company is not permitted to acquire the securities unless such person has obtained exchange control approval to do so.

Legal matters

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Cooley LLP, Reston, Virginia. Certain legal matters related to this offering will be passed upon for the underwriters by Latham & Watkins LLP.

Experts

The financial statements of Clearside Biomedical, Inc. at December 31, 2014 and 2015, and for each of the two years in the period ended December 31, 2015, appearing in this prospectus and registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

Where you can find additional information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the shares of common stock being offered by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information in the registration statement and its exhibits. For further information with respect to our company and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the internet at the SEC's website at *www.sec.gov*. You may also read and copy any document we file with the SEC at its public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

We are subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We also maintain a website at *www.clearsidebio.com*, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus.

Index to financial statements

Report of independent registered public accounting firm

The board of directors and stockholders of

Clearside Biomedical, Inc.

We have audited the accompanying balance sheets of Clearside Biomedical, Inc. (the Company) as of December 31, 2014 and 2015, and the related statements of operations, stockholders' deficit, and cash flows for each of the two years in the period ended December 31, 2015. 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. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Clearside Biomedical, Inc. at December 31, 2014 and 2015, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Atlanta, Georgia
March 18, 2016
except for Note 16, as to which the date is
May 11, 2016

CLEARSIDE BIOMEDICAL, INC.
Balance sheets
(in thousands, except share and per share data)

	December 31, 2014	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 8,269	$ 20,283
Prepaid expenses	47	159
Other current assets	7	40
Total current assets	8,323	20,482
Property and equipment, net	205	156
Deferred offering costs	1,750	410
Other assets	21	7
Total assets	$ 10,299	$ 21,055
Liabilities, convertible preferred stock and stockholders' deficit		
Current liabilities:		
Accounts payable	$ 1,257	$ 1,469
Accrued liabilities	1,157	1,985
Current portion of long-term debt	—	1,733
Current portion of deferred rent	10	9
Total current liabilities	2,424	5,196
Deferred revenue	200	700
Deferred rent	11	3
Long-term debt	—	4,243
Other non-current liabilities	42	258
Total liabilities	2,677	10,400
Convertible preferred stock:		
Series A preferred stock, $0.001 par value, 5,198,826 shares authorized, issued and outstanding at December 31, 2014 and 2015; liquidation preference of $4,086 at December 31, 2014 and 2015	4,086	4,086
Series A-1 preferred stock, $0.001 par value; 4,373,481 shares authorized at December 31, 2014 and 2015; 4,356,931 shares issued and outstanding at December 31, 2014 and 2015; liquidation preference of $7,900 at December 31, 2014 and 2015	7,858	7,900
Series B preferred stock, $0.001 par value, 7,413,365 shares authorized at December 31, 2014; 6,066,345 authorized at December 31, 2015; 6,009,202 shares issued and outstanding at December 31, 2014 and 2015; liquidation preference of $16,212 at December 31, 2014 and 2015	14,891	15,372
Series C preferred stock, $0.001 par value, 5,274,679 shares authorized at December 31, 2015; 5,274,674 shares issued and outstanding at December 31, 2015; liquidation preference of $20,000 at December 31, 2015	—	19,956
Total convertible preferred stock	26,835	47,314
Stockholders' (deficit) equity:		
Common stock, $0.001 par value; 30,000,000 shares authorized at December 31, 2014 and 40,000,000 shares authorized at December 31, 2015; 1,816,467 and 2,659,262 shares issued and outstanding at December 31, 2014 and 2015	2	3
Additional paid-in capital	2,509	2,701
Accumulated deficit	(21,724)	(39,363)
Total stockholders' (deficit) equity	(19,213)	(36,659)
Total liabilities, convertible preferred stock and stockholders' (deficit) equity	$ 10,299	$ 21,055

See accompanying notes to the financial statements.

CLEARSIDE BIOMEDICAL, INC.
Statements of operations
(in thousands, except share and per share data)

	Year Ended December 31,	
	2014	2015
License revenue	$ —	$ —
Operating expenses:		
Research and development	6,692	10,762
General and administrative	3,131	6,555
Total operating expenses	9,823	17,317
Loss from operations	(9,823)	(17,317)
Other income (expense):		
Interest expense	(371)	(330)
Interest income	5	8
Total other expense	(366)	(322)
Net loss	$ (10,189)	$ (17,639)
Net loss per share of common stock—basic and diluted	$ (5.86)	$ (7.54)
Weighted average shares outstanding—basic and diluted	1,738,660	2,338,950

See accompanying notes to the financial statements.

CLEARSIDE BIOMEDICAL, INC.
Statements of stockholders' deficit

(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount			
Balance at January 1, 2014	1,583,144	$ 2	$ 796	$ (11,535)	$ (10,738)
Exercise of stock options	24,803	—	5	—	5
Vesting of restricted stock	208,520	—	6	—	6
Issuance of warrants to purchase common stock	—	—	1,506	—	1,506
Accretion of stock issuance costs	—	—	(231)	—	(231)
Share-based compensation expense	—	—	427	—	427
Net loss	—	—	—	(10,189)	(10,189)
Balance at December 31, 2014	1,816,467	2	2,509	(21,724)	(19,213)
Exercise of stock options	50,980	—	14	—	14
Exercise of Series B common stock warrants	777,612	1	(2)	—	(1)
Vesting of restricted stock	14,203	—	—	—	—
Accretion of stock issuance costs	—	—	(525)	—	(525)
Share-based compensation expense	—	—	705	—	705
Net loss	—	—	—	(17,639)	(17,639)
Balance at December 31, 2015	2,659,262	$ 3	$ 2,701	$ (39,363)	$ (36,659)

See accompanying notes to the financial statements.

CLEARSIDE BIOMEDICAL, INC.
Statements of cash flows

(in thousands)

	Year Ended December 31,	
	2014	2015
Operating activities		
Net loss	$(10,189)	$(17,639)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	33	60
Share-based compensation expense	427	705
Non-cash interest expense	82	104
Accretion of debt discount	277	60
Change in fair value of warrant liability	18	52
Loss on sale of fixed assets	—	15
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	54	(145)
Other assets	(1,154)	1,763
Accounts payable and accrued liabilities	1,137	632
Deferred revenue	200	500
Deferred rent	(9)	(9)
Net cash used in operating activities	(9,124)	(13,902)
Investing activities		
Acquisition of property and equipment	(140)	(32)
Proceeds from the sale of fixed assets	—	4
Net cash used in investing activities	(140)	(28)
Financing activities		
Proceeds from issuance of long-term debt	3,000	5,976
Principal payments made on long-term debt	(125)	—
Proceeds from exercise of stock options	5	14
Proceeds from issuance of Series B Preferred Stock and common stock warrants, net of issuance cost	12,744	—
Proceeds from issuance of Series C Preferred Stock, net of issuance cost	—	19,954
Net cash provided by financing activities	15,624	25,944
Net increase (decrease) in cash and cash equivalents	6,360	12,014
Cash and cash equivalents, beginning of period	1,909	8,269
Cash and cash equivalents, end of period	$ 8,269	$ 20,283
Supplemental schedule of noncash investing and financing activities		
Conversion of stockholder loan, promissory note and accrued interest	$ 3,232	$ —
Issuance of warrant to purchase Series B preferred stock	—	164
Accretion of redeemable convertible preferred stock to redemption value	231	525
Interest paid	7	100
Deferred initial public offering costs in accounts payable and accrued expenses	602	410

See accompanying notes to the financial statements

CLEARSIDE BIOMEDICAL, INC.
Notes to the financial statements

1. The company

Clearside Biomedical, Inc. (the "Company") is a late-stage clinical biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye. The Company's current product candidates focus on diseases affecting the retina and choroid, especially diseases associated with macular edema, and are injected into the suprachoroidal space using its proprietary SCS Microinjector. Incorporated in the State of Delaware on May 26, 2011, the Company has its corporate headquarters in Alpharetta, Georgia.

The Company's activities since inception have primarily consisted of developing product and technology rights, raising capital and performing research and development activities. The Company has no current source of revenue to sustain present activities, and does not expect to generate revenue until and unless the Company receives regulatory approval of and successfully commercialize its product candidates. The Company is subject to a number of risks and uncertainties similar to those of other life science companies at a similar stage of development, including, among others, the need to obtain adequate additional financing, successful development efforts including regulatory approval of products, compliance with government regulations, successful commercialization of potential products, protection of proprietary technology and dependence on key individuals.

Liquidity

The Company has funded its operations to date primarily through the sale of convertible preferred stock and the issuance of long-term debt. The Company will need to obtain additional financing to fund future operations, including completing the development and commercialization of its primary product candidates. The Company will need to expend substantial resources for research and development, including costs associated with the clinical testing of its product candidates. The Company will need to obtain additional financing to conduct additional trials for the regulatory approval of its drug candidates if requested by regulatory bodies, and completing the development of any additional product candidates that might be acquired. If such products were to receive regulatory approval, the Company would need to prepare for the potential commercialization of its product candidates and fund the commercial launch of the products, if the Company decides to commercialize the products on its own. Moreover, the Company's fixed expenses such as rent and other contractual commitments are substantial and are expected to increase in the future.

The Company has incurred losses and experienced negative operating cash flows since inception, and has cumulative net cash flows used in operating activities of $33.1 million and cumulative net losses of $39.4 million for the period from May 26, 2011 (inception) to December 31, 2015. The total future need for operating capital and research and development funding significantly exceeds the cash and cash equivalents that the Company has on its balance sheet. As a result, the Company will require additional funding in the future and may not be able to raise such additional funds. In the absence of product or other revenues, the amount, timing, nature or source of which cannot be predicted, the Company's losses will continue as it conducts its research and development activities. Until the Company can generate a sufficient amount of revenue, the Company may finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic alliances and marketing or distribution arrangements. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in restrictive covenants, such as limitations on the Company's ability to incur additional debt, limitations on its ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact the ability of the Company to conduct its business. If adequate funds are not available, the Company plans to delay, reduce or

eliminate research and development programs or reduce administrative expenses. The Company may seek to access the public or private capital markets whenever conditions are favorable, even if the Company does not have an immediate need for additional capital at that time. In addition, if the Company raises additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, the Company may have to relinquish valuable rights to its technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to the Company. There is no assurance that the Company will be successful in obtaining sufficient financing on acceptable terms and conditions to fund continuing operations, if at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations and financial condition. However, the Company is able to control spending on development activities while still advancing clinical trials for key drug candidates through December 31, 2016 with the cash on hand as of December 31, 2015.

