# 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, 2020**

**OR**

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

**For the transition period from _____ to _____**

**Commission File Number: 001-37783**

## Clearside Biomedical, Inc.

**(Exact Name of Registrant as Specified in its Charter)**

| **Delaware**<br>**(State or other jurisdiction of incorporation or organization)** | **45-2437375**<br>**(I.R.S. Employer Identification No.)** |
|---|---|
| **900 North Point Parkway, Suite 200**<br>**Alpharetta, GA**<br>**(Address of principal executive offices)** | **30005**<br>**(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 | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, par value $0.001 per share | CLSD | 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 every Interactive Data File required to be submitted 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 such files). Yes ☒ No ☐

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 | ☒ | Smaller 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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, 2020 (the last business day of the registrant's most recently completed second fiscal quarter) based on the closing sale price of $1.88 as reported on the Nasdaq Global Market on that date was approximately $66,100,000.

As of March 10, 2021, the registrant had 57,422,475 shares of common stock, par value $0.001 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 2021 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 for the development and potential commercialization of our product candidates;
- our ongoing and planned preclinical studies and clinical trials for our product candidates;
- the timing of the availability of data from our clinical trials;
- the timing of our planned regulatory filings, including the resubmission of our new drug application for XIPERE™;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- our expectation that XIPERE, if approved, would be the first drug specifically indicated for the treatment of macular edema associated with uveitis;
- the clinical utility of our product candidates;
- our manufacturing capabilities and strategy;
- our intellectual property position;
- our plans to enter into and maintain collaborations with other companies;
- our ability to identify additional product candidates with significant commercial potential that are compatible with suprachoroidal injection and which are consistent with our commercial objectives; and
- our estimates regarding our cash resources, our future 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.

We have proprietary rights to a number of trademarks used in this Annual Report which are important to our business, including Clearside, XIPERE, SCS Microinjector 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.

**Risk Factors Summary**

The risk factors summarized below could materially harm our business, operating results, and/or financial condition, impair our future prospects, and/or cause the price of our common stock to decline. These risks are discussed more fully in the section titled "Risk Factors". Material risks that may affect our business, financial condition, results of operations, and trading price of our common stock include the following:

- 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 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.
- Our efforts are focused on the development of product candidates for treatment of eye disease through suprachoroidal injection and partnering with companies who can leverage our SCS Microinjector to deliver their ophthalmic product candidates to the suprachoroidal space. Suprachoroidal injection is a novel approach and may fail to achieve and sustain market acceptance.
- 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, either on our own or with a third party, or if we experience significant delays in doing so, our business may be harmed.
- 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 of our product candidates.
- We have granted an exclusive license to Bausch for the commercialization and development of XIPERE in the United States and Canada. If we are delayed in receiving FDA approval for XIPERE, or we are unable to maintain our partnership with Bausch, or if Bausch fails to successfully commercialize XIPERE, our business and prospects will be materially harmed.
- We have entered into, and intend to continue intend to enter into, collaborations with third parties for the development and commercialization of product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.
- 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.

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**PART I**

## ITEM 1. BUSINESS

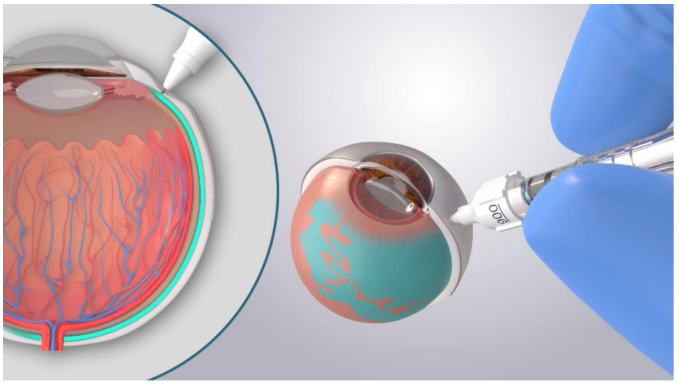
### Overview

We are a biopharmaceutical company dedicated to developing and delivering treatments that restore and preserve vision for people with serious back of the eye diseases. Our proprietary SCS Microinjector targeting the suprachoroidal space, or SCS, offers unique access to the macula, retina and choroid where sight-threatening disease often occurs. Our SCS injection platform is an inherently flexible, in-office, non-surgical procedure intended to provide targeted delivery to the site of disease and to work with both established and new formulations of medications, as well as future therapeutic innovations.

We are leveraging our SCS injection platform by building an internal research and development pipeline targeting retinal diseases and by creating external collaborations with other companies. Using our suprachoroidal injection technology in conjunction with proprietary formulations of existing drugs as well as novel therapies, we believe that we have created a broad therapeutic platform for developing product candidates to treat serious eye diseases.

***Our Suprachoroidal Injection Technology Platform***

Our suprachoroidal injection platform is a novel, patented approach for delivering pharmacotherapy to the back of the eye via the SCS. When fluid is injected between the choroid and sclera, the elasticity of the SCS allows the fluid to migrate and spread spherically toward the posterior regions of the eye where it is absorbed into adjacent tissue. Our proprietary microinjector is able to precisely administer drugs into the SCS utilizing a needle that is approximately one millimeter in length. This non-surgical method of administration facilitates more targeted delivery of therapeutic agents to chorioretinal structures and can be accomplished in an in-office setting. The suprachoroidal injection procedure is depicted in the picture below.

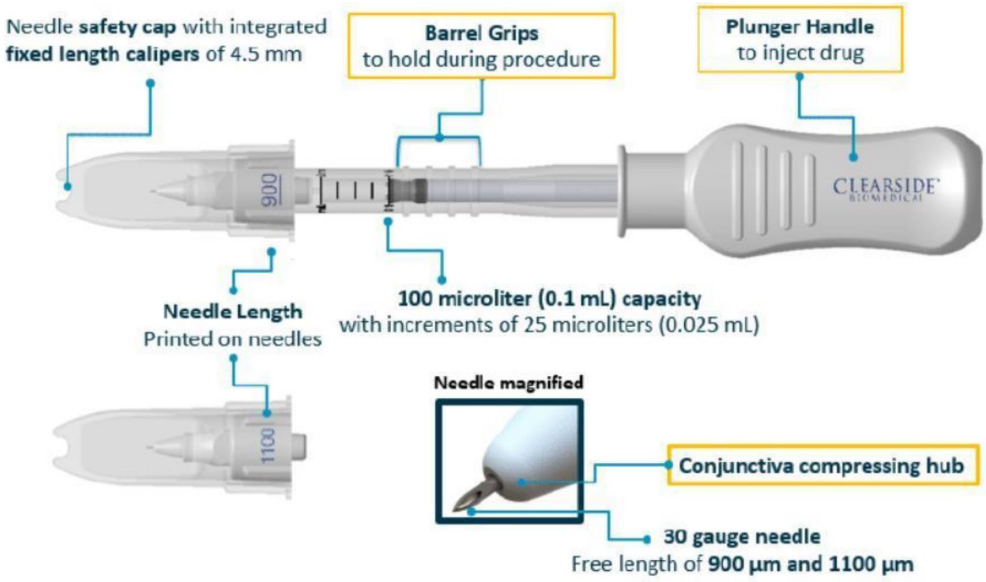


With suprachoroidal injections, product candidates are more directly administered to the retina and choroid, limiting exposure to non-target tissues as compared to other ocular drug administration techniques. Intravitreal injections, the current standard for delivery of many drugs for eye diseases, rely on diffusion of drug outward from the vitreous, a jelly-like substance that occupies the central portion of the eye, to the retina and choroid. This diffusion can result in lower concentrations of drug in these targeted areas and the drug spreading to unintended parts of the eye, potentially causing significant side effects. We believe treatment of eye disease via suprachoroidal injection of our product candidates may provide a number of benefits, including a non-surgical procedure, lower frequency of administration, limited exposure to non-targeted tissues, faster onset of therapeutic effect and an improved safety profile.

Our extensive patent portfolio provides us with exclusive rights to develop and commercialize pharmacological agents for treatment of eye diseases via suprachoroidal injection. We believe this proprietary method of administration has the potential to become the standard for the delivery of therapies intended to treat retinal and choroidal diseases. Our drug candidates, SCS Microinjector and method of drug administration into the SCS are protected by 22 issued U.S. patents and more than 50 European and international patents broadly directed to the use of the device, administration of any drug into the SCS by injection, as well as specific product candidates.

***Our SCS Microinjector***

Our proprietary SCS Microinjector, shown in the picture below, can be used to inject a wide variety of drugs into the SCS. Our internally developed and our collaborators' drug candidates are specifically formulated to be injected via suprachoroidal injection with our SCS Microinjector in order to flow to the back of the eye. The SCS Microinjector is composed of a syringe 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.




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. Intravitreal injections are typically performed using a needle that is approximately five millimeters in length, or five 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 reaches one of the layers between the sclera and the vitreous.

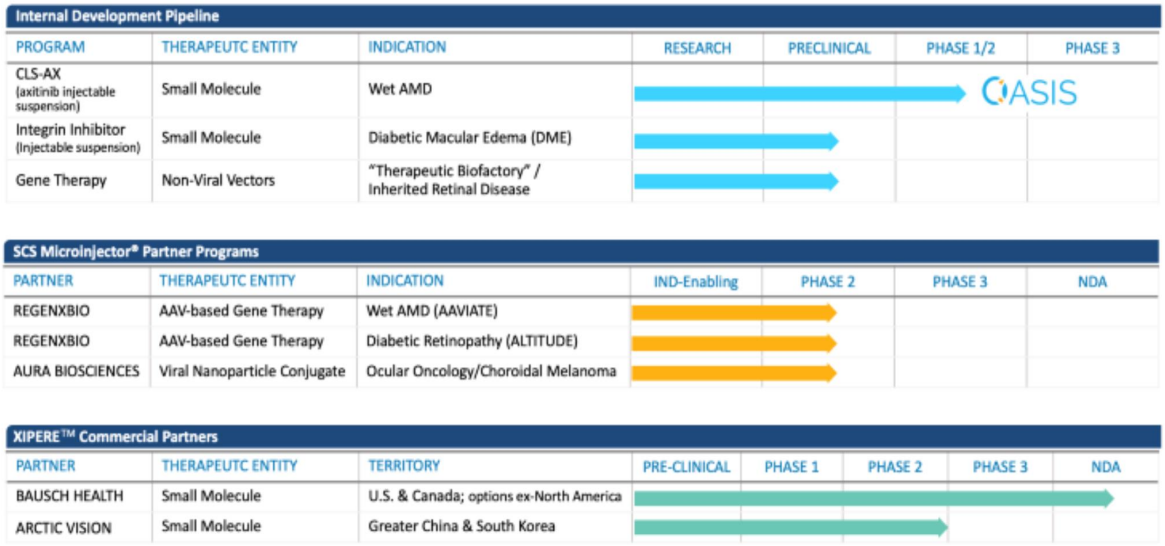
By contrast, our SCS Microinjector is designed to inject drug into the suprachoroidal space. This suprachoroidal injection is designed to be carried out perpendicular to the sclera, at a site similar to an intravitreal injection, under local anesthesia. Once the microneedle penetrates the sclera and 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, precisely targeting the cells of interest. Our SCS Microinjector has been used in over 1,200 suprachoroidal injections as part of our clinical trials.

***Our Pipeline***

We have research capabilities focused on developing proprietary therapeutic formulations to utilize with our SCS Microinjector. Our internal research and development initiatives are focused on small molecules and gene therapy to address unmet

needs in back-of-the-eye diseases. In addition to growing our internal pipeline, we are also focused on collaborating with other companies to provide access to the suprachoroidal space through the use of our SCS Microinjector.

The current development status of our pipeline of internal product candidates and external collaborations is summarized in the chart below:




*Internal Development Pipeline*

We are developing a proprietary suspension of axitinib, a tyrosine kinase inhibitor, or TKI, for suprachoroidal injection, which we refer to as CLS-AX. In our preclinical studies, administration of CLS-AX through suprachoroidal injection was well tolerated and showed durability over several months, providing us with the opportunity to potentially reduce treatment burden and address a primary need for wet age-related macular degeneration, or AMD, patients.

In August 2020, we announced that the U.S. Food and Drug Administration, or FDA, had accepted our Investigational New Drug application, or IND, for CLS-AX.

In January 2021, we announced that the first patients had been enrolled in our Phase 1/2a clinical trial of CLS-AX, known as OASIS. In March 2021, we completed patient dosing in the first cohort of OASIS and we expect to report initial safety data from this cohort in mid-2021.

We have initiated another small molecule program utilizing suprachoroidal administration of an integrin inhibitor suspension. Integrins play a role in pathologic processes, such as inflammation, angiogenesis and fibrosis. Integrin inhibition has had some recent preliminary validation in preclinical models and clinical studies of diabetic macular edema and macular degeneration conducted by others. We believe that integrin inhibition could potentially serve as primary therapy, adjunctive therapy to anti-VEGF agents or secondary therapy in refractory cases of diabetic macular edema and macular degeneration. Suprachoroidal delivery of an integrin inhibitor suspension could provide targeting, compartmentalization and durability advantages over topical or intravitreal delivery, similar to what we have observed in other preclinical studies of small molecule suspensions, such as triamcinolone acetonide and axitinib. Therefore, we are assessing ocular tolerability, distribution and pharmacokinetics of our integrin inhibitor suprachoroidal suspension in a series of preclinical studies. We expect to conclude these studies this year.

Based on our preclinical studies, we believe that gene therapy is a promising approach to treating retinal diseases, particularly those that are inherited, and that our suprachoroidal injection technology can enhance the benefits of this approach. Multiple, peer-reviewed publications have also validated a suprachoroidal gene therapy treatment approach. Our work in this area includes suprachoroidal administration of therapeutic transgenes and non-viral vector gene therapy. Our preclinical proof-of-concept studies utilizing suprachoroidal delivery of marker genes using DNA nanoparticles have shown the potential for suprachoroidal administration to deliver genes. We plan to present this data at a medical conference in the second quarter of 2021.

*External Collaborations Pipeline*

During the second half of 2019, we entered into three license and other agreements that we believe validate and expand the reach of our suprachoroidal injection platform. In October 2019, we announced that Bausch + Lomb, a division of Bausch Health Companies, Inc., or Bausch, acquired an exclusive license for the commercialization and development of XIPERE (triamcinolone acetonide suprachoroidal injectable suspension) in the United States and Canada. In April 2020, we granted Bausch an exclusive option to develop, manufacture, distribute, promote, market and commercialize XIPERE in one or more of the following regions: (i) the European Union, including the United Kingdom, (ii) Australia and New Zealand and (iii) South America and Mexico.

In October 2019, REGENXBIO Inc., or REGENXBIO, exercised its option to license our SCS Microinjector technology for in-office delivery of adeno-associated virus, or AAV,-based therapeutics to the SCS to potentially treat AMD, diabetic retinopathy and other conditions for which chronic anti-VEGF treatment is currently the standard of care. REGENXBIO has initiated their Phase 2 clinical trial, entitled AAVIATE, for the treatment of wet AMD and in January 2021 announced the completion of enrollment in Cohort 1. They also expect to report data from their Phase 2 clinical trial, entitled ALTITUDE, for the treatment of diabetic retinopathy, in 2021.

In July 2019, Aura Biosciences, or Aura, licensed our SCS Microinjector to deliver Aura's proprietary drug candidates into the SCS for the potential treatment of certain ocular cancers, including choroidal melanoma. Aura has initiated a Phase 2 clinical trial for the treatment of choroidal melanoma.

In March 2020, we entered into a license agreement, or the Arctic Vision License Agreement, with Arctic Vision (Hong Kong) Limited, or Arctic Vision. Pursuant to the Arctic Vision License Agreement, we granted an exclusive license to Arctic Vision to develop, distribute, promote, market and commercialize XIPERE, subject to specified exceptions, in China, Hong Kong, Macau, Taiwan and South Korea, or the Arctic Territory. In December 2020, Arctic Vision announced approval of its IND for a Phase 3 clinical trial of XIPERE in China.

By entering into these partnerships, we are able to expand the use of our suprachoroidal injection platform to other indications and geographies globally. Under these license agreements, we received $11.1 million of non-dilutive capital in the form of upfront payments during 2019 and 2020, and we are eligible to receive up to an aggregate of more than $200 million in potential future development and sales milestones, as well as and royalties from net sales of covered products.

**XIPERE (triamcinolone acetonide suprachoroidal injectable suspension)**

Our first candidate, XIPERE, formerly known as CLS-TA, is a proprietary, preservative-free suspension of the corticosteroid triamcinolone acetonide, or TA, formulated for administration via suprachoroidal injection. Corticosteroids are the standard of care in uveitis. They are effective at treating the inflammatory aspect of ocular disease, 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 intraocular pressure, or IOP, which can lead to glaucoma.

XIPERE is being developed for the treatment of macular edema associated with uveitis. Uveitis is a set of ocular inflammatory conditions affecting approximately 350,000 patients in the United States and more than one million worldwide. Approximately one-third of uveitis patients develop uveitic macular edema, a build-up of fluid in the macula, the area of the retina responsible for sharp, straight-ahead vision. Macular edema is the leading cause of vision loss and blindness in uveitis patients and can occur from uveitis affecting any anatomic location—anterior, intermediate, posterior or panuveitis. The uveitis market is expected to grow to nearly $550 million by 2024 in the United States, and over $1 billion globally.

***XIPERE regulatory approval pathway***

In December 2018, we submitted a New Drug Application, or NDA, to the FDA for XIPERE for the treatment of macular edema associated with uveitis. In February 2019, we announced that we had received notification that the FDA had accepted the NDA and assigned a Prescription Drug User Fee Act, or PDUFA, goal date for completion of its review by October 2019.

In October 2019, we received a complete response letter, or CRL, from the FDA regarding our NDA for XIPERE. The FDA did not identify any efficacy issues, and there were no requests for further clinical efficacy studies. As anticipated, the CRL included the FDA's request for additional stability data, additional clarifying information on components of the manufacturing process, and reinspection of the drug product manufacturer. The CRL included one new request for additional data on clinical use of the final to-be-marketed SCS Microinjector delivery system. In response to that request, we proposed the submission of SCS Microinjector clinical use information in 160 subjects from our TOPAZ study, as described below, for the treatment of macular edema associated with retinal vein occlusion, or RVO. In subsequent correspondence, the FDA agreed that it would be acceptable for us to submit such data in lieu of the requested clinical use evaluation.

