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, 2022

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

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

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

Title of each class	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. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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, 2022 (the last business day of the registrant's most recently completed second fiscal quarter) based on the closing sale price of $1.47 as reported on the Nasdaq Global Market on that date was approximately $80,000,000.

As of March 8, 2023, the registrant had 61,364,299 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 2023 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 expectations regarding the commercialization of XIPERE by our licensing partners;
- 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;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- 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, 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, or SCS. Suprachoroidal injection is a novel approach and may fail to achieve and sustain market acceptance.
- If we are unable to obtain regulatory approval for, and commercialize either on our own or with a third party, CLS-AX or our other product candidates, 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 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

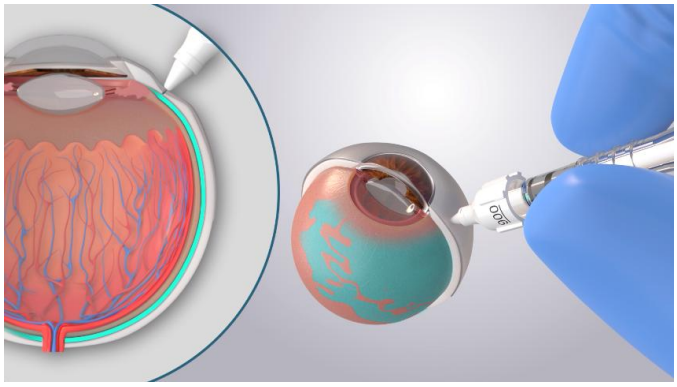
We are a biopharmaceutical company focused on revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space, or SCS. Our novel SCS injection platform, utilizing our proprietary SCS Microinjector, enables an in-office, repeatable, non-surgical procedure for the targeted and compartmentalized delivery of a wide variety of therapies to the macula, retina or choroid to potentially preserve and improve vision in patients with sight-threatening eye diseases. Our SCS injection platform can be used in conjunction with existing drugs designed for delivery to the SCS, novel therapies and future therapeutic innovations. We believe our proprietary suprachoroidal administration platform has the potential to become a standard for delivery of therapies intended to treat chorioretinal diseases.

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. We are developing our own pipeline of small molecule product candidates for administration via our SCS Microinjector, and we also strategically partner with companies developing other ophthalmic therapeutic innovations to be administered using our SCS injection platform. Our first product, XIPERE (triamcinolone acetonide injectable suspension) for suprachoroidal use, was approved by the U.S. Food and Drug Administration, or the FDA, in October 2021. Approval of XIPERE was a significant milestone for us as it is the first approved therapeutic delivered into the SCS, the first commercial product developed by us and the first therapy for macular edema associated with uveitis.

We believe that we are creating a broad therapeutic platform for developing product candidates to treat serious eye diseases.

Our Suprachoroidal Space (SCS) Injection 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 SCS 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. Furthermore, a natural pressure gradient between the intraocular pressure, or IOP, and the SCS pressure drives suprachoroidal injectates posteriorly towards the macula, which facilitates treatment of macular disorders with this office-based approach, without the need for an intraocular catheter or other surgical techniques. In contrast, 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 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.

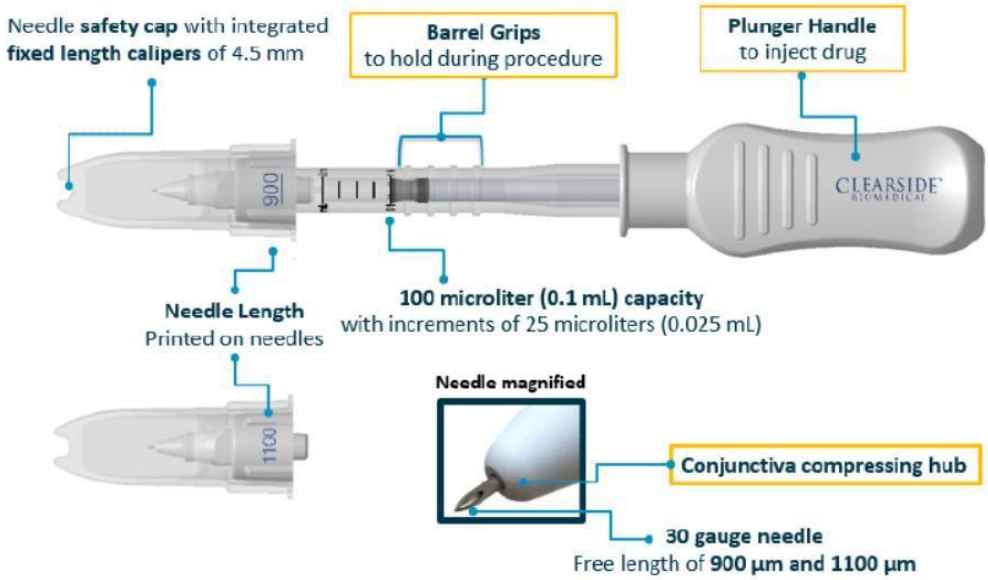
Our extensive patent portfolio provides us with the right to develop and commercialize pharmacological agents for treatment of eye diseases via suprachoroidal injection. We believe this proprietary method of administration has the potential to become the standard for the delivery of therapies intended to treat retinal and choroidal diseases. Our intellectual property portfolio consists of 26 issued U.S. patents and more than 70 European and international patents broadly directed to the use of the SCS Microinjector, administration of any drug into the SCS by injection, as well as XIPERE and our product candidates.

Our SCS Microinjector

Our proprietary SCS Microinjector can be used to inject a wide variety of therapies into the SCS, including our internally developed and our collaborators' drug candidates. Our SCS Microinjector provides targeted delivery to potentially improve efficacy and compartmentalization of medication to reduce or eliminate toxic effects on non-diseased cells. Suprachoroidal injection enables the rapid dispersion of medicine to the back of the eye, offering the potential for the medicine to act longer and minimize harm to the surrounding healthy parts of the eye.

Our SCS Microinjector has been used in over 2,000 suprachoroidal injections in our clinical trials and the clinical trials of our partners. It has been commercially accepted by retinal physicians following the launch of XIPERE in the United States by Bausch + Lomb with over 1,000 retinal physicians trained to date. Suprachoroidal injections using our SCS Microinjector have demonstrated a clinical safety profile comparable to intravitreal injections.

The SCS Microinjector, shown in the picture below, is composed of a syringe and two 30-gauge hollow microneedles of varying lengths, each approximately one millimeter, within a custom-designed hub that optimizes insertion and suprachoroidal administration of drugs.



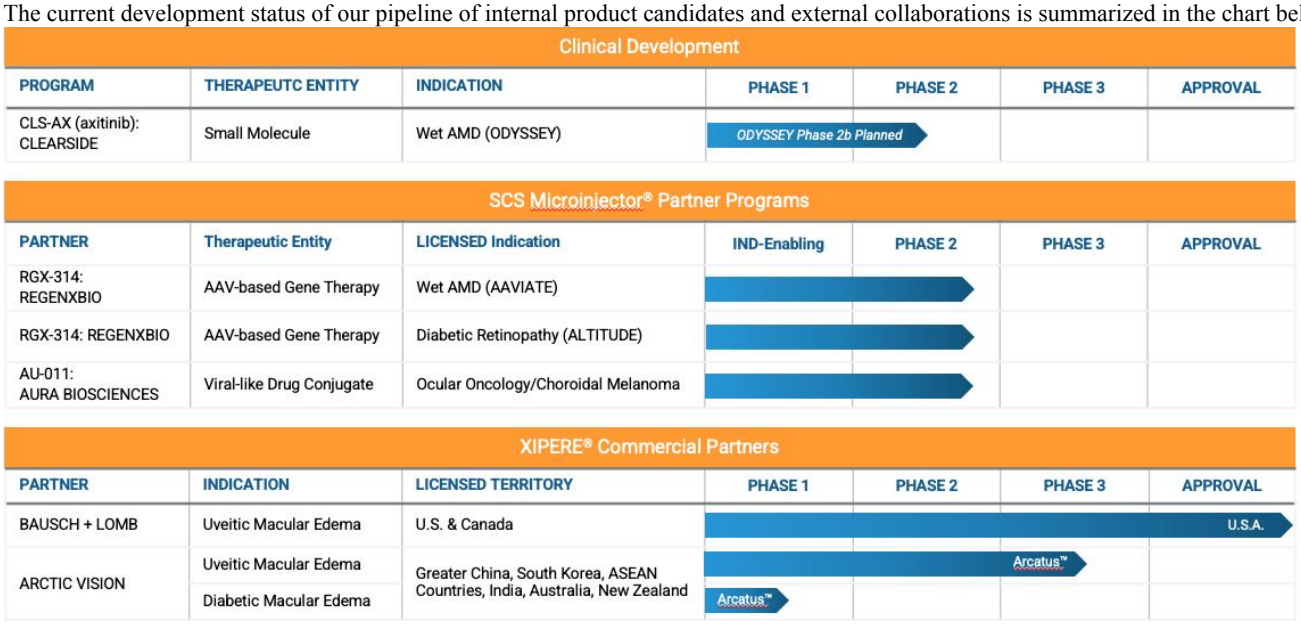
Current intravitreal injections are performed in a procedure similar to that of suprachoroidal injections, except that the hypodermic needles and syringes used in intravitreal injection procedures are designed so that the needle penetrates through all of the layers of the eye and drug is injected into 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 SCS. This suprachoroidal injection is designed to be carried out under local anesthesia, perpendicular to the sclera, at a site similar to an intravitreal injection. 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 to the back of the eye, due to a natural pressure gradient between the IOP and the SCS pressure, precisely targeting the cells of interest without the need for intraocular catheters or other surgical techniques.

Our Pipeline

We have research capabilities focused on developing proprietary therapeutic formulations to utilize with our SCS Microinjector. Our current internal research and development initiatives are focused on small molecules to address serious diseases that affect the back of the eye. In addition to growing our internal pipeline, we are also focused on strategically 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:



Clinical Development Pipeline

We are building a clinical development pipeline focused on small molecules. Our first product, XIPERE, was approved by the FDA in October 2021. The XIPERE approval supports our approach both clinically and preclinically to advance small molecule suspensions delivered into the SCS.

Our most advanced clinical development product candidate is a proprietary suspension of axitinib, a tyrosine kinase inhibitor, or TKI, for suprachoroidal injection, which we refer to as CLS-AX. We recently completed OASIS, a Phase 1/2a clinical trial in patients with neovascular age-related macular degeneration, commonly referred to as wet AMD. We are currently finalizing the trial design for ODYSSEY, our Phase 2b clinical trial of CLS-AX, and expect to initiate the trial in the second quarter of 2023.

CLS-AX (axitinib injectable suspension)

CLS-AX, our most advanced product candidate, is our proprietary suspension of the TKI axitinib for suprachoroidal injection delivered via our SCS Microinjector. CLS-AX is an inhibitor of vascular endothelial growth factor receptor-1, -2 and -3 that we believe may benefit patients who respond sub optimally to current anti-VEGF therapies. We are developing CLS-AX for administration to the SCS as a long-acting therapy for 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 of several drugs that generated aggregate 2020 sales of approximately $14.3 billion globally.

Axitinib is 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. 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. Importantly, we believe that administration of CLS-AX to the SCS using our SCS Microinjector, may minimize the occurrence of related adverse events, such as vitreous floaters, "snow globe" effect 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. These studies have also demonstrated 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.

In August 2020, we announced that the FDA had accepted our Investigational New Drug application, or IND, for CLS-AX. In January 2021, we announced the enrollment of our first participant in OASIS, a Phase 1/2a clinical trial of CLS-AX in participants with wet AMD. OASIS was 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. All participants were highly treatment-experienced wet AMD participants with active disease at screening. The primary endpoint for the trial assessed the safety and tolerability of CLS-AX for the three months following the administration of CLS-AX, and secondary endpoints evaluated the pharmacokinetics, visual function, ocular anatomy and the need for additional treatment with intravitreal aflibercept during the three- and six-month periods.

Participant inclusion criteria for enrollment in OASIS included: 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; and a best corrected visual acuity, or BCVA, score of $\geq$ 20 letters (20/400) and $\leq$ 75 letters (20/32) with < 5 letters change between screening and baseline to ensure patient stability after anti-VEGF treatment. Participants were assessed at weeks four, eight and twelve. Participants were assessed for additional therapy if they experienced 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; (2) increase in central subfield retinal thickness greater than 75 microns from baseline at visit 2 in the study eye; or (3) presence of vision-threatening hemorrhage due to AMD in the study eye. The trial consisted of four cohorts at the following doses of CLS-AX delivered via suprachoroidal injection: Cohort 1 at 0.03 mg; Cohort 2 at 0.1 mg; Cohort 3 at 0.5 mg; Cohort 4 at 1.0 mg. In January 2021, we announced that the first participants had been enrolled in OASIS. In December 2021, we announced that the primary endpoints were met in Cohorts 1 and 2. CLS-AX was well tolerated with no serious adverse events; there were no treatment emergent adverse events related to aflibercept, CLS-AX or the suprachoroidal injection procedure, no dispersion of drug into the vitreous, and no adverse events related to IOP, inflammation or vasculitis. In July 2022, we completed patient enrollment of OASIS and also completed dosing in Cohort 3 in which each patient received a dose of 0.5 mg, and in Cohort 4 in which each patient received a dose of 1.0 mg.

In the four OASIS cohorts we enrolled a total of 27 participants. All participants were highly treatment-experienced wet AMD participants with active disease at screening. These four cohorts allowed us to collect more CLS-AX patient data to help guide our selection of the most appropriate dosing protocol for ODYSSEY, our planned Phase 2b clinical trial of CLS-AX for the treatment of wet AMD.

Participants in Cohorts 2, 3, and 4 who elected to participate in an extension study were followed for an additional 3 months. On November 9, 2022, we reported positive results that included final three-month data from Cohorts 3 and 4, and interim data from the extension study. CLS-AX demonstrated a positive safety profile in all four cohorts. There were no serious adverse events and no treatment emergent adverse events related to aflibercept, CLS-AX, or the suprachoroidal injection procedure. There were also no dose limiting toxicities. There were no adverse events related to inflammation, vasculitis or vascular occlusion, and there were no vitreous "floaters" or dispersion of CLS-AX into the vitreous.