2. Significant accounting policies

Basis of presentation

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of income and expenses during the reporting periods. Significant items subject to such estimates and assumptions include the accounting for useful lives to calculate depreciation and amortization, accrued liabilities, share-based compensation expense and income tax valuation allowance. Actual results could differ from these estimates.

Segment 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 segment. All operations are located in the United States.

Property and equipment, net

Property and equipment is recorded at historical cost. Depreciation is calculated using the straight-line method over the estimated useful lives of the related assets. Repairs and maintenance are expensed when incurred. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are removed from the accounts, and any resulting gain or loss is included in the determination of net income.

Cash equivalents

Cash equivalents consist of short-term, highly liquid investments with an original term of three months or less at the date of purchase.

Concentration of credit risk arising from cash deposits in excess of insured limits

The Company maintains its cash in bank deposits that at times may exceed federally insured limits. The Company has not experienced any loss in such accounts. The Company believes it is not exposed to any significant risks with respect to its cash balances.

Deferred offering costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as other assets until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering or as a reduction to the carrying value of preferred stock issued, if such stock is classified outside of stockholders' equity (deficit). Should the equity financing no longer be considered probable of being consummated, the deferred offering costs would be expensed immediately as a charge to operating expenses in the statement of operations. As of December 31, 2014, the Company had recorded $1.8 million of deferred offering costs. In September 2015, $1.9 million of deferred offering costs were charged to operating expenses due to the postponement of the equity financing. As of December 31, 2015, the Company had recorded $0.4 million of deferred offering costs in connection with a new equity financing.

Research and development costs

Research and development costs are charged to expense as incurred and include, but are not limited to:

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense for research and development personnel;
- expenses incurred under agreements with contract research organizations, contract manufacturing organizations and consultants that conduct clinical and preclinical studies;
- costs associated with preclinical and development activities;
- costs associated with technology and intellectual property licenses;
- costs for the Company's research and development facility; and
- depreciation expense for assets used in research and development activities.

Costs for certain development activities, such as clinical studies, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the patterns of costs incurred, and are reflected in the financial statements as prepaid or accrued expense, which are reported in accounts payable. No material adjustments to these estimates have been recorded in these financial statements.

Share-based compensation

Compensation cost related to share-based awards granted to employees is measured at grant date, based on the estimated fair value of the award. The Company estimates the fair value of stock options using a Black-Scholes option pricing model. Compensation expense for options granted to non-employees is determined as the fair value of consideration received or the fair value of the equity instruments issued, whichever is more

reliably measured. The fair value of restricted stock awards is determined based on the fair value of the Company's common stock on the date of grant. Share-based compensation costs are expensed on a straight-line basis (net of estimated forfeitures) over the relevant vesting period. The fair value of awards granted to non-employees is re-measured each period until the related service is complete. All share-based compensation costs are recorded in general and administrative or research and development costs in the statements of operations based upon the underlying employees' roles within the Company.

Debt discount

The Company follows the authoritative guidance in Accounting Standards Codification ("ASC") 470-20-25-2, *Debt with Conversion of Other Options*, for accounting for debt discount related to the detachable stock purchase warrants issued in connection with a debt obligation. The fair value of the warrant is recorded as a discount against the related debt obligation, and is amortized using the effective interest rate method over the term of the underlying debt obligation and reflected in interest expense.

Fair value measurements

The Company records certain financial assets and liabilities at fair value in accordance with the provisions of ASC Topic 820, *Fair Value Measurements and Disclosures*, on fair value measurements. The Company's material financial instruments at December 31, 2014 and 2015 consisted primarily of cash and cash equivalents, long-term debt and stock purchase warrant liabilities. The fair value of cash and cash equivalents, other current assets, and accounts payable approximate their respective carrying values due to the short term nature of these instruments.

Stock purchase warrants

The Company accounts for stock purchase warrants as liabilities based upon the characteristics and provisions of the underlying instruments. These liabilities are recorded at their fair value on the date of issuance within other non-current liabilities on the balance sheet and are remeasured on each subsequent reporting date, with fair value changes recognized as income (decreases in fair value) or expenses (increases in fair value) in other income (expense), net in the statements of operations. The fair value of these liabilities is estimated using the Black-Scholes method.

Income taxes

Deferred tax assets or liabilities are recorded for temporary differences between financial statement and tax basis of assets and liabilities, using enacted rates in effect for the year in which the differences are expected to reverse. A valuation allowance is recorded if it is more likely than not that a deferred tax asset will not be realized. The Company has provided a full valuation allowance on its deferred tax assets, which primarily consist of cumulative net operating losses of $14.2 million for the period from May 26, 2011 (inception) to December 31, 2015. Due to its history of operating losses since inception and losses expected to be incurred in the foreseeable future, a full valuation allowance was considered necessary.

Recent accounting pronouncements

In March 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-09, *Compensation-Stock Compensation (Topic 718).* The new guidance simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. For

public companies, the amendments in this standard are effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted. The effects of this standard on the Company's financial statements or related disclosures are not expected to be material.

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

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 provides guidance about management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. The new standard is effective for the Company for the annual period ending after December 15, 2016 and for annual and interim periods thereafter, with early adoption permitted. The Company is currently evaluating the impact of this accounting standard update on the Company's financial statements or related disclosures.

Net loss per share of common stock

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period, without consideration of the dilutive effect of potential common stock equivalents. Diluted net loss per share gives effect to all dilutive potential shares of common stock outstanding during this period.

For all periods presented, the Company's potential common stock equivalents, which include convertible preferred stock, stock options, unvested restricted stock and stock purchase warrants, have been excluded from the computation of diluted net loss per share as their inclusion would have the effect of reducing the net loss per share. Therefore, the denominator used to calculate both basic and diluted net loss per share is the same in all periods presented.

The Company's potential common stock equivalents that have been excluded from the computation of diluted net loss per share for all periods presented because of their antidilutive effect consisted of the following:

	Year Ended December 31,	
	2014	**2015**
Convertible preferred stock	7,074,961	9,472,530
Outstanding stock options	1,098,486	1,261,637
Unvested restricted stock	20,688	6,485
Stock purchase warrants	900,724	146,298
	9,094,859	10,886,950

3. Property and equipment, net

Property and equipment, net consisted of the following (dollar amounts in thousands):

	Estimated Useful Lives (Years)	December 31, 2014	December 31, 2015
Furniture and fixtures	5	$ 95	$ 66
Machinery and equipment	5	105	121
Computer equipment	3	27	27
Leasehold improvements	Lesser of useful life or remaining lease term	33	45
		260	259
Less: Accumulated depreciation		(55)	(103)
		$205	$ 156

4. Accrued liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31, 2014	December 31, 2015
Accrued research and development	$ 427	$ 569
Accrued bonuses	279	530
Accrued professional fees	178	668
Accrued vacation	53	64
Accrued interest payable	—	15
Accrued expense	220	139
	$1,157	$1,985

5. Long-term debt

Note purchase agreement

In December 2012, the Company entered into a $150,000 unsecured note purchase agreement with a lender and borrowed $150,000 on that date. Amounts borrowed under the agreement bore interest at 5% per annum. All unpaid principal, together with the balance of unpaid and accrued interest, were due and payable on demand at any time after the earlier of (i) the maturity date of December 2017, (ii) the date on which the Company has achieved sustainable profitability for a period of at least two consecutive fiscal years in accordance with generally accepted accounting principles, (iii) without the prior written consent of the lender, the date on which an equity financing of the Company in which the Company issues shares of common stock, preferred stock or other equity interests in the Company in a transaction or series of related transactions and receives an investment of cash in consideration of such issuance in the amount of not less than $7.0 million or consolidation of the Company or the sale or transfer by the Company's stockholders of capital stock of the Company representing more than 50% of the voting power occurs or (iv) upon or after the occurrence of an event of default. The repayment acceleration provision specifically excluded the Series A-1 Preferred Stock financing that occurred in January 2013. The unsecured promissory note converted into 60,291 shares of Series B convertible preferred stock in connection with the Company's August 2014 Series B convertible preferred stock financing.

Interest expense on the borrowings under the note purchase agreement was $5,000 and $0 for the years ended December 31, 2014 and 2015, respectively. As of December 31, 2014 and 2015, the total amount of borrowings due under this note purchase agreement was $0.

Loan agreements

In April 2013, the Company borrowed $125,000 under a loan agreement, which borrowings bore interest at a compounded annual rate of 4.25%. As of December 31, 2013, the total amount of borrowings due under the loan agreement was $125,000. All unpaid principal, together with the balance of unpaid and accrued interest, was due and payable on demand at any time after the earlier of (i) the maturity date of February 2016, (ii) the date on which the Company sells, leases, transfers or otherwise disposes of all or substantially all of its assets now owned or hereafter acquired, (iii) the date on which the Company makes a public offering of the Company's capital stock or equity interests, (iv) the date on which the Company takes any action which would result in a change in the direct or indirect control of 50% or more of the capital stock or equity interest ownership of the Company, (v) the date after December 31, 2013 on which the Company had received additional equity investments or milestone payments or license fees totaling $2.5 million in the aggregate over any 12-month period or (vi) upon or after the occurrence of an event of default. In May 2014, the Company repaid this loan in full.

Interest expense on the borrowings under the loan agreement was $2,000 and $0 for the years ended December 31, 2014 and 2015, respectively.

As of December 31, 2013, the Company had recorded unamortized debt discount of $7,000, relating to the detachable warrants issued in conjunction with the loan agreement (Note 10). Debt discounts are amortized using the effective interest method through the earlier of the date of maturity or the conversion of the debt. As of December 31, 2013, cumulative amortization of debt discount amounted to $3,000. The remaining debt discount was written off to interest expense during 2014 when the loan was repaid.

In April 2015, the Company entered into a loan agreement with a bank for borrowings up to $6.0 million, with a floating interest rate equal to the Wall Street Journal's prime rate minus 0.50 percent. Under the terms of the loan, an initial tranche of $4.0 million was advanced on April 15, 2015 and an additional tranche of $2.0 million was advanced on May 15, 2015. The Company is required to pay accrued interest only for a period of 12 months from the date of each advance, followed by 30 equal monthly payments of principal and accrued interest. A final payment of $0.3 million, or 5.50% of the aggregate borrowed amount, is due at maturity of the loan in 2018 and is being accreted in long-term debt over the life of the loan. Closing costs of $24,000 were recorded in long-term debt and are also being accreted over the life of the loan.

