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As Confidentially Submitted to the Securities and Exchange Commission on December 23, 2014

Registration No. 333-

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

FORM S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Clearside Biomedical, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**45-2437375**
(State or other jurisdiction of incorporation or organization)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

1220 Old Alpharetta Road, Suite 300
Alpharetta, GA 30005
(678) 270-3631
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Daniel H. White
Chief Executive Officer
Clearside Biomedical, Inc.
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Alpharetta, GA 30005
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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration number of the earlier effective registration statement for the same offering. ☐

CALCULATION OF REGISTRATION FEE

Title of Securities being Registered	**Proposed Maximum Aggregate Offering Price(1)(2)**	**Amount of Registration Fee**
Common Stock, $0.001 par value per share	$	$

(1) In accordance with Rule 457(o) under the Securities Act of 1933, as amended, the number of shares being registered and the proposed maximum offering price per share are not included in this table.
(2) Estimated solely for purposes of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act. Includes offering price of additional shares that underwriters have the option to purchase.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 under the Securities Exchange Act of 1934. (Check one):

Large Accelerated Filer ☐ Accelerated Filer ☐ Non-accelerated Filer ☒ Smaller Reporting Company ☐

The registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is declared effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated December 23, 2014

Shares

COMMON STOCK

We are offering shares of our common stock. This is our initial public offering and no public market currently exists for our common stock. We expect the initial public offering price to be between $ and $ per share.

We have applied to list our common stock on The NASDAQ Global Market under the symbol "CLSD."

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, and will be subject to reduced public company reporting requirements.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 15.

	PER SHARE	TOTAL
Initial public offering price	$	$
Underwriting discount and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

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

We have granted the underwriters an option to purchase up to additional shares of common stock, exercisable at any time until 30 days after the date of this prospectus. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $ and the total proceeds to us, before expenses, will be $.

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

The underwriters expect to deliver the shares on or about , 2015.

RBC CAPITAL MARKETS **WELLS FARGO SECURITIES**

NEEDHAM & COMPANY **NOMURA**

Prospectus dated , 2015

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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.

Until and including , 2015, 25 days after the date of this prospectus, all dealers that buy, sell or trade our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.

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 clinical-stage 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 and choroid, especially diseases associated with macular edema, and are injected non-surgically into the suprachoroidal space, or SCS, adjacent to the choroid, using our proprietary microinjector. With the SCS injection procedure, our product candidates are more directly administered to the retina and choroid as compared to currently used intravitreal injections, which we believe 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 non-surgical administration into the SCS. Our most advanced product candidates, CLS-1001 and CLS-1003, are based on commonly used ophthalmic therapeutic agents, 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 Federal Food, Drug, and Cosmetic Act. Under Section 505(b)(2), if we can establish that reliance on the 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, 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. CLS-1001, for macular edema associated with non-infectious uveitis, is in an ongoing Phase 1/2 clinical trial, from which we expect final results in the first half of 2015. We expect to be able to conduct a single pivotal Phase 3 clinical trial in approximately 150 patients beginning in mid-2015, the results of which we believe, based on a meeting with the FDA and subsequent written correspondence, will be sufficient to support the filing of a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, in the first half of 2017. For CLS-1003, for macular edema associated with retinal vein occlusion, or RVO, we plan to initiate a Phase 2 clinical trial in early 2015 from which we expect to receive data in the second half of 2015. In our CLS-1002 program, for wet age-related macular degeneration, or wet AMD, we are evaluating drug compounds with anti-VEGF activity or dual anti-VEGF and anti-platelet derived growth factor, or anti-PDGF, activity for SCS injection, and plan to file an investigational new drug application, or IND, in the first half of 2016. We are also considering a development program for drug compounds to treat diabetic macular edema, or DME. 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 approximately $6 billion in 2013.

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, the tissue that lines the inside of the eye and is the part of the eye primarily responsible for vision, and the choroid, the layer adjacent to the retina that supplies the retina with blood, oxygen and nourishment. These diseases include

uveitis, RVO, wet AMD and DME. 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.

The most common treatments for diseases of the retina and choroid are corticosteroids and drugs that inhibit vascular endothelial growth factor, or anti-VEGF drugs. These corticosteroids and anti-VEGF drugs are often injected into the vitreous, a jelly-like substance that occupies the central portion of the eye. Intravitreal injections rely on drug to diffuse outward from the vitreous to the retina and choroid, which diffusion can result in lower concentrations of drug in these targeted areas. At the same time, this diffusion can result in drug spreading to unintended parts of the eye, where, for some drugs, it can cause significant side effects. By contrast, with our approach, drug is injected into and spreads within the SCS, which is the space located between the choroid and the outer protective layer of the eye known as the sclera, to reach the back of the eye. We believe SCS administration 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 inflammation aspects of ocular disease and at reducing macular edema, but when delivered intravitreally, they have been associated with significant side effects, such as cataracts and elevated intraocular pressure, or 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 SCS injection with our microinjector is conducted in an in-office setting and is similar to the procedure for intravitreal injection, and we therefore expect our products, if they achieve regulatory approval, to be easily incorporated into retinal specialists' standard medical practice.

We are developing CLS-1001 for the treatment of macular edema associated with non-infectious uveitis, an indication for which we are seeking orphan drug designation and exclusivity. CLS-1001 consists of an SCS injection of CLS-TA, our proprietary, preservative-free formulation of the corticosteroid triamcinolone acetonide, or TA, specifically designed to be administered through our SCS microinjector. We expect final results from our ongoing Phase 1/2 clinical trial with Triesence, a commonly used TA, in the first half of 2015, and we are currently screening patients for potential enrollment in a Phase 2 clinical trial that we intend to conduct with CLS-TA in approximately 30 patients, with data expected in mid-2015. We also plan to initiate a single pivotal Phase 3 clinical trial in approximately 150 patients in mid-2015, with the goal of filing a Section 505(b)(2) NDA in the first half of 2017. We are developing CLS-1003 for the treatment of macular edema associated with RVO. CLS-1003 consists of an SCS injection of CLS-TA with our microinjector, for administration together with an intravitreal injection of an anti-VEGF drug. We plan to initiate a Phase 2 clinical trial in approximately 40 patients in early 2015, with data expected in the second half of 2015. Under our CLS-1002 program, we are evaluating a number of compounds to develop as an SCS-injected therapy for the treatment of wet AMD, including compounds with anti-VEGF activity and compounds with dual anti-VEGF and anti-PDGF activity. We expect to select a lead drug candidate under this program for IND submission in early 2016.

Our drug candidates, microinjector and method of non-surgical drug administration into the SCS are protected by four issued U.S. patents and over 20 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 into the SCS by injection and are not scheduled to expire until between 2027 and 2029. Our patent applications relate to SCS administration 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 2034.

If our product candidates are approved, we plan to commercialize them with a specialty sales force of 30 to 40 representatives to target 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, CIBA Vision and ISTA Pharmaceuticals. Members of our team have contributed to the development, regulatory approval and commercialization of several retinal products, such as Triesence, Iluvien, Nevanac, Visudyne and Xibrom.

Anticipated Benefits from 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 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 SCS injection, as compared to the distribution of the same drug following intravitreal injection. We believe this suggests that SCS injection may have similar or better efficacy with a faster onset of therapeutic effect than intravitreal injection in diseases of the retina and choroid like uveitis, RVO, wet AMD and DME.
- ***Similar efficacy profile with lower drug amounts required.*** In a preclinical study in an animal model of uveitis, SCS 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 an SCS injection of CLS-TA, which addresses the inflammatory aspect of RVO, may have similar efficacy with a reduction in the frequency of required anti-VEGF treatments from once every 30 days to once every 90 days. In wet AMD, we believe that more direct application of drugs with anti-VEGF or dual anti-VEGF and anti-PDGF activity to the neovascularization in the choroid through SCS injection may

block the process of additional new vascular growth within the choroid before the vessels break into the retina and create further damage through leakage. We believe that such SCS injection of treatment therefore has the potential to 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.

- ***Enhanced safety profile.*** Intravitreal injections result in drugs diffusing throughout the eye, including into the lens, iris and ciliary body at the front of the eye, which for some drugs, has been associated with safety issues, such as cataracts and elevated IOP levels. Intravitreal administration of TA has been associated with cataracts and increases in IOP levels in 20% to 60% of patients. Because SCS injection of drugs appears to result in drug remaining localized in the retina and choroid without substantial diffusion to the vitreous or the front portion of the eye, we believe SCS injection has the potential to reduce the incidence of these side effects. Based on interim results from our ongoing Phase 1/2 clinical trial, none of the eight patients dosed in the trial have experienced cataracts, abnormally high levels of IOP or other treatment-related serious adverse events over the course of 26 weeks following a single SCS injection of TA.
- ***Incorporated into standard medical practice.*** If approved for marketing, our drugs will be packaged together with our SCS microinjector for one-time use by retinal specialists in their offices. Our product candidates are designed to be administered using a procedure similar to that used for intravitreal injections, without the need for any capital equipment to be installed in the office. Accordingly, we expect our products, if approved, will be easily 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 CLS-1001 and CLS-1003 to FDA approval under the Section 505(b)(2) NDA regulatory pathway.*** Our most advanced product candidates, CLS-1001 and CLS-1003, utilize CLS-TA, 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 plan to advance CLS-1001 into a single pivotal Phase 3 clinical trial for macular edema associated with non-infectious uveitis and, based on our pre-IND meeting in 2012 and subsequent written correspondence from the FDA, we expect this single trial to be sufficient to support a 505(b)(2) NDA filing. Our goal is to submit the 505(b)(2) NDA for CLS-1001 in the first half of 2017. Separately, we plan to initiate a Phase 2 clinical trial for CLS-1003 for macular edema associated with RVO in early 2015 and we expect to receive data from this trial in the second half of 2015.
- ***Maximizing the commercial potential of our product candidates.*** If either CLS-1001 or CLS-1003 is approved, we plan to build a specialized sales force of approximately 30 to 40 representatives 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 therapies for other back of the eye diseases that can be treated more effectively with SCS injection.*** We believe that SCS injection of ocular therapies could have benefits in a variety of other back of the eye indications. Our initial areas of focus for development include:
    - *Advancing our CLS-1002 wet AMD development program.* We are investigating opportunities to improve the treatment of wet AMD through SCS injection of compounds that are commonly used for this disease, such as anti-VEGF drugs, or have shown clinical promise, such as anti-VEGF drugs in combination with anti-PDGF drugs. These therapies are commonly administered by intravitreal injection. We have completed an exploratory Phase 1 clinical trial using an anti-VEGF drug, Avastin, administered into the SCS, rather than intravitreally, in four patients with wet AMD, from which we observed encouraging safety and efficacy results. We are conducting preclinical studies evaluating other compounds with dual anti-VEGF and anti-PDGF activity, with the goal of selecting a lead drug candidate under this program for IND submission in early 2016.
    - *Developing a product candidate to treat DME*. DME, like uveitis and RVO, is characterized by an inflammatory aspect. Once the data from the CLS-1003 Phase 2 clinical trial have been analyzed, we intend to initiate clinical trials to develop a product candidate to treat DME modeled after our approach for addressing macular edema associated with RVO.
    - *Developing additional therapies through collaborations with third parties*. We plan to explore collaborations with third parties to develop SCS-administered treatments for back of the eye diseases. These collaborations may take the form of in-licenses of the third parties' drugs or drug candidates for our own development for SCS injection, or out-licenses for third parties to use our intellectual property covering SCS injection as part of the development of their own drugs. We are currently studying several compounds under a research collaboration with Santen Pharmaceutical Co., Ltd.
- ***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 non-surgical SCS delivery methods, novel formulations of drugs, and microinjectors used to access 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 2034. 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:

Development Program	Indication	Route of Administration and Active Ingredient	Status and Upcoming Milestones
CLS-1001	Macular edema associated with non-infectious uveitis	SCS injection of CLS-TA	•Final results from ongoing Phase 1/2 clinical trial with Triesence expected 1H 2015 •Screening patients for ~30-patient Phase 2 clinical trial with CLS-TA, with data expected mid-2015 •Initiate ~150-patient single pivotal Phase 3 clinical trial in mid-2015 with CLS-TA, with 505(b)(2) NDA filing expected 1H 2017
CLS-1003	Macular edema associated with RVO	SCS injection of CLS-TA together with intravitreal injection of anti-VEGF compound	•Initiate ~40-patient Phase 2 clinical trial in early 2015, with data expected 2H 2015
CLS-1002	Wet AMD	SCS injection of anti-VEGF compound or compound with dual anti-VEGF and anti-PDGF activity	•Exploratory Phase 1 clinical trial with Avastin completed outside the U.S. •Selection of lead drug candidate for IND submission expected in early 2016

CLS-1001 Program Targeting 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. CLS-1001 consists of an SCS injection of CLS-TA with our microinjector. Under our CLS-1001 program, we are conducting a Phase 1/2 clinical trial in which we are evaluating the safety of SCS injection of Triesence, a TA formulation that is similar to CLS-TA and that has been approved by the FDA to treat non-infectious uveitis. While the trial is primarily a safety and tolerability study, we are also assessing efficacy measures. We intended to enroll approximately 10 patients in this trial. We completed enrollment after dosing the eighth patient. Interim data from these eight patients indicate that SCS injection of the drug has generally been well tolerated, with none of the eight patients having developed cataracts or experienced elevated IOP. At eight weeks after a single SCS injection, the visual acuity of all eight patients had improved by five or more letters on a standard eye chart over baseline, a clinically meaningful improvement, and the visual acuity of five of these eight patients improved by at least 15 letters. Because CLS-1001 is based on 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. Our preclinical studies suggest that SCS 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 early clinical trial results suggest the potential for CLS-1001 to effectively treat uveitis for at least 90 days following a single SCS injection. Currently used ocular injections of TA are typically effective for

approximately 90 days. We are currently screening patients for potential enrollment in a Phase 2 clinical trial in approximately 30 patients with macular edema associated with non-infectious uveitis to evaluate the safety and efficacy of our CLS-TA administered into the SCS. We also expect to initiate a single pivotal Phase 3 clinical trial in mid-2015 with our CLS-TA administered into the SCS in approximately 150 patients with macular edema associated with non-infectious uveitis, with the goal of being able to submit an NDA to the FDA in the first half of 2017. Based on our pre-IND meeting in 2012 and subsequent written correspondence from the FDA, we believe this single pivotal clinical trial will be sufficient to support a 505(b)(2) NDA filing for CLS-1001 for macular edema associated with non-infectious uveitis. If approved, CLS-1001 would be the first drug specifically indicated for macular edema associated with non-infectious uveitis.

CLS-1003 Program Targeting Macular Edema Associated with Retinal Vein Occlusion

Under our CLS-1003 program, we are planning to initiate a Phase 2 clinical trial in early 2015 in approximately 40 patients with 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 Avastin (bevacizumab). Although studies have shown that corticosteroids effectively address the inflammatory aspect of RVO, they are not used as first-line therapy because they are generally not considered to be as effective as anti-VEGF drugs and also have an unattractive side effect profile when injected intravitreally. In our Phase 2 clinical trial, we will evaluate the safety and efficacy of the injection of our CLS-TA into the SCS together with Eylea injected into the vitreous, as compared to an intravitreal injection of Eylea alone. We believe that SCS administration of our CLS-TA, 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, 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 CLS-1003 will be similar to that of current intravitreal anti-VEGF treatments alone, as SCS injections of CLS-TA should allow the corticosteroid to remain substantially localized in the retina and choroid without introducing the side effects that are commonly observed with other routes of administration of corticosteroids.

CLS-1002 Program Targeting Wet Age-Related Macular Degeneration

Under our CLS-1002 program, we are evaluating a number of compounds as potential therapies for the treatment of wet AMD by SCS injection, including compounds with anti-VEGF activity and compounds with dual anti-VEGF and anti-PDGF activity. 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. We have completed a Phase 1 clinical trial evaluating the safety and efficacy of SCS injection of Avastin, an anti-VEGF drug, in four patients with wet AMD. In this trial, SCS injection of Avastin was observed to be well tolerated, with no treatment-related serious adverse events. In addition, the four patients showed an average improvement in visual acuity of nine letters on a standard eye chart at the end of the eight-week post-treatment observation period. Two of the four patients showed an improvement in visual acuity of at least 13 letters. Because wet AMD manifests in the retina and choroid, we believe that SCS injection of drug

more directly to the retina and choroid may result in faster onset of therapeutic effect as compared to intravitreal injection, and could reduce the necessary frequency of treatment to once every 90 days.

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 SCS injection based on the results of our current and planned clinical trials. In addition to uveitis, RVO and wet AMD, there are a number of ophthalmic conditions affecting the retina and choroid with unmet medical need for which SCS injection of therapy may be beneficial. These indications include 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, 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.
- We are very early in our development efforts and none of our product candidates have completed a clinical trial.
- We have not yet dosed any patients using CLS-TA, our proprietary drug formulation of TA, for our two most advanced clinical programs.
- We have recently revised the design of our microinjector that we intend to utilize with any product candidate for which we ultimately seek marketing approval, but we do not yet have significant experience with this microinjector in humans.
- 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 SCS administration, which is a novel approach 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.
- An active trading market for our common stock may not develop and you may not be able to resell your shares of our common stock at or above the initial offering price, if at all.
- 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.

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® and the Clearside logo. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and TM 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 fifth anniversary of the completion of this offering, (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	shares
Common stock to be outstanding immediately after this offering	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 up to additional shares of our common stock.
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $ million, assuming the shares are offered at $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus. We anticipate that the majority of the net proceeds from this offering will be used to fund Phase 2 and Phase 3 clinical trials for CLS-1001, as well as a Phase 2 clinical trial for CLS-1003. The remaining proceeds will be used for further development of CLS-1003 and 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.
Proposed NASDAQ Global Market symbol	CLSD

The number of shares of our common stock that will be outstanding after this offering is based on 19,854,890 shares of common stock outstanding as of November 30, 2014, after giving effect to the automatic conversion of 15,564,959 shares of our convertible preferred stock outstanding as of November 30, 2014 and the exercise of warrants to purchase an aggregate of 248,175 shares of common stock that would otherwise expire upon the closing of this offering, and excludes:

- 1,759,246 shares of our common stock issuable upon the exercise of stock options outstanding under our 2011 stock incentive plan as of November 30, 2014, at a weighted average exercise price of $0.29 per share;
- 16,550 shares of our common stock issuable upon exercise of a warrant outstanding as of November 30, 2014, at an exercise price of $1.81 per share; and
- shares of our common stock reserved for future issuance under our equity incentive plans following this offering.

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

- -for- reverse stock split of our common stock expected to be completed prior to the completion of this offering;
- the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,564,959 shares of our common stock, which will occur automatically upon the closing of this offering;
- the exercise of all outstanding warrants to purchase shares of common stock that will otherwise expire upon the closing of this offering for an aggregate of 248,175 shares of common stock;
- the conversion of an outstanding warrant to purchase shares of Series A-1 convertible preferred stock into a warrant to purchase 16,550 shares of common stock upon the closing of this offering; and
- no exercise of the underwriters' option to purchase additional shares of common stock.

Summary Financial Data

In the tables below, we provide you with 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, 2012 and 2013 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, 2013 and 2014 and for the period from May 26, 2011 (date of inception) through September 30, 2014 and our balance sheet data as of September 30, 2014 from our unaudited interim financial statements appearing elsewhere in this prospectus.

The financial data for the nine months ended September 30, 2013 and 2014, for the period from May 26, 2011 (date of inception) through September 30, 2014 and as of September 30, 2014 includes, in the opinion of our management, all adjustments, consisting only of normal recurring adjustments that are 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, 2014 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 2014 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,		Period From May 26, 2011 (Date of Inception) to September 30, 2014
	2012	2013	2013	2014	
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Costs and expenses:					
Research and development	$ 2,354	$ 5,045	$ 3,647	$ 4,776	$ 12,382
General and administrative	1,575	2,193	1,665	2,398	6,307
Total costs and expenses	3,929	7,238	5,312	7,174	18,689
Loss from operations	(3,929)	(7,238)	(5,312)	(7,174)	(18,689)
Other income (expense):					
Interest expense	(3)	(23)	(9)	(353)	(381)
Interest income	1	7	6	1	9
Total other expense	(2)	(16)	(3)	(352)	(372)
Net loss	$ (3,931)	$ (7,254)	$ (5,315)	$ (7,526)	$ (19,061)
Net loss per share of common stock — basic and diluted	$ (2.12)	$ (2.45)	$ (1.87)	$ (2.00)	$ (7.72)
Weighted average shares outstanding, basic and diluted	1,853,423	2,956,285	2,835,897	3,769,091	2,470,630
Pro forma net loss per share — basic and diluted		$ (0.58)		$ (0.39)	
Pro forma weighted average shares outstanding — basic and diluted		12,512,042		19,334,050	

The following table presents our summary balance sheet data as of September 30, 2014:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,564,959 shares of our common stock, which will occur automatically upon the closing of this offering; and
  - the exercise of all outstanding warrants to purchase shares of common stock that will otherwise expire upon the closing of this offering for an aggregate of 248,175 shares of common stock; and
- on a pro forma as adjusted basis to give further effect to our sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	As of September 30, 2014		
	Actual	Pro forma	Pro forma as adjusted
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 11,067	$	$
Total assets	12,872		
Total liabilities	2,717		
Total convertible preferred stock	26,699		
Total stockholders' equity (deficit)	(16,544)		

The pro forma as adjusted information presented in the summary balance sheet data is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease each of cash and cash equivalents, total assets and total stockholders' equity on a pro forma as adjusted basis by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. Similarly, each increase or decrease of 1.0 million shares offered by us at the assumed initial public offering price would increase or decrease each of cash and cash equivalents, total assets and total stockholders' equity on a pro forma as adjusted basis by $ million.

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.

Since our inception through September 30, 2014, we have incurred net losses of $19.1 million. We incurred net losses of $3.9 million, $7.3 million and $7.5 million for the years ended December 31, 2012 and 2013 and the nine months ended September 30, 2014, respectively. As of September 30, 2014, we had a deficit accumulated during the development stage of $19.1 million. We financed our operations through September 30, 2014 with approximately $27.9 million of net cash proceeds raised in private placements of convertible preferred stock and convertible promissory notes.

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:

- continue our ongoing Phase 1/2 clinical trial evaluating the safety of SCS administration of a commercially available formulation of TA with our microinjector, and conduct planned clinical trials using CLS-TA in our CLS-1001 and CLS-1003 drug programs;
- continue the research and development of our other product candidates;
- seek to discover 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 the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 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 planned Phase 2 and Phase 3 clinical trials, both for CLS-1001 and for CLS-1003;
- 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, including purchasers of common stock in this offering, 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. 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 and our microinjector, 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.

Risks Related to the Development of Our Product Candidates

Our research and development efforts are focused on the development of product candidates for SCS administration, which is a novel approach and may fail to achieve and sustain market acceptance.

Administering drugs into the SCS is a novel approach for ophthalmic therapies, and there is no guarantee this approach will be accepted by physicians, patients or third-party payors. We believe we are the first and only company developing drugs specifically for non-surgical SCS administration. The scientific evidence to support the feasibility of developing drugs based on this approach is both preliminary and limited. Although preclinical studies suggest that SCS administration of drugs, such as CLS-1001, may be effective at treating back of the eye diseases, to date no company has developed a drug for administration through the SCS that has received marketing approval.

Additionally, we have very limited clinical experience in SCS drug administration. Our most advanced clinical development program, CLS-1001 for the treatment of macular edema associated with non-infectious uveitis, is currently in a Phase 1/2 clinical trial in which we have dosed eight patients to date with a commercially available formulation of the active ingredient in CLS-TA, only four of which have completed the 26 week post-treatment observation period. In addition to the preliminary data from the eight patients dosed in this trial, our only other human data involving SCS drug administration is from an exploratory Phase 1 clinical trial in four patients with wet AMD, which was conducted in Mexico without an IND from the FDA. To date, between these two trials, we have only dosed a total of twelve humans using our proprietary SCS injection method. Therefore, we cannot guarantee that SCS administration of drugs will prove in clinical trials to be a safe or effective approach for treating back of the eye diseases in humans.

Even if we are able to achieve marketing approval for one of our product candidates, the novelty of SCS injection may make it difficult to demonstrate to physicians and third-party payors that SCS administration of our drugs is the appropriate approach for treating diseases such as non-infectious uveitis, RVO and wet AMD and is superior to the current standard 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 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 CLS-1001, CLS-1003 and our other product candidates.

We are very early in our development efforts and none of our product candidates have completed a clinical trial. Our most advanced program, CLS-1001, is currently in a Phase 1/2 clinical trial. For our second program, CLS-1003, we plan to initiate our first clinical trial, a Phase 2 trial, in early 2015. All of our other product candidates are still in preclinical development. If we are unable to commercialize our product candidates or if we experience significant delays in doing so, our business may be harmed.

We are very early in our development efforts. For our most advanced clinical development program, CLS-1001 for the treatment of macular edema associated with non-infectious uveitis, we are currently conducting a Phase 1/2 clinical trial in which we have dosed eight patients to date with a commercially available formulation of the active ingredient in CLS-TA, only four of whom have completed the 26 week post-treatment observation period. As part of this program, we are also currently screening patients for potential enrollment in a Phase 2 trial administering CLS-TA with our microinjector. For our second clinical development program, CLS-1003 for the treatment of macular edema associated with RVO, we plan to initiate our first clinical trial, a Phase 2 trial, administering CLS-TA to patients in early 2015. In addition to the preliminary data from the eight patients dosed in our ongoing Phase 1/2 clinical trial, our only other human data is from an exploratory Phase 1 clinical trial conducted in Mexico without an IND from the FDA for our CLS-1002 program. 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, we will initiate our clinical development program for CLS-1003 with a Phase 2 clinical trial without having conducted a separate Phase 1 clinical trial for this program. We believe that we will be able to rely on our ongoing toxicology study of CLS-TA in rabbits, the preclinical studies and safety data generated by our ongoing Phase 1/2 clinical trial for CLS-1001 and other supportive literature to be able proceed directly into the Phase 2 clinical trial for CLS-1003, which has the same active pharmaceutical ingredient, CLS-TA, as CLS-1001. However, we have not yet confirmed this approach with the FDA, and the FDA may require that we conduct additional safety studies or trials before we are able to commence clinical trials under an IND for the CLS-1003 program. For our CLS-1002 program, the only clinical trial we have conducted to date is the Phase 1 exploratory trial in Mexico. Although the exploratory trial was conducted in accordance with good clinical practices and had approval and oversight of institutional review boards and institutional ethics committees, 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 CLS-1002.

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 microinjector for SCS administration 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;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining marketing approvals with labeling for sufficiently broad patient populations and indications, without unduly restrictive distribution limitations or safety warnings;

- 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 microinjector to administer drugs into the SCS;
- acceptance of the therapies and of the concept of SCS administration 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 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.

We have not yet dosed any patients using CLS-TA, our proprietary drug formulation of TA, for our two most advanced clinical programs.

To date, our clinical trial experience has involved the SCS injection of commercially available therapeutic agents. In our ongoing Phase 1/2 trial in our uveitis program, we are administering Triesence, a commercially available TA formulation, via SCS injection. However, in future clinical trials of our most advanced product candidates, including our planned Phase 2 clinical trials of CLS-1001 and CLS-1003, we intend to treat patients with CLS-TA, our proprietary drug formulation of TA. Although we have completed preclinical studies comparing CLS-TA to Triesence, we have never dosed this formulation in a human patient. Therefore, in addition to the risks associated with advancing our uveitis program from smaller scale to larger scale clinical trials and initiating our clinical trial program in RVO, there is also a risk that CLS-TA may have different pharmacokinetic or safety profiles in human subjects than the TA formulations that we have administered to date in animals. If CLS-TA does not exhibit similar safety and efficacy profiles to that of TA in humans, our ability to develop CLS-1001 and CLS-1003 may be harmed. Additionally, if the safety and efficacy profile of CLS-TA is not sufficiently comparable to that of previously commercialized TA formulations, we may be unable to rely on the Section 505(b)(2) regulatory approval pathway for CLS-1001 and CLS-1003, which would significantly lengthen our development process and the cost of developing and commercializing our product candidates.

The administration of CLS-1003 as a therapy together with anti-VEGF drugs for the treatment of macular edema associated with RVO is a novel approach and may fail to be successful.

We are developing our second drug program, CLS-1003, 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-vascular endothelial growth factor, or anti-VEGF, injections to quarterly injections. The scientific evidence to support the potential efficacy of this treatment approach is

limited and based on third party clinical trials studying intravitreal injections of steroids in patients with RVO, which, although effective in reducing edema, has been associated with side effects. While our preliminary clinical trial experience involving the SCS injection of steroids suggest that these adverse side effects may be avoided using SCS injection, to date no company has explored this concomitant treatment approach in clinical trials or preclinical studies.

Even if we are able to successfully develop, and achieve marketing approval of, CLS-1003, it may be difficult to demonstrate to physicians and third-party payors that the administration of CLS-1003 concomitantly with anti-VEGF drugs, and the reduction in frequency of anti-VEGF treatments, is the appropriate approach for treating RVO and is superior to the current standard of care. Further, if we are not successful in conveying to physicians, patients and third-party payors that the administration of CLS-1003 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, CLS-1003. Therefore, we may encounter significant difficulty in gaining broad market acceptance by physicians, third-party payors and potential patients using CLS-1003.

We have recently revised the design of our microinjector that we intend to utilize with any product candidate for which we ultimately seek marketing approval, but we do not yet have significant experience with this microinjector in humans.

We used an earlier design of our microinjector in our preclinical studies and clinical trials, including the first four patients dosed in our ongoing Phase 1/2 clinical trial. However, we have recently completed the design of a modified microinjector that we used in the most recent four patients in the Phase 1/2 trial, and we intend to use this design in our planned pivotal Phase 3 clinical trial of CLS-1001 and, if successful, ultimately include in the NDA of any drug for which we seek marketing approval. 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 ongoing Phase 1/2 clinical trial, 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, retinal 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 SCS administration 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. For example, the preliminary data obtained from our Phase 1/2 clinical trial for our CLS-1001 program is based on only eight patients and might not be achieved in any other patients treated with CLS-1001. 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 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;
- 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. We have very little experience enrolling patients in our clinical trials, and cannot predict how successful we will be at enrolling patients in future clinical trials. If we are not successful at enrolling patients in one clinical trial, it may effect 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.

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.

We expect to engage clinical research organizations, or CROs, for our planned Phase 2 and Phase 3 clinical trials for CLS-1001 and CLS-1003. 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 ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in FDA refusal to approve applications based on the clinical data, fines, 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 of any new drug application, or NDA, we submit by the FDA. Any such delay or rejection could prevent us from commercializing CLS-1001, CLS-1003 or our other future product candidates.

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

We contract with third parties for the manufacture of CLS-TA and our 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 CLS-TA and our 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 CLS-TA 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 CLS-TA with our 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 CLS-TA and our 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 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 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 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. If we do enter into any such 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 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. SCS administration 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 SCS administration of drugs;
- the willingness of retinal specialists to expend the time necessary to receive proper training on administering drugs into the SCS using our 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 CLS-TA, 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 macular edema following non-infectious uveitis 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. Alimera Sciences is developing Iluvien, an injectable form of fluocinolone acetonide, as a therapy for DME in the United States. Iluvien has been approved in 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 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 and the treatment of macular edema following RVO. Lucentis is the only ophthalmic drug therapy approved to treat 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 following retinal vein occlusion

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 central retinal vein occlusion, and is being reviewed for the treatment of macular edema following branch retinal vein occlusion.

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 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. Most recently, the Protecting Access to Medicare Act of 2014, signed into law in April 2014, provided for a 0.5% increase from 2013 payment rates under the Medicare Physician Fee Schedule through 2014 and a 0% increase from January 1 until April 1, 2015. If Congress fails to intervene to prevent the negative update factor in future years, the resulting decrease in payment may adversely affect our revenue and results of operations. 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. 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 Executive Vice President of Research and Development, as well as the other members of our scientific and clinical teams. Although we intend to enter into new employment agreements with our executive officers that will be effective upon the closing of this offering, each of them may currently terminate their employment with us at any time and will continue to be able to do so after the closing of this offering. 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, 2014, we had 19 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 SCS administration using our proprietary microinjector. 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 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. We have not yet selected trademarks for our product candidates and have not yet 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 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 our product candidates, such as CLS-1001. Our product candidates, including our proprietary drug formulations packaged together with our 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.

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).

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.

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 risk evaluation and mitigation strategy, 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.

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;
- 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 if we receive orphan drug designation for our most advanced product candidate, CLS-1001, we may not be able to obtain orphan drug marketing exclusivity for this product candidate or any of our future product candidates.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We have applied for orphan drug designation from the FDA, and intend to apply for orphan drug designation from the European Medicines Agency, or EMA, for CLS-1001 for the treatment of non-infectious uveitis, and we may seek orphan drug designation for our future drug candidates. However, we have not yet obtained orphan drug designation from either the FDA or the EMA, and there can be no assurance that we will receive this designation from either regulatory authority.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the United States and 10 years in the European Union. The European Union exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Even if we obtain orphan drug exclusivity for CLS-1001 for the treatment of non-infectious uveitis, that exclusivity may not effectively protect the drug candidate from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

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. 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 and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including 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 federal Open Payments program, created under Section 6002 of Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, and its implementing regulations, imposed new annual reporting requirements for 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 sales or 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 information related to 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 ACA, 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 ACA 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 ACA, 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 ACA 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, which currently includes, and we expect will continue to include, U.S. sales of drug and device combination products;
- 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 new requirements under the federal Open Payments program 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.

In addition, other legislative changes have been proposed and adopted since the ACA 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 will stay in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, 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.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we 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, Ownership of Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may not develop and you may not be able to resell your shares of our common stock at or above the initial offering price, if at all.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters and may not be indicative of the price at which our common stock will trade upon completion of this offering. Although we have applied to list our common stock on The NASDAQ Global Market, an active trading market for our

shares may never develop or be sustained following this offering. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares you purchased in this offering at an attractive price or 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 may be volatile. 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. We do not currently have and may never obtain research coverage by equity research analysts. Equity research analysts may elect not to provide research coverage of our common stock after the completion of this offering, and such lack of research coverage may adversely affect the market price of our common stock. In the event 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 us 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.

We expect the initial public offering price of our common stock to be 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 pro forma as adjusted net tangible book value per share after this offering. Based on an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of $ per share, representing the difference between our pro forma as adjusted net tangible book value per share after this offering and the assumed initial public offering price. After this offering, we will also have outstanding options and warrants to purchase common stock with exercise prices lower than the initial public offering price. To the extent these outstanding options and warrants are exercised, there will be further dilution to investors in this offering.

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 following this offering, the market price of our common stock could decline significantly.

Upon completion of this offering, we will have outstanding shares of common stock, assuming no exercise of outstanding options or warrants. Of these shares, the shares sold in this offering and additional shares will be freely tradable, additional shares of common stock will be eligible for sale in the public market beginning 90 days after the date of this prospectus under Rule 144 and Rule 701, and additional shares of common stock will be available for sale in the public market beginning 180 days after the date of this prospectus following the expiration of lock-up agreements between some of our stockholders and the underwriters. The representatives of the underwriters may release these stockholders from their lock-up agreements with the underwriters at any time and without notice, which would allow for earlier sales of shares in the public market.

In addition, promptly following the completion of this offering, we intend to file one or more registration statements on Form S-8 registering the issuance of approximately shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 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, after this offering, the holders of an aggregate of approximately shares of our common stock and shares of our common stock issuable upon the exercise of outstanding warrants, or their transferees, will 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 as they will be in effect following this offering 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 will have the authority to issue up to 5,000,000 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 will also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors will be elected each year;
- stockholders will not be entitled to remove directors other than by a 66 2⁄3% vote and only for cause;
- stockholders will not be 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.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Upon completion of this offering, our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates will, in the aggregate, beneficially own approximately % of our outstanding common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the price at which shares are being sold in this offering and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

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) following the fifth anniversary of the completion of this offering, (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.

After the completion of this offering, we will be 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, 2015, 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. Prior to this offering, 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 will 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 expect to use the net proceeds to us from this offering to advance the development of CLS-1001 into Phase 2 and Phase 3 clinical trials and CLS-1003 into a Phase 2 clinical trial, to fund the research and development of our earlier-stage programs, including drug discovery, and for working capital and general corporate purposes. Our failure to apply the net proceeds of 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, the terms of any existing or future debt agreements may 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, 2013, we had approximately $10.4 million of federal and $12.4 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, 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 will 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 will 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 planned clinical trials for CLS-1001 and CLS-1003;
- the timing of the availability of data from our clinical trials;
- the timing of our selection of a lead drug candidate for our CLS-1002 program;
- 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 CLS-1001, 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 SCS administration 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 shares of our common stock in this offering will be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional shares in full, based upon an assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, would increase or decrease the net proceeds to us from this offering by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million in the number of shares we are offering at the assumed initial public offering price would increase or decrease the net proceeds to us from this offering by $ million.