In August 2020, we secured a new contract manufacturing organization, or CMO, to manufacture the registration batches of XIPERE for the resubmission of our NDA, as well as to manufacture batches of XIPERE for potential commercialization. Our prior CMO notified us that they were no longer willing to serve as our commercial supplier for XIPERE and that they were uncertain about being prepared for an FDA pre-approval inspection on our timeline. We transferred the technology underlying the manufacturing process to the new CMO. We expect to resubmit the XIPERE NDA in the second quarter of 2021. We anticipate that the FDA will review the NDA within six months of the resubmission date.

We are also evaluating options for potential submissions to regulatory agencies in additional territories outside of the United States and Canada for XIPERE for the treatment of patients with macular edema associated with uveitis.

***License agreement for commercialization of XIPERE in United States and Canada***

In October 2019, we entered into an exclusive license agreement with Bausch for the commercialization and development of XIPERE in the United States and Canada, or the License Agreement. Pursuant to the License Agreement, Bausch paid us an upfront payment of $5.0 million, which is subject to a refund if the License Agreement is terminated in specified circumstances. In addition, Bausch has agreed to make additional payments of up to $15.0 million upon the achievement of specified pre-launch development and regulatory milestones and up to an aggregate of $56.0 million in additional milestone payments upon the achievement of regulatory approvals for specified additional indications of XIPERE and certain levels of annual net sales. Further, during the applicable royalty term, we will also be entitled to receive tiered royalties at increasing percentages, from the high-teens to twenty percent, based on XIPERE achieving certain annual net sales thresholds in the United States and Canada, as well as a lower royalty on annual net sales of other products, in each case subject to reductions in specified circumstances, although we will not receive any royalties on the first $30.0 million of cumulative net sales of all products.

We are responsible for all development expenses for XIPERE until our NDA for XIPERE is approved by the FDA, subject to specified exceptions, as well as manufacturing costs in connection with the NDA. We are also responsible for all clinical and development expenses conducted to satisfy the FDA's requests in the CRL and any subsequent CRL related to the NDA, or the CRL-related expenses. If XIPERE is approved by the FDA, Bausch will be responsible for all expenses following such approval, although we will be responsible for one-half of the costs of any post-approval clinical trials required by the FDA, up to a specified maximum amount.

In April 2020, we amended the License Agreement to grant Bausch an exclusive option, or the Option, to develop, manufacture, distribute, promote, market and commercialize XIPERE in one or more of the following regions: (i) the European Union, including the United Kingdom, (ii) Australia and New Zealand and (iii) South America and Mexico, or collectively the Additional Regions, in exchange for Bausch extending the deadline by which we must obtain regulatory approval for XIPERE in the United States. The Option may be exercised as to any or all of the Additional Regions any time before the earlier of regulatory approval of XIPERE in the United States and August 31, 2021. Under the terms of the amendment, we will not receive any royalties on the first $45.0 million of cumulative net sales of all products.

***License agreement for commercialization of XIPERE in China, Hong Kong, Macau, Taiwan and South Korea***

In March 2020, we entered into the Arctic License Agreement and granted an exclusive license to Arctic Vision to develop, distribute, promote, market and commercialize XIPERE, subject to specified exceptions, in the Arctic Territory. Under the terms of the Arctic License Agreement, neither party may commercialize XIPERE in the other party's territory. Arctic Vision has agreed to use commercially reasonably efforts to pursue development and commercialization of XIPERE for indications associated with uveitis in the Arctic Territory. In addition, upon receipt of the Company's consent, Arctic Vision will have the right, but not the obligation, to develop and commercialize XIPERE for additional indications in the Arctic Territory.

Pursuant to the Arctic License Agreement, Arctic Vision agreed to pay us up to a total of $35.5 million. This amount included an upfront payment of $4.0 million as well as an aggregate of up to $31.5 million in development milestone payments for specified events prior to and including receipt of approval of XIPERE in the United States and sales milestone payments for achievement of specified levels of net sales. Further, during the applicable royalty term, we will also be entitled to receive tiered royalties of 10% to 12% of net sales based on achieving certain annual net sales thresholds in the Arctic Territory, subject to customary reductions, payable on a product-by-product and country-by-country basis, commencing at launch in such country and lasting until the latest of (i) the date that all valid claims within the licensed patent rights covering XIPERE have expired, (ii) the date of the loss of marketing or regulatory exclusivity of XIPERE in a given country or (iii) ten years from the first commercial sale of XIPERE in a given country.

***XIPERE Phase 3 clinical trial data***

In PEACHTREE, a pivotal Phase 3 randomized, controlled, multi-center clinical trial, we evaluated the safety and efficacy of XIPERE administered through the SCS in patients with macular edema associated with non-infectious uveitis. PEACHTREE was conducted at 63 investigational sites and enrolled 160 patients with macular edema associated with non-infectious uveitis, randomized either to a treatment arm consisting of 96 patients who received a 4.0 mg dose of XIPERE or to a sham injection procedure arm consisting of 64 patients. We used a sham injection procedure as a comparator for XIPERE, as opposed to an active drug, because there were no approved therapies for macular edema associated with uveitis against which to compare XIPERE, and there were no controlled, randomized trials with data in patients who could be used as an appropriate comparator arm.

PEACHTREE was the first Phase 3 clinical trial of a drug candidate for patients with uveitic macular edema in which improvement in best corrected visual acuity, or BCVA, was the primary efficacy endpoint. It was also the first pivotal trial in which patients were evaluated across all types of uveitis: anterior, posterior, intermediate, and panuveitis. The trial met its primary endpoint with 47% of patients who received XIPERE every 12 weeks gaining at least 15 letters in 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 difference was statistically significant, with a p-value of less than 0.001. All key secondary and additional endpoints of the PEACHTREE trial were also achieved.

XIPERE 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 approximately 11.5% of patients in the treatment arm, compared to 15.6% of patients in the control arm, when including patients who received corticosteroid rescue medication. Specifically, 72% of patients in the control arm were administered rescue medication, with 37 of the 46 receiving intravitreal or periocular corticosteroid injections, such as intravitreal OZURDEX and periocular and intravitreal triamcinolone acetonide. Of those 37 control arm patients receiving local corticosteroid rescue medication, 10 patients, or 27%, experienced elevated IOP adverse events. In the PeriOcular and INTravitreal Corticosteroids for Uveitic Macular Edema Trial (POINT) Study, a recent National Eye Institute clinical trial studying the effect of current commercial treatments on macular edema associated with uveitis, over 30% of uveitis patients who received intravitreal steroid injections experienced steroid-related elevated IOP adverse events and received treatments to lower IOP. The reduced number of IOP adverse events in the XIPERE-treated patients in PEACHTREE suggest an IOP-sparing benefit, possibly due to the unique compartmentalization and ocular distribution of the drug inherent to administration via suprachoroidal injection. Preclinical studies investigating suprachoroidal administration support this assertion, with low corticosteroid exposure observed within the anterior chamber and trabecular meshwork.

In PEACHTREE, adverse events involving changes in cataract grading from baseline were similar in each arm, with approximately 7.3% and 6.3% of patients in the treatment arm and control arm showing adverse event changes in cataract grading, respectively. Further, no cataract surgeries resulted from this trial. Three serious adverse events occurred in the trial, all of which were identified in the CLS-TA arm: sialadenitis, posttraumatic compression fracture of the first lumbar vertebral body, and a retinal detachment approximately 8 weeks after the injection procedure. None of these serious adverse events were deemed treatment related by the study investigator or led to study discontinuation.

In January 2020, results of the PEACHTREE trial were published in *Ophthalmology*, the peer-reviewed journal of the American Academy of Ophthalmology.

In MAGNOLIA, our extension trial of PEACHTREE, we followed 28 of the 96 patients who were in the treatment arm of PEACHTREE across 22 clinical sites for six additional months without protocol-directed treatment to better understand XIPERE's long-term clinical profile. In MAGNOLIA, 50% of XIPERE-treated subjects maintained a mean improvement of 12.1 letters in BCVA from baseline through 36 additional weeks after their second suprachoroidal injection of XIPERE without requiring additional treatment.

In AZALEA, a Phase 3 safety trial, an additional 38 patients with non-infectious uveitis were enrolled in order to collect additional safety information required for our NDA submission. These patients were administered XIPERE at baseline and at week 12 and evaluated every 4 weeks after initial treatment, with a final evaluation at week 24. XIPERE was generally well tolerated, with no treatment-related serious adverse events reported in the trial.

In 2018, we were conducting SAPPHIRE, a Phase 3 trial, to assess the efficacy and safety of XIPERE together with intravitreal Eylea (aflibercept) in patients with RVO. We were also conducting TOPAZ, the companion Phase 3 trial to the SAPPHIRE trial assessing the efficacy and safety of suprachoroidal XIPERE together with an intravitreal anti-VEGF agent (either Lucentis, ranibizumab, or Avastin, bevacizumab) in patients with RVO. In November 2018, we announced that the primary endpoint of our Phase 3 clinical trial evaluating XIPERE together with intravitreal Eylea in patients with RVO was not achieved, and we discontinued the SAPPHIRE and TOPAZ trials at that time.

**CLS-AX (axitinib injectable suspension)**

Our most advanced internal development program is our proprietary suspension of axitinib for suprachoroidal injection, which we refer to as CLS-AX. CLS-AX is an inhibitor of vascular endothelial growth factor receptor-1, -2 and -3 that we believe may benefit patients who respond suboptimally to current anti-VEGF therapies. We are developing CLS-AX for administration to the SCS as a long-acting therapy for neovascular age-related macular degeneration, commonly referred to as wet AMD, a retinal degenerative disease that causes a progressive loss of central vision.

AMD is the leading cause of irreversible blindness in adults over 55 years old in developed countries. Approximately 11 million individuals in the United States are affected with AMD, with a global prevalence of 170 million. Aging is the greatest risk factor; therefore, the United States prevalence of AMD is anticipated to increase to 22 million by 2050, while the global prevalence is expected to increase to 288 million by 2040. An estimated 10% to 15% of people with AMD will develop the wet form, which refers to the advanced neovascular stage of the disease in which blood vessels leak blood and fluid into the macula and damage photoreceptor cells. Wet AMD often progresses rapidly and causes substantial loss of central vision if left untreated. Current wet AMD therapy has a ceiling of efficacy as increased dosage or more intense regimens yield limited or no additional visual benefit and require adherence to a regimen of frequent injections. This treatment burden is further highlighted by recent large “real-world” retrospective studies of wet AMD which underscore the difficulty in adhering to regimens. These real-world studies demonstrate that patients are undertreated, receiving only 6 to 7 injections per year on average, resulting in mean improvement of only one to three letters in visual acuity after one year of treatment. The current anti-VEGF market for the treatment of retinal diseases consists predominantly of several drugs that generated aggregate 2020 sales of approximately $14.3 billion globally.

CLS-AX combines our proprietary suspension of axitinib delivered via our SCS Microinjector. Based on preclinical data in multiple species, we believe that suprachoroidal injection of CLS-AX could benefit patients to yield potential safety, efficacy and durability benefits.

Axitinib is a TKI currently approved to treat renal cell cancer. Because it is a well-characterized small molecule instead of a novel complex biologic, we believe there is potential for less immune response and inflammation compared to some new, contemporary biologic agents. Also, compared to other TKIs, axitinib has shown better biocompatibility with ocular cells, including retinal pigment epithelial cells, which may potentially translate to safety benefits. Importantly, we believe that our unique route of SCS administration for CLS-AX, which is compartmentalized to the site of disease, may minimize treatment related adverse events, such as vitreous floaters, snow globe or corneal off-target effects seen with other TKI administration techniques.

With its broad VEGF blockade, we believe axitinib may have efficacy advantages over existing retinal therapies, which predominantly focus on VEGF-A blockade and may upregulate other forms of VEGF. Axitinib achieves pan-VEGF blockade by acting at a different level of the angiogenesis cascade, directly inhibiting VEGF receptors-1, -2, and -3 with high potency and specificity. In preclinical studies, axitinib was observed to be greater than ten times more potent than other TKIs. In multiple preclinical animal studies conducted by independent investigators, axitinib has inhibited corneal, retinal and choroidal angiogenesis. In addition, in preclinical models, axitinib more effectively inhibited and regressed experimental corneal neovascularization than other TKIs.

In our internal preclinical studies, CLS-AX delivered through suprachoroidal injection was well tolerated and showed durability over several months. This could lead to a longer lasting, highly effective treatment that may reduce the number of treatments and visits required for wet AMD patients to achieve optimal results.

In preclinical studies with our CLS-AX suspension of axitinib delivered via suprachoroidal injection, we have shown up to eleven times higher drug levels in affected tissues versus intravitreal administration of the same dose of axitinib. Therefore, suprachoroidal delivery of CLS-AX has the potential to compartmentalize therapy away from unaffected tissues for potential safety benefits and target the affected chorioretinal tissue layers for potential efficacy benefits.

Other TKIs have shown biologic effect in wet AMD clinical trials when delivered systemically, topically and intravitreally. However, each of these routes of administration have been associated with off-target effects. Consequently, a limitation of TKIs may be associated with the delivery of the drug and not a result of the mechanism of action.

In August 2020, we announced that the FDA had accepted our IND for CLS-AX. In January 2021, we announced the enrollment of our first patient in OASIS, a Phase 1/2a clinical trial of CLS-AX in patients with wet AMD. OASIS is an open-label, dose-escalation clinical trial to assess the safety and tolerability of single doses of CLS-AX administered through suprachoroidal injection following two or more prior treatments with aflibercept, an intravitreal anti-VEGF agent, dosed at screening. The primary endpoint for the trial will assess the safety and tolerability of CLS-AX for the three months following the administration of CLS-AX, and secondary endpoints will evaluate the pharmacokinetics, visual function, ocular anatomy and the need for additional treatment with intravitreal aflibercept during the three-month period.

Patient inclusion criteria for enrollment in OASIS include: active subfoveal choroidal neovascularization secondary to AMD; two or more anti-VEGF treatments with a meaningful response in the four months preceding the screening visit with a meaningful response; and best corrected visual acuity, or BCVA, score of ≥ 20 letters (20/400) and ≤ 75 letters (20/32) with < 5 letters change

between screening and baseline to ensure patient stability after anti-VEGF treatment. Patients are then assessed at weeks four, eight and twelve. Patients will be assessed for additional therapy if they experience any of the following: (1) loss of 10 or more letters in BCVA compared to the best prior study-assessed BCVA in the study eye that is attributed to intra- or sub-retinal fluid observed by the investigator; or (2) increase in central subfield retinal thickness greater than 75 microns from baseline at visit 2 in the study eye; or (3) presence of vison-threatening hemorrhage due to AMD in the study eye. The trial design consists of three cohorts of five patients each. Cohort 1 participants will receive the lowest dose, 0.03 mg of axitinib delivered via suprachoroidal injection. Dose escalation will then proceed following review of the safety data by the Safety Monitoring Committee for the trial and their recommendation to advance to the next higher dose cohort.

On March 2, 2021, we announced the completion of patient dosing for the first cohort and expect to announce initial safety data from this cohort in mid-2021.

**Gene Therapy**

We believe our platform offers the potential for safer, targeted ocular gene therapy without some of the risks of surgery and subretinal administration. Suprachoroidal administration of gene therapy could ultimately enhance access to care because it does not require specialized gene therapy surgery treatment centers. The procedure for suprachoroidal injection is conducted in an office setting and is similar in terms of patient preparation and duration to the procedure for intravitreal injection. Therefore, we believe our products could be incorporated into retina specialists' standard medical practice.

During the past several years, gene therapy has demonstrated in preclinical studies and clinical trials conducted by third parties that genetic material can be effectively and tolerably introduced to the retinal tissues, most often using an AAV. Safe and reproducible delivery of gene therapy vector into the subretinal space is essential for successful targeting of the retinal pigment epithelium, or RPE, and photoreceptor rods or cones. Currently, the only approved retinal gene therapy and most investigational retinal gene therapies are delivered via retinal surgery at a limited number of specialized ocular gene therapy treatment centers. During the pars plana vitrectomy surgery, the surgeon creates a small hole in the retina to inject the gene therapy beneath the retina to the subretinal space without tearing or damaging the retina and macula. This process creates a small retinal detachment, which separates and exposes the photoreceptors and RPE to the gene therapy. The retina is in a disease state and already compromised, and the procedure carries iatrogenic risk. However, the success of this surgery is critical for the clinical efficacy of retinal gene therapy. Consequently, the surgery requires extensive training and the limited number of specialized ocular gene therapy centers creates patient access issues. Unlike vitrectomy, suprachoroidal administration does not require detachment of the photoreceptors from the RPE, and consequently, avoids the risk of iatrogenic subretinal injection to an already-compromised retina. Suprachoroidal injection procedure training is minimal and could ultimately enhance access to care because it would not have to be administered at a specialized gene therapy surgery treatment center.

Inherited retinal diseases, or IRDs, such as Stargardt disease and Usher syndrome, represent some of the most challenging diseases that ophthalmologists encounter. They cause progressive, relentless vision loss due to changes in genes critical to the survival of photoreceptors and RPE cells, yet delivery of therapeutics to these cells is challenging. In preclinical animal studies from which data was presented at the American Academy of Ophthalmology 2019 Annual Meeting in October 2019, the suprachoroidal injection of luciferase DNA nanoparticles, or DNPs, in rabbits produced activity comparable to that seen from subretinal injections of luciferase DNPs. In these studies, SCS injections of DNPs were generally well tolerated across both rabbits and non-human primates, and no significant abnormalities were observed on ophthalmic exams. DNPs can also transfer large genes at potentially higher doses without the risks of subretinal surgery, which may allow for gene therapy in some of the most common IRDs.

We believe suprachoroidal administration may further enhance the value proposition of ocular gene therapy by potentially improving safety and expanding access. In preclinical studies we have observed that SCS injection can administer both viral and non-viral gene therapy. Using marker genes like green fluorescent protein and luciferase in both rabbits and non-human primates, gene therapy was delivered with our SCS injection to achieve expression in the retina and choroid.

We have also expanded the reach of our SCS Microinjector technology in gene therapy through a development and commercial partner. In August 2019, we entered into an option and license agreement with REGENXBIO, pursuant to which we granted REGENXBIO an exclusive option, or the Option, to enter into a commercial license agreement granting REGENXBIO an exclusive, worldwide and sublicensable license to our SCS Microinjector for the delivery of AAV-based gene therapies for the treatment of wet AMD, diabetic retinopathy and other conditions for which anti-VEGF treatment is currently the standard of care. REGENXBIO exercised the Option on October 29, 2019 and paid us an option fee equal to $2.0 million less $0.5 million received under a prior technology access agreement. Under the license agreement, REGENXBIO has agreed to make additional payments to us of up to an aggregate of $34.0 million upon the achievement of specified development milestones and up to $102.0 million in sales-based milestone payments, as well as mid-single digit royalties on net sales of products using the SCS Microinjector during the royalty term.