Interest expense on the borrowings under the loan agreement was $0.1 million for the year ended December 31, 2015. Accretion of the scheduled final payment was $0.1 million for the year ended December 31, 2015. Accretion of the deferred closing costs was $7,400 for the year ended December 31, 2015.

As of December 31, 2015, the annual payments for the loan agreement, including the scheduled final payment in 2018, were as follows (in thousands):

Year Ending December 31,	Principal	Interest and Final Payment	Total
2016	$ 1,733	$ 166	$1,899
2017	2,400	96	2,496
2018	1,867	354	2,221
	$ 6,000	$ 616	$6,616

6. Convertible shareholder notes payable

In April 2014, the Company authorized the sale of convertible promissory notes (the "Bridge Notes") to its existing stockholders, including two of its executive officers and one of its directors in their individual capacities, in the aggregate principal amount of $6.0 million. In April 2014, the Company issued $3.0 million in aggregate principal amount of Bridge Notes. The outstanding notes accrued interest at a rate of 7%, with principal plus interest due upon maturity in April 2015, unless earlier converted. The Bridge Notes were convertible upon the occurrence of a qualified financing. The Company's August 2014 Series B convertible preferred stock financing was a qualified financing as contemplated by the Bridge Notes, and accordingly the principal and interest under all of the Bridge Notes was converted automatically into an aggregate of 1,137,652 shares of Series B convertible preferred stock in connection with this financing. In connection with the issuance of the Bridge Notes, the Company also issued warrants to the lenders to purchase an aggregate of 112,802 shares of common stock at an exercise price of $0.02 per share. Unless earlier exercised, these warrants will expire upon the closing of an initial public offering.

Interest expense on the borrowings under the Bridge Notes was $69,000 for the year ended December 31, 2014.

7. Income taxes

No provision for U.S. federal or state income taxes has been recorded as the Company has incurred net operating losses since inception. Significant components of the Company's net deferred income tax assets consist of the following (in thousands):

	December 31,	
	2014	2015
Current		
Deferred tax asset (liability)		
Non-deductible accrued expenses	$ 20	$ 230
Deferred rent	4	3
Valuation allowance	(24)	(233)
Net current deferred tax asset	$ —	$ —
Non-current		
Deferred tax asset (liability)		
Stock compensation expense	$ 70	$ 88
Net operating loss carryforwards	7,891	14,169
Depreciation differences	(31)	(28)
Federal tax credits	447	850
State tax credits	196	262
Deferred revenue	—	77
Deferred rent	4	1
Charitable contributions	3	3
Valuation allowance	(8,580)	(15,422)
Net non-current deferred tax asset	$ —	$ —

A reconciliation of the statutory tax rates and the effective tax rates is as follows:

	Year Ended December 31,	
	2014	2015
U.S. federal tax rate	34.00%	34.00%
State tax rate	4.41	4.54
Permanent difference and other	(1.15)	(1.26)
Tax credit	4.54	2.66
Valuation allowance	(41.79)	(39.94)
	0.00%	0.00%

Realization of the future tax benefits is dependent on the Company's ability to generate sufficient taxable income within the carryforward period. Due to the Company's history of operating losses, the deferred tax assets arising from the aforementioned future tax benefits are currently not likely to be realized and, accordingly, are offset by a full valuation allowance. The income tax provision varies from the expected provision determined by applying the federal statutory income tax rate to income (loss). The reasons for the difference in the expected provision, as determined by applying the federal statutory income tax rate to net income (loss) is primarily due to the increase in the deferred income tax valuation allowance of $4.2 million and $7.0 million for the years ended December 31, 2014 and 2015, respectively.

As of December 31, 2015, the Company had net deferred tax assets primarily related to net operating loss carryforwards of $14.2 million, which expire through 2035. Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The effect of an ownership change could be an imposition of an annual limitation on the use of net operating loss carryforwards attributable to periods before the change.

The U.S. federal statute of limitations remains open for the periods from inception and forward. The Company has not been the subject of examination by the taxing authorities.

The Company has no uncertain tax positions.

8. Convertible preferred stock

The Company has authorized 20,913,331 shares of preferred stock. Of the authorized shares of preferred stock, 5,198,826 shares have been designated as Series A Convertible Preferred Stock ("Series A"), 4,373,481 shares have been designated as Series A-1 Preferred Stock ("Series A-1"), 6,066,345 shares have been designated as Series B Preferred Stock ("Series B") and 5,274,679 shares have been designated as Series C Preferred Stock ("Series C"). The Series A, Series A-1, Series B and Series C shares were issued at a price of $0.78589, $1.81320, $2.69783 and $3.79170 per share, respectively.

The following table summarizes the activity of convertible preferred stock (dollar amounts in thousands, except per share amounts):

	Series A Preferred Stock		Series A-1 Preferred Stock		Series B Preferred Stock		Series C Preferred Stock		Total Convertible Preferred Stock
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	
Balance at January 1, 2014	5,198,826	$ 4,040	4,356,931	$ 7,831	—	$ —	—	$ —	$ 11,871
Issuance of Series B at $2.69783 per share on August 29, 2014, net of issuance cost of $236	—	—	—	—	4,811,259	11,501	—	—	11,501
Conversion of promissory notes and interest payable at $2.69783 per share on August 29, 2014	—	—	—	—	1,197,943	3,232	—	—	3,232
Accretion of stock issuance costs	—	46	—	27	—	158	—	—	231
Balance at December 31, 2014	5,198,826	4,086	4,356,931	7,858	6,009,202	14,891	—	—	26,835
Issuance of Series C at $3.7917 per share in November and December 2015, net of issuance cost of $46	—	—	—	—	—	—	5,274,674	19,954	19,954
Accretion of stock issuance costs	—	—	—	42	—	481	—	2	525
Balance at December 31, 2015	5,198,826	$ 4,086	4,356,931	$ 7,900	6,009,202	$15,372	5,274,674	$19,956	$ 47,314

Dividends

Holders of Series A, Series A-1, Series B and Series C shares, in preference of common stockholders, shall be entitled to receive (a) when, as and if declared by the board of directors (the "Board"), but only out of funds that are legally available therefore, or (b) upon the liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, cumulative cash dividends at the rate of 8% per annum of the applicable original issuance price of such series of preferred stock.

The total cumulative preferred dividends in arrears, if declared, for the preferred stock as of December 31, 2014 and 2015 were $2.5 million and $5.0 million, respectively.

Liquidation

Upon a liquidation event (as defined in the amended and restated certificate of incorporation) the Series A, Series A-1, Series B and Series C holders will be paid their liquidation preference of $0.78589, $1.81320, $2.69783 and $3.79170 per share, respectively, which is the original issue price plus any accrued and declared but unpaid dividends on such class of capital stock. If the net assets of the Company are insufficient to cover the liquidation preference, the Company will distribute the available funds among the holders of Series A, Series A-1, Series B and Series C shares at the time outstanding, ratably in proportion to the full amounts to which they would otherwise be entitled if such amounts had been paid in full.

Conversion

Each share of Series A, Series A-1, Series B and Series C is convertible into a number of fully paid shares of common stock at any time at the option of the stockholder. The Series A, Series A-1, Series B and Series C shares may be converted into common stock at a conversion price per share of $1.72896, $3.98904, $5.93523, and $8.34174, respectively. In addition, the Series A, Series A-1, Series B and Series C shares are convertible into common stock immediately upon: (i) the closing of an initial public offering generating net proceeds of not less than $50.0 million to the Company, at a price per share of at least $12.51261; or (ii) the written consent of the holders of at least a majority of the outstanding shares of preferred stock and the holders of at least 50% of

the outstanding shares of Series C convertible preferred stock. As described in the amended and restated certificate of incorporation, a reduction in the conversion price will occur if the Company sells common stock for less than the conversion price of the Series A, Series A-1, Series B and Series C shares. Based on the conversion terms, there were no beneficial conversion features associated with Series A, Series A-1, Series B and Series C shares.

In addition, the potential reduction in the conversion price did not result in the conversion price feature meeting the definition of a derivative, which would require separate accounting.

Voting

Each holder of the Series A, Series A-1, Series B and Series C shares shall be entitled to the number of votes equal to the number of shares of common stock into which such shares of Series A, Series A-1, Series B and Series C may be converted, and shall have voting rights and powers equal to the voting rights and powers of the common stock, with certain limitations.

Redemption

Series A, Series A-1, Series B and Series C will be subject to redemption at the option of the investors holding a majority of the Series A, Series A-1, Series B and Series C shares at any time after the sixth anniversary of the issuance in an amount equal to the liquidation preference. On such redemption date, the Company shall redeem, on a pro rata basis in accordance with the number of shares of Series A, Series A-1, Series B and Series C owned by each holder, that number of outstanding shares of Series A, Series A-1, Series B and Series C determined by dividing (i) the total number of shares of Series A, Series A-1, Series B and Series C outstanding immediately prior to such redemption date by (ii) the number of remaining redemption dates including the redemption date to which such calculation applies. If the Company does not have sufficient funds legally available to redeem on any redemption date all Series A, Series A-1, Series B and Series C shares to be redeemed on such redemption date, the Company shall redeem a pro rata portion of each holder's Series A, Series A-1, Series B and Series C shares out of funds legally available therefor, based on the respective amounts which would otherwise be payable in respect of the shares to be redeemed if the legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares to have been redeemed as soon as practicable after the Company has funds legally available therefor.

9. Common stock

The Company’s amended and restated certificate of incorporation authorizes the Company to issue 40,000,000 shares of $0.001 par value common stock. As of December 31, 2014 and 2015, there were 1,816,467 and 2,659,262 shares of common stock outstanding, respectively, which excluded 20,688 and 6,485 shares, respectively, of unvested restricted stock. The terms, rights, preferences and privileges of the Company’s common stock are as follows:

Voting

Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of the stockholders, including the election of directors. The Company’s amended and restated certificate of incorporation and bylaws do not provide for cumulative voting rights.

Dividends

Subject to preferences that may be attributable to any then outstanding convertible preferred stock, the holders of the Company's outstanding shares of common stock are entitled to receive dividends, if any, as may be declared by the Company's board of directors out of legally available funds.

Liquidation

In the event of the Company's liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all the Company's debts and other liabilities, subject to satisfaction of the liquidation preferences granted to the holders of any outstanding preferred stock.

Rights and preference

Holders of the Company's common stock have no preemptive, conversion or subscription rights, and there are no redemption or other related provisions attributable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock of the Company that may be issued.

