UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

OR

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

Commission File Number: 001-37783

Clearside Biomedical, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**45-2437375**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
900 North Point Parkway, Suite 200 Alpharetta, GA	**30005**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (678) 270-3631

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

Title of Each Class	**Name of Each Exchange on which Registered**
Common Stock, $0.001 par value	The Nasdaq Stock Market, LLC

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐ (Do not check if a small reporting company)	Small reporting company	☐
		Emerging growth company	☒

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

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

The aggregate market value of Clearside Biomedical, Inc. voting and non-voting common equity held by non-affiliates as of June 30, 2017 (the last business day of the registrant's most recently completed second fiscal quarter) based on the closing sale price of $9.11 as reported on the Nasdaq Global Market on that date was $153,311,000.

As of March 12, 2018, the registrant had 31,913,113 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Company's definitive proxy statement, to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, for its 2018 Annual Meeting of Stockholders are incorporated by reference in Part III of the Form 10-K.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. "Business," Part I, Item 1A. "Risk Factors," and Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations," but are also contained elsewhere in this Annual Report. 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 Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

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

You should refer to Item 1A. "Risk Factors" in this Annual Report 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 Annual Report 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. The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, 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, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

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PART I

ITEM 1. BUSINESS

Overview

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

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

Our current and planned development programs aim to restore or improve visual function primarily by reducing the macular edema associated with a number of diseases affecting vision. Macular edema is the build-up of fluid that can cause abnormal swelling of the macula, the portion of the retina responsible for central vision and color perception. This swelling can rapidly result in deterioration of vision and can eventually lead to blindness. We are developing suprachoroidal CLS-TA, a proprietary, preservative-free formulation of the corticosteroid triamcinolone acetonide, or TA, specifically designed to be administered suprachoroidally using our SCS Microinjector for the treatment of macular edema associated with non-infectious uveitis, a condition characterized by inflammation of the choroid and surrounding tissues not caused by an infectious agent. We estimate that non-infectious uveitis affects over 350,000 patients in the United States, approximately one third of whom develop macular edema. The most common treatment for uveitic macular edema involves the use of corticosteroids, such as TA, or other immunosuppressive agents that are administered either systemically or locally.

On March 5, 2018, we announced positive topline results from our PEACHTREE Phase 3 clinical trial of CLS-TA for the treatment of macular edema associated with non-infectious uveitis. We enrolled 160 patients in the trial, of which 96 patients were randomized to the treatment arm to receive two 4.0 mg doses of suprachoroidal CLS-TA 12 weeks apart, and 64 patients were randomized to undergo a sham procedure at the same 12-week intervals. Patients were evaluated every four weeks for a total of 24 weeks, and a total of 155 patients, or 97% of those enrolled, completed the full evaluation period of the trial. The trial met the primary endpoint with 47% of patients who received suprachoroidal CLS-TA every 12 weeks gaining at least 15 letters in best corrected visual acuity, or BCVA, as measured using the Early Treatment of Diabetic Retinopathy Study, or ETDRS, scale, from baseline at week 24, compared to 16% of patients who underwent a sham procedure. This improvement was statistically significant, with a p-value of less than 0.001. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 or less represents statistical significance, meaning that there is a less than 1-in-20 likelihood that the observed results occurred by chance. The improvements in BCVA from baseline were better in the treatment arm than the sham arm at each monthly evaluation. The mean improvement from baseline was maintained throughout the evaluation period, with 9.6 letters gained at week 4 and 13.7 letters gained at week 24 in the active arm, compared to 1.2 letters gained at week 4 and 2.9 letters gained at week 24 in the control arm.

Administration of suprachoroidal CLS-TA also resulted in a mean reduction from baseline of 157 microns in central subfield thickness at week 24 in the active arm compared to a 19 micron mean reduction in the sham arm, a result that was also statistically significant with a p-value of less than 0.001.

Suprachoroidal CLS-TA was generally well tolerated, with no treatment-related serious adverse events reported in the trial. Through 24 weeks, steroid-related elevated intraocular pressure, or IOP, adverse events were reported for approximately 11.5% of patients in the CLS-TA treatment group, compared to no patients in the sham group.

Based in part on the results from PEACHTREE, we intend to submit a New Drug Application, or NDA, for CLS-TA for the treatment of patients with non-infectious uveitis by the end of 2018.

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

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

We have completed a Phase 2 clinical trial, known as TANZANITE, in 46 patients with macular edema associated with RVO. In this trial, 23 patients in the active arm initially received suprachoroidal CLS-TA together with an intravitreal injection of the anti-VEGF agent Eylea, or intravitreal Eylea, and 23 patients in the control arm initially received only intravitreal Eylea. The objective of the trial was to determine whether patients receiving suprachoroidal CLS-TA together with intravitreal Eylea could sustain improvements in visual acuity and reductions in macular edema over the three months of the clinical trial while requiring fewer additional Eylea treatments than patients receiving intravitreal Eylea alone. Patients in each arm were evaluated at months one, two and three after the initial treatment using pre-specified criteria to determine if they continued to experience macular edema or reductions in visual acuity and therefore required additional intravitreal Eylea treatments. The primary endpoint of the trial was met, with patients in the active arm requiring an aggregate of 60% fewer additional Eylea treatments than patients in the control arm over three months, a result that was statistically significant (p=0.013). In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant (p=0.003). In the same Phase 2 trial, patients in the active arm experienced greater improvement in visual acuity than those in the control arm, with patients in the active arm experiencing mean BCVA improvements at months one, two and three of 16, 20 and 19 letters, respectively, compared to improvements of 11, 12 and 11 letters, respectively, in the control arm at the same time points. We also extended our evaluation of the patients who participated in the trial and did not receive any additional Eylea treatment during the initial three-month evaluation period to further assess the durability of suprachoroidal CLS-TA in combination with intravitreal Eylea for an additional six months following completion of the trial. Of the 32 eligible patients, the medical records of 31 patients were obtained for review. Based on combined data from the initial and extended evaluation periods, 17 of the 23 patients in the combination arm, or 74%, did not receive any additional treatment over the nine-month period, compared to only 4 of 23 patients, or 17%, in the control arm.

Based on the results of TANZANITE and after incorporating feedback from an end-of-Phase 2 meeting with the FDA held in late 2016, we began to enroll patients in a Phase 3 clinical trial, which we refer to as SAPPHIRE, in the first quarter of 2017. We are continuing to enroll patients in SAPPHIRE, a multicenter, randomized, masked, controlled Phase 3 trial, to assess the efficacy and safety of suprachoroidal CLS-TA together with intravitreal Eylea in patients with RVO. Patients in the combination treatment arm will receive suprachoroidal CLS-TA together with intravitreal Eylea at the beginning of the trial, intravitreal Eylea alone at week 4, and suprachoroidal CLS-TA together with intravitreal Eylea at weeks 12 and 24. Patients in the control arm will receive intravitreal Eylea alone at the beginning of the trial and follow-up intravitreal Eylea alone every four weeks through and including week 24. After 24 weeks, patients will be followed for approximately an additional six months with patients in each arm having the opportunity to receive treatment as needed based on monthly evaluations. The primary objective of this trial will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at eight weeks after initial treatment. There will be several secondary efficacy and safety endpoints that will also be evaluated. We anticipate total enrollment of approximately 460 patients in the trial. We expect to report preliminary results from SAPPHIRE in the fourth quarter of 2018.

In addition, in the third quarter of 2017, we began the start-up activities for a second Phase 3 clinical trial in patients with RVO, which we refer to as TOPAZ. We enrolled the first patient in TOPAZ in March 2018. Similar to the SAPPHIRE trial, TOPAZ is a multicenter, randomized, masked, controlled Phase 3 trial, to assess the efficacy and safety of suprachoroidal CLS-TA together with an intravitreal anti-VEGF agent (either Lucentis or Avastin) in patients with RVO. Patients in the combination treatment arm will receive suprachoroidal CLS-TA together with an intravitreal anti-VEGF agent at the beginning of the trial, intravitreal anti-VEGF agent alone at week 4, and suprachoroidal CLS-TA together with intravitreal anti-VEGF agent at weeks 12 and 24. Patients in the control arm will receive intravitreal anti-VEGF agent alone at the beginning of the trial and follow-up intravitreal anti-VEGF agent alone every four weeks through and including week 24. After 24 weeks, patients will be followed for approximately an additional six months with patients in each arm having the opportunity to receive treatment as needed based on monthly evaluations. The primary objective of this trial will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at eight weeks after initial treatment. Several secondary efficacy and safety endpoints will also be evaluated. We anticipate total enrollment of approximately 460 patients in the trial.

We are also developing suprachoroidal CLS-TA for the treatment of diabetic macular edema, or DME. In April 2017, we completed enrollment of 20 patients with DME in an open-label, multi-center Phase 1/2 clinical trial, which we refer to as HULK, to obtain safety data and to observe efficacy outcomes from administering a combination of intravitreal Eylea and suprachoroidal CLS-TA, as well as suprachoroidal CLS-TA alone, over a six-month evaluation period. In November 2017, we announced preliminary results from the HULK trial. In the trial, we observed a visual benefit for patients receiving CLS-TA, with a greater benefit in treatment naïve eyes. Anatomic improvement was observed in all treated eyes, with more than two-thirds of those eyes achieving a greater than 50% reduction in excess central retinal thickness based on monthly measurements through six months after initial treatment. In the treatment naïve group, 40% of patients did not require retreatment over the entire six months, with an additional 20% requiring only one retreatment. Suprachoroidal CLS-TA, including in patients who received as many as five injections, was well tolerated, with a low incidence of ocular side effects, including IOP elevations.

In July 2017, we commenced a Phase 2 clinical trial, which we refer to as TYBEE, to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal CLS-TA to patients with DME, as compared to intravitreal Eylea alone. We completed enrollment of 71 patients in this trial in October 2017. Patient follow-up in TYBEE is six months after initial treatment and we expect to report preliminary data in the second quarter of 2018.

Finally, multiple nonclinical studies, both internally and with multiple collaborators, are underway in development areas such as gene therapy for inherited retinal disorders, neovascular age-related macular degeneration, also known as wet AMD, and other ocular diseases that may benefit from suprachoroidal administration of medication.

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

Our drug candidates, SCS Microinjector and method of drug administration into the SCS are protected by 12 issued U.S. patents and three allowed U.S. applications broadly directed to methods of administering drugs into the SCS by injection, including one design patent. In addition, our patent estate includes 17 patent applications pending in the United States, 18 issued foreign patents, eight pending international PCT applications and 37 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. Our issued patents are not scheduled to expire until 2027, 2029, 2033 and 2034, respectively. Our patent applications relate to suprachoroidal injection technology and methods, our current therapeutic drug candidates and formulations, various therapeutic uses, including treatment of specific indications such as non-infectious uveitis and RVO, as well as DME and wet AMD, and administration of classes of drugs to the SCS, including anti-inflammatory drugs and anti-VEGF drugs. Our pending patent applications are not projected to expire until between 2027 and 2035. If any of our product candidates are approved, we plan to build a specialized team of 30 to 40 sales and medical marketing support professionals to target

the approximately 1,900 uveitis and retina specialists in the United States, and we may also pursue collaborations with third parties to commercialize any of our drugs approved for marketing outside the United States.

We have proprietary rights to a number of trademarks used in this Annual Report which are important to our business, including Clearside, SCS 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 Annual Report are the property of their respective owners.

The Clearside approach

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

- *Improved bioavailability at the site of disease and faster onset of therapeutic effect.* In preclinical studies, we observed higher amounts of drug present in the retina and choroid following suprachoroidal injection, both at early time points and over the course of the experimental timeframe, as compared to the amounts of the same drug present over time in the retina and choroid following intravitreal administration. We believe this suggests that treatment using suprachoroidal injection of a drug may have a faster onset of therapeutic effect as compared to intravitreal administration, along with similar or better efficacy, in diseases such as uveitis, RVO and DME.
- *Similar efficacy profile with lower drug amounts required.* In a preclinical study in an animal model of uveitis, suprachoroidal injection of TA achieved similar efficacy results with only 10% of the drug amount 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. For RVO patients, we believe that a combination of an intravitreal injection of an anti-VEGF drug that addresses the vascular aspect of the disease, together with suprachoroidal CLS-TA, which addresses the inflammatory aspect of RVO, may have efficacy similar to that of monthly intravitreal anti-VEGF injections but with a reduction in the frequency of treatment to once every 90 days.
- *Enhanced safety profile.* Intravitreal injections result in drugs diffusing throughout the eye, including to the lens, iris and ciliary body at the front of the eye, which for some drugs, such as corticosteroids, has been associated with safety issues, such as cataract formation or exacerbation and elevated IOP levels, which can lead to glaucoma. Intravitreal administration of TA has been associated with cataracts and increases in IOP levels in 20% to 60% of patients. Because suprachoroidal injection of drugs in preclinical studies appeared to result in drug remaining mostly localized in the retina and choroid without substantial diffusion to the vitreous or the front portion of the eye, we believe suprachoroidal injection has the potential to reduce the incidence of these side effects. In our three clinical trials of CLS-TA, a total of 121 uveitis patients have been dosed, with follow-up evaluations for up to six months after initial treatment. No serious adverse events related to treatment were observed in these three trials. The incidence of IOP increase among these 121 uveitis patients administered with suprachoroidal injection of 4 mg of TA was 9%.
- *Incorporated into standard medical practice.* If approved for marketing, our drugs will be packaged together with our SCS Microinjector for use by uveitis and retina specialists. The procedure for suprachoroidal injection with our SCS Microinjector is intended to be conducted in an in-office setting and is similar in terms of patient preparation and duration of the procedure for intravitreal injection, and we therefore expect our products, if they achieve regulatory approval, to be incorporated into uveitis and retina specialists' standard medical practice.

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

Proposed Indication	Product Candidate	Status and Upcoming Milestones
Macular edema associated with non-infectious uveitis	Suprachoroidal CLS-TA	• Completed PEACHTREE with preliminary results reported in March 2018 • Intend to submit NDA by end of 2018
Macular edema associated with RVO	Suprachoroidal CLS-TA together with an intravitreal anti-VEGF agent	• Recruitment ongoing in SAPPHIRE with preliminary results expected in the fourth quarter of 2018 • Initiated TOPAZ in first quarter of 2018
DME	Suprachoroidal CLS-TA alone or together with intravitreal Eylea	• Completed HULK, with preliminary results reported in fourth quarter 2017 • Commenced TYBEE in July 2017, with preliminary data expected in second quarter of 2018

We have discussed our proposed development programs with the FDA for our uveitis and RVO programs, but we have not yet done so for our DME development program.

CLS-TA for macular edema associated with non-infectious uveitis

The most common treatment for non-infectious uveitis, a condition characterized by inflammation of the choroid and surrounding tissues, involves the use of corticosteroids, such as TA. CLS-TA is our formulation of TA, and TA is known to be effective in treating uveitis when administered to the eye by other routes of administration. We believe that our product candidate will be at least as effective as commonly used formulations of TA in treating complications of uveitis, including the associated macular edema. If approved, CLS-TA would be the first drug specifically indicated for macular edema associated with non-infectious uveitis. In August 2017, we completed enrollment of 160 patients with macular edema associated with non-infectious uveitis in PEACHTREE, a pivotal Phase 3 clinical trial in which CLS-TA was injected into the SCS with our SCS Microinjector. In PEACHTREE, we met the primary and secondary endpoints of the trial. The administration of suprachoroidal CLS-TA was generally well tolerated, with no treatment-related serious adverse events reported in the trial. Based on the results from PEACHTREE, we intend to submit an NDA for CLS-TA for the treatment of patients with non-infectious uveitis by the end of 2018.

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

Our clinical development

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

- a completed Phase 3 clinical trial in patients with macular edema associated with non-infectious uveitis evaluating suprachoroidal CLS-TA with our SCS Microinjector, from which we reported preliminary data in March 2018; and
- a completed 22-patient Phase 2 clinical trial in patients with macular edema associated with non-infectious uveitis evaluating suprachoroidal CLS-TA with our SCS Microinjector, from which we reported data in 2017.

Details of these clinical trials are summarized below.

Pivotal Phase 3 clinical trial

We have completed PEACHTREE, a pivotal Phase 3 randomized, controlled, multi-center clinical trial designed to evaluate the safety and efficacy of CLS-TA administered through the SCS in patients with macular edema associated with non-infectious uveitis.

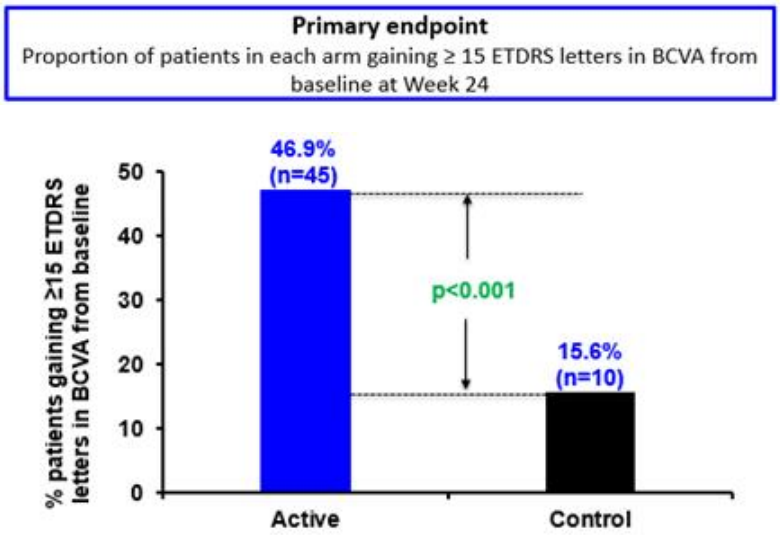
Based on feedback from our end-of-Phase 2 meeting with the FDA held in May 2015, we believe that this trial will be the only pivotal clinical trial necessary to support a filing of a Section 505(b)(2) NDA for this indication.

Clinical Trial Design.

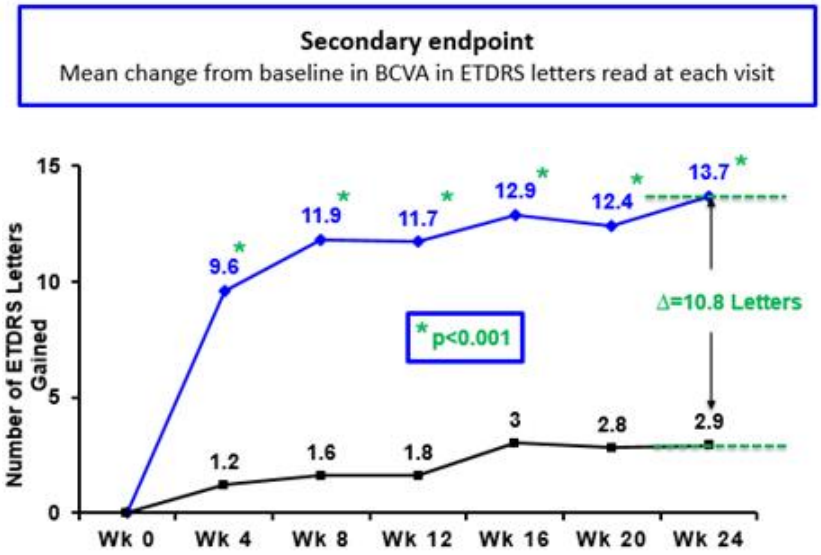
PEACHTREE was conducted at approximately 60 investigational sites and enrolled 160 patients with macular edema associated with non-infectious uveitis, randomized either to a treatment arm consisting of approximately 90 patients who received a 4.0 mg dose of suprachoroidal CLS-TA or to a sham injection procedure arm consisting of approximately 60 patients. We used a sham injection procedure as a comparator for suprachoroidal CLS-TA, 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-TA, and there are no controlled, randomized trials with data in patients who can be used as an appropriate comparator arm. In order to simulate an injection to maintain masking, the sham injection procedure included all steps involved in the suprachoroidal injection procedure, except that a syringe with a needleless hub was used to apply pressure to the eye. Patients in each arm received their designated procedure at the beginning of the trial and a second procedure of the same type at week 12. All patients were followed and evaluated for a period of six months following the initial procedure.