In Cohorts 3 and 4, the data showed favorable durability with a meaningful reduction in treatment burden at the 3-month endpoint and to date in the extension study. Of the 16 participants in Cohorts 3 and 4, at the 3-month endpoint, 69% did not receive additional therapy, 92% did not receive additional therapy per protocol criteria, and there was at least a 73% reduction in treatment burden from the average monthly injections in the three months before CLS-AX administration. Of the 12 participants in the extension study, based on interim data as of October 27, 2022, 88% (7/8) of participants did not receive additional therapy to the 5-month endpoint and 75% (3/4) of participants did not receive additional therapy to the 6-month endpoint. Further, in the extension study, there was at least a 90% reduction in treatment burden from the average monthly injections in the six months before CLS-AX administration. In Cohorts 3 and 4, CLS-AX also showed an observable biologic effect with stable mean BCVA, stable mean central subfield thickness, or CST, and anatomical signs of TKI biologic effect observed on Optical Coherence Tomography, or OCT, images.

On February 2, 2023, we announced positive results from the complete OASIS extension study.

CLS-AX was well-tolerated and demonstrated a favorable safety profile across all cohorts in both the three-month dose-escalation portion (n=27) and the extension study (n=14). No serious adverse events, treatment emergent adverse events related to study or dose limiting toxicities were observed. In addition, there were no adverse events related to inflammation, vasculitis or vascular occlusion, no vitreous "floaters" or dispersion of CLS-AX into the vitreous and no retinal detachments, endophthalmitis or adverse events related to IOP.

The full extension data for Cohorts 3 and 4 (n=12) showed promising durability, with a 77% - 85% reduction in treatment burden observed compared to the average monthly injections in the six months before CLS-AX administration. The table below details the length of time the participants went without additional therapy:

Duration Without Additional Therapy	Number of Participants (n=12)
≥ 3 Months	11/12 (92%)
≥ 4 Months	10/12 (83%)
≥ 6 Months	8/12 (67%)
> 6 Months	6/12 (50%)

In Cohorts 3 and 4 of the extension study, CLS-AX showed signs of biologic effect with stable mean BCVA and stable mean CST to the six-month timepoint. On optical coherent tomography images, anatomical signs of TKI biologic effect were observed in anti-VEGF treatment experienced sub-responders on optical coherent tomography images.

ODYSSEY Phase 2b Clinical Trial

Based on the results from the OASIS trial, we are planning to conduct a randomized, controlled, double-masked, Phase 2b clinical trial of CLS-AX for the treatment of wet AMD, which we refer to as ODYSSEY. Based on the issuance by the FDA of draft guidance on February 24, 2023 entitled Neovascular Age-Related Macular Degeneration: Developing Drugs for Treatment and subsequent interactions with the FDA, we intend to use aflibercept as the comparator drug in the ODYSSEY trial. We are currently finalizing the clinical trial design and plan to open enrollment in the second quarter of 2023, with data expected in the second half of 2024.

Preclinical

We have an experienced team of scientists and researchers evaluating small molecules that may be utilized as potential treatment options for back of the eye diseases. This work often entails developing a suspension formulation for delivery into the suprachoroidal space via our SCS Microinjector. Suprachoroidal delivery of a new suspension could provide targeting, compartmentalization and durability advantages over topical or intravitreal delivery, similar to what we observed with XIPERE and CLS-AX. Once a formulation is confirmed, we proceed with conducting non-human studies until enough data is collected to warrant submitting an IND for such a product candidate.

XIPERE (triamcinolone acetonide injectable suspension) for suprachoroidal use

Our first product, XIPERE, formerly known as CLS-TA, is a proprietary, preservative-free suspension of the corticosteroid triamcinolone acetonide, or TA, for suprachoroidal use. 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 IOP, which can lead to glaucoma.

XIPERE was approved 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.

We are evaluating options for potential submissions to regulatory agencies in additional territories not currently licensed for the treatment of patients with macular edema associated with uveitis.

External Collaborations Pipeline

In order to expand the global reach of our suprachoroidal injection platform, we have strategically partnered some of our assets for development and/or commercialization and intend to continue partnering our assets. By entering into these partnerships, we have been able to expand the use of our suprachoroidal injection platform to other indications and geographies globally. We currently have collaborations with Bausch Health, Arctic Vision, REGENXBIO, Inc., and Aura Biosciences. Under these license agreements, we have received an aggregate of $38.3 million of non-dilutive capital in the form of upfront and milestone payments since 2019, and we are eligible to receive up to an aggregate of more than $233 million in potential development and sales milestones, as well as royalties from net sales of covered products. As discussed below in "—Royalty Purchase and Sale Agreement", we are obligated to pay HCR any such royalties or milestone payments until we have satisfied our obligations under the Purchase and Sale Agreement.

License agreement for commercialization of XIPERE in United States and Canada

On October 22, 2019, we entered into a License Agreement with Bausch + Lomb or, as amended, the Bausch License Agreement. Pursuant to the Bausch License Agreement, we granted an exclusive license to Bausch to develop, manufacture, distribute, promote, market and commercialize XIPERE using our SCS Microinjector, as well as specified other steroids, corticosteroids and NSAIDs in combination with the SCS Microinjector, or together with XIPERE, the Products, subject to specified exceptions, in the United States and Canada, or the Territory for the treatment of ophthalmology indications, including non-infectious uveitis.

Pursuant to the Bausch License Agreement, Bausch paid us an upfront payment of $5.0 million in October 2019. In October 2021, the FDA approved XIPERE, and we received $5.0 million from Bausch as a result of the approval. In January 2022, we received an additional payment of $10.0 million related to the completion of pre-launch activities for XIPERE. In addition, Bausch has agreed to pay up to an aggregate of $55.0 million in additional milestone payments upon the achievement of (i) specified regulatory approvals for specified additional indications of XIPERE 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 Territory, as well as a lower royalty on annual net sales of other products, in each case subject to reductions in specified circumstances. However, we will not receive any royalties on the first $45.0 million of cumulative net sales of all products in the Territory. Bausch launched XIPERE in the United States in the first quarter of 2022. Our rights to these royalties and milestone payments have been sold pursuant to the terms and conditions of the Purchase and Sale Agreement described below in "—Royalty Purchase and Sale Agreement."

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. 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. 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.

License agreement for commercialization of XIPERE in China, Hong Kong, Macau, Taiwan and South Korea, India, ASEAN Countries, Australia and New Zealand

On March 10, 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. Under the terms of the Arctic Vision 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.

In December 2020, Arctic Vision announced clearance of its IND for a Phase 3 clinical trial of ARVN001 (XIPERE) in China for the treatment of macular edema associated with uveitis.

In November 2021, Arctic Vision announced dosing of the first patient in a Phase 3 clinical trial of ARVN001 for the treatment of macular edema associated with uveitis. Arctic Vision has also branded ARVN001 as Arcatus.

In March 2022, Arctic Vision announced dosing of the first patient in a Phase 1 clinical trial of ARVN011 in China for the treatment of diabetic macular edema.

Pursuant to the Arctic Vision License Agreement, Arctic Vision paid us an upfront payment of $4.0 million in March 2020. In December 2021, we received a milestone payment of $4.0 million following receipt of FDA approval of XIPERE in the United States. In addition, Arctic Vision has agreed to pay us up to a total of $22.5 million in development and sales milestone payments. Further, during the applicable royalty term, we are also 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. Our rights to these royalties and milestone payments have been sold pursuant to the terms and conditions of the Purchase and Sale Agreement described below in "—Royalty Purchase and Sale Agreement."

The Arctic Vision License Agreement will expire upon the expiration of the last-to-expire royalty term. Arctic Vision may terminate the License Agreement for convenience upon 45 days' notice if before regulatory approval in the Arctic Territory or 90 days' notice if after regulatory approval in the Arctic Territory. In addition, we can terminate the License Agreement if Arctic Vision commences a legal action challenging the validity, enforceability or scope of the licensed patents. Both parties may terminate the License Agreement (i) upon a material breach of the License Agreement, subject to a specified cure period, or (ii) if the other party enters bankruptcy. Upon termination, all licenses and other rights granted to Arctic Vision pursuant to the License Agreement would revert to us. If Arctic Vision exercises its termination right for convenience or if the License Agreement terminates as a result of Arctic Vision's material breach or bankruptcy, Arctic Vision will assign and transfer all regulatory approvals, related documents and trademarks (with respect to trademarks, only those specific to) pertaining to XIPERE in the Arctic Territory to us. If Arctic Vision terminates the Arctic Vision License Agreement as a result of material breach by us or our bankruptcy after regulatory approval of XIPERE in the Arctic Territory, we are obligated to pay Arctic Vision royalties equal to a low-single digit percentage of net sales of XIPERE in the Arctic Territory.

In August 2021, we entered into an amendment to the Arctic Vision License Agreement to expand the territories covered by the license to include India and the ASEAN Countries (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam). In September 2021, we entered into a second amendment to the Arctic Vision License Agreement to expand the Arctic Territory to include Australia and New Zealand. We received an aggregate of $3.0 million in consideration for the expansion of the Arctic Territory.

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 adeno-associated virus, or 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 diseased 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 and 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. To expand our overall development pipeline, we are looking to selectively partner our proprietary technology for use with novel gene therapies.

REGENXBIO, Inc.

We have expanded the reach of our SCS Microinjector technology in AAV-based gene therapy through a development and commercial partner.

In August 2019, we entered into an option and license agreement, or the REGENXBIO Option and License Agreement, with REGENXBIO Inc., or 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 in-office 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.

In October 2019, REGENXBIO exercised the Option 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 paid us $3.0 million in connection with a development milestone and has agreed to additional payments to us of up to an aggregate of $31.0 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. Our rights to these royalties and milestone payments have been sold pursuant to the terms and conditions of the Purchase and Sale Agreement described below in "—Royalty Purchase and Sale Agreement."

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.

REGENXBIO is currently conducting two multi-center, open-label, randomized, controlled, dose-escalation Phase 2 clinical trials evaluating the efficacy, safety and tolerability of suprachoroidal delivery of RGX-314 using our SCS Microinjector technology: a Phase 2 trial entitled AAVIATE for the treatment of wet AMD and a second Phase 2 trial entitled ALTITUDE for the treatment of

diabetic retinopathy. REGENXBIO has reported positive initial data from both clinical trials and the trials continue to enroll participants. In February 2022, REGENXBIO reported that both the wet AMD and diabetic retinopathy suprachoroidal clinical trials are on track to be completed in the first half of 2023, with additional interim trial data expected in the second half of 2023.

Ocular Oncology

Ocular cancers are a group of rare, life-threatening conditions that affect one or both eyes. The main indications include choroidal melanoma, choroidal metastases, cancers of the ocular surface and retinoblastoma, among others. Diagnosing and treating these cancers early is important because they have the potential to spread both within the eye and to other organs. The risk for ocular cancer increases with age and increases significantly after the age of 50. For cancers that occur inside the eye (e.g., choroidal melanoma), the typical treatment is radiotherapy in the form of plaque brachytherapy and proton beam therapy, but these treatments are highly invasive and result in major vision loss and other comorbidities for many patients.

Choroidal melanoma is the most common intraocular cancer in adults, with an incidence of approximately 11,000 patients per year in the United States and Europe. This comprises approximately 90% of all cases of uveal melanoma, consisting of melanomas in the choroid, ciliary body and iris, which are collectively referred to as the uvea. It is estimated that 96% of patients are diagnosed early without clinical evidence of metastatic disease. There are approximately 2,000 new cases treated each year in the United States and 1,600 new cases treated each year in Europe. However, despite the current treatments with radiotherapy, the long-term prognosis is poor with death occurring in more than 50% of cases. There are no FDA-approved therapies for choroidal melanoma. There is a need for treatment of early-stage disease which includes small melanomas and indeterminate lesions representing approximately 9,000 patients in the United States and Europe.

Aura Biosciences

On July 9, 2019, we entered into a worldwide licensing agreement with Aura Biosciences, or 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. Our SCS Microinjector may offer a non-surgical alternative to intravitreal delivery of Aura's oncology drug candidates, and we believe suprachoroidal administration may further enhance the value proposition of choroidal melanoma by potentially improving safety and expanding access. Pursuant to the licensing agreement, we are eligible to receive up to $21.1 million in payments related to pre-specified development and regulatory milestones, as well as low to mid-single digit royalties on net sales that utilize the SCS Microinjector. Our rights to these royalties and milestone payments have been sold pursuant to the terms and conditions of the Purchase and Sale Agreement described below in "—Royalty Purchase and Sale Agreement."

Aura is utilizing our SCS Microinjector to deliver their viral like drug conjugate, bel-sar, for the treatment of choroidal melanoma. In February 2022, Aura presented positive interim efficacy data from their ongoing Phase 2 clinical trial. The data presented showed a favorable safety profile along with an excellent response to the therapy with 89-100% tumor control. Based on their promising data, Aura announced final plans for its global Phase 3 trial utilizing the suprachoroidal route of administration. They expect to begin enrollment in that trial in 2023.

Royalty Purchase and Sale Agreement

On August 8, 2022, or the Closing Date, we, through our wholly-owned subsidiary Clearside Royalty LLC, a Delaware limited liability company, or Royalty Sub, entered into a Purchase and Sale Agreement, or the Purchase and Sale Agreement, with entities managed by HealthCare Royalty Management, LLC, or HCR, pursuant to which Royalty Sub sold to HCR certain of its rights to receive royalty and milestone payments payable to Royalty Sub under the Arctic Vision License Agreement, the Bausch License Agreement, that certain License Agreement, effective as of July 3, 2019, by and between the Company and Aura Biosciences, Inc., or the Aura License Agreement, the REGENXBIO Option and License Agreement and any and all out-license agreements following the Closing Date for, or related to XIPERE or the SCS Microinjector technology (to be used in connection with compounds or products of any third parties delivered, in whole or in part, by means of the SCS Microinjector technology), excluding, for the avoidance of doubt, any in-licensed or internally developed therapies following the Closing Date, or the Royalties, in exchange for up to $65 million. In connection with this transaction, we assigned the Arctic Vision License Agreement, Bausch License Agreement, Aura License Agreement, REGENXBIO Option and License Agreement, the Company's license agreement with Emory University and The Georgia Tech Research Corporation and related intellectual property rights to Royalty Sub.