10. Stock purchase warrants

During 2013, in connection with the loan agreement (Note 5), the Company issued a warrant to the lender to purchase up to 16,550 shares of Series A-1 preferred stock at a price per share of $1.8132. The term of the warrant extends until 10 years from the grant date and the warrant is exercisable at any time during that 10-year period. This warrant was outstanding at December 31, 2014 and 2015 and had a weighted average remaining life of 8.1 and 7.1 years, respectively.

The Company estimated the fair value of the warrants at issuance using the Black-Scholes option-pricing model utilizing the fair value of the underlying preferred stock. The estimates in the Black-Scholes option pricing model are based, in part, on assumptions, including but not limited to the volatility of comparable public companies, the expected life of the warrants, the risk-free interest rate and the fair value of the equity underlying the warrants.

Key assumptions utilized in the fair value calculation for the warrants appear in the table below:

	December 31,	
	2014	2015
Expected term (years)	5.00	5.00
Volatility	109.60%	113.50%
Risk-free interest rate	2.10%	2.13%
Dividend yield	0.00%	0.00%

The fair value of the Series A-1 warrant was $42,000 and $58,000 at December 31, 2014 and 2015, respectively.

During 2014, in connection with the issuance of the Bridge Notes (Note 6), the Company issued warrants to the lenders to purchase up to 112,802 shares of common stock at a price per share of $0.02. These warrants were outstanding at December 31, 2014 and December 31, 2015 and had a remaining life of 9.2 and 8.2 years, respectively. If unexercised, these warrants will expire upon the closing of an initial public offering.

In connection with its Series B convertible preferred stock financing in August 2014, the Company issued warrants to purchase an aggregate of 780,400 shares of common stock at an exercise price of $0.02 per share. These warrants were exercised on May 20, 2015.

At the date of issuance, the total value of the common stock warrants issued in connection with the Series B financing was estimated to be $1.2 million. In order to determine the fair value of these common warrants, the Company used a hybrid of an option pricing model and a probability-weighted expected return method ("PWERM"). The estimates in the option pricing model were based, in part, on assumptions, including but not limited to the volatility of comparable public companies, the expected life of the warrants, the risk-free interest rate and the fair value of the equity underlying the warrants. Significant inputs for the PWERM included an estimate of the Company's equity value and an estimated probability and timing for each valuation scenario. The Company attributed a 60% weighting to option pricing model, a 24% weighting to an early 2015 IPO scenario within the PWERM and a 16% weighting to a late 2015 IPO scenario within the PWERM.

In April 2015, in connection with the loan agreement, the Company issued a warrant to the lenders to purchase up to 57,143 shares of Series B preferred stock at a price per share of $3.50. The term of the warrant extends until 10 years from the grant date and the warrant is exercisable at any time during that 10-year period. This warrant was outstanding at December 31, 2015 and had a weighted average remaining life of 9.25 years.

The Company estimated the fair value of the Series B preferred warrants under three scenarios, the option price modeling, for which the Company took the value from the model discounted for the lack of marketability, and two IPO scenarios, early and late. Under the IPO scenarios, the Company calculated the value of the warrant based on a call option of the common share at IPO (assuming the Series B preferred stock would convert to common stock) given the time to exit and the term of the warrants stipulated in the contract. The Company then applied a discount for lack of marketability.

The Company also ran the valuation for the Series B preferred warrants at the issue date of April 15, 2015 based on the model, financials, and capitalization table as of March 31, 2015, assuming there had been no material changes to the business over the 15-day period since the March 31, 2015 valuation. The Company utilized the same methodology to calculate the value of the warrants as of December 31, 2015. The fair value of the Series B preferred warrant was $200,000 at December 31, 2015.

11. Share-based compensation

In November 2011, the Company's Board adopted and approved the Clearside Biomedical, Inc. 2011 Stock Incentive Plan (the "Plan") which provides for the grant of share-based awards to employees, directors and consultants of the Company. The Company has reserved 1,517,625 shares of common stock for issuance under the Plan. In February 2016, the Company awarded an option grant to a newly appointed board member. This option grant was outside of the Plan. The Board shall determine price, term and vesting conditions of all share-based awards at their grant date. Absent a public market price for the Company's common stock, the board of directors will determine the estimated fair value for the underlying common stock. Share-based awards vest over variable periods, generally from one to five years, and expire not more than ten years after the date of grant.

The total share-based compensation expense recognized is reflected in the statements of operations as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Research and development	$ 218	$ 327
General and administrative	209	378
Total	$ 427	$ 705

Share-based compensation is accounted for in accordance with the provisions of ASC 718, *Compensation-Stock Compensation*. The estimated fair value of options granted is determined as of the date of grant using the Black-Scholes option pricing model. The resulting fair value is recognized ratably over the requisite service period, which is generally the vesting period of the awards. Options granted to non-employees are re-measured at each financial reporting period until required services are performed.

The following table sets forth the weighted average assumptions utilized in the fair value calculation for the underlying common stock for the years ended December 31, 2014 and 2015.

	Year Ended December 31,	
	2014	2015
Expected term (years)	7.00	7.00
Expected stock price volatility	85.64%	86.63%
Risk-free interest rate	1.99%	2.09%
Expected dividend yield	0.00%	0.00%

Expected term (in years): The Company utilized the guidance set forth in ASC 718 to determine the expected term of options. The Company utilized the simplified method as prescribed by ASC 718, as the Company does not have sufficient historical exercise and post-vesting termination data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees.

Risk-free interest rate: The risk-free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected time to a possible liquidity event.

Expected dividend yield: The Company has not paid and does not anticipate paying any dividends in the foreseeable future.

Expected stock price volatility: The volatility assumption is based on the historical volatilities of the stock of several public entities that are similar to the Company, as the Company does not have sufficient historical transactions in its own shares on which to base expected volatility. The same peer group of companies was utilized for the years ended December 31, 2014 and 2015.

Stock options

The Company has granted stock option awards to employees, directors and consultants. Share-based compensation expense for options granted is reflected in the statements of operations as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Research and development	$ 91	$ 327
General and administrative	192	378
Total	$ 283	$ 705

The following table summarizes the activity related to stock options:

	Number of Shares	Weighted Average Exercise Price
Options outstanding at January 1, 2014	770,062	$ 0.34
Granted	376,126	3.38
Exercised	(24,803)	0.17
Cancelled/Forfeited	(22,899)	0.15
Options outstanding at December 31, 2014	1,098,486	1.39
Granted	289,619	5.68
Exercised	(50,980)	0.27
Cancelled/Forfeited	(75,488)	1.67
Options outstanding at December 31, 2015	1,261,637	2.40

The following table provides additional information about the Company's stock options that were outstanding and exercisable at December 31, 2015 (aggregate intrinsic values in thousands):

Exercise Price	Options Outstanding	Weighted Average Exercise Price	Aggregate Intrinsic Value	Average Remaining Contractual Life (Years)	Options Exercisable	Weighted Average Exercise Price	Aggregate Intrinsic Value
$0.02	11,363			5.9	11,363		
0.15	72,987			6.4	67,510		
0.40	544,493			7.6	329,131		
3.08	31,818			8.6	11,267		
3.41	311,357			9.0	79,254		
5.57	232,802			9.9	—		
6.16	56,817			9.5	2,272		
	1,261,637	$ 2.40	$ 7,210		500,797	$ 0.92	$ 3,606

As of December 31, 2015, the Company had $3.0 million of unrecognized compensation expense related to unvested stock options granted under the Plan. This cost is expected to be recognized over a weighted average period of 1.7 years as of December 31, 2015. The weighted average remaining contractual life of all outstanding options as of December 31, 2015 was 8.4 years.

The intrinsic value is calculated as the difference between the estimated fair market value and the exercise price per share of the stock options. The estimated fair market value per share of common stock as of December 31, 2015 was $8.12.

Restricted stock

In 2011, the founders of the Company purchased restricted common stock. These shares are subject to repurchase rights whereby the Company has the right to repurchase the unvested shares at price per share equal to the lesser of (i) the fair market value of the shares at the time the right of repurchase is exercised and (ii) the original issuance price of the shares. A summary of the status of unvested restricted stock is presented below:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at January 1, 2014	229,208	$ 0.51
Vested	(208,520)	0.40
Unvested at December 31, 2014	20,688	0.57
Vested	(14,203)	0.55
Unvested at December 31, 2015	6,485	0.57

Share-based compensation expense for restricted stock granted is reflected in the statements of operations as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Research and development	$ 127	$ —
General and administrative	17	—
Total	$ 144	$ —

As of December 31, 2014 and 2015, the Company had $0 of unrecognized compensation expense related to unvested restricted stock.

12. Commitments and contingencies

Lease commitment summary

The Company leases office space under non-cancelable operating leases which expire in March 2017. The operating leases have renewal options and rent escalation clauses. The following table presents future minimum commitments of the Company due under non-cancelable operating leases with original or remaining terms in excess of one year.

Minimum lease payments were as follows at December 31, 2015 (in thousands):

2016	$ 90
2017	23
Total minimum lease payments	$113

Rent expense, net of sublease income, was $198,000 and $150,000 for years ended December 31, 2014 and 2015, respectively.

Litigation

The Company is not party to any litigation and does not have contingency reserves established for any litigation liabilities.

Contract service providers

In the course of the Company's normal business operations, it has agreements with contract service providers to assist in the performance of its research and development, clinical research and manufacturing. Substantially all of these contracts are on an as needed basis.

Employment contracts

The Company has employment agreements with its executive officers and has at will employment contracts with substantially all other employees providing for salary, benefits and bonuses.

13. License agreements

In July 2012, the Company entered into an Exclusive License Agreement with Emory University and Georgia Tech Research Corporation ("Emory/GTRC"), whereby the Company purchased a license for Methods and Devices For Drug Delivery Using Microneedles. The Company paid $30,000 for the license and made a milestone payment of $35,000 during the year ended December 31, 2012. No payments were made to Emory/GTRC during the years ended December 31, 2014 or 2015. The Exclusive License Agreement requires the Company to make a milestone payment upon the occurrence of a specified event relating to the commercialization of a drug developed using the licensed patents. Beginning on the third anniversary of this license agreement, the Company will be obligated to pay an annual license maintenance fee of $25,000, which will continue until the first commercial sale of a product covered by the licensed patents. Additionally, the Company will owe a low single-digit royalty on any worldwide net product sales related to the licensed patents, with minimum annual royalties of $15,000 after commercialization. The minimum annual royalty increases thereafter to $100,000.