Endpoints. The primary efficacy outcome of the trial was the percentage of patients who experienced an improvement of at least 15 letters in BCVA from baseline at week 24. Secondary efficacy outcomes included additional measures of changes in BCVA and reductions in retinal thickness from baseline. Safety measures were monitored over the 24-week observation period and included the incidence of treatment emergent adverse events and serious adverse events, including cataracts and increases in IOP.

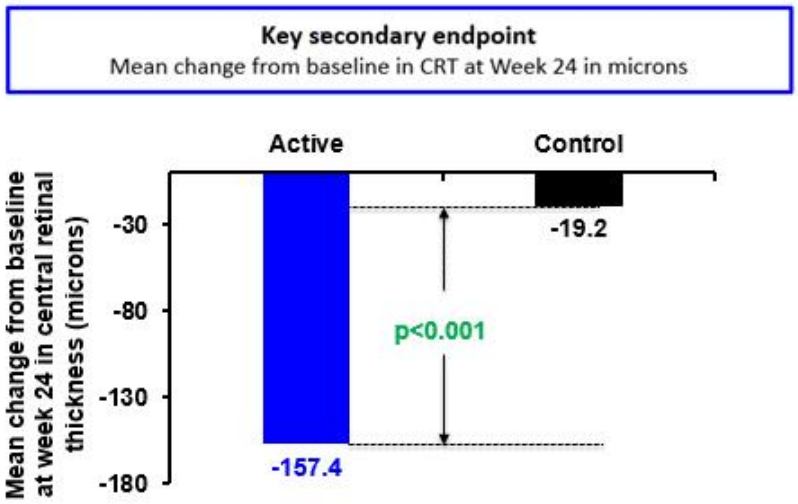
Efficacy results. In PEACHTREE, 45 of the 96 patients, or 47%, who received suprachoroidal CLS-TA at baseline and at 12 weeks gained at least 15 ETDRS letters in BCVA from baseline at week 24, compared to 10 of the 64 patients, or 16%, who underwent sham procedures at baseline and at week 12. This improvement, which was the primary endpoint of the trial, was statistically significant with a p-value of less than 0.001. These results are summarized in the figure below.



Further, in terms of improvements in BCVA, the mean change from baseline was better in the treatment arm than the sham arm at each monthly evaluation. The mean improvement from baseline was also maintained throughout the evaluation period, with 9.6 letters gained at week 4 and 13.7 letters at week 24 in the active arm, compared to 1.2 letters at week 4 and 2.9 letters at week 24 in the control arm. The mean improvements in BCVA were statistically significant at each 4-week evaluation point, each with a p-value of less than 0.001. The mean improvement from baseline at each 4-week evaluation point is shown in the figure below.



For the other key secondary endpoint, administration of suprachoroidal CLS-TA resulted in a mean reduction from baseline of 157 microns in central subfield thickness at week 24 in the active arm compared to a 19 micron mean reduction in the sham arm, a result that was also statistically significant with a p-value of less than 0.001. These results are summarized in the figure below.



Safety results. Suprachoroidal CLS-TA was generally well tolerated, with no treatment-related serious adverse events reported in the trial. Through 24 weeks, corticosteroid-related elevated IOP adverse events were reported for 11.5% of patients in the CLS-TA treatment group, compared to no patients in the sham group.

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

An additional 38 patients, with a diagnosis of non-infectious uveitis, were enrolled in a separate clinical trial in order to collect additional safety information to add to our overall safety database to reach the number required for our planned NDA submission. These additional patients will be administered suprachoroidal CLS-TA at baseline and at week 12, and they will be observed and evaluated at visits every 4 weeks after initial treatment, with a final evaluation at week 24.

Phase 2 clinical trial

In addition to PEACHTREE, we completed a Phase 2 multi-center, masked, randomized, dose controlled clinical trial designed to evaluate the safety and efficacy of a single 4.0 mg or a single 0.8 mg dose of CLS-TA administered through the SCS.

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

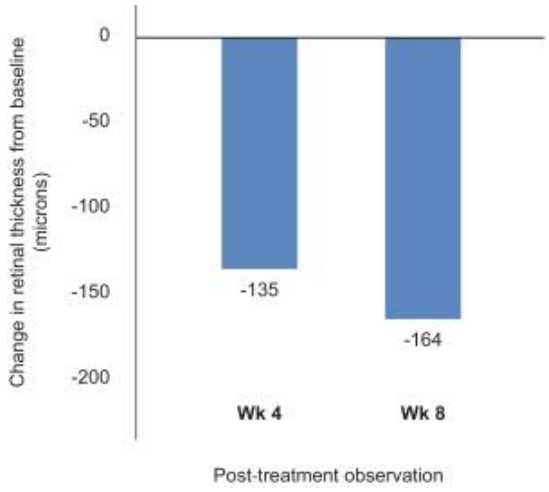
Patients enrolled in the trial ranged in age between 20 years and 83 years, with a median age of 53. Of the 22 patients enrolled, 12 were female and 10 were male; 18 were Caucasian and four were African-American.

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

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

Efficacy results—retinal thickness. Of the 17 patients who received the 4.0 mg dose of CLS-TA, 16 were evaluated for changes in retinal thickness. At four and eight weeks, the average reduction in retinal thickness was 135 and 164 microns, respectively, with p-values of 0.0056 and 0.0017, respectively. These results are summarized in the chart below.

Mean reduction in retinal thickness

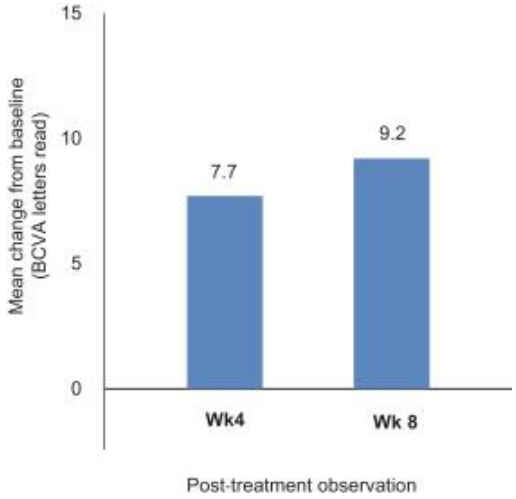


Of these 16 patients evaluated for changes in retinal thickness, nine patients achieved a reduction in retinal thickness to below 310 microns, which represents the maximum retinal thickness for approximately 95% of the population with normal retinas, at both

week 4 and week 8. In addition, nine patients had reductions in thickness of at least 20% from their baseline levels at week 4, while 11 patients achieved this level of reduction at week 8.

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

Improvement in best corrected visual acuity



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

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

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

Regulatory approval pathway

Based on the results from PEACHTREE, we intend to submit an NDA for CLS-TA for the treatment of patients with non-infectious uveitis by the end of 2018. We intend to utilize Section 505(b)(2) of the Food, Drug and Cosmetic Act, or FDCA. As part of our NDA submission under Section 505(b)(2), We intend to rely on the results from all of our clinical trials, as well as the FDA's previous findings of safety and efficacy for TA and an analysis of available data from clinical literature, in our planned NDA submission.

We are also evaluating a number of options for potential submissions to regulatory agencies in additional territories outside of the United States for CLS-TA for the treatment of patients with non-infectious uveitis. We intend to base any marketing applications in jurisdictions outside the United States, in part, on data obtained through these trials.

CLS-TA for macular edema associated with retinal vein occlusion

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

We have completed a 46-patient Phase 2 clinical trial with suprachoroidal CLS-TA together with intravitreal Eylea for the treatment of macular edema associated with RVO. Based on feedback from a meeting with the FDA in late 2016, we initiated a Phase 3 clinical trial in the first quarter of 2017 and a second Phase 3 clinical trial in the first quarter of 2018.

TANZANITE

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

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

For the primary endpoint, patients in the active arm, who initially received concomitant injections of CLS-TA into the SCS and Eylea into the vitreous, met the criteria for an aggregate of nine intravitreal Eylea follow-up injections over three months, while patients in the control arm, who initially received only intravitreal Eylea, met the criteria for an aggregate of 23 intravitreal Eylea follow-up injections. These results met the primary endpoint of the trial and were statistically significant, with a p-value of 0.013. In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant, with a p-value of 0.003. We also extended our evaluation of the patients who participated in the trial and did not receive any additional Eylea treatment during its initial three-month evaluation period to further assess the durability of suprachoroidal CLS-TA in combination with intravitreal Eylea for an additional six months following completion of the trial. Of the 32 eligible patients, the medical records of 31 patients were obtained for review. Based on combined data from the initial and extended evaluation periods, 17 of the 23 patients in the combination arm, or 74%, did not receive any additional treatment over the nine-month period, compared to only 4 of 23 patients, or 17%, in the control arm.

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

We have also completed a Good Laboratory Practices, or GLP, toxicology study in rabbits with suprachoroidal CLS-TA together with intravitreal Eylea.

SAPPHIRE AND TOPAZ

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

We initiated our first randomized, controlled, double-masked Phase 3 clinical trial, SAPPHIRE, with suprachoroidal CLS-TA and intravitreal Eylea for the treatment of RVO in the first quarter of 2017. We intend to conduct this trial at approximately 150 investigational sites and to enroll approximately 460 patients with macular edema associated with RVO, randomized either to a treatment arm consisting of approximately 230 patients or a control arm consisting of approximately 230 patients. Patients in the treatment arm will receive suprachoroidal CLS-TA together with intravitreal Eylea at the beginning of the trial, intravitreal Eylea alone at week 4, and suprachoroidal CLS-TA together with intravitreal Eylea at weeks 12 and 24. Patients in the control arm will receive intravitreal Eylea alone at the beginning of the trial and follow-up treatments of intravitreal Eylea alone every four weeks through week 24. After 24 weeks, patients will be followed for approximately an additional six months. The primary objective of this trial will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at eight weeks after initial treatment. There will be several secondary efficacy and safety endpoints that will also be evaluated. We expect to report preliminary results from SAPPHIRE in the fourth quarter of 2018.

In addition, in the first quarter of 2018, we enrolled the first patient in a second Phase 3 clinical trial in patients with RVO, which we refer to as TOPAZ. We intend to enroll approximately 460 patients in TOPAZ, a multicenter, randomized, masked, controlled Phase 3 trial, to assess the efficacy and safety of suprachoroidal CLS-TA together with an intravitreal anti-VEGF agent, which will be either Lucentis or Avastin, in patients with RVO. Patients in the combination treatment arm will receive suprachoroidal CLS-TA together with the intravitreal anti-VEGF agent at the beginning of the trial, the intravitreal anti-VEGF agent alone at week 4, and suprachoroidal CLS-TA together with the intravitreal anti-VEGF agent at weeks 12 and 24. Patients in the control arm will receive the intravitreal anti-VEGF agent alone at the beginning of the trial and follow-up intravitreal anti-VEGF agent injections alone every four weeks through and including week 24. After 24 weeks, patients will be followed for approximately an additional six months with patients in each arm having the opportunity to receive treatment as needed based on monthly evaluations. The primary objective of this trial will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at eight weeks after initial treatment. There will be several secondary efficacy and safety endpoints that will also be evaluated.

Regulatory approval pathway

Depending on the results of SAPPHIRE and TOPAZ, we intend to seek regulatory approval of CLS-TA for macular edema associated with RVO by utilizing Section 505(b)(2) of the FDCA. We intend to rely on the results from all of our clinical trials, as well as the FDA's previous findings of safety and efficacy for TA and an analysis of available data from clinical literature, in our planned NDA submission.

We also evaluating a number of options for potential submissions to regulatory agencies in additional territories outside of the United States for CLS-TA for the treatment of patients with non-infectious uveitis. We intend to base any marketing applications in jurisdictions outside the United States, in part, on data obtained through these trials.

CLS-TA for diabetic macular edema

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

HULK and TYBEE

Our development program for DME is modeled on our approach for the treatment of RVO. We have conducted a multi-center, open-label Phase 1/2 clinical trial, HULK, to evaluate safety data, and to collect efficacy observations, for the administration of CLS-TA, administered suprachoroidally, both alone and in combination with intravitreal Eylea, in patients with DME over a six-month evaluation period. We enrolled 20 patients in this trial. Efficacy observations included changes in retinal thickness and BCVA. In November 2017, we announced preliminary results from the HULK trial. In the trial, we observed a visual benefit for patients receiving CLS-TA, with a greater benefit in treatment naïve eyes. Anatomic improvement was observed in all treated eyes, with more than two-thirds of those eyes achieving a greater than 50% reduction in excess central retinal thickness based on monthly

measurements through 6 months after initial treatment. In the treatment naïve group, 40% of patients did not require retreatment over the entire 6 months, with an additional 20% requiring only one retreatment. Suprachoroidal CLS-TA, including in patients who received as many as five injections, was well tolerated, with a low incidence of ocular side effects, including IOP elevations.

In addition, in July 2017, we commenced a Phase 2 clinical trial, TYBEE, to evaluate the safety and efficacy of CLS-TA administered suprachoroidally together with intravitreal Eylea as compared to intravitreal Eylea only, in patients with DME over a nine-month evaluation period. We enrolled 71 patients in this trial. The primary endpoint is the change in BCVA from baseline. Patient follow-up in TYBEE is six months after initial treatment and we expect to report preliminary data in the second quarter of 2018.

Future potential product candidates

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

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

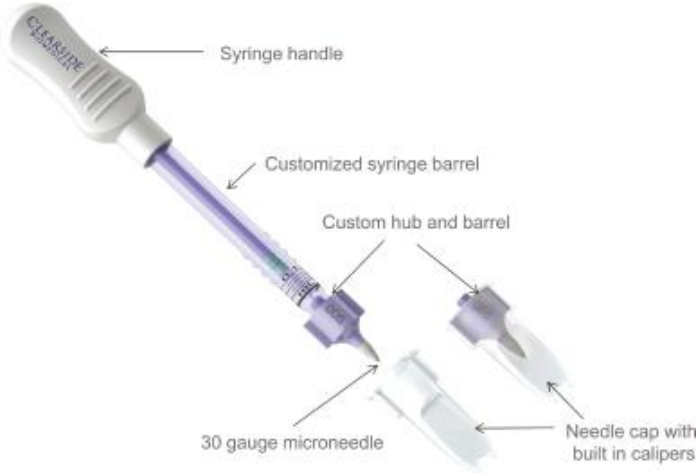
We are evaluating the use of our SCS Microinjector to administer sustained-release formulations of known glaucoma drugs. Glaucoma is a progressive eye disease in which elevated levels of IOP are associated with damage to the optic nerve, which results in irreversible vision loss and potentially blindness.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

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

The SCS Microinjector

Our drug candidates have been and will be specifically formulated to be injected with our SCS Microinjector via suprachoroidal injection in order to spread around to the back of the eye. The single-use microinjector is intended to consistently inject drug into the SCS, in volumes similar to the amount of drug commonly used in intravitreal injections. If our products are approved for marketing by applicable regulatory authorities, we will package the drug along with the SCS Microinjector and two 30-gauge hollow microneedles of varying lengths, each less than 1.2 millimeters, within a custom-designed hub that optimizes insertion and suprachoroidal administration of drugs.

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



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

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

Manufacturing

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

Commercialization

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

There are approximately 1,900 uveitis and retina specialists in the United States. We believe we will be able to reach this concentrated set of specialists efficiently, limiting the size of our sales force and other field team members required.

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, 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; however, it is used off-label for intraocular inflammation. There are also a number of generic equivalents of Kenalog. In addition, Alcon's injectable TA, Triesence, is approved in the United States for the treatment of uveitis and other inflammatory conditions unresponsive to topical corticosteroids, although it is not indicated for the treatment of macular edema associated with uveitis or RVO or DME. Ozurdex, marketed by Allergan, is a bioerodable extended release implant that delivers the corticosteroid dexamethasone and is approved for the treatment of non-infectious uveitis affecting the posterior segment of the eye and for macular edema due to RVO in both the United States and in the European Union, and received approval from the FDA to treat DME. Bausch + Lomb markets Retisert, an intravitreal implant of the corticosteroid fluocinolone acetonide for the treatment of non-infectious uveitis. Iluvien, an injectable form of fluocinolone acetonide marketed by Alimera Sciences, has been approved in both the United States and the European Union for the treatment of DME.

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

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 12 granted U.S. patents and three allowed U.S. applications broadly directed to methods of administering drugs into the SCS by injection, including one design patent. In addition, our patent estate includes 17 patent applications pending in the United States, 18 issued foreign patents, three pending international PCT applications and 37 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 five of the 12 issued U.S. patents, three pending U.S. applications, nine of the issued foreign patents, and eight foreign patent applications in major international markets, 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 applications, according to the terms of the license

agreement, we advise Georgia Tech and Emory regarding the countries in which patent applications should be pursued. Subject to payment of required maintenance fees, annuities and other charges, our issued in-licensed U.S. patents are expected to expire between 2027 and 2029, without taking into account possible patent term adjustments or extensions. Applications relating to SCS delivery technology and methods, our current therapeutic drug candidates and formulations, various therapeutic uses, including treatment of specific indications such as macular edema associated with non-infectious uveitis and RVO, wet AMD as well as DME and improvement of specified clinical parameters, are expected to expire between 2027 and 2037, without taking into account possible patent term adjustments or extensions.

The term of individual patents depends on the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be extended by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review.

Our product candidates are protected against genericization through several levels of patents, including the patented approach of administration into the SCS. In the case of 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 macular edema associated with uveitis, against our product, unless a biowaiver is obtained.

Third-party patent filings

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

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

License agreement with Emory and Georgia Tech

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

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

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

Royalties are calculated based on net sales of products covered by a patent licensed under the agreement, and are due on each such product sold as long as the patent covering that particular product is valid and unexpired. Unless otherwise terminated pursuant to its termination provisions, this license agreement will expire upon the expiration of the last to expire of the licensed patents. We have the right to terminate this license agreement at any time upon 60 days' written notice to Emory and GTRC. Emory and GTRC

may also terminate this license agreement in the event of a material breach by us. This license agreement will immediately terminate if we challenge the validity or enforceability of any of the licensed patents in a court or other governmental agency of competent jurisdiction.

Research, option and license agreement with Spark Therapeutics

In April 2015, we entered into a research, option and license agreement with Spark Therapeutics, Inc., or Spark, under which we granted Spark the option to license exclusive rights to our SCS Microinjector technology and related intellectual property for use in delivering gene therapies to the back of the eye. Under this agreement, we and Spark explored the feasibility of using our SCS Microinjector to deliver gene therapies to the choroid and the retina through the SCS for the treatment of several orphan diseases of the back of the eye.