REGENXBIO will be responsible for all development, regulatory and commercialization activities for their gene therapy product candidates. We will be responsible for supplying the SCS Microinjector in support of REGENXBIO's preclinical studies, clinical studies and commercial use.

**Ocular Oncology**

On July 9, 2019, we entered into a worldwide licensing agreement with Aura for the use of our SCS Microinjector to deliver Aura's proprietary drug candidates into the SCS for the potential treatment of certain ocular cancers, including choroidal melanoma. If the collaboration proves successful following preclinical and proof-of-concept studies, Aura may utilize the SCS Microinjector for certain future development programs. Pursuant to the licensing agreement, we are eligible to receive payments related to pre-specified development, regulatory and sales milestones, as well as royalties on product sales that utilize the SCS Microinjector.

**Manufacturing**

We do not own any manufacturing facilities. We utilize CMOs to formulate and produce our drug candidates and to produce our SCS Microinjector used for our clinical trials. We procure active pharmaceutical ingredients for our drugs from third-party suppliers. We expect to utilize third-party manufacturers to produce commercial quantities of our drugs and SCS Microinjector, if approved.

On May 8, 2018, we entered into a supply agreement with Gerresheimer Regensburg GmbH to supply our SCS Microinjector. Unless terminated earlier pursuant to its terms, the Gerresheimer agreement has an initial term of five years, after which it renews in three-year increments unless either party gives notice of non-renewal at least one year in advance. Each party has the right to terminate the agreement for customary reasons such as material breach and bankruptcy. The Gerresheimer agreement contains provisions relating to compliance by Gerresheimer with current Good Manufacturing Practices, regulations promulgated by the FDA, confidentiality and other customary matters for an agreement of this nature. We anticipate entering into commercial supply agreements with our other suppliers at a later date.

**Commercialization**

We have entered into exclusive license agreements for the commercialization and development of XIPERE with Bausch in the United States and Canada and with Arctic Vision in China, Hong Kong, Macau, Taiwan and South Korea. We may enter into distribution or licensing arrangements for commercialization rights for other regions. If any of our future product candidates, including CLS-AX, are approved by the applicable regulatory authorities, we may either commercialize those product candidates ourselves or through license or collaboration agreements with third parties.

**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.

XIPERE faces competition from other commercially available forms of TA and other topical, 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 using intravitreal and periocular administration. 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. 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 diabetic macular edema, or DME.

Additionally, our collaborator Bausch markets Retisert, an intravitreal implant of the corticosteroid fluocinolone acetonide for the treatment of non-infectious uveitis. Eyepoint Pharmaceuticals markets Yutiq, an injectable form of fluocinolone acetonide for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

Axitinib, also known by its brand name Inlyta, is currently marketed by Pfizer and is approved by the FDA for the treatment of advanced renal cell carcinoma, but not for any ophthalmology indications. Our product candidate, CLS-AX, could also compete with anti-VEGF drugs, which are the current standard of care for RVO and wet AMD. 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, 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 diabetic retinopathy. In the European Union, Eylea is approved for the treatment of wet AMD and RVO. Novartis' Beovu was recently approved for the treatment of wet AMD in the United States, and has been recommended for approval in the European Union at a recent meeting of European Medicines Agency's drug evaluation committee.

Axitinib may also compete with other drug candidates in development in other forms for ocular use and other development candidates for wet AMD. Companies developing potentially competitive TKIs for ocular use are Ocular Therapeutics, Graybug and Eyepoint. We expect that other established companies in the ocular space will seek to develop new products with the goal of superior efficacy and duration over the current standard of care.

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 before 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 may 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 22 granted U.S. patents broadly directed to devices and methods of administering drugs into the SCS by injection, including one design patent. In addition, our patent estate includes two allowed U.S. patent applications, 15 patent applications pending in the United States, 61 issued foreign patents and three allowed foreign patents, two pending international PCT applications and 49 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 seven of the 22 issued U.S. patents, 5 pending U.S. applications, 19 of the issued foreign patents and one of the allowed foreign patents, and seven 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 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 uveitis and RVO, wet AMD as well as DME and improvement of specified clinical parameters, are expected to expire, if issued, between 2027 and 2041, 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 numerous patents. In the case of XIPERE injected into the SCS, an applicant who files a paragraph 4 Abbreviated New Drug Application, or 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***

We have 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.

In addition to upfront and milestone payments of $65,000 in the aggregate made to date, the 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. On July 1, 2018 and 2019, we paid Emory and GTRC $75,000 and $50,000, respectively, to extend the date by which we may achieve the commercialization milestone. 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.

***Trademarks, trade secrets and know-how***

Our trademark portfolio currently consists of two registered trademarks in Australia and Korea, two registered trademarks in Russia, two registered trademarks in Singapore, six registered trademarks in Brazil, five registered trademarks in Canada, six registered trademarks in China, four registered trademarks in the European Union, two registered trademarks in each of India and New Zealand, two registered trademarks in Japan, three registered trademarks in Israel, seven registered trademarks in Mexico, four registered and three pending applications in South Africa, five registered trademarks in the United States and two pending applications in the United States and two registered trademarks in the United Kingdom. We also have two international registrations: the first with pending extensions of protection to Australia, Japan, Mexico and registered in the European Union, India, New Zealand, Korea and Singapore, and the second with extensions of protection pending in India and Mexico and registered in Australia, China, European Union, Israel, Japan, Korea, Russia, and Singapore. 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 Food, Drug and Cosmetic Act, or 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.

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.

***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 or an independent institutional review board, or IRB, may nevertheless initiate a clinical hold after the 30 days if, for example, significant health risks arise.

In the United States, each clinical trial must be reviewed and approved by an 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 and exemptions apply in limited cases. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

***Review of application***

Once an NDA has been accepted for filing, which occurs, if at all, 60 days after submission, the FDA sets a user fee goal date that informs the applicant of the specific date by which the FDA intends to complete its review. This is typically 10 months from the date of submission for drugs that are not new molecular entities, such as our product candidates. The review process can be expedited if priority review is granted. In such a case, the FDA review period is only 6 months. Alternatively, the FDA 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 boxed 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. The FDA will issue either an approval of the NDA or a CRL, 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 program user fee requirements for approved products, 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. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. However, companies may share truthful and not misleading information that is otherwise consistent with the product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, including without limitation the FDCA, the federal civil 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. As a condition for approval, the FDA may also require us to perform additional studies or measurements, including clinical trials, to support the change from the approved branded reference drug.

*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 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 file patent litigation 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 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 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 XIPERE for the treatment of 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. Therefore, even if we structure our programs with the intent of compliance with such laws, there can be no certainty that we would not need to defend ourselves against enforcement or litigation due to the fact that there is significant enforcement interest in life sciences companies in the United States and some of the applicable laws are broad in scope.

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 federal 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 federal civil False Claims Act. 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. 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 federal criminal False Claims Act. The federal 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 federal 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 and civil 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 certain health care providers, health plans, and healthcare clearinghouses. 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 their 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 and their subcontractors that use, disclose, access, or otherwise process protected health information. 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. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. Accordingly, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. New laws and regulations governing privacy and security may be adopted in the future as well.

In the EU/EEA, the General Data Protection Regulation (2016/679), or GDPR, went into effect on May 25, 2018 and replaced Directive 95/46/EC (the EU Privacy Directive). The GDPR applies to identified or identifiable personal data processed by automated means (for example, a computer database of customers) and data contained in, or intended to be part of, non-automated filing systems (traditional paper files) as well as transfer of such data to a country outside of the EU/EEA. The GDPR extends the geographical scope of EU data protection law to entities and operations outside of the EU/EEA under certain conditions and imposes substantial obligations upon companies and new rights for individuals, and by certain EU Member State-level legislation. Under the GDPR, fines of up to €20.0 million or up to 4% of the annual global turnover of the infringer, whichever is greater, could be imposed for significant non-compliance. The GDPR includes more stringent operational requirements for processors and controllers of personal data and creates additional rights for data subjects. In addition, the GDPR may increase our responsibility and liability in relation to personal data that we may process, and we may be required to put in place additional measures in an effort to comply with the GDPR and with other laws and regulations in the EU, including those of EU Member States, relating to privacy and data protection. This may be onerous and if our efforts to comply with GDPR or other applicable EU laws and regulations are not successful, or are perceived to be unsuccessful, it could adversely affect our business in the EU.

Further, the European Court of Justice (ECJ) invalidated the EU-U.S. Privacy Shield, which enabled the transfer of personal data from the EU to the U.S. for companies that had self-certified to the Privacy Shield in July 2020. The ECJ decision also raised questions about the continued validity of one of the primary alternatives to the EU-U.S. Privacy Shield, namely the European Commission's Standard Contractual Clauses, and EU regulators have issued additional guidance regarding considerations and requirements that we and other companies must consider and undertake when using the Standard Contractual Clauses. Although the EU has presented a new draft set of contractual clauses, at present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the Standard Contractual Clauses. To the extent that we were to rely on the EU-U.S. or Swiss-U.S. Privacy Shield programs, we will not be able to do so in the future, and the ECJ's decision and other regulatory guidance or developments otherwise may impose additional obligations with respect to the transfer of personal data from the EU and Switzerland to the U.S., each of which could restrict our activities in those jurisdictions, limit our ability to provide our products and services in those jurisdictions, or increase our costs and obligations and impose limitations upon our ability to efficiently transfer personal data from the EU and Switzerland to the U.S.

Additionally, in June 2016, United Kingdom voters approved an exit from the EU, commonly referred to as "Brexit," which could also lead to further legislative and regulatory changes. In March 2017, the United Kingdom began the process to leave the EU by April 2019. Under the post-Brexit Trade and Cooperation Agreement between the EU and the UK, the UK and EU have agreed that transfers of personal data to the UK from EEA member states will not be treated as 'restricted transfers' to a non-EEA country for a period of up to four months from January 1, 2021, plus a potential further two months extension (the "Extended Adequacy Assessment Period"). Although the current maximum duration of the Extended Adequacy Assessment Period is six months, it may end sooner, for example, in the event that the European Commission adopts an adequacy decision in respect of the UK, or the UK amends the UK GDPR and/or makes certain changes regarding data transfers under the UK GDPR/Data Protection Act 2018 without the consent of the EU (unless those amendments or decisions are made simply to keep relevant UK laws aligned with the EU's data protection regime). If the European Commission does not adopt an 'adequacy decision' in respect of the UK prior to the expiry of the Extended Adequacy Assessment Period, from that point onwards the UK will be an 'inadequate third country' under the GDPR and transfers of personal data from the EEA to the UK will require a 'transfer mechanism' such as the Standard Contractual Clauses. Beginning in 2021, the UK will be a "third country" under the GDPR. We may, however, incur liabilities, expenses, costs, and other operational losses under GDPR and applicable EU Member States and the United Kingdom privacy laws in connection with any measures we take to comply with them.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. Effective January 1, 2020, the CCPA requires covered companies to provide new disclosures to California consumers, provides such consumers new ways to opt-out of certain sales of personal information, and allows for a new cause of action for data breaches. The CCPA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

In addition, it is anticipated that the CCPA will be expanded on January 1, 2023, when the California Privacy Rights Act of 2020 ("CPRA") becomes operative. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive personal information, further restrict the use of cross-contextual advertising, establish restrictions on the retention of personal information, expand the types of data breaches subject to the CCPA's private right of action, provide for increased penalties for CPRA violations concerning California residents under the age of 16, and establish a new California Privacy Protection Agency to implement and enforce the new. Although there are limited exemptions for clinical trial data under the CCPA, the CCPA and other similar laws could impact our business activities depending on how it is interpreted.

With the GDPR, CCPA, CPRA, and other state and Federal laws, regulations and other obligations relating to privacy and data protection imposing new and relatively burdensome obligations, and with substantial uncertainty over the interpretation and application of these and other obligations, we may face challenges in addressing their requirements and making necessary changes to our policies and practices, and may incur significant costs and expenses in an effort to do so. Additionally, if third parties we work with, such as vendors or service providers, violate applicable laws or regulations or our policies, such violations may also put our or our customers' data at risk and could in turn have an adverse effect on our business.

Additionally, a trend has continued 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 (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their family members. Beginning in 2022, applicable manufacturers will

also be required to report information regarding payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants, and certified nurse-midwives. Certain states also mandate implementation of commercial compliance programs, impose restrictions on pharmaceutical manufacturer and device manufacturer marketing practices, require registration of pharmaceutical sales representatives, require drug manufacturers to report information on the pricing of certain drugs, 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 regulatory 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, civil and administrative penalties, damages, fines, disgorgement, individual 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 third-party payors, including private insurers and government-funded programs, like Medicare, and Medicare administrative contractors. We believe obtaining a separate CPT code for the use of our products is critical to maximizing our commercial success. 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 third-party payors to establish coverage, coding and reimbursement that will facilitate access to our product candidates and the SCS injection procedure as we expand our commercialization efforts in the United States. Our success in these efforts depends in part on the extent to which third-party payors provide coverage 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 adequate reimbursement from third-party payors for the procedures to administer our product candidates or for the product candidates themselves, or adverse changes in 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 procedures 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 established a quality payment program, also referred to as the Quality Payment Program. 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. In November 2019, CMS issued a final rule finalizing the changes to the Quality Payment Program. 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 third-party 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.

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. There remain judicial and Congressional challenges to certain aspects of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several 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, or Tax Act, includes a provision that repealed, 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". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's mandated medical device tax and "Cadillac" tax on high-cost employer-sponsored health coverage and, effective January 1, 2021, also eliminated the health insurer tax. The Bipartisan Budget Act of 2018, or BBA, among other things, amended 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". On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unknown when a decision will be made. Further, although the U.S. Supreme Court has not yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act and our business.

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 2030 with the exception of a temporary suspension from May 1, 2020 through March 31, 2021 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 used several means to propose or implement drug

pricing reform, including through federal budget proposals, executive orders and policy initiatives. HHS has solicited feedback on some of these measures and implemented others under its existing authority. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. At the state level, legislatures have increasingly passed legislation and implemented 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. It is also possible that additional governmental action will be taken in response to the COVID-19 pandemic.

***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 and Human Capital Resources**

We strive to recruit people who share our vision to develop technology that provides a ground-breaking impact to medicine and superior care to patients. We are proud of what we do and believe we create an excellent working environment that is inclusive and diverse with meaningful compensation, benefits and wellness programs that continue to facilitate the attraction, retention and motivation of talented employees.

As of December 31, 2020, we had 33 employees, all of whom were full-time and were located in the United States. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

**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. 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 $18.2 million, $30.8 million and $82.8 million for the years ended December 31, 2020, 2019 and 2018, respectively.

We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We have not completed development of, and obtained marketing approval for, 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;
- maintain, expand and protect our intellectual property portfolio; and
- hire additional clinical, manufacturing and scientific personnel.

To become and remain profitable, we must succeed in developing drugs that can generate significant revenue once commercialized. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, manufacturing, obtaining regulatory approval and potentially entering into agreements for the commercialization of 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.

***Our consolidated financial statements have been prepared assuming that we will continue as a going concern.***

We have incurred recurring losses from operations since inception which raises substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected, and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. In addition, if there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms, or at all.

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

We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2022. However, we will need to obtain substantial additional funding in connection with our continuing operations beyond the first quarter of 2022. 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, whether performed by us or third parties, 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, although as described in this report we have also entered into an at-the-market sales facility that allows us to sell shares 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 efforts 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.***

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 may not be successful in our transition from a company with a research and development focus to a company capable of supporting commercial activities.

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

**Risks Related to the Development of Our Product Candidates**

***Our efforts are focused on the development of product candidates for treatment of eye disease through suprachoroidal injection and partnering with companies who can leverage our SCS Microinjector to deliver their ophthalmic product candidates to the suprachoroidal space. Suprachoroidal injection 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 have also licensed our SCS Microinjector technology to third parties to deliver their proprietary drug candidates into the SCS for the potential treatment of certain ocular indications. Although our clinical trial results suggest that suprachoroidal injection of drugs, such as XIPERE, may be effective at treating back of the eye diseases, to date no company has developed a drug delivered via suprachoroidal administration that has received marketing approval.

We cannot guarantee that suprachoroidal injection of drugs will prove in ongoing and future clinical trials to be a safe or effective approach for treating eye diseases in humans, nor can we ensure that such drugs will achieve regulatory approval, even if the clinical trials are successful.

Even if our product candidate, or a product candidate of one of our collaboration partners, delivered via suprachoroidal injection achieves marketing approval, the novelty of suprachoroidal injection may make it difficult to demonstrate to physicians and third-party payors that suprachoroidal injection of drugs is an appropriate approach for treating eye diseases and provides advantages compared to the current standards of care. Further, if we or our commercialization and collaboration partners are not successful in conveying to physicians, patients and third-party payors that the suprachoroidal administration of drug candidates with our proprietary SCS Microinjector provides useful patient outcomes, we or our commercialization and collaboration partners may experience reluctance, or refusal, on the part of physicians to order and use, and third-party payors to cover and provide adequate reimbursement for, such product candidates. Additionally, in some cases, product candidates delivered using our SCS Microinjector will complement the current standard of care, rather than serve as a replacement for the current standard of care. Therefore, we or our commercialization and collaboration partners may encounter significant difficulty in gaining broad market acceptance by physicians, third-party payors and potential patients.

***Our licensing partners may require that we modify our SCS Microinjector to deliver their product candidates, and we may be unable to do so.***

We are currently partnering with companies who can leverage our SCS Microinjector to deliver their ophthalmic product candidates to the suprachoroidal space. Our current and future licensing partners may request modifications to the design of our SCS Microinjector to accommodate the delivery of their respective product candidates. If we are unable to make such modifications, we may not receive regulatory and development milestone payments that we otherwise would be eligible to receive, which could significantly harm our financial position.

***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, either on our own or with a third party, or if we experience significant delays in doing so, our business may be harmed.***

Given our 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 will depend heavily on their successful development and eventual commercialization, either by us or third parties. 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;
- the 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 from third-party payors;
- 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.

***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 data from our clinical studies. 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. 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, 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.

***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 receive marketing approval or achieve market acceptance. If we do not successfully develop 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 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. For example, we were previously developing XIPERE in combination with an anti-VEGF therapy for the treatment of macular edema associated with RVO. In November 2018, we announced that the primary endpoint of our Phase 3 clinical trial evaluating XIPERE together with intravitreal Eylea in patients with RVO was not achieved. In light of the 8-week topline data, we discontinued our Phase 3 trials of suprachoroidal XIPERE together with an intravitreal anti-VEGF agent in patients with RVO, as well as the clinical development of XIPERE in combination with anti-VEGF agents for the treatment of RVO.