We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $ million to complete our planned Phase 2 and Phase 3 clinical trials of CLS-1001 in uveitis patients;
- approximately $ million to complete our planned Phase 2 clinical trial of CLS-1003 in RVO patients; and
- the remainder to fund further development of CLS-1003 and continued research and development of our earlier-stage programs, including drug discovery for potential new applications for our SCS 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.

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. 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.

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.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of September 30, 2014:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,564,959 shares of our common stock, which will occur automatically upon the closing of this offering;
  - the filing of our amended and restated certificate of incorporation upon the closing of this offering; and
  - the exercise of all outstanding warrants to purchase shares of common stock that will otherwise expire upon the closing of this offering for an aggregate of 248,175 shares of common stock; and
- on a pro forma as adjusted basis to give further effect to our sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The following information is illustrative only of our cash and cash equivalents and capitalization following the completion of this offering and will change based on the actual initial public offering price and other terms of this offering determined at pricing. 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, 2014		
	Actual	Pro forma	Pro forma as adjusted
		(in thousands)	
Cash and cash equivalents	$ 11,067	$	$
Convertible preferred stock:			
Series A convertible preferred stock, $0.001 par value; 5,198,826 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 4,065		
Series A-1 convertible preferred stock, $0.001 par value; 4,373,481 shares authorized, 4,356,931 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	7,848		
Series B convertible preferred stock, $0.001 par value; 7,416,365 shares authorized, 6,009,202 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	14,786		
Stockholders' equity (deficit):			
Common stock, $0.001 par value; 30,000,000 shares authorized, 3,988,421 shares issued and outstanding, actual; shares authorized, shares issued and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted	4		
Preferred stock, $0.001 par value; no shares authorized, issued or outstanding, actual; shares authorized, no shares issued or outstanding, pro forma or pro forma as adjusted	—		
Additional paid-in-capital	2,513		
Deficit accumulated during the development stage	(19,061)		
Total stockholders' equity (deficit)	(16,544)		
Total capitalization	$ 10,155	$	$

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. Each increase or decrease of 1.0 million in the number of shares we are offering at the assumed initial public offering price would increase or decrease the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by $ million.

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

- 1,659,246 shares of our common stock issuable upon the exercise of stock options outstanding under our 2011 stock incentive plan as of September 30, 2014, at a weighted average exercise price of $0.21 per share;
- 16,550 shares of our common stock issuable upon exercise of a warrant outstanding as of September 30, 2014, at an exercise price of $1.81 per share; and
- shares of our common stock reserved for future issuance under our equity incentive plans following this offering.

DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the initial public offering price per share and the pro forma 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 and convertible preferred stock by the number of outstanding shares of our common stock.

As of September 30, 2014, we had a net tangible book deficit of $(16.5) million, or $(4.15) per share of common stock. On a pro forma basis, after giving effect to the conversion of the outstanding shares of our convertible preferred stock into 15,564,959 shares of our common stock upon the completion of this offering, and the exercise of all outstanding warrants to purchase shares of common stock that will otherwise expire upon the closing of this offering for 248,175 shares of common stock, our pro forma net tangible book value would have been $ million, or $ per share of common stock.

After giving effect to the issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2014 would have been $ million, or $ per share of common stock. This represents an immediate increase in the pro forma net tangible book value of $ per share to existing stockholders, and an immediate dilution in the pro forma net tangible book value of $ per share to investors purchasing shares of our common stock in this offering. The following table illustrates this per share dilution:

Assumed initial public offering price per share		$
Actual net tangible book deficit per share as of September 30, 2014	$(4.15)	
Increase per share attributable to conversion of convertible preferred stock and exercise of warrants		
Pro forma net tangible book value per share before this offering		
Increase in pro forma net tangible book value per share attributable to this offering		
Pro forma as adjusted net tangible book value per share after this offering		
Dilution per share to investors participating in this offering		$

The dilution information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, would increase or decrease our pro forma as adjusted net tangible book value by $ million, or $ per share, and the dilution per share to investors participating in this offering by $ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. Each increase or decrease of 1.0 million shares in the number of shares offered by us at the assumed initial public offering price would increase or decrease our pro forma as adjusted net tangible book value per share after this offering by $ per share and decrease or increase the dilution to investors participating in this offering by $ per share.

If the underwriters exercise their option in full to purchase additional shares of common stock in this offering, the pro forma as adjusted net tangible book value per share after the offering would be

$ per share, the increase in the pro forma net tangible book value per share to existing stockholders would be $ per share and the dilution to new investors purchasing common stock in this offering would be $ per share.

The following table sets forth as of September 30, 2014, on the pro forma basis described above, the differences between the number of shares of common stock purchased from us, the total consideration paid and the weighted average price per share paid by existing stockholders and by investors purchasing shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page on this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares purchased		Total consideration		Weighted average price per share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$	%	$
New investors					
Total		100%	$	100%	

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the range set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by $ million, and increase or decrease the percent of total consideration paid by new investors by percentage points, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The table above also excludes:

- 1,659,246 shares of our common stock issuable upon the exercise of stock options outstanding under our 2011 stock incentive plan as of September 30, 2014, at a weighted average exercise price of $0.21 per share;
- 16,550 shares of our common stock issuable upon exercise of a warrant outstanding as of September 30, 2014, at an exercise price of $1.81 per share; and
- shares of our common stock reserved for future issuance under our equity incentive plans following this offering.

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, 2012 and 2013 and the selected balance sheet data as of December 31, 2012 and 2013 are derived from our audited financial statements appearing elsewhere in this prospectus. The selected statement of operations data for the nine-month periods ended September 30, 2013 and 2014 and for the period from May 26, 2011 (date of inception) through September 30, 2014 and the selected balance sheet data as of September 30, 2014 are derived from unaudited condensed 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 condensed financial statements include all adjustments, consisting of normal recurring accruals, which management considers necessary for a fair presentation of the financial position and the 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, 2014 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 2014.

	Year Ended December 31,		Nine Months Ended September 30,		Period From May 26, 2011 (Date of Inception) to September 30, 2014
	2012	2013	2013	2014	
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Costs and expenses:					
Research and development	$ 2,354	$ 5,045	$ 3,647	$ 4,776	$ 12,382
General and administrative	1,575	2,193	1,665	2,398	6,307
Total costs and expenses	3,929	7,238	5,312	7,174	18,689
Loss from operations	(3,929)	(7,238)	(5,312)	(7,174)	(18,689)
Other income (expense):					
Interest expense	(3)	(23)	(9)	(353)	(381)
Interest income	1	7	6	1	9
Total other expense	(2)	(16)	(3)	(352)	(372)
Net loss	$ (3,931)	$ (7,254)	$ (5,315)	$ (7,526)	$ (19,061)
Net loss per share of common stock — basic and diluted	$ (2.12)	$ (2.45)	$ (1.87)	$ (2.00)	$ (7.72)
Weighted average shares outstanding, basic and diluted	1,853,423	2,956,285	2,835,897	3,769,091	2,470,630
Pro forma net loss per share — basic and diluted		$ (0.58)		$ (0.39)	
Pro forma weighted average shares outstanding — basic and diluted		12,512,042		19,334,050	

	As of December 31,		As of September 30,
	2012	2013	2014
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 856	$ 1,909	$ 11,067
Total assets	948	2,137	12,872
Long-term debt, including current portion	150	268	—
Total liabilities	709	1,004	2,717
Total convertible preferred stock	4,029	11,871	26,699
Total stockholders' deficit	(3,790)	(10,738)	(16,544)

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 clinical-stage 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 and choroid, especially diseases associated with macular edema, and are injected non-surgically into the suprachoroidal space, or SCS, using our proprietary microinjector. With the SCS injection procedure, our product candidates are more directly administered to the retina and choroid as compared to currently used intravitreal injections, which we believe 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 non-surgical administration into the SCS. Our most advanced product candidates, CLS-1001 and CLS-1003, are based on commonly used ophthalmic therapeutic agents, 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 Federal Food, Drug, and Cosmetic Act.

CLS-1001 is in an ongoing Phase 1/2 clinical trial of patients with non-infectious uveitis for which we expect final results in the first half of 2015. We are currently screening patients for potential enrollment in an additional Phase 2 clinical trial in approximately 30 patients with macular edema associated with non-infectious uveitis to evaluate the safety and efficacy of our CLS-1001 administered into the SCS. We also expect to initiate a single pivotal Phase 3 clinical trial in mid-2015 with our CLS-1001 administered into the SCS in approximately 150 patients with macular edema associated with non-infectious uveitis, with the goal of being able to submit a Section 505(b)(2) NDA to the FDA in the first half of 2017. Under our CLS-1003 program, we plan to initiate a Phase 2 clinical trial in early 2015 in approximately 40 patients with macular edema associated with RVO, a sight-threatening disorder resulting from the blockage of a retinal vein. Under our CLS-1002 program, we are evaluating a number of compounds for the treatment of wet AMD by SCS injection, including compounds with anti-VEGF activity and compounds with dual anti-VEGF and anti-PDGF activity. We plan to file an IND for this CLS-1002 program in the first half of 2016. We also intend to evaluate treatments for DME. If our product candidates are approved, we plan to commercialize them with a specialty sales force of 30 to 40 representatives to target 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 are a development-stage company and 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 a clinical trial of our most advance product candidate. To date, we have not generated any revenue and have primarily financed our operations through the private placement of our equity securities

and issuance of convertible promissory notes. We have raised net cash proceeds of $24.5 million from the sale of convertible preferred stock and $3.4 million from the sale of convertible promissory notes through September 30, 2014. As of September 30, 2014, we had a deficit accumulated during the development stage of $19.1 million. We recorded net losses of $3.9 million and $7.3 million for the years ended December 31, 2012 and 2013, respectively, and $5.3 million and $7.5 million for the nine months ended September 30, 2013 and 2014, respectively. We anticipate that a substantial portion of our capital resources and efforts in the foreseeable future will be focused on completing the development 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 development 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:

- initiate and conduct our planned Phase 2 and Phase 3 clinical trials of CLS-1001;
- initiate and conduct our planned Phase 2 clinical trial of CLS-1003;
- continue the research and development of our other product candidates;
- seek to evaluate 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 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 drug development and potential future commercialization efforts; and
- begin to operate as a public company.

We anticipate that we will use approximately $ million of the net proceeds from this offering for clinical and non-clinical costs associated with the initiation and completion of planned Phase 2 and Phase 3 clinical trials for CLS-1001 and approximately $ million for clinical and non-clinical costs associated with the initiation and completion of the planned Phase 2 clinical trial for CLS-1003. We intend to use the remainder of the proceeds of this offering to fund the research and development of our earlier-stage programs, including drug discovery and for working capital and general corporate purposes. We expect that these funds will not be sufficient to enable us to complete all necessary development and commercially launch both of these product candidates. Accordingly, we will be required to obtain further funding through other public or private offerings of our capital stock, debt financing, collaboration and licensing arrangements or other sources. Adequate additional funding may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or altogether cease our

research and development programs or future commercialization efforts. Although it is difficult to predict future liquidity requirements, we believe that the net proceeds of this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operations for at least the next 12 months. However, our ability to successfully transition to profitability will be dependent upon achieving a level of revenues adequate to support our cost structure. We cannot assure you that we will ever be profitable or generate positive cash flow from our operating activities.

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. Over time, we may also seek to earn revenue by out-licensing our proprietary microinjection technology for SCS drug administration to third-party strategic collaborators.

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 stock-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, stock-based compensation and depreciation, are not classified as direct clinical costs or non-clinical costs and are separately classified as unallocated.

For the year ended December 31, 2012, substantially all of our research and development expenses related to the non-clinical development of CLS-1001. For the year ended December 31, 2013 and the nine months ended September 30, 2013 and 2014, substantially all of our research and development expenses

related to the non-clinical and clinical development of CLS-1001. From inception through September 30, 2014, we have incurred $12.4 million in research and development expenses, of which only $0.2 million was expended prior to January 1, 2012. Prior to January 1, 2012, we did not allocate any research and development expenses to any specific product candidate.

The following table shows our research and development expenses by type of activity for the nine months ended September 30, 2013 and 2014, the years ended December 31, 2012 and 2013 and the period from May 26, 2011 (date of inception) to September 30, 2014.

	Nine Months Ended September 30,		Year Ended December 31,		Period from May 26, 2011 (Date of Inception) to September 30, 2014
	2013	2014	2012	2013	
	(in thousands)				
CLS-1001:					
Direct non-clinical	$ 931	$1,492	$ 926	$1,326	$ 3,744
Direct clinical	113	403	—	173	576
Total	1,044	1,895	926	1,499	4,320
CLS-1002:					
Direct non-clinical	55	204	—	153	357
Direct clinical	40	6	123	44	173
Total	95	210	123	197	530
CLS-1003:					
Direct non-clinical	—	100	—	45	145
Direct clinical	—	251	—	—	251
Total	—	351	—	45	396
Unallocated	2,508	2,320	1,305	3,304	7,136
Total research and development expense	$3,647	$4,776	$2,354	$5,045	$ 12,382

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 CLS-1001 and our other 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 trial is 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 profile of the product candidate.

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 stock-based compensation, for personnel in executive, finance, accounting, business development, and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to intellectual property and corporate matters and fees for accounting and consulting 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, insurance, and investor relations costs. In addition, if CLS-1001 or any of our other product candidates obtains regulatory approval for marketing, we expect to incur expenses associated with building a sales and marketing team. However, we do not expect to receive any such regulatory approval for at least the next several years.

Other Income (Expense)

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

Other expense consists of interest accrued under promissory notes and amortization of debt discounts arising from the preferred stock purchase warrant described in the footnotes to our financial statements appearing elsewhere in this prospectus.

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 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 GAAP, we evaluate our estimates and judgments on an ongoing basis. Significant estimates include assumptions used in the determination of stock-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, 2012, December 31, 2013 and September 30, 2014 consisted primarily of cash and cash equivalents, long-term debt and stock purchase warrant liabilities. The fair value of cash and cash equivalents and long-term debt approximate their respective carrying values due to the short-term nature of these instruments. We have determined the preferred stock purchase warrant, the value of which is recorded as an adjustment to long-term debt, to be valued under Level 3.

Stock-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.

Stock-based compensation expense was $0.3 million for each of the years ended December 31, 2012 and 2013 and $0.2 million and $0.3 million for the nine months ended September 30, 2013 and 2014, respectively.

Significant Factors, Assumptions and Methodologies Used in Determining Fair Value

Determining the appropriate fair value measurement of stock-based awards requires the use of subjective assumptions. In the absence of a public trading market for our common stock, and in preparation for this offering, we conducted retrospective assessments of the valuation of our common stock as of December 31, 2012 and 2013 and contemporaneous valuations as of June 30, 2014 and September 30, 2014, in each case as described below in “— Common Stock Valuations.” 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.* Since no public market exists for our stock, we must estimate its fair value, as discussed in "— Common Stock Valuations" below.
- *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 estimated our annual forfeiture rates to be zero for 2012 and 2013.
- *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, 2012 and 2013 and for the nine months ended September 30, 2013 and 2014.

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
Expected term (years)	7.00	7.00	7.00	7.00
Expected stock price volatility	156.84%	97.02%	99.81%	87.85%
Risk-free interest rate	1.07%	1.69%	1.42%	2.10%
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.

Common Stock Valuations

We are a private company with no active public market for our common stock. Our common stock valuations are 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 Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, referred to as the Practice Aid. The methodologies used to determine fair value of our common stock included estimating the fair value of the enterprise and then allocating this value to all classes of equity securities using a combination of the option pricing method and, beginning with our retrospective valuation as of December 31, 2013, the initial public offering scenario within the probability-weighted expected return method, described in more detail below.

The assumptions used in the valuation models that ultimately determine the fair value of our common stock as of the valuation date are based on numerous objective and subjective factors combined with management judgment, including the following:

- our results of operations, financial position and the status of our research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- our discounted future cash flows, based on our projected operating results;
- the potential impact on our common stock of liquidation preference rights of our convertible preferred stock;
- the valuation of publicly traded companies in the life sciences and pharmaceutical industry sectors, as well as recently completed mergers and acquisitions of peer companies;
- any external market conditions affecting the life sciences and pharmaceutical industry sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions;
- the state of the IPO market for similarly situated privately held biotechnology companies; and
- any recent contemporaneous valuations prepared in accordance with methodologies outlined in the Practice Aid.

The following table presents the grant dates and related exercise prices of stock options that we granted from January 1, 2013 through the date of this prospectus, along with the corresponding exercise price for each option grant and the fair values per share utilized to calculate stock-based compensation expense. Refer to “Estimate of Fair Value for Option Grants During Nine Months Ended September 30, 2013,” “Retrospective Valuation as of

December 31, 2013," "Contemporaneous Valuation as of June 30, 2014" and "Contemporaneous Valuation as of September 30, 2014" for additional information.

Date of Grant	Number of Shares Underlying Options	Exercise Price Per Option	Common Stock Fair Value Per Share on Grant Date
3/1/2013	585,500	$ 0.18	$ 0.50(1)
5/21/2013	5,000	0.18	0.50(1)
6/17/2013	100,000	0.18	0.50(1)
8/7/2013	165,000	0.18	0.66(1)
10/16/2013	50,000	0.18	0.66(1)
11/25/2013	500,000	0.18	0.66(1)
12/17/2013	30,000	0.18	0.66(1)
8/12/2014	70,000	1.40	1.40
11/26/2014	100,000	1.55	1.55
12/9/2014	132,500	1.55	1.55
12/19/2014	525,000	1.55	1.55

(1) We assessed the fair value of our common stock subsequent to the grant date of these awards, as described below.

Based on an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, the intrinsic value of all stock options outstanding as of September 30, 2014 was $ million, of which $ million and $ million related to stock options that were vested and unvested, respectively, at that date.

Common Stock Valuation Methodologies

The Practice Aid describes market, income and cost approaches to valuing equity securities, each of which approaches is summarized below.

Market Approach. The market approach uses similar companies or transactions in the marketplace. When using the guideline company method of the market approach in determining the fair value of common stock, a company identifies companies similar to its business and uses these guideline companies to develop relevant market multiples and ratios, which are then applied to its financial forecasts to create an indication of total equity value. When using the similar transaction methodology of the market approach in determining the fair value of common stock, a company uses publicly disclosed data from arm's-length transactions involving similar companies to develop relationships or value measures between the prices paid for the target companies and the underlying financial performance of those companies. These value measures are then applied to a company's applicable operating data to create an indication of total equity value.

Income Approach. For the income approach, a company uses the discounted free cash flow method, which is based on the premise that equity value as of the respective valuation date is equal to the projected future free cash flows and expected terminal value of the business, discounted by a required rate of return that investors would demand given the risks of ownership and the risks associated with achieving the stream of projected future free cash flows.

Cost Approach. The cost approach involves identifying a company's significant tangible assets, estimating the individual current market values of each and then totaling them to derive the value of the business as a whole. A company can use the cost approach to value its adjusted net assets available to

common stockholders if it were forced to liquidate its assets if its business model failed and the company was unable to raise additional financing.

Methods Used to Allocate Our Enterprise Value to Classes of Securities

In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at the valuation date. The methods we considered consisted of the following:

Current Value Method. Under the current value method, once the fair value of the enterprise is established, the value is allocated to the various series of preferred and common stock based on their respective seniority, liquidation preferences or conversion values, whichever is greatest.

Option Pricing Method, or OPM. Under the option pricing method, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options.

Probability-Weighted Expected Return Method, or PWERM. The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

Retrospective Valuation as of December 31, 2012

In view of our relatively early stage of development as of December 31, 2012, as well as the state of the market for biopharmaceutical initial public offerings at that time, we conducted a retrospective valuation of our common stock as of December 31, 2012 using the OPM. In conducting this valuation, we used a market approach to backsolve for an estimate of our enterprise value based on our Series A-1 convertible preferred stock financing, which occurred shortly thereafter in January 2013. Although we did not rely on the guideline company or similar transaction methodologies to determine our enterprise value as part of the market approach, we did review them to gain a deeper insight into the companies in the ophthalmic therapeutics market and to evaluate prevailing market conditions.

Once we determined an estimate of our enterprise value, we then allocated the estimated enterprise value to the various classes of our equity securities using the OPM, which analyzes the rights of the common stock relative to those of the preferred stock by assessing the “break points,” or the points at which it is economically viable for the holders of preferred stock to convert their preferred stock into common stock. At the December 31, 2012 valuation date, the model incorporated an assumed time to a liquidity event of 2.5 years. After applying a 40% discount for lack of marketability, the fair value per share of common stock on a non-marketable interest basis under the OPM was $0.30 as of December 31, 2012. We used basic put option and Finnerty put option analyses to estimate the discount for lack of marketability. These models are commonly used for estimating illiquidity discounts for securities.

Estimate of Fair Value for Option Grants During Nine Months Ended September 30, 2013

In January 2013, we completed our Series A-1 preferred stock financing, raising gross proceeds of $7.9 million, which we believe resulted in an increased value of our company and our common stock. Also in January 2013, we received approval of our IND from the FDA to initiate our Phase 1/2 clinical trial in our CLS-1001 program. Therefore, for purposes of our retrospective assessment of the fair value of our

common stock as of dates after January 2013, we believed that it was appropriate to increase our estimate of the fair value of our common stock from the December 31, 2012 estimated fair value of $0.30 per share. In deriving this estimate, we interpolated between $0.30 per share and the $0.66 per share estimated fair value that we utilized for our grants made in the second half of 2013, as described below. Based on this interpolation, we estimated the fair value per share of common stock to be $0.50 per share for the first and second quarters of 2013 and $0.66 per share for the third quarter of 2013, which we have applied retrospectively to all of our stock option grants made during the nine months ended September 30, 2013.

Retrospective Valuation as of December 31, 2013

By the end of 2013, based on our board of directors' review of overall market conditions, the improving market for biopharmaceutical initial public offerings and the progress of our clinical and preclinical development, our board of directors determined that a shift was occurring with respect to the potential valuation of our common stock in a liquidity event scenario, and we therefore performed a valuation for our common stock as of December 31, 2013.

In conducting this valuation, we used a market approach to backsolve for an estimate of our enterprise value based upon anticipated transactions involving convertible preferred stock. Specifically, based on our capital plan at the valuation date, we estimated that we would need additional funding during 2014. At the valuation date, we expected that such a new investment, a Series B preferred stock financing, would be completed at the same price as our prior Series A-1 convertible preferred stock, issued in January and February 2013, but would be senior to it in terms of liquidation preference. Although we did not rely on the guideline company or similar transaction methodologies to determine our enterprise value as part of the market approach, we did review them to gain a deeper insight into the companies in the ophthalmic therapeutics market and to evaluate prevailing market conditions.

Once we determined an estimate of our enterprise value, we then allocated the estimated enterprise value to the various classes of our equity securities using the OPM, which analyzes the rights of the common stock relative to those of the preferred stock by assessing the "break points," or the points at which it is economically viable for the holders of preferred stock to convert their preferred stock into common stock. At the December 31, 2013 valuation date, the model incorporated an assumed time to a liquidity event of two years. After applying a 30% discount for lack of marketability, the fair value per share of common stock on a non-marketable interest basis under the OPM was $0.32 as of December 31, 2013. We used basic put option and Finnerty put option analyses to estimate the discount for lack of marketability. These models are commonly used for estimating illiquidity discounts for securities.

As of December 31, 2013, our board of directors had authorized management to begin preparing for a potential initial public offering, or IPO, of our common stock, although we did not select underwriters for this offering until April 2014. Because an IPO scenario was considered to be a possible liquidity event, we also used the PWERM to estimate our enterprise value under this scenario and to estimate the fair value of our common stock in such a scenario. For this scenario, we assumed an IPO at the end of 2014. We reviewed a number of IPOs completed by life sciences and biopharmaceutical companies during 2013 and estimated an enterprise value for our company that would have been somewhat below the first quartile of the enterprise values of recent IPOs, after taking into account our stage of development as compared to the reviewed companies. After applying a 20% discount rate to the estimated future enterprise value at the time of an IPO, and after applying a 20% discount for lack of marketability using basic put option and Finnerty put option analyses, the fair value per share of common stock on a non-marketable basis under the PWERM was $2.01 as of December 31, 2013.

Based upon our estimates of the probabilities of the future outcomes, we then attributed an 80% weighting to the OPM and a 20% weighting to the IPO scenario within the PWERM. This resulted in a weighted per share value of $0.66 for our common stock as of December 31, 2013. For financial reporting purposes in determining the estimated fair value of the stock options, this value has been applied retrospectively to all of our stock option grants made during the six months ended December 31, 2013.

Contemporaneous Valuation as of June 30, 2014

We deemed it appropriate to obtain a valuation of our common stock as of June 30, 2014. In this valuation, we used the same methodology as we had used for our December 31, 2013 retrospective valuation.

Once we determined an estimate of our enterprise value, we allocated the estimated enterprise value to the various classes of our equity securities using the OPM. At the June 30, 2014 valuation date, the model incorporated an assumed time to a liquidity event of two years. After applying a 30% discount for lack of marketability using basic put option and Finnerty put option analyses, the fair value per share of common stock on a non-marketable interest basis under the OPM was $0.15 as of June 30, 2014.

Because an IPO scenario was considered to be a possible liquidity event as of June 30, 2014, we also used the PWERM to estimate our enterprise value under this scenario and to estimate the fair value of our common stock in such a scenario. For this scenario, we assumed an IPO at the end of 2014. We reviewed a number of IPOs completed by life sciences and biopharmaceutical companies during 2013 and 2014 and estimated an enterprise value for our company that would have been somewhat below the first quartile of the enterprise values of recent IPOs, after taking into account our stage of development as compared to the reviewed companies. After applying a 20% discount rate to the estimated future enterprise value at the time of an IPO, and after applying a 10% discount for lack of marketability using basic put option and Finnerty put option analyses, the fair value per share of common stock on a non-marketable basis under the PWERM was $3.89 as of June 30, 2014.

Based upon our estimates of the probabilities of the future outcomes, we then attributed a 67% weighting to the OPM and a 33% weighting to the IPO scenario within the PWERM. This resulted in a weighted per share value of $1.40 for our common stock as of June 30, 2014.

August 2014 Option Grants

Our board of directors granted options to purchase common stock on August 12, 2014, with each option having an exercise price of $1.40 per share. In establishing this exercise price, our board of directors considered input from management, giving substantial weight to the valuation we conducted of our common stock as of June 30, 2014. Our board of directors concluded that there were no events or circumstances that occurred between June 30, 2014 and August 12, 2014 that were indicative of a change in the fair value of our common stock and therefore determined that the fair value of our common stock on that grant date was $1.40 per share.

Contemporaneous Valuation as of September 30, 2014

We deemed it appropriate to obtain a valuation of our common stock as of September 30, 2014. In this valuation, we used the same methodology as we had used for our December 31, 2013 retrospective valuation and June 30, 2014 contemporaneous valuation.

Once we determined an estimate of our enterprise value, we allocated the estimated enterprise value to the various classes of our equity securities using the OPM. At the September 30, 2014 valuation date, the model incorporated an assumed time to a liquidity event of two years. After applying a 30% discount for lack of marketability using basic put option and Finnerty put option analyses, the fair value per share of common stock on a non-marketable interest basis under the OPM was $0.11 as of September 30, 2014.

Because we were continuing to make progress toward a potential IPO, we also used the PWERM to estimate our enterprise value under multiple IPO scenarios and to estimate the fair value of our common stock. In one scenario, we assumed an IPO in the first half of 2015 and in a second scenario we assumed an IPO in the second half of 2015. We reviewed a number of IPOs completed by life sciences and biopharmaceutical companies during 2013 and 2014 and estimated an enterprise value for our company that was close to the first quartile of the enterprise values of recent IPOs for the early 2015 IPO scenario and near the median of enterprise values of recent IPOs for the late 2015 IPO scenario, in each case after taking into account our stage of development as compared to the reviewed companies. After applying a 20% discount rate to the estimated future enterprise value at the time of each IPO scenario, and after applying a 10% discount for lack of marketability using basic put option and Finnerty put option analyses, the fair value per share of common stock on a non-marketable basis under the PWERM was $3.71 as of September 30, 2014.

Based upon our estimates of the probabilities of the future outcomes, we then attributed a 60% weighting to the OPM, a 24% weighting to the early 2015 IPO scenario within the PWERM and a 16% weighting to the late 2015 IPO scenario within the PWERM. This resulted in a weighted per share value of $1.55 for our common stock as of September 30, 2014.

November and December 2014 Option Grants

Our board of directors granted options to purchase common stock on November 26, 2014, December 9, 2014 and December 19, 2014, with each option having an exercise price of $1.55 per share. In establishing this exercise price, our board of directors considered input from management, giving substantial weight to the valuation we conducted of our common stock as of September 30, 2014. Our board of directors concluded that there were no events or circumstances that occurred between September 30, 2014 and December 19, 2014 that were indicative of a change in the fair value of our common stock and therefore determined that the fair value of our common stock on each grant date was $1.55 per share.

Determination of Estimated Offering Price

In April 2014, we selected underwriters for this offering. The midpoint of the preliminary range for the initial public offering as determined by us and the underwriters was $ per share. In comparison, our estimate of the fair value of our common stock was $1.55 per share as of the September 30, 2014 valuation. We note that, as is typical in IPOs, the preliminary range was not derived using a formal determination of fair value, but was determined based upon discussions between us and the underwriters. Among the factors that were considered in setting this range were our prospects and the history of and prospects for our industry, the general condition of the securities markets and the recent market prices of, and the demand for, publicly traded common stock of generally comparable companies. We believe that the difference between the fair value of our common stock as of September 30, 2014 and the midpoint of the price range for this offering is the result of these factors as well as the fact that the estimated IPO price range necessarily assumes that the initial public offering has occurred, a public market for our common stock has been created and that our preferred stock converted into common stock in connection with the IPO, and therefore

excludes any discount for lack of marketability of our common stock, which was factored into the September 30, 2014 valuation.

Results of Valuation Models May Vary

Valuation models require the input of highly subjective assumptions and estimates. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event and the determinations of the appropriate valuation methods. Because our common stock has characteristics significantly different from that of publicly traded common stock and because changes in the subjective input assumptions can materially affect our fair value estimates, the existing models do not necessarily provide a reliable, single measure of the fair value of our common stock. If we had made different assumptions, our stock-based compensation expense, our net loss and net loss per share could have been significantly different. The foregoing valuation methodologies are not the only valuation methodologies available and will not be used to value our common stock once this offering is complete. We cannot make assurances as to any particular valuation for our stock. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

Tax Valuation Allowance

We recorded deferred tax assets of $4.3 million as of December 31, 2013, 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 $10.4 million for the period from our inception on May 26, 2011 to December 31, 2013. We incurred a net loss of $7.5 million for the nine months ended September 30, 2014. 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, 2013, we had federal NOL carryforwards of $10.4 million and state NOL carryforwards of $12.4 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, 2013 and 2014

The following table sets forth our results of operations for the nine months ended September 30, 2013 and 2014.

	Nine Months Ended September 30,		Period-to-Period Change
	2013	2014	
	(in thousands)		
Costs and expenses:			
Research and development	$ 3,647	$ 4,776	$ 1,129
General and administrative	1,665	2,398	733
Total costs and expenses	5,312	7,174	1,862
Loss from operations	(5,312)	(7,174)	(1,862)
Other income (expense):			
Interest expense	(9)	(353)	(344)
Interest income	6	1	(5)
Total other expense	(3)	(352)	(349)
Net loss	$ (5,315)	$ (7,526)	$ (2,211)

Research and development. Research and development expense increased from $3.6 million for the nine months ended September 30, 2013 to $4.8 million for the nine months ended September 30, 2014, an increase of 31%. The increase was primarily attributable to a $0.7 million increase in costs related to the design, testing and manufacture of our microinjector, a $0.2 million increase in costs related to the Phase 2 program for CLS-1001 and a $0.4 million increase in costs for the startup of the Phase 2 clinical trial of CLS-1003 in RVO patients. We also incurred increased personnel costs during the nine months ended September 30, 2014 as compared to the prior year, offset by lower costs of pre-clinical studies for CLS-1001.

General and administrative. General and administrative expense increased by $0.7 million, from $1.7 million for the nine months ended September 30, 2013 to $2.4 million for the nine months ended September 30, 2014, an increase of 44%. The increase was primarily attributable to increases in personnel costs, including stock-based compensation and fees related to the audit of our financial statements in preparation for this offering.

Interest expense. Interest expense increased by $0.3 million for the nine months ended September 30, 2014. This increase was primarily due to the acceleration of the amortization of the debt discount related to the convertible promissory notes upon their conversion to Series B convertible preferred stock.

Results of Operations for the Years Ended December 31, 2012 and 2013

The following table sets forth our results of operations for the years ended December 31, 2012 and 2013.

	Year Ended December 31,		Period-to-Period Change
	2012	2013	
	(in thousands)		
Costs and expenses:			
Research and development	$ 2,354	$ 5,045	$ 2,691
General and administrative	1,575	2,193	618
Total costs and expenses	3,929	7,238	3,309
Loss from operations	(3,929)	(7,238)	(3,309)
Other income (expense):			
Interest expense	(3)	(23)	(20)
Interest income	1	7	6
Total other expense	(2)	(16)	(14)
Net loss	$(3,931)	$(7,254)	$ (3,323)

Research and development. Research and development expense increased by $2.7 million, from $2.4 million for the year ended December 31, 2012 to $5.0 million for the year ended December 31, 2013, an increase of 114%. The increase was primarily attributable to higher compensation, travel and facilities costs of $1.4 million resulting from new hires in 2013, as well as an increase of $0.6 million in direct clinical expenses for our CLS-1001 program, which began clinical development in the second half of 2013, and an increase of $0.7 million in preclinical expenses related to our other programs, including our earlier-stage RVO and wet AMD programs, during the year ended December 31, 2013.

General and administrative. General and administrative expense increased by $0.6 million, from $1.6 million for the year ended December 31, 2012 to $2.2 million for the year ended December 31, 2013, an increase of 39%. The increase was primarily attributable to an increase of $0.5 million in costs related to new hires in our general and administrative functions, including compensation and travel costs. Additionally, we had an increase of $0.1 million in professional fees as compared to the prior year.

Liquidity and Capital Resources

Sources of Liquidity

We have incurred losses and experienced negative operating cash flows since our inception and anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will increase over historical levels and, as a result, we will need additional capital to fund our operations, which we may obtain from additional public offerings, debt financing, collaboration and licensing arrangements or other sources.

For the period from our inception on May 26, 2011 to September 30, 2014, we have cumulative net cash used by operating activities of $16.5 million and cumulative net losses of $19.1 million. Since our inception, we have funded operations primarily through the sale of convertible preferred stock and the issuance of convertible promissory notes. We have raised net cash proceeds of $24.5 million from the sale of convertible preferred stock and $3.4 million from the sale of convertible promissory notes through September 30, 2014. As of December 31, 2013 and September 30, 2014, we had cash and cash equivalents of $1.9 million and $11.1 million, respectively. We invest any cash in excess of our immediate requirements

primarily with a view to liquidity and capital preservation. As of December 31, 2013 and September 30, 2014, our funds were held in cash and money market funds.

In April 2014, we authorized the sale of convertible promissory notes, or the bridge notes, to our existing stockholders, including two of our executive officers and one of our directors in their individual capacities, in the aggregate principal amount of $6.0 million. In April 2014, we issued $3.0 million in aggregate principal amount of bridge notes. We do not expect to issue the remaining $3.0 million in aggregate principal amount of bridge notes. The outstanding notes accrued interest at an annual 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. Our August 2014 Series B convertible preferred stock financing was a qualified financing as contemplated by the bridge notes, and the principal and interest under all of the bridge notes was converted automatically into an aggregate of 1,137,644 shares of Series B convertible preferred stock in connection with this financing. These shares of Series B convertible preferred stock are convertible into shares of our common stock upon the completion of this offering. In connection with the issuance of the bridge notes, we also issued warrants to the lenders to purchase an aggregate of 248,175 shares of our common stock at an exercise price of $0.01 per share. These warrants expire upon the closing of this offering, and therefore we expect that these warrants will be exercised in connection with the completion of this offering and that we will issue 248,175 shares of our common stock upon their exercise.