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

Trademarks, trade secrets and know-how

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

Government regulation

In the United States, the FDA regulates drug and device products under the FDCA and its implementing regulations. While it may be the case that when a drug and a device are used together, which is called a combination product, the FDA typically regulates the dispenser of a drug, such as a syringe co-packaged with a drug, as a drug itself. Based on our pre-IND meeting with the FDA, we believe that CLS-TA and our SCS Microinjector will be subject to regulation as drugs, as the SCS Microinjector used to dispense the drug will be packaged together with the CLS-TA.

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, or CDER, has primary jurisdiction over the premarket development, review and approval of our product candidates. We have been advised that, within CDER, the division responsible for ophthalmology, which will have primary jurisdiction, views our product candidate as a drug. 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 changes to this approach, although the FDA could change its position during the course of its review of any marketing application that we may submit.

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 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 GLP;
- the submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product and conducted in accordance with Good Clinical Practices, or GCP;
- the submission to the FDA of an NDA;

- FDA acceptance, review and approval of the NDA, which might include an Advisory Committee review; and
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with current Good Manufacturing Practices, or cGMPs.

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

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

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

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

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

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

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

Phase 4 clinical trials may be conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in enforcement action or withdrawal of approval.

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

Review of application

Once an NDA has been accepted for filing, which occurs, if at all, 60 days after submission, the FDA sets a user fee goal date that informs the applicant of the specific date by which the FDA intends to complete its review. The Company will be required to pay a user fee to the FDA to review the NDA, unless it receives a waiver or qualifies for an exemption. This is typically 10 months from the date of submission for drugs that are not new molecular entities, such as our product candidates. The review process can be extended by FDA requests for additional information or clarification. The FDA reviews NDAs to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMPs to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA may inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and may also inspect clinical trial sites for integrity of the data supporting safety and efficacy. The device component of our products will also be subject to review as part of the NDA review process and its manufacturers subject to inspection for

compliance with device cGMPs embodied in the Quality System Regulation, or QSR. During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS, and the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA could also require a special warning, known as a black box warning, to be included in the product label in order to highlight a particular safety risk. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA will issue either an approval of the NDA or a Complete Response Letter, detailing the deficiencies and information required for reconsideration of the application.

Post-approval requirements

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

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. The FDA may also require a REMS, which could involve requirements for, among other things, a medication guide, special training for prescribers and dispensers, and patient registries.

In addition, entities involved in the manufacture and distribution of approved devices or drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. The FDA has promulgated specific requirements for drug cGMPs, device cGMPs embodied in the QSR and combination product cGMPs that, for drug/device combination products, specify the requirements within the drug cGMPs and the QSR with which manufacturers must comply. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Corrective action could delay product distribution and require significant time and financial expenditures. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, , including without limitation the FDCA, the False Claims Act, other federal and state health care fraud and abuse laws and state consumer protection laws. 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 as Section 505(b)(2) NDAs under the FDCA. As an alternative path to FDA approval for modifications to formulations or uses of drugs previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This type of application permits reliance for such approvals on literature or on an FDA finding of safety, effectiveness or both for an approved drug product. As such, under Section 505(b)(2), the FDA may rely, for approval of an NDA, on data not developed by the applicant. Therefore, if we can satisfy the conditions required for a Section 505(b)(2) NDA submission, it may eliminate the need for us to conduct some of the preclinical studies or clinical trials for the new product candidate that might otherwise have been required, although the review time is not shortened. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved branded reference drug. The FDA may then approve the new product candidate for the new indication sought by the 505(b)(2) applicant.

Orange Book listing

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

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

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

Non-patent exclusivity

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

A drug, including one approved under a 505(b)(2) application, may obtain a three-year period of non-patent market exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, the FDA can accept an application and begin the review process during the three-year exclusivity period. A 505(b)(2) NDA may also be subject to a five-year exclusivity period for a new chemical entity, whereby the FDA will not accept for filing, with limited exception, a product seeking to rely upon the FDA's findings of safety or effectiveness for such new chemical entity.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the United States, or in other limited cases. Orphan drug designation does not convey any

advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan drugs are eligible for certain incentives, including tax credits for qualified clinical testing. In addition, an NDA for a product that has received orphan drug designation is not subject to a prescription drug user fee unless the application includes an indication other than the rare disease or condition for which the drug was designated.

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

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

Foreign regulation

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

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

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

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal 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 federal Anti-Kickback Statute has been violated.

Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, 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 additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

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

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

Under HIPAA, the U.S. Department of Health and Human Services, or HHS, has issued regulations to protect the privacy and security of protected health information used or disclosed by covered entities including health care providers. HIPAA also regulates standardization of data content, codes and formats used in health care transactions and standardization of identifiers for health plans and providers. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH and its implementing regulations, including the omnibus final rule published on January 25, 2013, also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that are applicable to our business. New laws governing privacy may be adopted in the future as well. Failure to comply with privacy requirements could result in civil or criminal penalties, which could have a materially adverse effect on our business.

Additionally, there has been a recent trend of increased federal and state regulation of payments and transfers of value provided to healthcare professionals and/or entities. On February 8, 2013, the Centers for Medicare & Medicaid Services, or CMS, released its final rule implementing the Physician Payments Sunshine Act that imposes annual reporting requirements on certain manufacturers of drugs, devices, biologicals and medical supplies for payments and other transfers of value provided by them, directly or indirectly, to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their family members. A manufacturer's failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in civil monetary penalties of up to an aggregate of $165,786 per year, and up to an aggregate of $1,105,241 per year for "knowing failures." Any failure to comply could result in significant fines and penalties. Certain states also mandate implementation of commercial compliance programs, impose restrictions on pharmaceutical manufacturer and device manufacturer marketing practices or require tracking and reporting of gifts, compensation and other remuneration to particular types of healthcare professionals and entities.

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

potentially significant criminal and civil and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage and reimbursement

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

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

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

In addition to uncertainties surrounding coverage policies, third-party payors from time to time update reimbursement amounts and also revise the methodologies used to determine reimbursement amounts. This includes annual updates to payments to ambulatory surgery centers, hospitals and physicians for the procedure performed administering our products, which could directly impact the demand for any of our product candidates that may be approved. An example of payment updates is the Medicare program updates to physician payments, which is done on an annual basis using a prescribed statutory formula. In the past, when the application of the formula resulted in lower payment, Congress has passed interim legislation to prevent the reductions. However, the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, ended the use of the statutory formula, and provided for a 0.5% annual increase in payment rates under the Medicare Physician Fee Schedule through 2019, but no annual update from 2020 through 2025. MACRA also introduced a quality payment program under which individual providers with Medicare billings of $30,000 or 100 patient visits per year will be subject to certain incentives or penalties based on new program quality standards. The quality payment program has two tracks, one known as the merit based incentive payment system for providers in the fee-for service Medicare program, and the advanced alternative payment model for providers in specific care models, such as accountable care organizations. Payment adjustments for the Medicare quality payment program will begin in 2019. At this time it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program. Any changes in coverage and reimbursement that further restricts coverage of our products or lowers reimbursement for procedures using our products could materially affect our business.

Healthcare reform

Current and future legislative proposals to further reform healthcare or reduce healthcare costs may result in lower reimbursement for our products, or for the procedures associated with the use of our products, or limit coverage of our products. The cost containment measures that payors and providers are instituting and the effect of any healthcare reform initiative implemented in the future could significantly reduce our revenues from the sale of our products. However, we believe that the shift away from fee-for-

service agreements to capitated payment models supports the value of our products, as we believe that our products reduce longitudinal resource utilization, which can be cost saving-for both payors and providers.

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

The Affordable Care Act imposed, among other things, a new federal excise tax on the sale of certain medical devices, established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, and provided incentives to programs that increase the federal government's comparative effectiveness research. In addition, the Affordable Care Act implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models. There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress could consider additional legislation to repeal or repeal and replace certain elements of the Affordable Care Act in the future.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to the BBA, will remain in effect through 2027 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.

Further, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. 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 December 31, 2017, we had 34 full-time employees, all of whom are located in the United States. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Information about Segments

We currently operate in a single business segment developing drug therapies to treat blinding diseases of the eye. See “Note 2—Significant Accounting Policies—Segment Information” to our financial statements contained in Part II, Item 8 of this Annual Report.

Corporate Information

We were incorporated under the laws of the State of Delaware in May 2011. Our principal executive offices are located at 900 North Point Parkway, Suite 200, Alpharetta, Georgia. Our telephone number is (678) 270-3631.

Available Information

Our internet website address is www.clearsidebio.com. In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission, or SEC. The public may read and copy the materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Additionally the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

ITEM 1A. RISK FACTORS

You should carefully consider the risks described below, as well as general economic and business risks and the other information in this Annual Report on Form 10-K. The occurrence of any of the events or circumstances described below or other adverse events could have a material adverse effect on our business, results of operations and financial condition and could cause the trading price of our common stock to decline. Additional risks or uncertainties not presently known to us or that we currently deem immaterial may also harm our business.

Risks Related to Our Financial Position and Capital Needs

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

We incurred net losses of $59.0 million, $25.9 million and $17.6 million for the years ended December 31, 2017, 2016 and 2015, respectively.

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

- conduct and complete our ongoing and planned clinical trials;
- seek to discover, research and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any drugs for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development and planned future commercialization efforts.

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 sufficient revenue to achieve profitability.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in the initiation and completion of our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations. A decline in our value could also cause you to lose all or part of your investment.

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

We believe that our existing cash, cash equivalents and short-term investments, including the net proceeds from the recent public offering of our common stock in March 2018, 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 ongoing, planned and future clinical trial programs;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other product candidates and technologies.

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

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements. We do not currently have any committed external source of funds other than our credit facility, although as described in this report we have also entered into an at-the-market sales facility that would allow us to sell up to $50.0 million of our common stock at prevailing market prices and on specified terms, depending on market conditions. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

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

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

We commenced active operations in 2012, and our operations to date have been largely focused on raising capital, identifying potential product candidates, broadening our expertise in the development of our product candidates, including our SCS Microinjector, and undertaking preclinical studies and conducting early clinical trials. We have not yet demonstrated an ability to successfully

complete multiple later-stage clinical trials, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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

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

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

We have entered into an amended and restated loan and security agreement with Silicon Valley Bank, or SVB, and entities affiliated with MidCap Financial Services, which we refer to collectively as the Lenders, pursuant to which we have borrowed an aggregate of $8.0 million as of December 31, 2017. We can draw an additional $7.0 million until March 31, 2018. Our obligations under the loan agreement are secured by substantially all of our assets except for our intellectual property, and we may not encumber our intellectual property without the Lenders' prior written consent. The amended and restated loan agreement contains negative covenants restricting our activities, including limitations on dispositions, mergers or acquisitions, incurring indebtedness or liens, paying dividends or making investments and other specified business transactions. Our obligations under the loan agreement are subject to acceleration upon the occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition. We were in compliance with these covenants as of December 31, 2017. We may also enter into other debt agreements in the future which may contain similar or more restrictive terms.

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

Risks Related to the Development of Our Product Candidates

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

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

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

Even if we are able to achieve marketing approval for one of our product candidates, the novelty of suprachoroidal injection may make it difficult to demonstrate to physicians and third-party payors that suprachoroidal injection of our drugs is an appropriate

approach for treating diseases such as non-infectious uveitis, RVO and DME and provides advantages compared to the current standards of care. Further, if we are not successful in conveying to physicians, patients and third-party payors that the suprachoroidal administration of our drug candidates with our proprietary SCS Microinjector provides useful 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-TA and our other product candidates.

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

Given our limited human experience with our clinical programs, the successful development of any of our product candidates is extremely uncertain, and we cannot guarantee that we will be successful in developing any of our product candidates. Further, the FDA may conclude that our clinical trials are not sufficient to support approval of our product candidates.

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

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

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

Interim, top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available, and such data are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, topline or preliminary data from our clinical studies, including the topline data from our Phase 3 PEACHTREE clinical trial published on March 5, 2018. Interim data from clinical trials are subject to the risk that one or

more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our prospects for obtaining regulatory approval of our product candidates.

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

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

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

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

In our preclinical studies and early clinical trials, we used several prototype iterations of the SCS Microinjector. We have since finalized the commercial design, which we have used in clinical trials since January 2017. We also plan to use this revised microinjector in our other ongoing and planned clinical trials. Accordingly, in addition to the risks associated with drug development, we are also subject to the risks associated with developing the microinjector. For example, in our Phase 1/2 clinical trial of CLS-TA for the treatment of macular edema associated with non-infectious uveitis, the needle of our earlier microinjector was not long enough to penetrate the scleras of two patients screened for the trial. If we encounter similar limitations with this design, or if it does not function properly in any way, we could be required to expend significant additional time and resources to redesign our microinjector, which would delay or compromise our drug development efforts. Additionally, our ability to successfully commercialize our product candidates will depend on uveitis and retina specialists being comfortable with the design and functionality of our microinjector. If, for any reason, these specialists were unsatisfied with the form or function of our microinjector, it would harm the market acceptance and potential commercial success of our product candidates, if any, that receive marketing approval.

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

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

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

The risk of failure for our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials

to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, including failure to demonstrate statistical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators may issue a clinical hold, or regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

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

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

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

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. We have relatively limited experience enrolling patients in our clinical trials, and cannot predict how successful we will be at enrolling patients in future clinical trials. In addition, if we are not successful at enrolling patients in one clinical trial, it may affect when we are able to initiate our next clinical trial, which could result in significant delays in our efforts to pursue regulatory approval of and commercialize our product candidates. In addition, some of our competitors have ongoing clinical trials to treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors. Patient enrollment is affected by other factors including:

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

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

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

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

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

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

Risks Related to Our Dependence on Third Parties

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

We have engaged contract research organizations, or CROs, for our ongoing and planned clinical trials. We also expect to engage CROs for any of our other product candidates that may progress to clinical development. We expect to rely on CROs, as well as other third parties, such as clinical data management organizations, medical institutions and clinical investigators, to conduct those

clinical trials. Agreements with such third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would delay our drug development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so by us or third parties can result in FDA refusal to approve applications based on the clinical data, enforcement actions, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA of any NDA we submit. Any such delay or rejection could prevent us from commercializing CLS-TA or our other current or 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 or regulatory noncompliance on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of CLS-TA and our SCS Microinjector for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of CLS-TA and our SCS Microinjector or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel. We currently procure the active pharmaceutical ingredient in 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 SCS Microinjector, as well as for commercial manufacture, if any of our product candidates receives marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of CLS-TA and our SCS Microinjector or such quantities at an acceptable cost or quality, which could delay, prevent or impair our ability to timely conduct our clinical trials or our other development or commercialization efforts.

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

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

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

Our product candidates, including our proprietary drug formulations packaged together with our SCS Microinjector, are regulated under the drug regulations of the Federal Food, Drug, and Cosmetic Act, or FDCA. Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations, regulations applicable to drug/device combination products, including applicable provisions of the FDA's drug cGMP regulations, device cGMP requirements embodied in the Quality System Regulation, or QSR, or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates.

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

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

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

We may seek third-party collaborators for the development and commercialization of our product candidates, particularly for the commercialization of any of our product candidates that are approved for marketing outside the United States or for product candidates targeted at larger indications in the United States such as DME. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. 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 1,900 uveitis and retina specialists in the United States for any of our product candidates that receive marketing approval. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities

is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

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

If we are unable to establish our own sales, marketing and distribution capabilities and, instead, enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to sell, market and distribute any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

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

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

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

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

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

Our product candidates will also compete with anti-VEGF drugs, which are the current standard of care for RVO and wet AMD and have also been approved for DME. Genentech's products Lucentis and Avastin are both anti-VEGF antibodies. Lucentis is currently approved in the United States and European Union for the treatment of wet AMD, macular edema associated with RVO and DME. Avastin is an anti-VEGF drug used off-label by uveitis and retina 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. Regeneron's anti-VEGF product, Eylea, is approved for the treatment of wet AMD, macular edema associated with RVO and DME and diabetic retinopathy in the United States. In the European Union, Eylea is approved for the treatment of wet AMD, DME and macular edema secondary to RVO.

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

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

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

Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and adequate reimbursement for our product candidates will be available from government payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers, managed care plans and other third-party payors. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medical products they will pay for and establish reimbursement levels. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs and products. Coverage and reimbursement

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

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

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

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

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

Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by

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

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

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

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

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

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

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Employee Matters and Managing Our Growth

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

We are highly dependent on the management, research and development, clinical, financial and business development expertise of Daniel White, our Chief Executive Officer, Charlie Deignan, our Chief Financial Officer, and Glenn Noronha, our Chief Scientific Officer, as well as the other members of our scientific and clinical teams. Although we have entered into employment agreements with

our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

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

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

As of December 31, 2017, we had 34 full-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our business and operations would suffer in the event of material computer system failures or security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, contract manufacturing organizations and other third parties on whom we rely, are vulnerable to damage from computer viruses, unauthorized access, security breaches, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could result in a material disruption of our clinical and product development activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur significant unexpected losses, expenses and liabilities, we could face litigation or suffer reputational harm and the further development of our product candidates could be delayed.

Risks Related to Our Intellectual Property

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

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

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. For example, we do not control the prosecution of the patent applications licensed to us under the Emory/GT License described below. Therefore,

these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States or visa-versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and drugs. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and may also affect patent litigation. The United States Patent and Trademark Office recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could significantly harm our business and financial condition. In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our owned and licensed patents and patent applications.

Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

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

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, or limit the duration of the patent protection of our technology and drugs. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours, and our business will suffer.

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

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent’s claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the

technology. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly, which would undermine our competitive position.

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

Our commercial success depends upon our ability, and the ability of any collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. In particular, we are focused on developing product candidates based on widely used therapeutic agents, many of which are protected by proprietary rights of third parties, and we are developing proprietary formulations of these therapeutic agents specifically for suprachoroidal injection using our proprietary SCS Microinjector. Although we seek to develop our proprietary drug formulations that don't infringe the intellectual property rights of others, we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our drugs or other aspects of our technology, including interference or derivation proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

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

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

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

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could hurt the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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

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

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

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

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

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

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

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

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

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. Other than the trade name Zuprata, which we previously sought to, but no longer plan to, use as the trade name for CLS-TA, we have not yet selected trademarks for our product candidates or begun the process of applying to register trademarks for our product candidates. Once we select trademarks and apply to register them, our trademark applications may not be approved. In addition, third parties may oppose our trademark applications, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

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

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

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

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

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

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

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

We intend to seek FDA approval through the Section 505(b)(2) regulatory pathway for CLS-TA and may pursue that pathway for our other product candidates. Our product candidates, including our proprietary drug formulations packaged together with our SCS Microinjector, will be regulated under the drug provisions of the FDCA, enabling us to submit NDAs for approval of our product candidates. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as anticipated, we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for our product candidates, and complications and risks associated with our product candidates, would likely substantially increase. We may need to obtain additional funding, which could result in significant dilution to the ownership interests of our then existing stockholders to the extent we issue equity securities or convertible debt. We cannot assure you that we would be able to obtain such additional financing on terms acceptable to us, if at all.

Moreover, inability to pursue the Section 505(b)(2) regulatory pathway could result in competitive products reaching the market before our product candidates, which could impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization, or that a competitor would not obtain approval first, including subsequent market exclusivity from the FDA, thereby delaying potential approval of our product.