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 for 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 or our potential collaborators' 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.

***COVID-19 could adversely impact our business, including our clinical trials or those of our licensing partners.***

In December 2019, a novel strain of coronavirus, SARS-CoV-2, causing COVID-19, was initially reported and has since been declared a pandemic by the World Health Organization. The COVID-19 pandemic has resulted in continuing travel and other restrictions in order to reduce the spread of the disease, including state and local orders across the country that, among other things, direct businesses and governmental agencies to cease non-essential operations at physical locations, prohibit certain non-essential gatherings, and order cessation of non-essential travel. In response to these public health directives and orders, we have implemented work-from-home policies for our employees. The effects of the executive orders and our work-from-home policies may negatively impact employee productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

Quarantines and similar government orders and employer restrictions related to COVID-19 may adversely impact our business operations and the business operations of third parties on which we rely. In addition, our clinical trials and those of our licensing partners may be affected by the COVID-19 pandemic. For example, clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic. Some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our ability, or that of our licensing partners, to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 may be impaired, which could adversely impact our clinical trial operations or those of our licensing partners and, as a result, negatively affect our ability to receive regulatory and development milestones under our license agreements.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a continued widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The extent to which the COVID-19 pandemic impacts our business, our clinical development and regulatory efforts and those of our licensing partners will depend on future developments that are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, travel restrictions, quarantines, social distancing requirements and business closures in the United States and other countries, business disruptions, the effectiveness of actions taken in the United States and other countries to contain the disease and the availability, timing and effectiveness of a vaccine, both domestically and abroad. Accordingly, we do not yet know the full extent of potential delays or impacts on our business, our clinical and regulatory activities, healthcare systems or the global economy as a whole.

***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 have granted an exclusive license to Bausch for the commercialization and development of XIPERE in the United States and Canada. If we are delayed in receiving FDA approval for XIPERE, or we are unable to maintain our partnership with Bausch, or if Bausch fails to successfully commercialize XIPERE, our business and prospects will be materially harmed.***

We have granted an exclusive license to Bausch for the commercialization and development of XIPERE in the United States and Canada. Pursuant to our agreement with Bausch, we are entitled to receive payments based on the achievement of specified sales and regulatory milestones and tiered royalties based on annual net sales of XIPERE. The successful or timely achievement of many of these milestones is outside of our control because the relevant activities will be conducted by Bausch. We expect to depend to a large degree on the payments from Bausch and future potential commercialization partners in order to fund our operations, and a failure to receive such payments may cause us to:

- delay, reduce or terminate certain research and development programs;
- reduce headcount;
- pursue the raising of additional funds through equity or convertible debt financings that could be dilutive to our stockholders;
- seek funds by entering into agreements that require us to assign rights to technologies or products that we would have otherwise retained;

- enter into new arrangements that may be less favorable than those we would have obtained under different circumstances; or
- consider strategic transactions or engaging in a joint venture with a third party.

In addition, Bausch may terminate the License Agreement immediately and have the upfront payment of $5.0 million refunded if the FDA has not approved the XIPERE NDA by August 31, 2021. Based upon our current expectations, it is likely that the FDA will not have approved the XIPERE NDA by such date. Therefore, if we are not able to enter into an amendment to the License Agreement or obtain a waiver from Bausch, it is possible that Bausch could terminate the License Agreement and that we would be required to refund the initial $5.0 million upfront payment. If this were to occur, our business prospects would be materially harmed, and we would need to seek a new partner to commercialize XIPERE in the United States and Canada and the Additional Regions.

***We have entered into, and intend to continue to enter into, collaborations with third parties for the development and commercialization of product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.***

We have entered into, and intend to continue to enter into, agreements with third-party collaborators for the development and commercialization of our product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and smaller 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 refuse to perform clinical trials or other obligations required for approval in a particular jurisdiction outside the United States;
- our collaborators' regulatory submissions may be denied by the applicable regulatory authorities;
- 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.

***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 or our potential collaborators' 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 the commercialization of XIPERE 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 do not have our own manufacturing capabilities and rely on third parties to produce clinical and commercial supplies of our current product candidates, including XIPERE, CLS-AX and our SCS Microinjector. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates, including the XIPERE drug product, CLS-AX 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 XIPERE on a purchase order basis from a third-party manufacturer, but we do not have a commercial supply agreement in place with that manufacturer. In addition, we have entered into a supply agreement with Gerresheimer, our SCS Microinjector supplier. Some of our current suppliers are based outside of the United States. In addition, some of the facilities of our third-party manufacturers have only undergone a limited number of FDA inspections or no inspections. We expect to continue to rely on third parties as we proceed with preclinical and clinical studies using 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

XIPERE including 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.

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 subject to the drug regulations of the 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. For example, in preparation for our NDA submission for XIPERE for the treatment of patients with macular edema associated with uveitis, we conducted audits of our third-party manufacturers, and identified items that require correction prior to the FDA's pre-approval inspection of those manufacturing facilities. Our prior CMO notified us that they were no longer willing to serve as our commercial supplier for XIPERE and that they were uncertain about being prepared for an FDA pre-approval inspection on our timeline. In August 2020, we secured a new CMO to manufacture the registration batches of XIPERE for the resubmission of our NDA, as well as to manufacture batches of XIPERE for potential commercialization. However, there can be no assurance that we or our suppliers will pass an FDA pre-approval inspection. 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, a refusal to file determination by the FDA, receipt of a CRL, 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 our ability to achieve regulatory approval of our product candidates, including XIPERE.

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 supply of 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.

***If we are not able to establish additional 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 and distribution capabilities for our product candidates for which we do not out-license commercialization rights, we may not be successful in commercializing those product candidates, if and when they are approved.***

We do not have a sales infrastructure. To achieve commercial success for any product candidate for which we may obtain marketing approval in the United States and have not licensed the commercialization rights to a third party, we will need to establish a sales organization. There are risks involved with establishing our own sales 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 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 educate an adequate number of physicians as to the benefits of our product candidates;
- 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 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 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 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 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 receive marketing approval, they 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 provided by us or our collaborators;
- the availability of third-party payor 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. We also are aware of companies that are developing suprachoroidal injectors which may compete with our SCS Microinjector.

With respect to XIPERE, 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. 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.

Additionally, our collaborator Bausch markets Retisert, an intravitreal implant of the corticosteroid fluocinolone acetonide for the treatment of non-infectious uveitis. Eyepoint Pharmaceuticals markets Yutiq, an injectable form of fluocinolone acetonide for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

Axitinib, also known by its brand name Inlyta, is currently marketed by Pfizer and is approved by the FDA for the treatment of advanced renal cell carcinoma, but not for any ophthalmology indications. Our product candidate CLS-AX could also compete with anti-VEGF drugs, which are the current standard of care for RVO and wet AMD. 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, 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 diabetic retinopathy. In the European Union, Eylea is approved for the treatment of wet AMD and RVO. Novartis' Beovu was recently approved for the treatment of wet AMD in the United States and has been recommended for approval in the European Union at a recent meeting of European Medicines Agency's drug evaluation committee.

Axitinib may also compete with other drug candidates in development in other forms for ocular use and other development candidates for wet AMD. Companies developing potentially competitive TKI's for ocular use are Ocular Therapeutics, Graybug and Eyepoint. We expect that other established companies in the ocular space will seek to develop new products with the goal of superior efficacy and duration over the current standard of care.

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 or our collaborators 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.

***Our product candidates may be subject to unfavorable pricing regulations, third-party coverage and reimbursement policies or healthcare reform initiatives.***

Our and our collaborators' 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 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 coverage and adequate reimbursement for our drugs may be difficult. We or our collaborators 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 or our collaborators 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 program 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, also referred to as the Sustainable Growth Rate, for clinician payment and established a quality payment incentive program, also referred to as the Quality Payment Program. This program provides clinicians with two ways to participate, including through the Advanced Alternative Payment Models, or APMs, and the Merit-based Incentive Payment System, or MIPS. In November 2019, CMS issued a final rule finalizing the changes to the Quality Payment Program. At this time, it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. 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 or that the Category III codes will remain in effect. Additionally, there is no guarantee that these billing codes or the payment amounts, if any, associated with such codes will be sufficient to successfully commercialize any approved product and, even if adequate payment amounts are obtained, they could 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 or our collaborators' 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 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.***

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 or collaborators 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
- our or our collaborators' 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 or our collaborators 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 our executive officers and senior management, as well as the other members of our scientific and clinical development teams. Our executive officers 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 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 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 and gain regulatory approval of 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 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.

**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 or that we have published an invention

prior to filing a relevant patent application. 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 be sold in countries in which our patent coverage might not exist or be as strong. If we lose a patent lawsuit alleging our infringement of a competitor's patent, or if FDA approval is stayed pending the outcome of patent litigation, we could be prevented from marketing our products. 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 or our collaborators 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 cease development of one or more or our product candidates or 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 or our collaborators' ability to commercialize our product candidates.

***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 XIPERE, 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. If 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.

***Some intellectual property that we have in-licensed may have been discovered through a government funded program and may be subject to certain federal regulations.***

Some of the intellectual property rights we have licensed, including such rights licensed from Emory University and Georgia Tech Research Corporation, may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government may have the right to require us to grant exclusive, partially exclusive or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention, (ii) government action is necessary to meet public health or safety needs or (iii)

government action is necessary to meet requirements for public use under federal regulations (also referred to as “march-in rights”). The U.S. government also could take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

***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**

***We have secured a new contract manufacturer for XIPERE to produce data necessary for the resubmission of our NDA for XIPERE. As a result, the timing of regulatory approval for XIPERE is uncertain, and we may never obtain regulatory approval for XIPERE in the United States.***

We have secured a new manufacturing partner for XIPERE. Our prior CMO notified us that they were no longer willing to serve as our commercial supplier for XIPERE and that they were uncertain about being fully prepared for an FDA pre-approval inspection on our timeline. Given our previously disclosed delays, we had begun evaluating alternative manufacturers. In August 2020, we engaged a new CMO to manufacture the registration batches of XIPERE for the resubmission of our NDA.

In connection with the engagement of the new CMO, the technology underlying the manufacturing process has been transferred to the new CMO so that they can generate the data required by the FDA. The timeline for the CMO’s ability to complete the necessary activities, implement the manufacturing processes and generate the necessary data is uncertain. While we believe, based on information received from the new CMO, that we will be able to resubmit the NDA no later than the second quarter of 2021, we cannot assure you that the CMO will be able to generate sufficient data to enable resubmission of the NDA, nor can we predict the outcome of any interactions with the FDA with respect to the resubmission of the XIPERE NDA or otherwise, We cannot guarantee when, or if, we will be successful in receiving regulatory approval for XIPERE. In addition, the FDA could require supplemental data or information from the new CMO, particularly if the FDA inspects the new CMO’s facilities. As a result, the timing of regulatory approval for XIPERE is uncertain, and we may never obtain regulatory approval for XIPERE in the United States. If we do not obtain approval for XIPERE or are delayed in obtaining such approval, it would have a material adverse effect on our operations and financial condition.

***If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we and our collaborators 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, or any collaborator to whom we grant rights, 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 are seeking FDA approval through the Section 505(b)(2) regulatory pathway for XIPERE and may pursue that pathway for our other product candidates. We believe that 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 or requirements. 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 in order for us or our collaborators 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;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- 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. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. However, companies may share truthful and not misleading information that is otherwise consistent with the product's FDA 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 federal civil 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 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 the treatment of non-infectious uveitis, and we may seek orphan drug designation from the FDA or EMA for our future product candidates. However, we cannot pursue orphan drug designation from the FDA for the treatment of uveitis.

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 even if we receive marketing authorization 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 substantial 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, 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, including 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 limitation, the federal civil False Claims Act which permits private individuals, on behalf of the government, to bring civil whistleblower or qui tam actions to enforce the law, prohibits individuals or entities from, 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 civil and 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 certain 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 and their subcontractors that use, disclose, access, or otherwise process individually identifiable health information, 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 (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members, and, beginning in 2022, will require applicable manufacturers to report information regarding payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants, and certified nurse-midwives;
- 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; state and local laws requiring the registration of pharmaceutical sales representatives; 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;

- U.S. data privacy regulations, such as the CCPA, which creates new individual privacy rights for consumers and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosures to California consumers, provides such consumers new ways to opt-out of certain sales of personal information, and allows for a new cause of action for data breaches; and
- foreign data privacy regulations, such as the General Data Protection Regulation (2016/679), or GDPR, which went into effect on May 25, 2018 and applies to identified or identifiable personal data in electronic or paper form. Under the GDPR, fines of up to €20.0 million or up to 4% of the annual global turnover of the infringer, whichever is greater, could be imposed for significant non-compliance. The GDPR includes more stringent operational requirements for processors and controllers of personal data and creates additional rights for data subjects.

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 order to have committed a violation. 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 and 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;
- 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 most branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the federal civil 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 now agree to offer 70% 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, 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 remain judicial and congressional challenges to certain aspects of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several 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, or the Tax Act, included a provision which repealed, 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". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it is unknown when a decision will be made. Further, although the U.S. Supreme Court has not yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act and 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 2030 with the exception of a temporary suspension from May 1, 2020 through March 31, 2021 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 used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule on September 24, 2020, effective

November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. At the state level, legislatures have increasingly passed legislation and implemented 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. It is also possible that additional governmental action will be taken in response to the COVID-19 pandemic.

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.

**Risks Related to Ownership of Our Common Stock**

***An active trading market for our common stock may not be sustained.***

We cannot assure you that an active trading market will continue to develop or be sustained. If an active market for our common stock is not 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 January 1, 2018, our common stock has traded at prices between $0.59 and $14.54 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;

- changes in the structure of healthcare payment systems;
- 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.

***If a significant number of our shares are sold into the market, it 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 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 and, in the case of our affiliates, the restrictions of Rule 144.

***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.

***Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.***

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine. However, this exclusive forum provision would not apply to suits brought to enforce a duty or liability created by the Securities Act or the Exchange Act. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

***We are an "emerging growth company" and a "smaller reporting company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting 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 December 31, 2021.

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.

We are also a "smaller reporting company," meaning that the market value of our shares held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We will continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our shares held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

***We have broad discretion in the use of our cash and cash equivalents and may invest or spend our cash in ways with which investors do not agree.***

We have broad discretion over the use of our cash and cash equivalents. Investors may not agree with our decisions, and our use of our cash may not yield any return on investment. Our failure to apply our resources effectively could compromise our ability to pursue our growth strategy. Investors will not have the opportunity to influence our decisions on how to use our cash and cash equivalents.

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

Investors 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 prior loan agreement prohibited us from paying dividends without the consent of the lenders under the agreement, and we expect that the terms of any future debt agreements would likewise preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be investors' sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

**General Risk Factors**

***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, inadvertent or accidental cyber issues caused by employees or other insiders, or external 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 or compromise 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 incident 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.

***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 2017 comprehensive tax reform bill, as modified by the CARES Act, and possible future changes in tax laws or regulations could adversely affect our business and financial condition.***

On December 22, 2017, President Trump signed into law the Tax Act, which significantly revised the Internal Revenue Code of 1986, as amended. In March 2020, the Tax Act was modified in certain respects by the CARES Act. Future guidance from the U.S. Internal Revenue Service and other tax authorities with respect to the Tax Act, as modified by the CARES Act, may affect us, and certain aspects of the Tax and CARES Act could be repealed or modified in future legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our U.S. operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act, the CARES Act, or future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges in the current or future taxable years, and could increase our future U.S. tax expense. The foregoing items, as well as any other future changes in tax laws, could have a material adverse effect on our business, cash flow, financial condition, or results of operations. In addition, it is uncertain if and to what extent various states will conform to the Tax Act and CARES Act or any newly enacted federal tax legislation.

***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 in which 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 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, 2020, we had approximately $232.7 million of federal and $40.7 million of state net operating loss, or NOL, carryforwards. If not utilized, the portion of these federal NOL carryforwards arising in tax years beginning before 2018 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. Under the Tax Act, as modified by the CARES Act, federal net operating losses incurred in taxable years beginning in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited for taxable years beginning after 2020. It is uncertain how various states will respond to the changes to the federal NOL rules included in the Tax Act and CARES Act. 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 stock ownership change of more than 50% over a three-year period. The completion of our IPO, follow-on public offerings, 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 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. At the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023.

***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.

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 incur significant costs and demands upon management as a result of being a public company.***

As a public company listed in the United States, we incur significant legal, accounting and other costs, which we expect to increase, especially after we cease to be an emerging growth company under SEC rules. 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 is listed on The Nasdaq Global Market under the symbol "CLSD".

**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.

**Stockholders**

As of March 10, 2021, we had 57,422,475 shares of common stock outstanding held by 11 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.

**Recent Sales of Unregistered Securities**

None.

**Purchases of Equity Securities by the Issuer and Affiliated Parties**

None.

**ITEM 6. SELECTED FINANCIAL DATA**

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

## 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 biopharmaceutical company dedicated to developing and delivering treatments that restore and preserve vision for people with serious back of the eye diseases. Our proprietary SCS Microinjector targeting the suprachoroidal space, or SCS, offers unique access to the macula, retina and choroid where sight-threatening disease often occurs. Our SCS injection platform is an inherently flexible, in-office, non-surgical procedure intended to provide targeted delivery to the site of disease and to work with both established and new formulations of medications, as well as future therapeutic innovations.

We are leveraging our SCS injection platform by building an internal research and development pipeline targeting retinal diseases and by creating external collaborations with other companies. Using our suprachoroidal injection technology in conjunction with proprietary formulations of existing drugs as well as novel therapies, we believe that we have created a broad therapeutic platform for developing product candidates to treat serious eye diseases.

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, conducting preclinical studies and clinical trials and undertaking other research and development initiatives. To date, we have not generated any revenue, other than license and other revenue generated from collaboration agreements, 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, 2020, we had an accumulated deficit of $255.9 million. We recorded net losses of $18.2 million, $30.8 million and $82.8 million for the years ended December 31, 2020, 2019 and 2018, 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 of our product candidates, as well as discovering compounds and developing proprietary solutions to utilize with our SCS Microinjector.

We expect to continue to incur significant and increasing operating losses at least for the next several years. We do not expect to generate significant product or license and other revenue unless and until we successfully complete necessary development of, obtain regulatory approval for and successfully commercialize one or more of our product candidates, either on our own or together with a third party. 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. Our clinical trial expenses have decreased significantly following our decision to discontinue late-stage clinical trials of XIPERE for indications other than uveitis. However, we will continue our efforts to seek to discover, research and develop additional product candidates and seek regulatory approvals in additional regions for XIPERE for the treatment of macular edema associated with uveitis. We have advanced our proprietary suspension of axitinib, which we refer to as CLS-AX, into clinical development, and if these trials are successful, we anticipate an increase in clinical trial expenses as we continue further development of that product candidate.