In April 2013, we entered into a loan agreement with an entity affiliated with the State of North Carolina under which we borrowed an aggregate of $125,000. The outstanding balance bore interest at an annual rate of 4.25%. All unpaid principal, together with unpaid and accrued interest, were due and payable in February 2016 or, if earlier, upon the occurrence of specified events. We repaid this note in full in May 2014. In connection with the initial loan, we also issued this lender a warrant to purchase 16,550 shares of our Series A-1 convertible preferred stock, which will become a warrant to purchase 16,550 shares of our common stock following the completion of this offering.

In December 2012, we entered into a $150,000 unsecured promissory note with a lender, which bore interest at an annual rate of 5%. All unpaid principal, together with unpaid and accrued interest converted into an aggregate of 60,291 shares of Series B convertible preferred stock in connection with our August 2014 Series B convertible preferred stock financing.

Between June 2011 and December 2011, we borrowed an aggregate of $100,000 from Daniel White, our chief executive officer. These advanced amounts, plus accrued interest of approximately $5,000, were converted into shares of our Series A convertible preferred stock during the year ended December 31, 2012.

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 CLS-1001, CLS-1002, CLS-1003 or any of our other product candidates. 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. 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. We estimate that we will annually incur approximately $1.5 million to $2.5 million in expenses to comply with these requirements.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 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

During the nine months ended September 30, 2013 and 2014, our operating activities used net cash of $4.8 million and $6.4 million, respectively. The use of net cash in each period primarily resulted from our net losses. The increase in net loss for the nine months ended September 30, 2014 as compared to the nine months ended September 30, 2013 was primarily attributable to higher research and development expenses. The other changes from operating activities were caused primarily by changes in our accounts payable, stock-based compensation, deferred offering costs and other accrued liabilities. During the nine months ended September 30, 2013 and 2014, we did not engage in any material investing activities. The net cash provided by financing activities during the nine months ended September 30, 2013 related to $7.8 million from the sale of our Series A-1 convertible preferred stock, net of issuance costs, while the net cash provided by financing activities during the nine months ended September 30, 2014 related primarily to $3.0 million received from the issuance of the bridge notes and $12.8 million from the sale of our Series B convertible preferred stock.

During the years ended December 31, 2012 and 2013, our operating activities used net cash of $3.2 million and $6.8 million, respectively. The use of net cash in each year primarily resulted from our net losses. The increase in net loss for the year ended December 31, 2013 as compared to the year ended December 31, 2012 was due primarily to the increase in research and development expenses and, to a lesser extent, an increase in general and administrative expenses. The other changes from operating activities were caused primarily by changes in our accounts payable and other accrued liabilities. During the years ended December 31, 2012 and 2013, our investing activities included primarily purchases of office furnishings and equipment to facilitate our increased research and development activities and headcount. During the years ended December 31, 2012 and 2013, our financing activities provided net cash of $4.1 million and $8.0 million, respectively. The net cash provided by financing activities during the year ended December 31, 2012 was primarily the result of $3.9 million in net proceeds from the sale of our Series A convertible preferred stock and $150,000 from the issuance of debt, while net cash provided by financing activities during the year ended December 31, 2013 was the result of $7.8 million from the sale of our Series A-1 convertible preferred stock as well as $125,000 from the issuance of debt.

Contractual Obligations

The following table summarizes our significant contractual obligations as of December 31, 2013, all of which consisted of obligations under leases for our corporate headquarters in Alpharetta, Georgia and our research facility in Durham, North Carolina.

	Payment due by period (in thousands)				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Operating lease obligations	$547	$ 254	$ 270	$ 23	$ —
Long-term debt obligations	275	—	125	150	—
Total	$822	$ 254	$ 395	$ 173	$ —

We have no material non-cancelable purchase commitments with contract manufacturers 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

We have considered all recently issued accounting pronouncements and do not believe the adoption of such pronouncements will have a material impact on our financial statements.

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. 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 December 31, 2012 and 2013 and September 30, 2014, we had cash and cash equivalents of $0.9 million, $1.9 million and $11.1 million, respectively. We generally hold our cash in interest-bearing money market accounts. 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 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.

We do not engage in any hedging activities against changes in interest rates. Our outstanding debt instruments carry a fixed interest rate and, as such, are not subject to interest rate risk.

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

BUSINESS

Overview

We are a clinical-stage 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 and choroid, especially diseases associated with macular edema, and are injected non-surgically into the suprachoroidal space, or SCS, adjacent to the choroid, using our proprietary microinjector. With the SCS injection procedure, our product candidates are more directly administered to the retina and choroid as compared to currently used intravitreal injections, which we believe 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 non-surgical administration into the SCS. Our most advanced product candidates, CLS-1001 and CLS-1003, are based on commonly used ophthalmic therapeutic agents, 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 Federal Food, Drug, and Cosmetic Act. Under Section 505(b)(2), if we can establish that reliance on the FDA's previous findings of safety or effectiveness or both for an approved product is scientifically appropriate, or there is scientific literature to support the product's safety or effectiveness, 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. CLS-1001, for macular edema associated with non-infectious uveitis, is in an ongoing Phase 1/2 clinical trial, from which we expect final results in the first half of 2015. We expect to be able to conduct a single pivotal Phase 3 clinical trial in approximately 150 patients beginning in mid-2015, the results of which we believe, based on a meeting with the FDA and subsequent written correspondence, will be sufficient to support the filing of a New Drug Application, or NDA, to the FDA in the first half of 2017. For CLS-1003, for macular edema associated with retinal vein occlusion, or RVO, we plan to initiate a Phase 2 clinical trial in early 2015 from which we expect to receive data in the second half of 2015. In our CLS-1002 program, for wet age-related macular degeneration, or wet AMD, we are evaluating drug compounds with anti-VEGF activity or dual anti-VEGF and anti-PDGF activity for SCS injection, and plan to file an investigational new drug application, or IND, in the first half of 2016. We are also considering a development program for drug compounds that may be able to treat diabetic macular edema, or DME. 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 approximately $6 billion in 2013.

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, the tissue that lines the inside of the eye and is the part of the eye primarily responsible for vision, and the choroid, the layer adjacent to the retina that supplies the retina with blood, oxygen and nourishment. These diseases include uveitis, RVO, wet AMD and DME. 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.

The most common treatments for diseases of the retina and choroid are corticosteroids and drugs that inhibit vascular endothelial growth factor, or anti-VEGF drugs. These corticosteroids and anti-VEGF drugs are often injected into the vitreous, a jelly-like substance that occupies the central portion of the eye. Intravitreal injections rely on drug to diffuse outward from the vitreous to the retina and choroid, which diffusion can result in lower concentrations of drug in these targeted areas. At the same time, this diffusion can result in drug spreading to unintended parts of the eye, where, for some drugs, it can cause significant side effects.

By contrast, with our approach, drug is injected into and spreads within the SCS, which is the space located between the choroid and the outer protective layer of the eye known as the sclera, to reach the back of the eye. We believe SCS administration 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 cataracts and elevated intraocular pressure, or 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 SCS injection with our microinjector is conducted in an in-office setting and is similar 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.

Under our CLS-1001 program, we are conducting a Phase 1/2 clinical trial in patients with non-infectious uveitis, a condition characterized by inflammation of the choroid and surrounding tissues. We intend to seek orphan drug designation and exclusivity for CLS-1001 for this indication. The most common treatment for non-infectious uveitis involves the use of corticosteroids, such as triamcinolone acetonide, or TA. CLS-1001 consists of an SCS injection of CLS-TA, our proprietary, preservative-free formulation of TA, specifically designed to be administered through our SCS microinjector. In this ongoing Phase 1/2 clinical trial, for which we have filed an IND with the FDA, we are evaluating the safety of SCS injection of Triesence, a TA formulation that is similar to CLS-TA and that has been approved by the U.S. Food and Drug Administration, or FDA, to treat non-infectious uveitis. While the trial is primarily a safety and tolerability study, we are also assessing efficacy measures. We intended to enroll approximately 10 patients in this trial. We completed enrollment after dosing the eighth patient. Interim data from these eight patients indicate that SCS injection of the drug has generally been well tolerated, with none of the eight patients having developed cataracts or experienced elevated IOP. At eight weeks after a single SCS injection, the visual acuity of all eight patients had improved by five or more letters on a standard eye chart over baseline, a clinically meaningful improvement, and the visual acuity of five of these eight patients improved by at least 15 letters. Because CLS-1001 is based on 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 the disease, including the associated macular edema. Our preclinical studies suggest that SCS 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 early clinical trial results suggest the potential for CLS-1001 to effectively treat uveitis for at least 90 days following a single SCS injection. Currently used ocular injections of TA are typically effective for approximately 90 days. We are currently screening patients for potential enrollment in a Phase 2 clinical trial in approximately 30 patients with macular edema associated with non-infectious uveitis to evaluate the safety and efficacy of our CLS-TA administered into the SCS. In mid-2015, we also expect to initiate a single pivotal Phase 3 clinical trial with our CLS-TA administered into the SCS in approximately 150 patients with macular edema associated with non-infectious uveitis, with the goal of being able to submit an NDA to the FDA in the first half of 2017. Based on our discussions with the FDA, which included both a pre-IND meeting in 2012 and subsequent written correspondence in 2013, we believe

this single pivotal clinical trial will be sufficient to support a 505(b)(2) NDA filing for CLS-1001 for macular edema associated with non-infectious uveitis. If approved, CLS-1001 would be the first drug specifically indicated for macular edema associated with non-infectious uveitis.

Under our CLS-1003 program, we plan to initiate a Phase 2 clinical trial in early 2015 in approximately 40 patients with macular edema associated with RVO, a sight-threatening disorder resulting from the blockage of a retinal vein. We have not yet discussed our clinical development plans for this program with the FDA, however. 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). Although studies have shown that corticosteroids effectively address the inflammatory aspect of RVO, they are not used as first-line therapy because they are generally not considered to be as effective as anti-VEGF drugs and also have an unattractive side effect profile when injected intravitreally. In our Phase 2 clinical trial, we will evaluate the safety and efficacy of the injection of our CLS-TA into the SCS together with Eylea injected into the vitreous, as compared to an intravitreal injection of Eylea alone. We believe that SCS administration of our CLS-TA, 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 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 CLS-1003 will be similar to that of current intravitreal anti-VEGF treatments alone, as SCS injections of CLS-TA should allow the corticosteroid to remain substantially localized in the retina and choroid without introducing the side effects that are commonly observed with other routes of administration of corticosteroids. Our planned clinical trials will evaluate this side effect profile.

Under our CLS-1002 program, we are evaluating a number of compounds as potential therapies for the treatment of wet AMD by SCS injection, including compounds with anti-VEGF activity and compounds with dual anti-VEGF and anti-platelet derived growth factor, or anti-PDGF, activity. 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. We have completed a Phase 1 clinical trial evaluating the safety and efficacy of SCS injection of Avastin, an anti-VEGF drug, in four patients with wet AMD. In this trial, SCS injection of Avastin was observed to be well tolerated, with no treatment-related serious adverse events and no unexpected adverse events. In addition, the four patients showed an average improvement in visual acuity of nine letters on a standard eye chart at the end of the eight-week post-treatment observation period. Two of the four patients showed an improvement in visual acuity of at least 13 letters. Because wet AMD manifests in the retina and choroid, we believe that SCS injection of drug more directly to the retina and choroid may result in faster onset of therapeutic effect as compared to intravitreal injection, and could reduce the necessary frequency of treatment to once every 90 days. We plan to further study this effect in any future clinical trials that we conduct as part of our CLS-1002 program.

Our drug candidates, microinjector, and method of non-surgical drug administration into the SCS are protected by four issued U.S. patents and over 20 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 into the SCS by injection and are not scheduled to expire until between 2027 and 2029. Our patent applications relate to SCS administration 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 2034.

If our product candidates are approved, we plan to commercialize them with a specialty sales force of 30 to 40 representatives to target 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, CIBA Vision and ISTA Pharmaceuticals. Members of our team have contributed to the development, regulatory approval and commercialization of several retinal products, such as Triesence, Iluvien, Nevanac, Visudyne and Xibrom.

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 CLS-1001 and CLS-1003 to FDA approval under the Section 505(b)(2) NDA regulatory pathway.*** Our most advanced product candidates, CLS-1001 and CLS-1003, utilize CLS-TA, 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 plan to advance CLS-1001 into a single pivotal Phase 3 clinical trial for macular edema associated with non-infectious uveitis and, based on our pre-IND meeting and subsequent written correspondence with the FDA, we expect this single trial to be sufficient to support a 505(b)(2) NDA filing. Our goal is to submit the 505(b)(2) NDA for CLS-1001 in the first half of 2017. Separately, we plan to initiate a Phase 2 clinical trial for CLS-1003 in early 2015 for macular edema associated with RVO, with data expected in the second half of 2015.
- ***Maximizing the commercial potential of our product candidates.*** If either CLS-1001 or CLS-1003 is approved, we plan to build a specialized sales force of approximately 30 to 40 representatives 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 therapies for other back of the eye diseases that can be treated more effectively with SCS injection.*** We believe that SCS injection of ocular therapies could have benefits in a variety of other back of the eye indications. Our initial areas of focus for development include:
    - *Advancing our CLS-1002 wet AMD development program.* We are investigating opportunities to improve the treatment of wet AMD through SCS injection of compounds that are commonly used for this disease, such as anti-VEGF drugs, or have shown clinical promise, such as anti-VEGF drugs in combination with anti-PDGF drugs. These therapies are commonly administered by intravitreal injection. We have completed an exploratory Phase 1 clinical trial using an anti-VEGF drug, Avastin, administered into the SCS, rather than intravitreally, in four patients with wet AMD, from which we observed encouraging safety and efficacy results. We are conducting preclinical studies evaluating other compounds with dual anti-VEGF and anti-PDGF activity, with the goal of selecting a lead drug candidate under this program for IND submission in early 2016.
    - *Developing a product candidate to treat DME.* DME, like uveitis and RVO, is characterized by an inflammatory aspect. Once the data from the CLS-1003 Phase 2 clinical trial have been analyzed, we intend to initiate clinical trials to develop a product candidate to treat DME modeled after our approach for addressing macular edema associated with RVO.
    - *Developing additional therapies through collaborations with third parties*. We plan to explore collaborations with third parties to develop SCS-administered treatments for back of the eye diseases. These collaborations may take the form of in-licenses of the third parties' drugs or drug candidates for our own development for SCS injection, or out-licenses for third parties to use our intellectual property covering SCS injection as part of the development of their own drugs. We are currently studying several compounds under a research collaboration with Santen Pharmaceutical Co., Ltd.
- ***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 non-surgical SCS delivery methods, novel formulations of drugs, and microinjectors used to access 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 2034. 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 back of the eye diseases to be administered to the retina and choroid through the SCS using our proprietary 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 SCS injection, as compared to the distribution of the same drug following intravitreal injection. We believe this suggests that SCS injection may have similar or better efficacy with a faster onset of therapeutic effect than intravitreal injection in diseases of the retina and choroid like uveitis, RVO, wet AMD and DME.

- ***Similar efficacy profile with lower drug amounts required.*** In a preclinical study in an animal model of uveitis, SCS 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 an SCS injection of CLS-TA, which addresses the inflammatory aspect of RVO, may have similar efficacy with a reduction in the frequency of required anti-VEGF treatments from once every 30 days to once every 90 days. In wet AMD, we believe that more direct application of drugs with anti-VEGF or dual anti-VEGF and anti-PDGF activity to the neovascularization in the choroid through SCS injection may block the process of additional new vascular growth within the choroid before the vessels break into the retina and create further damage through leakage. We believe that such SCS injection of treatment therefore has the potential to 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.
- ***Enhanced safety profile.*** Intravitreal injections result in drugs diffusing throughout the eye, including into the lens, iris and ciliary body at the front of the eye, which for some drugs, has been associated with safety issues, such as cataracts and elevated IOP levels. Intravitreal administration of TA has been associated with cataracts and increases in IOP levels in 20% to 60% of patients. Because SCS injection of drugs appears to result in drug remaining localized in the retina and choroid without substantial diffusion to the vitreous or the front portion of the eye, we believe SCS injection has the potential to reduce the incidence of these side effects. Based on interim results from our ongoing Phase 1/2 clinical trial, none of the eight patients dosed in the trial have experienced cataracts, abnormally high levels of IOP or other treatment-related serious adverse events over the course of 26 weeks following a single SCS injection of TA.
- ***Incorporated into standard medical practice.*** If approved for marketing, our drugs will be packaged together with our SCS microinjector for one-time use by retinal specialists in their offices. Our product candidates are designed to be administered using a similar procedure as is used for intravitreal injections, and no capital equipment will be required. Accordingly, we expect our products, if approved, will be easily incorporated into retinal specialists' standard medical practice.

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

Development Program	Indication	Route of Administration and Active Ingredient	Status and Upcoming Milestones
CLS-1001	Macular edema associated with non-infectious uveitis	SCS injection of CLS-TA	•Final results from ongoing Phase 1/2 clinical trial with Triesence expected 1H 2015 •Screening patients for ~30-patient Phase 2 clinical trial with CLS-TA, with data expected mid-2015 •Initiate ~150-patient single pivotal Phase 3 clinical trial in mid-2015 with CLS-TA, with 505(b)(2) NDA filing expected 1H 2017
CLS-1003	Macular edema associated with RVO	SCS injection of CLS-TA together with intravitreal injection of anti-VEGF compound	•Initiate ~40-patient Phase 2 clinical trial in early 2015 with data expected 2H 2015
CLS-1002	Wet AMD	SCS injection of anti-VEGF compound or compound with dual anti-VEGF and anti-PDGF activity	•Exploratory Phase 1 clinical trial with Avastin completed outside the U.S. •Selection of lead drug candidate for IND submission expected in early 2016

We have discussed our proposed clinical development program with the FDA for CLS-1001, but have not yet done so for our planned CLS-1003 and CLS-1002 development programs.

CLS-1001 Program Targeting Macular Edema Associated with Non-infectious Uveitis

We are developing CLS-1001 for treatment of macular edema associated with non-infectious uveitis, a condition characterized by inflammation of the choroid and surrounding tissues. CLS-1001 consists of an SCS injection of CLS-TA, our proprietary formulation of TA specifically designed to be administered through our SCS microinjector. We expect final results from our ongoing Phase 1/2 clinical trial in the first half of 2015. We are currently screening patients for potential enrollment in a Phase 2 clinical trial with CLS-TA in approximately 30 patients, with expected data in the mid-2015. We also plan to initiate a single pivotal Phase 3 clinical trial in approximately 150 patients in mid-2015, with a Section 505(b)(2) NDA filing expected in the first half of 2017. We believe that CLS-1001 will be at least as effective in treating uveitis, including the associated macular edema, as commonly used treatments with corticosteroids, but has the potential to 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 CLS-1001 may result in fewer side effects compared to commonly used corticosteroid treatments, and we are testing this potential side effect profile in clinical trials.

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 one or both eyes and accounts for approximately 10% of cases of blindness in the United States, according to a study published in *Journal of Ophthalmology*. Uveitis can be either infectious or non-infectious. Non-infectious uveitis accounts for approximately 80% of all uveitis cases. Macular edema related to uveitis is the predominant cause of blindness or visual impairment among patients with uveitis, accounting for approximately 30% of cases of blindness in uveitis patients. Because uveitis can become chronic or recurrent if not adequately treated, some patients may become refractory, or unresponsive, to treatment, leading to irreversible blindness.

Limitations of Currently Available Therapies for 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 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. Examples of intravitreal corticosteroid treatments include Ozurdex®, Retisert®, Kenalog® and Triesence. Ozurdex is a biodegradable dexamethasone implant that has been approved by the FDA as a treatment for non-infectious uveitis, but has been associated with increased IOP in 25% of patients, conjunctival hemorrhages in 22% of patients and cataracts in 5% of patients. Retisert, a non-biodegradable fluocinolone acetonide implant that requires surgical administration, has also been approved by the FDA as a treatment of 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 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 in uveitis or most of the other complications associated with uveitis.

Potential Benefits of CLS-1001

If approved by the FDA, CLS-1001 would be the first treatment specifically indicated for macular edema associated with non-infectious uveitis. Because CLS-1001 is based on our CLS-TA formulation of TA, a

corticosteroid known to be effective in treating uveitis, we believe that our product candidate will be at least as effective as TA in treating the disease, including the associated macular edema. Our clinical development program for CLS-1001 has been designed to test this hypothesis. Our preclinical studies suggest that SCS injection of TA may provide improved bioavailability of drug at the retina and choroid, which could result in faster onset of therapeutic effect and a similar efficacy profile with lower drug amounts required. Our early clinical trial results suggest the potential for CLS-1001 to be effective at treating uveitis for at least 90 days following a single SCS injection. Currently used ocular injections of TA are typically effective for approximately 90 days. In contrast to intravitreal injections, based on our preclinical studies, we believe that SCS injection will allow the drug to remain more localized in the diseased retina and choroid. As a result of this localization, we believe that CLS-1001 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 for CLS-1001.

Initial Clinical Research on Surgical Administration of TA into the SCS

In 2011, two separate studies were published by researchers evaluating administration of TA together with the anti-VEGF drug Avastin in a total of 27 patients with severe retinal disease. In one study, six patients had RVO or DME, and in the other study, 21 patients had wet AMD. In both studies, a surgical procedure was used to cut open the eye to expose the choroidal tissue and insert a small tube into the SCS, through which both TA and Avastin were administered. The six RVO and DME patients were followed for one year and the 21 wet AMD patients were followed for six months. Of the 27 patients, only one patient had developed cataracts, and one other patient was in the initial stages of cataract formation at the end of the observation period. In addition, only one patient showed elevated IOP, which was controlled with a topical glaucoma medication. We believe these studies suggest that surgical administration of TA into the SCS might present a lower risk of increased IOP and cataracts than intravitreal injection of TA, which has been associated with increases in IOP or cataract progression in 20% to 60% of patients.

Our Clinical and Preclinical Development of CLS-1001 for Non-Surgical Administration

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 non-surgically using a prototype of our microinjector, as part of our CLS-1001 development program:

- an ongoing Phase 1/2 clinical trial in non-infectious uveitis patients evaluating SCS injections of Triesence, a commercially available TA formulation, with our microinjector, from which we expect final safety and efficacy data in the first half of 2015;
- a completed preclinical study comparing the pharmacokinetic effects of SCS and intravitreal injection of Triesence in rabbits;
- a completed preclinical study comparing the pharmacokinetic effects of SCS injection of CLS-TA and Triesence in rabbits;
- a completed preclinical study evaluating the pharmacodynamic effects of SCS and intravitreal injection of Triesence in a pig model of uveitis; and
- completed preclinical studies evaluating the toxicology of SCS injection of CLS-TA and Triesence in rabbits.

Details of this trial and these studies are summarized below.

Ongoing Phase 1/2 Clinical Trial

In July 2013, we initiated 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 is being 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 add macular edema following non-infectious uveitis as a treatment indication. The primary purpose of this trial is to demonstrate the overall safety of treating uveitis patients by administering a commercially available formulation of TA into the SCS, rather than intravitreally. We expect to use CLS-TA for all future clinical trials intended to support a 505(b)(2) NDA submission for CLS-1001.

Clinical Trial Design. We intended to enroll approximately 10 patients at three centers in this trial. We completed enrollment after dosing the eighth patient. Eligibility criteria include adult patients with non-infectious uveitis experiencing either macular edema or vitreous haze, another common complication of uveitis. We are enrolling patients with either of these complications of uveitis in order to assess the safety and tolerability of SCS injection of TA and to determine whether SCS injection of TA can improve patient vision by reducing the effects of either of these conditions. For inclusion in the trial, patients must have IOP 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.

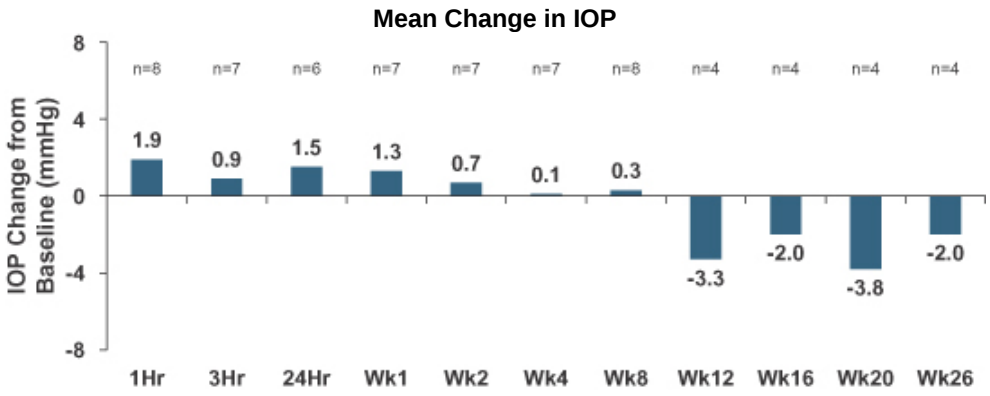
Each patient enrolled receives a single SCS microinjection of 4.0 mg of Triesence, a common intravitreal dose of TA, at a location at the front of the eye similar to the location typically used for intravitreal injection. Patients return for a follow-up examination on the day after the injection and then for eight additional evaluations at weeks 1, 2, 4, 8, 12, 16, 20 and 26 following the treatment. Patients may receive other treatment for non-infectious uveitis at any time during the trial with any accepted therapy, if the patient's condition deteriorates or if the treating physician otherwise determines it to be advisable. In the event a patient receives other treatment, we continue to follow the patient for the duration of the trial for safety purposes, but we thereafter no longer evaluate efficacy measures.

This Phase 1/2 clinical trial is 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 is not powered to show results with statistical significance, the results from the trial may be attributable to chance and not 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 is primarily a safety and tolerability study, although we are also assessing efficacy measures. The main safety endpoint relates to changes from baseline in IOP. We are also assessing 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 and is measured as the number of letters that the patient can read on the Early Treatment Diabetic Retinopathy Study, or ETDRS, eye chart. The ETDRS eye chart is a well-established standardized method of testing visual acuity.

Interim 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. Four of these eight patients have completed the full 26-week observation period. No patient has experienced a clinically meaningful increase in IOP, defined as a 10 mmHg increase in IOP from baseline, or an absolute increase in IOP to a level above 25 mmHg, which symptoms are typically seen at four to 12 weeks after administration. In contrast, the prescribing information for 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, no patient has 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 to these IOP observations, the drug has been generally well tolerated in the trial to date. 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.

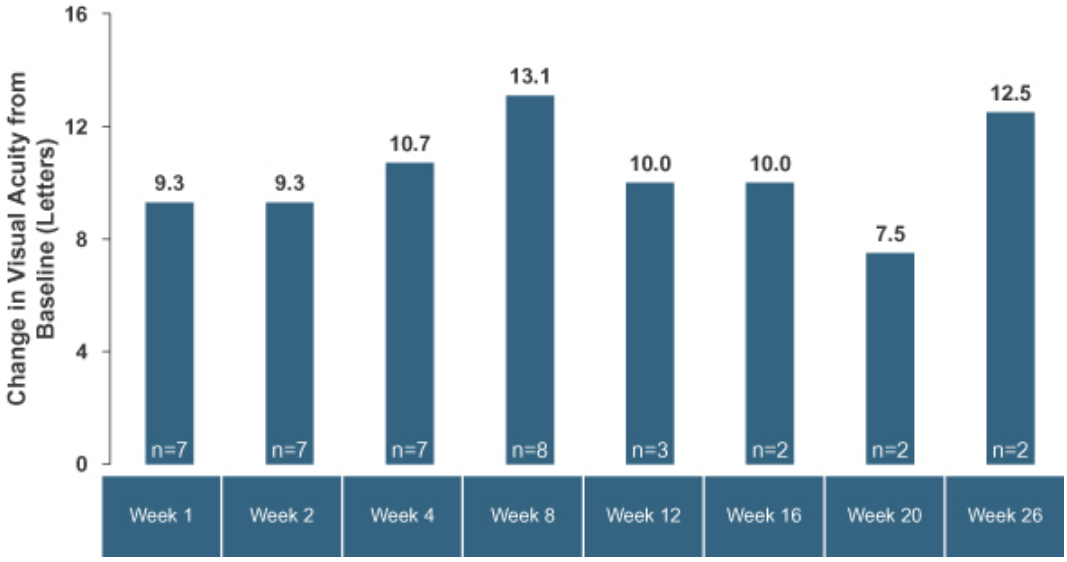
Interim Efficacy Results — Visual Acuity. Data are available at week 8 with respect to BCVA for each of the eight patients who have received treatment. At each follow-up examination, the change in BCVA was measured as the difference from the patient's baseline in the number of letters read on the ETDRS eye chart. Of these eight patients, two patients have completed the entire 26-week observation period without receiving other treatment for non-infectious uveitis. One patient received other treatment for non-infectious uveitis at week 8 and one patient received other treatment for non-infectious uveitis at week 16.

The chart below summarizes the mean improvement in BCVA observed to date in the trial for these eight patients. At eight weeks after a single SCS injection of Triesence, the visual acuity of all eight patients had improved by five or more letters on a standard eye chart over baseline, a clinically meaningful improvement. Five of the eight patients who have reached week 8, or approximately 63% of these patients,

had improved BCVA by at least 15 letters at week 8, compared to Ozurdex, for which approximately 40% of patients had improved BCVA by at least 15 letters at week 8.

In addition to the number of patients varying at each time point as a result of missing follow-up visits or inadvertently skipped measurements, as described above under "—Interim Safety Results," 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.

Improvement in Best Corrected Visual Acuity (Number of Letters Read on ETDRS Chart)



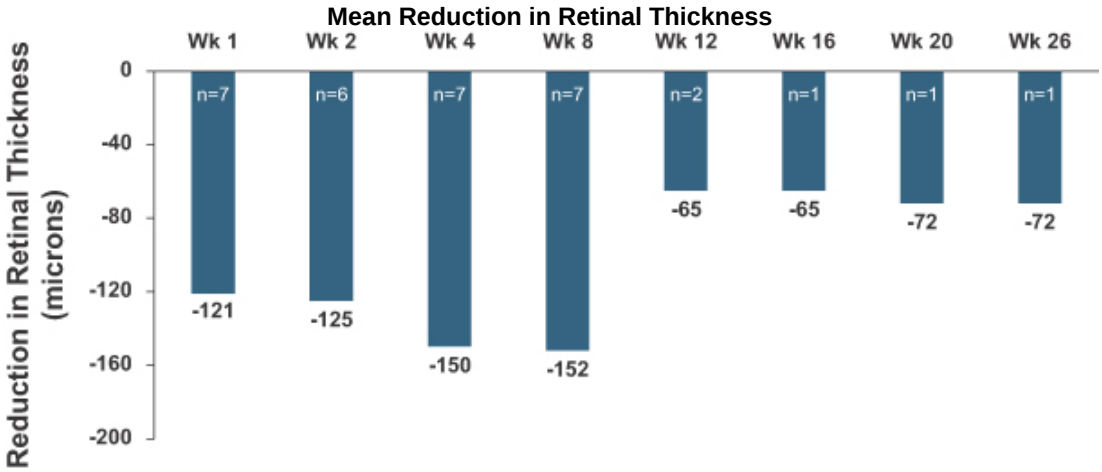
We believe these interim safety results are generally comparable to BCVA improvement observed in clinical trials of Ozurdex, in which patients with non-infectious uveitis achieved an average improvement of 13 letters at week 8 after treatment and 10 letters at week 26.

Interim Efficacy Results — Retinal Thickness. Of the eight patients treated in the trial, seven were experiencing macular edema 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 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 to date in the trial in the seven evaluated patients. Data are available at week 8 with respect to retinal thickness for each of the seven evaluated patients. Each of these seven patients achieved clinically meaningful reductions in retinal thickness

of at least 50 microns from their respective baselines by week 8 following treatment. In addition, by week 8, five of these seven evaluated patients experienced a reduction in retinal thickness to near or below 310 microns, which represents the maximum retinal thickness for 95% of the population with normal retinas. One micron is equal to one-thousandth of one millimeter. The reduction in retinal thickness experienced by one of the other two patients was over 20% from the patient's baseline. Both of these measures are considered clinically meaningful improvements. For the three patients experiencing macular edema who have completed the study, their levels of reduction were generally sustained throughout the remainder of their measurement periods of 8, 12 and 26 weeks, respectively.

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 "—Interim 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.



We believe these interim results are encouraging because we observed a rapid and persistent effect in the back of the eye after the SCS injection procedure at a location at the front of the eye similar to the location typically used for intravitreal 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 to date, in an open-label setting, were not statistically significant and might not be achieved by any additional patients observed in this trial or replicated in larger-scale trials that we intend to conduct.

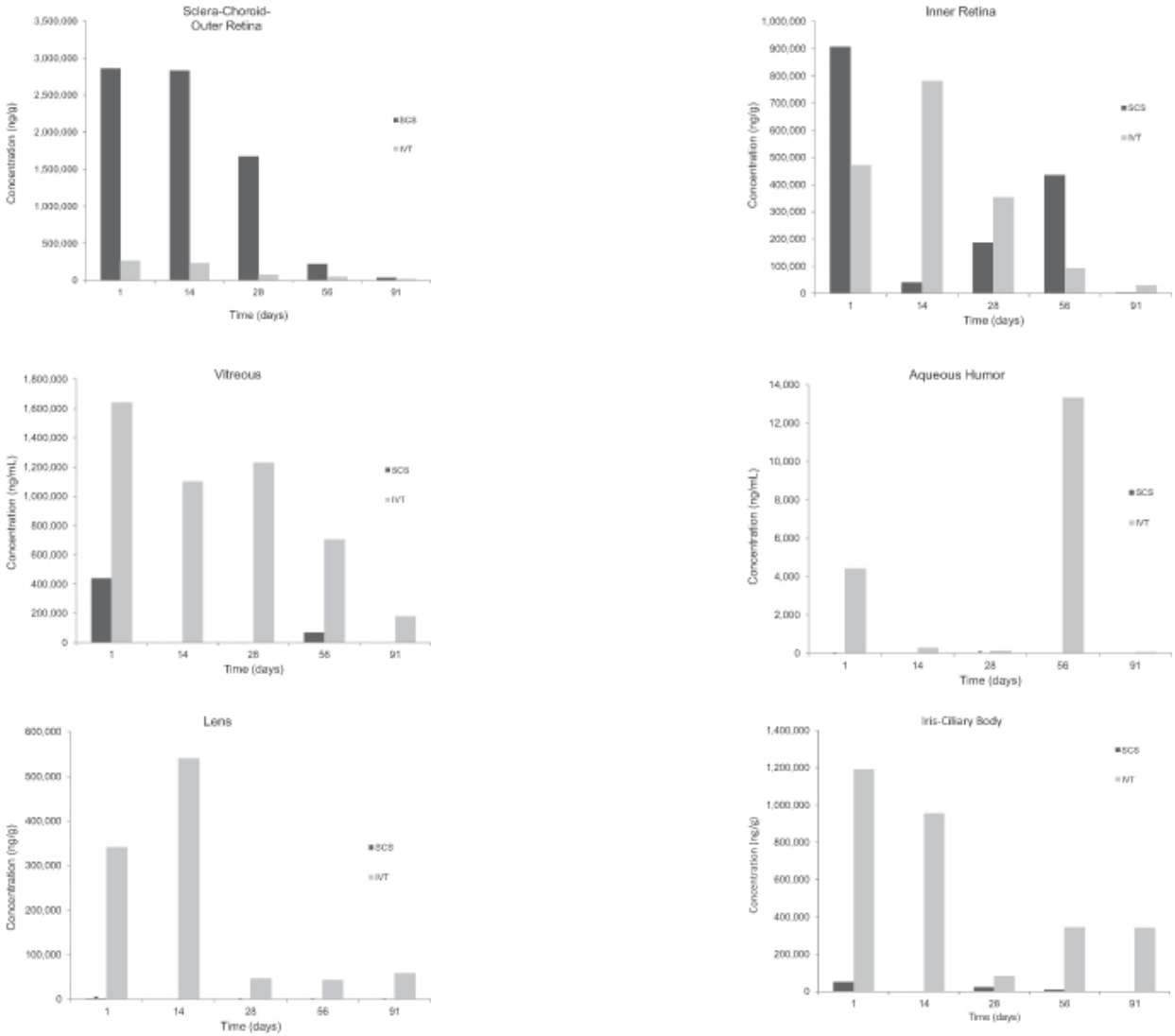
Preclinical Study Comparing the Pharmacokinetic Effects of SCS and Intravitreal Injection of Triesence in Rabbits

We conducted a preclinical study in rabbits to compare the pharmacokinetic results of SCS 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 SCS or Intravitreal (IVT) Injection



In the inner sclera, choroid and outer retina, significantly higher concentrations of TA administered into the SCS were present throughout the 91-day period as compared to TA administered 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 administered intravitreally as compared to its administration into the SCS. Only minimal levels of TA were present in the iris, ciliary body, lens and aqueous humor when administered 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.