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

Additional time may be required to obtain regulatory approval for our product candidates because of the complexity involved with co-packaging a drug with a dispensing device.

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

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

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

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

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

- differing regulatory requirements in foreign countries;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market with low or lower prices rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;

- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

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

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

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS, which could involve requirements for, among other things, a medication guide, special training for prescribers and dispensers, and patient registries. If any of our product candidates receives marketing approval, the accompanying label may limit its approved uses, which could limit sales of the product, or include a black box warning to highlight a specific health risk.

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

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

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

Non-compliance with European Union requirements regarding safety monitoring, or pharmacovigilance, and with requirements related to the development of drugs for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Even though we have received orphan drug designation in the European Union for CLS-TA for the treatment of non-infectious uveitis, we may not be able to obtain orphan drug marketing exclusivity for this product candidate.

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

Regulation (EC) No 141/2000 and Regulation (EC) No 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. In addition, the period of market exclusivity may be reduced to six years if it can be demonstrated based on available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity. There is no guarantee that we will be able to obtain or maintain orphan exclusivity for CLS-TA even if we receive marketing authorization for CLS-TA in Europe.

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

We are exposed to the risk of employee fraud or other misconduct or failure to comply with applicable regulatory requirements. Misconduct by employees and independent contractors, such as principal investigators, CROs, consultants, commercial partners and vendors, could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including 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, individual imprisonment, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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 civil False Claims Act, that may constrain the business or financial arrangements and relationships through which we sell, market and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy and security regulation by the federal government and by the states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws, including, without limitations, the federal civil False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, including federal health care programs, such as, 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;
- HIPAA, which created additional 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 HITECH, and their respective implementing regulations, which impose obligations on “covered entities,” including healthcare providers, health plans, and healthcare clearinghouses, as well as their respective “business associates” that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the Physician Payments Sunshine Act, created under Section 6002 of the Affordable Care Act, imposed annual reporting requirements for certain manufacturers of drugs, devices, biologics 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 $165,786 per year and up to an aggregate of $1,105,241 per year for “knowing failures,” for an aggregate potential annual liability of $1,271,027; 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 Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and the healthcare fraud statute. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them. In addition, the Affordable Care Act provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil 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, disgorgement, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, as well as reputational harm, 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 the same criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also affect our business.

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

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

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

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- a 2.3% medical device excise tax on certain transactions, including many U.S. sales of medical devices and drug and device combination products, which, under subsequent legislation, is suspended from January 1, 2016 to December 31, 2018, and, absent further legislative action, will be reinstated starting January 1, 2019;
- 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 federal 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% (and 70% starting January 1, 2019) 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.

There have been judicial and congressional challenges to certain aspects of the Affordable Care Act, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans and the annual fee imposed on certain health insurance providers based on market share. Further, the Bipartisan Budget Act of 2018, or BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress could consider additional legislation to repeal or repeal and replace certain elements of the Affordable Care Act. We continue to evaluate the potential impact of the Affordable Care Act and its possible repeal or replacement on our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to the BBA, will stay in effect through 2027 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.

Further, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government

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

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

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

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

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

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

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

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

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our

profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

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, 2017, we had approximately $116.3 million of federal and $79.1 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. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain how various states will respond to the newly enacted federal tax law. 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 our IPO, recent follow-on public offering[s], 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.

Risks Related to Ownership of Our Common Stock

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

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

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

Our stock price has been and may continue to be volatile. Since our IPO, our common stock has traded at prices between $5.30 and $25.08 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

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

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

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

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

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

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

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly. All of our outstanding shares of common stock are available for sale in the public market, subject only to the restrictions of Rule 144 under the Securities Act in the case of our affiliates.

In addition, we have filed registration statements on Form S-8 registering the issuance of approximately 4.5 million shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. These registered shares will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements described above and, in the case of our affiliates, the restrictions of Rule 144.

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

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

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

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

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

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

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

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

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

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) ending December 31, 2021, which is the end of the fiscal year following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

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

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

We are subject to the reporting requirements of the Securities Exchange Act of 1934, the Sarbanes-Oxley Act and the rules and regulations of The Nasdaq Stock Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. 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 this report and future annual reports on Form 10-K, as required by Section 404 of the Sarbanes-Oxley Act. This requires 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 the year ended December 31, 2017, 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 have broad discretion in the use of our cash, cash equivalents and short-term investments, including the proceeds from our recent follow-on public offering, and may invest or spend our cash in ways with which you do not agree.

We have broad discretion over the use of our cash, cash equivalents and short-term investments, including the proceeds from our recent follow-on public offering. You may not agree with our decisions, and our use of our cash may not yield any return on your investment. Our failure to apply our resources effectively could compromise our ability to pursue our growth strategy. You will not have the opportunity to influence our decisions on how to use our cash, cash equivalents and short-term investments.

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

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

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

As a public company listed in the United States, we have begun to incur significant additional legal, accounting and other costs. 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal offices occupy approximately 20,000 square feet of office space in Alpharetta, Georgia under a lease with an initial term until September 2023, with a renewal option for one additional five-year term.

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

ITEM 3. 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.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASE OF EQUITY SECURITIES

Market Information for Common Stock

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

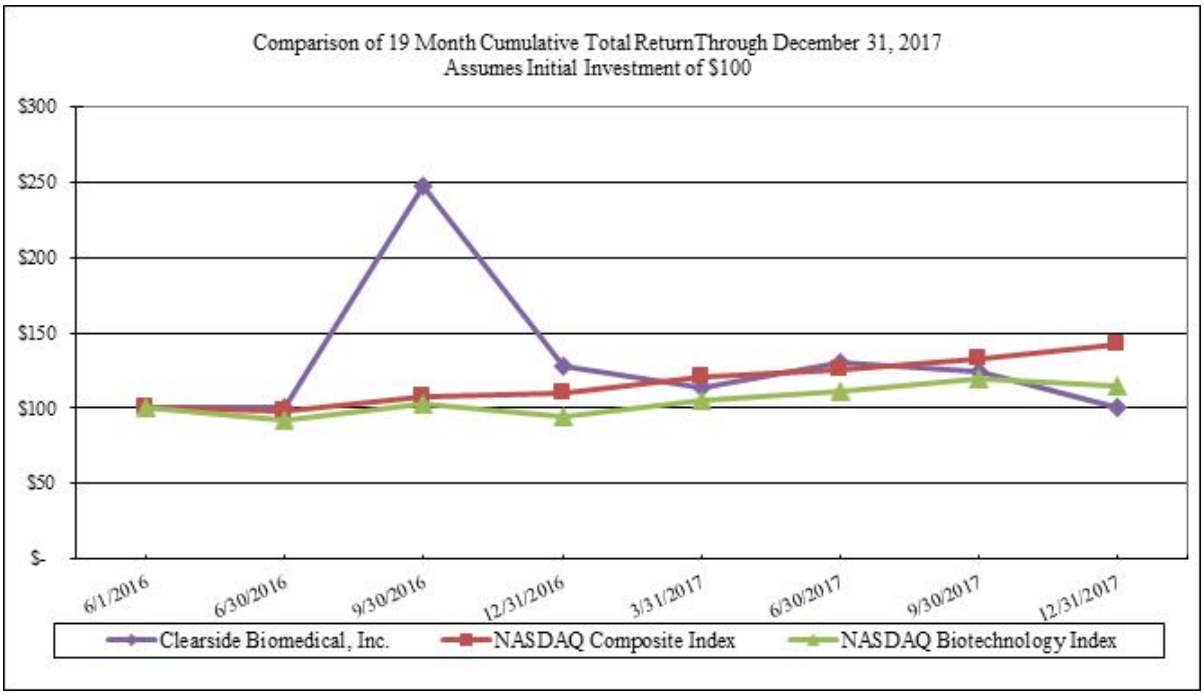
	High	Low
2017		
First quarter	$ 10.46	$ 5.44
Second quarter	$ 10.03	$ 6.80
Third quarter	$ 10.36	$ 6.42
Fourth quarter	$ 9.13	$ 5.70
2016		
Second quarter (from June 2, 2016)	$ 8.45	$ 6.67
Third quarter	$ 18.20	$ 5.65
Fourth quarter	$ 25.08	$ 8.09

The last reported sale price of our common stock on The Nasdaq Global Market on March 12, 2018 was $12.64 per share.

Stock Performance Graph

The following graph compares the performance of our common stock since June 1, 2016, the date of our IPO, with the performance of the Nasdaq Composite Index (U.S.) and the Nasdaq Biotechnology Index. The comparison assumes a $100 investment on June 1, 2016 in our common stock, the stocks comprising the Nasdaq Composite Index, and the stocks comprising the Nasdaq Biotechnology Index. We have not paid any cash dividends and, therefore, the cumulative total return calculation for us is based solely upon our stock price appreciation or depreciation and does not include any reinvestment of cash dividends. The graph assumes our closing sales price on June 1, 2016 of $7.00 per share as the initial value of our common stock.

The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock.



The information presented above in the stock performance graph shall not be deemed to be "soliciting material" or to be "filed" with the SEC or subject to Regulation 14A or 14C, except to the extent that we subsequently specifically request that such information be treated as soliciting material or specifically incorporate it by reference into a filing under the Securities Act of 1933, as amended, or a filing under the Securities Exchange Act of 1934, as amended.

Dividend Policy

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

Stockholders

As of March 12, 2018, we had 31,913,113 shares of common stock outstanding held by 21 holders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Use of Proceeds from Initial Public Offering of Common Stock

On June 1, 2016, our Registration Statement on Form S-1, as amended (File No. 333-208916) was declared effective in connection with our IPO, pursuant to which we sold 8,148,843 shares of our common stock, including the partial exercise of the underwriters' option to purchase additional shares, at a price to the public of $7.00 per share. The offering closed on June 7, 2016, and, as a result, we received net proceeds of $51.4 million (after underwriters' discounts and commissions of $4.0 million and additional offering related costs of $1.7 million). The joint managing underwriters of the offering were Cowen and Company, LLC and Stifel, Nicolaus & Company, Incorporated.

No expenses incurred by us in connection with our IPO were paid directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities, or (iii) any of our affiliates, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service.

There was no material change in the use of proceeds from our IPO from that described in the final prospectus filed with the SEC on June 2, 2016. As of December 31, 2017, we have used all of the proceeds from the IPO to fund our operations, consisting primarily of costs to conduct the Phase 3 clinical trials of CLS-TA for uveitis and RVO.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

ITEM 6. SELECTED FINANCIAL DATA

The following selected statement of operations data for the years ended December 31, 2017, 2016 and 2015, and balance sheet data as of December 31, 2017 and 2016 is derived from our audited financial statements included within this Annual Report. The balance sheet data as of December 31, 2015 and 2014, and the statement of operations data for the year ended December 31, 2014 have been derived from our audited financial statements which are not included herein. Our historical results are not necessarily indicative of the results to be expected in the future. The selected financial data should be read together with Item 7. “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 Annual Report.

	Year Ended December 31,			
	2017	**2016**	**2015**	**2014**
	(in thousands, except share and per share data)			
License and collaboration revenue	$ 345	$ 520	$ —	$ —
Operating expenses:				
Research and development	49,053	19,455	10,762	6,692
General and administrative	9,700	6,263	6,555	3,131
Total operating expenses	58,753	25,718	17,317	9,823
Loss from operations	(58,408)	(25,198)	(17,317)	(9,823)
Other expense	(567)	(684)	(322)	(366)
Net loss	$ (58,975)	$ (25,882)	$ (17,639)	$ (10,189)
Net loss per share of common stock — basic and diluted	$ (2.33)	$ (1.97)	$ (7.54)	$ (5.86)
Weighted average shares outstanding — basic and diluted	25,311,614	13,111,067	2,338,950	1,738,660

	December 31,			
	2017	**2016**	**2015**	**2014**
	(in thousands)			
Balance sheet data:				
Cash and cash equivalents	$ 9,224	$ 34,824	$ 20,283	$ 8,269
Short-term investments	28,416	48,807	—	—
Restricted cash	360	360	—	—
Total assets	40,493	84,813	21,055	10,299
Debt	8,009	7,586	5,976	—
Total liabilities	19,078	13,154	10,400	2,677
Total stockholders' equity (deficit)	21,415	71,659	(36,659)	(19,213)

ITEM 7. 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 in conjunction with the financial statements and the related notes to those statements included later in this Annual Report. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates, beliefs and expectations that involve risks and uncertainties. Our actual results and the timing of events could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, particularly in Item 1A. "Risk Factors" and "Special Note Regarding Forward-Looking Statements."

Overview

We are a late-stage clinical biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye. Our current product candidates focus on treatments for diseases affecting the retina and choroid, especially diseases associated with macular edema, and are injected into the suprachoroidal space, or SCS, using our proprietary SCS Microinjector. With the suprachoroidal injection procedure, our product candidates are more directly administered to the retina and choroid as compared to other ocular drug administration techniques such as intravitreal injections. We believe treatment of eye disease via suprachoroidal injection may provide a number of benefits, including lower frequency of administration and faster onset of therapeutic effect. We hold the exclusive rights to develop and commercialize drugs for treatment via injection into the SCS. Our most advanced product candidates are based on commonly used ophthalmic drugs, which we believe will allow us to more efficiently and predictably pursue the regulatory approval of these product candidates under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act.

We are developing suprachoroidal CLS-TA, our proprietary, preservative-free formulation of the corticosteroid triamcinolone acetonide, or TA, to be administered suprachoroidally, for the treatment of patients with non-infectious uveitis. On March 5, 2018, we announced positive topline results from our PEACHTREE Phase 3 clinical trial of CLS-TA for the treatment of macular edema associated with non-infectious uveitis. We enrolled 160 patients in the trial, of which 96 patients were randomized to the treatment arm to receive two 4.0 mg doses of suprachoroidal CLS-TA 12 weeks apart, and 64 patients were randomized to undergo a sham procedure at the same 12-week intervals. Patients were evaluated every four weeks for a total of 24 weeks, and a total of 155 patients, or 97% of those enrolled, completed the full evaluation period of the trial. The trial met the primary endpoint with 47% of patients who received suprachoroidal CLS-TA every 12 weeks gaining at least 15 letters in best corrected visual acuity, or BCVA, as measured using the Early Treatment of Diabetic Retinopathy Study, or ETDRS, scale, from baseline at week 24, compared to 16% of patients who underwent a sham procedure. This improvement was statistically significant, with a p-value of less than 0.001. The improvement in BCVA from baseline was better in the treatment arm than the sham arm at each monthly evaluation. The mean improvement from baseline was maintained throughout the evaluation period, with 9.6 letters gained at week 4 and 13.7 letters gained at week 24 in the active arm, compared to 1.2 letters gained at week 4 and 2.9 letters gained at week 24 in the control arm.

Administration of suprachoroidal CLS-TA also resulted in a mean reduction from baseline of 157 microns in central subfield thickness at week 24 in the active arm compared to a 19 micron mean reduction in the sham arm, a result that was also statistically significant with a p-value of less than 0.001.

Suprachoroidal CLS-TA was generally well tolerated, with no treatment-related serious adverse events reported in the trial. Through 24 weeks, steroid-related elevated IOP adverse events were reported for approximately 11.5% of patients in the CLS-TA treatment group, compared to no patients in the sham group.

Based on the results from PEACHTREE, we intend to submit an NDA for CLS-TA for the treatment of patients with non-infectious uveitis by the end of 2018.

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

We have completed a Phase 2 clinical trial, which we refer to as TANZANITE, in 46 patients with macular edema associated with RVO. In this trial, 23 patients in the active arm initially received suprachoroidal CLS-TA together with an intravitreal injection of the anti-VEGF agent Eylea, or intravitreal Eylea, and 23 patients in the control arm initially received only intravitreal Eylea. The objective of the trial was to determine whether patients receiving suprachoroidal CLS-TA together with intravitreal Eylea could sustain this improved visual acuity over the three months of the clinical trial while requiring fewer additional Eylea treatments than patients receiving intravitreal Eylea alone. Patients in each arm were evaluated at months one, two and three after the initial treatment using pre-specified criteria to determine if they continued to experience macular edema or reductions in visual acuity and therefore

required additional intravitreal Eylea treatments. The primary objective of the trial was met, with patients in the active arm requiring an aggregate of 60% fewer additional Eylea treatments than patients in the control arm over three months, a result that was statistically significant (p=0.013). In addition, based on a post-hoc analysis, 18 of the 23 patients, or 78%, in the active arm of the trial did not require additional treatments during the three-month trial compared to 7 of the 23 patients, or 30%, in the control arm, a result that was also statistically significant (p=0.003). In the same Phase 2 trial, patients in the active arm experienced greater improvement in visual acuity than those in the control arm, with patients in the active arm experiencing mean BCVA improvements at months one, two and three of 16, 20 and 19 letters, respectively, compared to improvements of 11, 12 and 11 letters, respectively, in the control arm at the same time points. We also extended our evaluation of the patients who participated in the trial and did not receive any additional Eylea treatment during its initial three-month evaluation period to further assess the durability of suprachoroidal CLS-TA in combination with intravitreal Eylea for an additional six months following completion of the trial. Of the 32 eligible patients, the medical records of 31 patients were obtained for review. Based on combined data from the initial and extended evaluation periods, 17 of the 23 patients in the combination arm, or 74%, did not receive any additional treatment over the nine-month period, compared to only 4 of 23 patients, or 17%, in the control arm.

Based on the results of TANZANITE and after incorporating feedback from an end-of-Phase 2 meeting with the FDA held in late 2016, we began to enroll patients in a Phase 3 clinical trial, which we refer to as SAPPHIRE, in the first quarter of 2017.We are continuing to enroll patients in SAPPHIRE, a multicenter, randomized, masked, controlled trial, to assess the efficacy and safety of suprachoroidal CLS-TA together with intravitreal Eylea in patients with RVO. Patients in the combination treatment arm will receive suprachoroidal CLS-TA together with intravitreal Eylea at the beginning of the trial, intravitreal Eylea alone at week 4, and suprachoroidal CLS-TA together with intravitreal Eylea at weeks 12 and 24. Patients in the control arm will receive intravitreal Eylea alone at the beginning of the trial and follow-up intravitreal Eylea alone every four weeks through and including week 24. After 24 weeks, patients will be followed for approximately an additional six months. The primary objective of this trial will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at eight weeks after initial treatment. There will be several secondary efficacy and safety endpoints that will also be evaluated. We anticipate total enrollment of approximately 460 patients in the trial. We expect to report preliminary results from SAPPHIRE in the fourth quarter of 2018.

In addition, in the third quarter of 2017, we began the start-up activities for a second Phase 3 clinical trial in patients with RVO, which we refer to as TOPAZ. We enrolled the first patient in TOPAZ in March 2018. Similar to the SAPPHIRE trial, TOPAZ is a multicenter, randomized, masked, controlled Phase 3 trial, to assess the efficacy and safety of suprachoroidal CLS-TA together with an intravitreal anti-VEGF agent (either Lucentis or Avastin) in patients with RVO. Patients in the combination treatment arm will receive suprachoroidal CLS-TA together with an intravitreal anti-VEGF agent at the beginning of the trial, intravitreal anti-VEGF agent alone at week 4, and suprachoroidal CLS-TA together with intravitreal anti-VEGF agent at weeks 12 and 24. Patients in the control arm will receive intravitreal anti-VEGF agent alone at the beginning of the trial and follow-up intravitreal anti-VEGF agent alone every four weeks through and including week 24. After 24 weeks, patients will be followed for approximately an additional six months with patients in each arm having the opportunity to receive treatment as needed based on monthly evaluations. The primary objective of this trial will be to determine the proportion of patients in each arm with a BCVA improvement of at least 15 letters from baseline at eight weeks after initial treatment. Several secondary efficacy and safety endpoints will also be evaluated. We anticipate total enrollment of approximately 460 patients in the trial.