### 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, either on our own or with a third party. Our revenue in recent years has been generated primarily from our license agreements. We are seeking to enter into additional license and other agreements with third parties to evaluate the potential use of our proprietary SCS Microinjector with the third party's product candidates for the treatment of various eye diseases. These agreements may include payments to us for technology access, upfront license payments, regulatory and commercial milestone payments and royalties.

***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 clinical trials;
- costs associated with submitting regulatory approval applications for our product candidates;
- costs associated with training physicians on the suprachoroidal injection procedure and educating and providing them with appropriate product candidate information;
- 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. These costs include preclinical activities, such as manufacturing and stability and toxicology studies, that are supportive of a product candidate itself. In addition, there are expenses related to clinical trials and similar activities for each program, including costs associated with CROs. Clinical costs 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 support more than one development program or activity, such as salaries, share-based compensation and depreciation, are not classified as direct preclinical costs or clinical costs and are separately classified as unallocated.

The following table shows our research and development expenses by type of activity for the years ended December 31, 2020, 2019 and 2018.

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2020** | **2019** | **2018** |
| | (in thousands) | | |
| XIPERE (uveitis program) | $ 3,841 | $ 2,947 | $ 8,803 |
| XIPERE (RVO program) | 84 | 2,323 | 44,432 |
| XIPERE (DME program) | — | (133) | 3,062 |
| CLS-AX (wet AMD program) | 2,169 | 67 | 3 |
| Total program expense | 6,094 | 5,204 | 56,300 |
| Unallocated | 8,979 | 10,454 | 11,991 |
| Total research and development expense | $ 15,073 | $ 15,658 | $ 68,291 |

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.

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. 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 XIPERE and the SCS Microinjector for clinical trials and for requirements associated with regulatory filings associated with approval;
- the 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 potential impact of the COVID-19 pandemic on the enrollment in, and timing of, our clinical trials;
- 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 product 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 historically included commercial pre-launch preparations for XIPERE, and also include facility related costs not otherwise included in research and development expenses, as well as professional fees for legal, patent, consulting, and accounting and audit services.

***Other Income (Expense)***

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

Other expense consists of interest expense incurred under our loan agreements.

**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, in accordance with U.S. GAAP, as those 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.

***Revenue recognition***

On January 1, 2018, we adopted Accounting Standards Update, or ASU, 2014-09, *Revenue from Contracts with Customers (Topic 606)*, or ASC 606, as amended by ASU 2016-08, 2016-10, 2016-12 and 2016-20 using the modified retrospective method. Under ASC 606, we recognize revenue in an amount that reflects the consideration to which we expect to be entitled in exchange for the transfer of promised goods or services to customers. To determine revenue recognition for contracts with customers that are within the scope of ASC 606, we perform the following steps: (1) identify the contract with the customer, (2) identify the performance obligations in the contract, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations in the contract, and (5) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services transferred to the customer.

As part of the accounting for our revenue arrangements, we develop assumptions that require judgment such as the estimate of the stand-alone selling price for each performance obligation identified in the contract.

*Licenses of intellectual property:* If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promised goods or services, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

*Milestone Payments:* At the inception of each arrangement that includes development, commercialization, and regulatory milestone payments, we evaluate whether the achievement of the milestones is considered probable and estimate the amount to be included in the transaction price using the most likely amount method. Performance milestone payments represent a form of variable consideration. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Achievement of milestones that are not within our or our licensee's control, such as regulatory approvals, are not considered probable until the approvals are achieved. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis and we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

*Manufacturing Supply Services:* Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer's discretion are generally considered options. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations at the outset of the arrangement.

*Royalties:* For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not received any royalty revenue resulting from any of our licensing arrangements.

***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.

***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. Share-based compensation costs are expensed on a straight-line basis over the relevant vesting period. The fair value of restricted stock units, or RSUs, granted is measured based on the market value of our common stock on the date of grant and is recognized ratably over the requisite service period, which is generally the vesting period of the awards. 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 estimate 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.* 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.* We calculate expected volatility based on the historical volatility of our common stock.
- *Expected term.* We use 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, the employee stock purchase plan and RSUs aggregated $3.6 million, $4.6 million and $4.8 million for the years ended December 31, 2020, 2019 and 2018, respectively.

***Tax valuation allowance***

We recorded aggregate deferred tax assets of $63.4 million, primarily related to our net operating losses, as of December 31, 2020, 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 for the period from our inception through December 31, 2020. We incurred a net loss for tax purposes of $12.3 million for the year ended December 31, 2020. 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, 2020, we had federal NOL carryforwards of $232.7 million and state NOL carryforwards of $40.7 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, 2020 and 2019**

The following table sets forth our results of operations for the years ended December 31, 2020 and 2019.

| | Year Ended December 31, | | Period-to-Period Change |
|---|---|---|---|
| | 2020 | 2019 | |
| | (in thousands) | | |
| License and other revenue | $ 7,894 | $ 2,173 | $ 5,721 |
| Operating expenses: | | | |
| Research and development | 15,073 | 15,658 | (585) |
| General and administrative | 10,756 | 16,819 | (6,063) |
| Total operating expenses | 25,829 | 32,477 | (6,648) |
| Loss from operations | (17,935) | (30,304) | 12,369 |
| Other expense | (275) | (466) | 191 |
| Net loss | $ (18,210) | $ (30,770) | $ 12,560 |

*Revenue*. In the years ended December 31, 2020 and 2019 we recognized $7.7 million and $2.1 million, respectively, of revenue associated with our license agreements. In the years ended December 31, 2020 and 2019, we recognized $0.2 million and $0.1 million, respectively, of revenue associated with other agreements to evaluate the potential use of our proprietary SCS Microinjector with third-party product candidates for the treatment of various diseases.

*Research and development*. Research and development expense decreased by $0.6 million, from $15.7 million for the year ended December 31, 2019 to $15.1 million for the year ended December 31, 2020. This decrease was primarily attributable to the $2.2 million in costs incurred during the year ended December 31, 2019 to close down the SAPPHIRE and TOPAZ trials. Additionally, there was a $0.9 million decrease in employee-related costs and a $0.2 million decrease in travel costs between the periods. These decreases were partially offset by a $3.0 million increase in costs related to device and drug manufacturing for XIPERE and CLS-AX, as well as the initial startup costs for the Phase 1/2a clinical trial of CLS-AX referred to as OASIS.

*General and administrative*. General and administrative expenses decreased by $6.1 million, from $16.8 million for the year ended December 31, 2019 to $10.8 million for the year ended December 31, 2020. This decrease was primarily attributable to a $4.1 million reduction in marketing-related expenses related to the change of our business strategy to seek partners for XIPERE rather than commercializing XIPERE on our own, a decrease of $1.4 million of employee-related costs due to expenses incurred in the prior year primarily related to the departure of our former chief executive officer and a $0.9 million decrease in professional fees.

*Other expense*. Other expense for each of the years ended December 31, 2020 and 2019 primarily consisted of interest on long-term debt, the amortization of financing costs, the accretion of warrants and the final payment related to our loan agreements. The decrease in other expense for the year ended December 31, 2020 as compared to the year ended December 31, 2019 is primarily due to lower costs on our loan agreement that we prepaid in full in May 2020.

**Results of Operations for the Years Ended December 31, 2019 and 2018**

The following table sets forth our results of operations for the years ended December 31, 2019 and 2018.

| | Year Ended December 31, | | Period-to-Period Change |
|---|---|---|---|
| | 2019 | 2018 | |
| | (in thousands) | | |
| License and other revenue | $ 2,173 | $ 30 | $ 2,143 |
| Operating expenses: | | | |
| Research and development | 15,658 | 68,291 | (52,633) |
| General and administrative | 16,819 | 14,684 | 2,135 |
| Total operating expenses | 32,477 | 82,975 | (50,498) |
| Loss from operations | (30,304) | (82,945) | 52,641 |
| Other (expense) income | (466) | 127 | (593) |
| Net loss | $ (30,770) | $ (82,818) | $ 52,048 |

*Revenue*. In the year ended December 31, 2019 we recognized $2.1 million of revenue associated with our license agreements. In the years ended December 31, 2019 and 2018, we recognized $0.1 million and $30,000, respectively, of revenue associated with other agreements.

*Research and development*. Research and development expense decreased by $52.6 million, from $68.3 million for the year ended December 31, 2018 to $15.7 million for the year ended December 31, 2019. This was primarily attributable to a $42.1 million decrease due to closing down the SAPPHIRE and TOPAZ trials. Additionally, there was a $4.6 million decrease due to the completion of the PEACHTREE trial during the first quarter of 2018, a $3.2 million decrease in costs related to our DME program, as the TYBEE trial was completed in the second quarter of 2018, a $1.2 million decrease in costs related to device and drug manufacturing, a $0.6 million decrease in costs related to quality assurance as audits related to our NDA filing were completed during 2018 and a $1.4 million decrease in regulatory expenses as the NDA submission for XIPERE was completed in the fourth quarter of 2018. These decreases were partially offset by a $0.4 million increase in employee-related costs and a $0.5 million increase in nonclinical activities.

*General and administrative*. General and administrative expenses increased by $2.1 million, from $14.7 million for the year ended December 31, 2018 to $16.8 million for the year ended December 31, 2019. The increase was primarily attributable to a $1.9 million increase in employee-related costs, including accrued expenses related to the resignation of our former CEO, and an increase of $0.9 million in professional fees. These increases were partially offset by a $0.4 million decrease that was primarily attributable to marketing-related expenses related to the change of our business strategy to seek partners for XIPERE rather than commercialize it on our own.

*Other (expense) income*. The decrease from other income of $0.1 million in 2018 to other expense of $0.5 million in 2019 was the result of higher interest income on short-term investment balances in the first quarter of 2018 following our public offering of common stock, which balances decreased over time.

**Liquidity and Capital Resources**

***Sources of Liquidity***

We have funded our operations primarily through the proceeds of public offerings of our common stock, sales of convertible preferred stock and the issuance of long-term debt. As of December 31, 2020, we had cash and cash equivalents of $17.3 million. We invest any cash in excess of our immediate requirements primarily with a view to liquidity and capital preservation. As of December 31, 2020, our funds were held in cash and money market funds.

On January 6, 2021, we entered into a securities purchase agreement with certain institutional purchasers pursuant to which we issued and sold 4.2 million shares of our common stock in a registered direct offering at a price of $2.851 per share. We raised net cash proceeds of $11.1 million after deducting offering expenses.

During the year ended December 31, 2020, we sold 6.2 million shares of our common stock for net proceeds of $12.0 million under the at-the-market, or ATM, agreement, Cowen and Company LLC, or Cowen. Under the ATM agreement, we may offer and

sell, from time to time at our sole discretion, shares of our common stock through Cowen acting as our sales agent. As of December 31, 2020, there was $27.0 million available for future sales under the ATM agreement. Subsequent to December 31, 2020, we sold 1.2 million shares of our common stock for net proceeds of $3.3 million.

In September 2020, we received $3.0 million in milestone payments under the REGENXBIO agreement.

On April 20, 2020, we entered into a loan agreement with Silicon Valley Bank under the terms of which Silicon Valley Bank loaned us $1.0 million, or the PPP Loan, pursuant to the Paycheck Protection Program, or PPP, under the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act. In accordance with the requirements of the CARES Act, we used the proceeds primarily for payroll costs and other eligible expenses. The CARES Act and the PPP provided a mechanism for forgiveness of up to the full amount borrowed. On January 11, 2021, we received notification from Silicon Valley bank that the full amount borrowed under the PPP Loan and approximately $7,000 of accrued interest was forgiven.

On March 10, 2020, we entered into the Arctic License Agreement, under which Arctic Vision has agreed to pay us up to a total of $35.5 million. This amount includes an upfront payment of $4.0 million, which we received in March 2020, as well as an aggregate of up to $31.5 million in potential development milestone payments for specified events prior to and including receipt of regulatory approval of XIPERE in the United States and potential sales milestone payments for achievement of specified levels of net sales. Further, during the applicable royalty term, we will also be entitled to receive tiered royalties of 10-12% of net sales in the Arctic Territory, subject to customary reductions.

We previously entered into a loan and security agreement with Silicon Valley Bank and MidCap Financial Services, or collectively the Lenders, under which we borrowed $10.0 million in May 2018. In October 2019, we repaid $5.0 million of the outstanding principal balance. Under the loan agreement, we were required to pay accrued interest only on the $5.0 million remaining outstanding balance through October 31, 2020, followed by consecutive equal monthly payments of principal and interest in arrears continuing through the maturity date of October 1, 2022. We had the option to prepay the outstanding balance in full, subject to a prepayment fee. In May 2020, we prepaid in full the outstanding $5.0 million principal balance, plus $0.3 million reflecting a final payment fee and accrued interest. The prepayment fees were waived by the Lenders.

***Funding Requirements***

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, ongoing costs related to our NDA submission for XIPERE, research and development costs to build our product candidate pipeline, 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 XIPERE or any future product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from product sales. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

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

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license and development agreements. Other than potential payments we may receive under our license and other agreements, we do not currently have any committed external source of funds, though, as described above, we may also be able to sell our common stock under the ATM agreement with Cowen subject to the terms of that agreement and depending on market conditions. We expect that we will require additional capital to fund our ongoing operations. Additional funds may not be available to us on a timely basis, on commercially reasonable terms, or at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. 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 funds through additional collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, including any future collaboration or licensing arrangement for XIPERE outside the U.S. and Canada, we may be required to relinquish additional 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, including costs and expenses for fees to members of our board of directors, accounting and finance personnel costs, 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***

We have suffered recurring losses and negative cash flows from operations since inception and anticipate incurring additional losses until such time, if ever, that we can obtain FDA approval to market and then generate significant royalties from XIPERE and other licensing arrangements or revenues from other product candidates. We will need additional financing to fund our operations. These conditions raise substantial doubt about our ability to continue as a going concern within one year after the date of this report. Our plans primarily consist of raising additional capital, potentially in a combination of equity or debt financings or restructurings, or potentially entering into additional collaborations, partnerships and other strategic arrangements.

Based on our current plans and forecasted expenses, we expect that our cash and cash equivalents as of the filing date, March 15, 2021, will enable us to fund our planned operating expenses and capital expenditure requirements into the first quarter of 2022. This estimate does not give effect to additional development milestone payments we might receive under the agreements with Bausch, REGENXBIO or Arctic Vision or in connection with any other potential license or collaboration agreement for XIPERE or any future product candidates. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our capital resources sooner than we expect.

Our financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result should we be unable to continue as a going concern.

***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, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| | (in thousands) | | |
| Net cash (used in) provided by: | | | |
| Operating activities | $ (13,120) | $ (27,068) | $ (79,200) |
| Investing activities | (55) | 32,925 | (3,760) |
| Financing activities | 7,867 | 8,695 | 81,779 |
| Net change in cash and cash equivalents | $ (5,308) | $ 14,552 | $ (1,181) |

During the years ended December 31, 2020, 2019 and 2018, our operating activities used net cash of $13.0 million, $27.1 million and $79.2 million, respectively. The use of cash in each period primarily resulted from our net losses.

The decrease in the net loss for the year ended December 31, 2020 as compared to the year ended December 31, 2019 was primarily attributable to lower research and development expenses as a result of the discontinuation of the SAPPHIRE and TOPAZ trials and ceasing of commercialization activities in 2019. The losses were partially offset by non-cash items, made up primarily of share-based compensation, of $3.6 million and $4.6 million for the years ended December 31, 2020 and 2019, respectively.

The decrease in net loss for the year ended December 31, 2019 as compared to the year ended December 31, 2018 was primarily attributable to lower research and development expenses as a result of the completion of the PEACHTREE and TYBEE trials in the prior year and the discontinuation of the SAPPHIRE and TOPAZ trials. The year ended December 31, 2019 also included a net cash outflow of $5.1 million from a decrease in accounts payable, which was the result of payments we made in connection with winding down the clinical trials.

The increase in net loss for the year ended December 31, 2018 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. In addition, for the year ended December 31, 2018, we incurred regulatory costs in preparation for an NDA submission and costs associated with the planned commercialization of XIPERE.

In the year ended December 31, 2020, our investing activities used net cash of $55,000 for the purchase of machinery and equipment. In the year ended December 31, 2019, net cash provided by investing activities of $32.9 million consisted of maturities of short-term available-for-sale investments. In the year ended December 31, 2018, net cash used in investing activities of $3.8 million was primarily for the purchase of $80.1 million of short-term, available-for-sale investments, which included commercial paper and treasury bills, offset by the maturities of $76.5 million of short-term, available-for-sale investments, which included corporate bonds, commercial paper and treasury bills and $88,000 for the purchase of furniture and fixtures.

During the years ended December 31, 2020, 2019 and 2018, our net cash provided by financing activities was $7.9 million, $8.7 million and $81.8 million, respectively. The net cash provided by financing activities for the year ended December 31, 2020 was primarily comprised of $12.0 million of net proceeds from the sale of shares of common stock under the ATM agreement and $1.0 million of proceeds from the PPP Loan, partially offset by the full prepayment of the remaining $5.3 million owed under our loan agreement. The net cash provided by financing activities for the year ended December 31, 2019 was primarily comprised of $10.3 million of net proceeds from sales of common stock pursuant to our ATM agreement and $3.3 million of net proceeds from a private placement of common stock, partially offset by a $5.0 million principal payment made under our Loan Agreement. The net cash provided by financing activities for the year ended December 31, 2018 was primarily comprised of the $79.6 million of net proceeds received from a public follow-on offering of our common stock in March 2018, $1.7 million of net proceeds received from the Loan Agreement and $0.5 million of proceeds received from shares issued from the exercise of stock options and the employee stock purchase plan.