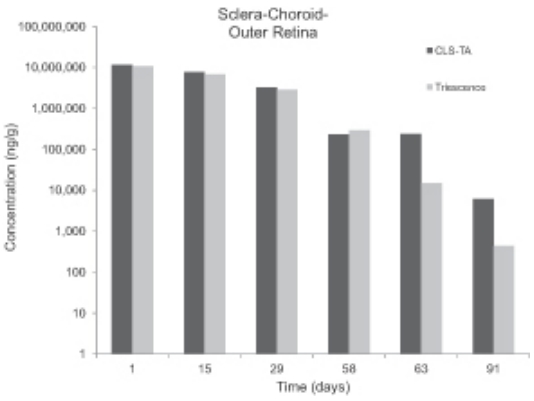
We believe these preclinical study results suggest that drugs administered through the SCS can remain substantially localized within the targeted retina and choroid, and away from other parts of the eye, where they could result in a higher incidence of side effects. We also believe these results suggest that SCS 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.

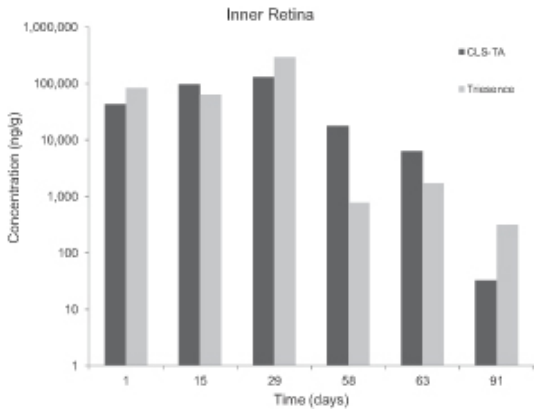
Preclinical Study Comparing the Pharmacokinetic Effects of SCS Injection of CLS-TA and Triesence in Rabbits

In order to establish that our CLS-TA 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 our CLS-TA 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 our CLS-TA 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, our CLS-TA and Triesence had comparable distributions throughout the eye over the 90-day period. As shown in the graphs below, both our CLS-TA and Triesence, administered through the SCS, remained present in the retina and choroid throughout the 90-day period following injection.

Concentration of Either CLS-TA or Triesence Following SCS Injection

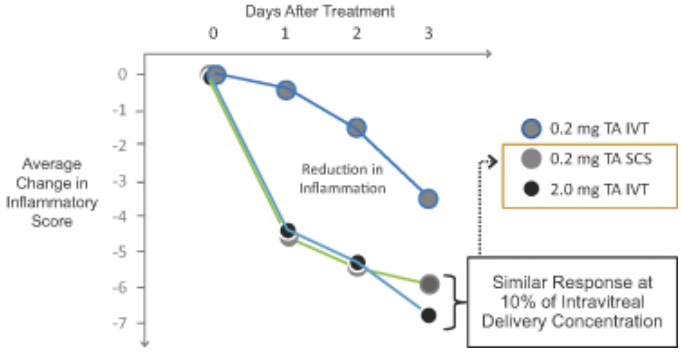




Preclinical Study Evaluating the Pharmacodynamic Effects of SCS and Intravitreal Injection of Triesence in a Pig Model of Uveitis

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 SCS 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, SCS injection of Triesence had a similar pharmacodynamic response to intravitreal administration at only 10% of the dose. The graph below illustrates these results.

Reduction in Inflammation Following Either SCS or Intravitreal Injection of Triesence in a Pig Model of Uveitis



Preclinical Studies Evaluating the Toxicology of SCS Injection of CLS-TA and Triesence in Rabbits

We have conducted toxicology studies in rabbits in which both our CLS-TA and Triesence were well tolerated when injected into the SCS. In one study, 110 rabbits received a single SCS 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 SCS injection of either 4.0 mg of our CLS-TA or of vehicle control and were then evaluated for the following 13 weeks. A subgroup of the 48 rabbits received a second SCS injection of our CLS-TA 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 our CLS-TA and Triesence were well-tolerated. In the study in which rabbits received our CLS-TA, 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.

Planned Phase 2 Clinical Trial

Based on our preclinical data and on our consultation with the FDA, we plan to conduct a Phase 2 randomized, controlled, multi-center clinical trial in the United States in approximately 30 patients with macular edema associated with non-infectious uveitis. We are currently screening patients for enrollment in this trial. Of the approximately 30 patients to be enrolled, approximately equal numbers of patients will receive either a 4.0 mg dose of our CLS-TA, which is the standard dose of TA when administered intravitreally, or a lower dose of 0.8 mg of our CLS-TA, in both cases administered through the SCS with our microinjector. The trial will provide safety and efficacy information on SCS injection of our CLS-TA using the standard dose. We intend to explore the lower dose in this trial to assess whether efficacy may be observed at the lower dose. If the results of the Phase 2 clinical trial suggest that a lower dose is effective, we may seek to explore, and potentially seek approval of, the lower dose subsequent to the completion of our planned Phase 3 clinical trial using the standard 4.0 mg dose.

The primary efficacy endpoint will be the mean change from baseline in retinal thickness at two months after treatment. Secondary efficacy endpoints will include visual acuity improvements at one and two months post-treatment, measured by the mean change in BCVA from baseline. Safety measures will be monitored over the two-month observation period and will include the incidence of adverse events and serious adverse events, including cataracts and increases in IOP.

Planned Pivotal Phase 3 Clinical Trial

We intend to conduct a single pivotal Phase 3 randomized, controlled, multi-center clinical trial in patients with macular edema associated with non-infectious uveitis to support a Section 505(b)(2) NDA for this indication, which we expect to be able to file in the first half of 2017. We expect to commence this trial in mid-2015.

We held a pre-IND meeting with the FDA in September 2012, at which we discussed our proposed clinical development plan for CLS-1001. We then scheduled a meeting with the FDA for August 2013 and submitted questions related to our planned clinical trials. Based on the written responses that we received from the FDA, we elected not to proceed with the requested meeting, and the responses from the FDA became the final minutes for the meeting. Based on these discussions and this correspondence with the FDA, we do not expect to be required to wait for findings from our Phase 2 clinical trial to begin the single pivotal Phase 3 clinical trial and we expect that the single pivotal trial will be sufficient to support a potential Section 505(b)(2) NDA filing. We expect to enroll approximately 150 patients with macular edema associated with non-infectious uveitis, randomized 1:1 either to a treatment arm or to a sham injection arm. We expect to use a sham injection as a comparator for CLS-1001, as opposed to an active drug, because there are no approved therapies for macular edema associated with non-infectious uveitis against which to compare CLS-1001. All of the approximately 75 patients in the treatment arm will receive a 4.0 mg dose of our CLS-TA injected into the SCS using our microinjector. In order to simulate an injection to maintain masking, the sham injection procedure will include all steps involved in the SCS injection procedure, except that an empty microinjector without a needle will be used to apply pressure to the eye. We anticipate that the treatment arm will receive an initial SCS injection of our CLS-TA at the beginning of the trial and a second SCS injection of our CLS-TA at week 12.

The primary efficacy endpoint of the trial will be mean change in BCVA from baseline at week 26. Secondary efficacy endpoints will include additional measures of change in visual acuity and reductions in

retinal thickness from baseline. Safety measures will be monitored over the 26-week observation period and will include the incidence of adverse events and serious adverse events, including cataracts and increases in IOP.

Regulatory Approval Pathway of CLS-1001

If our single pivotal Phase 3 clinical trial is successful, we intend to seek regulatory approval of CLS-1001 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 our ongoing Phase 1/2 clinical trial, our planned Phase 2 and single pivotal Phase 3 clinical trials conducted under our existing IND for CLS-TA, as well as the FDA's previous findings of safety and efficacy for TA and an analysis of available data from clinical literature.

Based on our pre-IND meeting and subsequent written correspondence with the FDA, we believe this single pivotal Phase 3 clinical trial will be sufficient to support our NDA filing for macular edema associated with non-infectious uveitis pursuant to Section 505(b)(2). We also intend to base any foreign marketing applications, in part, on data obtained through these trials.

Orphan Drug Application for CLS-1001

We have applied for orphan drug designation from the FDA in the United States, and intend to apply for orphan drug designation from the European Medicines Agency in the European Union for CLS-1001 for the treatment of non-infectious uveitis. Orphan drug designation for this indication would make us eligible for seven years of marketing exclusivity in the United States and 10 years of marketing exclusivity in the European Union, if we receive the first marketing approval of TA for macular edema associated with non-infectious uveitis. Orphan drug designation would also provide us with certain tax incentives and user fee waivers. However, even if we are able to obtain orphan drug designation, it will not convey any advantage in, or shorten the duration of, the regulatory review and approval process for our marketing application. In addition, even if we ultimately obtain marketing exclusivity, competition is still possible if, for example, different drugs are approved for the same indication, a similar drug is shown to be clinically superior to ours, doctors prescribe a competitor's products for off-label use, or a patent to which we do not have rights covers our drug product, in each case undermining our orphan drug exclusivity and our opportunity to market our drug successfully, if at all.

CLS-1003 Program Targeting Macular Edema Associated with Retinal Vein Occlusion

We are developing CLS-1003 for treatment of macular edema associated with RVO, a sight-threatening disorder resulting from the blockage of a retinal vein. CLS-1003 consists of an SCS injection of CLS-TA with our microinjector, for administration together with an intravitreal injection of an anti-VEGF drug. We plan to initiate a Phase 2 clinical trial in approximately 40 patients in early 2015, with data expected in the second half of 2015. We believe that CLS-1003 may provide faster onset of therapeutic effect compared to currently used intravitreal anti-VEGF injections alone, while also reducing the frequency of required intravitreal anti-VEGF treatments from once every 30 days to once every 90 days. In addition, we believe that the side effect profile of CLS-1003 will be similar to that of current intravitreal anti-VEGF injections alone.

Market Opportunity for Treatment of Macular Edema Associated with 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 macular edema caused by 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. In these studies, approximately 20% 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 therapy, Ozurdex, an extended release corticosteroid implanted in the vitreous, has also been approved by the FDA for the treatment of RVO, but has also been associated with increased IOP in 25% of patients, conjunctival hemorrhages in 22% 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 CLS-1003

We believe that SCS administration of CLS-TA, 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 compared to currently used intravitreal anti-VEGF treatment alone. Based on the SCORE studies described above and our findings in preclinical studies, we believe that each SCS injection of CLS-TA 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 CLS-1003 will be similar to that of current intravitreal anti-VEGF treatments alone, as SCS injections of CLS-TA should allow the corticosteroid to remain substantially localized in the retina and choroid without introducing the side effects that are commonly observed with other routes of administration of corticosteroids.

Planned Clinical Trials

In support of our planned clinical development program for CLS-1003, we are in the process of completing a toxicology study in rabbits with the SCS injection of CLS-TA together with the intravitreal injection of the anti-VEGF drug Eylea. Depending on the outcome of this study, we intend to initiate a Phase 2 randomized, multi-center, double-masked clinical trial of CLS-1003 in early 2015.

Based on our ongoing toxicology study and our clinical and preclinical experience with SCS administration of TA in our CLS-1001 program, we anticipate being able to proceed directly into a Phase 2 clinical trial for CLS-1003. The goal of the Phase 2 clinical trial will be to demonstrate that patients treated with CLS-TA administered into the SCS together with Eylea administered intravitreally may require less frequent treatments than monotherapy of Eylea administered intravitreally.

We expect to enroll approximately 40 patients at 10 sites in the United States for the Phase 2 clinical trial. All patients will start by receiving one intravitreal injection of 2.0 mg of Eylea, in a total volume of 50 microliters, and will then be randomized on a 1:1 basis to receive an SCS injection of either 4.0 mg of our CLS-TA, in a total volume of 100 microliters, or a sham procedure in the same visit. After randomization, patients will be seen in the clinic once per month for three months. Patients in the CLS-TA treatment arm will receive additional intravitreal injections of Eylea at the subsequent visits one and two months after the initial injection if they continue to experience increases in macular edema or reductions in visual acuity. If they do not experience increases in macular edema or reductions in visual acuity at these subsequent visits, they will not receive additional intravitreal Eylea treatment. Patients in the control arm will receive monthly intravitreal Eylea injections, as specified on the Eylea label.

The primary objective of the trial will be to evaluate the safety and efficacy of a single SCS injection of CLS-TA together with the initial intravitreal injection of Eylea, compared to monthly intravitreal Eylea injections alone. The primary efficacy endpoints in the trial will include determining the number of required Eylea treatments in each arm, which we believe will provide an indication of whether concomitant therapy provides any advantage to the patient in reducing the number of required Eylea treatments. Secondary efficacy endpoints will include measures of change in visual acuity and reductions in retinal thickness from baseline. The safety endpoints will be the incidence of adverse events and serious adverse events, including increases in IOP.

Regulatory Approval Pathway

To date, we have not met formally with the FDA to discuss our clinical development plan for the CLS-1003 program. However, we intend to meet with the FDA following the completion of our Phase 2 clinical trial to discuss the details of the regulatory approval pathway for CLS-1003. If the results of our planned Phase 2 clinical trial are positive, we expect to be able to follow a 505(b)(2) NDA regulatory approval pathway and to conduct one or two pivotal Phase 3 clinical trials in order to support an NDA submission for CLS-1003 in macular edema associated with RVO. In pursuing the 505(b)(2) regulatory pathway, we intend to rely on the results from our planned CLS-1003 clinical trials, the FDA's previous findings of safety and efficacy for TA, and peer-reviewed literature.

CLS-1002 Program Targeting Wet Age-Related Macular Degeneration

Under our CLS-1002 program, we intend to develop a treatment for wet AMD that, through SCS administration with our microinjector, could 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. We have completed a Phase 1 clinical trial evaluating the safety and efficacy of SCS injection of Avastin, an anti-VEGF drug, in four patients with wet AMD. We are evaluating a number of compounds as SCS-injected therapies for the treatment of wet AMD, including compounds with anti-VEGF activity, and compounds with dual anti-VEGF and anti-PDGF activity, and expect to select a lead drug candidate for IND submission in early 2016. We believe that CLS-1002 may show faster onset of therapeutic effect as compared to intravitreal injection, while potentially reducing the frequency of necessary treatment. We plan to further study this effect in any future clinical trials that we conduct as part of our CLS-1002 program.

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, 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 Lucentis alone. However, no anti-PDGF therapy has been approved by the FDA for the treatment of wet AMD. Even if approved, we expect that anti-PDGF therapy would also require regular injections indefinitely.

Even though anti-VEGF and anti-PDGF therapies may be effective in treating wet AMD, intravitreal administration 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 CLS-1002

The compounds we are evaluating have anti-VEGF activity, and we believe these compounds should provide the clinically established advantages that currently used anti-VEGF drugs provide, especially the reduction in macular edema and improvements in visual outcomes. Some of the compounds we are evaluating have dual anti-VEGF and anti-PDGF activity. We believe that the anti-PDGF properties together with anti-VEGF properties may provide superior visual outcomes to standalone anti-VEGF drugs. We believe that the SCS administration of drugs with anti-VEGF, or dual anti-VEGF and anti-PDGF, activity more directly to the neovascularization in the choroid through SCS 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 SCS 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 administration, potentially only once every 90 days. We will test this hypothesis in any future clinical trials that we may conduct as part of our clinical development program for CLS-1002.

Clinical and Preclinical Development of CLS-1002

We have completed the following clinical trial and preclinical studies as part of our CLS-1002 development program:

- a completed Phase 1 clinical trial in wet AMD patients evaluating the safety and tolerability of SCS injection of Avastin, an anti-VEGF drug, with our microinjector;
- a completed preclinical efficacy study of a compound with dual anti-VEGF and anti-PDGF activity in a rabbit model of wet AMD; and
- a completed preclinical safety study of SCS injection of compounds with dual anti-VEGF and anti-PDGF activity.

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 SCS administration of Avastin, an anti-VEGF drug, in humans with our 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 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 SCS 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. SCS 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 SCS 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 SCS 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 SCS 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 CLS-1002 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 SCS injection. In this study, the treatment arm of three rabbits received an SCS injection of the drug and the control arm of three rabbits received an SCS 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 Safety Study of SCS 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 SCS injection. In this study, a total of 18 rabbits received an SCS 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.

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 SCS injection, and we will evaluate this hypothesis as part of any clinical development program for CLS-1002. We will continue to evaluate the SCS injection of a number of compounds with anti-VEGF and anti-PDGF activity to assess their potential for clinical development for the treatment of wet AMD. Once we select a lead compound for clinical development, we expect to perform pharmacokinetic and toxicology studies, as well as additional preclinical testing, to support an IND filing in the first half of 2016.

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 SCS 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 and wet AMD, there are a number of ophthalmic conditions affecting the retina and choroid with unmet medical need for which SCS injection of therapy may be beneficial, including:

- *Diabetic macular edema*, or 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;
- *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; and

- *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.

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 21.0 million in 2010. 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.

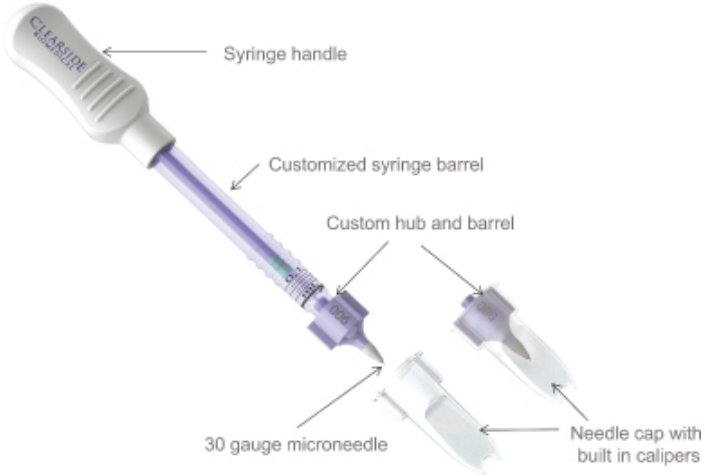
Currently, the only FDA-approved drugs for the treatment of DME are the anti-VEGF drugs Lucentis and Eylea and the intravitreal corticosteroid implant Ozurdex. Some retinal specialists also prescribe other anti-VEGF drugs for off-label use, such as Avastin, as well as corticosteroid therapies, primarily Kenalog and Triesence, and laser photocoagulation to treat DME. 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.

Our development program for DME will be modeled after our approach for addressing macular edema associated with RVO. We expect that any clinical trials we may conduct for this indication will be designed based on the results observed in our Phase 2 clinical trial of CLS-1003 in RVO patients.

Our Proprietary SCS Microinjector

Our drug candidates have been and will be specifically formulated to be injected with our microinjector into the SCS in order to spread around to the back of the eye. The single-use microinjector is intended to consistently administer 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 microinjector will be packaged with two 30-gauge hollow microneedles of varying lengths, each less than 1.2 millimeters, to account for varying scleral thicknesses, within a custom-designed hub that optimizes insertion 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 microinjector, but this could change during the course of its review of any marketing application that we may submit.

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

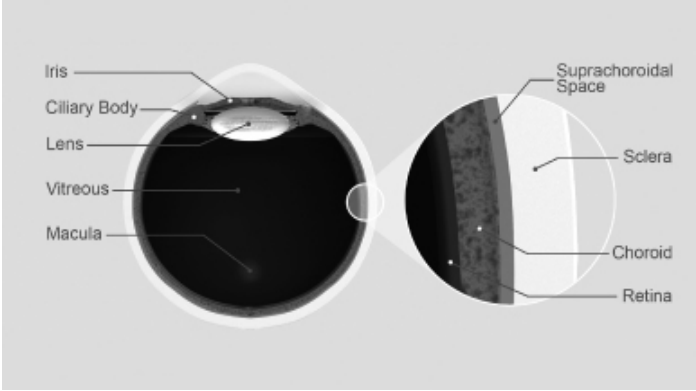


The SCS microinjection is designed to be made perpendicular to the sclera, at a site similar to an intravitreal administration, under local anesthesia. Once the microneedle penetrates the sclera and reaches the SCS, the boundary between the sclera and the choroid, the open bevel of the needle releases 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 SCS injections, except that the hypodermic needles and syringes used in intravitreal injection procedures are designed to inject through all of the layers of the eye and into the vitreous, where the precise spacial 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. With our microinjector, however, the needle hub is designed to enable the release of the drug into the SCS only after the needle passes the sclera and to prevent penetration into the layers beyond the SCS.

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 a group of ocular conditions that are characterized by inflammation that typically affects the choroid and surrounding tissues. 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. Macular edema 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.

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 AMD.

Wet AMD occurs when new blood vessels in the choroid intrude into the retinal layers. This is referred to as choroidal neovascularization. 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 scarring, resulting in irreversible destruction of the macula and 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 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 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. Patients typically receive injections as often as seven times per year to manage this chronic disease.

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 21.0 million in 2010. 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 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, both anti-VEGF drugs and corticosteroids administered intravitreally are limited by a need for frequent injections to maintain a therapeutic effect. 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. Laser photocoagulation can also have undesirable side effects, including partial loss of peripheral and night vision.

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 deliver 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 SCS 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 microinjector components used for our clinical trials. We assemble our microinjector ourselves 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 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, ISTA and Novartis.

For marketing in the United States, we intend to hire a dedicated field sales force consisting of approximately 30 to 40 sales 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 CLS-TA, 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 DME. Ozurdex, marketed by Allergan, is a bioerodable extended release implant that delivers the corticosteroid dexamethasone and is approved for the treatment of macular edema following non-infectious uveitis 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. Alimera Sciences is developing Iluvien, an injectable form of fluocinolone acetonide, as a therapy for DME in the United States Iluvien has been approved in 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 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 and the treatment of macular edema following RVO and 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 retinal vein occlusion and DME. In the European Union, Eylea is approved for the treatment of wet AMD, DME and macular edema secondary to central retinal vein occlusion, and is being reviewed for the treatment of macular edema following branch retinal vein occlusion.

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 four granted U.S. patents broadly directed to methods of administering drugs into the SCS by injection. In addition, our patent estate includes five patent applications pending in the United States, two issued foreign patents, four pending international PCT applications and 13 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 the four issued U.S. patents, one pending U.S. application, the two issued foreign patents, one of the pending international PCT applications and the 13 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 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 2034, 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 non-surgical administration into the SCS. In the case of CLS-TA 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 uveitic macular edema 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.

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 the 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 refusal by FDA to approve applications, withdrawal of an approval, imposition of a clinical hold, import/export delays, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by 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 are 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 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. 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 withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, 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. 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 all, or some, of the label indications for which the branded reference drug has been approved, as well as for any 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. There might also be no relevant patent certification. 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.

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 intend to seek orphan drug designation and exclusivity for CLS-1001 for the treatment of non-infectious uveitis in the United States and Europe, and we may seek designation for other products in the future, but 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 Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively 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 new federal criminal statutes that prohibit among other actions, 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, such as us. HIPAA also regulates standardization of data content, codes and formats used in health care transactions and standardization of identifiers for health plans and providers. 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 section 6002 of the Affordable Care Act known as the Physician Payment Sunshine Act that imposes new annual reporting requirements on 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 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 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 products 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 SCS injection using our microinjector and for the drug itself. We intend to seek a specific Current Procedural Terminology, or CPT, code as established and maintained by the American Medical Association, or AMA, for the SCS injection of pharmacologic agents using our microinjector, and a separate Healthcare Common Procedure Coding System, or HCPCS, code as maintained by the Centers for Medicare and Medicaid Services, or 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 the AMA or CMS will approve the creation of such new codes applicable to our products.

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 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. Most recently, the Protecting Access to Medicare Act of 2014, signed into law in April 2014, provided for a 0.5% change from 2013 payment rates under the Medicare Physician Fee Schedule through 2014 and a 0% update from January 1 until April 1, 2015. If Congress fails to intervene to prevent the negative update factor in future years, the resulting decrease in payment may adversely affect our revenues and results of operations. 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.

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 will remain in effect through 2024 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. 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, 2014, we had 19 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. We also lease approximately 6,600 square feet of space in Durham, North Carolina for our clinical development and regulatory functions under a lease agreement that expires in May 2015. We believe that our current 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, executive officers and other key employees, including their ages as of August 31, 2014:

Name	Age	Position
Executive Officers:		
Daniel H. White	47	President, Chief Executive Officer and Director
Charles A. Deignan	50	Chief Financial Officer
Glenn Noronha, Ph.D.	49	Executive Vice President, Research and Development
Other Key Employees:		
Rafael V. Andino	49	Vice President, Product Development
Stephen H. Lang	57	Vice President, Commercial Operations
Non-Management Directors:		
Christy L. Shaffer, Ph.D	56	Chairman of the Board of Directors
Clay B. Thorp	46	Director
Evgeny Zaytsev, M.D.	46	Director
Gerald D. Cagle, Ph.D.	70	Director
William D. Humphries	48	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. 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.

Other Key Employees

Rafael V. Andino

Mr. Andino has served as our Vice President, Product Development since February 2013. Since June 2013, Mr. Andino has also served as an adjunct professor of biomedical engineering at the Georgia Institute of Technology. From January 2009 to February 2013, he served as Director of Research and Development for Bard Medical, a division of C.R. Bard, Inc., a publicly traded company. In 1999, Mr. Andino founded, and until 2008 served as President and Chief Executive Officer of Biofisica, Inc., a biotechnology company that developed technology to expedite wound healing and regeneration of connective tissue in humans. Prior to founding Biofisica, from 1995 to 2005 Mr. Andino was a mechanical engineer, research and development director and senior project manager for CIBA Vision, a Novartis company. He has also worked for the global technology companies E.I. Dupont de Nemours, General Electric and IBM. Mr. Andino received his Bachelor's degree in Mechanical Engineering from the Georgia Institute of Technology, a Master of Science in Biomedical Engineering from the University of Alabama at Birmingham and an M.B.A. degree from Mercer University.

Stephen H. Lang

Mr. Lang has served as our Vice President, Commercial Operations since March 2013. From 2006 to June 2012, Mr. Lang served as Vice President of Sales for ISTA Pharmaceuticals, Inc., an ophthalmic product company acquired by Bausch + Lomb in 2012. Previously, Mr. Lang held leadership roles in sales and marketing, serving with Novartis Ophthalmics, Inc. from 1995 to 2003, including as its Senior Vice President of U.S. Sales from 2002 to 2003. Mr. Lang began his career with Allergan, Inc. where he served for more than 16 years in various positions, including sales, marketing, national accounts and global business development. He earned his B.B.A. degree in Management from Georgia Southern University.

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, lnc., 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 lnc. 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 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.

Board Composition

Our board of directors currently consists of six members. Each director is currently elected to the board for a one-year term, to serve until the election and qualification of successor directors at the annual meeting of stockholders, or until the director's earlier removal, resignation or death.

Our directors were elected to and currently serve on the board pursuant to a voting agreement among us and several of our largest stockholders. This agreement will terminate upon the completion of this offering, after which there will be no further contractual obligations regarding the election of our directors.

In accordance with our amended and restated certificate of incorporation, which will be in effect upon the closing of this offering, our board of directors will be divided into three classes, each of which will

consist, as nearly as possible, of one-third of the total number of directors constituting our entire board and which will serve 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 will be divided among the three classes as follows:

- Class I, which will consist of and , and their term will expire at our first annual meeting of stockholders to be held after the completion of this offering;
- Class II, which will consist of and , and their term will expire at our second annual meeting of stockholders to be held after the completion of this offering; and
- Class III, which will consist of and , and their term will expire at our third annual meeting of stockholders to be held after the completion of this offering.

Our amended and restated bylaws, which will become effective upon completion of this offering, will 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

Our board of directors has undertaken a review of 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 and Thorp, representing five of our six 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, , and , and our board of directors has determined that each of them is independent within the meaning of the applicable stock exchange listing requirements and the independence requirements contemplated by Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. is the chairman of the audit committee and our board of directors has determined that is an “audit committee financial expert” as defined by SEC rules and regulations. Our board of directors has determined that the composition of our audit committee meets the criteria for independence under, and the functioning of our audit committee complies with, the

applicable requirements of the Sarbanes-Oxley Act, applicable stock exchange listing requirements and SEC rules and regulations. 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 directors, , each of whom is a non-employee member of our board of directors as defined in Rule 16b-3 under the Exchange Act. 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 directors, . 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

Effective upon completion of this offering, we will adopt a Code of Business Conduct and Ethics, or the Code of Conduct, applicable to all of our employees, executive officers and directors. Following the completion of this offering, the Code of Conduct will be available on our website at *www.clearsidebio.com*. The nominating and corporate governance committee of our board of directors will be 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

We have not historically paid 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. In January 2012, we awarded an option to purchase 50,000 shares of our common stock to Mr. Humphries at an exercise price of $0.07 per share. In October 2013, we awarded an option to purchase 50,000 shares of our common stock to Mr. Humphries at an exercise price of $0.18 per share. In June 2013, in connection with his appointment to our board of directors, we awarded an option to purchase 100,000 shares of our common stock to Dr. Cagle at an exercise price of $0.18 per share. Other than Mr. Humphries and Mr. Cagle, none of our non-employee directors serving as of December 31, 2013 held any options to purchase our common stock.

The following table sets forth information regarding compensation earned for service on our board of directors during the year ended December 31, 2013 by our non-employee directors. Mr. White, our President and Chief Executive Officer, is also a director but does not receive any additional compensation for his service as director. Mr. White's compensation as an executive officer is set forth below under "Executive Compensation — Summary Compensation Table."

Name	Stock Awards ($)	Option Awards ($)(1)
Gerald D. Cagle, Ph.D.	—	44,900(2)
William D. Humphries	—	29,800(3)
Mark R. Prausnitz, Ph.D.	—(4)	—
Christy L. Shaffer, Ph.D.	—	—
Clay B. Thorp	—	—

(1) This column reflects the full grant date fair value for options granted during the year as measured pursuant to ASC Topic 718 as stock-based compensation in our consolidated financial statements. 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 director 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 audited consolidated financial statements included in this prospectus.

(2) As of December 31, 2013, Dr. Cagle held an option to purchase 100,000 shares of common stock, which vests in 16 equal quarterly installments at the end of each calendar quarter beginning September 30, 2013 and is subject to full acceleration of vesting upon a change of control of our company.

(3) As of December 31, 2013, Mr. Humphries held options to purchase 100,000 shares of common stock, of which 50,000 shares were vested and the remainder vests in eight equal quarterly installments at the end of each calendar quarter beginning March 31, 2014 and are subject to full acceleration of vesting upon a change of control of our company.

(4) As a founder of our company, Dr. Prausnitz acquired 617,500 shares of common stock from us in August 2011, which shares were subject to a right of repurchase in favor of us through June 30, 2014. Dr. Prausnitz resigned from our board of directors in August 2014. As of December 31, 2013, there were 77,188 shares not yet vested.

We expect that our board of directors will adopt a director compensation policy for non-employee directors to be effective following the completion of this offering.

EXECUTIVE COMPENSATION

Our named executive officers for the year ended December 31, 2013 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 Executive Vice President of Research and Development.

No other individuals served as executive officers of our company at any point during 2013.

2013 Summary Compensation Table

The following table presents the compensation awarded to, earned by or paid to each of our named executive officers for the year ended December 31, 2013.

Name and Principal Position	Salary ($)(1)	Bonus ($)(2)	Option Awards ($)(3)	Non-Equity Incentive Plan Compensation ($)	All Other Compensation ($)	Total ($)
Daniel H. White President and Chief Executive Officer	256,771	12,906	102,225	51,625	—	423,527
Charles A. Deignan Chief Financial Officer	179,740	—	68,025	28,910	—	276,675
Glenn Noronha, Ph.D. Executive Vice President, Research and Development(4)	108,333	—	105,250	17,333	48,809(5)	279,725

(1) Salary amounts represent actual amounts paid during 2013. 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. The compensation committee exercised its discretion to award Mr. White additional compensation in light of his role 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 2013. 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.

(4) Dr. Noronha became an executive officer of our company in August 2013, and amounts represent compensation earned since that date.

(5) Amount represents relocation allowance plus associated tax gross-up.

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. 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. 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.

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 2013 and 2014, the target bonus was and is as follows:

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

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. For 2013, 40% of each executive officer's target bonus was attributable to the commencement of our Phase 1/2 clinical trial for CLS-1001, 30% was attributable to our further drug and product development efforts and 30% was attributable to our capital raising activities. In 2014, our compensation

committee determined that the performance goals had been achieved at an 80% level in the aggregate. The bonuses to be paid to the named executive officers for 2013 performance at the 80% 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 authorizes 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 2013, 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 February 2013, our compensation committee awarded options to Messrs. White and Deignan to purchase 128,000 shares and 52,000 shares, respectively. Each of these options has an exercise price of $0.18 per share. In August 2013, in connection with the commencement of Dr. Noronha's employment with us, our board of directors approved the grant of an option to purchase 125,000 shares of our common stock with an exercise price of $0.18 per share. In November 2013, our board of directors approved additional options grants to Messrs. White and Deignan and Dr. Noronha to purchase 75,000 shares, 75,000 shares and 50,000 shares, respectively.

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. The agreement is renewable for one-year terms beginning in September 2014, unless either we or Dr. White give written notice of non-renewal at least 60 days prior to the end of the term. Under this agreement, Mr. White is eligible to receive severance benefits in specified circumstances.

In the event that we terminate Mr. White without cause, he resigns for good reason or we elect not to renew the term of the 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 nine 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.

The following definitions have been adopted in Mr. White's employment agreement:

- "cause" means that our board of directors, without Mr. White, has determined that any of the following occurred: (a) Mr. White's material breach of the employment agreement, his failure to diligently and properly perform his duties or his failure to achieve the objectives specified by the board of directors, and any such breach or failure has not been cured within 30 days after written notice thereof, (b) his 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) his material failure to comply with our company 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 company policies relating to harassment, unlawful discrimination, retaliation or workplace violence do not require notice or permit a cure period, (d) his use of illegal drugs or any illegal substance, or his use of alcohol in any manner that materially interferes with the performance of his duties to the company, (e) any dishonest or illegal action by him, or any action determined to be materially detrimental to the interest and well-being of our company, including harm to our reputation, (f) his failure to fully disclose any material conflict of interest that he may have in a transaction between us and a third party, which conflict is materially detrimental to our interest and well-being, or (g) any adverse action or omission by him that 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 Mr. White'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 terminates his employment with us no later than two years after the initial existence of the event.

Outstanding Equity Awards at End of 2013

The following table provides information about outstanding stock options held by each of our executive officers at December 31, 2013. 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 ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($)(8)
Daniel H. White	—	128,000(1)	0.18	02/28/2023	118,750(4)	78,375
		75,000(3)	0.18	11/24/2023		
Charles A. Deignan	—	52,000(1)	0.18	02/28/2023	20,833(5)	13,750
		75,000(3)	0.18	11/24/2023	38,750(6)	25,575
					17,188(7)	11,344
Glenn Noronha, Ph.D.	—	125,000(2)	0.18	08/06/2023		
		50,000(3)	0.18	11/24/2023		

(1) The unvested shares underlying this option vest 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 unvested shares underlying this option vest 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 unvested shares underlying this option vest 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) These restricted shares will vest in equal monthly installments through June 30, 2014. These restricted shares are subject to full acceleration of vesting upon a change of control or in the event the officer's employment is terminated without cause.

(5) These restricted shares will vest in equal monthly installments through January 31, 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.

(6) These restricted shares will vest 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.

(7) These restricted shares will vest 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.

(8) Based on the valuation of our common stock of $0.66 per share as of December 31, 2013.

Stock Option Exercises and Stock Vested During 2013

The following table shows information regarding options exercised and stock awards vested during the year ended December 31, 2013 with respect to our named executive officers.

	Option Awards		Stock Awards	
Name	Number of Shares Acquired on Exercise (#)	Value Realized on Exercise ($)	Number of Shares Acquired on Vesting (#)	Value Realized on Vesting ($)
Daniel H. White	—	—	237,500	137,750(2)
Charles A. Deignan	46,875	27,655(1)	1,354(3)	799(4)

(1) The aggregate dollar amount represents the amount by which the aggregate fair value of the shares of our common stock on the date of exercise, as calculated using an assumed per share value of $0.66,

which is the assumed fair value as of the date of exercise, exceeds the aggregate exercise price of the option, as calculated using the per share exercise price of $0.07.

(2) For shares that vested during the first six months of 2013, we have determined the value realized by Mr. White using an assumed value of $0.50 per share. For shares vested during the last six months of 2013, we have determined the value of such shares using an assumed value of $0.66 per share.