We are also developing suprachoroidal CLS-TA for the treatment of diabetic macular edema, or DME. In April 2017, we completed enrollment of 20 patients with DME in an open-label, multi-center Phase 1/2 clinical trial, which we refer to as HULK, to obtain safety data and to observe efficacy outcomes from administering a combination of intravitreal Eylea and suprachoroidal CLS-TA, as well as suprachoroidal CLS-TA alone, over a six-month evaluation period. In November 2017, we announced preliminary results from the HULK trial. In the trial, we observed a visual benefit for patients receiving suprachoroidal CLS-TA, with a greater benefit in treatment naïve eyes. Anatomic improvement was observed in all treated eyes, with more than two-thirds of those eyes achieving a greater than 50% reduction in excess central retinal thickness based on monthly measurements through six months after initial treatment. In the treatment naïve group, 40% of patients did not require retreatment over the entire six months, with an additional 20% requiring only one retreatment. Suprachoroidal CLS-TA, including in patients who received as many as five injections, was well tolerated, with a low incidence of ocular side effects, including IOP elevations.

In July 2017, we commenced a Phase 2 clinical trial, which we refer to as TYBEE, to evaluate the safety and efficacy of administering a combination of intravitreal Eylea and suprachoroidal CLS-TA to patients with DME, as compared to intravitreal Eylea alone. We completed enrollment of 71 patients in this trial in October 2017. Patient follow-up in TYBEE is six months after initial treatment and we expect to report preliminary data in the second quarter of 2018.

Finally, multiple nonclinical studies, both internally and with multiple collaborators, are underway in development areas such as gene therapy for inherited retinal disorders, neovascular age-related macular degeneration, also known as wet AMD, and other ocular diseases that may benefit from suprachoroidal administration of medication.

If any of our product candidates are approved, we plan to commercialize them with a specialty team of 30 to 40 sales and medical marketing professionals to target the approximately 1,900 uveitis and retina specialists in the United States, and we may also pursue collaborations with third parties to commercialize any of our drugs approved for marketing outside the United States.

We have incurred net losses since our inception in May 2011. Our operations to date have been limited to organizing and staffing our company, raising capital, undertaking preclinical studies and other research and development initiatives and, beginning in 2013, conducting clinical trials of our most advanced drug candidates. To date, we have not generated any revenue, other than license and collaboration revenue, and we have primarily financed our operations through public offerings and private placements of our equity securities, issuances of convertible promissory notes and loan agreements. As of December 31, 2017, we had an accumulated deficit of $124.2 million. We recorded net losses of $59.0 million, $25.9 million and $17.6 million for the years ended December 31, 2017, 2016 and 2015, respectively. We anticipate that a substantial portion of our capital resources and efforts in the foreseeable future will be focused on completing the necessary development for and obtaining regulatory approval and preparing for potential commercialization of our product candidates.

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

- complete our ongoing PEACHTREE, SAPPHIRE, TOPAZ and TYBEE clinical trials;
- initiate and conduct our planned future clinical trials;
- seek to discover, research and develop additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials and other developmental efforts necessary to seek such approvals;
- establish sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any product candidates for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our development and potential future commercialization efforts; and
- operate as a public company.

Components of Operating Results

Revenue

We have not generated any revenue from the sale of any drugs, and we do not expect to generate any product revenue unless or until we obtain regulatory approval of and commercialize our product candidates. In 2014, we executed a license agreement with NovaMedica LLC, or NovaMedica, and in 2015, we executed a license agreement with Spark Therapeutics, Inc., or Spark. In connection with these agreements, we received up-front payments of $200,000 from NovaMedica and $500,000 from Spark. We deferred recognizing these payments through 2015. In the first quarter of 2016, we began recognizing revenue related to the NovaMedica payment and we recognized the entire payment from Spark. In the second quarter of 2017, we entered into additional collaboration agreements to evaluate the potential use of our proprietary SCS microinjector with third-party product candidates for the treatment of various diseases. We recognized $325,000 in collaboration revenue from these agreements during the year ended December 31, 2017.

Research and Development

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

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense for research and development personnel;
- expenses incurred under agreements with contract research organizations, or CROs, as well as contract manufacturing organizations and consultants that conduct clinical trials and preclinical studies;
- costs associated with preclinical activities and development activities;
- costs associated with technology and intellectual property licenses;

- costs for our research and development facility; and
- depreciation expense for assets used in research and development activities.

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

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

For the years ended December 31, 2017, 2016 and 2015, substantially all of our research and development expenses have been related to the non-clinical and clinical development of our product candidates.

The following table shows our research and development expenses by type of activity for the years ended December 31, 2017, 2016 and 2015.

	Year Ended December 31,		
	2017	2016	2015
	(in thousands)		
CLS-TA (uveitis program)	$ 12,702	$ 8,411	$ 3,877
CLS-TA (RVO program)	23,487	3,677	1,462
CLS-TA (DME program)	4,217	—	—
Wet AMD program	252	2,930	1,259
Total program expense	40,658	15,018	6,598
Unallocated	8,395	4,437	4,164
Total research and development expense	$ 49,053	$ 19,455	$ 10,762

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

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

The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors that include the following:

- the costs associated with process development, scale-up and manufacturing of CLS-TA and the microinjector for clinical trials and for requirements associated with regulatory filings associated with approval;
- number of trials required for approval and any requirement for extension trials;
- per patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;

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

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

General and Administrative

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

We anticipate that our general and administrative expenses will increase in the future to support our continued research and development activities and the potential commercialization of our product candidates. Additionally, we anticipate increased costs associated with being a public company including expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC requirements, director and officer insurance, and investor and public relations costs.

Other Income (Expense)

Other income consists of interest income earned on our cash and cash equivalents. Interest income is not currently significant to our financial statements.

Other expense consisted of interest accrued under our loan agreements for the years ended December 31, 2017, 2016 and 2015. Additionally, during the years ended December 31, 2016 and 2015, other expense included changes in the value of a liability related to a warrant to purchase preferred stock, which warrant automatically converted into a warrant to purchase common stock in connection with our initial public offering, or IPO, in June 2016. After the conversion, no further income or expense was recognized in connection with changes in the fair value of that warrant, which was subsequently exercised in October 2016.

Critical Accounting Policies and Significant Judgments and Estimates

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

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. While our significant accounting policies are more fully described in Note 2 to our financial statements appearing elsewhere in this Annual Report, 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, 2017 and 2016 consisted primarily of cash and cash equivalents, short-term investments and long-term debt. The fair value of cash and cash equivalents, other current assets and accounts payable approximate their respective carrying values due to the short term nature of these instruments. The fair value of long-term debt approximates the carrying value due to variable interest rates that correspond to market rates. We have determined our cash and cash equivalents and government bonds to be Level 1 in the fair value hierarchy. We have determined our short-term investments, comprised of certificates of deposit, government and corporate bonds, treasury bills, commercial paper and agency obligations, to be Level 2 in the fair value hierarchy. The fair value was determined using a market approach, based on prices and other relevant information generated by market transactions involving similar assets. The short-term investments consist of investments with original maturity dates from date of acquisition of 90 to 365 days and are classified as available-for-sale. We have determined our stock purchase warrants liability to be Level 3 in the fair value hierarchy.

Share-based compensation

Compensation cost related to share-based awards granted to employees is measured based on the estimated fair value of the award at the grant date. We estimate 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 awards granted to non-employees is re-measured each period until the related service is complete. Share-based compensation costs are expensed on a straight-line basis (net of estimated forfeitures) over the relevant vesting period. All share-based compensation costs are recorded in general and administrative or research and development costs in the statements of operations based upon the underlying employees' roles.

Significant factors, assumptions and methodologies used in determining fair value

Determining the appropriate fair value measurement of share-based awards requires the use of subjective assumptions. 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 Black-Scholes option pricing model with the following assumptions:

- *Fair value of our common stock.* Prior to the IPO, no public market existed for our stock, and we estimated its fair value using retrospective assessments and contemporaneous valuations of our common stock. For stock options granted after June 1, 2016, the date of our IPO, we estimate the fair value of our common stock by reference to the closing price of our common stock on The Nasdaq Global Market on the date of grant.
- *Volatility.* As we do not have a trading history for our common stock, we utilize data from a representative group of publicly traded companies to estimate expected stock price volatility. We selected representative companies from the pharmaceutical industry with similar characteristics to us, including stage of product development and therapeutic focus.
- *Expected term.* We used the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, as we do not have sufficient historical exercise and post-vesting termination data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees.
- *Risk-free rate.* The risk-free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected time to liquidity.
- *Forfeitures.* Forfeitures are accounted for as they occur.
- *Dividend yield.* We have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future.

We have an employee stock purchase plan that is considered a compensatory plan. The fair value of the discount and the look-back period of the employee stock purchase plan are estimated using the Black-Scholes option pricing model and expense is recognized over the six month withholding period prior to the purchase date.

Share-based compensation expense related to stock options and the employee stock purchase plan aggregated $3.4 million, $1.3 million and $0.7 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Tax valuation allowance

We recorded deferred tax assets of $28.0 million, related to our net operating losses, as of December 31, 2017, 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 $116.3 million for the period from our inception on May 26, 2011 to December 31, 2017. We incurred a net loss for tax purposes of $55.5 million for the year ended December 31, 2017. 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, 2017, we had federal NOL carryforwards of $116.3 million and state NOL carryforwards of $79.1 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 as a result of future offerings or 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 Years Ended December 31, 2017 and 2016

The following table sets forth our results of operations for the years ended December 31, 2017 and 2016.

	Year Ended December 31,		Period-to-Period Change
	2017	2016	
	(in thousands)		
License and collaboration revenue	$ 345	$ 520	$ (175)
Operating expenses:			
Research and development	49,053	19,455	29,598
General and administrative	9,700	6,263	3,437
Total operating expenses	58,753	25,718	33,035
Loss from operations	(58,408)	(25,198)	(33,210)
Other expense	(567)	(684)	117
Net loss	$ (58,975)	$ (25,882)	$ (33,093)

Revenue. In each of the years ended December 31, 2017 and 2016, we recognized $20,000 of revenue associated with our NovaMedica agreement. In the year ended December 31, 2017, we recognized $0.3 million of revenue associated with our other collaboration agreements. In the year ended December 31, 2016, we recognized $0.5 million of revenue associated with our collaboration agreement with Spark.

Research and development. Research and development expense increased by $29.6 million, from $19.5 million for the year ended December 31, 2016 to $49.1 million for the year ended December 31, 2017. This increase was primarily attributable to an increase in costs related to our clinical programs. Costs for our uveitis program increased $4.2 million, costs for our RVO program increased $21.3 million, which included purchases of Eylea for SAPPHIRE and start-up costs for TOPAZ, and costs for our DME program increased $4.2 million. In addition to the increase in the cost of our clinical programs, we also incurred a $0.7 million increase in the cost of producing drug product for the registration batches to support an NDA submission, a $0.3 million increase in regulatory costs in preparation for a potential NDA submission, a $0.7 million increase in other research and development activities and a $2.4 million increase in employee-related costs due to an increase in headcount to support the increased clinical trial activities. These increases were partially offset by a $2.0 million decrease resulting from the completion in 2016 of two Phase 2 clinical trials for CLS-TA and a $2.7 million decrease in costs resulting from the discontinuation of nonclinical development for our wet AMD program in the first quarter of 2017.

General and administrative. General and administrative expenses increased by $3.4 million, from $6.3 million for the year ended December 31, 2016 to $9.7 million for the year ended December 31, 2017. The increase was primarily attributable to an increase of $1.6 million of employee-related costs, a $0.4 million increase in patent and trademark costs, a $0.2 million increase in marketing expenses and a $0.8 million increase related to the costs of operating as a public company for a full year, including an increase in director and officer insurance premiums, professional fees and non-employee director compensation.

Other expense. Other expense for the year ended December 31, 2017 was $0.6 million, compared to $0.7 million for the year ended December 31, 2016, in each case primarily consisting of interest on long-term debt and the amortization of financing costs, partially offset by interest income from our short-term investments. Other expense in the year ended December 31, 2016 also included a change in the mark-to-market warrant liability and the acceleration of the final payment from the original loan agreement with Silicon Valley Bank, or SVB.

Results of Operations for the Years Ended December 31, 2016 and 2015

The following table sets forth our results of operations for the years ended December 31, 2016 and 2015.

	Year Ended December 31,		Period-to-Period Change
	2016	2015	
	(in thousands)		
License and collaboration revenue	$ 520	$ —	$ 520
Operating expenses:			
Research and development	19,455	10,762	8,693
General and administrative	6,263	6,555	(292)
Total operating expenses	25,718	17,317	8,401
Loss from operations	(25,198)	(17,317)	(7,881)
Other expense	(684)	(322)	(362)
Net loss	$ (25,882)	$ (17,639)	$ (8,243)

Revenue. In the year ended December 31, 2016, we recognized $0.5 million of revenue associated with our agreement with NovaMedica and the license and collaboration agreement with Spark. We did not recognize any revenue in the year ended December 31, 2015.

Research and development. Research and development expense increased by $8.7 million, from $10.8 million for the year ended December 31, 2015 to $19.5 million for the year ended December 31, 2016. This increase was primarily attributable to a $2.8 million increase in costs related to the ongoing Phase 3 clinical trial for CLS-TA for the treatment of non-infectious uveitis, a $1.7 million increase in costs associated with preclinical studies for our wet AMD program, a $2.2 million increase for costs related to the initial preparation of the Phase 3 clinical trial for CLS-TA for the treatment of macular edema associated with RVO and a $2.2 million increase in device manufacturing costs. These increases were partially offset by a $1.0 million decrease in costs for the completed Phase 2 clinical trial for CLS-TA for the treatment of non-infectious uveitis and Phase 2 clinical trial for CLS-TA for the treatment of macular edema associated with RVO.

General and administrative. General and administrative expenses decreased by $0.3 million, from $6.6 million for the year ended December 31, 2015 to $6.3 million for the year ended December 31, 2016. The decrease was primarily attributable to recognizing $1.9 million of expenses related to previously deferred offering costs in 2015, offset by increases in 2016 of $1.0 million for employee-related costs and $0.5 million for costs of operating as a public company.

Other expense. Other expense increased in the year ended December 31, 2016 by $0.4 million compared to 2015, from $0.3 million to $0.7 million. This increase was primarily the result of an increase in the mark-to-market warrant liability and the acceleration of the final payment from the original loan agreement with SVB in addition to the amortization of financing costs, the accretion of warrants and the final payment related to our new loan agreements.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2017, we had an accumulated deficit of $124.2 million and cash, cash equivalents and short-term investments of $37.6 million. We invest any cash in excess of our immediate requirements primarily with a view to liquidity and capital preservation. As of December 31, 2017, our funds were held in cash, money market funds, certificates of deposit, corporate bonds, government bonds, commercial paper and treasury bills.

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

On December 14, 2016, we closed a follow-on public offering in which we sold 4,000,000 shares of common stock at a public offering price of $9.00 per share. On December 30, 2016, the underwriters exercised their option to purchase 600,000 additional shares, and on January 6, 2017, we sold the 600,000 additional shares at $9.00 per share. These issuances collectively resulted in net proceeds of $38.5 million after deducting underwriting discounts and commissions and offering expenses.

On June 30, 2017, we entered into an at-the-market sales agreement with Cowen and Company LLC, or Cowen, under which we may offer and sell, from time to time at our sole discretion, shares of our common stock having an aggregate offering price of up to $50.0 million through Cowen acting as our sales agent. As of the date of this report, we have not sold any shares of our common stock under the at-the-market facility.

On March 12, 2018, we closed a follow-on public offering in which we sold 6,538,462 shares of common stock at a public offering price of $13.00 per share, resulting in net proceeds of $79.6 million after deducting underwriting discounts and commissions and estimated offering expenses. We have granted the underwriters an option, exercisable through April 6, 2018, to purchase up to an additional 980,769 shares of common stock at the public offering price.

Prior to our IPO, we funded operations primarily through the sale of convertible preferred stock, a long-term loan agreement and the issuance of convertible promissory notes. We raised net cash proceeds of $44.5 million from the sale of convertible preferred stock, $6.0 million from a long-term loan agreement and $3.4 million from the sale of convertible promissory notes through December 31, 2016.

On September 28, 2016, we entered into an amended and restated loan and security agreement, which we subsequently amended on October 31, 2017, or as amended the Loan Agreement, with SVB and entities affiliated with MidCap Financial Services, which we refer to collectively with SVB as the Lenders. The Loan Agreement amended and restated in its entirety our prior loan and security agreement with SVB. The Loan Agreement provides for new term loans of up to $15.0 million, with a floating interest rate equal to 7% plus the greater of (i) the 30-day U.S. LIBOR, reported in the Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, or (ii) 0.50%. We borrowed an initial tranche of $8.0 million on September 28, 2016, of which $5.3 million was used to repay all amounts outstanding under our prior loan agreement with SVB. We may draw the remaining $7.0 million through March 31, 2018. We were required to pay accrued interest only through December 31, 2017 on the outstanding amount, followed by 30 equal payments of principal and accrued interest. We have the option to prepay the outstanding balance of the term loans in full, subject to a prepayment fee of 2% of the original principal amount of the aggregate term loans for any prepayments through May 31, 2020. A final payment of $0.5 million, or 6.50% of the aggregate borrowed amount, is due at maturity of the loan on June 1, 2020, or upon the prepayment of the facility or the acceleration of amounts due under the facility as a result of an event of default.

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

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

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-TA or any future product candidates, although we will require additional funding to complete our Phase 3 clinical program for CLS-TA as a potential treatment, together with an anti-VEGF agent, for RVO. We are also unable to predict when, if ever, material net cash inflows will commence from product sales. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

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

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements. We do not currently have any committed external source of funds other than under the Loan Agreement, and as described above we may also be able to sell up to $50.0 million of our common stock under the at-the-market sales agreement with Cowen subject to the terms of that agreement and depending on market conditions. 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 also incur costs as a public company that we have not previously incurred or have previously incurred at lower rates, including increased costs and expenses for fees to members of our board of directors, increased personnel costs, increased directors and officers insurance premiums, audit and legal fees, investor relations fees and expenses for compliance with reporting requirements under the Exchange Act and rules implemented by the SEC and Nasdaq.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, including our ability to control spending by delaying, reducing or eliminating research and development programs or reducing administrative expense while still advancing clinical trials for our most advanced product candidates, we expect that our existing cash, cash equivalents and short-term investments, including the net proceeds from our public offering of common stock in March 2018, 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 exhaust our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress in these trials is uncertain.