**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**

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**Index to financial statements**

## 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, 2020 and 2019, and the related statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

**The Company's Ability to Continue as a Going Concern**

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses, negative cash flows from operations, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

**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 15, 2021

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

| | December 31, 2020 | December 31, 2019 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 17,287 | $ 22,595 |
| Prepaid expenses | 722 | 1,139 |
| Other current assets | 109 | 1,485 |
| Total current assets | 18,118 | 25,219 |
| Property and equipment, net | 416 | 541 |
| Operating lease right-of-use asset | 528 | 656 |
| Restricted cash | 260 | 360 |
| Total assets | $ 19,322 | $ 26,776 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 1,997 | $ 1,280 |
| Accrued liabilities | 1,582 | 2,930 |
| Current portion of long-term debt | 991 | 1,333 |
| Current portion of operating lease liabilities | 373 | 360 |
| Deferred revenue | 5,000 | 5,000 |
| Total current liabilities | 9,943 | 10,903 |
| Long-term debt | — | 3,819 |
| Operating lease liabilities | 616 | 897 |
| Total liabilities | 10,559 | 15,619 |
| Commitments and contingencies | | |
| Stockholders' equity: | | |
| Preferred stock, $0.001 par value; 10,000,000 shares authorized and no shares issued at December 31, 2020 and 2019 | — | — |
| Common stock, $0.001 par value; 100,000,000 shares authorized at December 31, 2020 and 2019; 51,860,941 and 44,413,372 shares issued and outstanding at December 31, 2020 and 2019, respectively | 52 | 44 |
| Additional paid-in capital | 264,578 | 248,770 |
| Accumulated deficit | (255,867) | (237,657) |
| Total stockholders' equity | 8,763 | 11,157 |
| Total liabilities and stockholders' equity | $ 19,322 | $ 26,776 |

*See accompanying notes to the financial statements*

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| License and other revenue | $ 7,894 | $ 2,173 | $ 30 |
| Operating expenses: | | | |
| Research and development | 15,073 | 15,658 | 68,291 |
| General and administrative | 10,756 | 16,819 | 14,684 |
| Total operating expenses | 25,829 | 32,477 | 82,975 |
| Loss from operations | (17,935) | (30,304) | (82,945) |
| Other (expense) income | (275) | (466) | 127 |
| Net loss | $ (18,210) | $ (30,770) | $ (82,818) |
| Net loss per share of common stock — basic and diluted | $ (0.39) | $ (0.81) | $ (2.69) |
| Weighted average shares outstanding — basic and diluted | 46,506,540 | 38,170,830 | 30,733,600 |

*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 |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| Balance at December 31, 2017 | 25,354,651 | $ 25 | $ 145,618 | $ (124,220) | $ (8) | $ 21,415 |
| Cumulative effect of accounting change | — | — | — | 151 | 8 | 159 |
| Issuance of common shares under follow-on offering | 6,548,712 | 7 | 79,557 | — | — | 79,564 |
| Issuance of common shares under employee stock purchase plan | 12,595 | — | 50 | — | — | 50 |
| Exercise of stock options | 203,269 | — | 465 | — | — | 465 |
| Share-based compensation expense | — | — | 4,785 | — | — | 4,785 |
| Net loss | — | — | — | (82,818) | — | (82,818) |
| Balance at December 31, 2018 | 32,119,227 | 32 | 230,475 | (206,887) | — | 23,620 |
| Issuance of common shares under at-the-market sales agreement | 8,976,940 | 9 | 10,310 | — | — | 10,319 |
| Issuance of common shares under private placement | 3,178,367 | 3 | 3,321 | — | — | 3,324 |
| Issuance of common shares under employee stock purchase plan | 52,476 | — | 45 | — | — | 45 |
| Exercise of stock options | 16,362 | — | 7 | | — | 7 |
| Vesting and settlement of restricted stock units | 70,000 | — | — | — | — | — |
| Share-based compensation expense | — | — | 4,612 | — | — | 4,612 |
| Net loss | — | — | — | (30,770) | — | (30,770) |
| Balance at December 31, 2019 | 44,413,372 | 44 | 248,770 | (237,657) | — | 11,157 |
| Issuance of common shares under at-the-market sales agreement | 6,176,415 | 6 | 11,952 | — | — | 11,958 |
| Issuance of common shares under employee stock purchase plan | 35,359 | — | 31 | — | — | 31 |
| Exercise of stock options | 254,466 | 2 | 225 | — | — | 227 |
| Vesting and settlement of restricted stock units | 981,329 | — | — | — | — | — |
| Share-based compensation expense | — | — | 3,600 | — | — | 3,600 |
| Net loss | — | — | — | (18,210) | — | (18,210) |
| Balance at December 31, 2020 | 51,860,941 | $ 52 | $ 264,578 | $ (255,867) | $ — | $ 8,763 |

*See accompanying notes to the financial statements.*

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| **Operating activities** | | | |
| Net loss | $ (18,210) | $ (30,770) | $ (82,818) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Depreciation | 180 | 211 | 189 |
| Share-based compensation expense | 3,600 | 4,612 | 4,785 |
| Non-cash interest expense | 59 | 163 | 154 |
| Accretion of debt discount | 129 | 67 | 112 |
| Loss on disposal of fixed assets | — | 63 | — |
| Amortization and accretion on available-for-sale investments, net | — | (115) | (748) |
| Changes in operating assets and liabilities: | | | |
| Prepaid expenses and other current assets | 1,893 | (558) | (505) |
| Other assets and liabilities | (140) | (159) | (55) |
| Accounts payable and accrued liabilities | (631) | (5,582) | (314) |
| Deferred revenue | — | 5,000 | — |
| Net cash used in operating activities | (13,120) | (27,068) | (79,200) |
| **Investing activities** | | | |
| Maturities of available-for-sale-investments | — | 32,950 | 76,470 |
| Purchase of available-for-sale investments | — | — | (80,142) |
| Acquisition of property and equipment | (55) | (25) | (88) |
| Net cash (used in) provided by investing activities | (55) | 32,925 | (3,760) |
| **Financing activities** | | | |
| Proceeds from at-the-market sales agreement, net of issuance costs | 11,958 | 10,319 | — |
| Proceeds from private placement, net of issuance costs | — | 3,324 | — |
| Proceeds from follow-on offering, net of issuance costs | — | — | 79,564 |
| Proceeds from exercise of stock options | 227 | 7 | 465 |
| Proceeds from shares issued under employee stock purchase plan | 31 | 45 | 50 |
| Proceeds from issuance of long-term debt | 991 | — | 10,000 |
| Principal payments made on long-term debt | (5,340) | (5,000) | (8,300) |
| Net cash provided by financing activities | 7,867 | 8,695 | 81,779 |
| Net (decrease) increase in cash, cash equivalents and restricted cash | (5,308) | 14,552 | (1,181) |
| Cash, cash equivalents and restricted cash, beginning of period | 22,955 | 8,403 | 9,584 |
| Cash, cash equivalents and restricted cash, end of period | $ 17,647 | $ 22,955 | $ 8,403 |
| **Supplemental disclosure** | | | |
| Interest paid | $ 524 | $ 843 | $ 751 |

**Reconciliation of cash, cash equivalents and restricted cash:**

| | December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| Cash and cash equivalents | $ 17,287 | $ 22,595 | $ 8,043 |
| Restricted cash | 360 | 360 | 360 |
| Cash, cash equivalents and restricted cash at end of period | $ 17,647 | $ 22,955 | $ 8,403 |

*See accompanying notes to the financial statements.*

**CLEARSIDE BIOMEDICAL, INC.**

**Notes to the Financial Statements**

## 1. The Company

Clearside Biomedical, Inc. (the "Company") is a biopharmaceutical company dedicated to developing and delivering treatments that restore and preserve vision for people with serious back of the eye diseases. The Company's proprietary SCS Microinjector targeting the suprachoroidal space offers unique access to the macula, retina and choroid where sight-threatening disease often occurs. This suprachoroidal space injection platform is an inherently flexible, in-office, non-surgical procedure, intended to provide targeted delivery to the site of disease and to work with both established and new formulations of medications, as well as future therapeutic innovations such as gene therapy. 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, either on its own or with a third party. The Company is subject to a number of risks and uncertainties similar to those of other life science companies at a similar stage of development, including, among others, the need to obtain adequate additional financing, successful development efforts including regulatory approval of products, compliance with government regulations, successful commercialization of potential products, protection of proprietary technology and dependence on key individuals.

***Liquidity***

The Company had cash and cash equivalents of $17.3 million as of December 31, 2020. On January 6, 2021, the Company entered into a securities purchase agreement with certain institutional purchasers that purchased 4.2 million shares of its common stock in a registered direct offering at a price of $2.851 per share. The Company raised net proceeds of $11.1 million after deducting offering expenses. In addition, subsequent to December 31, 2020, the Company sold 1.2 million shares of its common stock for net proceeds of $3.3 million under its at-the-market agreement with Cowen and Company, LLC.

The Company has funded its operations primarily through the sale of convertible preferred stock and common stock and the issuance of long-term debt. The Company will continue to need to obtain additional financing to fund future operations, including completing the development, partnering and potential commercialization of its primary product candidates. The Company will need to obtain financing to conduct additional trials for the regulatory approval of its product candidates if requested by regulatory bodies, and completing the development of any product candidates that might be acquired. If such products were to receive regulatory approval, the Company would need to obtain additional financing to prepare for the potential commercialization of its product candidates, if the Company decides to commercialize the products on its own.

The Company has suffered recurring losses and negative cash flows from operations since inception and anticipates incurring additional losses until such time, if ever, that it can obtain FDA approval to sell, and then generate significant revenue from commercializing its lead product candidate, XIPERE (triamcinolone acetonide suprachoroidal injectable suspension formulated for administration to the back of the eye), with its licensees. 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.

These conditions raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the financial statements are issued. Based on its current plans and forecasted expenses, the Company expect that its cash and cash equivalents as of the filing date, March 15, 2021, will enable it to fund its planned operating expenses and capital expenditure requirements into the first quarter of 2022. This estimate does not give effect to additional development milestone payments the Company might receive under the agreements with Bausch, REGENXBIO or Arctic Vision or in connection with any other potential license or collaboration agreement for XIPERE or any future product candidates. The Company has based this estimate on assumptions that may prove to be wrong, and it could exhaust its capital resources sooner than expected.

The Company's financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result should the Company be unable to continue as a going concern.

**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 revenue recognition, the accounting for useful lives to calculate depreciation and amortization, clinical trial expense accruals, share-based compensation expense and income tax valuation allowance. Actual results could differ from these estimates.

***Effects of COVID-19***

The COVID-19 pandemic is expected to continue to result in a global slowdown of economic activity. Estimates and assumptions about future events and their effects cannot be determined with certainty and therefore require the exercise of judgment. As of the date of issuance of these financial statements, the Company is not aware of any specific event or circumstance that would require it to update its estimates, assumptions and judgments or revise the carrying value of its assets or liabilities. These estimates may change as new events occur and additional information is obtained and are recognized in the consolidated financial statements as soon as they become known. Actual results could differ from those estimates and any such differences may be material to the financial statements.

***Revenue Recognition***

The Company recognizes revenue from its contracts with customers under Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers* ("ASC Topic 606"). The Company's primary revenue arrangements are license agreements which typically include upfront payments, regulatory and commercial milestone payments and royalties based on future product sales. The arrangements may also include payments for the Company's SCS Microinjector devices as well as payments for assistance and oversight of the customer's use of the Company's technology. In determining the amount of revenue to be recognized under these agreements, the Company performs the following steps: (i) identifies the promised goods and services to be transferred in the contract, (ii) identifies the performance obligations, (iii) determines the transaction price, (iv) allocates the transaction price to the performance obligations and (v) recognizes revenue as the performance obligations are satisfied.

The Company receives payments from its customers based on billing schedules established in each contract. Up-front and other payments may require deferral of revenue recognition to a future period until the Company performs its obligations under the arrangement. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

***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.

***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 for the period from May 26, 2011 (inception) to December 31, 2020. 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.

Liabilities for uncertain tax positions are recognized based on a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. Once it is determined that the position meets the recognition threshold, the second step requires estimating and measuring the largest amount of tax benefit that is more likely than not to be realized upon ultimate settlement. The difference between the amount of recognizable tax benefit and the total amount of tax benefit from positions filed or to be filed with the tax authorities is recorded as a liability for uncertain tax benefits.

***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 preclinical studies and clinical trials;
- costs associated with preclinical and clinical development activities;
- costs associated with submitting regulatory approval applications for the Company's product candidates;
- costs associated with training physicians on the suprachoroidal injection procedure and educating and providing them with appropriate product candidate information;
- 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 expenses.

***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 restricted stock units granted is measured based on the market value of the Company's common stock on the date of grant. Share-based compensation costs are expensed on a straight-line basis 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.

***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, 2020, the restricted cash balance was invested in a commercial money market account. The current portion of the restricted cash is recorded in other current assets and the long-term portion is recorded in restricted cash.

***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 2018, the FASB issued Accounting Standards Update ("ASU") 2018-13, *Fair Value Measurement (Topic 820-10): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which changes the fair value measurement disclosure requirements of ASC Topic 820, *Fair Value Measurements and Disclosures*. Under this ASU, certain disclosure requirements for fair value measurements are eliminated, amended or added. These changes aim to improve the overall usefulness of disclosures to financial statement users and reduce unnecessary costs to companies when preparing the disclosures. The Company adopted ASU 2018-13 on January 1, 2020, and the adoption did not have a material impact on its financial statements and disclosures.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost, including trade receivables. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model that requires the use of forward-looking information to calculate credit loss estimates. The Company adopted ASU 2016-13 on January 1, 2020, and the adoption did not have a material impact on its financial statements and related disclosures.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which simplifies the accounting for income taxes by removing certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. The new ASU also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates. These changes aim to improve the overall usefulness of disclosures to financial statement users and reduce unnecessary costs to companies when preparing the disclosures. The guidance is effective for the Company beginning on January 1, 2021 and prescribes different transition methods for the various provisions. The Company does not expect the adoption of ASU 2019-12 to have a material impact 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) | December 31, 2020 | December 31, 2019 |
|---|---|---|---|
| Furniture and fixtures | 5 | $ 337 | $ 337 |
| Machinery and equipment | 5 | 176 | 121 |
| Computer equipment | 3 | 13 | 13 |
| Leasehold improvements | Lesser of useful life or remaining lease term | 667 | 667 |
| Total property and equipment | | 1,193 | 1,138 |
| Less: Accumulated depreciation | | (777) | (597) |
| Property and equipment, net | | $ 416 | $ 541 |

**4. Accrued Liabilities**

Accrued liabilities consisted of the following (in thousands):

| | December 31, 2020 | December 31, 2019 |
|---|---|---|
| Accrued research and development | $ 234 | $ 359 |
| Accrued employee costs | 1,132 | 1,530 |
| Accrued severance | — | 751 |
| Accrued professional fees | 56 | 58 |
| Accrued expense | 160 | 232 |
| | $ 1,582 | $ 2,930 |

**5. Long-Term Debt**

***Loan and Security Agreements***

On May 14, 2018, the Company entered into a second amended and restated loan and security agreement (the "2nd A&R Loan Agreement") with Silicon Valley Bank ("SVB"), MidCap Funding III Trust and MidCap Financial Trust (together, "MidCap" and collectively with SVB, the "Lenders"). The 2nd A&R Loan Agreement provided for new term loans of up to $20.0 million, with a floating interest rate equal to 6.50% plus the greater of (i) the 30-day U.S. LIBOR, as reported in the Wall Street Journal on the last business day of the month the immediately precedes the month in which the interest will accrue, or (ii) 1.89%. The 2nd A&R Loan Agreement included, among other things, the ability of the Lenders to accelerate the payment of the term loan in the event of a material adverse change and restrictions on the Company's ability to sell, assign, license, transfer or otherwise dispose of its assets, including intellectual property assets, without the prior written consent of the Lenders.

The Company borrowed an initial tranche of $10.0 million on May 14, 2018, of which $7.0 million was used to repay all amounts outstanding under a prior loan agreement, including fees associated with the final payment. The prepayment fees were waived. Of the remaining $10.0 million available under the 2nd A&R loan agreement, the Company elected not to draw $5.0 million and the other $5.0 million was not available for draw.

On October 18, 2019, the Company entered into an amendment to the 2nd A&R Loan Agreement with the Lenders. Pursuant to the amendment, the Company repaid $5.0 million of the outstanding principal balance of the $10.0 million term loan. The Company did not pay any final payment or termination fees in connection with the $5.0 million prepayment. In addition, the Company and the Lenders agreed to modify the term loan repayment schedule. As amended, the term loan repayment schedule provided for interest only payments through October 31, 2020, followed by consecutive equal monthly payments of principal and interest in arrears continuing through the maturity date of October 1, 2022. The Company had the option to prepay the outstanding balance in full, subject to a prepayment fee. A final payment of 5.50% of the aggregate borrowed amount was due at maturity of the loan on October 1, 2022, 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 2nd A&R loan agreement were secured by substantially all of the Company's assets.

On May 7, 2020, due to various restrictions and other limiting covenants of the 2nd A&R Loan Agreement, the Company prepaid in full the outstanding $5.0 million principal balance, plus $0.3 million reflecting the final payment fee and accrued interest. The prepayment fees were waived by the Lenders.

Interest expense on the borrowings under the loan agreements described above was $147,000, $804,000 and $791,000 for the years ended December 31, 2020, 2019 and 2018, respectively. Accretion of the scheduled final payment was $59,000, $163,000 and $154,000 for the years ended December 31, 2020, 2019 and 2018, respectively. Accretion of the deferred closing costs was $129,000, $67,000 and $112,000 for the years ended December 31, 2020, 2019 and 2018, respectively.

**6. CARES Act Paycheck Protection Program Loan**

On April 20, 2020, the Company entered into a loan agreement with SVB (the "PPP Lender") under the terms of which the PPP Lender made a loan to the Company in an aggregate principal amount of $1.0 million (the "PPP Loan") pursuant to the Paycheck Protection Program (the "PPP") under the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act"). The PPP Loan was evidenced by a promissory note (the "Note") containing the terms and conditions for repayment of the PPP Loan.

Under the terms of the Note and the PPP Loan, interest accrued on the outstanding principal amount at the rate of 1.0% per annum. The term of the Note was until April 2022, with the Company obligated to make equal monthly payments of principal and interest, beginning in November 2020 and continuing until the maturity date.

The CARES Act and the PPP provided a mechanism for forgiveness of up to the full amount borrowed. Under the PPP, the Company could apply for forgiveness for all or a portion of the PPP Loan based on a formula that takes into account a number of factors, including the amount of loan proceeds used by the Company during the 24-week period after the loan origination for certain purposes, including payroll costs, interest on certain mortgage obligations, rent payments on certain leases, and certain qualified utility payments, provided that at least 60% of the loan amount has been used for eligible payroll costs; the employer maintaining or rehiring employees and maintaining salaries at certain levels; and other factors. Subject to the other requirements and limitations on loan forgiveness, only loan proceeds spent on payroll and other eligible costs qualified for forgiveness.