Under the terms of the Purchase and Sale Agreement, Royalty Sub received an initial payment of $32.1 million, representing the $32.5 million to which we were entitled, net of certain of HCR's transaction-related expenses which we agreed to reimburse. An additional $12.5 million was deposited by HCR in an escrow account to be released to Royalty Sub upon attainment of a pre-specified

XIPERE sales milestone achieved no later than March 31, 2024. The terms of the Purchase and Sale Agreement also provide for an additional $20 million milestone payment to Royalty Sub upon attainment of a second pre-specified sales milestone related to 2024 XIPERE sales, or the Second Milestone Event.

The Purchase and Sale Agreement will automatically expire, and the payment of Royalties from the Royalty Sub to HCR will cease, when HCR has received payments of the Royalties equal to 2.5 times the aggregate amount of payments made by HCR under the Agreement if the Second Milestone Event is achieved on or prior to December 31, 2024, or the Initial Cap. If the Second Milestone Event is not achieved on or prior to December 31, 2024, payment of Royalties from Royalty Sub to HCR will cease when HCR has received Royalties payments equal to 3.4 times the aggregate amount of payments under the Purchase and Sale Agreement, or the Alternative Cap. In the event of a change in control, acquiror will have the option to make a payment to HCR of the Initial Cap or the Alternative Cap, depending on which is then in effect, less the aggregate amount of Royalty payments made by Royalty Sub to HCR under the Purchase and Sale Agreement as a one-time payment at which time, payment of Royalties to HCR will cease. Alternatively, in the event of a change in control, the acquiror will have the option to make an initial payment of 1.0 times the aggregate amount of payments made by HCR under the Purchase and Sale Agreement as of the date of such change in control, then in that event, payment of Royalties from Royalty Sub to HCR will cease when HCR has received total Royalties payments (including the initial payment) equal to the Alternative Cap. After the Purchase and Sale Agreement expires, all rights to receive the Royalties return to Royalty Sub.

Manufacturing

We do not own any manufacturing facilities. We utilize CMOs to formulate and produce our drug candidates and to produce our SCS Microinjector. We procure active pharmaceutical ingredients for our drugs from third-party suppliers. We expect to continue to utilize third-party manufacturers to produce quantities of our drug candidates and the SCS Microinjector.

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 may enter into commercial supply agreements with our other suppliers.

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, South Korea, India, the ASEAN Countries, Australia and New Zealand. 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 companies, specialty pharmaceutical and biotechnology companies, government agencies and public, and private research and academic 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, although none are approved for the indication of macular edema associated with uveitis. Bristol-Myers Squibb markets TA, under the brand name Kenalog, for which a number of generic equivalents are currently available. Kenalog is indicated only for intramuscular or intraarticular injection; however, it is used off-label for intraocular inflammation using intravitreal and periocular administration. In addition, Alcon’s injectable TA, Triesence, is approved in the United States for the treatment of uveitis and other ocular inflammatory conditions unresponsive to topical corticosteroids, but it is not indicated for the treatment of macular edema associated with uveitis. Ozurdex, marketed by Allergan, is a bio-erodible, extended-release implant that delivers the corticosteroid and dexamethasone, and is approved for the treatment of non-infectious uveitis affecting the posterior segment of the eye and for macular

edema due to retinal vein occlusion, or RVO in both the United States and in the European Union. Ozurdex is also approved in the United States for the treatment of diabetic macular edema, or DME. Retisert and Yutiq, both intravitreal implants of fluocinolone acetonide, are marketed by Bausch and Eyepoint Pharmaceuticals, respectively, and are approved in the United Sates for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye. In addition, Oxular is developing OXU-001 which is dexamethasone delivered via the Oxulumis suprachoroidal device for the treatment of Diabetic Macular Edema. It is possible physicians may use OXU-001 off label to treat macular edema associated with uveitis once approved.

CLS-AX faces competition with anti-VEGF drugs, the current standard of care for RVO and wet AMD, as well as other drug candidates in development for ocular use for the treatment of wet AMD, such as other TKI's. Axitinib, also known by its brand name Inlyta, is not currently approved for an ocular indication but is approved by the FDA and marketed by Pfizer for the treatment of advanced renal cell carcinoma. Genentech has several products which serve as competitors in this space, including anti-VEGF agents Lucentis, Avastin, and Susvimo. 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 routinely 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. Susvimo, an ocular implant that releases ranibizumab over time, received approval from the FDA in October 2021 for the treatment of wet AMD in patients who have previously responded to anti-VEGF therapy. Additionally, Genentech's product, Vabysmo (faricimab-svoa), an intravitreal injection which blocks two disease pathways, including (Ang-2) and vascular endothelial growth factor-A (VEGF-A), received approval in January 2022 for the treatment of wet AMD and diabetic macular edema.

In addition to Genentech's products, Regeneron's anti-VEGF product, Eylea and Novartis' product, Beovu, also present potential competition for CLS-AX in both the United States and Europe. Eylea is approved for the treatment of wet AMD, macular edema following RVO and diabetic retinopathy and DME in the United States and for the treatment of wet AMD, RVO and DME in the European Union. Novartis' Beovu was approved in 2019 for the treatment of wet AMD in the United States and in 2020 in Europe.

Additional future competition may emerge from biosimilar anti-VEGF products as they are approved and enter the market.

Ocular drug candidates being investigated for treatment of wet AMD may also represent potential competition for CLS-AX. Ocular Therapeutics and Eyepoint are companies currently investigating TKIs for ocular use. We expect other established companies will seek to develop new products in the ocular space with the goal of superior efficacy and duration over the current standard of care.

The SCS Microinjector faces competition from other devices being developed to access ocular posterior tissues via the SCS. Oxular Limited announced plans to file for a 510(k) clearance of its Oxulumis device which is designed to administer therapy to the SCS via a microcatheter, and Gyroscope Therapeutics also announced 510(k) clearance for its Orbit Subretinal Delivery System which uses a catheter to access the subretinal space via the SCS.

Both large and established companies, as well as smaller or early-stage companies could represent challenges in the competitive space. Larger established companies may have greater resources such as greater financial resources, deeper expertise and personnel in nonclinical development, clinical development, manufacturing and regulatory sectors. Smaller or early-stage companies could pose a challenge competitively through collaborative arrangements with large and established companies. Lastly, both small and large companies will compete in areas such as recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient recruitment for competing clinical trials.

Several key competitive factors affecting the potential success of our product candidates are likely to be the efficacy, safety, method of administration, convenience, price and the availability of coverage and reimbursement from government and other third-party payors. Additionally, our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, more convenient or are less expensive than any drugs we develop. The timing of competitors' regulatory approval and patent protection could also impact commercial opportunities. Competitors receiving approval prior to us could result in stronger market positioning and/or obtaining FDA market exclusivity. Competitors' patent protection could potentially delay FDA approval of our product candidates for up to 30 months, as well as subject us to potential patent litigation that might arise beyond the 30 months.

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 27 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 23 patent applications pending in the United States, 75 issued foreign patents and one allowed foreign patents, three pending international PCT applications and 44 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 eight issued U.S. patents, five pending U.S. applications, 21 of the issued foreign patents, and four 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 2042, 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, we made a $75,000 payment related to a milestone that was achieved in December 2021 for 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. Additionally, we are currently paying 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 and one pending application in Canada, five registered trademarks in China, four registered and two pending applications in the European Union, two registered trademarks in each of India and New Zealand, two registered trademarks in Japan, three registered and 1 pending application in Israel, eight registered trademarks in Mexico, four registered and three pending applications in South Africa, six registered trademarks in the United States and four pending applications in the United States and six registered trademarks in the United Kingdom. We also have three international registrations: the first with registered protection in the European Union, India, Japan, New Zealand, Korea and Singapore; the second with extensions of protection pending in India and registered in Australia, China, European Union, Israel, Japan, Korea, Mexico, New Zealand, Russia, and Singapore; and the third with extensions of protection pending in Australia, Brazil, Canada, Japan and Mexico.

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. This includes combination products where a drug and a device are used together.

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

One of our regulatory strategies 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 may seek orphan drug designation for 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.

Outside the United States, an increasing number of laws, regulations, and industry standards govern data privacy and security. For example, the European Union's General Data Protection Regulation, or EU GDPR, and the United Kingdom's GDPR, or UK GDPR, impose strict requirements for processing personal data. Under the EU GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. In Canada, the Personal Information Protection and Electronic Documents Act and various related provincial laws, as well as Canada's Anti-Spam Legislation, may, in the future, apply to our operations.

In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area (EEA) and the United Kingdom (UK) have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA and UK's standard contractual clauses, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups.

Additionally, California has 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 applies to personal information of consumers, business representatives, and employees, and requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights. The CCPA provides for civil penalties of up to $7,500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA increases compliance costs and potential liability with respect to other personal data we maintain about California residents. In addition, the California Privacy Rights Act of 2020, or CPRA expands the CCPA's requirements, including by adding a new right for individuals to correct their personal information and establishing a new regulatory agency to implement and enforce the law. Other states, such as Virginia, Colorado, Utah, and Connecticut have also passed comprehensive privacy laws, and similar laws are being considered in several other states, as well as at the federal and local levels. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us, the third parties upon whom we rely.

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), other healthcare professionals (such as physicians assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their family members. 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. CPT code 0465T became effective on January 1, 2017. With respect to our product candidates, we or our partners may seek a separate Healthcare Common Procedure Coding System, or HCPCS, code as maintained by CMS for the drug itself. We believe obtaining billing codes for the use of our products is critical to maximizing our commercial success. There is no guarantee that these billing codes, once granted, 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. In addition, beginning on January 1, 2023, certain manufacturers will be required to pay quarterly refunds to CMS for discarded amounts of single-dose container and single-use package drugs covered under Medicare Part B. Refunds will be based on the discarded volume above 10% of the total allowed amount, except in unique circumstances as determined by CMS. 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 have been 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. Further, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated 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 instructed 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. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear any additional 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 until 2031. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. 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, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" for such drugs and biologics under the law, and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. 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.

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, 2022, we had 36 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 30005. 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 a net loss of $32.9 million in 2022, net income of $0.4 million in 2021 and net loss of $18.2 million in 2020. We expect to incur significant expenses and operating losses over the next several years. Our financial results may fluctuate significantly from quarter to quarter and year to year.

We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. 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;
- establish additional partnerships for the development and commercialization of our assets;
- 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.

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 second quarter of 2024. However, we will need to obtain substantial additional funding in connection with our continuing operations beyond the second quarter 2024, including additional funding to complete clinical development of CLS-AX. Our future capital requirements will depend on many factors, including:

- the progress and results of our ongoing, planned and future clinical trial programs;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval and intend to commercialize ourselves;
- the amount of revenue, if any, received from commercial sales of any 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 of our product candidates and achieve product sales. In addition, XIPERE and our other product candidates, if approved, may

not achieve commercial success. 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 grant licenses on terms that may not be favorable to or relinquish valuable rights to our technologies, research programs, product candidates or future revenue streams. For example, we, through our wholly-owned subsidiary, sold our rights to receive certain royalty and milestone payments under the Arctic Vision License Agreement, Bausch License Agreement, the Aura License Agreement, the REGENXBIO Option and License Agreement and any out-license agreements for, or related to, XIPERE or our SCS Microinjector technology to be used in connection with compounds or products of any third parties in exchange for up to $65 million. 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 agreements with HCR contain various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.

On August 8, 2022, we, through Royalty Sub, entered into the Purchase and Sale Agreement, with HCR pursuant to which we sold our rights to royalty and milestone payments due to us from XIPERE and certain license agreements related to our SCS Microinjector, or the Royalties, subject to a cap of 2.5 times the total purchase price paid by HCR under the Purchase and Sale Agreement, which cap can be increased to 3.4 times under certain circumstances. Under the terms of the Purchase and Sale Agreement, Royalty Sub received an initial payment of $32.5 million, less certain expenses. An additional $12.5 million was placed in an escrow account to be released to Royalty Sub upon attainment of a pre-specified XIPERE sales milestone achieved no later than March 31, 2024. The terms of the Purchase and Sale Agreement also provide for an additional $20 million milestone payment to Royalty Sub upon attainment of a second pre-specified sales milestone related to 2024 XIPERE sales.

In connection with the Purchase and Sale Agreement, we entered into a Contribution and Servicing Agreement with Royalty Sub, pursuant to which we assigned the Arctic Vision License Agreement, Bausch License Agreement, Aura License Agreement, REGENXBIO Option and License Agreement, our license agreement with Emory University and The Georgia Tech Research Corporation and related intellectual property rights, or collectively the Contributed Assets, to Royalty Sub. The Contribution and Servicing Agreement contains various representations and warranties, covenants, indemnification obligations and other provisions related to the contribution of the Contributed Assets and our maintenance and servicing obligations with respect to the same.

In connection with the Purchase and Sale Agreement, we also entered into a Pledge and Security Agreement with HCR. The Pledge and Security Agreement contains various representations, warranties and covenants, and includes a limited recourse guaranty of Royalty Sub's obligations under the Purchase and Sale Agreement which is secured by the pledge in favor of HCR all of the capital stock of Royalty Sub. HCR is entitled to foreclose on the capital stock of Royalty Sub following the occurrence of certain remedies events, including, without limitation, a bankruptcy of us, our failure of to perform our obligations under the Contribution and Servicing Agreement or in the event of a change of control of us, any failure to make the payment required under Section 2.3 of the Purchase Agreement within the time period required thereunder. Such foreclosure, if it were to occur, could have a material adverse effect on our financial condition as HCR, by virtue of owning Royalty Sub, would own the Royalties and the Contributed Assets.

Our business could be adversely affected by economic downturns, inflation, increases in interest rates, natural disasters, public health crises such as the COVID-19 pandemic, political crises, geopolitical events, such as the crisis in Ukraine, or other macroeconomic conditions.