Cash Flows

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

	Year Ended December 31,		
	2017	**2016**	**2015**
	(in thousands)		
Net cash (used in) provided by:			
Operating activities	$ (51,083)	$ (22,709)	$ (13,902)
Investing activities	20,121	(49,140)	(28)
Financing activities	5,362	86,390	25,944
Net change in cash and cash equivalents	$ (25,600)	$ 14,541	$ 12,014

During the years ended December 31, 2017, 2016 and 2015, our operating activities used net cash of $51.1 million, $22.7 million and $13.9 million, respectively. The use of cash in each period primarily resulted from our net losses. The increase in net loss for the year ended December 31, 2017 as compared to the years ended December 31, 2016 and 2015 was primarily attributable to higher research and development expenses related to our Phase 3 clinical trials PEACHTREE, SAPPHIRE and TOPAZ and the related expenses to support them including employee-related costs.

During the year ended December 31, 2017, our net cash provided by investing activities was $20.1 million, compared to net cash used in investing activities of $49.1 million and $28,000 during the years ended December 31, 2016 and 2015, respectively. In the year ended December 31, 2017, cash flows provided by investing activities was primarily from $68.5 million for the maturities of short-term, available-for-sale investments, which include certificates of deposit, corporate bonds and government bonds, commercial paper, treasury bills and agency obligations, partially offset by the purchase of $48.1 million of short-term, available-for-sale investments and $0.3 million for the purchase of furniture and fixtures for our corporate office. In the year ended December 31, 2016, cash flows used in investing activities resulted primarily from the purchase of $54.5 million of short-term, available-for-sale

investments, partially offset by $5.7 million for the maturities of short-term, available-for-sale investments. Net cash used in investing activities during the years ended December 31, 2015 was comprised of the purchase of fixed assets.

During the years ended December 31, 2017, 2016 and 2015, our net cash provided by financing activities was $5.4 million, $86.4 million and $25.9 million, respectively. The net cash provided by financing activities for the year ended December 31, 2017 was comprised primarily of the $5.1 million of net proceeds received from the underwriters' exercise of their option to purchase additional shares as part of our public offering of common stock that initially closed in December 2016. The net cash provided by financing activities for the year ended December 31, 2016 was comprised primarily of the $84.8 million of net proceeds received from our IPO and follow-on public offering of common stock and from the Loan Agreement with SVB, partially offset by $6.3 million in payments of long-term debt, which includes the $5.3 million to repay all amounts owed under the prior loan agreement with SVB. The net cash provided by financing activities during the year ended December 31, 2015 was primarily due to $20.0 million received from the sale of our Series C convertible preferred stock and amounts borrowed under the prior loan agreement with SVB.

Contractual Obligations

The following table summarizes our significant contractual obligations as of December 31, 2017, all of which consisted of obligations under the lease for our corporate headquarters in Alpharetta, Georgia and obligations under the Loan Agreement.

	Payments due by period				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
	(in thousands)				
Operating lease obligations	$ 2,665	$ 431	$ 1,374	$ 860	$ —
Long-term debt obligations [1]	9,255	3,676	5,579	—	—
Total	$ 11,920	$ 4,107	$ 6,953	$ 860	$ —

1. Includes estimated interest expense at the minimum rate of 7.50% and the final payment.

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

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Recent Accounting Pronouncements

See Item 8. "Financial Statements and Supplementary Data – Note 2, Significant Accounting Policies" for a discussion of recent accounting pronouncements and their effect on us.

JOBS Act

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

ITEM 7A. 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, 2017 and 2016, we had cash and cash equivalents of $9.2 million and $34.8 million, respectively. We generally hold our cash in interest-bearing money market accounts. As of December 31, 2017 and 2016, we had short-term investments of $28.4 million and $48.8 million, respectively. The short-term investments include certificates of deposit, corporate bonds and government bonds, commercial paper, treasury bills and agency obligations. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term

maturities of our cash equivalents and short-term investments and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents and short-term investments.

We do not engage in any hedging activities against changes in interest rates. Our outstanding debt instruments carry a floating interest rate that is 7.0% plus the greater of (i) the 30-day U.S. LIBOR, reported in the Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, or (ii) 0.50%. A 100 basis point increase in the variable interest rate would have resulted in an $80,000 increase in interest expense for each of the years ended December 31, 2017 and 2016.

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

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Clearside Biomedical, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Clearside Biomedical, Inc. (the Company) as of December 31, 2017 and 2016, and the related statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2014.

Atlanta, Georgia
March 16, 2018

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

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 9,224	$ 34,824
Short-term investments	28,416	48,807
Prepaid expenses	1,445	396
Other current assets	116	290
Total current assets	39,201	84,317
Property and equipment, net	885	94
Restricted cash	360	360
Other assets	47	42
Total assets	$ 40,493	$ 84,813
Liabilities, convertible preferred stock and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,384	$ 2,594
Accrued liabilities	4,716	2,791
Current portion of long-term debt	3,200	—
Current portion of deferred rent	199	3
Other current liabilities	20	20
Total current liabilities	13,519	5,408
Long-term debt	4,809	7,586
Deferred rent	610	—
Deferred revenue	140	160
Total liabilities	19,078	13,154
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized and no shares issued at December 31, 2017 and 2016	—	—
Common stock, $0.001 par value; 100,000,000 shares authorized at December 31, 2017 and 2016; 25,354,651 and 24,573,033 shares issued and outstanding at December 31, 2017 and 2016, respectively	25	25
Additional paid-in capital	145,618	136,892
Accumulated deficit	(124,220)	(65,245)
Accumulated other comprehensive loss	(8)	(13)
Total stockholders' equity	21,415	71,659
Total liabilities and stockholders' equity	$ 40,493	$ 84,813

See accompanying notes to the financial statements

CLEARSIDE BIOMEDICAL, INC.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,		
	2017	2016	2015
License and collaboration revenue	$ 345	$ 520	$ —
Operating expenses:			
Research and development	49,053	19,455	10,762
General and administrative	9,700	6,263	6,555
Total operating expenses	58,753	25,718	17,317
Loss from operations	(58,408)	(25,198)	(17,317)
Other expense	(567)	(684)	(322)
Net loss	$ (58,975)	$ (25,882)	$ (17,639)
Net loss per share of common stock — basic and diluted	$ (2.33)	$ (1.97)	$ (7.54)
Weighted average shares outstanding — basic and diluted	25,311,614	13,111,067	2,338,950
Net loss	$ (58,975)	$ (25,882)	$ (17,639)
Unrealized gain (loss) on available-for-sale investments	5	(13)	—
Comprehensive loss	$ (58,970)	$ (25,895)	$ (17,639)

See accompanying notes to the financial statements.

CLEARSIDE BIOMEDICAL, INC.
Statement of Stockholders' Equity (Deficit)
(in thousands, except share data)

	Common Stock		Additional Paid-In-Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance at January 1, 2015	1,816,467	$ 2	$ 2,509	$ (21,724)	$ —	$ (19,213)
Exercise of stock options	50,980	—	14	—	—	14
Vesting of restricted stock	14,203	—	—	—	—	—
Issuance of common stock upon exercise of warrants	777,612	1	(2)	—	—	(1)
Accretion of stock issuance costs	—	—	(525)	—	—	(525)
Share-based compensation expense	—	—	705	—	—	705
Net loss	—	—	—	(17,639)	—	(17,639)
Balance at December 31, 2015	2,659,262	3	2,701	(39,363)	—	(36,659)
Exercise of stock options	10,724	—	31	—	—	31
Vesting of restricted stock	6,485	—	—	—	—	—
Issuance of common stock upon exercise of warrants	133,560	—	410	—	—	410
Issuance of common stock in initial public offering	8,148,843	8	51,369	—	—	51,377
Issuance of common stock in follow-on offering	4,000,000	4	33,455	—	—	33,459
Conversion of preferred stock to common stock	9,614,159	10	48,188	—	—	48,198
Issuance of warrants to purchase common stock	—	—	308	—	—	308
Accretion of redeemable convertible preferred stock to redemption value	—	—	(884)	—	—	(884)
Share-based compensation expense	—	—	1,314	—	—	1,314
Net loss	—	—	—	(25,882)	—	(25,882)
Other comprehensive loss	—	—	—	—	(13)	(13)
Balance at December 31, 2016	24,573,033	25	136,892	(65,245)	(13)	71,659
Issuance of common shares in follow-on offering	600,000	—	5,057	—	—	5,057
Issuance of common shares under employee stock purchase plan	9,692	—	66	—	—	66
Exercise of stock options	171,926	—	239	—	—	239
Share-based compensation expense	—	—	3,364	—	—	3,364
Net loss	—	—	—	(58,975)	—	(58,975)
Other comprehensive gain	—	—	—	—	5	5
Balance at December 31, 2017	25,354,651	$ 25	$ 145,618	$ (124,220)	$ (8)	$ 21,415

See accompanying notes to the financial statements.

CLEARSIDE BIOMEDICAL, INC.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2017	2016	2015
Operating activities			
Net loss	$ (58,975)	$ (25,882)	$ (17,639)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	182	65	60
Share-based compensation expense	3,364	1,314	705
Non-cash interest expense	211	283	104
Accretion of debt discount	212	108	60
Change in fair value of warrant liability	—	156	52
Amortization and accretion on available-for-sale investments, net	(31)	(43)	—
Loss on sale of fixed assets	—	—	15
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(833)	(487)	(145)
Other assets	(5)	882	1,763
Accounts payable and accrued liabilities	4,715	1,424	632
Deferred revenue	(20)	(520)	500
Deferred rent	97	(9)	(9)
Net cash used in operating activities	(51,083)	(22,709)	(13,902)
Investing activities			
Purchase of available-for-sale investments	(48,116)	(54,485)	—
Maturities of available-for-sale-investments	68,543	5,708	—
Change in restricted cash	—	(360)	—
Acquisition of property and equipment	(306)	(3)	(32)
Proceeds from the sale of fixed assets	—	—	4
Net cash provided by (used in) investing activities	20,121	(49,140)	(28)
Financing activities			
Proceeds from follow-on offering, net of issuance costs	5,057	33,456	—
Proceeds from initial public offering, net of issuance costs	—	51,376	—
Proceeds from the issuance of Series C Preferred Stock, net of issuance costs	—	—	19,954
Proceeds from exercise of stock options	239	31	14
Proceeds from shares issued under employee stock purchase plan	66	—	—
Proceeds from issuance of long-term debt	—	7,857	5,976
Principal payments made on long-term debt	—	(6,330)	—
Net cash provided by financing activities	5,362	86,390	25,944
Net (decrease) increase in cash and cash equivalents	(25,600)	14,541	12,014
Cash and cash equivalents, beginning of period	34,824	20,283	8,269
Cash and cash equivalents, end of period	$ 9,224	$ 34,824	$ 20,283
Supplemental disclosure			
Interest paid	$ 653	$ 250	$ 100
Supplemental disclosure of noncash investing and financing activities			
Tenant improvements paid by landlord	$ 637	$ —	$ —
Conversion of convertible preferred stock to common stock	—	48,198	—
Reclassification of deferred initial public offering costs	—	1,597	—
Issuance of warrants to purchase common stock	—	308	—
Issuance of warrant to purchase Series B preferred stock	—	—	164
Accretion of redeemable convertible preferred stock to redemption value	—	884	525
Unpaid initial public offering costs in accounts payable and accrued expenses	—	507	410

See accompanying notes to the financial statements.

1. The Company

Clearside Biomedical, Inc. (the "Company") is a late-stage clinical biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye. The Company's current product candidates focus on treatments for diseases affecting the retina and choroid, especially diseases associated with macular edema, and are injected into the suprachoroidal space ("SCS") using its proprietary SCS Microinjector. Incorporated in the State of Delaware on May 26, 2011, the Company has its corporate headquarters in Alpharetta, Georgia.

The Company's activities since inception have primarily consisted of developing product and technology rights, raising capital and performing research and development activities. The Company has no current source of revenue to sustain present activities, and does not expect to generate meaningful revenue until and unless the Company receives regulatory approval of and successfully commercializes its product candidates. The Company is subject to a number of risks and uncertainties similar to those of other life science companies at a similar stage of development, including, among others, the need to obtain adequate additional financing, successful development efforts including regulatory approval of products, compliance with government regulations, successful commercialization of potential products, protection of proprietary technology and dependence on key individuals.

Liquidity

On June 1, 2016, the Company's registration statement on Form S-1 relating to its initial public offering of its common stock (the "IPO") was declared effective by the Securities and Exchange Commission ("SEC"). The IPO closed on June 7, 2016 and the Company sold 7,200,000 shares of common stock at a price to the public of $7.00 per share, for net proceeds of $45.3 million. On June 30, 2016, the underwriters of the IPO partially exercised their option to purchase additional shares, and on July 6, 2016, the Company sold 948,843 additional shares of common stock at a price to the public of $7.00 per share, for net proceeds of $6.1 million. The Company paid to the underwriters underwriting discounts and commissions of $4.0 million in connection with the IPO, including the underwriters' exercise of their option to purchase additional shares. In addition, the Company incurred expenses of $1.6 million in connection with the IPO. Thus, the aggregate net offering proceeds to the Company, after deducting underwriting discounts and commissions and offering expenses, were $51.4 million.

On December 9, 2016, the Company's registration statement on Form S-1 relating to its follow-on public offering of its common stock was declared effective by the SEC. The follow-on public offering closed on December 14, 2016 and the Company sold 4,000,000 share of common stock at a price to the public of $9.00 per share, for net proceeds of $33.4 million. On December 30, 2016, the underwriters of the follow-on public offering exercised their option to purchase additional shares and on January 6, 2017, the Company sold 600,000 additional shares of common stock at a price to the public of $9.00 per share, for net proceeds of $5.1 million. The Company paid to the underwriters underwriting discounts and commissions of $2.5 million in connection with the follow-on public offering, including the underwriters' exercise of their option to purchase additional shares, and incurred expenses of $0.4 million in connection with the follow-on public offering.

On June 30, 2017, the Company entered into an at-the-market sales agreement with Cowen and Company LLC ("Cowen"), under which the Company may offer and sell, from time to time at its sole discretion, shares of its common stock having an aggregate offering price of up to $50.0 million through Cowen acting as its sales agent. As of the date of this report, the Company has not sold any shares of its common stock under the at-the-market facility.

On March 12, 2018, the Company closed a follow-on public offering in which it sold 6,538,462 shares of common stock at a public offering price of $13.00 per share, resulting in net proceeds of $79.6 million after deducting underwriting discounts and commissions and estimated offering expenses.

Prior to the IPO, the Company had funded its operations primarily through the sale of convertible preferred stock and the issuance of long-term debt, resulting in aggregate proceeds of approximately $53.9 million. Even with the completion of the IPO and the subsequent public offerings of common stock, the Company will continue to need to obtain additional financing to fund future operations, including completing the development and commercialization of its primary product candidates. The Company will need to expend substantial resources for research and development, including costs associated with the clinical testing of its product candidates. The Company will also need to obtain additional financing to conduct additional trials for the regulatory approval of its drug candidates if requested by regulatory bodies, and completing the development of any additional product candidates that might be acquired. If such products were to receive regulatory approval, the Company would need to prepare for the potential commercialization of its product candidates and fund the commercial launch of the products, if the Company decides to

commercialize the products on its own. Moreover, the Company's fixed expenses such as rent and other contractual commitments are substantial and are expected to increase in the future.

The Company had cash, cash equivalents and short-term investments of $37.6 million as of December 31, 2017. 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 sufficient revenue, the Company may finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic alliances and marketing or distribution arrangements. The Company has incurred losses and negative cash flows since inception and expects operating losses and negative cash flows to continue into the foreseeable future. However, the Company is able to control spending on development activities while proceeding with a new drug application and still advancing clinical trials for key drug candidates and the Company expects that the cash on hand as of the filing date, March 16, 2018, will be sufficient to fund its operations for at least the next 12 months from that date.

2. Significant Accounting Policies

Basis of Presentation

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP").

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, clinical trial accruals, 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.

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, or for leasehold improvement the lesser of the useful life or remaining lease term . 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.

Debt Discount

All debt discounts are recorded against the related debt obligation and are 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 Accounting Standards Codification ("ASC") Topic 820, *Fair Value Measurements and Disclosures*, on fair value measurements. The Company's material financial instruments at December 31, 2017 and 2016 consisted primarily of cash and cash equivalents, short-term investments and long-term debt. The fair value of cash and cash equivalents, other current assets, and accounts payable approximate their respective carrying values due to the short term nature of these instruments.

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 $28.0 million for the period from May 26, 2011 (inception) to December 31, 2017. 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.

Reverse Stock Split

On May 11, 2016, the Company effected a 1-for-2.2 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's convertible preferred stock. Accordingly, all share and per share amounts for all periods presented in these financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios. The adjustment to the conversion ratio for the Series C convertible preferred stock also included an anti-dilution adjustment based on the initial public offering price of the Company's common stock.

Research and Development Costs

Research and development costs are charged to expense as incurred and include:

- employee-related expenses, including salaries, benefits, travel and share-based compensation expense for research and development personnel;
- expenses incurred under agreements with contract research organizations, contract manufacturing organizations and consultants that conduct clinical and preclinical studies;
- costs associated with nonclinical 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 liabilities No material adjustments to these estimates have been recorded in these financial statements.

Share-Based Compensation

Compensation cost related to share-based awards granted to employees is measured based on the estimated fair value of the award at the grant date. 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 awards granted to non-employees is re-measured each period until the related service is complete. Share-based compensation costs are expensed on a straight-line basis (net of estimated forfeitures) over the relevant vesting period.

Compensation cost related to shares purchased through the Company's employee stock purchase plan, which is considered compensatory, is based on the estimated fair value of the shares on the offering date, including consideration of the discount and the look back period. The Company estimates the fair value of the shares using a Black-Scholes option pricing model. Compensation expense is recognized over the six month withholding period prior to the purchase date.

All share-based compensation costs are recorded in general and administrative or research and development costs in the statements of operations based upon the underlying employees' roles within the Company.

Cash Equivalents

Cash equivalents consist of short-term, highly liquid investments with an original term of three months or less at the date of purchase.

Short-Term Investments

Short-term investments are investments with original maturities of between 90 and 365 days when purchased and are comprised of certificates of deposit, commercial paper, corporate and government bonds and treasury bills. The Company classifies its short-term investments as available-for-sale securities. Short-term investments are recorded at fair value and unrealized gains and losses are recorded within accumulated other comprehensive loss until realized. In addition, the Company evaluates the short-investments with unrealized losses to determine whether such losses are other-than-temporary.

Restricted Cash

The Company is required to maintain a stand-by letter of credit as a security deposit for its facility lease in Alpharetta, Georgia. The Company's bank requires the Company to maintain a restricted cash balance to serve as collateral for the letter of credit issued to the landlord by the bank. As of December 31, 2017, the restricted cash balance was invested in a commercial money market account.

Concentration of Credit Risk Arising From Cash Deposits in Excess of Insured Limits

The Company maintains its cash in bank deposits that at times may exceed federally insured limits. The Company has not experienced any loss in such accounts. The Company believes it is not exposed to any significant risks with respect to its cash balances.

Recent Accounting Pronouncements

Accounting Pronouncements Recently Adopted

In August 2016, Financial Accounting Standards Board ("FASB") issued ASU 2016-15, *Statement of Cash Flows Classification of Certain Cash Receipts and Cash Payments*. The update addresses eight specific cash flow matters with the objective of reducing diversity in practice in how certain cash receipts and payments are classified in the statement of cash flows. The update is effective for annual periods beginning after December 15, 2017, and interim periods within the period. Early adoption is permitted. The Company adopted the standard effective January 1, 2018, and the adoption did not have a material impact on its financial statements and related disclosures.