As of December 31, 2020, the Company had recorded the $1.0 million principal balance of the PPP Loan in current portion of long-term debt on the balance sheet. On January 11, 2021, the Company was notified by the PPP Lender that the PPP Loan had been forgiven for the full amount borrowed under the PPP Loan as well as approximately $7,000 of accrued interest. In accordance with ASC 405-20, *Extinguishment of Liabilities*, the income from the forgiveness of the amount borrowed amount and the accrued interest will be recognized in the statement of operations as a gain on loan extinguishment in the next reporting period.

**7. Preferred and Common Stock**

The Company's amended and restated certificate of incorporation authorizes the Company to issue 10,000,000 shares of $0.001 par value of preferred stock. As of December 31, 2020 and 2019, there were 10,000,000 shares of preferred stock authorized, none of which were issued and outstanding.

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, 2020 and 2019, there were 51,860,941 and 44,413,372 shares of common stock outstanding, respectively.

**8. Common Stock Warrants**

In September 2016, in connection with a 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 are fully exercisable and expire in September 2026, or earlier upon the occurrence of specified mergers or acquisitions of the Company. The warrants were recorded in equity at the time of issuance and had a remaining life of 5.75 years as of December 31, 2020.

**9. 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 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, 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, 2020, under the 2016 Plan, options to purchase 3,794,184 shares of the Company's common stock were outstanding at a weighted average price of $4.09 per share and 1,068,601 shares remained available for future grant. As of January 1, 2021, the number of shares of common stock that may be issued under the 2016 Plan was automatically increased by 2,074,437 shares, representing 4% of the total number of shares of common stock outstanding on December 31, 2020, increasing the number of shares of common stock available for issuance under the 2016 Plan as of that date to 3,143,038 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, 2020, options to purchase 436,773 shares of the Company's common stock were outstanding under the 2011 Plan at a weighted average exercise price of $2.53 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, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| Research and development | $ 1,183 | $ 1,379 | $ 1,766 |
| General and administrative | 1,574 | 2,728 | 3,004 |
| Total | $ 2,757 | $ 4,107 | $ 4,770 |

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 Black-Scholes option pricing model to calculate the fair value of the underlying common stock for the years ended December 31, 2020, 2019 and 2018.

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| Expected term (years) | 7.00 | 7.00 | 7.00 |
| Expected stock price volatility | 108.13% | 109.49% | 93.08% |
| Risk-free interest rate | 1.52% | 2.49% | 2.87% |
| Expected dividend yield | 0.00% | 0.00% | 0.00% |

*Expected term* (in years): 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 Company calculates expected volatility based on the historical volatility of its common stock.

*Forfeitures:* The Company records forfeitures as they occur.

The following table summarizes the activity related to stock options during the year ended December 31, 2020:

| | Number of Shares | Weighted Average Exercise Price |
|---|---|---|
| Options outstanding at December 31, 2019 | 4,104,450 | $ 4.63 |
| Granted | 1,100,250 | 2.31 |
| Exercised | (254,466) | 0.89 |
| Cancelled/Forfeited | (702,041) | 6.49 |
| Options outstanding at December 31, 2020 | 4,248,193 | 3.95 |
| | | |
| Options exercisable at December 31, 2019 | 2,452,764 | 5.44 |
| | | |
| Options exercisable at December 31, 2020 | 2,355,900 | 4.96 |

The following table provides additional information about the Company's stock options that were outstanding and exercisable at December 31, 2020 (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) |
|---|---|---|---|---|---|---|---|---|
| $0.00 - $2.99 | 2,598,987 | | | 8.12 | 1,011,680 | | | 7.08 |
| $3.00 - $6.99 | 998,120 | | | 6.59 | 725,221 | | | 6.25 |
| $7.00 - $8.99 | 449,308 | | | 6.16 | 432,847 | | | 6.12 |
| $9.00 - $20.84 | 201,778 | | | 6.76 | 186,152 | | | 6.71 |
| | 4,248,193 | $ 3.95 | $ 2,753 | 7.49 | 2,355,900 | $ 4.96 | $ 1,551 | 6.62 |

As of December 31, 2020, the Company had $3.4 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 2.1 years. The weighted average fair values of all stock options granted for the years ended December 31, 2020, 2019 and 2018 was $1.97 per share, $1.09 per share and $5.98 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 31, 2020 was $2.74, which was the closing sale price of the Company's common stock on the Nasdaq Global Market on that date.

***Restricted Stock Units***

The Company has granted restricted stock units ("RSUs") to employees under the 2016 Plan. The shares underlying the RSU awards have vesting terms of two to four years from the date of grant, subject to the employees' continuous service and subject to accelerated vesting in specified circumstances. The fair value of the RSUs granted is measured based on the market value of the Company's common stock on the date of grant and is recognized ratably over the requisite service period, which is generally the vesting period of the awards.

The total share-based compensation expense related to RSUs is reflected in the statements of operations as follows (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| Research and development | $ 375 | $ 177 | $ — |
| General and administrative | 427 | 306 | — |
| Total | $ 802 | $ 483 | $ — |

The following table summarizes the activity related to RSUs during the year ended December 31, 2020:

| | Number of Shares | Weighted Average Grant Date Fair Value |
|---|---|---|
| Non-vested RSUs outstanding at December 31, 2019 | 1,269,300 | $ 0.87 |
| Granted | 486,000 | 2.39 |
| Vested | (981,329) | 0.91 |
| Forfeited | (6,700) | 0.91 |
| Non-vested RSUs outstanding at December 31, 2020 | 767,271 | 1.78 |

As of December 31, 2020, the Company had $1.0 million of unrecognized compensation expense related to the RSUs, which amount is expected to be recognized over a weighted average period of 2.5 years.

***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 number of shares reserved for issuance under the 2016 ESPP will automatically increase on January 1 of each year, 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. The Company's board of directors elected not to increase the shares reserved for issuance on January 1, 2021. The number of shares of common stock available for issuance under the 2016 ESPP as of December 31, 2020 was 570,972 shares.

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 years ended December 31, 2020, 2019 and 2018, the Company issued 35,359, 52,476 and 12,595 shares, respectively, of common stock purchased under the 2016 ESPP.

The share-based compensation expense recognized for the 2016 ESPP is reflected in the statements of operations and comprehensive loss as follows (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| Research and development | $ 19 | $ 11 | $ 5 |
| General and administrative | 22 | 9 | 10 |
| Total | $ 41 | $ 20 | $ 15 |

**10. Income Taxes**

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's net deferred income tax assets consist of the following (in thousands):

| | December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| Deferred tax asset (liability) | | | |
| Net operating loss carryforwards | $ 51,414 | $ 46,305 | $ 41,152 |
| Non-deductible accrued expenses | 263 | 422 | 245 |
| Right-of-use asset | (132) | (138) | - |
| Lease liability | 247 | 264 | - |
| Deferred rent | — | — | 148 |
| Deferred revenue | 1,247 | — | — |
| Stock compensation expense | 2,044 | 1,472 | 899 |
| Depreciation differences | (82) | (94) | (125) |
| Federal tax credits | 8,015 | 7,249 | 6,481 |
| State tax credits | 381 | 623 | 757 |
| Disallowed interest expense | 7 | 99 | — |
| Charitable contributions | — | 4 | 6 |
| Valuation allowance | (63,404) | (56,206) | (49,563) |
| Net deferred tax asset | $ — | $ — | $ — |

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| U.S. federal tax rate | 21.00% | 21.00% | 21.00% |
| State tax rate | 14.28 | — | (0.73) |
| Permanent difference and other | 1.42 | (1.33) | (0.33) |
| Tax credit | 2.89 | 2.06 | 3.96 |
| Valuation allowance | (39.66) | (21.73) | (20.39) |
| ASC 740-10 | (0.26) | — | (4) |
| Impact of federal rate change | — | — | — |
| | 0.33% | 0.00% | 0.00% |

Certain items of income and expense are not reported in tax returns and financial statements in the same year. The tax effect of such temporary differences is reported as deferred income taxes. The measurement of deferred tax assets is reduced, if necessary, by the amount of any tax benefit that, based on available evidence, is not expected to be realized. The Company establishes a valuation allowance for deferred tax assets for which realization is not likely. As of each reporting date, management considers new evidence, both positive and negative, that could affect its view of the future realization of deferred tax assets.

At December 31, 2020, the Company had a valuation allowance of $63.4 million recorded against the benefit of certain deferred tax assets. The valuation allowance was primarily related to federal and state net operating loss ("NOL") carryforwards that, in the judgment of management, are not more likely than not to be realized. In assessing the recoverability of the Company's deferred tax assets, management considered, among other things, its deferred tax liabilities, its historical earnings and losses, projections of future income, and tax-planning strategies available to the Company in the relevant jurisdiction. The Company will release this valuation allowance when management determines that it is more likely than not that its deferred tax asset will be realized.

At December 31, 2020, the Company had income tax NOL carryforwards for federal and state purposes of $232.7 million and $40.7 million, respectively. The Company has recorded a deferred tax asset for both federal and state NOL carryforwards of $48.9 million and $2.5 million, respectively. If not utilized, the federal NOL carryforwards will begin to expire beginning in 2031, and the state NOL carryforwards will begin to expire at various dates beginning in 2027. Additionally, under the 2017 Tax Cuts and Jobs Act, federal net operating losses incurred in 2018 and beyond may be carried forward indefinitely. However, the deductibility of such

federal net operating losses is limited beginning in 2021. Certain states have also adopted the indefinite carryforward period beginning with the 2018 tax year, but state conformity varies state by state.

Liabilities for uncertain tax positions are recognized based on a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. Once it is determined that the position meets the recognition threshold, the second step requires the Company to estimate and measure the largest amount of tax benefit that is more likely than not to be realized upon ultimate settlement. The difference between the amount of recognizable tax benefit and the total amount of tax benefit from positions filed or to be filed with the tax authorities is recorded as a liability for uncertain tax benefits.

The following is a rollforward of the Company's uncertain tax positions (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | **2020** | **2019** |
| Balance of uncertain tax positions at the beginning of the year | $ 2,903 | $ 2,903 |
| Gross increases - tax positions in prior period | 4,665 | — |
| Balance of uncertain tax positions at the end of the year | $ 7,568 | $ 2,903 |

As of December 31, 2020 and 2019, there was $7.6 million and $2.9 million, respectively, of unrecognized tax benefit that if recognized would be in the form of a net operating loss carryforward, which is expected to require a full valuation allowance based on present circumstances. The Company accrued $4.6 million of unrecognized tax benefit and $48,000 of unrecognized tax expenses for the year 2020. The Company recognizes accrued interest related to unrecognized tax expenses and penalties as income tax expense. No significant amounts of interest or penalties have been recorded as of December 31, 2020

Ownership changes, as defined by Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), may limit the amount of net operating losses that a company may utilize to offset future taxable income and taxes payable. Pursuant to Section 382 of the Code, an ownership change occurs when the stock ownership of 5% stockholders increases by more than 50% over a testing period of three years. It is possible that the Company has undergone an ownership change as defined by Section 382 of the Code or that the Company may undergo such a change in the future. Any such ownership change may limit the Company's ability to utilize net operating losses.

The Company is subject to taxation in the United States and certain state jurisdictions. As of December 31, 2020, the Company's tax returns for 2017, 2018 and 2019 are subject to full examination by the tax authorities. As of December 31, 2020, the Company is generally no longer subject to state or local examinations by tax authorities for years before 2017, except to the extent of NOLs generated in prior years claimed on a tax return.

## 11. Commitments and Contingencies

***Lease Commitment Summary***

The Company leases its facilities and some of its equipment under noncancelable operating lease arrangements that expire at various dates through 2023. In November 2016, the Company signed an 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. Operating lease cost 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 space in March 2017.

In August 2018, the Company signed an office lease agreement to lease approximately 3,500 square feet of office space in Berkeley, California for its commercial operations. The lease agreement was for a two-year term with a renewal option for an additional one-year term. The Company did not exercise the renewal option for the Berkeley lease and terminated the lease on December 15, 2019, with no further payments due. The termination of the lease did not have a material impact on the Company's statements of operations. Operating lease cost under this lease was recognized on a straight-line basis over the term of the lease. The Company also paid a pro-rata share of the annual operating expenses associated with the premises.

The Company's operating leases included on the balance sheet are as follows (in thousands):

| | December 31, 2020 |
|---|---|
| Operating lease right-of-use asset | $ 528 |
| Liabilities | |
| Current portion of operating lease liabilities | $ 373 |
| Operating lease liabilities | 616 |
| Total operating lease liabilities | $ 989 |

The Company recognizes a right-of-use asset for the right to use the underlying asset for the lease term, and a lease liability, which represents the present value of the Company's obligation to make payments over the lease term. The renewal option is not included in the calculation of the right-of-use asset and the lease liabilities as the Company has not yet determined if the Alpharetta, Georgia lease will be renewed. The present value of the lease payments is calculated using an incremental borrowing rate as the Company's leases do not provide an implicit interest rate. At December 31, 2020, the Company's incremental borrowing rate was 11.0% and the remaining lease term was 2.75 years.

Minimum lease payments were as follows at December 31, 2020 (in thousands):

| **Year ending December 31,** | |
|---|---|
| 2021 | $ 392 |
| 2022 | 407 |
| 2023 | 316 |
| Total minimum lease payments | 1,115 |
| Less imputed interest | (126) |
| Total operating lease liabilities | $ 989 |

Operating lease cost was $247,000 and $393,000 for the years ended December 31, 2020 and 2019, respectively. Variable lease cost was $95,000 and $83,000 for the years ended December 31, 2020 and 2019, respectively. Short-term lease cost was $12,000 and $20,000 for the years ended December 31, 2020 and 2019, 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.

In May 2018, the Company entered into a manufacturing supply agreement (the "Supply Agreement"), with Gerresheimer Regensburg GmbH, a company incorporated under the laws of Germany ("Gerresheimer"). Gerresheimer will manufacture and supply the Company's proprietary SCS Microinjector. The Company will provide Gerresheimer with a rolling forecast schedule of its projected purchase orders for at least the next four calendar quarters. The Supply Agreement contains an initial five-year term that will automatically renew for successive periods of three years, unless terminated by either party at least 12 months prior to the end of the applicable term.

**12. License and Other Agreements**

*Bausch + Lomb*

On October 22, 2019, the Company entered into a License Agreement with Bausch + Lomb, a division of Bausch Health Companies, Inc. ("Bausch"). Pursuant to the Bausch License Agreement, the Company has granted an exclusive license to Bausch to develop, manufacture, distribute, promote, market and commercialize XIPERE using the Company's proprietary microinjector (the "Device"), as well as specified other steroids, corticosteroids and NSAIDs in combination with the Device ("Other Products," and

together with XIPERE, the "Products"), subject to specified exceptions, in the United States and Canada (the "Original Territory") for the treatment of ophthalmology indications, including non-infectious uveitis.

On April 27, 2020, the Company and Bausch entered into an amendment to the Company's License Agreement with Bausch dated October 22, 2019 (as amended, the "Bausch License Agreement"). Pursuant to the Bausch License Agreement, the Company has granted Bausch an exclusive option (the "Option") to develop, manufacture, distribute, promote, market and commercialize XIPERE in one or more of the following regions: (i) the European Union, including the United Kingdom, (ii) Australia and New Zealand and (iii) South America and Mexico (such regions, the "Additional Regions" and together with the Original Territory, the "Territory"). The Option may be exercised any time before the earlier of regulatory approval of XIPERE in the United States and August 31, 2021.

Pursuant to the Bausch License Agreement, Bausch made an upfront payment of $5.0 million (the "Upfront Payment") in October 2019, which is subject to a refund if the Bausch License Agreement is terminated in specified circumstances. In addition, Bausch has agreed to make additional payments of up to $15.0 million upon the achievement of specified pre-launch development and regulatory milestones (the "Pre-Launch Milestone Payments") and up to an aggregate of $57.3 million in additional milestone payments upon the achievement of (i) specified regulatory approvals for specified additional indications of XIPERE (including certain regulatory and commercial milestones if Bausch exercises its Option in the European Union) and (ii) specified levels of annual net sales (as defined in the Bausch License Agreement). Further, during the applicable royalty term, the Company will also be entitled to receive tiered royalties at increasing percentages, from the high-teens to twenty percent, based on XIPERE achieving certain annual net sales thresholds in the Original Territory, as well as a lower royalty on annual net sales of Other Products in the Original Territory and on annual net sales of XIPERE in the Additional Regions if Bausch exercises its Option, in each case subject to reductions in specified circumstances; provided that the Company will not receive any royalties on the first $45.0 million of cumulative net sales of all products in the Original Territory.

During the term of the Bausch License Agreement, and in the Territory, the Company has agreed not to (i) develop or commercialize XIPERE alone or in combination with an Other Device (as defined in the Bausch License Agreement) in the licensed field, (ii) develop or commercialize any corticosteroid with the Device or an Other Device in the licensed field, (iii) develop or commercialize the Device or an Other Device with any active pharmaceutical ingredient for non-infectious uveitis or macular edema associated with non-infectious uveitis, including with any Other Drug (as defined in the Bausch License Agreement, which are restricted to those steroids, corticosteroids and non-steroidal anti-inflammatory drugs specifically identified in the Bausch License Agreement), (iv) develop or commercialize any Other Drug in combination with the Device and (v) commercialize any Other Device for achieving non-surgical access to the suprachoroidal space where such device is sold as a stand-alone product, subject to specified exceptions. The Bausch License Agreement will expire upon expiration of the royalty terms for all Products and countries in the Territory, with each royalty term for a given Product and country ending on the latest of (i) the date of expiration of the last-to-expire valid claim of any licensed patent rights covering such Product in such country in the Territory, (ii) the date of the loss of regulatory exclusivity for such Product in such country in the Territory, or (iii) ten years from the later of the first sale of such Product in such country in the Territory. For a specified period of time, Bausch may terminate the Bausch License Agreement immediately and have the Upfront Payment refunded if the U.S. Food and Drug Administration (the "FDA") has not approved the Company's New Drug Application ("NDA") for XIPERE by August 31, 2021. Following the payment of the Pre-Launch Milestone Payments, Bausch may also terminate the Bausch License Agreement for convenience upon 180 days' written notice. In addition, the Company can terminate the Bausch License Agreement if Bausch commences a legal action challenging the validity, enforceability or scope of any of the licensed patents. If the FDA requires an additional clinical trial prior to approving the NDA for XIPERE and the Company notifies Bausch that the Company will not conduct the trial at the Company's expense, then Bausch may terminate the Bausch License Agreement and have the Upfront Payment refunded within 60 days of the receipt of such notice from the Company. Both parties may terminate the Bausch License Agreement (i) upon a material breach of the Bausch License Agreement, subject to a specified cure period and specified exceptions, or (ii) if the other party encounters bankruptcy or insolvency. Upon termination (other than for a material breach by or bankruptcy or insolvency event of the Company), all licenses and other rights granted by the Company to Bausch pursuant to the Bausch License Agreement would revert to the Company.