In August 2014, the Company entered into a royalty-bearing license agreement with NovaMedica LLC ("NovaMedica"). Under this agreement, the Company granted to NovaMedica the right to use the Company's intellectual property to develop and commercialize the intended products (the "Covered Products") and to have the exclusive right to sell those products in Russia and specified adjacent territories involving the use of the corticosteroid triamcinolone acetonide as the sole active pharmaceutical ingredient for administration in the suprachoroidal space. In addition, NovaMedica agreed to make royalty payments equal to the amount of any royalties the Company owes to Emory or GTRC pursuant to the Emory/GTRC License Agreement as a result of NovaMedica's sales of products and services covered by the license granted to NovaMedica, up to a maximum of a low single-digit percentage of net sales of such products or services by NovaMedica. NovaMedica has also agreed to make milestone payments, totaling $12.7 million in the aggregate, primarily related to the achievement of specified commercial product sales. The agreement also includes provisions whereby the Company and NovaMedica may enter into a future development and research collaboration agreement and a supply agreement for the Company to manufacture and supply the Covered Products. Terms and conditions of these agreements would be negotiated in good faith in the future. The term of the NovaMedica license agreement will expire upon the expiration of the last-to-expire valid claim within the patents licensed to NovaMedica pursuant to the agreement. Either the Company or NovaMedica may terminate the agreement

upon written notice in the event of the other party's material breach that is not cured within 20 business days of receiving written notice requesting a cure of a payment breach, and within 60 business days of receiving written notice requesting a cure in the case of all other breaches. Each party also has the right to terminate the agreement in the event of the other party's bankruptcy or insolvency. The Company may terminate the agreement immediately upon written notice in the event that NovaMedica commences or participates in any action challenging the validity or enforceability of the patents licensed to NovaMedica under the agreement. In connection with this royalty-bearing license, NovaMedica made an upfront payment to the Company of $200,000. The Company is currently developing product candidates that when completed would be subject to this license giving NovaMedica the exclusive right to then sell the products in the specified geographic territories. During 2014 and 2015, the Company deferred the $200,000 given the early stage of development of the intellectual property and uncertainty regarding commercial feasibility. In mid-December 2015, the Company received positive results from the Phase 2 clinical trial relating to the product candidate and determined, based on these results, that the intellectual property could become commercially feasible. Beginning in the first quarter ended March 31, 2016, the Company began recognizing the $200,000 to revenue over the period of time to complete clinical development and commercialization of the Covered Products and the beginning of the first set of patent expirations in 2027. NovaMedica is jointly owned by Rusnano MedInvest LLC, or Rusnano MedInvest, and Domain Russia Investments Limited. RMI, which beneficially owns approximately 11% of the Company's voting securities, is a wholly owned subsidiary of Rusnano MedInvest.

On April 27, 2015, the Company entered into a license and collaboration agreement (the "Spark Agreement") with Spark Therapeutics, Inc. ("Spark") under which Spark could acquire the exclusive rights to license the Company's microinjector technology and access to the suprachoroidal space within the eye (collectively "the IP") for development and ultimate commercialization of Spark's gene therapy treatments to be delivered via the microinjector. If Spark made the decision to license the IP, Spark would be responsible for the costs of the future development and commercialization. The Company would be responsible for providing the microinjector technology as well as other defined support to Spark as part of Spark's development efforts.

The Spark Agreement was structured to allow Spark certain periods of time (the "Option Periods") before actually entering into the IP license. In conjunction with executing the Spark Agreement, Spark made an upfront, non-refundable payment to the Company of $500,000. During the initial Option Period, the parties agreed to have a third-party research organization perform an initial preclinical study under the direction of the Company. At any time during this Option Period, Spark could exercise its option to license the IP by paying an additional $2.0 million, or could elect to initiate a second Option Period during which the Company and Spark would conduct further studies specified in the Spark Agreement. If Spark elected to initiate the second Option Period, Spark would be required to pay the Company $1.0 million. If Spark exercised its option to license the IP during the second Option Period, then Spark would be required to pay the Company an additional $3.0 million. If Spark did not exercise its option to license the IP or elect to initiate the second Option Period, then the Spark Agreement would terminate at the end of the first Option Period. Spark had the right to terminate the Spark Agreement at any time upon written notice to the Company. The Company and Spark could also terminate the Spark Agreement upon 90 days' written notice in the event of an uncured material breach by the other party.

If Spark decided to license the technology, the Company would be eligible to receive aggregate payments of up to $13.5 million from Spark upon the achievement of specified future development and commercialization milestones as described in the agreement, as well as aggregate payments of up to $12.0 million upon the achievement of specified annual net sales milestones. In addition, the Company would be eligible to receive low to mid single-digit percentage royalties on net sales of licensed products. Subject to specified exceptions, the license would expire on a licensed product-by-licensed product basis and on a country-by-country basis upon the expiration of the specified licensed intellectual property.

In evaluating the Option Periods granted to Spark to determine whether Spark would license the IP, the Company determined that these Option Periods combined had stand-alone value apart from the IP license as Spark was deriving value from its ability to evaluate the technology through defined preclinical studies conducted by the Company and Spark during these Option Periods. The Company also determined that the two Option Periods represented one unit of accounting providing Spark with an overall evaluation period in which to decide whether to license the IP. This determination was made based on the fact that the planned studies are not independent of each other, but instead are designed to build on the results of the prior studies in order to further the preclinical analysis to be in a position to ultimately file an investigational new drug application and begin the onset of clinical trials in human patients as contemplated in the Spark Agreement.

The Company determined that the $500,000 upfront payment should be recognized to revenue over the expected period of time to perform and complete the planned studies during the Option Periods contemplated at the date the agreement was executed. The Company estimated that this time period would be approximately 30 months from the start of the initial study to the end and evaluation of the planned studies to be performed during the Option Periods. The Company did not record any revenue from the $500,000 upfront payment during 2015.

In February 2016, the initial study was completed and Spark elected not to extend the arrangement nor license the technology which terminated the agreement in accordance with the agreement terms. During the quarter ended March 31, 2016, the Company recorded as revenue the $500,000 upfront payment as the amount was non-refundable and the Company had no further obligations under this arrangement.

14. Collaborative agreement

In January 2013, the Company entered into a collaborative research agreement with one of the holders of the Series A-1 preferred stock, whereby the two parties agreed to conduct feasibility studies for certain compounds. Each party to the collaborative research agreement will bear its own costs, except that certain costs incurred by the Company are limited to a defined maximum amount. The Company incurred research and development costs in relation to the collaborative research agreement of $98,000 and $145,000 for the years ended December 31, 2014 and 2015, respectively.

15. Fair value measurements

The Company records certain financial assets and liabilities at fair value in accordance with the provisions of ASC Topic 820, *Fair Value Measurements and Disclosures*, on fair value measurements. As defined in the guidance, fair value, defined as an exit price, represents the amount that would be received to sell an asset or pay to transfer a liability in an orderly transaction between market participants. As a result, fair value is a market-based approach that should be determined based on assumptions that market participants would use in pricing an asset or a liability. As a basis for considering these assumptions, the guidance defines a three-tier value hierarchy that prioritizes the inputs used in the valuation methodologies in measuring fair value.

- Level 1—Unadjusted quoted prices in active, accessible markets for identical assets or liabilities.
- Level 2—Other inputs that are directly or indirectly observable in the marketplace.
- Level 3—Unobservable inputs that are supported by little or no market activity.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The Company’s material financial instruments at December 31, 2014 and 2015 consisted primarily of cash and cash equivalents, long-term debt and stock purchase warrant liabilities. The fair value of cash and cash

equivalents, other current assets and accounts payable approximate their respective carrying values due to the short term nature of these instruments. The fair value of long-term debt approximates the carrying value due to variable interest rates that correspond to market rates. The Company has determined its stock purchase warrants liability to be a Level 3 fair value measurement.

There were no significant transfers between Levels 1, 2 and 3 during the years ended December 31, 2014 and 2015.

The following tables summarize the fair value of financial assets and liabilities that are measured at fair value and the classification by level of input within the fair value hierarchy (in thousands):

	December 31, 2014			
	Level 1	Level 2	Level 3	Recorded Value
Financial Assets:				
Money markets (included in cash and cash equivalents)	$7,951	$ —	$ —	$ 7,951
Financial Liabilities:				
Stock purchase warrants	$ —	$ —	$ 42	$ 42

	December 31, 2015			
	Level 1	Level 2	Level 3	Recorded Value
Financial Assets:				
Money markets (included in cash and cash equivalents)	$20,076	$ —	$ —	$ 20,076
Financial Liabilities:				
Stock purchase warrants	$ —	$ —	$ 258	$ 258

The determination of the fair value of the stock purchase warrants is discussed in Note 10. Changes in the fair value of the stock purchase warrants are recorded in other income (expense), net in the statements of operations. The following table summarizes the changes in fair value of the Level 3 liability, stock purchase warrants (in thousands):

	Level 3 Liabilities	
	Year Ended December 31,	
	2014	2015
Stock purchase warrants		
Balance at beginning of period	$ 24	$ 42
Issuance of stock purchase warrants	—	164
Net increase (decrease) in fair value remeasurement	18	52
Balance at period end of period	$ 42	$ 258

16. Subsequent events

Reverse stock split

On May 11, 2016, the Company effected a 1-for-2.2 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's convertible preferred stock (see Notes 8 and 9). Accordingly, all share and per share amounts for all periods presented in these financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios.