(3) 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.

(4) Represents the difference between the estimated value of the shares for which our repurchase right lapsed and the exercise price of $0.07 per share paid by Mr. Deignan in respect of such shares upon the early exercise of the options. The assumed value of such shares upon vesting was $0.66 per share.

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 is $17,500 for 2014. Participants who are at least 50 years old can also make "catch-up" contributions, which in 2014 may be up to an additional $5,500 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

2014 Equity Incentive Plan

We expect that our board of directors will adopt, and our stockholders will approve, prior to the completion of this offering our 2014 Equity Incentive Plan, or our 2014 plan. We do not expect to issue equity awards under our 2014 plan until after the completion of this offering. No awards have been granted and no shares of our common stock have been issued under our 2014 plan. Our 2014 plan will provide for the grant of incentive stock options within the meaning of Section 422 of the Internal Revenue Code, or 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 2014 plan will also provide 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 2014 plan is shares. The number of shares of our common stock reserved for issuance under our 2014 plan will

automatically increase on January 1 of each year, for a period of 10 years, from January 1, 2015 continuing through January 1, 2024, by % 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 2014 plan is .

Shares issued under our 2014 plan may be authorized but unissued or reacquired shares of our common stock. Shares subject to stock awards granted under our 2014 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 2014 plan. Additionally, shares issued pursuant to stock awards under our 2014 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 2014 plan.

Administration

Our board of directors, or a duly authorized committee thereof, has the authority to administer our 2014 plan. Our board of directors has delegated its authority to administer our 2014 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 2014 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 2014 plan.

The administrator has the power to modify outstanding awards under our 2014 plan. Subject to the terms of our 2014 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 shares of our common stock under our 2014 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 shares of our common stock or a performance cash award having a maximum value in excess of $ under our 2014 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 2014 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 2014 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;
- 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 2014 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 date our board of directors adopts our 2014 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 provides 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

There are 3,338,776 shares of our common stock reserved for issuance under our 2011 plan. As of September 30, 2014, 450,923 shares of our common stock have been issued upon the exercise of options granted under our 2011 plan and options to purchase 1,659,246 shares of our common stock were outstanding at a weighted average exercise price of $0.21 per share. Effective upon the completion of this offering, no further options or stock awards may be granted under our 2011 plan, but all outstanding stock awards will 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.

2014 Employee Stock Purchase Plan

We expect that our board of directors will adopt, and our stockholders will approve, prior to the completion of this offering, our 2014 Employee Stock Purchase Plan, or our 2014 ESPP. We expect that the

2014 ESPP will become effective upon the completion of this offering, but we have no current plans to grant purchase rights under our 2014 ESPP.

The maximum number of shares of our common stock that may be issued under our 2014 ESPP is shares. Additionally, the number of shares of our common stock reserved for issuance under our 2014 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, 2024, 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) 1,000,000 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 2014 ESPP that terminate without having been exercised in full will not reduce the number of shares available for issuance under our 2014 ESPP.

Our board of directors, or a duly authorized committee thereof, will administer our 2014 ESPP. Our board of directors has delegated its authority to administer our 2014 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 2014 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 2014 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 2014 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 2014 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 2014 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 2014 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 2014 ESPP.

Our 2014 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 2014 ESPP other than by will, the laws of descent and distribution or as otherwise provided under our 2014 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 2014 ESPP, at any time and for any reason. Our 2014 ESPP will remain in effect until terminated by our board of directors in accordance with the terms of the 2014 ESPP.

Limitations on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective upon the completion of this offering, 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 will provide that we are required to indemnify our directors to the fullest extent permitted by Delaware law. Our amended and restated bylaws will 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 will 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. Prior to 180 days after the date of this offering, subject to early termination, the sale of any shares under such plan would be prohibited by the lock-up agreement that the director or officer has entered into with the underwriters.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since our inception on May 26, 2011 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."

Sales of Series A Convertible Preferred Stock

In January 2012, February 2012 and July 2012, we sold an aggregate of 5,198,826 shares of our Series A convertible preferred stock at a price of $0.78589 per share for an aggregate price of $4.1 million, 5,071,582 shares of which were sold to holders of more than 5% of our voting securities and members of our board of directors. The table below summarizes these sales.

Purchaser	Shares of Series A Convertible Preferred Stock Purchased	Aggregate Purchase Price
Entities affiliated with Hatteras Venture Partners(1)	4,071,815	$ 3,199,999
Entities affiliated with GRA Venture Fund(2)	866,533	681,000
Daniel H. White(3)	133,234	104,707
Total	5,071,582	$ 3,985,706

(1) Consists of 1,866,418 shares purchased by Hatteras Venture Partners III, LP, 169,489 shares purchased by Hatteras Venture Affiliates III, LP and 2,035,908 shares purchased by Hatteras Venture Partners IV SBIC, LP. Entities affiliated with Hatteras Venture Partners are holders of more than 5% of our voting securities, and Christy L. Shaffer, Ph.D. and Clay B. Thorp are affiliated with Hatteras Venture Partners and are members of our board of directors.

(2) Consists of 547,492 shares purchased by GRA Venture Fund, LLC and 319,041 shares purchased by GRA Venture Fund (T.E.), LLC. Entities affiliated with GRA Venture Fund are holders of more than 5% of our voting securities.

(3) Mr. White's investment represented the conversion of $100,000 in principal amount under convertible promissory notes issued to Mr. White between June 2011 and December 2011, plus accrued interest of $4,707.

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. 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. Entities affiliated with Hatteras Venture Partners are holders of more than 5% of our voting securities, and Christy Shaffer, Ph.D. and Clay B. Thorp are affiliated with Hatteras Venture Partners and are members of our board of directors.

(2) Consists of 174,226 shares purchased by GRA Venture Fund, LLC and 101,528 shares purchased by GRA Venture Fund (T.E.), LLC. Entities affiliated with GRA Venture Fund are holders of more than 5% of our voting securities.

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 248,175 shares of our common stock at an exercise price of $0.01 per share. We issued an aggregate principal amount of $2,196,993 of our bridge notes and warrants to purchase up to 181,750 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	95,508
Entities affiliated with GRA Venture Fund(2)	499,997	41,363
Santen Pharmaceutical Co., Ltd.	500,000	41,363
Daniel H. White	17,500	1,448
Charles A. Deignan	12,500	1,034
Gerald D. Cagle, Ph.D.	12,500	1,034
Total	$ 2,196,993	181,750

(1) Consists of bridge notes and warrants issued to Hatteras Venture Partners III, LP. Entities affiliated with Hatteras Venture Partners are holders of more than 5% of our voting securities, and Christy L. Shaffer, Ph.D. and Clay B. Thorp are affiliated with Hatteras Venture Partners and are members of our board of directors.

(2) Consists of a principal amount of $315,911 of our bridge notes and warrants to purchase 31,023 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 10,341 shares of our common stock issued to GRA Venture Fund (T.E.), LLC. Entities affiliated with GRA Venture Fund are holders of more than 5% of our voting securities.

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 1,716,914 shares of common stock at an exercise price of $0.01 per share, which will become exercisable in February 2015 if we have not completed an initial public offering by then, but otherwise will terminate upon the closing of our initial public offering. Of these warrants issued, warrants to purchase an aggregate of 1,229,248 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. 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	247,395	$1,154,492	$1,181,508
Entities affiliated with GRA Venture Fund(2)	434,937	124,268	499,994	673,394
Santen Pharmaceutical Co., Ltd.	375,004	107,144	499,998	511,699
RMI Investments(3)	2,594,677	741,340	6,999,997	—
Daniel H. White	13,110	3,745	17,499	17,871
Charles A. Deignan	9,375	2,678	12,500	12,792
Gerald D. Cagle	9,375	2,678	12,500	12,792
Total	4,302,359	1,229,248	$9,196,980	$2,410,056

(1) Consists of (i) 396,920 shares of Series B convertible preferred stock and a warrant to purchase 113,406 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 10,291 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 123,698 shares of common stock issued to Hatteras Venture Partners IV SBIC, LP. Entities affiliated with Hatteras Venture Partners are holders of more than 5% of our voting securities, and Christy L. Shaffer, Ph.D. and Clay B. Thorp are affiliated with Hatteras Venture Partners and are members of our board of directors.

(2) Consists of (i) 236,711 shares of Series B convertible preferred stock and a warrant to purchase 67,632 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 39,410 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 17,226 shares of common stock issued to Georgia Research Alliance, Inc. Entities affiliated with GRA Venture Fund are holders of more than 5% of our voting securities.

(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.

NovaMedica License Agreement

In connection with our Series B financing, 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 will make 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 incurred research and development costs under this agreement of $162,000 during the year ended December 31, 2013 and $51,000 during the nine months ended September 30, 2014.

Investor Rights Agreement

We have entered into an investor rights agreement, as amended, with our preferred stockholders, including entities affiliated with Hatteras, Santen, GRA and RMI, each of which beneficially own more than 5% of our common stock. The investor rights agreement, among other things:

- grants our preferred stockholders specified registration rights with respect to shares of our common stock, including shares of common stock issued or issuable upon conversion of shares of our convertible preferred stock held by them;
- obligates us to deliver periodic financial statements to some of the stockholders who are parties to the investor rights agreement; and
- grants a right of first refusal with respect to sales of our shares by us, subject to specified exclusions, which exclusions include the sale of the shares pursuant to this prospectus, to the stockholders who are parties to the investor rights agreement.

For more information regarding the registration rights provided in this agreement, please refer to the section titled "Description of Capital Stock — Registration Rights." The provisions of this agreement other than those relating to registration rights will terminate upon the completion of this offering.

Voting Agreement

We have entered into a voting agreement, as amended, with some of our stockholders, including entities affiliated with Hatteras, Santen, GRA and RMI. The voting agreement, among other things, provides for the voting of shares with respect to the constituency of our board of directors. The voting agreement will terminate upon the completion of this offering.

Stock Sale Agreement

We have entered into a stock sale agreement, as amended, with some of our stockholders, including entities affiliated with Hatteras, Santen, GRA and RMI. The stock sale agreement, among other things:

- grants our investors and our founders rights of first refusal and co-sale with respect to proposed transfers of our securities by specified stockholders;
- grants us rights of first refusal with respect to proposed transfers of our securities by specified stockholders; and
- provides 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 will terminate upon the completion of this offering.

Indemnification Agreements

Our amended and restated certificate of incorporation will contain provisions limiting the liability of directors, and our amended and restated bylaws will provide 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 will 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

Prior to this offering, we have not had a formal policy regarding approval of transactions with related parties. Prior to the completion of this offering, we expect to adopt a related person transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. The policy will become effective immediately upon the execution of the underwriting agreement for this offering. 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 that we expect to adopt prior to the completion of this offering, 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 August 31, 2014 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 table is based upon 19,580,059 shares of common stock outstanding as of August 31, 2014, after giving effect to the conversion of all of our convertible preferred stock into 15,564,959 shares of common stock, which will occur automatically upon the closing of this offering.

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 October 30, 2014, which is 60 days after August 31, 2014. 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. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

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)	6,687,733	34.1%	
Santen Pharmaceutical Co., Ltd.(2)	2,346,655	12.0	
Entities affiliated with GRA Venture Fund(3)	1,618,586	8.3	
RMI Investments(4)	2,594,677	13.3	
Executive Officers and Directors:			
Daniel H. White(5)	1,309,881	6.7	
Charles A. Deignan(6)	155,991	*	
Glenn Noronha, Ph.D.(7)	36,458	*	
Christy L. Schaffer, Ph.D.(1)	—	—	
Clay B. Thorp(1)	6,687,733	34.1	
William D. Humphries(8)	68,750	*	
Gerald D. Cagle, Ph.D.(9)	41,659	*	
Evgeny Zaytsev, M.D.(4)	2,594,677	13.3	
All current directors and executive officers as a group (8 persons)(10)	10,895,149	54.8	

* Represents beneficial ownership of less than 1%.

(1) Consists of (a) 2,895,335 shares of common stock issuable upon conversion of shares of preferred stock and 43,780 shares of common stock issuable upon exercise of immediately exercisable warrants held by Hatteras Venture Partners III, LP (“HVP III”), (b) 262,900 shares of common stock issuable upon conversion of shares of preferred stock and 3,973 shares of common stock issuable upon exercise of immediately exercisable warrants held by Hatteras Venture Affiliates III, LP (“HVA III”), (c) 3,158,237 shares of common stock issuable upon conversion of shares of preferred stock and 47,753 shares of common stock issuable upon exercise of immediately exercisable warrants held by Hatteras Venture Partners IV SBIC, LP (“HVP IV SBIC”) and (d) 275,755 shares of common stock issuable upon conversion of shares of preferred stock held by Hatteras NC Fund (“Hatteras NC” and together with HVP III, HVA III, and HVP IV SBIC, the “Hatteras Entities”). The shares directly held by HVA III and HVP III are indirectly held by Hatteras Venture Advisors III, LLC (“HVA III LLC”), their general partner. The individual general partners of HVA III LLC are Clay B. Thorp, Robert A. Ingram, Kenneth B. Lee, Douglas Reed, MD and John Crumpler (the “HVA III LLC Directors”). HVA III LLC and the HVA III LLC Directors may be deemed to have shared voting and dispositive power over, and be deemed indirect beneficial owners of, the shares directly held by Hatteras Venture Affiliates III and Hatteras Venture Partners III. The shares directly held by HVP IV SBIC are indirectly held by Hatteras Venture Advisors IV SBIC, LLC (“HVA IV SBIC LLC”), its general partner. The individual general partners of HVA IV SBIC LLC are Clay B. Thorp, Robert A Ingram, Kenneth B. Lee, Douglas Reed, MD and John Crumpler (the “HVA IV SBIC LLC Directors”). HVA IV SBIC LLC and the HVA IV SBIC LLC Directors may be deemed to have shared voting and dispositive power over, and be deemed indirect beneficial owners

of, the shares directly held by HVA IV SBIC. The shares directly held by Hatteras NC are indirectly held by Hatteras Venture Advisors IV, LLC ("HVA IV"), its general partner. The individual general partners of HVA IV are Clay B. Thorp, Robert A. Ingram, Kenneth B. Lee, Douglas Reed, MD and John Crumpler (the "HVA IV Directors"). HVA IV and the HVA IV Directors may be deemed to have shared voting and dispositive power over, and be deemed indirect beneficial owners of, the shares directly held by Hatteras NC. Christy Shaffer, one of our directors, is a Venture Partner with Hatteras Venture Partners, but she does not have beneficial ownership over the shares held by HVP III, HVA III, HVP IV SBIC and Hatteras NC. The principal business address of the Hatteras Entities is 280 S. Mangum St., Suite 350, Durham, NC 27701.

(2) Consists of (a) 2,305,292 shares of common stock issuable upon conversion of shares of preferred stock and (b) 41,363 shares of common stock issuable upon exercise of immediately exercisable warrants, in each case held by Santen Pharmaceutical Co., Ltd. ("Santen"). The principal business address of Santen is 9-19 Shimoshinjo 3-chome, Higashiyodogawa-ku, Osaka 533-8651, Japan.

(3) Consists of (a) 958,429 shares of common stock issuable upon conversion of shares of preferred stock and 26,134 shares of common stock issuable upon exercise of immediately exercisable warrants held by GRA Venture Fund, LLC ("GRAVF"), (b) 558,504 shares of common stock issuable upon conversion of shares of preferred stock and 15,228 shares of common stock issuable upon exercise of immediately exercisable warrants held by GRA Venture Fund (T.E.), LLC ("GRAVF TE") and (c) 60,291 shares of common stock issuable upon conversion of shares of preferred stock held in the name of Georgia Research Alliance, Inc. ("GRA, Inc." and, together with GRAVF and GRAVF TE, the "GRA Entities") in an account administered by GRA, Inc. pursuant to a contract with the State of Georgia's Department of Economic Development. The shares directly held by GRAVF are indirectly held by the members of its board of managers, Duane Ackerman, Jim Balloun, Chris Carr, Russ Chandler, Frederick E. Cooper, Brad Currey, Bill Fickling, Rusty French, William Linginfelter, Diana M. Murphy, Sig Mosley, Tom Parker, David Ratcliffe and Fran Rogers (the "GRAVF Directors"). The GRAVF Directors may be deemed to have shared voting and dispositive power over, and be deemed indirect beneficial owners of, the shares directly held by GRAVF. The shares directly held by GRAVF TE are indirectly held by the members of its board of managers, who are the same individuals as the GRAVF Directors (the "GRAVF TE Directors"). The GRAVF TE Directors may be deemed to have shared voting and dispositive power over, and be deemed indirect beneficial owners of, the shares directly held by GRAVF TE. The shares directly held by GRA, Inc. are indirectly held by the members of its board of trustees, Clyde Tuggle, Douglas Hertz, Kathelen Amos, Paul Amos, Dr. Ricardo Azziz, Dr. Mark Becker, Paul Bowers, Carlton Brown, Chris Carr, Dr. Max Cooper, Kenneth Cornelius, Thomas Cousins, Larry Gellerstedt III, George Deese, James Hannan, Robert Hatcher, Edward Heys, William Linginfelter, Kelly Loeffler, Charles McTier, Jere Morehead, Allen Mosley, Thomas Noonan, Charles Ogburn, Kenneth Ostrowski, G.P. Peterson, Parker Petit, David Ratcliffe, Joseph Rogers, William Rogers, John Somerhalder II, Lizanne Thomas, T. Rogers Wade, James Wagner and Felker Ward (the "GRA, Inc. Trustees"). The GRA, Inc. Trustees may be deemed to have shared voting and dispositive power over, and be deemed indirect beneficial owners of, the shares directly held in the name of GRA, Inc. pursuant to a contact with the State of Georgia's Department of Economic Development. The principal business address of the GRA Entities is 191 Peachtree Street, NE, Suite 846, Atlanta, Georgia 30303.

(4) Consists of 2,594,677 shares of common stock issuable upon conversion of shares of preferred stock held by RMI. The shares directly held by RMI are indirectly held by Rusnano MedInvest, the parent company of RMI. RMI Partners LLC is the management company for RusnanoMedInvest. The CEO of RMI Partners

LLC is Vladimir Gurdus and the Managing Partner of RMI Partners LLC is Evgeny Zaytsev, M.D., a member of our board of directors (the "RMI Partners LLC Directors"). RusnanoMedInvest, RMI Partners LLC and the RMI Partners LLC Directors 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) Consists of (a) 1,016,290 shares of common stock held by Mr. White directly and vested within 60 days of August 31, 2014, (b) 90,000 shares of common stock held by the White Family Trust, for which Mr. White's wife serves as trustee, (c) 5,136 shares of common stock held for the benefit of Mr. White's children under the Georgia Uniform Transfers to Minors Act, for which Mr. White serves as custodian, (d) 141,617 shares of common stock issuable upon conversion of shares of preferred stock held by Mr. White directly, (e) 4,727 shares of common stock issuable upon conversion of shares of preferred stock held by the Daniel H. White (IRA), for which Mr. White serves as trustee, (f) 50,663 shares of common stock underlying options that are exercisable and vested within 60 days of August 31, 2014 and (g) 1,448 shares of common stock issuable upon exercise of immediately exercisable warrants.

(6) Consists of (a) 79,686 shares of common stock that are vested within 60 days of August 31, 2014, (b) 45,314 shares of restricted stock that are not vested within 60 days of August 31, 2014, (c) 9,375 shares of common stock issuable upon conversion of shares of preferred stock, (d) 20,582 shares of common stock underlying options that are exercisable and vested within 60 days of August 31, 2014 and (e) 1,034 shares of common stock issuable upon exercise of immediately exercisable warrants. Shares of restricted stock that are not vested are subject to a repurchase right in favor of the company if Mr. Deignan does not satisfy the applicable vesting requirements. In any event, unvested restricted shares may not be disposed of until the vesting period has been satisfied.

(7) Consists of 36,458 shares of common stock underlying options that are exercisable and vested within 60 days of August 31, 2014.

(8) Consists of 68,750 shares of common stock underlying options that are exercisable and vested within 60 days of August 31, 2014.

(9) Consists of (a) 9,375 shares of common stock issuable upon conversion of shares of preferred stock (b) 31,250 shares of common stock underlying options that are exercisable and vested within 60 days of August 31, 2014 and (c) 1,034 shares of common stock issuable upon exercise of immediately exercisable warrants.

(10) Consists of (a) 1,191,112 shares of common stock that are vested within 60 days of August 31, 2014, (b) 9,351,998 shares of common stock issuable upon conversion of shares of preferred stock, (c) 45,314 shares of restricted stock that are not vested within 60 days of August 31, 2014, (d) 207,703 shares of common stock underlying options that are exercisable and vested within 60 days of August 31, 2014 and (e) 99,022 shares of common stock issuable upon exercise of immediately exercisable warrants. Shares of restricted stock that are not vested are subject to a repurchase right in favor of the company if the officer or director does not satisfy the applicable vesting requirements. In any event, unvested restricted shares may not be disposed of until the vesting period has been satisfied.

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 filed as exhibits to the registration statement of which this prospectus is part.

General

Upon the completion of this offering, our amended and restated certificate of incorporation will authorize us to issue up to shares of common stock, $0.001 par value per share, and 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. As of August 31, 2014, we had outstanding 4,015,100 shares of common stock, held by 17 stockholders of record. As of August 31, 2014, after giving effect to the conversion of all outstanding preferred stock into shares of common stock, there would have been 19,580,059 shares of common stock issued and outstanding, held of record by 46 stockholders.

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 will 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.

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

As of August 31, 2014, there were outstanding 15,564,959 shares of convertible preferred stock. All currently outstanding shares of convertible preferred stock will be converted automatically into an aggregate of 15,564,959 shares of common stock immediately prior to the completion of this offering.

Following the completion of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 5,000,000 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.

We have no present plans to issue any shares of preferred stock following completion of this offering.

Options

As of August 31, 2014, under our 2011 plan, options to purchase an aggregate of 1,685,902 shares of common stock were outstanding. For additional information regarding the terms of this plan, see “Executive Compensation — Equity Incentive Plans.”

Warrants

We have outstanding an immediately exercisable warrant to purchase 16,550 shares of our Series A-1 convertible preferred stock at an exercise price of $1.81 per share, which expires in February 2023. This warrant has a net exercise provision under which the holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of our stock at the time of exercise of the warrant after deduction of the aggregate exercise price. The warrant also contain provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of certain stock dividends, stock splits, reorganizations, reclassifications and consolidations. Upon the completion of this offering, unless earlier exercised, this warrant will be converted into a warrant to purchase 16,550 shares of our common stock at $1.81 per share.

We also have outstanding immediately exercisable warrants to purchase an aggregate of 248,175 shares of our common stock at an exercise price of $0.01 per share, which expire in April 2024. These warrants have net exercise provisions under which the holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of our common stock at the time of exercise of the warrant after deduction of the aggregate exercise price. These

warrants also contain provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of certain stock dividends, stock splits, reorganizations, reclassifications and consolidations. If unexercised, these warrants will expire upon the closing of this offering, and therefore we expect that these warrants will be exercised in connection with the completion of this offering and that we will issue approximately 248,175 shares of our common stock upon their exercise.

Registration Rights

We and the holders of our existing convertible preferred stock have entered into an investor rights agreement. The registration rights provisions of this agreement provide those holders with demand and piggyback registration rights with respect to the shares of our common stock currently held by them and issuable to them upon exercise of warrants and upon conversion of our convertible preferred stock in connection with this offering.

Demand Registration Rights

At any time beginning 180 days following the effective date of the registration statement of which this prospectus is a part, the holders of at least 40% of the shares issuable upon conversion of our convertible preferred stock 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. An aggregate of shares of common stock and shares issuable upon the exercise of warrants will be entitled to these demand registration rights.

Piggyback Registration Rights

At any time after the completion of this offering, 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 holders of shares of common stock that are issued upon conversion of our convertible preferred stock, some holders of shares of our common stock and the holders of our currently outstanding warrants 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. An aggregate of shares of common stock and shares issuable upon the exercise of warrants will be entitled to these piggyback registration rights.

Registration on Form S-3

At any time after we become eligible to file a registration statement on Form S-3, holders of shares of our common stock that are issued upon conversion of our convertible preferred stock will be entitled, upon their written request, to have such shares registered by us on a Form S-3 registration statement at our expense, provided that such requested registration has an anticipated aggregate offering size to the public of at least $1.0 million and subject to other specified conditions and limitations. An aggregate of shares of common stock and shares issuable upon the exercise of warrants will be entitled to these Form S-3 registration rights.

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) the fifth anniversary of the completion of this offering 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 to be in Effect Upon the Completion of this Offering

Our amended and restated certificate of incorporation to be in effect upon the completion of this offering, or our restated certificate, will provide for our board of directors to be divided into three classes with staggered three-year terms. Only one class of directors will be 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 will be able to elect all of our directors. Our restated certificate and our amended and restated bylaws to be effective upon the completion of this offering, or our restated bylaws, will 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 will also provide that all stockholder actions must be effected at a duly called meeting of stockholders and will eliminate the right of stockholders to act by written consent without a meeting. Our restated bylaws will also provide 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 will also provide 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 will specify requirements as to the form and content of a stockholder's notice.

Our restated certificate and restated bylaws will 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 will provide 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

We have applied for listing of our common stock on The NASDAQ Global Market under the trading symbol "CLSD."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, no public market existed for our common stock. Future sales of shares of our common stock in the public market after this offering, or the perception that these sales could occur, could adversely affect prevailing market prices for our common stock and could impair our future ability to raise equity capital.

Based on the number of shares outstanding as of August 31, 2014, upon completion of this offering and assuming no exercise of the underwriters' option to purchase additional shares, shares of common stock will be outstanding, assuming no outstanding options or warrants are exercised. All of the shares of common stock sold 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 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.

As a result of contractual restrictions described below and the provisions of Rules 144 and 701, the shares sold in this offering and the restricted securities will be available for sale in the public market as follows:

- the shares sold in this offering and of the existing restricted shares will be eligible for immediate sale upon the completion of this offering;
- approximately restricted shares will be eligible for sale in the public market 90 days after the date of this prospectus, subject to the volume, manner of sale and other limitations under Rule 144 and Rule 701; and
- approximately restricted shares will be eligible for sale in the public market upon expiration of lock-up agreements 180 days after the date of this prospectus, subject in certain circumstances to the volume, manner of sale and other limitations under Rule 144 and Rule 701.

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 approximately shares immediately after the completion of this offering based on the number of shares outstanding as of August 31, 2014; 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.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and in the section of this prospectus titled “Underwriting” and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Form S-8 Registration Statements

As soon as practicable after the completion of this offering, we intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act to register the shares of our common stock that are issuable pursuant to our 2011 plan, 2014 plan and 2014 ESPP. These registration statements will become effective immediately upon filing. Shares covered by these registration statements will then be 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

We and the holders of substantially all of our common stock outstanding on the date of this prospectus, including each of our executive officers and directors, 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 a period of 180 days from the date of this prospectus.

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a general discussion of the material U.S. federal income and estate 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 own 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 and estate 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. 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 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 subject to the alternative minimum tax or the Medicare contribution tax, 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 own 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 or estate 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 own 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). 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 will generally apply to dividends on our common stock paid on or after July 1, 2014 and with respect to gross proceeds of a sale or other disposition of our common stock on or after January 1, 2017. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, to be dated the date of this prospectus, between us and RBC Capital Markets, LLC and Wells Fargo Securities, LLC, as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

Underwriter	Number of Shares
RBC Capital Markets, LLC	
Wells Fargo Securities, LLC	
Needham & Company, LLC	
Nomura Securities International, Inc.	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters, their affiliates and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not expect sales to accounts over which they have discretionary authority to exceed 5% of the common stock being offered.

Commissions and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $ per share of common stock. After the offering, the initial public offering price and the concession to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share		Total	
	Without Option To Purchase Additional Shares	With Option To Purchase Additional Shares	Without Option To Purchase Additional Shares	With Option To Purchase Additional Shares
Public offering price	$	$	$	$
Underwriting discounts and commissions paid by us	$	$	$	$
Proceeds to us, before expenses	$	$	$	$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $ million. We have agreed to reimburse the underwriters for certain expenses in an amount up to $.

Determination of Offering Price

Prior to this offering, there has not been a public market for our common stock. Consequently, the initial public offering price for our common stock will be determined by negotiations between us and the representatives. Among the factors to be considered in these negotiations will be prevailing market conditions, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which the common stock will trade in the public market subsequent to the offering or that an active trading market for the common stock will develop and continue after the offering.

Listing

We have applied to list our common stock on The NASDAQ Global Market under the symbol "CLSD."

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

No Sales of Similar Securities

We, our officers, directors and holders of substantially all of our outstanding capital stock 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 a period of 180 days after the date of this prospectus without the prior written consent of the representatives.

The lock-up restrictions terminate after the close of trading of the common stock on and including the 180th 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 180-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; and
- 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 180-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;

provided, however, that in the case of any transfer or distribution pursuant to the first, third, ninth and tenth 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, sixth and eleventh 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 restricted period.

There are no existing agreements between the underwriters and any of our stockholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares of our common stock in this offering. The underwriters may close out any

covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. 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 shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' websites and any information contained in any other website maintained by any of the underwriters is not part of this prospectus, has not been approved or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their respective affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Notice to Residents of Canada

The securities may be sold only to purchasers purchasing as principal that are both "accredited investors" as defined in National Instrument 45-106 Prospectus and Registration Exemptions and "permitted clients" as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from the prospectus requirements and in compliance with the registration requirements of applicable securities laws.

Notice to Prospective Investors in the EEA

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), including each Relevant Member State that has implemented amendments to Article 3(2) of the Prospectus Directive introduced by the 2010 PD Amending Directive (each, an "Early Implementing Member State"), an offer of shares of common stock to the public may not be made in that Relevant Member State and each initial purchaser represents and agrees that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "Relevant Implementation Date") it has not made and will not make an offer of the shares of common stock to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares of common stock 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 Prospectus Directive, except that an offer of the shares of common stock to the public in that Relevant Member State may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;

(b) to fewer than 100 (or, in the case of Early Implementing Member States, 150) natural or legal persons (other than "qualified investors" as defined in the Prospectus Directive) subject to obtaining the prior consent of the Subscribers; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of the shares of common stock referred to in (a) to (c) above shall require the issuer or any Subscriber to publish a prospectus pursuant to Article 3 of the Prospectus Directive or

supplement a prospectus pursuant to Article 16 of the Prospectus Directive and each person who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, warranted and agreed to and with the issuer or any Subscriber that it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of common stock 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 shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe to the shares of common stock, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC of the European Parliament and of the Council of 4 November 2003 (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State. The expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case 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 in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571 Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Israel

The securities offered by this prospectus have not been approved or disapproved by the Israeli Securities Authority, or the ISA, nor have such securities been registered for sale in Israel. The shares of common stock may not be offered or sold, directly or indirectly, to the public in Israel, absent the publication of a prospectus. The ISA has not issued permits, approvals or licenses in connection with the Offering or publishing the prospectus; nor has it authenticated the details included herein, confirmed their reliability or completeness, or rendered an opinion as to the quality of the securities being offered. Any resale in Israel, directly or indirectly, to the public of the securities offered by this prospectus is subject to restrictions on transferability and must be effected only in compliance with the Israeli securities laws and regulations.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and 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 a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

Notice to Prospective Investors in 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 the shares may not be circulated or distributed, nor may the shares 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 (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) 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 (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, which we refer to as the Order, or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The Prospectus does not constitute an issue prospectus pursuant to Article 652a or Article 1156 of the Swiss Code of Obligations ("CO") and the shares will not be listed on the SIX Swiss Exchange. Therefore, the Prospectus may not comply with the disclosure standards of the CO or the listing rules (including any prospectus schemes) of the SIX Swiss Exchange. Accordingly, the shares may not be offered to the public in or from Switzerland, but only to a selected and limited circle of investors, which do not subscribe to the shares with a view to distribution.

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, Boston, Massachusetts.

EXPERTS

The financial statements of Clearside Biomedical, Inc. at December 31, 2012 and 2013, and for each of the two years in the period ended December 31, 2013, and for the period from May 26, 2011 (date of inception) to December 31, 2013, 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.