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in inflation rates, higher interest rates and uncertainty about economic stability. For example, the COVID-19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. The Federal Reserve recently raised interest rates multiple times in response to concerns about inflation and it may raise them again. Higher interest rates, coupled with reduced government spending and volatility in financial markets may increase economic uncertainty and affect consumer spending. Similarly, the ongoing military conflict between Russia and Ukraine has created extreme volatility in the global capital markets and is expected to have further global economic consequences, including disruptions of the global supply chain and energy markets. Any such volatility and disruptions may adversely affect our or our partners' business. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more costly or more dilutive or more difficult to obtain in a timely manner or on favorable terms, if at all. Increased inflation rates can adversely affect us by increasing our costs, including clinical trials costs and labor and employee benefit costs.

Adverse developments affecting financial institutions, companies in the financial services industry or the financial services industry generally, such as actual events or concerns involving liquidity, defaults or non-performance, could adversely affect our operations and liquidity.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank, or SVB, was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation, or the FDIC, as receiver. As of March 10, 2023, we had nearly all of our cash and cash equivalent balances on deposit with SVB.

Although a statement by the U.S. Department of the Treasury, the Federal Reserve and the FDIC stated that all depositors of SVB would have access to all of their money after only one business day following the date of closure and we and other depositors with SVB received such access on March 13, 2023, uncertainty and liquidity concerns in the broader financial services industry remain. Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. The U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25 billion of loans to financial institutions secured by such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments. However, widespread demands for customer withdrawals or other needs of financial institutions for immediate liquidity may exceed the capacity of such program. There is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions in a timely fashion or at all.

Our access to our cash and cash equivalents in amounts adequate to finance our operations could be significantly impaired by the financial institutions with which we have arrangements directly facing liquidity constraints or failures. In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any material decline in available funding or our ability to access our cash and cash equivalents could adversely impact our ability to meet our operating expenses, result in breaches of our contractual obligations or result in violations of federal or state wage and hour laws, any of which could have material adverse impacts on our operations and liquidity.

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 SCS. 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 the FDA approved XIPERE for suprachoroidal use for the treatment of macular edema associated with uveitis, we cannot guarantee that suprachoroidal injection of other 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 other drugs will achieve regulatory approval, even if the clinical trials are successful.

In addition, 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 drugs 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 drugs. Additionally, in some cases, drugs 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 SCS. 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 after we have satisfied our obligations under the Purchase and Sale Agreement, which could significantly harm our financial position.

If we are unable to obtain regulatory approval for, and commercialize either on our own or with a third party, CLS-AX or our other product candidates, or if we experience significant delays in doing so, our business may be harmed.

Given our 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 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 trials. 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 CLS-AX or 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.

For example, our initiation of the ODYSSEY trial will be delayed by one quarter due to the issuance by FDA of draft guidance on February 6, 2023 entitled Neovascular Age-Related Macular Degeneration: Developing Drugs for Treatment. As announced by us on February 3, 2023, the ODYSSEY trial originally was planned to have intravitreal faricimab as the comparator drug and would have been initiated in the first quarter of 2023. Based on the draft guidance publication and subsequent interaction with FDA, we intend to amend the protocol to have aflibercept as the comparator drug. As we finalize the protocol amendment in consultation with FDA there may be additional changes to our originally announced design. Despite changing the protocol in response to FDA's draft guidance, the guidance document could be finalized in the future with different recommendations at a time at which the ODYSSEY trial can no longer be amended, potentially requiring longer or additional clinical development of CLS-AX for the treatment of wet AMD.

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 cannot predict how successful we will be at enrolling patients in future clinical trials. In addition, if we are not successful at enrolling patients in one clinical trial, it may affect when we are able to initiate our next clinical trial, which could result in significant delays in our efforts to pursue regulatory approval of and commercialize our product candidates. In addition, some of our competitors have ongoing clinical trials to treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors. Patient enrollment is affected by other factors including:

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

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

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

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

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

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

Risks Related to Our Dependence on Third Parties

We have granted an exclusive license to Bausch for the commercialization and development of XIPERE in the United States and Canada. After we have satisfied our obligations under the Purchase and Sale Agreement, if 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. We will not retain these royalties and milestone

payments until our obligations under the Purchase and Sale Agreement described above in "Business—Royalty Purchase and Sale Agreement" are satisfied. The successful or timely achievement of many of these milestones is outside of our control because the relevant activities will be conducted by Bausch or third parties engaged by Bausch, including manufacturers and suppliers. We expect to depend to a large degree on the payments from Bausch after we have satisfied our obligations under the Purchase and Sale Agreement as well as payments from 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.

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

We have entered into, and intend to continue to enter into, agreements with third-party collaborators for the development and commercialization of XIPERE and 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 XIPERE and 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 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 our 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 and our SCS Microinjector. This reliance on third parties increases the risk that we will not have

sufficient quantities of our drug products 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 of our product candidates 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, for any of our product candidates that receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug products 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. In addition, 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. 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.

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/or our commercialization partner's 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.

XIPERE and any of our product candidates that receive marketing approval, 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.

XIPERE and any of our product candidates that receive marketing approval 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 XIPERE or 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 XIPERE and 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 products 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, for which a number of generic equivalents are currently available. Kenalog is indicated only for intramuscular or intraarticular injection; however, it is commonly used off-label for intraocular inflammation using intravitreal and periocular administration. In addition, Alcon's injectable TA, Triesence, is approved in the United States for the treatment of uveitis and other ocular inflammatory conditions unresponsive to topical corticosteroids, although it is not indicated for the treatment of macular edema associated with uveitis. 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. Ozurdex is also approved in the United States for the treatment of DME. Retisert and Yutiq, both intravitreal implants of fluocinolone acetonide, are marketed by Bausch and Eyepoint Pharmaceuticals, respectively, and are approved in the United Sates for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

CLS-AX faces competition with anti-VEGF drugs, the current standard of care for RVO and wet AMD, as well as other drug candidates in development for ocular use for the treatment of wet AMD, such as other TKI's. Axitinib, also known by its brand name Inlyta, is not currently approved for an ocular indication but is approved by the FDA and marketed by Pfizer for the treatment of advanced renal cell carcinoma. Genentech has several products which serve as competitors in this space, including anti-VEGF agents Lucentis, Avastin, and Susvimo. 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 routinely 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. Susvimo, an ocular implant that releases ranibizumab over time, received approval from the FDA in October 2021 for the treatment of wet AMD in patients who have previously responded to anti-VEGF therapy. Additionally, Genentech's product, Vabysmo (faricimab-svoa), an intravitreal injection which blocks two disease pathways, including (Ang-2) and vascular endothelial growth factor-A (VEGF-A), received approval in January 2022 for the treatment of wet AMD and diabetic macular edema. In addition to Genentech's products, Regeneron's anti-VEGF product, Eylea and Novartis' product, Beovu, also present potential competition for CLS-AX in both the United States and Europe. Eylea is approved for the treatment of wet AMD, macular edema following RVO and diabetic retinopathy and DME in the United States and for the treatment of wet AMD, RVO and

DME in the European Union. Novartis' Beovu was approved in 2019 for the treatment of wet AMD in the United States and in 2020 in Europe.

Ocular drug candidates being investigated for treatment of wet AMD may also represent potential competition for CLS-AX. Ocular Therapeutics and Eyepoint are companies currently investigating TKIs for ocular use. We expect other established companies will seek to develop new products in the ocular space with the goal of superior efficacy and duration over the current standard of care.

The SCS Microinjector faces competition from other devices being developed to access ocular posterior tissues via the SCS. Oxular Limited recently announced plans to file for a 510(k) clearance of its Oxulumis device which is designed to administer therapy to the SCS via a microcatheter, and Gyroscope Therapeutics also announced 510(k) clearance for its Orbit Subretinal Delivery System which uses a catheter to access the subretinal space via the SCS.

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.

XIPERE and 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 XIPERE and any of our 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, the Centers for Medicare and Medicaid Services, or 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. For our product candidates, 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. Additionally, coverage policies and reimbursement rates may change at any time. For example, beginning on January 1, 2023, certain manufacturers will be required to pay quarterly refunds to CMS for discarded amounts of single-dose container and single-use package drugs covered under Medicare Part B. Refunds will be based on the discarded volume above 10% of the total allowed amount, except in unique circumstances, as determined by CMS. 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. Further, 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.

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 sale of XIPERE as well as the testing of our product candidates in human clinical trials. 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.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

The United States has enacted and implemented wide-ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future. For example, the complexity and uncertainty of European patent laws have also increased in recent years. In Europe, a new unitary patent system will likely be introduced by the end of 2023, which would significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

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

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 expect to rely on third-party CROs to assist us in preparing some or all aspects of the applications necessary to gain marketing approvals. 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 a product candidate satisfies 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 in this pathway 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 believe that certain of 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 for a product candidate 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-device combination product.

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

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 research, 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 (including privacy and cybersecurity laws and regulations) 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;
- the Health Insurance Portability and Accountability Act, or 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 the Health Information Technology for Economic and Clinical Health Act of 2019, or 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, 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), other healthcare professionals (such as physicians assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- 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;
- new U.S. data privacy regulations, such as the California Privacy Rights Act of 2020, or CPRA, which establishes a new California Privacy Protection Agency to implement and enforce the CPRA. Other states, such as Virginia, Colorado, Utah, and Connecticut have also passed comprehensive privacy laws that have or will go into effect during 2023, and similar laws are being considered in several other states, as well as at the federal and local levels. While these new state laws, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us, the third parties upon whom we rely. If we become subject to new data privacy laws, at the state level, the risk of enforcement action against us could increase because we may become subject to additional obligations, and the number of individuals or entities that can initiate actions against us may increase (including individuals, via a private right of action, and state actors);
- foreign data privacy regulations, such as the General Data Protection Regulation (2016/679), or GDPR, which 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, including a private right of action. Also under the EU GDPR, companies may face temporary or definitive bans on data processing and other corrective actions. Other such foreign data privacy obligations include the EU GDPR as it forms part of United Kingdom ("UK") law by virtue of section 3 of the European Union (Withdrawal) Act 2018 ("UK GDPR"); and
- In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area (EEA) and the United Kingdom (UK) have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA and UK's standard contractual clauses, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups.

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 have been judicial and congressional challenges to certain aspects of the Affordable Care Act. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period 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. The Affordable Care Act may be subject to additional judicial or Congressional challenges in the future. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear how any additional 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 2031 with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. 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, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, , the Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. In addition, the IRA, among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" for such drugs and biologics under the law, and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. 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

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, 2021, our common stock has traded at prices between $0.98 and $7.73 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated or disproportionate to the operating performance of particular companies, including in connection with the COVID-19 pandemic. Broad market and industry factors, including potentially worsening economic conditions, inflation and other adverse effects or developments relating to the ongoing COVID-19 pandemic, may negatively affect the market price of our common stock, regardless of our actual operating performance. 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;
- sales of our common stock, including sales by our directors and officers or specific stockholders; and
- general political and economic conditions.

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.

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 a "smaller reporting company" and as a result of the reduced disclosure and governance requirements applicable to smaller reporting companies, our common stock may be less attractive to investors.

We are 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. 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 we have reduced disclosure obligations regarding executive compensation. In addition, as a smaller reporting company and non-accelerated filer, we are not required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. We cannot predict whether investors will find our securities less attractive because we will rely on these exemptions. If some investors find our securities less attractive as a result of our reliance on these exemptions, the trading prices of our securities may be lower than they otherwise would be, there may be a less active trading market for our securities and the trading prices of our securities may be more volatile.

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, including but not limited to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits and other adverse consequences.

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. Cyberattacks, malicious internet-based activity, and online and offline fraud are prevalent and continue to increase. These threats are becoming increasingly difficult to detect. These threats come from a variety of sources. In addition to traditional computer "hackers," threat actors, personnel (such as through theft or misuse), sophisticated nation-states, and nation-state-supported actors now engage in attacks. We and the third parties upon which we rely may be subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing), personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fires, floods, and other similar threats.

Any of the foregoing 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, or any personal data for which we are responsible, 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. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

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, the Inflation Reduction 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, or the Code. In March 2020, the Tax Act was modified in certain respects by the Coronavirus Aid, Relief, and Economic Security (CARES) Act. More recently, the Inflation Reduction Inflation of 2022, or the IRA, was enacted which includes provisions that impact the U.S. federal income taxation of corporations, including imposing a minimum tax on the book income of certain large corporations and an excise tax on certain corporate stock repurchases that would be imposed on the corporation repurchasing such stock. 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, and the IRA, may affect us, and certain aspects of the Tax Act, CARES Act and IRA 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, the IRA, 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, the CARES Act, the IRA, 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, 2022, we had approximately $216.1 million of federal and $78.4 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 NOLs incurred in taxable years beginning in 2018 and in later years may be carried forward indefinitely, but the deductibility of such federal NOLs is limited for taxable years beginning after 2020 to 80% of taxable income. Certain states have conformed to the federal NOL rules included in the Tax Act and CARES Act. However, under Section 382 of the Code of 1986, 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 ownership changes. The completion of our IPO, follow-on public offerings, private placements and other transactions that have occurred, and future offerings of our securities have triggered, and may in the future trigger additional, ownership changes. We have determined that three such ownership changes have occurred in the past. We have determined that $38,000 and $2,000 of our deferred tax assets related to federal NOL and R&D credits, respectively, will expire due to Section 382.

In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo ownership changes in the future. Any such additional limitations 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 limitations. 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.

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. Because we are a smaller reporting company and a non-accelerated filer, we are not required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. However, 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 if we cease to be a smaller reporting 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.

Climate change, extreme weather events, earthquakes and other natural disasters could adversely affect our business.

In recent years, extreme weather events and changing weather patterns such as storms, flooding, droughts, fires and temperature changes have become more common. As a result, we are potentially exposed to varying natural disaster or extreme weather risks such as hurricanes, tornadoes, fires, droughts or floods, or other events that may result from the impact of climate change on the environment, such as sea level rise. The potential impacts of climate change may also include increased operating costs associated with additional regulatory requirements and investments in reducing energy, water use and greenhouse gas emissions.