The Company is responsible for all development expenses for XIPERE in the Original Territory until the NDA is approved by the FDA, subject to specified exceptions, as well as manufacturing costs in connection with the NDA. The Company is also responsible for all clinical and development expenses conducted to satisfy the FDA's requests in the complete response letter issued on October 18, 2019 related to the NDA and any subsequent complete response letter related to the NDA (the "CRL-related expenses"). If XIPERE is approved by the FDA, Bausch will be responsible for all expenses following such approval; provided that the Company will be responsible for the CRL-related expenses and for one-half of the costs of any post-approval clinical trials required by the FDA, up to a specified maximum amount.

Due to the refund provisions in the License Agreement, the upfront payment of $5.0 million received from Bausch was included on the balance sheet as deferred revenue as of December 31, 2020 and 2019 and will remain in deferred revenue until the refund provisions lapse.

*REGENXBIO, Inc.*

On August 29, 2019, the Company entered into an option and license agreement with REGENXBIO, Inc. ("REGENXBIO") pursuant to which the Company granted REGENXBIO an exclusive option to enter into a commercial license agreement (the "Option"), which grants REGENXBIO an exclusive, worldwide and sublicensable license to the Company's SCS Microinjector for the delivery of adeno-associated virus-based gene therapies for the treatment of wet age-related macular degeneration, diabetic retinopathy and other conditions for which anti-vascular endothelial growth factor treatment is currently the standard of care. REGENXBIO exercised the Option in October 2019 and paid the Company an option fee equal to $2.0 million, less a credit of $0.5 million previously received under a technology access agreement. In addition, REGENXBIO has agreed to pay the Company up to an aggregate of $34.0 million in milestone payments upon the achievement of specified development milestones and up to an aggregate of $102.0 million in sales-based milestone payments, as well as mid-single digit royalties on net sales of products using the SCS Microinjector during the royalty term. In September 2020, the Company received $3.0 million in milestone payments under the Option.

*Arctic Vision (Hong Kong) Limited*

On March 10, 2020, the Company entered into a License Agreement (the "License Agreement") with Arctic Vision (Hong Kong) Limited ("Arctic Vision"). Pursuant to the License Agreement, the Company has granted an exclusive license to Arctic Vision to develop, distribute, promote, market and commercialize XIPERE, subject to specified exceptions, in China, Hong Kong, Macau, Taiwan and South Korea (the "Territory"). Under the terms of the License Agreement, neither party may commercialize XIPERE in the other party's territory. Arctic Vision has agreed to use commercially reasonably efforts to pursue development and commercialization of XIPERE for indications associated with uveitis in China, Hong Kong, Macau, Taiwan and South Korea (the "Arctic Territory"). In addition, upon receipt of the Company's consent, Arctic Vision will have the right, but not the obligation, to develop and commercialize XIPERE for additional indications in the Arctic Territory.

Pursuant to the License Agreement, Arctic Vision has agreed to pay the Company up to a total of $35.5 million. This amount includes an upfront payment of $4.0 million as well as an aggregate of up to $31.5 million in development milestone payments for specified events prior to and including receipt of approval of XIPERE in the United States and sales milestone payments for achievement of specified levels of net sales. Further, during the applicable royalty term, the Company will also be entitled to receive tiered royalties of ten to twelve percent of net sales based on achieving certain annual net sales thresholds in the Territory, subject to customary reductions, payable on a product-by-product and country-by-country basis, commencing at launch in such country and lasting until the latest of (i) the date that all valid claims within the licensed patent rights covering XIPERE have expired, (ii) the date of the loss of marketing or regulatory exclusivity of XIPERE in a given country, or (iii) ten years from the first commercial sale of XIPERE in a given country. In March 2020, the Company received an upfront payment of $4.0 million under the License Agreement.

*Other*

The Company periodically enters into short-term agreements with other customers 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 agreements are recognized as revenue over the term of the agreement. The Company recorded $200,000, $105,000 and $30,000 of revenue from these agreements during the years ended December 31, 2020, 2019 and 2018, respectively.

**13. Fair Value Measurements**

The Company's material financial instruments at December 31, 2020 and 2019 consisted primarily of cash and cash equivalents 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 and are classified as Level 1 in the fair value hierarchy. The fair value of long-term debt approximates the carrying value due to variable interest rates that correspond to market rates.

There were no significant transfers between Levels 1, 2 and 3 during the years ended December 31, 2020 and 2019.

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, 2020 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Recorded Value |
| **Financial Assets:** | | | | |
| Cash and money markets | $ 17,287 | $ — | $ — | $ 17,287 |
| Restricted cash money market | 360 | — | — | 360 |
| Total financial assets | $ 17,647 | $ — | $ — | $ 17,647 |

| | December 31, 2019 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Recorded Value |
| **Financial Assets:** | | | | |
| Cash and money markets | $ 22,595 | $ — | $ — | $ 22,595 |
| Restricted cash money market | 360 | — | — | 360 |
| Total financial assets | $ 22,955 | $ — | $ — | $ 22,955 |

**14. 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, | | |
|---|---|---|---|
| | 2020 | 2019 | 2018 |
| Outstanding stock options | 4,248,193 | 4,104,450 | 3,075,349 |
| Non-vested restricted stock units | 767,271 | 1,269,300 | — |
| Stock purchase warrants | 29,796 | 29,796 | 29,796 |
| | 5,045,260 | 5,403,546 | 3,105,145 |

**15. Related Party Transactions**

On November 22, 2019, the Company issued shares of common stock in a private placement offering at an offering price of $1.054 per share. Two of the purchasers, Hatteras Venture Partners IV SBIC, LP and Hatteras Venture Partners IV, LP, are affiliated with certain of the Company's directors and purchased 1,347,629 and 170,397 shares, respectively.

## 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, 2020. 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, 2020 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, 2020, 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

On December 10, 2020, the board of directors of the Company adopted resolutions (the "Resolutions") approving the ratification of the issuance of certain shares of Common Stock, pursuant to Section 204 of the Delaware General Corporation Law (the "Ratification"). A copy of the Resolutions adopted by the board of directors setting forth the information with respect to the Ratification required under Section 204 of the Delaware General Corporation Law is attached hereto as Exhibit 99.1. Any claim that any defective corporate act or putative stock ratified pursuant to the Ratification is void or voidable due to the failure of authorization specified in the Resolutions, or that the Delaware Court of Chancery should declare in its discretion that the Ratification in accordance with Section 204 of the Delaware General Corporation Law not be effective or be effective only on certain conditions, must be

brought within the later of (i) 120 days from the validation effective time (which is December 10, 2020) and (ii) the giving of this notice (which is deemed given on the date that this Annual Report on Form 10-K is filed with the Securities and Exchange Commission).

## PART III

We will file a definitive Proxy Statement for our 2021 Annual Meeting of Stockholders (the “2021 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 2021 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 2021 Proxy Statement under the captions "Information Regarding the Board of Directors and Corporate Governance," "Election of Directors," and "Information About Our Executive Officers."

### ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 is hereby incorporated by reference to the sections of the 2021 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 2021 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 2021 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 2021 Proxy Statement under the caption "Ratification of Selection of Independent Auditors."

## PART IV

### ITEM 15. EXHIBITS, 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). |
| 4.4 | | Description of Common Stock of Clearside Biomedical, Inc. (incorporated herein by reference to Exhibit 4.4 to the Registrant’s Annual Report on Form 10-K (File No. 001-37783), filed with the Commission on March 13, 2020). |
| 4.5 | | Registration Rights Agreement, by and among the Registrant and the Investors named therein, dated as of November 22, 2019 (incorporated herein by reference to Exhibit 10.2 to the Registrant’s Current Report on Form 8-K (File No. 001-37783), filed with the Commission on November 25, 2019). |
| 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 | | 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). |
| 10.11 | | 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). |
| 10.12 | | 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). |
| 10.13 | + | 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). |
| 10.14 | + | 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). |
| 10.15 | | Supply Agreement, by and among the Registrant and Gerresheimer Regensburg GmbH, dated as of May 8, 2018 (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 August 8, 2018). |
| 10.16 | + | Change in Control Equity Acceleration Plan, amending the Registrant's 2016 Equity Incentive Plan (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 August 8, 2018.) |
| 10.17 | | Third Amendment to License Agreement, by and among the Registrant, Emory University and The Georgia Tech Research Corporation, dated April 1, 2018 (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 August 8, 2019). |
| 10.18 | ## | License Agreement, by and between the Registrant and Bausch Health Ireland Limited, dated as of October 22, 2019 (incorporated herein by reference to Exhibit 10.26 to the Registrant's Annual Report on Form 10-K (File No. 001-37783), filed with the Commission on March 13, 2020). |
| 10.19 | ## | First Amendment to License Agreement, by and between the Registrant and Bausch Health Ireland Limited, dated as of April 27, 2020. (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 August 10, 2020). |
| 10.20 | + | Letter Agreement, by and between the Registrant and George Lasezkay, dated April 16, 2019 (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 April 17, 2019). |
| 10.21 | + | Amendment to Offer Letter Agreement, by and between the Registrant and George Lasezkay, dated as of August 6, 2019 (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 August 8, 2019). |
| 10.22 | ## | Option and License Agreement by and between the Registrant and REGENXBIO Inc., dated as of August 29, 2019 (incorporated herein by reference to Exhibit 10.30 to the Registrant's Annual Report on Form 10-K (File No. 001-37783), filed with the Commission on March 13, 2020). |
| 10.23 | ## | License Agreement by and between the Registrant and Arctic Vision (Hong Kong) Limited, dated as of March 20, 2020 (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 May 8, 2020). |
| 10.24 | + | Executive Employment Agreement, by and between the Registrant and Thomas Ciulla, dated as of June 24, 2019 (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 August 10, 2020). |
| 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. |
| 99.1 | * | Resolutions adopted by the Board of Directors of the Registrant setting forth the information with respect to the Ratification required under Section 204 of the Delaware General Corporation Law. |
| 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 |

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* Filed herewith.
\+ 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.
## Pursuant to Item 601(b)(10)(iv) of Regulation S-K promulgated by the Securities and Exchange Commission, certain portions of this exhibit (indicated by asterisks) have been omitted. The Registrant hereby agrees to furnish supplementally to the Securities and Exchange Commission, upon its request, an unredacted copy of this exhibit.

**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/ *George Lasezkay, Pharm.D., J.D.*
George Lasezkay, Pharm.D., J.D.
*President and Chief Executive Officer*

March 15, 2021

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints George Lasezkay, Charles A. Deignan and Leslie Zacks, 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/ George Lasezkay, Pharm.D., J.D.*<br>George Lasezkay, Pharm.D., J.D. | President, Chief Executive Officer and Director<br>*(Principal Executive Officer)* | March 15, 2021 |
| */s/ Charles A. Deignan*<br>Charles A. Deignan | Chief Financial Officer<br>*(Principal Financial Officer and Principal Accounting Officer)* | March 15, 2021 |
| */s/ William D. Humphries*<br>William D. Humphries | Director | March 15, 2021 |
| */s/ Richard Croarkin*<br>Richard Croarkin | Director | March 15, 2021 |
| */s/ Jeffrey L. Edwards*<br>Jeffrey L. Edwards | Director | March 15, 2021 |
| */s/ Nancy J. Hutson*<br>Nancy J. Hutson | Director | March 15, 2021 |
| */s/ Christy L. Shaffer, Ph.D.*<br>Christy L. Shaffer, Ph.D. | Director | March 15, 2021 |
| */s/Clay B. Thorp*<br>Clay B. Thorp | Director | March 15, 2021 |

**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.,

(3) Registration Statement (Form S-3 No. 333-219132) of Clearside Biomedical, Inc.,

(4) Registration Statement (Form S-8 No. 333-224826) pertaining to the 2016 Equity Incentive Plan and 2016 Employee Stock Purchase Plan of Clearside Biomedical, Inc., and

(5) Registration Statement (Form S-8 No. 333-231383) pertaining to the 2016 Equity Incentive Plan of Clearside Biomedical, Inc.,

(6) Registration Statement (Form S-8 No. 333-238133) pertaining to the 2016 Equity Incentive Plan of Clearside Biomedical, Inc.

of our report dated March 15, 2021, 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, 2020.

/s/ Ernst & Young LLP

Atlanta, Georgia
March 15, 2021

**Exhibit 31.1**

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

I, George Lasezkay, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2020 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 15, 2021

/s/ George Lasezkay, Pharm.D., J.D.
George Lasezkay, Pharm.D., J.D.
President and Chief Executive Officer
(principal executive officer)

**Exhibit 31.2**

**CERTIFICATION OF PRINCIPAL FINANCIAL 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, 2020 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 15, 2021

/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), George Lasezkay, 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, 2020, 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 15th day of March, 2021.

/s/ George Lasezkay, Pharm.D., J.D.
George Lasezkay, Pharm.D., J.D.
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.

**ACTION BY WRITTEN CONSENT**
**OF THE BOARD OF DIRECTORS OF**
**CLEARSIDE BIOMEDICAL, INC.**

**DECEMBER 10, 2020**

The undersigned, being all of the members of the Board of Directors (the "***Board***") of **CLEARSIDE BIOMEDICAL, INC.**, a Delaware corporation (the "***Company***"), hereby take the following actions by written consent without a meeting pursuant to Sections 141(f) and 204 of the General Corporation Law of the State of Delaware (the "***DGCL***"), to, among other things, ratify and correct certain defective corporate acts as described below, and hereby direct that this consent be filed with the minutes of the proceedings of the Board:

**RATIFICATION OF STOCK ISSUANCES**

**WHEREAS**, Section 204 of the DGCL ("***Section 204***") provides that, if a "defective corporate act" and "putative stock" (as such terms are defined therein) is ratified as provided in that section, it shall not be void or voidable solely as a result of a failure to authorize or effect an act or transaction in compliance with the provisions of the DGCL, the certificate of incorporation, or the bylaws of the corporation;

**WHEREAS**, between October 5, 2020 and October 9, 2020, Company purported to issue an aggregate of 126,510 shares of the Company's common stock, par value $0.001 per share ("***Common Stock***"), as detailed on **Exhibit A** attached hereto (each a "***Stock Issuance***" and collectively, the "***Stock Issuances***") pursuant to the Company's Registration Statement on Form S-3 (File No. 333-238128) in one or more "at-the-market" offerings with Cowen and Company, LLC acting as agent or principal (the "***ATM Program***");

**WHEREAS**, the Board has determined that each of the Stock Issuances may have been a "defective corporate act" (as defined in Section 204) and the shares of Common Stock purported issued in the Stock Issuances (collectively, the "***Putative Stock***") may be "putative stock" (as defined in Section 204) because the authority the Board had previously delegated to management to issue shares of Common Stock pursuant to the ATM Program had expired as of the close of business on September 30, 2020; and

**WHEREAS**, the Board desires to ratify the Stock Issuances and the Putative Stock pursuant to and in accordance with Section 204.

**NOW, THEREFORE, BE IT RESOLVED**, that the Stock Issuances are the defective corporate acts to be ratified hereby;

**RESOLVED FURTHER**, that the date of each Stock Issuance is as set forth on Exhibit A;

**RESOLVED FURTHER**, that the numbers of shares of Putative Stock purportedly issued, the dates such shares of Putative Stock were purportedly issued, and the consideration received by the corporation for such Putative Shares are as set forth on Exhibit A, all of which Putative Shares were shares of Common Stock;

**RESOLVED FURTHER**, that the nature of the failure of authorization in respect of the Stock Issuances is the failure of the Board or a duly authorized Committee thereof to have

authorized the Stock Issuances in accordance with Sections 152 and 153 of the DGCL prior to thereto; and

**Resolved Further**, that, pursuant to and in accordance with Section 204, the ratification of the Stock Issuances and the issuance of the Putative Stock be, and hereby is, approved, adopted and confirmed in all respects.

**Actions in Furtherance of Ratification**

**Whereas**, any claim that any defective corporate act or putative stock referenced herein being ratified under Section 204 is void or voidable due to the failure of authorization, or that the Delaware Court of Chancery should declare in its discretion that the ratification thereof in accordance with Section 204 not be effective or be effective only on certain conditions must be brought within the later of 120 days from the relevant validation effective time (which, in the case of the Stock Issuances, will be the date and time of the adoption of these resolutions) and the time at which the notice required by Section 204(g) is given.

**Resolved Further**, that the officers of the Company be, and each of them hereby is, authorized, empowered and directed, for and on behalf of the Company, to deliver a notice of the ratification of the Stock Issuances and Putative Stock set forth herein in the form and containing the information required by Section 204 of the General Corporation Law.

**Resolved Further**, that the officers of the Company be, and each of them hereby is, authorized, empowered and directed, for and on behalf of the Company, to take any and all actions, to negotiate for and enter into agreements and amendments to agreements, to perform all such acts and things, to execute, file, deliver or record in the name and on behalf of the Company, all such certificates, instruments, agreements or other documents, and to make all such payments as they, in their judgment, or in the judgment of any one or more of them, may deem necessary, advisable or appropriate in order to carry out the purpose and intent of, or consummate the transactions contemplated by the foregoing resolutions and/or all of the transactions contemplated therein or thereby, the authorization therefor to be conclusively evidenced by the taking of such action or the execution and delivery of such certificates, instruments, agreements or documents.

This Unanimous Written Consent may be executed in one or more counterparts. An electronic transmission expressing the consent of a director to the approval and adoption of the resolutions set forth herein shall be deemed the same as the delivery of an original counterpart.

**[This Space Intentionally Left Blank]**

The undersigned have executed this Action by Written Consent of the Board of Directors on the date set forth above.

/s/ George Lasezkay
**GEORGE LASEZKAY**

/s/ Christy L. Shaffer
**CHRISTY L. SHAFFER**

/s/ Clay B. Thorp
**CLAY B. THORP**

/s/ William D. Humphries
**WILLIAM D. HUMPHRIES**

/s/ Richard Croarkin
**RICHARD CROARKIN**

/s/ Jeffrey L. Edwards
**JEFFERY L. EDWARDS**

/s/ Nancy J. Hutson
**NANCY J. HUTSON**

**EXHIBIT A**

**STOCK ISSUANCES**

| ***Number of Shares*** | ***Date of Issuance*** | ***Price Per Share*** |
|---|---|---|
| 17,237 | October 5, 2020 | $1.6000 |
| 39,561 | October 8, 2020 | $1.5500 |
| 69,712 | October 9, 2020 | $1.5958 |