CLEARSIDE BIOMEDICAL, INC.
Balance sheets
(in thousands, except share and per share data)

	September 30, 2016	December 31, 2015
	(unaudited)	
Assets		
Current assets:		
Cash and cash equivalents	$ 36,876	$ 20,283
Short-term investments	20,043	—
Prepaid expenses	662	159
Other current assets	73	40
Total current assets	57,654	20,482
Property and equipment, net	110	156
Deferred offering costs	—	410
Other assets	7	7
Total assets	$ 57,771	$ 21,055
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,347	$ 1,469
Accrued liabilities	1,556	1,985
Current portion of long-term debt	—	1,733
Other current liabilities	25	9
Total current liabilities	2,928	5,196
Deferred revenue	165	700
Long-term debt	7,489	4,243
Other non-current liabilities	251	261
Total liabilities	10,833	10,400
Commitments and contingencies		
Convertible preferred stock:		
Series A preferred stock, $0.001 par value, no shares authorized, issued and outstanding at September 30, 2016; 5,198,826 shares authorized, issued and outstanding at December 31, 2015; liquidation preference of $4,086 at December 31, 2015	—	4,086
Series A-1 preferred stock, $0.001 par value; no shares authorized, issued and outstanding at September 30, 2016; 4,373,481 shares authorized and 4,356,931 shares issued and outstanding at December 31, 2015; liquidation preference of $7,900 at December 31, 2015	—	7,900
Series B preferred stock, $0.001 par value, no shares authorized, issued and outstanding at September 30, 2016; 6,066,345 authorized and 6,009,202 shares issued and outstanding at December 31, 2015; liquidation preference of $16,212 at December 31, 2015	—	15,372
Series C preferred stock, $0.001 par value, no shares authorized, issued and outstanding at September 30, 2016; 5,274,679 shares authorized and 5,274,674 shares issued and outstanding at December 31, 2015; liquidation preference of $20,000 at December 31, 2015	—	19,956
Total convertible preferred stock	—	47,314
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares authorized and no shares issued at September 30, 2016; no shares authorized or issued at December 31, 2015	—	—
Common stock, $0.001 par value; 100,000,000 shares authorized and 20,545,752 shares issued and outstanding at September 30, 2016; 40,000,000 shares authorized and 2,659,262 shares issued and outstanding at December 31, 2015	21	3
Additional paid-in capital	102,481	2,701
Accumulated deficit	(55,559)	(39,363)
Accumulated other comprehensive loss	(5)	—
Total stockholders' equity (deficit)	46,938	(36,659)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 57,771	$ 21,055

See accompanying notes to the financial statements

CLEARSIDE BIOMEDICAL, INC.
Statements of operations and comprehensive loss
(in thousands, except share and per share data)

	Nine Months Ended September 30,	
	2016	2015
	(unaudited)	
License revenue	$ 515	$ —
Operating expenses:		
Research and development	12,484	6,964
General and administrative	3,872	5,337
Total operating expenses	16,356	12,301
Loss from operations	(15,841)	(12,301)
Other income (expense)	(355)	(168)
Net loss	$ (16,196)	$ (12,469)
Net loss per share of common stock—basic and diluted	$ (1.54)	$ (5.59)
Weighted average shares outstanding—basic and diluted	10,502,459	2,231,830
Net loss	$ (16,196)	$ (12,469)
Unrealized loss on available-for-sale investments	(5)	—
Comprehensive loss	$ (16,201)	$ (12,469)

See accompanying notes to the financial statements

CLEARSIDE BIOMEDICAL, INC.
Statements of cash flows

(in thousands)

	Nine Months Ended September 30,	
	2016	2015
	(unaudited)	
Operating activities		
Net loss	$(16,196)	$ (12,469)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	49	45
Share-based compensation expense	776	502
Non-cash interest expense	224	66
Accretion of debt discount	60	32
Change in fair value of warrant liability	16	(1)
Amortization and accretion on available-for-sale investments, net	17	—
Loss on sale of fixed assets	—	15
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(536)	(122)
Other assets	426	1,764
Accounts payable and accrued liabilities	(567)	(399)
Deferred revenue	(515)	500
Deferred rent	(7)	(6)
Net cash used in operating activities	(16,253)	(10,073)
Investing activities		
Purchase of available-for-sale investments	(20,065)	—
Acquisition of property and equipment	(3)	(8)
Proceeds from the sale of fixed assets	—	4
Net cash used in investing activities	(20,068)	(4)
Financing activities		
Proceeds from initial public offering, net of issuance costs	51,377	—
Proceeds from issuance of long-term debt	7,867	5,981
Principal payments made on long-term debt	(6,330)	—
Proceeds from exercise of stock options	—	13
Net cash provided by financing activities	52,914	5,994
Net increase (decrease) in cash and cash equivalents	16,593	(4,083)
Cash and cash equivalents, beginning of period	20,283	8,269
Cash and cash equivalents, end of period	$ 36,876	$ 4,186
Supplemental schedule of noncash investing and financing activities		
Conversion of convertible preferred stock to common stock	$ 48,198	$ —
Reclassification of deferred initial public offering costs	1,597	—
Issuance of warrant to purchase common stock	308	—
Issuance of warrant to purchase Series B preferred stock	—	164
Accretion of redeemable convertible preferred stock to redemption value	883	392
Unpaid initial public offering costs in accounts payable and accrued expenses	16	228

See accompanying notes to the financial statements

CLEARSIDE BIOMEDICAL, INC.
Notes to the financial statements
(unaudited)

1. The company

Clearside Biomedical, Inc. (the "Company") is a late-stage clinical biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye. The Company's current product candidates focus on treatments for diseases affecting the retina and choroid, especially diseases associated with macular edema, and are injected into the suprachoroidal space using its proprietary SCS Microinjector. Incorporated in the State of Delaware on May 26, 2011, the Company has its corporate headquarters in Alpharetta, Georgia.

The Company's activities since inception have primarily consisted of developing product and technology rights, raising capital and performing research and development activities. The Company has no current source of revenue to sustain present activities, and does not expect to generate meaningful revenue until and unless the Company receives regulatory approval of and successfully commercializes its product candidates. The Company is subject to a number of risks and uncertainties similar to those of other life science companies at a similar stage of development, including, among others, the need to obtain adequate additional financing, successful development efforts including regulatory approval of products, compliance with government regulations, successful commercialization of potential products, protection of proprietary technology and dependence on key individuals.

Liquidity

On June 1, 2016, the Company's registration statement on Form S-1 relating to its initial public offering of its common stock (the "IPO") was declared effective by the Securities and Exchange Commission ("SEC"). The IPO closed on June 7, 2016 and the Company sold 7,200,000 shares of common stock at a price to the public of $7.00 per share, for net proceeds of $45.3 million. On June 30, 2016, the underwriters of the IPO partially exercised their option to purchase additional shares, and on July 6, 2016, the Company sold 948,843 additional shares of common stock at a price to the public of $7.00 per share, for net proceeds of $6.1 million. The Company paid to the underwriters underwriting discounts and commissions of $4.0 million in connection with the IPO, including the underwriters' exercise of their option to purchase additional shares. In addition, the Company incurred expenses of $1.6 million in connection with the IPO. Thus, the aggregate net offering proceeds to the Company, after deducting underwriting discounts and commissions and offering expenses, were $51.4 million.

Prior to the IPO, the Company had funded its operations primarily through the sale of convertible preferred stock and the issuance of long-term debt, resulting in aggregate proceeds of approximately $53.9 million. Even with the completion of the IPO, the Company will continue to need to obtain additional financing to fund future operations, including completing the development and commercialization of its primary product candidates. The Company will need to expend substantial resources for research and development, including costs associated with the clinical testing of its product candidates. The Company will also need to obtain additional financing to conduct additional trials for the regulatory approval of its drug candidates if requested by regulatory bodies, and completing the development of any additional product candidates that might be acquired. If such products were to receive regulatory approval, the Company would need to prepare for the potential commercialization of its product candidates and fund the commercial launch of the products, if the Company decides to commercialize the products on its own. Moreover, the Company's fixed expenses such as rent and other contractual commitments are substantial and are expected to increase in the future.

The Company had cash, cash equivalents and short-term investments of $56.9 million as of September 30, 2016 and cumulative net cash flows used in operating activities of $49.4 million and cumulative net losses of $55.6 million through September 30, 2016. In the absence of product or other revenues, the amount, timing, nature or source of which cannot be predicted, the Company's losses will continue as it conducts its research and development activities. Until the Company can generate a sufficient amount of revenue, the Company may finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic alliances and marketing or distribution arrangements. The Company has incurred losses and negative cash flows since inception and expects operating losses and negative cash flows to continue into the foreseeable future. However, the Company is able to control spending on development activities while still advancing clinical trials for key drug and candidates and expects that the cash on hand as of September 30, 2016 will be sufficient to fund its operations for at least the next 12 months from that date.

2. Significant accounting policies

Basis of presentation

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Unaudited interim financial information

The accompanying balance sheet as of September 30, 2016, statements of operations for the nine months ended September 30, 2016 and 2015 and statements of cash flows for the nine months ended September 30, 2016 and 2015 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair presentation of the Company's financial position as of September 30, 2016 and its results of its operations for the nine months ended September 30, 2016 and 2015 and its cash flows for the nine months ended September 30, 2016 and 2015. The financial data and other information disclosed in these notes related to the nine months ended September 30, 2016 and 2015 are unaudited. The results for the nine months ended September 30, 2016 are not indicative of results to be expected for the year ending December 31, 2016, any other interim periods or any future year or period. These unaudited financial statements should be read in conjunction with the audited financial statements and related footnotes for the year ended December 31, 2015, which are included in the Company's prospectus dated June 1, 2016, as filed pursuant to Rule 424(b) under the Securities and Exchange Act of 1933 filed, as amended, with the SEC.

Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of income and expenses during the reporting periods. Significant items subject to such estimates and assumptions include the accounting for useful lives to calculate depreciation and amortization, accrued liabilities, share-based compensation expense and income tax valuation allowance. Actual results could differ from these estimates.

Reverse stock split

On May 11, 2016, the Company effected a 1-for-2.2 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's

convertible preferred stock. Accordingly, all share and per share amounts for all periods presented in these financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios. The adjustment to the conversion ratio for the Series C convertible preferred stock also included an anti-dilution adjustment based on the initial public offering price of the Company's common stock.

Research and development costs

Research and development costs are charged to expense as incurred and include, but are not limited to:

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense for research and development personnel;
- expenses incurred under agreements with contract research organizations, contract manufacturing organizations and consultants that conduct clinical and preclinical studies;
- costs associated with preclinical and development activities;
- costs associated with technology and intellectual property licenses;
- costs for the Company's research and development facility; and
- depreciation expense for assets used in research and development activities.

Costs for certain development activities, such as clinical studies, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the patterns of costs incurred, and are reflected in the financial statements as prepaid or accrued expense, which are reported in accounts payable. No material adjustments to these estimates have been recorded in these financial statements.

Share-based compensation

Compensation cost related to share-based awards granted to employees is measured at grant date, based on the estimated fair value of the award. The Company estimates the fair value of stock options using a Black-Scholes option pricing model. Compensation expense for options granted to non-employees is determined as the fair value of consideration received or the fair value of the equity instruments issued, whichever is more reliably measured. The fair value of restricted stock awards is determined based on the fair value of the Company's common stock on the date of grant. Share-based compensation costs are expensed on a straight-line basis (net of estimated forfeitures) over the relevant vesting period. The fair value of awards granted to non-employees is re-measured each period until the related service is complete. All share-based compensation costs are recorded in general and administrative or research and development costs in the statements of operations based upon the underlying employees' roles within the Company.