Upon completion of this offering, we will be 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. (a development stage enterprise) (the Company) as of December 31, 2012 and 2013, and the related statements of operations, stockholders' deficit, and cash flows for each of the two years in the period ended December 31, 2013 and for the period from May 26, 2011 (date of inception) to December 31, 2013. 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, 2012 and 2013, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2013 and for the period from May 26, 2011 (date of inception) to December 31, 2013, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Atlanta, Georgia
June 23, 2014

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)
Balance Sheets
(in thousands, except share and per share data)

	December 31,			Pro forma Liabilities, Convertible Preferred Stock and Stockholders' Deficit
	2012	2013	September 30, 2014 (unaudited)	September 30, 2014 (unaudited)
Assets				
Current assets:				
Cash and cash equivalents	$ 856	$ 1,909	$ 11,067	
Prepaid expenses	27	63	62	
Other current assets	—	45	—	
Total current assets	883	2,017	11,129	
Property and equipment, net	50	98	164	
Deferred offering costs	—	—	1,558	
Other assets	15	22	21	
Total assets	$ 948	$ 2,137	$ 12,872	
Liabilities, convertible preferred stock and stockholders' deficit				
Current liabilities:				
Accounts payable	$ 129	$ 248	$ 1,508	$ 1,508
Accrued liabilities	400	427	955	955
Current portion of deferred rent	2	8	11	11
Total current liabilities	531	683	2,474	2,474
Deferred revenue	—	—	200	200
Deferred rent	26	22	15	15
Long-term debt	150	268	—	—
Other non-current liabilities	2	31	28	28
Total liabilities	709	1,004	2,717	2,717
Convertible preferred stock:				
Series A preferred stock, $0.001 par value, 5,200,000 shares authorized at December 31, 2012 and 2013 and 5,198,826 shares authorized at September 30, 2014; 5,198,826 shares issued and outstanding at December 31, 2012 and 2013 and September 30, 2014 (unaudited); no shares authorized, issued or outstanding, pro forma; liquidation preference of $4,085,705 at December 31, 2013 and September 30, 2014 (unaudited)	4,029	4,040	4,065	—
Series A-1 preferred stock, $0.001 par value; no shares authorized, issued or outstanding at December 31, 2012; 4,800,000 shares authorized, 4,356,931 shares issued and outstanding at December 31, 2013; 4,373,481 shares authorized, 4,356,931 shares issued and outstanding at September 30, 2014 (unaudited); no shares authorized, issued or outstanding, pro forma; liquidation preference of $7,899,987 at December 31, 2013 and September 30, 2014 (unaudited)	—	7,831	7,848	—
Series B preferred stock, $0.001 par value, 7,413,365 shares authorized; 6,009,202 shares issued and outstanding at September 30, 2014 (unaudited); no shares authorized, issued, or outstanding, pro forma; liquidation preference of $16,211,805 at September 30, 2014 (unaudited)	—	—	14,786	—
Total convertible preferred stock	4,029	11,871	26,699	—
Stockholders' deficit:				
Common stock, $0.001 par value; 17,000,000 shares authorized, 2,547,243 and 3,482,916 shares issued and outstanding at December 31, 2012 and 2013, respectively; 30,000,000 shares authorized, 3,988,421 shares issued and outstanding at September 30, 2014 (unaudited); 30,000,000 shares authorized, 19,533,380 shares issued and outstanding, pro forma at September 30, 2014 (unaudited)	2	3	4	20
Additional paid-in capital	489	794	2,513	29,196
Deficit accumulated during the development stage	(4,281)	(11,535)	(19,061)	(19,061)
Total stockholders' deficit	(3,790)	(10,738)	(16,544)	10,155
Total liabilities, convertible preferred stock and stockholders' deficit	$ 948	$ 2,137	$ 12,872	$ 12,872

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)
Statements of Operations
(in thousands, except share and per share data)

	Year Ended December 31,		Nine Months Ended September 30,		Period From May 26, 2011 (Date of Inception) to December 31, 2013	Period From May 26, 2011 (Date of Inception) to September 30, 2014
	2012	2013	2013	2014		
			(unaudited)			(unaudited)
Operating expenses:						
Research and development	$ 2,354	$ 5,045	$ 3,647	$ 4,776	$ 7,606	$ 12,382
General and administrative	1,575	2,193	1,665	2,398	3,909	6,307
Total operating expenses	3,929	7,238	5,312	7,174	11,515	18,689
Loss from operations	(3,929)	(7,238)	(5,312)	(7,174)	(11,515)	(18,689)
Other income (expense):						
Interest expense	(3)	(23)	(9)	(353)	(28)	(381)
Interest income	1	7	6	1	8	9
Total other expense	(2)	(16)	(3)	(352)	(20)	(372)
Net loss	$ (3,931)	$ (7,254)	$ (5,315)	$ (7,526)	$ (11,535)	$ (19,061)
Net loss per share of common stock — basic and diluted	$ (2.12)	$ (2.45)	$ (1.87)	$ (2.00)	$ (5.50)	$ (7.72)
Weighted average shares outstanding, basic and diluted	1,853,423	2,956,285	2,835,897	3,769,091	2,097,885	2,470,630
Pro forma net loss per share — basic and diluted (unaudited)		$ (0.58)		$ (0.39)		
Pro forma weighted average shares outstanding — basic and diluted (unaudited)		12,512,042		19,334,050		

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)
Statements of Stockholders' Deficit
(in thousands, except share and per share data)

	Common Stock		Additional Paid-In Capital	Deficit Accumulated During Development Stage	Total Stockholders' Deficit
	Shares	Amount			
Balance at May 26, 2011 (inception)	—	$ —	$ —	$ —	$ —
Issuance of Common Stock at par value on August 4, 2011	50,000	—	—	—	—
Vesting of restricted stock	1,315,833	1	—	—	1
Stock-based compensation expense	—	—	217	—	217
Net loss	—	—	—	(350)	(350)
Balance at December 31, 2011	1,365,833	1	217	(350)	(132)
Exercise of stock options at $0.07 per share on August 24, 2012	77,484	—	6	—	6
Exercise of stock options at $0.07 per share on December 18, 2012	161,426	—	11	—	11
Vesting of restricted stock	942,500	1	—	—	1
Accretion of stock issuance costs	—	—	(11)	—	(11)
Stock-based compensation expense	—	—	266	—	266
Net loss	—	—	—	(3,931)	(3,931)
Balance at December 31, 2012	2,547,243	2	489	(4,281)	(3,790)
Exercise of stock options at $0.07 per share on October 1, 2013	41,664	—	3	—	3
Exercise of stock options at $0.07 per share on November 26, 2013	13,853	—	1	—	1
Exercise of stock options at $0.07 per share on December 16, 2013	18,591	—	1	—	1
Vesting of restricted stock	861,565	1	—	—	1
Accretion of stock issuance costs	—	—	(22)	—	(22)
Stock compensation expense	—	—	322	—	322
Net loss	—	—	—	(7,254)	(7,254)
Balance at December 31, 2013	3,482,916	3	794	(11,535)	(10,738)
Vesting of restricted stock (unaudited)	450,936	1	2	—	3
Exercise of stock options at $0.07 per share on June 9, 2014 (unaudited)	24,580	—	2	—	2
Exercise of stock options at $0.07 per share on August 18, 2014 (unaudited)	3,333	—	1	—	1
Exercise of stock options at $0.07 per share on September 24, 2014 (unaudited)	26,656	—	2	—	2
Issuance of warrants to purchase common stock (unaudited)	—	—	1,506	—	1,506
Accretion of stock issuance costs (unaudited)	—	—	(84)	—	(84)
Stock compensation expense (unaudited)	—	—	290	—	290
Net loss (unaudited)	—	—	—	(7,526)	(7,526)
Balance at September 30, 2014 (unaudited)	3,988,421	$ 4	$ 2,513	$ (19,061)	$ (16,544)

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)
Statements of Cash Flows
(in thousands)

	Year Ended December 31,		Nine Months Ended September 30,		Period From May 26, 2011 (Date of Inception) to December 31, 2013	Period From May 26, 2011 (Date of Inception) to September 30, 2014
	2012	2013	2013	2014		
			(unaudited)			(unaudited)
Operating activities						
Net loss	$(3,931)	$(7,254)	$ (5,315)	$ (7,526)	$ (11,535)	$ (19,061)
Adjustments to reconcile net loss to net cash used in operating activities:						
Depreciation	7	15	9	22	22	44
Stock-based compensation expense	266	322	220	290	805	1,095
Non-cash interest expense	—	—	—	82	—	82
Accretion of debt discount	—	—	—	277	—	277
Change in fair value of warrant liability	—	6	5	—	6	6
Changes in operating assets and liabilities:						
Prepaid expenses and other current assets	19	(78)	(11)	(617)	(105)	(722)
Other assets	(15)	2	1	(3)	(13)	(16)
Accounts payable and accrued liabilities	450	146	323	870	680	1,550
Deferred revenue	—	—	—	200	—	200
Deferred rent	28	2	—	(4)	30	26
Net cash used in operating activities	(3,176)	(6,839)	(4,768)	(6,409)	(10,110)	(16,519)
Investing activities						
Acquisition of property and equipment	(57)	(63)	(60)	(68)	(120)	(188)
Net cash used in investing activities	(57)	(63)	(60)	(68)	(120)	(188)
Financing activities						
Proceeds from issuance of convertible shareholder note	—	—	—	—	100	100
Proceeds from issuance of long-term debt	150	125	125	3,000	275	3,275
Principal payments made on long-term debt	—	—	—	(125)	—	(125)
Proceeds from issuance of common stock and restricted stock	—	—	—	—	8	8
Purchase of restricted stock	(4)	—	—	—	(4)	(4)
Proceeds from exercise of stock options	17	10	—	5	27	32
Proceeds from issuance of Series A Preferred Stock, net of issuance cost	3,913	—	—	—	3,913	3,913
Proceeds from issuance of Series A-1 Preferred Stock, net of issuance cost	—	7,820	7,820	—	7,820	7,820
Proceeds from issuance of Series B Preferred Stock, net of issuance cost	—	—	—	12,755	—	12,755
Net cash provided by financing activities	4,076	7,955	7,945	15,635	12,139	27,774
Net increase in cash and cash equivalents	843	1,053	3,117	9,158	1,909	11,067
Cash and cash equivalents, beginning of period	13	856	856	1,909	—	—
Cash and cash equivalents, end of period	$ 856	$ 1,909	$ 3,973	$ 11,067	$ 1,909	$ 11,067
Supplemental schedule of noncash investing and financing activities						
Acquisition of property and equipment	$ —	$ —	$ —	$ 20	$ —	$ 20
Conversion of notes payable and accrued interest into Series A preferred stock	105	—	—	—	105	105
Conversion of shareholder loan, promissory note and accrued interest	—	—	—	3,232	—	3,232
Issuance of warrant to purchase Series A-1 preferred stock	—	19	19	—	19	19
Issuance of warrant to purchase common stock	—	—	—	1,506	—	1,506
Accretion of redeemable convertible preferred stock to redemption value	11	22	16	84	33	117
Vesting of restricted stock	1	1	—	3	3	6
Amortization of debt discount	—	2	1	(7)	2	(5)
Deferred initial public offering costs in accounts payable and accrued expenses	—	—	—	898	—	898

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)

Notes to the Financial Statements

1. The Company

Clearside Biomedical, Inc. (the "Company") is a clinical-stage 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 non-surgically into the suprachoroidal space using its proprietary microinjector. Incorporated in the State of Delaware on May 26, 2011, the Company has its corporate headquarters in Alpharetta, Georgia.

To date, the Company is in the development stage since it has not yet commenced primary operations or generated significant revenue as defined by Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 915, *Development Stage Entities*. 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 development stage life science companies, 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. 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 $10.1 million and $16.5 million and cumulative net losses of $11.5 million and $19.1 million for the period from May 26, 2011 (inception) to December 31, 2013 and for the period from May 26, 2011 (inception) to September 30, 2014 (unaudited), respectively. 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.

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, 2014, statements of operations and statements of cash flows for the nine months ended September 30, 2013 and 2014 and the period from May 26, 2011 (inception) to September 30, 2014 and statement of stockholders' deficit as of September 30, 2014 are unaudited. The interim unaudited 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, 2014 and the results of its operations and its cash flows for the nine months ended September 30, 2013 and 2014 and the period from May 26, 2011 (inception) to September 30, 2014. The financial data and other information disclosed in these notes related to the nine months ended September 30, 2013 and 2014 and the period from May 26, 2011 (inception) to September 30, 2014 are unaudited. The results for the nine months ended September 30, 2014 are not indicative of results to be expected for the year ending December 31, 2014, any other interim periods or any future year or period.

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)

Notes to the Financial Statements (Continued)

Unaudited Pro Forma Information

The unaudited pro forma balance sheet data as of September 30, 2014 gives effect to the automatic conversion of all outstanding shares of the Company's convertible preferred stock into an aggregate of 15,564,959 shares of common stock upon completion of the Company's planned initial public offering. The unaudited pro forma basic and diluted net loss per share for the year ended December 31, 2013 and nine months ended September 30, 2014 gives effect to such automatic conversion as if it had occurred as of the beginning of the periods presented.

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.

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)

Notes to the Financial Statements (Continued)

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. The Company did not record any deferred offering costs as of December 31, 2012 or 2013. As of September 30, 2014 (unaudited), the Company had recorded $1.6 million of deferred offering costs.

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 stock-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.

Stock-Based Compensation

Compensation cost related to stock-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. Stock-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 stock-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 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 warrants 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. 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, 2012 and 2013 and September 30, 2014 (unaudited) 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, accounts payable and accrued expenses approximate their respective carrying values due to the short term nature of these instruments. The Company has determined its stock purchase warrants liability to be a Level 3 fair value measurement (Note 10).

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.

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)

Notes to the Financial Statements (Continued)

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 $10.4 million for the period from May 26, 2011 (inception) to December 31, 2013. 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

Management has considered all recently issued accounting pronouncements and does not believe the adoption of such pronouncements will have a material impact on the Company's financial statements.

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,		Nine Months Ended September 30,		Period From May 26, 2011 (Inception) to December 31, 2013	Period From May 26, 2011 (Inception) to September 30, 2014
	2012	2013	2013	2014		
			(unaudited)			(unaudited)
Convertible preferred stock	5,198,826	9,555,757	9,555,757	15,564,959	9,555,757	15,564,959
Outstanding stock options	617,250	1,694,198	1,336,603	1,659,246	1,694,198	1,659,246
Unvested restricted stock	1,282,500	504,271	641,250	53,335	504,271	53,335
Stock purchase warrants	—	16,550	—	1,981,639	16,550	1,981,639
	7,098,576	11,770,776	11,533,610	19,259,179	11,770,776	19,259,179

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)

Notes to the Financial Statements (Continued)

3. Property and Equipment, Net

Property and equipment, net consisted of the following (dollar amounts in thousands):

	Estimated Useful Lives (Years)	December 31, 2012	December 31, 2013	September 30, 2014 (unaudited)
Furniture and fixtures	5	$ 51	$ 77	$ 85
Machinery and equipment	5	—	26	70
Computer equipment	3	—	7	21
Leasehold improvements	Lesser of useful life or remaining lease term	6	10	32
		57	120	208
Less: Accumulated depreciation		(7)	(22)	(44)
		$ 50	$ 98	$ 164

Depreciation expense was $7,000 and $15,000 for the years ended December 31, 2012 and 2013, respectively; $9,000 and $22,000 for the nine months ended September 30, 2013 (unaudited) and 2014 (unaudited), respectively; and $22,000 and $44,000 for the period from May 26, 2011 (inception) to December 31, 2013 and the period from May 26, 2011 (inception) to September 30, 2014 (unaudited), respectively.

4. Other Current Liabilities

Other current liabilities consisted of the following (in thousands):

	December 31, 2012	December 31, 2013	September 30, 2014 (unaudited)
Accrued expenses	$164	$ 93	$ 564
Accrued bonuses	215	289	311
Accrued vacation	21	33	80
Accrued interest payable	—	12	—
	$400	$427	$ 955

5. Long-Term Debt

Note Purchase Agreement

On December 20, 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 $7,000,000 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 an aggregate of 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 $0 and $8,000 for the years ended December 31, 2012 and 2013, respectively; $5,000 for each of the nine months ended September 30, 2013 (unaudited) and 2014 (unaudited); and $8,000 and $13,000 for the period from May 26, 2011 (inception) to December 31, 2013 and the period from May 26, 2011 (inception) to September 30, 2014 (unaudited), respectively. As of December 31, 2013 and September 30, 2014 (unaudited), the total amount of borrowings due under this note purchase agreement was $150,000 and $0, respectively.

Loan Agreement

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 $2,500,000 in the aggregate over any 12-month period or (vi) upon or after the occurrence of an event of default. Subsequent to December 31, 2013, the Company repaid this loan in full.

Interest expense on the borrowings under the loan agreement was $0 and $4,000 for the years ended December 31, 2012 and 2013, respectively; $2,000 for each of the nine months ended September 30, 2013 (unaudited) and 2014 (unaudited); and $4,000 and $6,000 for the period from May 26, 2011 (inception) to December 31, 2013 and the period from May 26, 2011 (inception) to September 30, 2014 (unaudited), 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.

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

6. Convertible Shareholder Notes Payable

During 2011, the Company issued a convertible promissory note (the "Note") to Daniel H. White, the Company's chief executive officer, under which $100,000 was advanced to the Company in a series of advances between June 2011 and December 2011. The Note, which totaled $104,707, including accrued interest of $4,707, was converted, in two tranches, into 133,234 shares of Series A preferred stock of the Company during the year ended December 31, 2012.

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. As of June 30, 2014 (unaudited), the total amount of borrowings due under the loan agreement was $3.0 million. 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 1,137,644 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 248,175 shares of common stock at an exercise price of $0.01 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 nine months ended September 30, 2014 (unaudited) and for the period from May 26, 2011 (inception) to September 30, 2014 (unaudited).

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

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, 2012	December 31, 2013
Current		
Deferred tax asset (liability)		
Non-deductible accrued expenses	$ 8	$ 125
Deferred rent	1	3
Valuation allowance	(9)	(128)
Net current deferred tax asset	$ —	$ —
Non-current		
Deferred tax asset (liability)		
Stock compensation expense	$ 27	$ 39
Net operating loss carryforwards	1,447	4,005
Depreciation differences	—	(17)
Tax credits	1	181
Deferred rent	10	8
Charitable contributions	—	2
Valuation allowance	(1,485)	(4,218)
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, 2012	Year Ended December 31, 2013
U.S. federal tax rate	34.00%	34.00%
State tax rate	4.62	4.43
Permanent Difference and Other	(0.62)	(1.60)
Tax Credit	0.03	2.47
Valuation allowance	(38.03)	(39.30)
	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 $1.5 million and $2.8 million for the years ended December 31, 2012 and 2013, respectively.

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

As of December 31, 2013, the Company has net deferred tax assets primarily related to net operating loss carryforwards of $4.0 million, which expire through 2033. 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 16,985,672 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”) and 7,413,365 shares have been designated as Series B Preferred Stock (“Series B”). The Series A, Series A-1 and Series B shares were issued at a price of $0.78589, $1.81320 and $2.69783 per share, respectively.

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

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		Total Convertible Preferred Stock
	Shares	Amount	Shares	Amount	Shares	Amount	
Balance at December 31, 2011	—	$ —	—	$ —	—	$ —	$ —
Issuance of Series A at $0.78589 per share on January 2, 2012, net of issuance cost of $26	1,479,213	1,137	—	—	—	—	1,137
Issuance of Series A at $0.78589 per share on January 15, 2012, net of issuance cost of $31	420,382	300	—	—	—	—	300
Issuance of Series A at $0.78589 per share on July 23, 2012, net of issuance cost of $12	3,165,997	2,476	—	—	—	—	2,476
Conversion of related party note and interest payable at $0.78589 per share on January 3, 2012	48,598	38	—	—	—	—	38
Conversion of related party note and interest payable at $0.78589 per share on July 23, 2012	84,636	67	—	—	—	—	67
Accretion of preferred stock issuance costs	—	11	—	—	—	—	11
Balance at December 31, 2012	5,198,826	4,029	—	—	—	—	4,029
Issuance of Series A-1 at $1.81320 per share, on January 31, 2013, net of issuance cost of $75	—	—	4,081,177	7,325	—	—	7,325
Issuance of Series A-1 at $1.81320 per share, on February 12, 2013, net of issuance cost of $5	—	—	275,754	495	—	—	495
Accretion of preferred stock issuance costs	—	11	—	11	—	—	22
Balance at December 31, 2013	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 $225	—	—	—	—	4,811,259	11,512	11,512
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 preferred stock issuance costs (unaudited)	—	25	—	17	—	42	84
Balance at September 30, 2014 (unaudited)	5,198,826	$ 4,065	4,356,931	$ 7,848	6,009,202	$ 14,786	$ 26,699

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

Dividends

Holders of Series A, Series A-1 and Series B 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 for the preferred stock as of December 31, 2013 and September 30, 2014 (unaudited) were $1.1 million and $1.9 million, respectively.

Liquidation

Upon a liquidation event (as defined in the amended and restated certificate of incorporation) the Series A, Series A-1 and Series B holders will be paid their liquidation preference of $0.78589, $1.81320 and $2.69783 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 and Series B 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 and Series B 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 and Series B shares may be converted into common stock at a conversion price of $0.78589, $1.81320 and $2.69783, respectively. In addition, the Series A, Series A-1 and Series B 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 $4.04675 if the initial public offering closes on or before February 20, 2015 or $8.09349 if the initial public offering closes after February 20, 2015; 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 70% of the outstanding shares of Series B 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 and Series B shares. Based on the conversion terms, there were no beneficial conversion features associated with Series A, Series A-1 and Series B 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 and Series B 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 and Series B may be converted, and shall have voting rights and powers equal to the voting rights and powers of the common stock, with certain limitations.

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

Redemption

Series A, Series A-1 preferred stock and Series B will be subject to redemption at the option of the investors holding a majority of the Series A, Series A-1 and Series B 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 and Series B owned by each holder, that number of outstanding shares of Series A, Series A-1 and Series B determined by dividing (i) the total number of shares of Series A, Series A-1 and Series B 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 and Series B 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 and Series B 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 30,000,000 shares of $0.001 par value common stock. As of December 31, 2013 and September 30, 2014 (unaudited), there were 3,482,916 and 3,988,421 shares of common stock outstanding, respectively, which excludes 504,271 and 53,335 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.

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

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, 2013 and September 30, 2014 (unaudited) and had a weighted average remaining life of 9.12 and 8.38 years, 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 248,175 shares of common stock at a price per share of $0.01. The terms of these warrants extend until one year from the grant date and the warrants are exercisable at any time during that one-year period. These warrants were outstanding at September 30, 2014 (unaudited) and had a weighted average remaining life of 0.5 years. If unexercised, these warrants will expire upon the closing of an initial public offering.

The Company recognizes the warrants on its balance sheet as an adjustment to its long-term debt, which had no effect on the Company's cash flows for any period presented.

The Company estimated the fair value of the warrant 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 warrant, the risk-free interest rate and the fair value of the equity underlying the warrant.

Key assumptions utilized in the fair value calculation for the warrant at issuance appear in the table below:

Expected term (years)	5.00
Volatility	100.28%
Risk-free interest rate	1.38%
Dividend yield	0.00%

In connection with its Series B convertible preferred stock financing in August 2014, the Company issued warrants to purchase an aggregate of 1,716,914 shares of common stock at an exercise price of $0.01 per share, which will become exercisable in February 2015 if the Company has not completed an initial public offering by then, but otherwise will terminate upon the closing of the Company's initial public offering.

As of September 30, 2014, the total value of the common stock warrants issued in connection with the Series B financing was estimated to be $1,345,964. 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

CLEARSIDE BIOMEDICAL, INC.
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Notes to the Financial Statements (Continued)

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.

11. Stock-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 stock-based awards to employees, directors and consultants of the Company. The Company has reserved 3,338,776 shares of common stock for issuance under the Plan. The Board shall determine price, term and vesting conditions of all stock-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. Stock-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 stock-based compensation expense recognized is reflected in the statements of operations as follows (in thousands):

	Year Ended December 31,		Nine Months Ended September 30,		Period From May 26, 2011 (Inception) to December 31, 2013	Period From May 26, 2011 (Inception) to September 30, 2014
	2012	2013	2013	2014		
			(unaudited)			(unaudited)
Research and development	$158	$213	$ 148	$ 166	$ 531	$ 697
General and administrative	108	109	72	124	274	398
Total	$266	$322	$ 220	$ 290	$ 805	$ 1,095

Stock-based payments are 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, 2012 and 2013 and for the nine months ended September 30, 2013 (unaudited) and 2014 (unaudited).

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
Expected term (years)	7.00	7.00	7.00	7.00
Expected stock price volatility	156.84%	97.02%	99.81%	87.85%
Risk-free interest rate	1.07%	1.69%	1.42%	2.10%
Expected dividend yield	0.00%	0.00%	0.00%	0.00%

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Notes to the Financial Statements (Continued)

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 both for 2012 and for 2013.

Stock Options

The Company has granted stock option awards to employees, directors and consultants. Stock-based compensation expense for options granted is reflected in the statements of operations as follows (in thousands):

	Year Ended December 31,		Nine Months Ended Sept 30,		Period From May 26, 2011 (Inception) to December 31, 2013	Period From May 26, 2011 (Inception) to Sept 30, 2014
	2012	2013	2013	2014		
			(unaudited)			(unaudited)
Research and development	$ 17	$ 50	$ 28	$ 80	$ 67	$ 147
General and administrative	70	71	44	107	141	248
Total	$ 87	$ 121	$ 72	$ 187	$ 208	$ 395

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Notes to the Financial Statements (Continued)

The following table summarizes the activity related to stock options:

	Number of Shares	Weighted Average Exercise Price
Options outstanding at May 26, 2011, inception	—	$ —
Granted	50,000	0.04
Options outstanding at December 31, 2011	50,000	0.04
Granted	823,660	0.07
Exercised	(238,910)	0.07
Cancelled/Forfeited	(17,500)	0.07
Options outstanding at December 31, 2012	617,250	0.07
Granted	1,435,500	0.18
Exercised	(157,444)	0.07
Cancelled/Forfeited	(201,108)	0.13
Options outstanding at December 31, 2013	1,694,198	0.16
Granted	70,000	1.40
Exercised (unaudited)	(54,569)	0.08
Cancelled/Forfeited (unaudited)	(50,383)	0.07
Options outstanding at September 30, 2014 (unaudited)	1,659,246	0.21
Options exercisable at December 31, 2013	205,136	0.07
Options exercisable at September 30, 2014 (unaudited)	440,842	0.13

The following table provides additional information about the Company's stock options that were outstanding and exercisable at December 31, 2013 (aggregate intrinsic values in thousands):

Exercise Price	Options Outstanding	Weighted Average Exercise Price	Aggregate Intrinsic Value	Weighted Average Remaining Contractual Life (Years)	Options Exercisable	Weighted Average Exercise Price	Aggregate Intrinsic Value
$0.01	25,000			7.9	16,667		
0.07	349,698			8.2	182,226		
0.18	1,319,500			9.5	6,243		
	1,694,198	$ 0.16	$ 886		205,136	$ 0.07	$ 121

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Notes to the Financial Statements (Continued)

The following table provides additional information about the Company's stock options that were outstanding and exercisable at September 30, 2014 (unaudited) (aggregate intrinsic values in thousands):

Exercise Price	Options Outstanding	Weighted Average Exercise Price	Aggregate Intrinsic Value	Weighted Average Remaining Contractual Life (Years)	Options Exercisable	Weighted Average Exercise Price	Aggregate Intrinsic Value
$0.01	25,000			7.12	22,907		
0.07	248,079			7.80	150,322		
0.18	1,316,167			8.83	267,613		
1.40	70,000			9.87	—		
	1,659,246	$ 0.21	$ 2,219		440,842	$ 0.13	$ 624

As of December 31, 2013 and September 30, 2014 (unaudited), the Company had $0.7 million and $0.6 million of unrecognized compensation expense, respectively, related to unvested stock options granted under the Plan. This cost is expected to be recognized over a weighted average period of 1.5 years as of September 30, 2014 (unaudited). The weighted average remaining contractual life of all outstanding options as of December 31, 2013 and September 30, 2014 (unaudited) was 9.3 and 8.7 years, respectively.

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, 2013 and September 30, 2014 (unaudited) was $0.66 and $1.55, respectively.

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Notes to the Financial Statements (Continued)

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:

	Shares	Weighted Average Grant Date Fair Value
Unvested at May 26, 2011 (inception)	—	$ —
Granted	3,970,000	0.16
Vested	(1,315,833)	0.16
Cancelled	(50,000)	0.16
Unvested at December 31, 2011	2,604,167	0.16
Vested	(942,500)	0.16
Forfeited	(379,167)	0.16
Unvested at December 31, 2012	1,282,500	0.16
Granted	83,336	0.61
Vested	(861,565)	0.16
Unvested at December 31, 2013	504,271	0.23
Vested (unaudited)	(450,936)	0.18
Unvested at September 30, 2014 (unaudited)	53,335	0.61

Stock-based compensation expense for restricted stock granted is reflected in the statements of operations as follows (in thousands):

	Year Ended December 31,		Nine Months Ended September 30,		Period From May 26, 2011 (Inception) to December 31, 2013	Period From May 26, 2011 (Inception) to September 30, 2014
	2012	2013	2013	2014		
			(unaudited)			(unaudited)
Research and development	$ 141	$ 163	$ 120	$ 86	$ 464	$ 550
General and administrative	38	38	28	17	133	150
Total	$ 179	$ 201	$ 148	$ 103	$ 597	$ 700

As of December 31, 2013 and September 30, 2014 (unaudited), the Company had $106,000 and $0 of unrecognized compensation expense, respectively, related to unvested restricted stock.

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Notes to the Financial Statements (Continued)

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 at December 31, 2013.

Minimum lease payments were as follows at December 31, 2013 (in thousands):

2014	$254
2015	180
2016	90
2017	23
Total minimum lease payments	$547

Rent expense, net of sublease income, was $102,000 and $182,000 for years ended December 31, 2012 and 2013, respectively; $127,000 and $155,000 for the nine months ended September 30, 2013 (unaudited) and 2014 (unaudited), respectively; and $284,000 and $439,000 for the period from May 26, 2011 (inception) to December 31, 2013 and the period from May 26, 2011 (inception) to September 30, 2014 (unaudited), respectively. Total future rent income from the sub-lease agreement on an operating lease due through May 2015 was $59,000 as of December 31, 2013.

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 at will employment contracts with substantially all employees providing for salary, benefits and bonuses.

13. License Agreements

On July 4, 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 year ended December 31, 2013 or the nine months ended September 30, 2014. 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 connection with the Company's Series B financing, in August 2014, the Company entered into a license agreement with NovaMedica LLC ("NovaMedica"). Under this agreement, the Company granted to NovaMedica the exclusive right in Russia and specified adjacent territories to use the Company's intellectual property to develop and commercialize products involving the use of the corticosteriod triamcinolone acetonide as the sole active pharmaceutical ingredient for administration in the suprachoroidal space. In connection with this license, NovaMedica made an upfront payment to the Company of $200,000. In addition, NovaMedica has 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, upon the achievement of specified development and commercial milestones. 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.

14. Collaborative Agreement

On January 31, 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 $162,000 in 2013 and $51,000 for the nine months ended September 30, 2014 (unaudited).

CLEARSIDE BIOMEDICAL, INC.
(A Development Stage Enterprise)

Notes to the Financial Statements (Continued)

15. Unaudited Pro Forma Net Loss Per Share

The unaudited pro forma basic and diluted net loss per share for the year ended December 31, 2013 and nine months ended September 30, 2014 gives effect to the conversion of outstanding convertible preferred stock, which will occur automatically upon the completion of the planned initial public offering, as if such conversion occurred as of the beginning of the periods presented. The following table sets forth the computation of unaudited pro forma basic and diluted net loss per share of common stock for the periods indicated (in thousands except share and per share amounts):

	Year Ended December 31, 2013	Nine Months Ended September 30, 2014
Numerator for pro forma calculation:		
Net loss	$ (7,254)	$ (7,526)
Denominator for pro forma calculation:		
Weighted-average number of shares outstanding—basic and diluted	2,956,285	3,769,091
Pro forma adjustment to reflect automatic conversion of outstanding convertible preferred stock	9,555,757	15,564,959
Weighted-average number of pro forma shares outstanding—basic Diluted	12,512,042	19,334,050
Pro forma net loss per share—basic and diluted	$ (0.58)	$ (0.39)

16. Subsequent Events (Unaudited)

The Company evaluated subsequent events through December 23, 2014, the date on which these financial statements were issued.

Shares

COMMON STOCK

RBC CAPITAL MARKETS **WELLS FARGO SECURITIES**

NEEDHAM & COMPANY **NOMURA**

, 2015

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. ***Other Expenses of Issuance and Distribution.***

The following table sets forth all costs and expenses, other than underwriting discounts and commissions, payable by us in connection with the sale of the common stock being registered. All amounts shown are estimates except for the SEC registration fee, the Financial Industry Regulatory Authority, or FINRA, filing fee and The NASDAQ Global Market initial listing fee.

	Amount to be Paid
SEC registration fee	$ *
FINRA filing fee	*
NASDAQ Global Market initial listing fee	*
Blue sky fees and expenses	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees and expenses	*
Miscellaneous fees and expenses	*
Total	$ *

* To be filed by amendment.

Item 14. ***Indemnification of Directors and Officers.***

We are incorporated under the laws of the State of Delaware. Section 102 of the Delaware General Corporation Law permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit.

Section 145 of the Delaware General Corporation Law provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

As permitted by the Delaware General Corporation Law, our amended and restated certificate of incorporation and bylaws to be in effect upon the closing of this offering will provide that: (i) we are required to indemnify our directors to the fullest extent permitted by the Delaware General Corporation Law; (ii) we may, in our discretion, indemnify our officers, employees and agents as set forth in the Delaware General Corporation Law; (iii) we are required, upon satisfaction of certain conditions, to advance all expenses incurred by our directors in connection with certain legal proceedings; (iv) the rights conferred in the bylaws are not exclusive; and (v) we are authorized to enter into indemnification agreements with our directors, officers, employees and agents.

We have entered into agreements with our directors that require us to indemnify them against expenses, judgments, fines, settlements and other amounts that any such person becomes legally obligated to pay (including with respect to a derivative action) in connection with any proceeding, whether actual or threatened, to which such person may be made a party by reason of the fact that such person is or was a director or officer of us or any of our affiliates, provided such person acted in good faith and in a manner such person reasonably believed to be in, or not opposed to, our best interests. The indemnification agreements also set forth certain procedures that will apply in the event of a claim for indemnification thereunder. We intend to enter into similar indemnification agreements with our executive officers prior to the completion of this offering. At present, no litigation or proceeding is pending that involves any of our directors or officers regarding which indemnification is sought, nor are we aware of any threatened litigation that may result in claims for indemnification.

We maintain a directors' and officers' liability insurance policy. The policy insures directors and officers against unindemnified losses arising from certain wrongful acts in their capacities as directors and officers and reimburses us for those losses for which we have lawfully indemnified the directors and officers. The policy contains various exclusions.

In addition, the underwriting agreement filed as Exhibit 1.1 to this Registration Statement provides for indemnification by the underwriters of us and our officers and directors for certain liabilities arising under the Securities Act, or otherwise.

Item 15. *Recent Sales of Unregistered Securities.*

Issuances of Capital Stock, Promissory Notes and Warrants

The following list sets forth information regarding all unregistered securities sold by us since May 26, 2011, the date of our inception, through December 23, 2014.

1) Between June 2011 and December 2011, we borrowed an aggregate of $100,000 from Daniel H. White pursuant to a series of convertible promissory notes.

2) In January 2012, February 2012 and July 2012, we issued an aggregate of 5,198,826 shares of our Series A convertible preferred stock to seven accredited investors at a per share price of $0.78589, for aggregate consideration of approximately $4.1 million, including the conversion of the promissory notes described above.

3) In December 2012, we borrowed $150,000 from a lender pursuant to an unsecured promissory note.

4) In January 2013, we issued an aggregate of 4,356,931 shares of our Series A-1 convertible preferred stock to 13 accredited investors at a per share price of $1.8132, for aggregate consideration of approximately $7.9 million.

5) In February 2013, in connection with a loan agreement, we borrowed $125,000 from a lender pursuant to a promissory note and issued a warrant to purchase 16,550 shares of our Series A-1 convertible preferred stock, which will become a warrant to purchase 16,550 shares of our common stock following the completion of this offering.

6) In April and May 2014, we issued an aggregate principal amount of $3.0 million of unsecured 7% convertible promissory notes and warrants to purchase 248,175 shares of our common stock at an exercise price of $0.01 per share to 10 accredited investors.

7) In August 2014, we issued an aggregate of 6,009,202 shares of our Series B convertible preferred stock at a per share price of $2.69783 and warrants to purchase 1,716,914 shares of our common stock at an exercise price of $0.01 per share to 31 accredited investors, for aggregate consideration of approximately $16.2 million. In some cases, some or all of the purchase price for these shares took the form of conversion of principal and interest under outstanding convertible promissory notes held by the respective investors.

The offers, sales and issuances of the securities described in the paragraphs above were exempt from registration under Section 4(a)(2) of the Securities Act and Regulation D promulgated under the Securities Act. The recipients represented to us that they acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. The recipients also represented to us that they were accredited investors as defined in Rule 501 promulgated under the Securities Act.

Stock Option Grants

From May 26, 2011, the date of our inception, through December 23, 2014, we have granted options under our 2011 stock incentive plan to purchase an aggregate of 3,446,660 shares of our common stock to employees, consultants and directors, having exercise prices ranging from $0.01 to $1.55 per share. Of these, options to purchase an aggregate of 578,991 shares have been cancelled without being exercised and 450,923 shares were issued upon the exercise of stock options, at a weighted average exercise price of $0.07 per share, for aggregate proceeds of approximately $32,000.

The offers, sales and issuances of the securities described in the foregoing paragraph were exempt from registration under Rule 701 promulgated under the Securities Act in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were our employees, directors or consultants and received the securities under our 2011 stock incentive plan. Appropriate legends were affixed to the securities issued in these transactions.

Item 16. *Exhibits and Financial Statement Schedules.*

The exhibits to the registration statement are listed in the Exhibit Index attached hereto and are incorporated by reference herein.

Item 17. *Undertakings.*

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Alpharetta, State of Georgia, on the day of , 2015.

CLEARSIDE BIOMEDICAL, INC.

By: _____

Daniel H. White
President and Chief Executive Officer

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Daniel H. White, Charles A. Deignan and Brent B. Siler, and each of them, his or her true and lawful agent, proxy and attorney-in-fact, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to (i) act on, sign and file with the Securities and Exchange Commission any and all amendments (including post-effective amendments) to this registration statement together with all schedules and exhibits thereto and any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, together with all schedules and exhibits thereto, (ii) act on, sign and file such certificates, instruments, agreements and other documents as may be necessary or appropriate in connection therewith, (iii) act on and file any supplement to any prospectus included in this registration statement or any such amendment or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and (iv) take any and all actions which may be necessary or appropriate to be done, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
Daniel H. White	President, Chief Executive Officer and Director *(Principal Executive Officer)*	, 2015
Charles A. Deignan	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	, 2015
Christy L. Shaffer, Ph.D.	Director	, 2015
Clay B. Thorp	Director	, 2015

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Signature	Title	Date
William D. Humphries	Director	, 2015
Evgeny Zaytsev, M.D.	Director	, 2015
Gerald D. Cagle, Ph.D.	Director	, 2015

EXHIBIT INDEX

Exhibit Number		Description of Document
1.1	†	Form of Underwriting Agreement.
3.1	**	Fourth Amended and Restated Certificate of Incorporation, as currently in effect.
3.2	†	Form of Certificate of Amendment of Fourth Amended and Restated Certificate of Incorporation to be filed prior to the completion of this offering.
3.3	†	Form of Fifth Amended and Restated Certificate of Incorporation to be effective upon completion of this offering.
3.4	**	Bylaws, as currently in effect.
3.5	†	Form of Amended and Restated Bylaws to be effective upon completion of this offering.
4.1	†	Specimen stock certificate evidencing shares of Common Stock.
4.2	**	Second Amended and Restated Investor Rights Agreement, dated as of August 29, 2014, by and among the Registrant and certain of its stockholders.
4.3	**	Form of Common Stock Purchase Warrant issued in bridge financing.
4.4	**	Stock Warrant issued to North Carolina Biotechnology Center, dated as of February 12, 2013.
5.1	†	Opinion of Cooley LLP as to legality.
10.1	#	License Agreement, by and among the Registrant, Emory University and The Georgia Tech Research Corporation, dated as of July 4, 2012, as amended by the First Amendment to License Agreement, dated April 2, 2014.
10.2	**	Lease Agreement, dated as of March 14, 2012, by and between the Registrant and McDonald Ventures XI, LLC, as amended by the renewal letter from McDonald Ventures XI, LLC to the Registrant, dated March 18, 2014, and by the First Amendment to the Lease Agreement, dated August 22, 2014.
10.3	+**	2011 Stock Incentive Plan, as amended to date.
10.4	+**	Form of Incentive Stock Option Grant Notice and Incentive Stock Option Agreement under 2011 Stock Incentive Plan.
10.5	+**	Form of Nonqualified Stock Option Grant Notice and Nonqualified Stock Option Agreement under 2011 Stock Incentive Plan.
10.6	+†	Form of 2014 Equity Incentive Plan
10.7	+†	Form of Stock Option Grant Notice and Stock Option Agreement under 2014 Equity Incentive Plan.
10.8	+†	Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under 2014 Equity Incentive Plan.
10.9	+**	Form of Indemnification Agreement with non-employee directors.