Adverse global economic conditions and geopolitical tensions could have a negative effect on our business, results of operations and financial condition and liquidity.

In recent years, concerns about the global economic outlook have adversely affected market and business conditions in general. Macroeconomic weakness and uncertainty could make it more difficult for us or the licensing partners on whom we depend to commercialize XIPERE to manage our respective operations. Geopolitical tensions, such as Russia's recent incursion into Ukraine, ongoing conflicts between the United States and China, tariff and trade policy changes, economic sanctions and increasing potential of conflict involving countries in Asia, including countries that are part of the Artic Territory under our license agreement with Arctic Vision, create uncertainty for us and for global commerce generally. Sustained or worsening of global economic conditions and increasing geopolitical tensions may increase our cost of doing business, limit our ability to access capital, disrupt our supply chain operations or the supply chain operations of our licensing partners and intensify pricing pressures. Any or all of these factors could negatively affect our business, financial condition and result of operations.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal offices occupy approximately 14,000 square feet of office space in Alpharetta, Georgia under a lease with an initial term until November 2026, with a renewal option for one additional three-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 8, 2023, we had 61,364,299 shares of common stock outstanding held by 7 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. [Reserved].

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 focused on revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS). Our SCS injection platform, utilizing our proprietary SCS Microinjector, enables an in-office, repeatable, non-surgical procedure for the targeted and compartmentalized delivery of a wide variety of therapies to the macula, retina or choroid to potentially preserve and improve vision in patients with sight-threatening eye diseases. Our suprachoroidal injection technology can be used in conjunction with existing drugs designed for delivery to the SCS, novel therapies, and future therapeutic innovations. We believe our proprietary suprachoroidal administration platform has the potential to become a standard for delivery of therapies intended to treat chorioretinal diseases.

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. We are developing our own pipeline of small molecule product candidates for administration via our SCS Microinjector, and we also strategically partner with companies developing other ophthalmic therapeutic innovations to be administered using our SCS injection platform. Our first product, XIPERE (triamcinolone acetonide injectable suspension) for suprachoroidal use, was approved by the U.S. Food and Drug Administration, or the FDA, in October 2021. Approval of XIPERE was a significant milestone for us as it is the first approved therapeutic delivered into the SCS, the first commercial product developed by us, and the first therapy for macular edema associated with uveitis.

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 only generated revenue through upfront payments and milestone payments related to license agreements and other revenue generated from collaboration agreements. 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, 2022, we had an accumulated deficit of $288.3 million. We recorded net losses of $32.9 million for the year ended December 31, 2022, net income of $0.4 million for the year ended December 31, 2021 and net losses of $18.2 million for the year ended December 31, 2020. 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 therapeutics 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 XIPERE is successfully commercialized by its licensees or until we successfully complete development of, obtain regulatory approval for and commercialize additional product candidates, either on our own or together with a third party. Our financial results may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials and our expenditures on other research and development activities. We expect clinical trial expenses to increase in 2023 as a result of the implementation of a Phase 2b clinical trial of CLS-AX as well as continuing our pipeline development. We also 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. Based on our current research and development plans, we expect to have sufficient resources to fund our planned operations into the second quarter of 2024. We will require additional capital in order to complete clinical development of CLS-AX.

Components of Operating Results

Revenue

We have not generated any revenue from the sale of XIPERE and we do not expect to generate any other product revenue unless or until we obtain regulatory approval of and commercialize our other product candidates, either on our own or with a third party. The revenue received under the Bausch license agreement, as well as other certain payments from our licensees, will be recorded as non-cash revenue until we have fulfilled our obligations under the Purchase and Sale Agreement. 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, 2022, 2021 and 2020.

	Year Ended December 31,		
	2022	**2021**	**2020**
		(in thousands)	
XIPERE (uveitis program)	$ 339	$ 2,612	$ 3,841
CLS-AX (wet AMD program)	5,449	4,515	2,169
CLS-301 (DME program)	911	966	240
Total program expense	6,699	8,093	6,250
Unallocated	12,931	10,444	8,823
Total research and development expense	$ 19,630	$ 18,537	$ 15,073

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 our product candidates including the SCS Microinjector for clinical trials and for requirements associated with regulatory filings;
- 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 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 (Other Expense)

Other income consists of the gain on the extinguishment of the PPP Loan and accrued interest and 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.

Non-cash Interest Expense on Liability Related to the Sales of Future Royalties

Non-cash interest expense on liability related to the sales of future royalties consists of imputed interest on the carrying value of the liability and the amortization of the related issuance costs.

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 consolidated 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 consolidated 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

We recognize revenue from our contracts with customers under Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 606, Revenue from Contracts with Customers ("ASC 606"). 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. The arrangements may also include assistance and oversight of the customer's use of the drug substance or drug product. 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 consolidated 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, directors and consultants 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. 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.* In the year ended December 31, 2022, we used historical data to calculate the expected term. In the years ended December 31, 2021 and 2020, we used the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, as we did 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 $4.9 million, $5.1 million and $3.6 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Liabilities Related to the Sales of Royalties and Non-Cash Interest Expense

We recognized a liability related to the sales of future royalties under ASC 470-10 Debt and ASC 835-30 Interest - Imputation of Interest. The initial funds received by us pursuant to the terms of the Purchase and Sale Agreement were recorded as a liability and will be accreted under the effective interest method up to the estimated amount of future royalties and milestone payments to be made under the Purchase and Sale Agreement. The issuance costs were recorded as a direct deduction to the carrying amount of the liability and will be amortized under the effective interest method over the estimated period the liability will be repaid. We estimated the total amount of future royalty revenue and milestone payments to be generated over the life of the Purchase and Sale Agreement, and a significant increase or decrease in these estimates could materially impact the liability balance and the related interest expense. If the timing of the receipt of royalty payments or milestones is materially different from the original estimates, we will prospectively adjust the effective interest and the related amortization of the liability and related issuance costs.

Tax valuation allowance

We recorded aggregate deferred tax assets of $73.7 million, primarily related to our net operating losses, as of December 31, 2022, 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, 2022. We incurred a net income for tax purposes of $19.3 million for the year ended December 31, 2022 which was offset by utilizing NOLs for the same amount. 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, 2022, we had federal NOL carryforwards of $216.1 million and state NOL carryforwards of $78.4 million available to reduce future taxable income, if any. These federal NOL carryforwards will begin to expire at various dates starting in 2031. The state NOL carryforwards will begin to expire at various dates starting in 2027. In general, if we experience a greater than 50 percentage point aggregate change in ownership of specified significant stockholders over a three-year period, utilization of our pre-change NOL carryforwards will be subject to an annual limitation under Section 382 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and similar state laws. Such limitations may result in expiration of a portion of the NOL carryforwards before utilization and may be substantial. The completion of our IPO, follow-on public offerings, private placements and other transactions that have occurred, and future offerings of our securities have triggered, and may in the future trigger additional, ownership changes. We have determined that three such ownership changes have occurred in the past. We have determined that $38,000 and $2,000 of our deferred tax assets related to federal NOL and R&D credits, respectively, will expire due to Section 382. In addition, 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, 2022 and 2021

The following table sets forth our results of operations for the years ended December 31, 2022 and 2021.

	Year Ended December 31,		Period-to-Period Change
	2022	2021	
		(in thousands)	
License and other revenue	$ 1,327	$ 29,575	$ (28,248)
Operating expenses:			
Cost of goods sold	204	—	204
Research and development	19,630	18,537	1,093
General and administrative	11,770	11,665	105
Total operating expenses	31,604	30,202	1,402
Loss from operations	(30,277)	(627)	(29,650)
Other income	669	1,003	(334)
Non-cash interest expense on liability related to the sales of future royalties	(3,339)	—	(3,339)
Net (loss) income	$ (32,947)	$ 376	$ (33,323)

Revenue. In the year ended December 31, 2022 and 2021, we recognized $1.3 million and $29.6 million of revenue associated with our license agreements. License revenue for the year ended December 31, 2022 was primarily from providing training materials and clinical trial products to our licensees. License revenue for the year ended December 31, 2021 was primarily a result of (i) the milestone payments from Bausch that consisted of $5.0 million received upon FDA approval of XIPERE, the recognition of $5.0 million of deferred revenue for the upfront milestone payment and the recognition of a $10.0 million milestone for pre-launch activities and (ii) an aggregate of $8.0 million received from Arctic Vision for FDA approval of XIPERE, territory expansion and certain development milestones.

Cost of Goods Sold. In the year ended December 31, 2022, we recognized $0.2 million in cost of goods sold related to the sales of our SCS Microinjector kits to our licensees.

Research and development. Research and development expense increased by $1.1 million, from $18.5 million for the year ended December 31, 2021 to $19.6 million for the year ended December 31, 2022. This increase was primarily due to a $0.9 million increase in costs for the CLS-AX program, including costs for OASIS, a Phase 1/2a clinical trial of CLS-AX, the OASIS extension study and the preliminary startup costs of ODYSSEY, a Phase 2b clinical trial of CLS-AX. Additionally, there was $1.2 million in costs related to our other programs and a $0.7 million increase in costs related to an increase in headcount. This is partially offset by a $2.3 million decrease in costs related to XIPERE.

General and administrative. General and administrative expenses increased by $0.1 million for the years ended December 31, 2022 and 2021. This increase was primarily a result of a $0.4 million increase in patent related expenses and a $0.5 million decrease in costs related to employee benefits.

Other income. Other income for the year ended December 31, 2022 was primarily comprised of interest income from the cash and cash equivalents. Other income for the year ended December 31, 2021 was primarily comprised of the gain on the extinguishment of debt from the forgiveness of the PPP Loan and accrued interest.

Non-cash interest expense from liability related to the sales of future royalties. Non-cash interest expense for the year ended December 31, 2022 was comprised of imputed interest on the liability related to the sales of future royalties and the amortization of the associated issuance costs.

Results of Operations for the Years Ended December 31, 2021 and 2020

The following table sets forth our results of operations for the years ended December 31, 2021 and 2020.

	Year Ended December 31,		Period-to-Period Change
	2021	2020	
		(in thousands)	
License and other revenue	$ 29,575	$ 7,894	$ 21,681
Operating expenses:			
Research and development	18,537	15,073	3,464
General and administrative	11,665	10,756	909
Total operating expenses	30,202	25,829	4,373
Loss from operations	(627)	(17,935)	17,308
Other income	1,003	—	1,003
Other expense	—	(275)	275
Net income (loss)	$ 376	$ (18,210)	$ 18,586

Revenue. In the year ended December 31, 2021, we recognized $29.6 million of revenue associated with our license agreements. For the year ended December 31, 2020, we recognized $7.7 million of revenue associated with our license agreements and $0.2 million 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. License revenue for the year ended December 31, 2021 was primarily a result of (i) the milestone payments from Bausch that consisted of $5.0 million received upon FDA approval of XIPERE, the recognition of $5.0 million of deferred revenue for the upfront milestone payment and the recognition of a $10.0 million milestone for pre-launch activities and (ii) an aggregate of $8.0 million received from Arctic Vision for FDA approval of XIPERE, territory expansion and certain development milestones. License revenue for the year end December 31, 2020 was primarily a result of milestone payments of $4.3 million received from Arctic Vision and $3.0 million milestone payment received from REGENXBIO.

Research and development. Research and development expense increased by $3.5 million, from $15.1 million for the year ended December 31, 2020 to $18.5 million for the year ended December 31, 2021. This increase was primarily due to a $2.3 million increase in costs for the CLS-AX program, including costs for OASIS, a Phase 1/2a clinical trial of CLS-AX, and a $0.7 million increase in costs for the CLS-301 program. Additionally, there was an $0.8 million increase in costs related to share-based compensation and a $0.9 million increase in costs related to an increase in headcount, salary increases and bonuses. This is partially offset by a $1.1 million decrease in costs related to XIPERE.

General and administrative. General and administrative expenses increased by $0.9 million for the years ended December 31, 2021 and 2020. This increase was primarily a result of a $0.7 million increase in costs related to share-based compensation and a $0.5 million increase in costs related to salary increases and bonuses, partially offset by a $0.2 million decrease in professional fees.

Other income. Other income for the year ended December 31, 2021 was primarily comprised of the gain on the extinguishment of debt from the forgiveness of the PPP Loan and accrued interest.

Other expense. Other expense for the year ended December 31, 2020 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 agreement.

Liquidity and Capital Resources

Sources of Liquidity

We have funded our operations primarily through the proceeds from public offerings of our common stock, sales of convertible preferred stock and the issuance of long-term debt. As of December 31, 2022, we had cash and cash equivalents of $48.3 million. We invest any cash in excess of our immediate requirements primarily with a view to liquidity and capital preservation. As of December 31, 2022, our funds were held in cash and money market funds.

During the year ended December 31, 2022, we sold 425,460 shares of our common stock for net proceeds of $0.6 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,

2022, there was $13.8 million available for future sales under the ATM agreement. Subsequent to December 31, 2022, we sold 214,128 shares of our common stock for net proceeds of $0.3 million under the ATM agreement.

On August 8, 2022, or the Closing Date, we, through our wholly-owned subsidiary Clearside Royalty LLC, a Delaware limited liability company, or Royalty Sub, entered into a Purchase and Sale Agreement with entities managed by HealthCare Royalty Management, LLC, or HCR, pursuant to which Royalty Sub sold to HCR certain of its rights to receive royalty and milestone payments payable to Royalty Sub under the Arctic Vision License Agreement, Bausch License Agreement, that certain License Agreement, effective as of July 3, 2019, by and between us and Aura Biosciences, Inc., that certain Option and License Agreement, dated as of August 29, 2019, by and between REGENXBIO Inc. and us, and any and all out-license agreements following the Closing Date for, or related to XIPERE or the SCS Microinjector technology to be used in connection with compounds or products of any third parties delivered, in whole or in part, by means of the SCS Microinjector technology, excluding, for the avoidance of doubt, any in-licensed or internally developed therapies following the Closing Date, in exchange for up to $65 million. Under the terms of the Purchase and Sale Agreement, Royalty Sub received a payment of $32.1 million, representing the $32.5 million to which we were entitled less certain expenses. There were additional issuance costs of $1.5 million related to the Purchase and Sale Agreement resulting in net proceeds of $30.6 million. An additional $12.5 million was deposited in an escrow account by HCR to be released to Royalty Sub upon attainment of a pre-specified XIPERE sales milestone achieved no later than March 31, 2024. The terms of the Purchase and Sale Agreement also provide for an additional $20 million milestone payment to Royalty Sub upon attainment of a second pre-specified sales milestone related to 2024 XIPERE sales.