In November 2016, the FASB issued ASU 2016-18, *Restricted Cash*, which addresses diversity in practice in the classification and presentation of a change in restricted cash on the statement of cash flows. The amendments in this update require that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. The Company adopted the standard effective January 1, 2018, and the adoption did not have a material impact on its financial statements and related disclosures.

Recent Accounting Pronouncements Not Yet Adopted

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers*. Under ASU 2014-09, companies will be required to recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration (that is, payment) to which the company expects to be entitled in exchange for those goods or services. The new standard also will result in enhanced disclosures about revenue, provide guidance for transactions that were not previously addressed comprehensively (for example, service revenue and contract modifications) and modify guidance for multiple-element arrangements. In August 2015, the FASB issued ASU 2015-14, which deferred by one year the effective date of ASU 2014-09.

The Company plans to adopt the standard using the modified retrospective transition method. After evaluating its current and prior license agreements, as well as its other collaboration agreements, the Company does not expect that the adoption of ASU 2014-09 will not have a material impact on its financial statements and related disclosures.

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

3. Property and Equipment, Net

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

	Estimated Useful Lives (Years)	December31, 2017	December31, 2016
Furniture and fixtures	5	$ 303	$ 69
Machinery and equipment	5	121	121
Computer equipment	3	41	27
Leasehold improvements	Lesser of useful life or remaining lease term	667	45
Total property and equipment		1,132	262
Less: Accumulated depreciation		(247)	(168)
Property and equipment, net		$ 885	$ 94

4. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31, 2017	December 31, 2016
Accrued research and development	$ 3,360	$ 1,153
Accrued bonuses	920	870
Accrued professional fees	62	410
Accrued vacation	113	72
Accrued interest payable	58	52
Accrued expense	203	234
	$ 4,716	$ 2,791

5. Long-Term Debt

Loan and Security Agreements

In April 2015, the Company entered into a loan agreement (the “original loan agreement”) with Silicon Valley Bank (“SVB”) for borrowings up to $6.0 million, with a floating interest rate equal to the Wall Street Journal’s prime rate minus 0.50%. Under the terms of the original loan agreement, an initial tranche of $4.0 million was advanced on April 15, 2015 and an additional tranche of $2.0 million was advanced on May 15, 2015. The Company was required to pay accrued interest only for a period of 12 months from the date of each advance, followed by 30 equal monthly payments of principal and accrued interest. A final payment of $0.3 million, or 5.50% of the aggregate borrowed amount, was due at maturity of the loan in 2018 and was being accreted in long-term debt over the life of the loan. Closing costs of $24,000 were recorded against the long-term debt liability and were also being accreted over the life of the loan.

In September 2016, the Company entered into an amended and restated loan and security agreement, which was subsequently amended on October 31, 2017 (as amended, the “loan agreement”) with SVB, MidCap Funding XII Trust and MidCap Financial Trust (together, “MidCap” and collectively with SVB, the “Lenders”), which amended and restated in its entirety the Company’s original loan agreement. The loan agreement provides for new term loans of up to $15.0 million, with a floating interest rate equal to 7% plus the greater of (i) the 30-day U.S. LIBOR, reported in the Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue, or (ii) 0.50%.

Under the terms of the loan agreement, an initial tranche of $8.0 million was advanced on September 28, 2016. The Company may draw the remaining $7.0 million through March 31, 2018. The Company was required to pay accrued interest only through December 31, 2017 on the outstanding amount, followed by 30 equal payments of principal and accrued interest. The Company has the option to prepay the outstanding balance of the term loans in full, subject to a prepayment fee of 2% of the original principal amount of the aggregate term loans for any prepayment through May 31, 2020. A final payment of $0.5 million, or 6.50% of the aggregate borrowed amount, is due at maturity of the loan on June 1, 2020, or upon the prepayment of the facility or the acceleration

of amounts due under the facility as a result of an event of default, and is being accreted in long-term debt over the life of the loan. Of the initial $8.0 million advanced on September 28, 2016, $5.3 million was used to repay all amounts outstanding under the original loan agreement. Closing costs incurred in the refinancing portion of the loan were recorded as expense while the financing costs for the new portion of the loan are recorded in long-term debt and being accreted over the life of the loan. Upon repayment of the original loan agreement, all remaining closing costs associated with the original loan agreement are being accreted to long-term debt over the life of the new loan.

The term loans under the loan agreement are secured by substantially all of the Company's assets, except that the collateral does not include any of the Company's intellectual property. However, pursuant to the terms of a negative pledge arrangement, the Company has agreed not to encumber any of its intellectual property.

Interest expense on the borrowings under the original loan agreement and the loan agreement was $653,000, $287,000 and $115,000 for the years ended December 31, 2017, 2016 and 2015, respectively. Accretion of the scheduled final payment under the original loan agreement and the loan agreement was $211,000, $283,000 and $101,000 for the years ended December 31, 2017, 2016 and 2015, respectively. Accretion of the deferred closing costs under the original loan agreement and the loan agreement was $62,000, $17,000 and $7,400 for the years ended December 31, 2017, 2016 and 2015, respectively.

As of December 31, 2017, the scheduled payments for the loan agreement, including the scheduled final payment in 2020, were as follows (in thousands):

Year Ending December 31,	Principal	Interest and Final Payment	Total
2018	$ 3,200	$ 476	$ 3,676
2019	3,200	234	3,434
2020	1,600	545	2,145
	$ 8,000	$ 1,255	$ 9,255

6. Convertible Shareholder Notes Payable

In April 2014, the Company authorized the sale of convertible promissory notes (the "Bridge Notes") to its existing stockholders, including two of its executive officers and one of its directors in their individual capacities, in the aggregate principal amount of $6.0 million. In April 2014, the Company issued $3.0 million in aggregate principal amount of Bridge Notes. The outstanding notes accrued interest at a rate of 7%, with principal plus interest due upon maturity in April 2015, unless earlier converted. The Bridge Notes were convertible upon the occurrence of a qualified financing which occurred in August 2014, and accordingly the principal and interest under all of the Bridge Notes was converted automatically into an aggregate of 1,137,652 shares of Series B convertible preferred stock in connection with the financing. In connection with the issuance of the Bridge Notes, the Company also issued warrants to the lenders to purchase an aggregate of 112,802 shares of common stock at an exercise price of $0.02 per share. These warrants, which would have otherwise expired upon the closing of the IPO, were automatically net exercised for an aggregate of 112,441 shares of common stock upon the closing of the IPO.

7. Convertible Preferred Stock

As of December 31, 2015, the Company had authorized an aggregate of 20,913,331 shares of Series A, A-1, B and C convertible preferred stock, par value $0.001 per share. Upon the closing of the Company's IPO, all 20,839,633 shares of the Company's convertible preferred stock that were issued and outstanding on that date were automatically converted into an aggregate of 9,614,159 shares of its common stock.

The following table summarizes the activity of convertible preferred stock (in thousands, except per share amounts):

	Series A Preferred Stock		Series A-1 Preferred Stock		Series B Preferred Stock		Series C Preferred Stock		Total Convertible Preferred Stock
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	
Balance at January 1, 2016	5,198,826	$ 4,086	4,356,931	$ 7,900	6,009,202	$ 15,372	5,274,674	$ 19,956	$ 47,314
Accretion of redeemable convertible preferred stock to redemption value	—	—	—	—	—	840	—	44	884
Conversion of preferred stock to common stock at closing of IPO	(5,198,826)	(4,086)	(4,356,931)	(7,900)	(6,009,202)	(16,212)	(5,274,674)	(20,000)	(48,198)
Balance at December 31, 2016	—	$ —	—	$ —	—	$ —	—	$ —	$ —

As of December 31, 2017 and 2016, there were 10,000,000 shares of preferred stock authorized, none of which were issued and outstanding.

8. Common Stock

The Company's amended and restated certificate of incorporation authorizes the Company to issue 100,000,000 shares of $0.001 par value common stock. As of December 31, 2017 and 2016, there were 25,354,651 and 24,573,033 shares of common stock outstanding, respectively.

9. Stock Purchase Warrants

Preferred Stock Warrants

During 2013, in connection with a loan agreement, the Company issued a warrant to the lender to purchase up to 16,550 shares of Series A-1 preferred stock at a price per share of $1.8132. The term of the warrant extended until 10 years from the grant date and the warrant was exercisable at any time during that 10-year period. This warrant was outstanding at December 31, 2015 and had a weighted average remaining life of 6.8 years and a fair value of $58,000. The warrant was automatically converted to a common stock warrant and was net exercised on June 6, 2016, in connection with the IPO, resulting in the issuance of 3,236 shares of common stock.

In April 2015, in connection with the original loan agreement, the Company issued a warrant to the lenders to purchase up to 57,143 shares of Series B preferred stock at a price per share of $3.50. The term of the warrant extends until 10 years from the grant date and the warrant is exercisable at any time during that 10-year period. The warrant was automatically converted into a warrant to purchase 25,974 shares of common stock at an exercise price of $7.70 upon the closing of the IPO. This warrant was outstanding at December 31, 2015 and had a weighted average remaining life of 9.25 years and a fair value of $0.2 million. This warrant was net exercised on October 12, 2016, resulting in the issuance of 17,883 shares of common stock.

Common Stock Warrants

During 2014, in connection with the sale of convertible promissory notes in connection with a preferred stock financing, the Company issued warrants to the lenders to purchase up to an aggregate of 112,802 shares of common stock at a price per share of $0.02. These warrants were outstanding at December 31, 2015 and had a remaining life of 8.2 years. These warrants, which would have otherwise expired upon the closing of the IPO, were automatically net exercised for an aggregate of 112,441 shares of common stock upon the closing of the IPO.

In September 2016, in connection with the loan agreement, the Company issued warrants to the Lenders to purchase up to 29,796 shares of common stock at a price per share of $10.74. The warrants expire in September 2026, or earlier upon the occurrence of specified mergers or acquisitions of the Company, and are immediately exercisable. The warrants were recorded in equity and had a remaining life of 8.75 years as of December 31, 2017.

10. Share-Based Compensation

Stock Options

In January 2016, the Company's board of directors adopted and approved the Clearside Biomedical, Inc. 2016 Equity Incentive Plan (the "2016 Plan") which became effective on June 1, 2016. The 2016 Plan provides for the grant of share-based awards to employees, directors and consultants of the Company. The Company reserved 1,818,182 shares of common stock for issuance under the 2016 Plan. The 2016 Plan provides for the grant of incentive stock options to employees, and for the grant of nonqualified stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of stock compensation to the Company's employees, directors, and non-employee third parties. The number of shares of common stock reserved for issuance under the 2016 Plan will automatically increase on January 1 each year, for a period of ten years, from January 1, 2017 through January 1, 2026, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Company's board of directors. At December 31, 2017, under the 2016 Plan, options to purchase 2,044,400 shares of the Company's common stock were outstanding at a weighted average price of $7.98 per share and 751,078 shares remained available for future grant. As of January 1, 2018, the number of shares of common stock that may be issued under the 2016 Plan was automatically increased by 1,014,186 shares, representing 4% of the total number of shares of common stock outstanding on December 31, 2017, increasing the number of shares of common stock available for issuance under the 2016 Plan as of that date to 1,765,264 shares.

As a result of the adoption of the 2016 Plan, no further grants may be made under the Company's 2011 Stock Incentive Plan (the "2011 Plan"). The 2011 Plan provided for the grant of share-based awards to employees, directors and consultants of the Company. At December 31, 2017, options to purchase 1,013,713 shares of the Company's common stock were outstanding under the 2011 Plan at a weighted average exercise price of $2.47 per share.

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

	Year Ended December 31,		
	2017	2016	2015
Research and development	$ 1,348	$ 539	$ 327
General and administrative	1,988	775	378
Total	$ 3,336	$ 1,314	$ 705

Share-based compensation is accounted for in accordance with the provisions of ASC 718, *Compensation-Stock Compensation*. The estimated fair value of options granted is determined as of the date of grant using the Black-Scholes option pricing model. The resulting fair value is recognized ratably over the requisite service period, which is generally the vesting period of the awards.

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, 2017, 2016 and 2015.

	Year Ended December 31,		
	2017	2016	2015
Expected term (years)	7.00	7.00	7.00
Expected stock price volatility	96.85%	97.45%	86.63%
Risk-free interest rate	2.20%	2.20%	2.09%
Expected dividend yield	0.00%	0.00%	0.00%

Expected term (in years): The Company utilized the guidance set forth in ASC 718 to determine the expected term of options. The Company utilized the simplified method as prescribed by ASC 718, as the Company does not have sufficient historical exercise and post-vesting termination data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees.

Risk-free interest rate: The risk-free interest rate is based on the yields of U.S. Treasury securities with maturities similar to the expected time to a possible liquidity event.

Expected dividend yield: The Company has not paid and does not anticipate paying any dividends in the foreseeable future.

Expected stock price volatility: The volatility assumption is based on the historical volatilities of the stock of several public entities that are similar to the Company, as the Company does not have sufficient historical transactions in its own shares on which to base expected volatility. A similar peer group of companies was utilized for 2017 and 2016.

Forfeitures: As of January 1, 2017, upon adopting ASU 2016-09, the Company began recording forfeitures as they occurred. In prior years, the Company had estimated its forfeiture rate to be zero for the periods presented and any expense true-ups for terminated employees have been immaterial.

The following table summarizes the activity related to stock options during the year ended December 31, 2017:

	Number of Shares	Weighted Average Exercise Price
Options outstanding at January 1, 2017	2,243,575	$ 5.78
Granted	1,127,950	6.45
Exercised	(171,926)	1.37
Cancelled/Forfeited	(124,250)	8.40
Options outstanding at December 31, 2017	3,075,349	6.17
Options exercisable at December 31, 2016	789,120	1.55
Options exercisable at December 31, 2017	1,114,286	3.94

The following table provides additional information about the Company's stock options that were outstanding and exercisable at December 31, 2017 (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	Weighted Average Remaining Contractual Life (Years)
$0.02 - $0.40	465,265			5.4	465,265			5.4
$3.08 - $5.89	1,385,871			8.9	356,632			7.2
$6.16 - $8.90	1,105,921			8.9	264,161			8.2
$9.11 - $20.84	118,292			9.0	28,228			8.9
	3,075,349	$ 6.17	$ 5,598	8.4	1,114,286	$ 3.94	$ 4,180	6.7

As of December 31, 2017, the Company had $11.6 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 3.1 years. The weighted-average fair values of all stock options granted for the years ended December 31, 2017, 2016 and 2015 was $5.25 per share, $7.89 per share and $5.72 per share, respectively. The intrinsic value is calculated as the difference between the fair market value and the exercise price per share of the stock options. The fair market value per share of common stock as of December 29, 2017 was $7.00, which was the closing sale price of the Company's common stock on the Nasdaq Global Market on that date.

Employee Stock Purchase Plan

In January 2016, the Company's board of directors adopted and approved the Clearside Biomedical, Inc. 2016 Employee Stock Purchase Plan (the "2016 ESPP") which became effective on June 1, 2016. The 2016 ESPP permits employees to purchase shares of the Company's common stock through payroll deductions up to 15% of their earnings. The Company reserved 181,818 shares of common stock for issuance under the 2016 ESPP. Additionally, the number of shares reserved for issuance under the 2016 ESPP will automatically increase for a period of ten years, from January 1, 2017 through January 1, 2026, by the lesser of (i) 1% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, (ii) 454,545 shares of common stock or (iii) a lesser number of shares as may be determined by the Company's board of directors. As of January 1, 2018, the number of shares of common stock that may be issued under the 2016 ESPP was automatically increased by 253,546 shares, representing 1% of the total number of shares of common stock outstanding on December 31, 2017, increasing the number of shares of common stock available for issuance under the 2016 ESPP as of that date to 671,402 shares.

The first offering period for the 2016 ESPP commenced on January 1, 2017. The 2016 ESPP is considered a compensatory plan and the fair value of the discount and the look-back period are estimated using the Black-Scholes option pricing model and expense is recognized over the six month withholding period prior to the purchase date. During the year ended December 31, 2017, the Company issued 9,692 shares of common stock purchased under the 2016 ESPP, and $21,000 and $7,000 of share-based compensation expense was recorded in general and administration expense and research and development expense, respectively.

11. 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,		
	2017	2016	2015
Deferred tax asset (liability)			
Net operating loss carryforwards	$ 27,999	$ 23,391	$ 14,119
Non-deductible accrued expenses	248	358	230
Deferred rent	49	1	4
Deferred revenue	38	69	77
Stock compensation expense	387	101	88
Depreciation differences	(18)	(13)	(28)
Federal tax credits	3,437	1,232	850
State tax credits	524	301	262
Charitable contributions	6	6	3
Valuation allowance	(32,670)	(25,446)	(15,605)
Net deferred tax asset	$ —	$ —	$ —

A reconciliation of the statutory tax rates and the effective tax rates is as follows:

	Year Ended December 31,		
	2017	2016	2015
U.S. federal tax rate	34.00%	34.00%	34.00%
State tax rate	2.42	3.79	4.54
Permanent difference and other	(2.84)	(1.98)	(1.26)
Tax credit	3.97	1.62	2.66
Valuation allowance	(12.42)	(37.43)	(39.94)
Impact of federal rate change	(25.13)	—	—
	0.00%	0.00%	0.00%

In December 2017, the 2017 Tax Cuts and Jobs Act (the "2017 Tax Act") was signed into law. The 2017 Tax Act significantly revises the U.S. corporate income tax by, among other things, lowering the statutory corporate tax rate from 34% to 21%, eliminating certain deductions, imposing a mandatory one-time tax on accumulated earnings of foreign subsidiaries, introducing new tax regimes, and changing how foreign earnings are subject to U.S. tax. The 2017 Tax Act also enhanced and extended through 2026 the option to claim accelerated depreciation deductions on qualified property. The Company has not completed its determination of the accounting implications of the 2017 Tax Act on its tax accruals. However, the Company has reasonably estimated the effects of the 2017 Tax Act and recorded provisional amounts in its financial statements as of December 31, 2017. The Company recorded a provisional tax expense of the impact of the 2017 Tax Act of approximately $14.9 million. This amount is primarily comprised of the re-measurement of federal deferred tax liabilities resulting from the permanent reduction in the U.S. statutory corporate tax rate to 21% from 34%. As the Company completes its analysis of the 2017 Tax Act, collects and prepares necessary data, and interprets any additional guidance issued by the U.S. Treasury Department, the IRS, and other standard-setting bodies, the Company may make adjustments to the provisional amounts. Those adjustments may materially impact the Company's provision for income taxes in the period in which the adjustments are made. Based on the Company's history of net operating losses, any benefit that is being or will be derived from the 2017 Tax Act will be offset by a full valuation allowance, as discussed further below.

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 difference in the expected provision, as determined by applying the federal statutory income tax rate to income (loss) is primarily due to the increase in the deferred income tax valuation allowance of $7.2 million, $9.8 million and $7.0 million for the years ended December 31, 2017, 2016 and 2015, respectively, and in 2017, the impact of the federal rate change because of the 2017 Tax Act.

As of December 31, 2017, the Company had net deferred tax assets primarily related to net operating loss carryforwards of $28.0 million, which expire through 2037. 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.