Cash equivalents

Cash equivalents consist of short-term, highly liquid investments with an original term of three months or less at the date of purchase.

Short-term investments

Short-term investments are investments with original maturities of between 90 and 365 days when purchased and are comprised of corporate and government bonds and government agency securities. The Company classifies its short-term investments as available-for-sale securities. Short-term investments are recorded at fair value and unrealized gains and losses are recorded within accumulated other comprehensive income (loss) until realized. In addition, the Company evaluates the short-investments with unrealized losses to determine whether such losses are other-than-temporary.

Concentration of credit risk arising from cash deposits in excess of insured limits

The Company maintains its cash in bank deposits that at times may exceed federally insured limits. The Company has not experienced any loss in such accounts. The Company believes it is not exposed to any significant risks with respect to its cash balances.

Recent accounting pronouncements

In August 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2016-15, *Statement of Cash Flows Classification of Certain Cash Receipts and Cash Payments*. The update addresses eight specific cash flow matters with the objective of reducing diversity in practice in how certain cash receipts and payments are classified in the statement of cash flows. The update is effective for annual periods beginning after December 15, 2017, and interim periods within the period. Early adoption is permitted. The Company is currently evaluating the impact the adoption of ASU 2016-15 will have on its financial statements and related disclosures.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718).* The new guidance simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. For public companies, the amendments in this standard are effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted. The effects of this standard on the Company's financial statements and related disclosures are not expected to be material.

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

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 provides guidance about management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. The new standard is effective for the Company for the annual period ending after December 15, 2016 and for annual and interim periods thereafter, with early adoption permitted. The Company does not expect this accounting standard to have an impact on its financial statements and related disclosures.

In May 2014, FASB issued ASU 2014-09, *Revenue from Contracts with Customers*. Under ASU 2014-09, companies will be required to recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration (that is, payment) to which the company expects to be entitled in exchange for those goods or services. The new standard also will result in enhanced disclosures about revenue, provide guidance for transactions that were not previously addressed comprehensively (for example, service revenue and contract modifications) and modify guidance for multiple-element arrangements. In August 2015, the FASB issued ASU 2015-14, which deferred by one year the effective date of ASU 2014-09. The one year deferral of the effective date of this standard changes the effective date for the Company to January 1, 2018. Early adoption is permitted, but not before the original effective date. The Company is currently evaluating the effect this standard may have on its financial statements and related disclosures.

3. Property and equipment, net

Property and equipment, net consisted of the following (dollar amounts in thousands):

	Estimated Useful Lives (Years)	September 30, 2016	December 31, 2015
Furniture and fixtures	5	$ 69	$ 66
Machinery and equipment	5	121	121
Computer equipment	3	27	27
Leasehold improvements	Lesser of Useful life or remaining lease term	45	45
		262	259
Less: Accumulated depreciation		(152)	(103)
		$ 110	$ 156

4. Accrued liabilities

Accrued liabilities consisted of the following (in thousands):

	September 30, 2016	December 31, 2015
Accrued research and development	$ 790	$ 569
Accrued bonuses	478	530
Accrued professional fees	78	668
Accrued vacation	88	64
Accrued interest payable	5	15
Accrued expense	117	139
	$ 1,556	$ 1,985

5. Long-term debt

Loan and security agreements

In September 2016, the Company entered into an amended and restated loan and security agreement (the “loan agreement”) with Silicon Valley Bank (“SVB”), MidCap Funding XII Trust and MidCap Financial Trust (together,

"MidCap" and collectively with SVB, the "Lenders"), which amended and restated in its entirety the Company's prior loan and security agreement with SVB dated as of April 14, 2015 (the "original loan agreement"), under which the Company had borrowed $6.0 million in April and May 2015. The loan agreement provides for new term loans of up to $15.0 million, with a floating interest rate equal to 7% plus the greater of (i) the 30-day U.S. LIBOR, reported in the Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, or (ii) 0.50%. The interest rate on the original loan agreement was equal to the lender's prime rate less 0.50 percent.

Under the terms of the new loan, an initial tranche of $8.0 million was advanced on September 28, 2016. The remaining $7.0 million will become available beginning on the later of (i) September 30, 2017 and (ii) the date on which the Lenders have received evidence, in form and substance reasonably satisfactory to them, that the Company has produced clinical trial data sufficient to file a New Drug Application, or NDA, for its drug candidate CLS-1001 for the treatment of uveitis. Once the draw period for the remaining $7.0 million has commenced, the Company may draw funds at its discretion until the earlier of (i) December 31, 2017 and (ii) the occurrence of an event of default under the loan agreement. The Company is required to pay accrued interest only through December 31, 2017 on the outstanding amount, followed by 30 equal payments of principal and accrued interest. The Company has the option to prepay the outstanding balance of the term loans in full, subject to a prepayment fee of (i) 3% of the original principal amount of the aggregate term loans for any prepayment prior to September 28, 2017 or (ii) 2% of the original principal amount of the aggregate term loans for any prepayment between September 28, 2017 and May 31, 2020. A final payment of $0.5 million, or 6.50% of the aggregate borrowed amount, is due at maturity of the loan on June 1, 2020, or upon the prepayment of the facility or the acceleration of amounts due under the facility as a result of an event of default, and is being accreted in long-term debt over the life of the loan. Of the initial $8.0 million advanced on September 28, 2016, $5.3 million was used to repay all amounts outstanding under the original loan agreement. Closing costs incurred in the refinancing portion of the loan were recorded as expense while the financing costs for the new portion of the loan are recorded in long-term debt and being accreted over the life of the loan. Upon repayment of the original loan agreement, all remaining closing costs associated with the original loan agreement are being accreted to long-term debt over the life of the new loan.

The term loans under the loan agreement are secured by substantially all of the Company's assets, except that the collateral does not include any of the Company's intellectual property. However, pursuant to the terms of a negative pledge arrangement, the Company has agreed not to encumber any of its intellectual property.

Interest expense on the borrowings under the original loan agreement was $129,000 and $72,000 for the nine months ended September 30, 2016 and 2015, respectively. Accretion of the scheduled final payment was $224,000 and $64,000 for the nine months ended September 30, 2016 and 2015, respectively. Accretion of the deferred closing costs was $7,000 and $5,000 for the nine months ended September 30, 2016 and 2015, respectively.

As of September 30, 2016, the scheduled payments for the loan agreement, including the scheduled final payment in 2020, were as follows (in thousands):

Year Ending December 31,	Principal	Interest and Final Payment	Total
2016	$ —	$ 158	$ 158
2017	—	608	608
2018	3,200	476	3,676
2019	3,200	234	3,434
2020	1,600	545	2,145
	$ 8,000	$ 2,021	$10,021

6. Convertible debt

As of December 31, 2015, the Company had authorized an aggregate of 20,913,331 shares of Series A, A-1, B and C convertible preferred stock, par value $0.001 per share. Upon the closing of the Company's IPO on June 1, 2016, all 20,839,633 shares of the Company's convertible preferred stock that were issued and outstanding on that date were automatically converted into an aggregate of 9,614,159 shares of its common stock.

As of September 30, 2016, there were 10,000,000 shares of preferred stock authorized, none of which were issued and outstanding.

7. Common stock

The Company's amended and restated certificate of incorporation authorizes the Company to issue 100,000,000 shares of $0.001 par value common stock. As of September 30, 2016 and December 31, 2015, there were 20,545,752 and 2,659,262 shares of common stock outstanding, respectively, which excluded 6,478 shares of unvested restricted stock at December 31, 2015. There was no unvested restricted stock as of September 30, 2016.

8. Stock purchase warrants

Preferred stock warrants

During 2013, in connection with a loan agreement, the Company issued a warrant to the lender to purchase up to 16,550 shares of Series A-1 preferred stock at a price per share of $1.8132. The term of the warrant extended until 10 years from the grant date and the warrant was exercisable at any time during that 10-year period. This warrant was outstanding at December 31, 2015 and had a weighted average remaining life of 6.8 years and a fair value of $58,000. The warrant was automatically converted to a common stock warrant and was net exercised on June 6, 2016, resulting in the issuance of 3,236 shares of common stock.

In April 2015, in connection with another loan agreement, the Company issued a warrant to the lenders to purchase up to 57,143 shares of Series B preferred stock at a price per share of $3.50. The term of the warrant extends until 10 years from the grant date and the warrant is exercisable at any time during that 10-year period. The warrant was automatically converted into a warrant to purchase 25,974 shares of common stock at an exercise price of $7.70 upon the closing of the IPO. This warrant was outstanding at September 30, 2016 and December 31, 2015 and had a weighted average remaining life of 8.5 and 9.25 years, respectively. The fair value of the warrant was $0.3 million and $0.2 million at September 30, 2016 and December 31, 2015, respectively.

Common stock warrants

During 2014, in connection with the sale of convertible promissory notes in connection with a preferred stock financing, the Company issued warrants to the lenders to purchase up to an aggregate of 112,802 shares of common stock at a price per share of $0.02. These warrants were outstanding at December 31, 2015 and had a remaining life of 8.2 years. These warrants, which would have otherwise expired upon the closing of the IPO, were automatically net exercised for an aggregate of 112,441 shares of common stock upon the closing of the IPO.

In September 2016, in connection with the amended and restated loan and security agreement, the Company issued warrants to the lenders to purchase up to 29,796 shares of common stock at a price per share of $10.74. The warrants expire in September 2026, or earlier upon the occurrence of specified mergers or acquisitions of the Company, and are immediately exercisable. The warrants were recorded in equity and have a weighted average remaining life of 10 years and a fair value of $0.3 million at September 30, 2016.

9. Share-based compensation

In January 2016, the Company's board of directors adopted and approved the Clearside Biomedical, Inc. 2016 Equity Incentive Plan (the "2016 Plan") which became effective in connection with the IPO on June 1, 2016. The 2016 Plan provides for the grant of share-based awards to employees, directors and consultants of the Company. The Company has reserved 1,818,182 shares of common stock for issuance under the 2016 Plan. The 2016 Plan provides for the grant of incentive stock options to employees, and for the grant of nonqualified stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of stock compensation to the Company's employees, directors, and non-employee third parties. The number of shares of common stock reserved for issuance under the 2016 Plan will automatically increase on January 1 each year, for a period of ten years, from January 1, 2017 through January 1, 2026, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Company's board of directors. At September 30, 2016, under the 2016 Plan, options to purchase 157,500 shares of the Company's common stock were outstanding at a weighted average price of $6.64 per share and 1,660,682 shares remained available for future grant.