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.

In April 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 provide a mechanism for forgiveness of up to the full amount borrowed. On January 11, 2021, we received notification from Silicon Valley Bank that the PPP Loan was forgiven in full, including approximately $7,000 of accrued interest.

Pursuant to the Arctic Vision License Agreement, Arctic Vision paid us an upfront payment of $4.0 million in March 2020. In December 2021, we received a milestone payment of $4.0 million following receipt of FDA approval of XIPERE in the United States. In addition, Arctic Vision has agreed to pay us up to a total of $22.5 million in development and sales milestone payments. 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. In August 2021, we entered into an amendment to the Arctic Vision License Agreement to expand the territories covered by the license to include India and the ASEAN Countries (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam). In September 2021, we entered into a second amendment to the Arctic Vision License Agreement to expand the Arctic Territory to include Australia and New Zealand. We received an aggregate of $3.0 million in consideration for the expansion of the Arctic Territory.

In October 2019, we announced that Bausch acquired an exclusive license for the commercialization and development of XIPERE in the United States and Canada. On October 25, 2021, we announced that the FDA approved XIPERE for the treatment of macular edema associated with uveitis. We received a $5.0 million milestone payment from Bausch within 30 days of FDA approval. In December 2021, $10.0 million was recorded as revenue upon completion of pre-launch activities for XIPERE and the payment was received in January 2022. Bausch launched XIPERE in the United States in the first quarter of 2022.

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, research and development costs to build our product candidate pipeline, legal and other regulatory expenses and general overhead costs. In

addition, we have certain contractual obligations for future payments. Refer to Footnote 12 to our financial statements included this Annual Report on Form 10-K.

The successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of CLS-AX 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 and related macroeconomic changes, such as rising inflation. 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 of the territories in which we have previously licensed or granted options to license XIPERE, 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 generate significant milestone payments and royalties from XIPERE and other licensing arrangements or revenues from other product candidates. We will need additional financing to fund our operations. Our plans primarily consist of raising additional capital, potentially in a combination of equity or debt financings, monetizing royalties, 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 14, 2023, will enable us to fund our planned operating expenses and capital expenditure requirements into the second quarter of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our capital resources sooner than we expect. We will require additional capital in order to complete clinical development of CLS-AX.

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,		
	2022	2021	2020
		(in thousands)	
Net cash (used in) provided by:			
Operating activities	$ (13,365)	$ (10,733)	$ (13,120)
Investing activities	(246)	—	(55)
Financing activities	31,333	23,782	7,867
Net change in cash and cash equivalents	$ 17,722	$ 13,049	$ (5,308)

During the years ended December 31, 2022, 2021 and 2020, our operating activities used net cash of $13.4 million, $10.7 million and $13.1 million, respectively. The increase in cash used in operating activities for the year ended December 31, 2022 as compared to the year ended December 31, 2021 was primarily due to research and development expenses related to the preclinical and clinical programs offset by the receipt of the $10.0 million milestone payment received from Bausch in connection with pre-launch activities for XIPERE.

The decrease in cash used in operating activities for the year ended December 31, 2021 as compared to the year ended December 31, 2020 was primarily due to an increase in accounts receivable related to the achievement of pre-launch activities milestone pursuant to our agreement with Bausch. This was partially offset by the decrease in deferred revenue related to the upfront milestone payment from Bausch and an increase of $1.5 million in share-based compensation for the year ended December 31, 2021 compared to prior year.

In the year ended December 31, 2022 and 2020, our investing activities used net cash of $0.2 million and $55,000, respectively, for the purchase of machinery and equipment.

During the years ended December 31, 2022, 2021 and 2020, our net cash provided by financing activities was $31.3 million, $23.8 million and $7.9 million, respectively. The net cash provided by financing activities for the year ended December 31, 2022 was primarily comprised of $30.6 million from the Purchase and Sale Agreement, net of issuance costs and $0.6 million of net proceeds from the sale of shares of our common stock under the ATM agreement. The net cash provided by financing activities for the year ended December 31, 2021 was primarily comprised of $11.1 million of net proceeds from the sale of shares of our common stock in a registered direct offering and $12.2 million of net proceeds from the sale of shares of our common stock under the ATM agreement. 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.

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.

Smaller Reporting Company Status

We are 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. 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 we have reduced disclosure obligations regarding executive compensation.

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 consolidated balance sheets of Clearside Biomedical, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the account or disclosure to which it relates.

Valuation of Liability Related to the Sales of Future Royalties, Net

Description of the Matter	As discussed in Note 2 and 5 to the consolidated financial statements, on August 8, 2022, the Company entered into a Royalty Purchase and Sale Agreement with a third party, pursuant to which the Company sold certain of its rights to receive royalty and milestone payments. The Company received proceeds of $32.1 million, representing the $32.5 million to which the Company was entitled, net of certain transaction related expenses. The Company will repay the lender at a multiple of the initial proceeds received, which may vary based on timing and amount of cash flows received from its licensing partners. The Company recorded the financing as Liability related to the sales of future royalties, net on the balance sheet at its carrying value of $34.0 million as of December 31, 2022. The Company imputes interest expense associated with this liability using the effective interest rate method. Such interest expense is recorded in the statement of operations for the year ended December 31, 2022 as Non-cash interest expense on liability related to the sales of future royalties. The effective interest rate is calculated based on the rate that would enable the estimated liability to be repaid in full over the anticipated life of the arrangement. The Company utilizes the prospective method to record interest expense by updating its estimate of the new effective interest rate each period, based on its current estimate of remaining cash flows under the arrangement. The Company estimates the amount and timing of expected royalty and milestone payments using a combination of internal projections and forecasts from external sources. Auditing the liability related to the sales of future royalties, net was complex and highly judgmental due to the estimation uncertainty in determining the effective interest rate. The Company's effective interest rate model includes cash flow projections for future royalty and milestone payments, which are sensitive to certain assumptions (including market size, market penetration, and sales price) that are forward looking and could be affected by future market conditions.
How We Addressed the Matter in Our Audit	To test the liability related to the sales of future royalties, net as of December 31, 2022, our audit procedures included, among others, assessing the underlying data and significant assumptions used by the Company in determining the timing and amount of future cash flows used within its effective interest rate model. With the support of a specialist, we assessed the reasonableness of the significant assumptions used in the cash flow projections to current industry, market and economic trends. We recalculated the current year interest expense and performed sensitivity analyses to evaluate the changes in the effective interest rate, and associated interest expense, that would result from changes in the assumptions.

/s/ Ernst & Young LLP

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

Atlanta, Georgia
March 14, 2023

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

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	$ 48,258	$ 30,436
Accounts receivable	—	10,000
Prepaid expenses	704	921
Other current assets	439	779
Total current assets	49,401	42,136
Property and equipment, net	755	238
Operating lease right-of-use asset	1,117	369
Restricted cash and other assets	30	160
Total assets	$ 51,303	$ 42,903
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,050	$ 941
Accrued liabilities	4,179	3,312
Current portion of operating lease liabilities	349	387
Deferred revenue	205	—
Total current liabilities	5,783	4,640
Liability related to the sales of future royalties, net	33,977	—
Operating lease liabilities	936	288
Total liabilities	40,696	4,928
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized and no shares issued at December 31, 2022 and 2021	—	—
Common stock, $0.001 par value; 200,000,000 and 100,000,000 shares authorized at December 31, 2022 and 2021, respectively; 60,639,827 and 59,722,930 shares issued and outstanding at December 31, 2022 and 2021, respectively	61	60
Additional paid-in capital	298,984	293,406
Accumulated deficit	(288,438)	(255,491)
Total stockholders' equity	10,607	37,975
Total liabilities and stockholders' equity	$ 51,303	$ 42,903

See accompanying notes to the financial statements

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

	Year Ended December 31,		
	2022	2021	2020
License and other revenue	$ 1,327	$ 29,575	$ 7,894
Operating expenses:			
Cost of goods sold	204	—	—
Research and development	19,630	18,537	15,073
General and administrative	11,770	11,665	10,756
Total operating expenses	31,604	30,202	25,829
Loss from operations	(30,277)	(627)	(17,935)
Other income	669	1,003	—
Non-cash interest expense on liability related to the sales of future royalties	(3,339)	—	—
Other expense	—	—	(275)
Net (loss) income	$ (32,947)	$ 376	$ (18,210)
Net (loss) income per share of common stock — basic and diluted	$ (0.55)	$ 0.01	$ (0.39)
Weighted average shares outstanding — basic	60,204,862	58,491,986	46,506,540
Weighted average shares outstanding — diluted	60,204,862	59,906,602	46,506,540

See accompanying notes to the financial statements.

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

	Common Stock		Additional Paid-In-Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
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
Issuance of common shares under at-the-market sales agreement	2,891,419	3	12,202	—	12,205
Issuance of common shares under a direct registered offering	4,209,050	4	11,074	—	11,078
Issuance of common shares under employee stock purchase plan	65,481	—	111	—	111
Exercise of stock options	280,771	1	387	—	388
Vesting and settlement of restricted stock units	415,268	—	—	—	—
Share-based compensation expense	—	—	5,054	—	5,054
Net income	—	—	—	376	376
Balance at December 31, 2021	59,722,930	60	293,406	(255,491)	37,975
Issuance of common shares under at-the-market sales agreement	425,460	1	565	—	566
Issuance of common shares under employee stock purchase plan	66,919	—	112	—	112
Exercise of stock options	49,187	—	17	—	17
Vesting and settlement of restricted stock units	375,331	—	—	—	—
Share-based compensation expense	—	—	4,884	—	4,884
Net loss	—	—	—	(32,947)	(32,947)
Balance at December 31, 2022	60,639,827	$ 61	$ 298,984	$ (288,438)	$ 10,607

See accompanying notes to the financial statements.

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

	Year Ended December 31,		
	2022	2021	2020
Operating activities			
Net (loss) income	$ (32,947)	$ 376	$ (18,210)
Adjustments to reconcile net (loss) income to net cash used in operating activities:			
Non-cash interest expense on liability related to the sales of future royalties, net of issuance costs accretion	3,339	—	—
Depreciation	145	178	180
Share-based compensation expense	4,884	5,054	3,600
Gain on termination of operating lease	(55)	—	—
Loss on disposal of fixed assets	33	—	—
Gain on extinguishment of debt	—	(998)	—
Non-cash interest expense	—	—	59
Accretion of debt discount	—	—	129
Changes in operating assets and liabilities:			
Accounts receivable, prepaid expenses and other current assets	10,420	(10,869)	1,893
Other assets and liabilities	(83)	(155)	(140)
Accounts payable and accrued liabilities	694	681	(631)
Deferred revenue	205	(5,000)	—
Net cash used in operating activities	(13,365)	(10,733)	(13,120)
Investing activities			
Acquisition of property and equipment	(246)	—	(55)
Net cash used in investing activities	(246)	—	(55)
Financing activities			
Proceeds from royalty purchase and sale agreement, net of $1.9 million of issuance costs	30,638	—	—
Proceeds from at-the-market sales agreement, net of issuance costs	566	12,205	11,958
Proceeds from registered direct offering, net of issuance costs	—	11,078	—
Proceeds from shares issued under employee stock purchase plan	112	111	31
Proceeds from exercise of stock options	17	388	227
Proceeds from issuance of long-term debt	—	—	991
Principal payments made on long-term debt	—	—	(5,340)
Net cash provided by financing activities	31,333	23,782	7,867
Net increase (decrease) in cash, cash equivalents and restricted cash	17,722	13,049	(5,308)
Cash, cash equivalents and restricted cash, beginning of period	30,696	17,647	22,955
Cash, cash equivalents and restricted cash, end of period	$ 48,418	$ 30,696	$ 17,647
Supplemental disclosure			
Interest paid	$ —	$ —	$ 524
Purchase of property and equipment in accounts payable and accrued liabilities	$ 282	$ —	$ —
Forgiveness of PPP Loan and accrued interest	$ —	$ 998	$ —

Reconciliation of cash, cash equivalents and restricted cash:

	December 31,		
	2022	2021	2020
Cash and cash equivalents	$ 48,258	$ 30,436	$ 17,287
Restricted cash ($160 and $100 as of December 31, 2022 and 2021, respectively, is recorded in other current assets)	160	260	360
Cash, cash equivalents and restricted cash at end of period	$ 48,418	$ 30,696	$ 17,647

See accompanying notes to the financial statements.

CLEARSIDE BIOMEDICAL, INC.

Notes to the Consolidated Financial Statements

1. The Company

Clearside Biomedical, Inc. (the "Company") is a biopharmaceutical company focused on revolutionizing the delivery of therapies to the back of the eye through the suprachoroidal space (SCS). 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 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 $48.3 million as of December 31, 2022.

Historically, the Company has funded its operations primarily through the sale of common stock and convertible preferred stock, the issuance of long-term debt, and license agreements. On October 25, 2021, the Company announced that the U.S. Food and Drug Administration (the "FDA") approved XIPERE® (triamcinolone acetonide injectable suspension) for the treatment of macular edema associated with uveitis, a form of eye inflammation. In January 2022, the Company received $10.0 million from Bausch + Lomb, a division of Bausch Health Companies, Inc. ("Bausch"), upon completion of pre-launch activities for XIPERE pursuant to the license agreement granting Bausch an exclusive license to develop and commercialize XIPERE in the United States and Canada. Bausch launched XIPERE in the United States in the first quarter of 2022.