Exhibit Number	Description of Document
10.10**	Office Lease, dated as of June 17, 2013, by and between the Registrant and Highwoods Realty Limited Partnership.
10.11#**	Collaboration Agreement, dated as of January 31, 2013, by and among the Registrant and Santen Pharmaceutical Co., Ltd., as amended by Amendment No. 1 to Collaboration Agreement, dated as of April 29, 2014.
10.12+†	Form of 2014 Employee Stock Purchase Plan.
10.13+†	Form of Employment Agreement with executive officers to be in effect upon completion of this offering.
10.14+†	Non-Employee Director Compensation Policy to be in effect upon completion of this offering.
10.15#**	License Agreement, by and between the Registrant and NovaMedica LLC, dated as of August 29, 2014.
23.1†	Consent of Ernst & Young LLP, independent registered public accounting firm.
23.2†	Consent of Cooley LLP (included in Exhibit 5.1).

† To be filed by amendment.

+ Indicates management contract or compensatory plan.

** Previously submitted.

Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and have been separately filed with the Securities and Exchange Commission.

Exhibit 10.1

*****Text Omitted and Filed Separately**
Confidential Treatment Requested
Under 17 CFR §§ 200. 80(b)(4) and 230.406

LICENSE AGREEMENT

between

EMORY UNIVERSITY,

THE GEORGIA TECH RESEARCH CORPORATION

and

CLEARSIDE BIOMEDICAL, INC.

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CONFIDENTIAL TREATMENT HAS BEEN REQUESTED FOR PORTIONS OF THIS EXHIBIT. THE COPY FILED HEREWITH OMITS THE INFORMATION SUBJECT TO A REQUEST FOR CONFIDENTIAL TREATMENT. OMISSIONS ARE DESIGNATED BY [* * *]. A COMPLETE VERSION OF THIS EXHIBIT HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

THIS LICENSE AGREEMENT is made and entered into as of the 4th day of July, 2012, (hereinafter referred to as the "**Effective Date**") by and among EMORY UNIVERSITY, a nonprofit Georgia corporation with offices located at 1599 Clifton Road NE, 4th Floor, Mailstop 1599/001/1AZ Atlanta, Georgia 30322, (hereinafter referred to as "**EMORY**"), "), the GEORGIA TECH RESEARCH CORPORATION, a nonprofit corporation with offices located at 505 10th Street, NW, Atlanta, Georgia 30332-0415 (hereinafter referred to as "**GTRC**") and Clearside Biomedical, Inc., a corporation organized under the laws of the state of Delaware having a principal place of business located at, 1220 Old Alpharetta Road—Suite 300, Alpharetta, Georgia 30005 (hereinafter referred to as "**COMPANY**").

WHEREAS, EMORY and **GTRC** (hereinafter together, **"LICENSOR"**) are the owners of all right, title, and interest in inventions and technology, developed by their respective employees and are responsible for their protection and commercial development; and

WHEREAS, LICENSOR has developed certain inventions and technology related to "Microneedle for Ocular Procedure" and "Microneedles for Tissue Injections", which is in part described in [* * *]; and

WHEREAS, COMPANY wishes to obtain and **LICENSOR** wishes to grant certain rights to pursue the development and commercialization of the inventions in accordance with the terms and conditions of the Agreement;

WHEREAS, COMPANY understands and acknowledges that **GTRC** may have one or more patent(s) which may be required to practice the inventions licensed in this Agreement, and subject to a separate agreement with **GTRC**, **COMPANY** may obtain commercial rights that may be available at that time;

NOW, THEREFORE, for and in consideration of the mutual covenants and the premises herein, the parties, intending to be legally bound, hereby agree as follows.

ARTICLE 1. DEFINITIONS

The following terms as used herein shall have the following meaning:

"**Affiliate**" shall mean any corporation or non-corporate business entity which controls, is controlled by, or is under common control with a party to this Agreement. A corporation or non-corporate business entity shall be regarded as in control of another corporation if it owns, or directly or indirectly controls, at least fifty (50%) percent of the voting stock of the other corporation, or if it possesses, directly or indirectly, the power to direct or cause the direction of the management and policies of such entity.

"**Agreement**" or "**License Agreement**" shall mean this Agreement, including all APPENDICES.

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"**COMPANY's Development Plan**" shall mean the plan detailed in **APPENDIX A** of this Agreement, which may be amended upon written agreement by the parties.

"**Dollars**" shall mean United States dollars.

"**Field of Use**" shall mean all ophthalmic uses in mammals and birds.

"**Indemnitees**" shall mean the Inventors, EMORY, GTRC, the Georgia Institute of Technology, ("GIT"), the Board of Regents of the University System of Georgia, its directors, officers, employees and students, and their heirs, executors, administrators, successors and legal representatives.

"Improvements" shall mean any inventions with utility solely in the Field of Use (a) that are claimed in patent applications filed or identified in invention disclosures made to Licensor within two years of the Effective Date, (b) which if practiced would infringe any Valid Claim of any of the Licensed Patents listed in Appendix B, and (c) are invented solely by Inventors of one or more Licensed Patents.

"**Inventors**" shall mean the named inventors of the Licensed Patents.

"**Licensed Patents**" shall mean the patent applications identified in APPENDIX B, together with any and all substitutions, extensions, divisionals, continuations, continuations-in-part (to the extent that the claimed subject matter of such continuations-in-part is disclosed and enabled in the parent Licensed Patent application or extensions based thereon), foreign counterparts of such patent applications and any patents which issue thereon anywhere in the world, including reexamined and reissued patents.

"**Licensed Product(s)**" shall mean any process, service or product covered by a Valid Claim of any Licensed Patent. For purposes of clarity, Licensed Product specifically includes any proprietary needle having measured gauge of thirty (30) or smaller and length of less than [* * *] millimeters, or any product that may be packaged in combination with a syringe containing drug active, excipient, or similar substance (for example balanced saline), in each case to the extent covered by Licensed Patents.

"**Licensed Know-How**" shall mean certain techniques, technology, prototypes, data, methods and other information known to the Inventors of the Licensed Patents and owned by LICENSOR as of the Effective Date that is reasonably necessary to practice the Licensed Patents that is disclosed but not claimed in a patent or patent application. For clarification, any information available in the public domain or that may otherwise be used by any person who is not an employee of LICENSOR without violating the intellectual property rights of LICENSOR shall no longer constitute Licensed Know-How and COMPANY may use any such information without any restriction or obligation hereunder.

"**Licensed Technology**" means Licensed Patents and Licensed Know-How.

"**Licensed Territory**" means the world.

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"**Net Selling Price**" of Licensed Products shall mean the gross selling price paid by a purchaser of a Licensed Product to COMPANY, an Affiliate or Sublicensee of COMPANY, or any other party authorized by COMPANY to sell Licensed Products less the following discounts:

a) customary trade, quantity and cash discounts, service allowances (including without limitation wholesalers' fees for services and stocking fees) and retroactive price adjustments actually allowed and taken, including rebates granted to vendors, managed health care or governmental organizations and independent brokers or agents' commissions, if any, as accrued and adjusted for actual amounts taken, allowed or paid;

b) credits actually given for rejected or returned Licensed Products;

c) freight, postage, shipping, transportation and insurance costs, third-party handling charges and other costs directly related to bringing Licensed Product to the purchaser or end user, in each case in accordance with industry norms; and

d) sales, excise taxes and customs duties included in the invoiced amount.

Notwithstanding the foregoing in this Section, amounts received by COMPANY, its Affiliates or Sublicensees of COMPANY or its Affiliates for the sale of Licensed Products among COMPANY, its Affiliates and Sublicensees for resale shall not be included in the computation of Net Selling Price hereunder.

Notwithstanding anything in this Agreement to the contrary, in the event that COMPANY grants a sublicense to a third party in a bona fide, arm's length transaction and the Sublicensee requires, as a condition to entering into the sublicense agreement, that running royalties on sales of Licensed Product by or on behalf of the sublicensee be calculated and paid based on a different definition of Net Selling Price, then a substitute definition of Net Selling Price may be used with respect to such sublicense provided that the substitute definition (i) is consistent with generally accepted accounting principles as consistently applied by such sublicensee and (ii) does not materially reduce royalties payable hereunder to LICENSOR.

"**Prosecution and Maintenance**" or "**Prosecute and Maintain**" shall mean, with respect to a particular patent application or patent, means the preparation, filing, prosecution and maintenance of such patent or patent application, as well as re-examinations, reissues, applications for patent term extensions and the like with respect to such patent or patent application, together with the conduct of interferences, the defense of oppositions and other similar proceedings with respect to such patent or patent application.

"**Sale**," "**Sell**" or "**Sold**" shall mean the sale, transfer, exchange, or other disposition of Licensed Products whether by gift or otherwise by COMPANY, its Affiliates, Sublicensees or any third party authorized by COMPANY to make such sale, transfer, exchange or disposition. Sales of

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Licensed Products shall be deemed consummated upon the first to occur of: (a) receipt of payment from the purchaser; (b) delivery of Licensed Products to the purchaser or a common carrier; (c) release of Licensed Products from consignment; (d) if deemed Sold by use, when first put to such use; or (e) if otherwise transferred, exchanged, gifted, or disposed of, when such transfer, exchange, gift, or other disposition occurs.

"**U.S. Government Licenses**" shall mean the non-exclusive license to the U.S. Government or agencies thereof pursuant to 37 CFR Section 401 in connection with NIH grant Nos.: [* * *].

"**Valid Claim**" shall mean a claim in an unexpired patent or pending patent application so long as such claim shall not have been irrevocably abandoned or held invalid in an unappealable decision of a court or other authority of competent jurisdiction in the relevant country.

ARTICLE 2. GRANT OF LICENSE

2.1. License.

2.1.1. LICENSOR hereby grants COMPANY and its Affiliates an exclusive right and license under the Licensed Patents, subject to Sections 2.2 through 2.4, including the right to sublicense, to make, have made, use, perform, sell, offer for sale, import, manufacture and distribute Licensed Products in the Field of Use in the Licensed Territory during the term of the Agreement.

2.1.2. LICENSOR hereby grants COMPANY and its Affiliates a non-exclusive right and license to the Licensed Know-How, subject to Sections 2.2 through 2.4, including the right to sublicense, to make, have made, use, perform, sell, offer for sale, import, manufacture and distribute Licensed Products and products that would be Licensed Products if covered by one or more Valid Claims in the Field of Use in the Licensed Territory during the term of the Agreement.

2.2. Government Rights. COMPANY acknowledges that LICENSOR and COMPANY may have certain obligations and the United States government may have certain rights in the Licensed Technology if such was developed with any assistance through grants or contracts from the United States government. COMPANY hereby warrants that it shall take all action requested to enable LICENSOR to satisfy such obligations. If the United States government should take action which renders it impossible or impractical for LICENSOR to grant, or which conditions or reduces the rights and licenses granted herein, LICENSOR or COMPANY may terminate this Agreement upon reasonable prior notice or cause it to be equitably reformed upon reasonable prior notice to reflect such conditioned or reduced rights and licenses (including without limitation with respect to the value and price of such rights and licenses). COMPANY shall not have any right to the return of any payments of any kind made by it to EMORY prior to the date of such action. To LICENSOR's knowledge as of the Effective Date, the only rights of the United States Federal government with respect to the Licensed Patent are the U.S. Government Licenses.

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2.3. Option. LICENSOR hereby grants COMPANY, subject to third party rights, an exclusive option to an exclusive license to Improvements for a period of two years from the Effective Date. LICENSOR agrees to disclose, within a reasonable amount of time, any Improvements to COMPANY. COMPANY shall provide LICENSOR written notice of its intent to exercise its option within [* * *] days of notification by LICENSOR. Unless otherwise agreed, if COMPANY exercises its option to license any IMPROVEMENT, such Improvements shall be included in the definition of Licensed Patent herein.

2.4. Retained License. The exclusive license granted herein is further conditional on the right retained by LICENSOR, on behalf of itself, its employees and LICENSOR research collaborators, to make, have made, use, import, and transfer Licensed Products and practice Technology for research, educational and non-commercial and humanitarian clinical purposes, subject to the following limitations: LICENSOR shall not engage in any human use of any of the Licensed Technology in the Field of Use without the express written consent of COMPANY and shall not transfer microneedles to any third party for research purposes in the Field of Use without COMPANY's permission, such permission not to be unreasonably withheld. Should COMPANY not provide a response within [* * *] days of a request for permission, permission shall be presumed. Should COMPANY deny permission to transfer microneedles, then COMPANY shall provide the microneedles requested to the third party on reasonable and appropriate terms and conditions.

2.5. Sublicenses. COMPANY may grant sublicenses to third parties ("**Sublicensees**") provided that COMPANY shall be responsible for the operations of its Sublicensees that are relevant to this Agreement and remain responsible for any reporting and any payment of all fees and royalties due under this Agreement.

2.5.1. COMPANY shall include in any sublicense granted pursuant to this Agreement which sublicense provides a Sublicense with the right to sell Licensed Products, a provision requiring the Sublicensee to indemnify Indemnitees and maintain liability coverage to the same extent that COMPANY is so required pursuant to Section 10.3 of this Agreement.

2.5.2. COMPANY shall include in any sublicense granted pursuant to this Agreement that provides a Sublicensee with the right to sell Licensed Products, a provision that grants LICENSOR the right to audit the Sublicensee to the same extent that LICENSOR has the right to audit the COMPANY pursuant to Section 4.4 of this Agreement.

2.5.3. COMPANY shall provide LICENSOR with copies of all sublicense agreements within [* * *] days of their execution date, which, if redacted, must include the relevant provisions under this Article 2 and a disclosure of the financial terms of the sublicense (the use and disclosure of such sublicense agreement and information contained therein by LICENSOR shall be subject to the confidentiality provisions set forth in Section 11 unless otherwise obligated to disclose to the federal government under Bayh-Dole provisions);

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2.5.4. COMPANY shall ensure that any sublicense or distributor agreements will include a provision that causes automatic termination of the sublicense or distribution agreement in the event that a Sublicensee or distributor challenges, either directly or indirectly, the validity, enforceability or scope of any claim within the Licensed Patent in a court or other governmental agency of competent jurisdiction, including in a reexamination or opposition proceeding.

2.5.5. If this Agreement terminates for any reason, any Sublicensee shall, unless the sublicense agreement also terminates, from the effective date of such termination, automatically become a direct licensee of LICENSOR with respect to the rights originally sublicensed to it by COMPANY, provided such Sublicensee did not cause the termination of the Agreement, Sublicensee agrees to comply with all the terms of this Agreement and Sublicensee assumes the responsibilities of COMPANY hereunder, to the extent applicable to the sublicense originally granted to it.

2.5.6. If COMPANY does not enter into a sublicense to the Licensed Patents with [* * *] in a field of use for [* * *] to ocular tissue using microneedle for the purpose of [* * *], with the right to grant further sublicenses in the [* * *], no later than [* * *] from the Effective Date unless Licensee demonstrates to LICENSOR's reasonable satisfaction that such a sublicense could reasonably be expected to interfere with COMPANY's business as evidenced by documentation of secured funding in and business development plan for the [* * *], all rights and licenses to the Licensed Technology in the [* * *] shall revert to LICENSOR. Such license to [* * *] shall generally be in accordance with the term sheet attached hereto as **Appendix I** and shall include such other terms and conditions as COMPANY may reasonably require to protect its business interests with respect to Licensed Products. Should no sublicense agreement be executed by [* * *] from the Effective Date despite reasonable commercial efforts, this paragraph shall not apply unless LICENSOR confirms in writing that [* * *] is still interested in obtaining a license to the Licensed Patents in the [* * *].

2.6. No Implied License. The license and rights granted in this Agreement shall not be construed to confer any rights upon COMPANY by implication, estoppel, or otherwise as to any technology not specifically identified in this Agreement as Licensed Technology.

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2.7. U.S. Manufacturing. To the extent that any Licensed Technology is developed using any funding from the United States, COMPANY agrees that any Licensed Products used or sold in the United States will be manufactured substantially in the United States unless any waivers required are obtained from the United States Government by COMPANY.

ARTICLE 3. CONSIDERATION FOR LICENSE

3.1. License Fee. As partial consideration for the license granted to COMPANY under this Agreement, COMPANY shall pay LICENSOR a license fee in the amount of thirty thousand ($30,000) Dollars (less the $10,000 option fee paid) within thirty (30) days of the Effective Date of this Agreement.

3.2. Running Royalties. As partial consideration for the license granted to COMPANY under this Agreement, COMPANY shall pay LICENSOR a total royalty equal to the percentage set forth on **APPENDIX D** times the Net Selling Price of all Licensed Products Sold during the term of this Agreement by COMPANY, its Affiliates, its Sublicensees or any third party authorized by COMPANY to Sell Licensed Products. Royalties shall be due and payable on a quarterly basis (March 31, June 30, September 30 and December 31).

3.2.1. Sublicensee Royalties. As partial consideration for the license granted to COMPANY under this Agreement, COMPANY shall pay LICENSOR a total royalty equal to, (a) the greater of the royalty rate listed in **Appendix D** or [* * *] of the running royalty payable to the COMPANY or its Affiliates on sales of any Licensed Product Sold during the term of this Agreement by a Sublicensee, if the sublicense is granted prior to the $35,000 Milestone Event referenced in **Appendix F**, or (b) otherwise, the greater of the royalty rate listed in **Appendix D** or [* * *] of the running royalty payable to the COMPANY or its Affiliates on sales of any Licensed Product Sold during the term of this Agreement by a Sublicensee. Any such Sublicense Royalties due under this Agreement shall be due and payable on a quarterly basis (March 31, June 30, September 30 and December 31) and payments due LICENSOR on such Sublicense Royalty payments shall be due and payable thirty (30) days from receipt by COMPANY.

3.2.2. Reduction of Running Royalties-Compulsory Licenses. Should a compulsory license be granted to a third party with respect to Licensed Products in the Licensed Field of Use in any country in the Licensed Territory with a royalty rate lower than the royalty rate provided herein, then the royalty rate to be paid by COMPANY on Sales of Licensed Product in that country under Article 3.2 shall be reduced to the rate paid by the compulsory third party licensee. COMPANY shall provide LICENSOR with prompt written notice of any governmental or judicial procedures initiated in any country to impose a compulsory

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license of which it is aware. If permitted by law, COMPANY shall use commercially reasonable efforts to oppose such compulsory license. At COMPANY's request, LICENSOR will cooperate reasonably in any legal action which COMPANY may wish to take to oppose such compulsory license, which action shall be at COMPANY's sole expense.

3.2.3. Reduction of Royalties-Third Party Royalties. In the event it becomes necessary for COMPANY or its Sublicensee, in the reasonable opinion of its counsel, to obtain a license from a third party in order to make, have made, develop, import, export, use, sell, offer for sale, have sold or otherwise exploit any Licensed Product because, except for a license granted by the third party, sale of a Licensed Product in the relevant country would infringe an intellectual property right of a third party in that country, COMPANY or its Sublicensee may offset the royalty rate paid to LICENSOR on a Licensed Product-by-Licensed Product and country-by-country basis by up to [* * *] of the royalties paid to such third party in any calendar quarter. Notwithstanding the foregoing, however, in no event shall the royalties due to LICENSOR on Net Sales of such Licensed Products in any country be reduced by more than [* * *] of the Running Royalty Percent as identified in **APPENDIX D**.

3.3. Minimum Royalties. In the event that, following the first Sale of a Licensed Product ("First Sale"), the aggregate royalties paid to LICENSOR pursuant to Section 3.2 hereof during any calendar year after the calendar year in which the First Sale occurs do not exceed the minimum royalty set forth in **APPENDIX E**, COMPANY shall pay to LICENSOR no later than [* * *] following the last day of such calendar year the difference between such minimum royalty amount and the actual royalties paid. This Section 3.3 shall terminate upon expiration of the last Valid Claim of a Licensed Patent in the United States.

3.4. Sublicensee Payments. Within thirty (30) days of receipt by COMPANY, COMPANY shall pay LICENSOR [* * *] of any fees or payments paid to COMPANY by a Sublicensee ("Sublicensee Percentage") as consideration for a sublicense grant under this Agreement. Such Sublicense Percentage shall be applied to any payments made to COMPANY by a Sublicensee as consideration for a sublicense grant, including but not limited to any initial licensing fees, milestone fees, maintenance fees and minimum royalty payments, to the extent any such payment is directly attributable to the sublicense of the Licensed Patents and Licensed Technology, but excluding (i) amounts paid to reimburse COMPANY for actual costs (including overhead but excluding profit) incurred in connection with research and development of Licensed Products and the prosecution, maintenance and enforcement of intellectual property rights covering Licensed Products, (ii) the value of any intellectual property rights transferred or granted to COMPANY if such rights are necessary or helpful to the development or commercialization of Licensed Products and (iii) amounts paid for shares of Company stock. If COMPANY in-licenses third

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party technology and/or intellectual property rights and incorporates it into Licensed Product, and receives sublicense revenue with respect to such Licensed Product, then the [* * *] sublicense revenue sharing provided for above shall apply to that portion of the value of the Licensed Product that is attributable to the intellectual property licensed from LICENSOR. For example, the sublicense revenue that is subject to sharing with LICENSOR shall be that fraction A/(A+B) of non-royalty revenue received where A is the amount attributable to the LICENSOR intellectual property, and B is the aggregate amount attributable to the remainder of the technology so licensed. If it is not feasible to accurately determine such amounts, then the allocation shall be commercially reasonable and determined by good faith negotiation between COMPANY and LICENSOR.

3.5. Milestone Payments. COMPANY shall pay LICENSOR a one-time Milestone Payment in the amount specified in **APPENDIX F** no later than [* * *] after the first occurrence of the corresponding Milestone Event. To the extent that a Milestone Payment is due to the COMPANY from a Sublicensee, the COMPANY shall pay LICENSOR the amount of the Milestone Payment due, as well as a Sublicense Percentage of any additional amount paid to COMPANY.

3.6. License Maintenance Fees. In the event no Milestone Payment has been paid to LICENSOR prior to an anniversary of the Effective Date as set forth on **APPENDIX G**, COMPANY shall pay to LICENSOR the corresponding Maintenance Fee. No Maintenance Fee pursuant to this Section 3.6 shall be payable by COMPANY during any year in which (a) it has achieved at least one Milestone Event, (b) it has spent at least $100,000 on research and development of the Licensed Products or (c) it has sold a Licensed Product.

3.7. Reimbursement for Patent Expenses.

(i) COMPANY shall reimburse LICENSOR for all fees, costs, and expenses incurred by LICENSOR after the Effective Date and during the term of this Agreement related to Prosecuting or Maintaining the Licensed Patents in the Licensed Territory, as provided for in Section 7. COMPANY shall deliver such payment to LICENSOR within [* * *] days after LICENSOR notifies COMPANY of the amount of such fees, costs, and expenses.

(ii) COMPANY shall reimburse LICENSOR for all previously unreimbursed fees, costs, and expenses incurred by LICENSOR as of the Effective Date related to Prosecuting or Maintaining the Licensed Patents. These unreimbursed fees, costs, and expenses incurred up to the Effective Date are estimated to be $[* * *], however this amount may be subject to change upon final notification, but in no event shall it be greater than $50,000. COMPANY shall deliver such payment to LICENSOR within [* * *] days after LICENSOR notifies COMPANY of the amount.

3.8. Tax Payments. All payments made to LICENSOR under this Agreement shall be made free and clear of any tax, withholding or other governmental charge or levy (other than taxes imposed on the net income of LICENSOR), all such non-excluded amounts being “Taxes.” However, should the

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COMPANY (or a Sublicensee) be obligated by law to withhold any Taxes on such payments. COMPANY shall promptly pay such tax, levy or charge for and on behalf of LICENSOR to the proper governmental authority, and shall promptly furnish LICENSOR with receipt evidencing such payment. COMPANY shall have the right to deduct any such tax, levy or charge actually paid from payment due LICENSOR. COMPANY shall promptly advise LICENSOR in the event it determines that any tax withholding may be required. COMPANY shall reasonably cooperate with LICENSOR in any lawful action to claim exemption from such deductions or withholdings and otherwise to minimize the amount required to be so withheld or deducted.

ARTICLE 4. REPORTS AND ACCOUNTING

4.1. Progress Reports. Within five (5) days after the Board Meetings directly following each January 1st and July 1st of each calendar year until the First Sale, COMPANY shall provide LICENSOR with a written report detailing the activities of the COMPANY relevant to the COMPANY's Development Plan and the development and commercialization of Licensed Products. For avoidance of doubt, non-receipt of such written report within the specified time period shall be considered a material breach of this Agreement under Section 12.2. For clarification, delivery to Licensor of the materials provided to COMPANY's Board of Directors related to the development and commercialization of Licensed Products shall be deemed to satisfy the written report requirement. If Licensor reasonably determines that such information is not sufficient to determine that Company has met its obligations hereunder or that such information is not sufficient to enable LICENSOR to fulfill its obligation of reporting under Bayh-Dole, Licensor may notify COMPANY of such matter and Licensor shall promptly provide such additional information as may be reasonably necessary to verify or enable such compliance.

4.2. Royalty Reports. During the term of this Agreement, COMPANY shall provide LICENSOR written reports semiannually until the first Sale of a Licensed Product and quarterly thereafter showing:

i. the occurrence of any event triggering a Milestone Payment obligation or any other payment in accordance with Article 3; and

ii. a summary of all reports provided to COMPANY by COMPANY'S Sublicensees, including the names and addresses of all Sublicensees; and

iii. the amount of any consideration received by COMPANY from Sublicensees and an explanation of the contractual obligation satisfied by such consideration;

iv. within a given fiscal quarter, the gross selling price and the number of units of all Licensed Products (identified by product number/name) Sold in each country of the Licensed Territory, together with the calculations of Net Selling Price; and

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v. within a given fiscal quarter, the royalties payable in Dollars which accrued hereunder; and

vi. within a given fiscal quarter, the exchange rates, if any, used in determining the amount due

4.3. Records. During the term of this Agreement and for a period of [* * *] thereafter, COMPANY shall keep at its principal place of business true and accurate records of all Sales in accordance with generally accepted accounting principles in the respective country where such Sales occur and in such form and manner so that all royalties owed to LICENSOR may be readily and accurately determined. COMPANY shall furnish LICENSOR copies of such records upon LICENSOR's request.

4.4. Right to Audit. LICENSOR shall have the right, upon prior notice to COMPANY or a Sublicensee, not more than once in each calendar year and the calendar year immediately following termination of the Agreement, through an independent certified public accountant selected by LICENSOR, to have access during normal business hours as may be reasonably necessary to examine the records of COMPANY or Sublicensee to include, but not be limited to, sales invoice registers, sales analysis reports, original invoices, inventory records, price lists, sublicense and distributor agreements, accounting general ledgers, and sales tax returns, in order to verify the accuracy of the of the calculation of any payment due under this Agreement. Such audit shall be limited in scope to the preceding [* * *] from the date of the notice of audit. If such independent public accountant's report shows any underpayment of royalties by COMPANY, its Affiliates or Sublicensees, within [* * *] days after COMPANY'S receipt of such report, COMPANY shall remit or shall cause its Sublicensees to remit to LICENSOR:

i. the amount of such underpayment; and

ii. if such underpayment exceeds [* * *] of the total royalties owed for the fiscal year then being reviewed, the reasonably necessary fees and expenses of such independent public accountant performing the audit. Otherwise, LICENSOR's accountant's fees and expenses shall be borne by LICENSOR.

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ARTICLE 5. PAYMENTS

5.1. Payment Due Dates. Royalties shall be due commencing upon the first Sale of a Licensed Product in the Licensed Field of Use in any country in the Licensed Territory. Royalties and sublicense fees payable to LICENSOR as a result of activities occurring during the period covered by each royalty report provided for under Article 4 of this Agreement shall be due and payable on the date such royalty report is due. All other payments required under this Agreement, if not specified otherwise in this Agreement, shall be payable within [* * *] days of the due date for each payment.

5.2. Payment Delivery. Unless otherwise requested by LICENSOR, all payments due to LICENSOR under this Agreement shall be made in person or via the United States mail or private carrier to the following address:

Emory University
Attn: Director, Office of Technology Transfer
1599 Clifton Rd. 4th Floor
Atlanta, Georgia 30322
Facsimile: (404) 727-1271

Any payment in excess of [* * *] or originating outside of the United States shall be made by wire transfer to an account of LICENSOR designated by LICENSOR from time to time and royalty reports shall be sent by facsimile or express courier to the Director, Office of Technology Transfer on the same date. Royalty reports may also be transmitted via email to [* * *], provided that if no confirmation of receipt is received, COMPANY agrees to forward the report via facsimile.

5.3. Currency Conversion. Except as hereinafter provided in this Section 5.3, all royalties shall be paid in Dollars. If any Licensed Products are Sold for consideration other than Dollars, the Net Selling price of such Licensed Products shall first be determined in the foreign currency of the country in which such Licensed Products are Sold and then converted to Dollars at a ninety (90)-day trailing average published by the Wall Street Journal (U.S. editions) for conversion of the foreign currency into Dollars on the last day of the quarter for which such payment is due.

5.4. Interest. Royalties and other payments, including patent expense reimbursements, required to be paid by COMPANY pursuant to this Agreement shall, if overdue, bear interest until payment at a rate [* * *] per month. The interest payment shall be due from the day the original payment was due until the day that the payment was received by LICENSOR. The payment of such interest shall not foreclose LICENSOR from exercising any other rights it may have because any payment is overdue.

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ARTICLE 6. DILIGENCE AND COMMERCIALIZATION

6.1. Diligence. COMPANY represents and warrants that it has the necessary expertise and will, as appropriate, acquire the necessary resources to reasonably develop and commercialize Licensed Products. COMPANY shall use its commercially reasonable efforts, either directly or through Affiliates or Sublicensees, throughout the term of this Agreement to comply with COMPANY's Development Plan and to bring Licensed Products to market through a commercially reasonable and diligent program for exploitation of the right and license granted in this Agreement to COMPANY and to create, supply, and service in the Licensed Territory as extensive a market as reasonably commercially practicable. In no instance shall COMPANY's commercially reasonable efforts be less than efforts customary in COMPANY's industry.

6.2. Development Milestones. COMPANY shall adhere to the schedule of development milestones and dates set forth in **APPENDIX H**. If COMPANY fails to meet any deadline set forth in **APPENDIX H**, COMPANY shall provide LICENSOR with a written report outlining the efforts undertaken thus far and the steps COMPANY will take to meet the unsatisfied milestone, which shall also include an adjustment in the time required to meet such milestone or a substitute milestone ("Time Adjustment Proposal"). For clarity, a non-limiting example of a reasonable request for a Time Adjusted Delay contemplated herein is regulatory review delay of the responsible agency. Such report shall be submitted to LICENSOR for consideration within [* * *] days after the failure to meet the milestone. If COMPANY fails to provide the report, LICENSOR reasonably declines to accept the Time Adjustment Proposal, or if COMPANY fails to meet the new deadlines set in the Time Adjustment Proposal approved by LICENSOR, LICENSOR shall have the option in its sole discretion and following [* * *] days written notice to COMPANY to terminate the license granted hereunder, to allow this Agreement to continue in full force and effect, or to convert the license granted hereunder to a nonexclusive license upon written notice to COMPANY. Notwithstanding the foregoing, if COMPANY effects an assignment permitted by Article 13 prior to the first commercial Sale of a Licensed Product, the deadline set forth on Appendix H for such due diligence milestone event may, at the election of the COMPANY, be extended by a period of [* * *], with the option to extend by a period of an additional [* * *] with payment of a nonrefundable fee of [* * *], provided, however that such extensions shall not relive COMPANY of its obligation to continue to use commercially reasonable efforts to bring Licensed Product to market.

6.3. Sublicensee Performance. LICENSOR agrees that a Sublicensee's performance of its diligence obligations regarding a Licensed Product as set forth in the sublicense agreement shall be deemed to be performance by COMPANY of its diligence obligations for such Licensed Product under this License Agreement, including, but not limited to, those set forth in Article 6 hereof. COMPANY further agrees to attach copies of pertinent portions of this Agreement to executed sublicense agreements.

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ARTICLE 7. PATENT PROSECUTION

7.1. Licensed Patents. The Prosecution and Maintenance of the Licensed Patents shall be the primary responsibility of LICENSOR. LICENSOR shall utilize patent counsel that is acceptable to COMPANY for the Prosecution and Maintenance of the Licensed Patents.

i. Comment. LICENSOR shall use reasonable efforts to provide COMPANY with copies of all filings and official correspondence pertaining to such Prosecution and Maintenance of the Licensed Patents at least thirty days prior to any deadline so as to give COMPANY an opportunity to advise and cooperate with LICENSOR in such Prosecution and Maintenance. In the event LICENSOR desires to transfer the prosecution of any of the Licensed Patents to new patent counsel, LICENSOR shall be responsible for costs associated with effecting the transfer and COMPANY's written consent shall be obtained, which consent shall not be unreasonably withheld or delayed.

ii. New Applications. COMPANY shall notify LICENSOR in writing of the countries in which COMPANY wishes additional patent applications to be filed, including but not limited to national phase filings and regional registrations. LICENSOR shall, at COMPANY's expense, file such additional patent applications. LICENSOR may, at its own expense, file patent applications in any country in which COMPANY elects not to file and such applications shall not be subject to any license granted to COMPANY hereunder.

iii. Reimbursement. If COMPANY should fail to timely make reimbursement for patent expenses for any Licensed Patent, LICENSOR, in addition to any other remedies under the Agreement, shall have no further obligation to Prosecute or Maintain such Licensed Patent(s). COMPANY, upon [* * *] days written notice, may advise LICENSOR that it no longer wishes to pay expenses for Prosecution or Maintenance of one or more Licensed Patents on a country-by-country basis. LICENSOR may, at its sole option, elect to pay such expenses and, if so, such patents or patent applications shall cease to be subject to any license granted to COMPANY hereunder.

7.2 Extension of Licensed Patents. COMPANY, at its expense, may request that LICENSOR have the normal term of any Licensed Patents extended or restored under any country's procedure for extending patent term and LICENSOR shall use all reasonable efforts to do so. Royalties shall be payable until the end of the extended term of the patent. LICENSOR acknowledges that there are limits on the number of patents that may be extended with respect to any product and that COMPANY shall have the right in its sole discretion to determine which patent, if any, shall be extended with respect to any Licensed Product.

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ARTICLE 8. INFRINGEMENT

8.1 The parties shall promptly notify each other of any suspected infringement of any Licensed Patents.

i. During the Term, COMPANY shall, at its expense, have the right to enforce any Licensed Patents against such infringer and may defend any declaratory judgment action brought against it alleging the invalidity of a Licensed Patent. COMPANY agrees to defend LICENSOR against any counterclaim brought against it in such action. LICENSOR shall cooperate with COMPANY in such effort, and EMORY agrees that it will, at COMPANY'S expense, be joined as a party to such action, if necessary. It is LICENSOR's intention that COMPANY be able to prosecute an alleged infringement without including LICENSOR as a party to the litigation, should LICENSOR choose at its discretion not to be a party to the litigation, and as such herein grants COMPANY the rights in Licensed Patents to sue an infringer alone. Should GTRC choose not to join in such action and COMPANY is unable to initiate or prosecute such action in its name only by a ruling of a court of competent jurisdiction, GTRC shall assign to EMORY only such rights to the applicable Licensed Patent that may be necessary to permit COMPANY to initiate or prosecute such action without GTRC, provided that COMPANY shall be responsible for all reasonable attorney's fees and costs associated with LICENSOR's participation in such suit. COMPANY shall reimburse LICENSOR for any costs incurred, including reasonable attorneys' fees, as part of any action brought by COMPANY.

ii. COMPANY shall not enter into any settlement agreement, voluntary dismissal, consent judgment or other voluntary final disposition in any action regarding the Licensed Patents, without the express written consent of LICENSOR if such agreement would or would be reasonably likely to have a material adverse effect on the validity or enforceability of the Licensed Patents, which consent shall not be unreasonably withheld, conditioned or delayed. Consent shall be deemed given hereunder if no objection is provided in writing within fifteen days of delivery of the request for such consent. Any recovery or settlement received (whether for punitive or exemplary damages, or any other recovery or settlement received, including compensatory damages or damages based on loss or revenues (hereinafter referred to as "Recovery")), shall first be used to reimburse the documented out-of-pocket costs and expenses incurred by COMPANY and LICENSOR in pursuing such action, and to the extent any portion of the balance of the

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Recovery represents compensatory damages, for example, compensation for loss of revenues, such portion shall be deemed to be the Sales of Licensed Products in the fiscal quarter received by COMPANY, and COMPANY shall pay to LICENSOR an amount representing the royalty which would have been paid by COMPANY in accordance with the provisions of Article 3.2 had such portion of the Recovery been accrued by COMPANY as Sales. Any remaining amounts of such Recovery that represents, for example, additional damages (such as enhanced or punitive damages) shall be paid (a) [* * *] to the extent the Recovery is attributable to infringement in the United States of Licensed Patents and (b) otherwise [* * *].