12. Commitments and Contingencies

Lease Commitment Summary

The Company had previously leased office space under non-cancelable operating leases which expired in March 2017.

In November 2016, the Company signed a new office lease agreement to lease approximately 20,000 square feet of office space in Alpharetta, Georgia for its corporate headquarters. The lease agreement is for a six and one-half year term with a renewal option for one additional five-year term. Rental payments are $35,145 per month subject to an increase of 3% per year. Rent expense under this lease is recognized on a straight-line basis over the term of the lease. In addition, the lease agreement requires payment of the pro-rata share of the annual operating expenses associated with the premises. The Company relocated to this new space in March 2017.

Minimum lease payments were as follows at December 31, 2017 (in thousands):

Year ending December 31,		
2018	$	431
2019		444
2020		458
2021		472
2022		487
Thereafter		373
Total minimum lease payments	$	2,665

Rent expense was $214,000, $81,000 and $150,000 for the years ended December 31, 2017, 2016 and 2015, respectively.

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.

13. License and Collaboration Agreements

In August 2014, the Company entered into a royalty-bearing license agreement with NovaMedica LLC ("NovaMedica"). Under this agreement, the Company granted to NovaMedica the right to use the Company's intellectual property to develop and commercialize the intended products (the "Covered Products") and to have the exclusive right to sell those products in Russia and specified adjacent territories involving the use of the corticosteroid triamcinolone acetonide as the sole active pharmaceutical ingredient for administration in the SCS. In connection with this royalty-bearing license, NovaMedica made an upfront payment to the Company of $200,000. The Company is currently developing product candidates that when completed would be subject to this license giving NovaMedica the exclusive right to then sell the products in the specified geographic territories. In mid-December 2015, the Company received positive results from the Phase 2 clinical trial relating to the product candidate and determined, based on these results, that the intellectual property could become commercially feasible. Beginning in the first quarter ended March 31, 2016, the Company began recognizing the $200,000 to revenue over the period of time to complete clinical development and commercialization of the Covered Products and the beginning of the first set of patent expirations in 2027. The Company recorded $20,000 of license revenue during each of the years ended December 31, 2017 and 2016 for this license agreement. NovaMedica is jointly owned by Rusnano MedInvest LLC ("Rusnano MedInvest") and Domain Russia Investments Limited. RMI Investments, which beneficially owned approximately 6% of the Company's voting securities as of December 31, 2017, is a wholly owned subsidiary of Rusnano MedInvest.

In April 2015, the Company entered into a license and collaboration agreement (the "Spark Agreement") with Spark Therapeutics, Inc. ("Spark") under which Spark could acquire the exclusive rights to license the Company's microinjector technology and access to the SCS within the eye for development and ultimate commercialization of Spark's gene therapy treatments to be delivered via the microinjector. In conjunction with executing the Spark Agreement, Spark made an upfront, non-refundable payment to the Company of $500,000.

In February 2016, the initial study was completed and Spark elected not to extend the arrangement nor license the technology which terminated the Spark Agreement in accordance with the agreement terms. During the quarter ended March 31, 2016, the Company recorded as revenue the $500,000 upfront payment as the amount was non-refundable and the Company had no further obligations under the Spark Agreement.

The Company has periodically entered into other short-term collaboration agreements to evaluate the potential use of its proprietary SCS microinjector with third-party product candidates for the treatment of various diseases. Funds received from these collaboration agreements are recognized as revenue over the term of the agreement. The Company recorded $325,000 of revenue from these collaboration agreements during the year ended December 31, 2017.

14. Available-for-Sale Investments

The following table summarizes the Company's available-for-sale investments as of December 31, 2017 (in thousands):

	December 31, 2017		
	Amortized Cost	Unrealized Loss	Fair Value
Government bonds and agency obligations	$ 11,241	$ (3)	$ 11,238
Commercial paper	10,154	—	10,154
Corporate bonds	5,069	(5)	5,064
Certificates of deposit	1,960	—	1,960
Total available-for-sale investments	$ 28,424	$ (8)	$ 28,416

15. Fair Value Measurements

The Company records certain financial assets and liabilities at fair value in accordance with the provisions of ASC Topic 820, *Fair Value Measurements and Disclosures*. 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, 2017 and 2016 consisted primarily of cash and cash equivalents, short-term investments and long-term debt and stock purchase warrant liabilities. The fair value of cash and cash equivalents, government bonds, other current assets and accounts payable approximate their respective carrying values due to the short term nature of these instruments and are classified as Level 1 in the fair hierarchy. The fair value of long-term debt approximates the carrying value due to variable interest rates that correspond to market rates. The Company has determined its short-term investments, comprised of certificates of deposit, corporate bonds, commercial paper, treasury bills and agency obligations, to be Level 2 in the fair value hierarchy. The fair value was determined using a market approach, based on prices and other relevant information generated by market transactions involving similar assets. The short-term investments consist of investments with original maturity dates from date of acquisition of 90 to 365 days and are classified as available-for-sale. The Company has determined its stock purchase warrants liability to be Level 3 in the fair value hierarchy.

There were no significant transfers between Levels 1, 2 and 3 during the years ended December 31, 2017 and 2016.

The following tables summarize the fair value of financial assets and liabilities that are measured at fair value and the classification by level of input within the fair value hierarchy (in thousands):

	December 31, 2017			
	Level 1	Level 2	Level 3	Recorded Value
Financial Assets:				
Cash and money markets	$ 9,224	$ —	$ —	$ 9,224
Restricted cash money market	360	—	—	360
Government bonds and treasury bills	11,238	—	—	11,238
Certificates of deposit	—	1,960	—	1,960
Corporate bonds	—	5,064	—	5,064
Commercial paper	—	10,154	—	10,154
Total financial assets	$ 20,822	$ 17,178	$ —	$ 38,000

	December 31, 2016			
	Level 1	Level 2	Level 3	Recorded Value
Financial Assets:				
Cash and money markets	$ 29,928	$ —	$ —	$ 29,928
Restricted cash money market	360	—	—	360
Government bonds	19,027	—	—	19,027
Certificates of deposit	—	6,579	—	6,579
Agency obligations	—	4,179	—	4,179
Corporate bonds	—	7,262	—	7,262
Commercial paper	—	16,656	—	16,656
Total financial assets	$ 49,315	$ 34,676	$ —	$ 83,991

Prior to the IPO, the Company estimated the fair value of its warrants to purchase preferred stock using an option pricing model that included three valuation scenarios, a non-IPO scenario and two IPO scenarios. Under the IPO scenarios, the Company calculated the value of the warrant based on a call option of the common share at IPO (assuming the underlying preferred stock would convert to common stock) given the time to exit and the term of the warrants stipulated in the contract. The Company then applied a discount for lack of marketability. Subsequent to the IPO, the Company used the Black-Scholes option pricing model to estimate the fair value of the remaining warrants. The estimates in the Black-Scholes option pricing model are based, in part, on assumptions related to the volatility of comparable public companies, the expected life of the warrants, the risk-free interest rate and the fair value of the underlying warrants. Changes in the fair value of the stock purchase warrants were recorded in other expense, net in the statements of operations. The following table summarizes the changes in fair value of the Level 3 liability, stock purchase warrants (in thousands):

	Level 3 Liabilities
	Year Ended December 31, 2016
Stock purchase warrants	
Balance at beginning of period	$ 258
Issuance of stock purchase warrants	—
Exercise of stock purchase warrants	(414)
Net increase in fair value remeasurement	156
Balance at end of period	$ —

16. Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period, without consideration of the dilutive effect of potential common stock equivalents. Diluted net loss per share gives effect to all dilutive potential shares of common stock outstanding during this period.

For all periods presented, the Company’s potential common stock equivalents, which included 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,		
	2017	2016	2015
Convertible preferred stock	—	—	9,472,530
Outstanding stock options	3,075,349	2,243,575	1,261,637
Unvested restricted stock	—	—	6,485
Stock purchase warrants	29,796	29,796	146,298
	3,105,145	2,273,371	10,886,950

17. Quarterly Financial Information (unaudited)

Summarized quarterly financial information for each of the years ended December 31, 2017 and 2016 are as follows (in thousands except per share data):

	Quarter Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Operating expenses	$ (10,261)	$ (13,768)	$ (18,348)	$ (16,376)
Net loss	$ (10,373)	$ (13,773)	$ (18,336)	$ (16,493)
Net loss per share of common stock — basic and diluted	$ (0.41)	$ (0.54)	$ (0.72)	$ (0.65)

	Quarter Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
Operating expenses	$ (5,862)	$ (5,183)	$ (5,311)	$ (9,362)
Net loss	$ (5,449)	$ (5,102)	$ (5,645)	$ (9,686)
Net loss per share of common stock — basic and diluted	$ (2.05)	$ (0.62)	$ (0.28)	$ (0.45)

18. Subsequent Events

On March 12, 2018, the Company closed a follow-on public offering in which it sold 6,538,462 shares of common stock at a public offering price of $13.00 per share, resulting in net proceeds of $79.6 million after deducting underwriting discounts and commissions and estimated offering expenses. The Company has granted the underwriters of the offering an option, exercisable through April 6, 2018, to purchase up to an additional 980,769 shares of common stock at the public offering price.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), refers to controls and procedures that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that such information is accumulated and communicated to a company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

In designing and evaluating our disclosure controls and procedures, management recognizes that disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the disclosure controls and procedures are met. Additionally, in designing disclosure controls and procedures, our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a control system, misstatements due to error or fraud may occur and not be detected.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this report at the reasonable assurance level.

Changes in Internal Controls over Financial Reporting

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting and Attestation Report of the Registered Public Accounting Firm

Our management is responsible for establishing and maintaining an adequate system of internal control over financial reporting, as defined in the Exchange Act Rule 13a-15(f). Management conducted an assessment of our internal control over financial reporting based on the framework established in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework. Based on the assessment, management concluded that, as of December 31, 2017, our internal control over financial reporting was effective.

This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting as required by Section 404(c) of the Sarbanes Oxley Act of 2002. Because we qualify as an emerging growth company under the JOBS Act, management's report was not subject to attestation by our independent registered public accounting firm.

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

We will file a definitive Proxy Statement for our 2018 Annual Meeting of Stockholders (the “2018 Proxy Statement”) with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the 2018 Proxy Statement that specifically address the items set forth herein are incorporated by reference.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by Item 10 is hereby incorporated by reference to the sections of the 2018 Proxy Statement under the captions "Information Regarding the Board of Directors and Corporate Governance," "Election of Directors," "Executive Officers" and "Section 16(a) Beneficial Ownership Reporting Compliance."

ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 is hereby incorporated by reference to the sections of the 2018 Proxy Statement under the captions "Executive Compensation" and "Non-Employee Director Compensation."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by Item 12 is hereby incorporated by reference to the sections of the 2018 Proxy Statement under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under Equity Compensation Plans."

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by Item 13 is hereby incorporated by reference to the sections of the 2018 Proxy Statement under the captions "Transactions with Related Persons" and "Independence of the Board of Directors."

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by Item 14 is hereby incorporated by reference to the sections of the 2018 Proxy Statement under the caption "Ratification of Selection of Independent Auditors."

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

We have filed the following documents as part of this Annual Report:

1. Financial Statements

The financial statements are included in Item 8. “Financial Statements and Supplementary Data.”

2. Financial Statement Schedules

All schedules are omitted as information required is inapplicable or the information is presented in the financial statements and the related notes.

3. Exhibits

Exhibit number	Description of document
3.1	Amended and Restated Certificate of Incorporation (incorporated herein by reference to Exhibit 3.1 to the Registrant’s Current Report on Form 8-K (File No. 001-37783) filed with the SEC on June 7, 2016).
3.2	Amended and Restated Bylaws (incorporated herein by reference to Exhibit 3.2 to the Registrant’s Current Report on Form 8-K (File No. 001-37783) filed with the SEC on June 7, 2016).

4.1		Specimen stock certificate evidencing shares of Common Stock (incorporated herein by reference to Exhibit 4.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916) filed with the SEC on March 18, 2016).
4.2		Third Amended and Restated Investor Rights Agreement, dated as of November 23, 2015, by and among the Registrant and certain of its stockholders (incorporated herein by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on January 8, 2016).
4.3		Form of Warrant to Purchase Common Stock issued to lenders in September 2016 in connection with Amended and Restated Loan and Security Agreement (incorporated herein by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37783), filed with the Commission on October 4, 2016).
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 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on January 8, 2016).
10.2	+	2011 Stock Incentive Plan, as amended to date (incorporated herein by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on January 8, 2016).
10.3	+	Form of Incentive Stock Option Grant Notice and Incentive Stock Option Agreement under 2011 Stock Incentive Plan (incorporated herein by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on January 8, 2016).
10.4	+	Form of Nonqualified Stock Option Grant Notice and Nonqualified Stock Option Agreement under 2011 Stock Incentive Plan (incorporated herein by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on January 8, 2016).
10.5	+	2016 Equity Incentive Plan (incorporated herein by reference to Exhibit 4.7 to the Registrant's Registration Statement on Form S-8 (File No. 333-212014), file with the Commission on June 14, 2016).
10.6	+	Form of Stock Option Grant Notice and Stock Option Agreement under 2016 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on March 18, 2016).
10.7	+	Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under 2016 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on March 18, 2016).
10.8	+	Form of Indemnification Agreement with non-employee directors (incorporated herein by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on January 8, 2016).
10.9	+	Form of 2016 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.12 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on March 18, 2016).
10.10	#	License Agreement, by and between the Registrant and NovaMedica LLC, dated as of August 29, 2014 (incorporated herein by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1 (File No. 333-208916), filed with the Commission on January 8, 2016).
10.11		Amended and Restated Loan and Security Agreement, dated as of September 28, 2016, by and among the Registrant, Silicon Valley Bank, MidCap Funding XIII Trust and MidCap Financial Trust (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37783) filed with the SEC on October 4, 2016).
10.12		Office Lease Agreement, dated November 21, 2016, by and between the Registrant and BRE/COH GA LLC (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37783), filed with the Commission on November 23, 2016).
10.13		Second Amendment to License Agreement, by and among the Registrant, Emory University and The Georgia Tech Research Corporation, dated December 12, 2016 (incorporated herein by reference to Exhibit 10.21 to the Registrant's Annual Report on Form 10-K (File No. 001-37783), filed with the Commission on March 16, 2017).
10.14		Sales Agreement, dated June 30, 2017, by and between the Registrant and Cowen and Company, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37783), filed with the SEC on July 3, 2017).
10.15	+	Amended and Restated Executive Employment Agreement, by and between Clearside Biomedical, Inc. and Daniel H. White, dated as of August 3, 2017 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37783), filed with the Commission on November 9, 2017).
10.16	+	Amended and Restated Executive Employment Agreement, by and between Clearside Biomedical, Inc. and Charles A. Deignan, dated as of August 3, 2017 (incorporated herein by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37783), filed with the Commission on November 9, 2017).

10.17	+	Amended and Restated Executive Employment Agreement, by and between Clearside Biomedical, Inc. and Glenn Noronha, dated as of August 3, 2017 (incorporated herein by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37783), filed with the Commission on November 9, 2017).
10.18	+	Amended and Restated Non-Employee Director Compensation Policy (incorporated herein by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37783), filed with the Commission on November 9, 2017).
10.19		First Amendment to Amended and Restated Loan and Security Agreement, by and among the Company, Silicon Valley Bank, ELM 2016-1 Trust and Midcap Financial Trust, dated as of October 31, 2017 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37783), filed with the Commission on November 2, 2017).
23.1		Consent of Ernst & Young LLP, independent registered public accounting firm.
24.1		Power of Attorney (included on signature page).
31.1		Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2		Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to section 302 of the Sarbanes-Oxley Act of 2002.
32.1	^	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rules 13a-14(b) and 15d-14(b) promulgated under the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to section 906 of The Sarbanes-Oxley Act of 2002.
101.INS		XBRL Instance Document
101.SCH		XBRL Taxonomy Extension Schema Document
101.CAL		XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF		XBRL Taxonomy Extension Definition Linkbase Document
101.LAB		XBRL Taxonomy Extension Label Linkbase Document
101.PRE		XBRL Taxonomy Extension Presentation Linkbase Document

+ Indicates management contract or compensatory plan.

Confidential treatment has been granted with respect to portions of this exhibit (indicated by asterisks) and those portions have been separately filed with the Securities and Exchange Commission.

^ These certifications are being furnished solely to accompany this Annual Report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

ITEM 16. FORM 10-K SUMMARY

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CLEARSIDE BIOMEDICAL, INC.

By: /s/ *Daniel H. White*
Daniel H. White
President and Chief Executive Officer

March 16, 2018

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Daniel H. White and Charles A. Deignan, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of Clearside Biomedical, Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Daniel H. White Daniel H. White	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 16, 2018
/s/ Charles A. Deignan Charles A. Deignan	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 16, 2018
/s/Christy L. Shaffer, Ph.D. Christy L. Shaffer, Ph.D.	Director	March 16, 2018
/s/Clay B. Thorp Clay B. Thorp	Director	March 16, 2018
/s/William D Humphries William D. Humphries	Director	March 16, 2018
/s/Evgeny Zaytsev, M.D. Evgeny Zaytsev, M.D.	Director	March 16, 2018
/s/Gerald D. Cagle, Ph. D. Gerald D. Cagle, Ph.D.	Director	March 16, 2018
/s/George Lasezkay, Pharm.D., J.D. George Lasezkay, Pharm.D., J.D.	Director	March 16, 2018
/s/Richard Croarkin Richard Croarkin	Director	March 16, 2018

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-212014) pertaining to the 2011 Stock Incentive Plan, as amended, Stock Option Awards, 2016 Equity Incentive Plan, and 2016 Employee Stock Purchase Plan of Clearside Biomedical, Inc.,
(2) Registration Statement (Form S-8 No. 333-216750) pertaining to the 2016 Equity Incentive Plan and 2016 Employee Stock Purchase Plan of Clearside Biomedical, Inc., and
(3) Registration Statement (Form S-3 No. 333-219132) of Clearside Biomedical, Inc.

of our report dated March 16, 2018, with respect to the financial statements of Clearside Biomedical, Inc. included in this Annual Report (Form 10-K) of Clearside Biomedical, Inc. for the year ended December 31, 2017.

/s/Ernst & Young LLP

Atlanta, Georgia
March 16, 2018

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Daniel H. White, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2017 of Clearside Biomedical, Inc. (the "registrant");

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

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

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

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

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

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

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

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

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

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

Date: March 16, 2018

/s/ Daniel H. White
Daniel H. White
President and Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Charles A. Deignan, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2017 of Clearside Biomedical, Inc. (the "registrant");

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

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

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

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

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

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

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

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

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

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

Date: March 16, 2018

/s/ Charles A. Deignan
Charles A. Deignan
Chief Financial Officer
(principal financial officer)

Exhibit 32.1

CERTIFICATIONS OF
PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Daniel H. White, President and Chief Executive Officer of Clearside Biomedical, Inc. (the "Company"), and Charles A. Deignan, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the year ended December 31, 2017, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

IN WITNESS WHEREOF, the undersigned have set their hands hereto as of the 16th day of March, 2018.

/s/ Daniel H. White
Daniel H. White
President and Chief Executive Officer
(principal executive officer)

/s/ Charles A. Deignan
Charles A. Deignan
Chief Financial Officer
(principal financial officer)

* This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.