As a result of the adoption of the 2016 Plan, no further grants may be made under the Company's 2011 Stock Incentive Plan (the "2011 Plan"). The 2011 Plan provided for the grant of share-based awards to employees, directors and consultants of the Company. At September 30, 2016, options to purchase 1,239,858 shares of the Company's common stock were outstanding under the 2011 Plan at a weighted average exercise price of $2.35 per share.

Share-based compensation is accounted for in accordance with the provisions of ASC 718, *Compensation-Stock Compensation*. The estimated fair value of options granted is determined as of the date of grant using the Black-Scholes option pricing model. The resulting fair value is recognized ratably over the requisite service period, which is generally the vesting period of the awards. Options granted to non-employees are re-measured at each financial reporting period until required services are performed.

The Company has granted stock option awards to employees, directors and consultants. Share-based compensation expense for options granted is reflected in the statements of operations as follows (in thousands):

	Nine Months Ended September 30,	
	2016	2015
Research and development	$ 375	$ 229
General and administrative	401	273
Total	$ 776	$ 502

The following table summarizes the activity related to stock options during the nine months ended September 30, 2016:

	Number of Shares	Weighted Average Exercise Price
Options outstanding at January 1, 2016	1,261,638	$ 2.41
Granted	174,736	6.79
Exercised	(1,326)	0.40
Cancelled/Forfeited	(20,454)	6.03
Options outstanding at September 30, 2016	1,414,594	2.90
Options exercisable at December 31, 2015	500,797	0.92
Options exercisable at September 30, 2016	686,439	1.22

As of September 30, 2016, the Company had $3.1 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 1.5 years.

10. Commitments and contingencies

Lease commitment summary

The Company leases office space under non-cancelable operating leases which expire in March 2017. The operating leases have renewal options and rent escalation clauses.

Minimum lease payments were as follows at September 30, 2016 (in thousands):

2016	$23
2017	23
Total minimum lease payments	$46

Rent expense, net of sublease income, was $61,000 for the nine months ended September 30, 2016 and 2015.

Contract service providers

In the course of the Company's normal business operations, it has agreements with contract service providers to assist in the performance of its research and development, clinical research and manufacturing. Substantially all of these contracts are on an as needed basis.

11. License agreements

In August 2014, the Company entered into a royalty-bearing license agreement with NovaMedica LLC ("NovaMedica"). Under this agreement, the Company granted to NovaMedica the right to use the Company's intellectual property to develop and commercialize the intended products (the "Covered Products") and to have the exclusive right to sell those products in Russia and specified adjacent territories involving the use of the corticosteroid triamcinolone acetonide as the sole active pharmaceutical ingredient for administration in the suprachoroidal space. In connection with this royalty-bearing license, NovaMedica made an upfront payment to the Company of $200,000. The Company is currently developing product candidates that when completed would be subject to this license giving NovaMedica the exclusive right to then sell the products in the specified geographic territories. In mid-December 2015, the Company received positive results from the Phase 2 clinical

trial relating to the product candidate and determined, based on these results, that the intellectual property could become commercially feasible. Beginning in the first quarter ended March 31, 2016, the Company began recognizing the $200,000 to revenue over the period of time to complete clinical development and commercialization of the Covered Products and the beginning of the first set of patent expirations in 2027. The Company recorded $5,000 and $15,000 of license revenue during the three and nine months ended September 30, 2016, respectively, for this license agreement. NovaMedica is jointly owned by Rusnano MedInvest LLC, or Rusnano MedInvest, and Domain Russia Investments Limited. RMI, which beneficially owns approximately 11% of the Company's voting securities, is a wholly owned subsidiary of Rusnano MedInvest.

In April 2015, the Company entered into a license and collaboration agreement (the "Spark Agreement") with Spark Therapeutics, Inc. ("Spark") under which Spark could acquire the exclusive rights to license the Company's microinjector technology and access to the suprachoroidal space within the eye for development and ultimate commercialization of Spark's gene therapy treatments to be delivered via the microinjector. In conjunction with executing the Spark Agreement, Spark made an upfront, non-refundable payment to the Company of $500,000.

In February 2016, the initial study was completed and Spark elected not to extend the arrangement nor license the technology which terminated the agreement in accordance with the agreement terms. During the quarter ended March 31, 2016, the Company recorded as revenue the $500,000 upfront payment as the amount was non-refundable and the Company had no further obligations under this arrangement.

12. Collaborative agreement

In January 2013, the Company entered into a collaborative research agreement with a stockholder, whereby the parties agreed to conduct feasibility studies for certain compounds. Each party to the collaborative research agreement will bear its own costs, except that certain costs incurred by the Company are limited to a defined maximum amount. The Company incurred research and development costs in relation to the collaborative research agreement of $85,000 and $124,000 for the nine months ended September 30, 2016 and 2015, respectively.

13. Available-for sale securities

The following table summarizes the Company's available-for-sale investments as of September 30, 2016:

	September 30, 2016		
	Amortized Cost	Unrealized Loss	Fair Value
Government bonds and agency obligations	$ 11,032	$ (3)	$11,029
Certificates of deposit	4,658	—	4,658
Corporate bonds	4,358	(2)	4,356
Total available-for-sale investments	$ 20,048	$ (5)	$20,043

14. Fair value measurements

The Company records certain financial assets and liabilities at fair value in accordance with the provisions of ASC Topic 820, *Fair Value Measurements and Disclosures*, on fair value measurements. As defined in the guidance, fair value, defined as an exit price, represents the amount that would be received to sell an asset or pay to transfer a liability in an orderly transaction between market participants. As a result, fair value is a market-based approach that should be determined based on assumptions that market participants would use in

pricing an asset or a liability. As a basis for considering these assumptions, the guidance defines a three-tier value hierarchy that prioritizes the inputs used in the valuation methodologies in measuring fair value.

- Level 1—Unadjusted quoted prices in active, accessible markets for identical assets or liabilities.
- Level 2—Other inputs that are directly or indirectly observable in the marketplace.
- Level 3—Unobservable inputs that are supported by little or no market activity.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The Company's material financial instruments at September 30, 2016 and December 31, 2015 consisted primarily of cash and cash equivalents, short-term investments, long-term debt and stock purchase warrant liabilities. The fair value of cash and cash equivalents, other current assets and accounts payable approximate their respective carrying values due to the short term nature of these instruments. The fair value of long-term debt approximates the carrying value due to variable interest rates that correspond to market rates. The Company has determined its short-term investments, comprised of certificates of deposit, corporate bonds and government bonds and agency obligations, to be Level 2 in the fair value hierarchy. The fair value was determined using a market approach, based on prices and other relevant information generated by market transactions involving similar assets. The short-term investments consist of investments with original maturity dates from date of acquisition of 90 to 365 days and are classified as available-for-sale. The Company has determined its stock purchase warrants liability to be Level 3 in the fair value hierarchy.

There were no significant transfers between Levels 1, 2 and 3 during the nine months ended September 30, 2016 and the year ended December 31, 2015.

The following tables summarize the fair value of financial assets and liabilities that are measured at fair value and the classification by level of input within the fair value hierarchy (in thousands):

	September 30, 2016			
	Level 1	Level 2	Level 3	Recorded Value
Financial Assets:				
Cash and money markets	$35,666	$ —	$ —	$ 35,666
Certificates of deposit	5,868	—	—	5,868
Government bonds	2,499	—	—	2,499
Agency obligations	—	8,530	—	8,530
Corporate bonds	—	4,356	—	4,356
Total financial assets	$44,033	$12,886	$ —	$ 56,919
Financial Liabilities:				
Stock purchase warrants	$ —	$ —	$ 251	$ 251

	December 31, 2015			
	Level 1	Level 2	Level 3	Recorded Value
Financial Assets:				
Money markets (included in cash and cash equivalents)	$20,076	$ —	$ —	$ 20,076
Financial Liabilities:				
Stock purchase warrants	$ —	$ —	$ 258	$ 258

Prior to the IPO, the Company estimated the fair value of its warrants to purchase preferred stock using an option pricing model that included three valuation scenarios, a non-IPO scenario and two IPO scenarios. Under the IPO scenarios, the Company calculated the value of the warrant based on a call option of the common share at IPO (assuming the underlying preferred stock would convert to common stock) given the time to exit and the term of the warrants stipulated in the contract. The Company then applied a discount for lack of marketability. Changes in the fair value of the stock purchase warrants were recorded in other income (expense), net in the statements of operations. Subsequent to the IPO, the Company used the Black-Scholes option pricing model to estimate the fair value of the remaining warrants. The estimates in the Black-Scholes option pricing model are based, in part, on assumptions, including but not limited to the volatility of comparable public companies, the expected life of the warrants, the risk-free interest rate and the fair value of the underlying warrants. The following table summarizes the changes in fair value of the Level 3 liability, stock purchase warrants (in thousands):

	Level 3 Liabilities	
	Nine Months Ended September 30, 2016	Year Ended December 31, 2015
Stock purchase warrants		
Balance at beginning of period	$ 258	$ 42
Issuance of stock purchase warrants	—	164
Exercise of stock purchase warrants	(23)	—
Net increase in fair value remeasurement	16	52
Balance at end of period	$ 251	$ 258

15. Net loss per share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period, without consideration of the dilutive effect of potential common stock equivalents. Diluted net loss per share gives effect to all dilutive potential shares of common stock outstanding during this period.

For all periods presented, the Company's potential common stock equivalents, which include convertible preferred stock, stock options, unvested restricted stock and stock purchase warrants, have been excluded from the computation of diluted net loss per share as their inclusion would have the effect of reducing the net loss per share. Therefore, the denominator used to calculate both basic and diluted net loss per share is the same in all periods presented.

The Company's potential common stock equivalents that have been excluded from the computation of diluted net loss per share for all periods presented because of their antidilutive effect consisted of the following:

	Nine Months Ended September 30,	
	2016	2015
Convertible preferred stock	—	7,074,961
Outstanding stock options	1,414,594	1,030,025
Unvested restricted stock	—	10,030
Stock purchase warrants	55,770	146,298
	1,470,364	8,261,314

16. Subsequent events

Subsequent to September 30, 2016, we entered into a new office lease agreement for our corporate headquarters, under which we have agreed to lease approximately 20,000 square feet of space in Alpharetta, Georgia. We expect to move into this new space in the first half of 2017. Under this lease, we will pay an initial annual base rent of $421,740, or $35,145 per month, subject to an increase of 3% per year.

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Stifel

Co-manager

Wedbush PacGrow

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