8.2 If COMPANY fails, within [* * *] days after receiving notice of a potential infringement that would or would be reasonably likely to have a material adverse effect the validity or enforceability of the Licensed Patents , to institute an action against such infringer or notifies LICENSOR that it does not plan to institute such action, then LICENSOR shall have the right to do so at its own expense unless COMPANY notifies LICENSOR that COMPANY is engaged in bona fide negotiations for the grant to the alleged infringer of a sublicense. COMPANY shall cooperate with LICENSOR in such effort including being joined as a party to such action if necessary. LICENSOR shall be entitled to retain all damages or costs awarded in such action. Should either LICENSOR or COMPANY be a party to a suit under the provisions of this Article and thereafter elect to abandon such suit, the abandoning party shall give timely notice to the other party who may, at its discretion, continue prosecution of such suit.

ARTICLE 9. LIMITED WARRANTY AND EXCLUSION OF WARRANTIES

9.1 Representation by Licensor. LICENSOR represents that it has the right and authority to enter into this Agreement and that, to the best of its knowledge, neither the execution of this Agreement nor the performance of its obligations hereunder will constitute a breach of the terms and provisions of any other agreement to which LICENSOR is a party. LICENSOR represents that, to the best of its knowledge, it is an owner of the Licensed Technology and has the right to issue licenses to the same. LICENSOR has provided to the COMPANY copies of assignments whereby each inventor named in a Licensed Patent has assigned to LICENSOR all of such inventor’s interest in any inventions claimed in any such Licensed Patent.

It is hereby acknowledged and expressly understood by COMPANY that GTRC and EMORY do not represent or warrant that COMPANY may practice the Licensed Technology hereunder without infringing one or more patents, which may be owned by GTRC. Furthermore, GTRC and EMORY do not warrant that the Licensed Patents licensed hereunder or Licensed Technology may be exploited by COMPANY or its Affiliates or Sublicensees without infringing other patents, which may be owned by GTRC. To the extent GTRC is able and GRTC and COMPANY can reach agreement, and upon COMPANY’s election, GTRC will grant COMPANY non-exclusive rights to additional technologies owned by GTRC under a completely separate agreement.

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LICENSOR does not warrant the validity of the Licensed Patents licensed hereunder and makes no representation whatsoever with regard to the scope of the Licensed Patents or that such Licensed Patents or Licensed Technology may be exploited by COMPANY or its Affiliates or Sublicensees without infringing other patents including those owned by GTRC.

9.2 Merchantability and Exclusion of Warranties. COMPANY possesses the necessary expertise and skill in the technical areas pertaining to the Licensed Products and Licensed Technology to make, and has made, its own evaluation of the capabilities, safety, utility and commercial application of the Licensed Products and Licensed Technology. ACCORDINGLY, LICENSOR DOES NOT MAKE ANY REPRESENTATION OR WARRANTY OF ANY KIND WITH RESPECT TO THE LICENSED TECHNOLOGY OR LICENSED PRODUCTS AND EXPRESSLY DISCLAIMS ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE AND ANY OTHER IMPLIED WARRANTIES WITH RESPECT TO THE CAPABILITIES, SAFETY, UTILITY, OR COMMERCIAL APPLICATION OF THE LICENSED TECHNOLOGY OR LICENSED PRODUCTS.

9.3 FDA and Other Regulations. COMPANY represents and warrants that any Products made or Sold by COMPANY or its Affiliates pursuant to this Agreement shall comply with all applicable federal and state law regulations, including but not limited to regulations of the Federal Drug Administration, the Environmental Protection Agency, and their state equivalents. COMPANY further warrants to include in any sublicense agreement in which a Sublicensee is granted the right to make and sell Licensed Products, that such agreement shall include a comparable covenant by the Sublicensee.

ARTICLE 10. DAMAGES, INDEMNIFICATION AND INSURANCE

10.1 No Liability. LICENSOR shall not be liable to COMPANY or COMPANY'S Affiliates, or customers and/or Sublicensees of COMPANY or COMPANY'S Affiliates, for compensatory, special, incidental, indirect, consequential or exemplary damages resulting from the manufacture, testing, design, labeling, use or sale of Licensed Products.

10.2 Indemnification. COMPANY shall defend, indemnify, and hold harmless the Indemnitees, from and against any and all claims, demands, loss, liability, expense, or damage (including investigative costs, court costs and attorneys' fees) Indemnitees may suffer, pay, or incur as a result of claims, demands or actions against any of the Indemnitees caused or contributed to, in whole or in part, by COMPANY'S or COMPANY'S Affiliates, contractors, agents, or Sublicensees manufacture, testing, design, use, Sale, or labeling of any Licensed Products or the use of any Licensed Technology. COMPANY'S obligations under this Article shall survive the expiration or termination of this Agreement for any reason.

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COMPANY agrees to provide attorneys reasonably acceptable to LICENSOR to defend against such a claim. LICENSOR shall cooperate with COMPANY in any defense of such claim. COMPANY shall not settle any such claims, demands or actions under this Section 10.2, without the express, prior written consent of LICENSOR, which consent shall not be unreasonably withheld or delayed. COMPANY'S obligations under this Article shall survive the expiration or termination of this Agreement for any reason. Notwithstanding the foregoing, in the case of both the Georgia Institute of Technology and the Board of Regents of the State of Georgia, at their sole discretion, the Attorney General of the State of Georgia may represent them on any such matter.

10.3 Insurance. Without limiting COMPANY'S indemnity obligations under the preceding paragraph, COMPANY shall, prior to any clinical trial or Sale of any Licensed Product, cause to be in force a products liability insurance (or, prior to first commercial Sale, general commercial liability and/or clinical trials insurance) policy. Such polic(y)(ies) shall:

i. provide Indemnitees product liability, clinical trial and/or general liability coverage in an amount no less than $Two Million Dollars ($2,000,000.00) per occurrence for personal injury and $1,000,000 per occurrence for property damage;

ii. insure Indemnitees for all claims, damages, and actions mentioned in Section 10.2 of this Agreement;

iii. include contractual liability coverage for all liability which may be incurred by Indemnitees in connection with this Agreement;

iv. require the insurance carrier to provide LICENSOR with no less than thirty (30) days' written notice of any change in the terms or coverage of the policy or its cancellation; and

v. If written on a "claims made" basis, the Company agrees to provide coverage for five years after termination of the Agreement.

Company shall purchase statutory Workers Compensation insurance including employers liability as required by applicable law

All insurance coverage required under this Agreement shall be primary to any coverage carried by LICENSOR, shall waive all rights of subrogation against any additional insured and shall be placed with insurers whose A.M. Best's rating is at least A-X.

As detailed in Section 2.5, COMPANY agrees to require any Sublicensee under Section 2.5 of this Agreement to maintain insurance coverage consistent with this Section 10.3. Notwithstanding the foregoing, self-insurance may be substituted for insurance meeting the above standards if (a) Company has become an Affiliate of a company with a market capitalization in excess of US$10 billion or (b) trials are conducted by or on behalf of a Sublicensee that, together with its Affiliates, meets the foregoing market capitalization test.

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10.4 Notification. COMPANY shall provide to LICENSOR prior to its, Affiliate's and/or Sublicensee's first clinical trial or commercial Sale of any Licensed Product, certificates of insurance evidencing the coverages required in section 10.3 above and adding LICENSOR as an additional insured.

10.5 Notice of Claims. COMPANY shall promptly notify LICENSOR of all claims involving the Indemnitees and shall advise LICENSOR of the amounts that might be needed to defend and pay any such claims. LICENSOR shall promptly notify COMPANY of any and all claims brought to its attention relating to COMPANY's indemnity obligations under this Agreement.

ARTICLE 11. CONFIDENTIALITY

11.1 Treatment of Confidential Information. Except as otherwise provided hereunder, during the term of this Agreement and for a period of five (5) years thereafter:

i. COMPANY and its Affiliates and Sublicensees shall retain in confidence and use only for purposes of this Agreement, any written information and data supplied by LICENSOR under this Agreement;

ii. LICENSOR shall retain in confidence and use only for purposes of this Agreement any written information and data supplied by COMPANY under this Agreement and marked as proprietary, except for any information required to be provided to the federal funding agency under 35 CFR Part 401 and its accompanying legislation (commonly referred to as the "Bayh-Dole Act").

For purposes of this Agreement, all such information and data which a party is obligated to retain in confidence shall be called "Confidential Information."

11.2 Right to Disclose. To the extent that it is reasonably necessary to fulfill its obligations or exercise its rights under this Agreement, or any rights which survive termination or expiration hereof, each party may disclose Confidential Information to its Affiliates, Sublicensees, consultants, outside contractors, governmental regulatory authorities and clinical investigators on condition that such entities or persons agree:

i. to keep the Confidential Information confidential for at least the same time periods and to the same extent as each party is required to keep it confidential;

ii. to use the Confidential Information only for such purposes as such parties are authorized to use it.

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11.3 Release from Restrictions. Each party or its Affiliates or Sublicensees may use or disclose Confidential Information to the government or other regulatory authorities to the extent that such disclosure is reasonably necessary for the prosecution and enforcement of patents, or to obtain or maintain any regulatory approval, including authorizations to conduct clinical trials, or commercially market or obtain pricing approval of any Licensed Products, provided that such party is otherwise entitled to engage in such activities under this Agreement.

The obligation not to disclose Confidential Information shall not apply to any part of such Confidential Information that:

i. is or becomes patented, published or otherwise part of the public domain, other than by unauthorized acts of the party obligated not to disclose such Confidential Information (for purposes of this Article 11 the "receiving party") or its Affiliates or Sublicensees in contravention of this Agreement;

ii. is disclosed to the receiving party or its Affiliates or Sublicensees by a third party provided that such Confidential Information was not obtained by such third party directly or indirectly from the other party under this Agreement; or

iii. prior to disclosure under this Agreement, was already in the possession of the receiving party, its Affiliates or Sublicensees, provided that such Confidential Information was not obtained directly or indirectly from the other party under this Agreement; or

iv. results from research and development by the receiving party or its Affiliates or Sublicensees, independent of disclosures from the other party of this Agreement, provided that the persons developing it have not had exposure to the Confidential Information from the disclosing party; or

v. is required by law to be disclosed by the receiving party, provided that the receiving party uses its best efforts to notify the other party immediately upon learning of such requirement in order to give the other party reasonable opportunity to oppose such requirement; or

vi. COMPANY and LICENSOR agree in writing may be disclosed; or

vii. is subject to an open records request under the laws of the State of Georgia. LICENSOR shall reasonably cooperate with COMPANY in any lawful effort requested by COMPANY to minimize disclosures pursuant to any such law.

ARTICLE 12. TERM AND TERMINATION

12.1 Term. Unless sooner terminated as otherwise provided in this Agreement, the term of this Agreement shall commence on the effective date hereof and shall continue in full force and effect until the expiration of the last to expire of the Licensed Patents. Following termination resulting from expiration of Licensed Patents only, on a country by country basis, COMPANY shall have a perpetual, irrevocable non-exclusive royalty-free license to the Licensed Know-How.

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12.2 Termination. LICENSOR shall have the right to terminate this Agreement upon the occurrence of a material breach. Without limitation, any one or more of the following shall each be deemed a material breach of this Agreement by COMPANY:

i. failure of COMPANY to make any payment required under this Agreement when due; or

ii. failure of COMPANY to provide Progress Reports or Royalty Reports; or

iii. lack of Diligence as set forth in Article 6; or

iv. the dissolution of the Company, the institution of any proceeding under any bankruptcy, insolvency, or moratorium law, by or on behalf of COMPANY or its creditors (excluding a reorganization under Chapter 11 of the US Bankruptcy Code or similar law of another jurisdiction in which the reorganized entity assumes and timely satisfies the obligations under this Agreement and excluding an involuntary bankruptcy, insolvency or similar proceeding initiated by creditors and dismissed within sixty days of commencement); or

v. any COMPANY decision to cease developing or quit the business of selling Licensed Products; or

vi. the breach by COMPANY of any other material term of this Agreement.

12.3 LICENSOR shall provide COMPANY written notice describing the breach, which notice shall include LICENSOR's intention to terminate the Agreement. If COMPANY does not cure the breach within thirty (30) days after receipt of such notice, this Agreement will terminate immediately without further action by LICENSOR. If COMPANY disputes such breach in good faith by written notice to LICENSOR within the thirty (30) day period, the matter will be submitted to dispute resolution as described under Article 14. LICENSOR's right to terminate shall be suspended until resolution of the dispute. The procedures set forth in this Section 12.2 shall not prejudice LICENSOR's right to receive royalties or other sums due hereunder and shall not prejudice any cause of action or claim due to any breach or default by the COMPANY.

Notwithstanding the foregoing, if the COMPANY challenges the validity or enforceability of any Licensed Patents in a court or other governmental agency of competent jurisdiction, this Agreement shall terminate immediately.

12.4 Notice of Bankruptcy. COMPANY must inform LICENSOR of its intention to file a voluntary petition in bankruptcy or of another's intention to file an involuntary petition in bankruptcy to be received at least forty five (45) days prior to filing such a petition. If COMPANY files a petition of bankruptcy without conforming to this requirement, this shall be deemed a material, pre-petition, incurable breach.

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12.5 Failure to Enforce. The failure of LICENSOR, at any time, or for any period of time, to enforce any of the provisions of this Agreement, shall not be construed as a waiver of such provisions or as a waiver of the right of LICENSOR thereafter to enforce each and every such provision of this Agreement.

12.6 Termination by COMPANY. COMPANY shall have the right to terminate this Agreement at its sole discretion upon sixty (60) days written notice to LICENSOR and upon payment of any amounts due to LICENSOR under this Agreement through the effective date of such termination.

12.7 Effect. If this Agreement is terminated for any reason whatsoever (other than expiration or as a result of material breach by LICENSOR), COMPANY shall return, or at LICENSOR's direction, destroy, all tangible materials (including plans, documents, samples, biological materials, models and the like) pertaining to the Licensed Patents or Licensed Technology supplied to COMPANY by LICENSOR, retaining archival copies in its corporate legal or data management department as required so that compliance with any continuing obligations may be determined. Within [* * *] days after termination of this Agreement for any reason (other than expiration or as a result of material breach by LICENSOR), COMPANY shall provide LICENSOR full and complete copies of development information, including in vitro studies, toxicology, pharmacokinetic, efficacy, clinical and other technical data and all correspondence to and from regulatory agencies relating to approval of Licensed Products generated by COMPANY and/or its Affiliates, contractors and agents to the extent the Company can do so without violating the rights of any third party (hereinafter "Development Information"). Development Information shall remain the Confidential Information of Licensee, subject to the protections of Article 11 and subject to the rights in favor of LICENSOR set forth in Section 12.8. Upon termination of this Agreement (other than upon expiration), COMPANY shall cease manufacturing, processing, producing, using, importing or Selling Licensed Products; provided, however, that COMPANY may continue to Sell in the ordinary course of business for a period of [* * *] reasonable quantities of Licensed Products which are fully manufactured or on order at the date of termination if (a) all monetary obligations of COMPANY to LICENSOR have been satisfied and (b) royalties on such sales are paid to LICENSOR in the amounts and in the manner provided in this Agreement. However, nothing herein shall be construed to release either party of any obligation which matured prior to the effective date of such termination.

12.8 Development Information. COMPANY shall, subject to any rights any Sublicensees or other third parties may have with respect to Development Information, grant to LICENSOR a right for LICENSOR to access and to refer to all Development Information delivered or required to be delivered pursuant to Section 12.7, and to provide a copy thereof to potential licensees of the Licensed Patents (under conditions of confidentiality consistent with Article 11), solely for use in LICENSOR's efforts to license the Licensed Patents to any third party; LICENSOR shall not be entitled to license, grant, or transfer to any third party any rights in such Development Information. In the event LICENSOR agrees

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in writing to material economic terms with a third party concerning the grant of a license to such third party under the Licensed Patents formerly licensed to COMPANY hereunder, LICENSOR shall provide written notice thereof to COMPANY and COMPANY shall enter into good faith negotiations with such third party concerning the granting of rights to, or transfer of title in, the Development Information to such third party on commercially reasonable terms, subject to any rights any Sublicensees or other third parties may have with respect to any of the foregoing that survive termination of this Agreement.

ARTICLE 13. ASSIGNMENT

COMPANY may grant, transfer, convey, or otherwise assign any or all of its rights and obligations under this Agreement in conjunction with the transfer of all, or substantially all, of the business interests of COMPANY related to Licensed Products. LICENSOR's written consent, which shall not be unreasonably withheld, shall be required prior to any other assignment of COMPANY'S rights or obligations under this Agreement. This Agreement shall be assignable by LICENSOR to any other nonprofit corporation which promotes the research purposes of LICENSOR, including but not limited to GIT, the Georgia Tech Foundation, and/or the Board of Regents of the University System of Georgia.

ARTICLE 14. DISPUTE RESOLUTION

14.1. Negotiation. Any dispute related to this License Agreement shall be settled in accordance with the procedures specified in this Section. COMPANY and LICENSOR agree to attempt to settle any claim or controversy arising out of this Agreement through consultation and negotiation in good faith and spirit of mutual cooperation. Any dispute between the parties relating to this Agreement will first be submitted in writing to a senior executive of COMPANY and LICENSOR (the "Dispute Notice"), who will promptly meet and confer in an effort to resolve such dispute. Any agreed decisions of the executives will be final and binding on the parties. All negotiations pursuant to this Section are confidential and shall be treated as compromise and settlement negotiations for purposes of applicable rules of evidence.

14.2. Non-binding Mediation. If the parties are unable to resolve any dispute by negotiation within [* * *] days of the Dispute Notice, then either party may initiate mediation upon written notice to the other party demanding mediation (the "Mediation Notice"), whereupon the dispute will be mediated by a mutually acceptable mediator to be chosen within [* * *] days after the Mediation Notice. The parties will share the costs of the mediator equally. If the parties cannot agree upon selection of a mediator within [* * *] days of the notice, then upon request of either party, the AAA shall appoint the mediator. Mediation shall take place in Atlanta, Georgia and shall proceed under the then current American Arbitration Association Model Commercial Mediation Procedures to the extent that the Model Procedure does not conflict with provisions of this article.

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14.3. Costs. The fees and expenses, but not attorney's fees, incurred in connection with any non-binding mediation shall be borne by the party initiating the non-binding mediation proceeding (or equally by both parties if both parties jointly initiate such proceeding) subject to reimbursement by the party which does not prevail in such proceeding promptly upon the termination thereof in the event that the party initiating such proceeding is the prevailing party.

14.4. Continued Obligations. Each party shall continue to perform its undisputed obligations under this Agreement, including payments due, pending final resolution of any dispute arising out of or relating to this Agreement; provided, however that a party may suspend performance during any period in which the other party fails to perform its undisputed obligations.

ARTICLE 15. MISCELLANEOUS

15.1 Export Controls. COMPANY acknowledges that Licensed Products and Licensed Technology may be subject to United States laws and regulations controlling the export of technical data, biological materials, chemical compositions, computer software, laboratory prototypes and other commodities and that LICENSOR's obligations under this Agreement are contingent upon compliance with applicable United States export laws and regulations. The transfer of technical data and commodities may require a license from the cognizant agency of the United States government or written assurances by COMPANY that COMPANY shall not export data or commodities to certain foreign countries without the prior approval of certain United States agencies. LICENSOR neither represents that an export license shall not be required nor that, if required, such export license shall issue.

15.2 Legal Compliance. COMPANY shall comply in all material respects with all laws and regulations relating to its manufacture, processing, producing, using, importing Selling, labeling or distribution of Licensed Products and Licensed Technology and shall not take any action which would cause LICENSOR to violate any laws or regulations.

15.3 Independent Contractor. COMPANY's relationship to LICENSOR shall be that of a licensee only. COMPANY shall not be the agent of LICENSOR and shall have no authority to act for, or on behalf of, LICENSOR in any matter. Persons retained by COMPANY as employees or agents shall not, by reason thereof, be deemed to be employees or agents of LICENSOR.

15.4 Patent Marking. COMPANY shall mark Licensed Products Sold in the United States with United States patent numbers. Licensed Products manufactured or Sold in other countries shall be marked in compliance with the intellectual property laws in force in such foreign countries.

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15.5 Use of Names. COMPANY shall obtain the prior written approval of LICENSOR prior to making use of their names for any commercial purpose, except as required by law. As an exception to the foregoing, both COMPANY and LICENSOR shall have the right to publicize the existence of this Agreement; however, neither COMPANY nor LICENSOR shall disclose the terms and conditions of this Agreement without the other party's consent, except as required by law. Notwithstanding the foregoing, (a) COMPANY shall not use the names of Georgia Tech Research Corporation, the Georgia Institute of Technology, Georgia Tech, the Georgia Tech Foundation or any of their respective affiliates or divisions or any derivations thereof in any advertisement, publications, or sales materials without the prior written consent of GTRC and (b) COMPANY may disclose this Agreement and the terms hereof on a confidential basis to actual or prospective acquirors, merger partners, sources of funding, professional advisors, Sublicensees and research and commercialization collaborators.

15.6 Place of Execution. This Agreement and any subsequent modifications or amendments hereto shall be deemed to have been executed in the State of Georgia, U.S.A.

15.7 Governing Law. This Agreement and all amendments, modifications, alterations, or supplements hereto, and the rights of the parties hereunder, shall be construed under and governed by the laws of the State of Georgia and the United States of America.

15.8 Venue. Only courts in the State of Georgia, U.S.A., shall have jurisdiction to hear and decide any controversy or claim between the parties arising under or relating to this Agreement.

15.9 Entire Agreement. This Agreement constitutes the entire agreement between LICENSOR and COMPANY with respect to the subject matter hereof and shall not be modified, amended or terminated, except as herein provided or except by another agreement in writing executed by the parties hereto.

15.10 Survival. Articles 9, 10, 11, 12.7 and 12.8 shall survive termination of this Agreement for any reason.

15.11 Severability. All rights and restrictions contained herein may be exercised and shall be applicable and binding only to the extent that they do not violate any applicable laws and are intended to be limited to the extent necessary so that they will not render this Agreement illegal, invalid or unenforceable. If any provision or portion of any provision of this Agreement, not essential to the commercial purpose of this Agreement, shall be held to be illegal, invalid or unenforceable by a court of competent jurisdiction, it is the intention of the parties that the remaining provisions or portions thereof shall constitute their agreement with respect to the subject matter hereof, and all such remaining provisions, or portions thereof, shall remain in full force and effect. To the extent legally permissible, any illegal, invalid or unenforceable provision of this Agreement shall be replaced by a valid provision which shall implement the commercial purpose of the illegal, invalid, or unenforceable provision.

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15.12 Force Majeure. Any delays in, or failure of performance of any party to this Agreement, shall not constitute a default hereunder, or give rise to any claim for damages, if and to the extent caused by occurrences beyond the control of the party affected, including, but not limited to, acts of God, strikes or other concerted acts of workmen, civil disturbances, fires, floods, explosions, riots, war, rebellion, sabotage, acts of governmental authority or failure of governmental authority to issue licenses or approvals which may be required.

15.13 Counterparts. This Agreement may be executed by facsimile and in counterparts, each of which is deemed an original, but all of which together shall constitute one and the same instrument

ARTICLE 16. NOTICES

All notices, statements, and reports required to be given by one party to the other shall be in writing. Progress and Royalty reports required under Article 4 may be delivered electronically with a copy to [* * *] and to [* * *].

Except for progress and royalty reports required under Article 4, all reports shall be hand delivered, sent by private overnight mail service, or sent by registered or certified U.S. mail, postage prepaid, return receipt requested and addressed as follows:

If to EMORY:

Emory University
Office of Technology Transfer
1599 Clifton Rd., 4th Floor
Atlanta, Georgia 30322
ATTN: Director
Facsimile: (404) 727-1271

If to GTRC:

Director, Office of Innovation Commercialization
Georgia Tech Research Corporation
505 Tenth St NW
Atlanta, GA 30332-0415
Fax: (404) 894-9728

If to COMPANY:

Clearside Biomedical, Inc.
1220 Old Alpharetta Rd. Suite 300
Alpharetta GA 30005
Attn: CEO

With a copy to

Hutchison Law Group
5410 Trinity Road, Suite 400
Raleigh, NC 27607
bwofford@hutchlaw.com

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Such notices or other communications shall be effective upon receipt by an employee, agent or representative of the receiving party authorized to receive notices or other communications sent or delivered in the manner set forth above. Any party hereto may change the address to which notices to such party are to be sent by giving notice to the other party at the address and in the manner provided above. Any notice may be given, in addition to the manner set forth above by facsimile provided that the party giving such notice obtains acknowledgement by facsimile that such notice has been received by the party to be notified. Notice made in this manner shall be deemed to have been given when such acknowledgement has been transmitted.

[signature page follows]

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IN WITNESS WHEREOF, LICENSOR and COMPANY have caused this Agreement to be signed by their duly authorized representatives as of the Effective Date.

EMORY UNIVERSITY

By: /s/ Todd Sherer
Name: Todd T. Sherer, Ph.D.
Title: Assistant Vice President for Research and Director office of Technology Transfer

CLEARSIDE BIOMEDICAL, INC.

By: /s/ Daniel H. White
Name: Daniel H. White
Title: President & CEO

LIC.__.__

GEORGIA TECH RESEARCH CORPORATION

By: /s/ Jilda Diehl Garton
Name: Jilda Diehl Garton
Title: General Manager

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APPENDIX A

COMPANY'S DEVELOPMENT PLAN

[* * *]

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APPENDIX B

LICENSED PATENTS

U.S. Patent No. 7,918,814 entitled “Method for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Patent Serial No. 12/767,768 “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

PCT Patent Application No. PCT/US2011/033987 “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Patent Serial No. 13/447,246 “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Patent Serial No. 13/453,407 “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Draft provisional patent application based on the invention disclosure [* * *], which application is titled, “METHODS AND DEVICES FOR DRUG DELIVERY USING MICRONEEDLES” .

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APPENDIX C

[omitted]

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APPENDIX D

RUNNING ROYALTY PERCENTAGES

	Percentage of Net Selling Price
510k/CE device disposable tip	[***]%
510k/CE device syringe plus tip	[***]%
Device in combination or packaged with enabling instrument	[***]%
Device in combination with Patent Protected Active Pharmaceutical Ingredient (API)	[***]%
Device in combination with a Generic active pharmaceutical ingredient	[***]%
Device in combination with Non API (e.g., balanced saline)	[***]%

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APPENDIX E

MINIMUM ROYALTIES

Calendar Year after First commercial Sale	Minimum Royalty
Year 1 and 2 (1st and 2nd calendar year following First Sale)	$ 15,000
Year 3	$ 25,000
Year 4	$ 50,000
Year 5	$ 75,000
Year 6 and subsequent years	$ 100,000

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APPENDIX F

MILESTONES

	Milestone Event	Milestone Payment
a)	First FDA 510(k) regulatory approval, CE Mark approval or dosing of a first human patient in a Company-sponsored clinical trial	$ 35,000
b)	First commercial Sale of an FDA approved product as a human therapeutic	$ 75,000

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APPENDIX G

LICENSE MAINTENANCE FEES

Effective Date Anniversary	License Maintenance Fee
First and Second Anniversary	None
Third and Each Subsequent Anniversary	$ 25,000

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APPENDIX H

DEVELOPMENT MILESTONES AND DATES

1. Initiate GLP safety studies in a suitable animal model within [* * *] of the Effective Date of this Agreement; and

2. Submission of first application for FDA 510(k) or CE Mark or IND within [* * *] of the Effective Date of this Agreement; and

3. Initiate human clinical studies within [* * *] of successful completion of GLP safety studies; and

4. First commercial Sale of a Licensed Product within [* * *] of the Effective Date of this Agreement. *

* Company may extend the date for achievement of this milestone by [* * *] by providing written notice to LICENSOR together with the $75,000 milestone payment set forth on Appendix F, with the option to extend by a period of an additional [* * *] with payment of a nonrefundable fee of [* * *], provided, however that such extension shall not relive COMPANY of its obligation to continue to use commercially reasonable efforts to bring Licensed Product to market.

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APPENDIX I

[* * *] TERM SHEET

[* * *]

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Exhibit A
Patent Rights

Emory File No [* * *]**.**

U.S. Patent No. 7,918,814 entitled “Method for Drug Delivery to Ocular Tissue Using Microneedle”

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FIRST AMENDMENT TO

LICENSE AGREEMENT

This First Amendment (the "**First Amendment**") to the License Agreement (the "**Agreement**") dated July 4, 2012, by and among Clearside Biomedical, Inc., a Delaware corporation having a principal place of business at 1220 Old Alpharetta Road, Suite 300, Alpharetta, Georgia 30005 ("**Clearside**" or "**COMPANY**"), Emory University, a nonprofit Georgia corporation having offices located at 1599 Clifton Road NE, 4th Floor, Mailstop 1599/001/1AZ, Atlanta, Georgia 30322 ("**Emory**") and the Georgia Tech Research Corporation, a nonprofit corporation with offices located at offices located at 505 10th Street NW, Atlanta, Georgia 30332-0415 ("**GTRC**" and together with Emory, "**LICENSOR**") is effective this 2nd day of April, 2014 (the "**First Amendment Effective Date**").

WHEREAS, the parties have made joint advances to the technology licensed pursuant to the Agreement;

WHEREAS, the parties desire to treat patents that may issue based on certain joint discoveries as "Licensed Patents" during the term of the Agreement;

WHEREAS, the parties also desire to treat patents that may issue based on U.S. Provisional Patent Application Serial No. 61/918,992 (the "**2014 Patent Application**") as "**Licensed Patents**" during the term of the Agreement.

WHEREAS, in connection with such advances, the parties hereto wish to make certain changes to the Agreement.

NOW THEREFORE, in consideration of the promises, undertakings and covenants set forth in this First Amendment, the receipt and sufficiency of which are hereby agreed and acknowledged, the parties agree as follows:

1. Additional License Fee. As partial consideration for the license granted to COMPANY with respect to the 2014 Patent Application, COMPANY shall pay LICENSOR a license fee in the amount of fifteen thousand ($15,000) Dollars within thirty (30) days of the First Amendment Effective Date.

2. Amendment of Section 2.5.6. Section 2.5.6 shall be revised to read as follows: "Notwithstanding anything herein to the contrary, in no event shall Clearside have any obligation to grant any sublicense to any person with respect to any Licensed Patent that is jointly owned by Clearside and Licensor during the term of this License."

3. Amendment to Section 11. The following sentence shall be added at the end of Section 11.1(i):

   "COMPANY and its Affiliates and Sublicensees shall retain in confidence and use only for the purposes of this Agreement any written information and data supplied by LICENSOR before the First Amendment Effective Date regarding the 2014 Patent Application.

4. Amendment of Section 12. The following sentence shall be added at the end of Section 12.7:

   "Notwithstanding the foregoing, with respect to any Licensed Patents that are jointly owned by COMPANY and Licensor, upon termination of this Agreement, COMPANY agrees, at LICENSOR's request within one year of termination to negotiate in good faith an exclusive license to any jointly owned rights."

5. Amendment of Appendix B. Appendix B shall be deleted and replaced with the Appendix B attached hereto.

CONFIDENTIAL TREATMENT HAS BEEN REQUESTED FOR PORTIONS OF THIS EXHIBIT. THE COPY FILED HEREWITH OMITS THE INFORMATION SUBJECT TO A REQUEST FOR CONFIDENTIAL TREATMENT. OMISSIONS ARE DESIGNATED BY [* * *]. A COMPLETE VERSION OF THIS EXHIBIT HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

6. Miscellaneous.

6.1. Defined Terms. Capitalized terms undefined herein shall have the meaning ascribed to them in the Agreement.

6.2. No Other Amendment; Effectiveness. Except as expressly amended herein, the Agreement remains in full force and effect according to its original terms.

6.3. Governing Law. This First Amendment shall be construed under and governed by the laws of the State of Georgia and the United States of America.

6.4. Severability. All rights and restrictions contained herein may be exercised and shall be applicable and binding only to the extent that they do not violate any applicable laws and are intended to be limited to the extent necessary so that they will not render this Agreement illegal, invalid or unenforceable. If any provision or portion of any provision of this Agreement, not essential to the commercial purpose of this Agreement, shall be held to be illegal, invalid or unenforceable by a court of competent jurisdiction, it is the intention of the parties that the remaining provisions or portions thereof shall constitute their agreement with respect to the subject matter hereof, and all such remaining provisions, or portions thereof, shall remain in full force and effect. To the extent legally permissible, any illegal, invalid or unenforceable provision of this Agreement shall be replaced by a valid provision which shall implement the commercial purpose of the illegal, invalid, or unenforceable provision.

6.5. Counterparts. This First Agreement may be executed electronically and in counterparts, each of which is deemed an original, but all of which together shall constitute one and the same instrument.

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IN WITNESS WHEREOF, the parties have caused this First Amendment to be executed by their duly authorized representatives as of the First Amendment Effective Date.

EMORY UNIVERSITY

By: /s/ Todd Sherer
Name: Todd Sherer
Title: Director, OTT
Date: April 3, 2014

GEORGIA TECH RESEARCH CORPORATION

By: /s/ Lauren MacLanahan
Name: Lauren MacLanahan
Title: Director
Date: April 1, 2014

CLEARSIDE BIOMEDICAL, INC.

By: /s/ Daniel H. White
Name: Daniel White
Title: President and CEO
Date: April 11, 2014

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APPENDIX B

LICENSED PATENTS

Licensor solely owned

U.S. Patent No. 7,918,814, issued April 5, 2011, entitled “Method for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Patent No. 8,197,435, issued June 12, 2012, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Patent No. 8,636,713, issued January 28, 2014, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Patent Application Serial No. 13/447,246, filed April 15, 2012, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Patent Application Serial No. 14/136,657, filed December 20, 2013, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle

PCT Patent Application No. PCT/US2011/033987, filed April 26, 2011, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Australia Patent Application No. 2011248624, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Brazil Patent Application No. 11 2012 027416-3, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Canada Patent Application No. 2797258, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

China national phase of PCT/US2011/033987, filed April 26, 2011, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

European Patent Application No. 11777924.9, filed April 26, 2011, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

India Patent Application No. 10099/DELNP/2012, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Israel Patent Application No. 222638, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

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Japan Patent Application No. 2013-508168, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Mexico Patent Application No. MX/a/2012/012495, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

New Zealand Patent Application No. 603185, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Russia Patent Application No. 2012147341, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

Singapore Patent Application No. 201207910-9, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

South Africa Patent Application No. 2012/08069, filed April 26, 2011, which is the National Phase of PCT/US2011/033987, entitled “Methods and Devices for Drug Delivery to Ocular Tissue Using Microneedle”

U.S. Provisional Patent Application Serial No. 61/698,254, filed September 7, 2012, entitled “Microneedles and Systems for Administration of Drug to the Suprachoroidal Space and Other Tissue Sites”

U.S. Provisional Patent Application Serial No. 61/918,992, filed December 20, 2013, entitled “Ocular Drug Delivery”

Jointly Owned Patents

U.S. Provisional Patent Application Serial No. 61/693,542, filed August 27, 2012, entitled “Apparatus and Methods for Drug Delivery Using Microneedles”

U.S. Provisional Patent Application Serial No. 61/754,495, filed January 18, 2013, entitled “Apparatus and Methods for Drug Delivery Using Microneedles”

U.S. Provisional Patent Application Serial No. 61/784,817, filed March 14, 2013, entitled “Apparatus and Methods for Drug Delivery Using Microneedles”

PCT Patent Application No. PCT/US2013/056863, filed August 27, 2013, entitled “Apparatus and Methods for Drug Delivery Using Microneedles”

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