On August 8, 2022, the Company entered into a Purchase and Sale Agreement (the "Purchase and Sale Agreement") pursuant to which it sold its rights to receive royalty and milestone payments due to the Company from XIPERE and certain SCS Microinjector license agreements subject to a cap which may be increased under certain circumstances. The Company received a payment of $32.1 million in September 2022, representing the $32.5 million to which the Company was entitled, net of certain of HCR's transaction-related expenses which the Company agreed to reimburse. There were additional issuance costs of $1.5 million related to the Purchase and Sale Agreement resulting in net proceeds of $30.6 million.

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.

During the year ended December 31, 2021, the Company sold 2.9 million shares of its common stock for net proceeds of $12.2 million under its at-the-market agreement with Cowen and Company, LLC. During the year ended December 31, 2022, the Company sold 425,460 shares of its common stock for net proceeds of $0.6 million under its at-the-market agreement with Cowen and Company, LLC. Subsequent to December 31, 2022, the Company sold an additional 214,128 shares of its common stock for net proceeds of $0.3 million.

In August 2021, the Company entered into an amendment to the Arctic Vision License Agreement (as defined in Note 10 - License and Other Agreements) to expand the territories covered by the license to include India and the ASEAN Countries (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam). In September 2021, the Company entered into a second amendment to the Arctic Vision License Agreement to expand the territories covered by the license to include Australia and New Zealand. The Company received an aggregate of $3.0 million in consideration for the expansion of the licensed territory.

In April 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 provide a mechanism for forgiveness of up to the full amount borrowed. On January 11, 2021, we received notification from Silicon Valley Bank that the PPP Loan was forgiven in full, including approximately $7,000 of accrued interest.

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 generate significant revenue. The Company has no current source of revenue to sustain present activities. The Company does not expect to generate other meaningful revenue until and unless the Company's licensees successfully commercialize XIPERE and the Company has fulfilled its obligations under the Purchase and Sale Agreement, its other licensees receive regulatory approval and successfully commercialize its product candidates, or the Company commercializes its product candidates either on its own or with a third party. 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.

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 complete the development and conduct clinical trials for the regulatory approval of its product candidates if requested by regulatory bodies. If such product candidates were to receive regulatory approval, the Company would need to obtain financing to prepare for the potential commercialization of its product candidates, if the Company decides to commercialize the products on its own.

Based on its cash and cash equivalents as of the filing date, March 14, 2023, its current plans and forecasted expenses the Company expects that it will be able to fund its planned operating expenses and capital expenditure requirements into the second quarter of 2024. The Company has based this estimate on assumptions that may prove to be wrong, and it could exhaust its capital resources sooner than expected. Until the Company can generate sufficient revenue, the Company will need to finance future cash needs through public or private equity offerings, license agreements, debt financings or restructurings, collaborations, strategic alliances and marketing or distribution arrangements.

2. Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The Company's consolidated financial statements include the results of the financial operations of Clearside Biomedical, Inc. and its wholly-owned subsidiary, Clearside Royalty, LLC. a Delaware limited liability company, which was formed for the purposes of the transactions contemplated by the Purchase and Sale Agreement describe in Note 5. All intercompany balances and transactions have been eliminated.

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 consolidated 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 consolidated 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 continues to result in global economic uncertainty. 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 us 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 Company's consolidated financial statements.

Revenue Recognition

The Company recognizes revenue from its contracts with customers under Financial Accounting Standards Board Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers*. 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.

In the year ended December 31, 2022, 2021, and 2020, the Company recognized $1.3 million, $29.6 million, and $7.7 million of revenue associated with its license agreements, respectively. License revenue for the year ended December 31, 2022 was primarily from providing training materials and clinical trial products to the Company's licensees. License revenue for the year ended December 31, 2021 was primarily a result of (i) the milestone payments from Bausch that consisted of $5.0 million received upon FDA approval of XIPERE, the recognition of $5.0 million of deferred revenue for the upfront milestone payment and the recognition of a $10.0 million milestone for pre-launch activities and (ii) an aggregate of $8.0 million received from Arctic Vision for FDA approval of XIPERE, territory expansion and certain development milestones. License revenue for the year end December 31, 2020 was primarily a result of milestone payments of $4.3 million received from Arctic Vision and $3.0 million milestone payment received from REGENXBIO.

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, 2022. 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 trial activities, are recognized based on an evaluation of the estimated total costs for the clinical trial, progress to completion of specific tasks, using data such as patient enrollment, pass through expenses, clinical site activations, data from the clinical sites 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 contracts and any subsequent amendments, 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, directors and consultants is measured based on the estimated fair value of the award at the grant date. 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, 2022, 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.

Liability Related to the Sales of Future Royalties and Non-Cash Interest Expense

The Company recognizes a liability related to the sales of future royalties under ASC 470-10 Debt and ASC 835-30 Interest - Imputation of Interest. The initial funds received by the Company pursuant to the terms of the Purchase and Sale Agreement were recorded as a liability and will be accreted under the effective interest method up to the estimated amount of future royalties and milestone payments to be made under the Purchase and Sale Agreement. The issuance costs were recorded as a direct deduction to the carrying amount of the liability and will be amortized under the effective interest method over the estimated period the liability will be repaid. The Company estimated the total amount of future royalty revenue and milestone payments to be generated over the life of the Purchase and Sale Agreement, and a significant increase or decrease in these estimates could materially impact the liability balance and the related interest expense. If the timing of the receipt of royalty payments or milestones is materially different from the original estimates, the Company will prospectively adjust the effective interest and the related amortization of the liability and related issuance costs.

3. Property and Equipment, Net

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

	Estimated Useful Lives (Years)	December 31, 2022	December 31, 2021
Furniture and fixtures	5	$ 249	$ 337
Machinery and equipment	5	343	176
Computer equipment	3	13	13
Leasehold improvements	Lesser of useful life or remaining lease term	476	667
Work in process		527	—
Total property and equipment		1,608	1,193
Less: Accumulated depreciation		(853)	(955)
Property and equipment, net		$ 755	$ 238

4. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Accrued research and development	$ 1,817	$ 1,083
Accrued employee costs	1,837	1,854
Accrued professional fees	49	30
Accrued expense	476	345
	$ 4,179	$ 3,312

5. Royalty Purchase and Sale Agreement

On August 8, 2022 (the “Closing Date”), the Company, through its wholly-owned subsidiary Clearside Royalty LLC, a Delaware limited liability company (“Royalty Sub”), entered into a Purchase and Sale Agreement (the “Purchase and Sale

Agreement") with entities managed by HealthCare Royalty Management, LLC ("HCR"), pursuant to which Royalty Sub sold to HCR certain of its rights to receive royalty and milestone payments payable to Royalty Sub under the Arctic Vision License Agreement, the Bausch License Agreement, that certain License Agreement, effective as of July 3, 2019, by and between the Company and Aura Biosciences, Inc. (the "Aura License Agreement"), that certain Option and License Agreement, dated as of August 29, 2019, by and between REGENXBIO Inc. and the Company (the "REGENXBIO License Agreement") and any and all out-license agreements following the Closing Date for, or related to XIPERE or the SCS Microinjector technology (to be used in connection with compounds or products of any third parties) delivered, in whole or in part, by means of the SCS Microinjector technology), excluding, for the avoidance of doubt, any in-licensed or internally developed therapies following the Closing Date (collectively, the "Royalties"), in exchange for up to $65 million. In connection with this transaction, the Company assigned the Arctic Vision License Agreement, Bausch License Agreement, Aura License Agreement, REGENXBIO License Agreement, the Company's license agreement with Emory University and The Georgia Tech Research Corporation and related intellectual property rights to Royalty Sub.

Under the terms of the Purchase and Sale Agreement, Royalty Sub received an initial payment of $32.1 million, representing the $32.5 million to which the Company was entitled, net of certain of HCR's transaction-related expenses which the Company agreed to reimburse. There were additional issuance costs of $1.5 million related to the Purchase and Sale Agreement resulting in net proceeds of $30.6 million. An additional $12.5 million was deposited by HCR in an escrow account to be released to Royalty Sub upon attainment of a pre-specified XIPERE sales milestone achieved no later than March 31, 2024. The terms of the Purchase and Sale Agreement also provide for an additional $20 million milestone payment to Royalty Sub upon attainment of a second pre-specified sales milestone related to 2024 XIPERE sales (the "Second Milestone Event").

The Purchase and Sale Agreement will automatically expire, and the payment of Royalties from the Royalty Sub to HCR will cease, when HCR has received payments of the Royalties equal to 2.5 times the aggregate amount of payments made by HCR under the Agreement if the Second Milestone Event is achieved on or prior to December 31, 2024 (the "Initial Cap"). If the Second Milestone Event is not achieved on or prior to December 31, 2024, payment of Royalties from Royalty Sub to HCR will cease when HCR has received Royalties payments equal to 3.4 times the aggregate amount of payments under the Purchase and Sale Agreement (the "Alternative Cap", and together with the Initial Cap, the "Cap Amount"). In the event of a change in control, acquiror will have the option to make a payment to HCR of the Cap Amount then in effect, less the aggregate amount of Royalty payments made by Royalty Sub to HCR under the Purchase and Sale Agreement as a one-time payment at which time, payment of Royalties to HCR will cease. Alternatively, in the event of a change in control, the acquiror will have the option to make an initial payment of 1.0 times the aggregate amount of payments made by HCR under the Purchase and Sale Agreement as of the date of such change in control, then in that event, payment of Royalties from Royalty Sub to HCR will cease when HCR has received total Royalties payments (including the initial payment) equal to the Alternative Cap. After the Purchase and Sale Agreement expires, all rights to receive the Royalties return to Royalty Sub.

Issuance costs pursuant to the Purchase and Sale Agreement consisting primarily of advisory and legal fees, totaled $1.9 million including the amount of HCR's transaction-related expenses that the Company reimbursed. The effective interest rate includes cash flow projections for future royalty and milestone payments, which are sensitive to certain assumptions, including market size, market penetration and sales price, that are forward looking and could be affected by future market conditions.

The following table summarizes the activity of the Purchase and Sale Agreement (in thousands):

Royalty purchase and sale agreement effective August 8, 2022	$	32,500
Issuance costs		(1,862)
Non-cash interest expense		3,339
Balance at December 31, 2022	$	33,977
Effective interest rate		26.5%

6. 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 for the year ended December 31, 2020. Accretion of the scheduled final payment was $59,000 for the year ended December 31, 2020. Accretion of the deferred closing costs was $129,000 for the year ended December 31, 2020.

7. **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 provide a mechanism for forgiveness of up to the full amount borrowed. On January 11, 2021, the Company was notified by the PPP Lender that the PPP Loan had been forgiven in full, including approximately $7,000 of accrued interest. In accordance with ASC 405-20, *Extinguishment of Liabilities*, the income from the forgiveness of the amount borrowed and the accrued interest was recognized in the statement of operations in other income as a gain on extinguishment of debt.

8. 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, 2022 and 2021, there were 10,000,000 shares of preferred stock authorized, none of which were issued and outstanding.

At the Company's Annual Meeting of Stockholders held on June 22, 2022, the Company's stockholders approved an amendment to the amended and restated certificate of incorporation to increase the Company's authorized number of shares of common stock from 100,000,000 shares to 200,000,000 shares. As of December 31, 2022 the Company was authorized to issue 200,000,000 shares of $0.001 par value common stock. As of December 31, 2022 and 2021, there were 60,639,827 and 59,722,930 shares of common stock outstanding, respectively.

9. 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 3.75 years as of December 31, 2022.

10. Share-Based Compensation

Stock Options

In January 2016, the Company's board of directors adopted and approved the Clearside Biomedical, Inc. 2016 Equity Incentive Plan (the "2016 Plan") which became effective on June 1, 2016. The 2016 Plan provides for the grant of share-based awards to employees, directors and consultants of the Company. The 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, 2022, under the 2016 Plan, options to purchase 6,590,838 shares of the Company's common stock were outstanding at a weighted average price of $3.59 per share and 1,035,374 shares remained available for future grant. As of January 1, 2023, the number of shares of common stock that may be issued under the 2016 Plan was automatically increased by 2,425,593 shares, representing 4% of the total number of shares of common stock outstanding on December 31, 2022, increasing the number of shares of common stock available for issuance under the 2016 Plan as of that date to 3,460,967 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, 2022, options to purchase 307,256 shares of the Company's common stock were outstanding under the 2011 Plan at a weighted average exercise price of $3.26 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,		
	2022	2021	2020
Research and development	$ 1,616	$ 1,570	$ 1,183
General and administrative	1,785	1,985	1,574
Total	$ 3,401	$ 3,555	$ 2,757

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, 2022, 2021 and 2020.

	Year Ended December 31,		
	2022	2021	2020
Expected term (years)	6.00	7.00	7.00
Expected stock price volatility	98.24%	101.43%	108.13%
Risk-free interest rate	2.09%	0.75%	1.52%
Expected dividend yield	0.00%	0.00%	0.00%

Expected term (in years): In the year ended December 31, 2022, the Company began using historical data to calculate the expected term. In the years ended December 31, 2021 and 2020, the Company utilized the simplified method as prescribed by ASC

718, as the Company did 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, 2022:

	Number of Shares	Weighted Average Exercise Price
Options outstanding at December 31, 2021	5,762,328	$ 4.07
Granted	1,782,440	1.98
Exercised	(49,187)	0.35
Forfeited or expired	(580,251)	3.73
Options outstanding at December 31, 2022	6,915,330	3.58
Options exercisable at December 31, 2021	3,148,502	4.59
Options exercisable at December 31, 2022	4,223,931	4.22

The following table provides additional information about the Company's stock options that were outstanding and exercisable at December 31, 2022 (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	3,777,873			7.61	1,865,987			6.31
$3.00 - $6.99	2,506,371			6.85	1,726,858			6.30
$7.00 - $8.99	429,308			4.17	429,308			4.17
$9.00 - $20.84	201,778			4.76	201,778			4.76
	6,915,330	$ 3.58	$ 66	7.03	4,223,931	$ 4.22	$ 64	6.02

As of December 31, 2022, the Company had $4.4 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 2.3 years. The weighted average fair values of all stock options granted for the years ended December 31, 2022, 2021 and 2020 was $1.55 per share, $3.24 per share and $1.97 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 30, 2022 was $1.12, 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 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,		
	2022	2021	2020
Research and development	$ 794	$ 723	$ 375
General and administrative	658	715	427
Total	$ 1,452	$ 1,438	$ 802

The following table summarizes the activity related to RSUs during the year ended December 31, 2022:

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested RSUs outstanding at December 31, 2021	1,317,347	$ 3.58
Granted	648,460	2.19
Vested	(375,331)	3.44
Forfeited	(127,544)	3.04
Non-vested RSUs outstanding at December 31, 2022	1,462,932	3.04

As of December 31, 2022, the Company had $3.1 million of unrecognized compensation expense related to the RSUs, which amount is expected to be recognized over a weighted average period of 2.3 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, 2023. The number of shares of common stock available for issuance under the 2016 ESPP as of December 31, 2022 was 438,572 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, 2022, 2021 and 2020, the Company issued 66,919, 65,481 and 35,359 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,		
	2022	2021	2020
Research and development	$ 21	$ 41	$ 19
General and administrative	10	20	22
Total	$ 31	$ 61	$ 41

11. 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,		
	2022	2021	2020
Deferred tax asset (liability):			
Net operating loss carryforwards	$ 50,267	$ 53,966	$ 51,414
Non-deductible accrued expenses	386	469	263
Right-of-use asset	(238)	(96)	(132)
Lease liability	274	176	247
Deferred revenue	—	—	1,247
Stock compensation expense	2,678	2,768	2,044
Depreciation differences	(40)	(44)	(82)
Federal tax credits	9,742	9,012	8,015
State tax credits	326	342	381
Disallowed interest expense	—	—	7
Charitable contributions	—	6	—
Royalty purchase and sale agreement	7,247	—	—
Capitalized research and development expenses	3,057	—	—
Valuation allowance	(73,699)	(66,599)	(63,404)
Net deferred tax asset	$ —	$ —	$ —

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

	Year Ended December 31,		
	2022	2021	2020
U.S. federal tax rate	21.00%	21.00%	21.00%
State tax rate	(0.85)	(599.32)	14.28
Permanent difference	(1.34)	(3.15)	1.42
Tax credit	2.18	(253.97)	2.89
Valuation allowance	(21.57)	847.82	(39.66)
ASC 740-10	—	(3.19)	(0.26)
Adjustment to prior year tax provision	0.67	(13.16)	—
Other	(0.09)	3.97	—
	0.00%	0.00%	(0.33)%

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, 2022, the Company had a valuation allowance of $73.7 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, 2022, the Company had income tax NOL carryforwards for federal and state purposes of $216.1 million and $78.4 million, respectively. The Company has recorded a deferred tax asset for both federal and state NOL carryforwards of $45.4 million and $4.9 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 roll forward of the Company's uncertain tax positions (in thousands):

	Year Ended December 31,	
	2022	2021
Balance of uncertain tax positions at the beginning of the year	$ 7,520	$ 7,568
Gross decreases - tax positions in prior period	—	(12)
Gross decreases - settlements with taxing authorities	—	(36)
Balance of uncertain tax positions at the end of the year	$ 7,520	$ 7,520

As of December 31, 2022 and 2021, there was $7.5 million in each period 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 reversed $48,000 of previously recorded unrecognized tax expenses for the year 2021. 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, 2022.

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. In general, if the Company experiences a greater than 50% aggregate change in ownership over a 3-year period (a Section 382 ownership change), utilization of the Company's pre-change NOL carryforwards may be subject to limitation under the Code. The annual limitation generally is determined by multiplying the value of the Company's stock at the time of such ownership change (subject to certain adjustments) by the applicable long-term tax-exempt rate for the month in which the ownership change occurred. Such limitation may result in expiration of a portion of the NOL carryforwards before utilization. The Company has completed an owner shift analysis to determine the dates in which the Company may have experienced a Section 382 ownership change, and determined that the Company experienced ownership changes for Section 382 purposes in January 2012, December 2013, and July 2016. Further, the Company has determined that $38,000 and $2,000 of its deferred tax asset related to Federal NOL and Federal R&D Credit, respectively, will expire due to Section 382.

The NOL DTA has a full valuation allowance as it is deemed that it is more likely than not to be utilized. The Company will continue to monitor equity movement and its impact on the utilization of the NOLs and credits. The Company's ability to use the remaining NOL carryforwards may be further limited if the Company experiences an additional Section 382 ownership change as a result of future changes in its stock ownership.

The Company is subject to taxation in the United States and certain state jurisdictions. As of December 31, 2022, the Company's tax returns for 2019, 2020 and 2021 are subject to full examination by the tax authorities. As of December 31, 2022, the Company is generally no longer subject to state or local examinations by tax authorities for years before 2019, except to the extent of NOLs generated in prior years claimed on a tax return.

12. 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 was for a six and one-half year term with a renewal option for one additional five-year term. Rental payments were $35,145 per month subject to an increase of 3% per year.

In November 2022, the Company amended the office lease agreement and decreased the square footage to approximately 14,000 square feet. The amended office lease agreement is for a four year term with a renewal option for an additional thirty-eight months. Rental payments are $30,437 per month subject to an increase of 3% per year. Operating lease cost under this lease and the amendment is recognized on a straight-line basis over the term of the lease. In addition, the office lease agreement requires payment of the 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, 2022
Operating lease right-of-use asset	$ 1,117
Liabilities	
Current portion of operating lease liabilities	$ 349
Operating lease liabilities	936
Total operating lease liabilities	$ 1,285

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 is not reasonably certain 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, 2022, the Company's incremental borrowing rate was 8.0% and the remaining lease term was 4.0 years. Cash payments included in operating activities on the consolidated statement of cash flows for operating lease liabilities were $339,000, $392,000 and $378,000 for the years ended December 31, 2022, 2021 and 2020, respectively.

Minimum lease payments were as follows at December 31, 2022 (in thousands):

Year ending December 31,	
2023	$ 362
2024	378
2025	389
2026	367
Total minimum lease payments	1,496
Less imputed interest	(211)
Total operating lease liabilities	$ 1,285

Equipment leases with an initial term of 12 months or less are not recorded with operating lease liabilities. The Company recognizes expense for these leases on a straight-line basis over the lease term. The equipment leases were deemed to be immaterial.

Operating lease cost was $262,000 for the year ended December 31, 2022 and $247,000 for each of the years ended December 31, 2021 and 2020. Variable lease cost was $87,000 for the year ended December 31, 2022 and $95,000 for the years ended December 31, 2021 and 2020. Short-term lease cost was $86,000, $12,000 and $20,000 for the years ended December 31, 2022, 2021 and 2020, 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.

13. License and Other Agreements

Bausch + Lomb

On October 22, 2019, the Company entered into a License Agreement (as amended, the "Bausch 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 SCS 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 “Territory”) for the treatment of ophthalmology indications, including non-infectious uveitis.

Pursuant to the Bausch License Agreement, Bausch paid the Company an upfront payment of $5.0 million (the “Upfront Payment”) in October 2019. In October 2021, the FDA approved XIPERE. The Company received $5.0 million from Bausch as a result of the approval. In December 2021, $10.0 million was recorded upon completion of pre-launch activities for XIPERE and payment was received in January 2022. In addition, Bausch has agreed to pay up to an aggregate of $55.0 million in additional milestone payments upon the achievement of (i) specified regulatory approvals for specified additional indications of XIPERE 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 Territory, 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 Territory. Bausch launched XIPERE in the United States in the first quarter of 2022. The Company's rights to these royalties and milestone payments have been sold pursuant to the terms and conditions of the Purchase and Sale Agreement described in Note 5 to the consolidated financial statements.

The Company was responsible for all development expenses for XIPERE in the Territory until the Company's New Drug Application ("NDA") was approved by the FDA, subject to specified exceptions, as well as manufacturing costs in connection with the NDA. The Company was 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. Following FDA approval of XIPERE, Bausch is responsible for all such expenses.

Due to the refund provisions in the License Agreement, the Upfront Payment was included on the balance sheet as deferred revenue as of December 31, 2020. The refund provisions lapsed upon FDA approval of XIPERE and the $5.0 million was recognized as revenue in the fourth quarter of 2021.

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 $31.0 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. The Company's rights to these royalties and milestone payments have been sold pursuant to the terms and conditions of the Purchase and Sale Agreement described in Note 5 to the consolidated financial statements.

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 "Arctic 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 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 paid the Company an upfront payment of $4.0 million in March 2020. In December 2021, the Company received a milestone payment of $4.0 million following the receipt of FDA approval of XIPERE in the United States. In addition, Arctic Vision has agreed to pay the Company up to $22.5 million in development and sales milestones. 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 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. The Company's rights to these royalties and milestone payments have been sold pursuant to the terms and conditions of the Purchase and Sale Agreement described in Note 5 to the consolidated financial statements.

In August 2021, the Company entered into an amendment to the Arctic Vision License Agreement to expand the territories covered by the license to include India and the ASEAN Countries (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam). In September 2021, the Company entered into a second amendment to the Arctic Vision License Agreement to expand the Arctic Territory to include Australia and New Zealand. The Company received an aggregate of $3.0 million in consideration for the expansion of the Arctic Territory.

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 $13,000, $200,000 and $105,000 of revenue from these agreements during the years ended December 31, 2021, 2020 and 2019, respectively.

14. Fair Value Measurements

The Company's material financial instruments at December 31, 2022 and 2021, consisted primarily of cash and cash equivalents. 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 liability related to the sales of future royalties approximates the carrying value due to the short period of time that has elapsed from the origination date.

There were no transfers between Levels 1, 2 and 3 during the years ended December 31, 2022 and 2021.

15. Net Income (Loss) Per Share

Basic net income (loss) per share is calculated by dividing the net income (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 income (loss) per share gives effect to all dilutive potential shares of common stock outstanding during this period.

For periods in which the Company incurred net losses, common stock equivalents were excluded which included 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.

	Year Ended December 31,		
	2022	2021	2020
Net (loss) income - basic and diluted	$ (32,947)	$ 376	$ (18,210)
Weighted average shares - basic	60,204,862	58,491,986	46,506,540
Effect of dilutive securities:			
Stock options	—	1,058,134	—
Restricted stock	—	342,943	—
ESPP	—	13,539	—
Weighted average shares - diluted	60,204,862	59,906,602	46,506,540
Net (loss) income per share - basic	$ (0.55)	$ 0.01	$ (0.39)
Net (loss) income per share - diluted	$ (0.55)	$ 0.01	$ (0.39)

The Company's potential common stock equivalents that have been excluded from the computation of diluted net income (loss) per share for all periods presented because of their antidilutive effect consisted of the following:

	Year Ended December 31,		
	2022	2021	2020
Outstanding stock options	6,915,330	4,704,194	4,248,193
Non-vested restricted stock units	1,462,932	974,404	767,271
Stock purchase warrants	29,796	29,796	29,796
	8,408,058	5,708,394	5,045,260

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, 2022. 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, 2022 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, 2022, 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 a non-accelerated filer and a smaller reporting company under SEC rules, management's report was not subject to attestation by our independent registered public accounting firm.

ITEM 9B. OTHER INFORMATION

Not applicable.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

We will file a definitive Proxy Statement for our 2023 Annual Meeting of Stockholders (the "2023 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 2023 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 2023 Proxy Statement under the captions "Information Regarding the Board of Directors and Corporate Governance," "Election of Directors," and "Information About Our Executive Officers."

Code of Ethics

We have adopted a Code of Business Conduct and Ethics (the "Code of Conduct") applicable to all of our employees, executive officers and directors. The Code of Conduct is available on our website at www.clearsidebio.com. The Audit Committee is responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for executive officers and directors. If we make any substantive amendments to the Code of Conduct or grant any waiver from a provision of the Code of Conduct to any executive officer or director, we will promptly disclose the amendment or waiver on our website.

ITEM 11. EXECUTIVE COMPENSATION

The information required by Item 11 is hereby incorporated by reference to the sections of the 2023 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 2023 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 2023 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 2023 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		Certificate of Amendment to 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 23, 2022).
3.3		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).
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	+	Fourth Amended and Restated Non-Employee Director Compensation Policy (incorporated 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 12, 2022).
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).
10.25	##	First Amendment to the License Agreement, by and between the Registrant and Arctic Vision (Hong Kong) Limited, dated as of August 15, 2021 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form-10 (File No. 001-37783), filed with the Commission on November 10, 2021.

10.26	##	Second Amendment to the License Agreement, by and between the Registrant and Arctic Vision (Hong Kong) Limited, dated as of September 9, 2021 (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 10, 2021.
10.27		Second Amendment to the License Agreement, by and between the Registrant and Bausch + Lomb Ireland Limited (as assignee of Bausch Health Ireland Limited), dated as of September 27, 2021 (incorporated herein by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37783), filed with the Commission on November 10, 2021.
10.28	##◆	Purchase and Sale Agreement, by and among Clearside Royalty LLC, Healthcare Royalty Partners IV, L.P. and HCR Collateral Management, LLC (in its capacity as agent for Purchaser), dated as of August 8, 2022 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37783), filed with the Commission on November 9, 2022).
10.29	*	First Amendment to Office Lease Agreement, by and between the Registrant and Radiant-North Point Properties, LLLP, dated as of November 1, 2022.
10.30	##*	First Amendment to Option and License Agreement, by and between the Registrant and REGENXBIO, Inc., dated as of January 14, 2023.
10.31	+	Consulting Agreement, by and between the Registrant and Thomas Ciulla, dated as of February 17, 2023 (incorporated herein by reference to Exhibit 10.1 to the (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 February 21, 2023).
23.1	*	Consent of Ernst & Young LLP, independent registered public accounting firm.
24.1	*	Power of Attorney (included on signature page).
31.1	*	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	*	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	*^	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rules 13a-14(b) and 15d-14(b) promulgated under the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002.
101.INS		Inline XBRL Instance Document
101.SCH		Inline XBRL Taxonomy Extension Schema Document
101.CAL		Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF		Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB		Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE		Inline XBRL Taxonomy Extension Presentation Linkbase Document
104		Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

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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 because they are not material and are the type that the Registrant treats as private or confidential. The Registrant hereby agrees to furnish supplementally to the Securities and Exchange Commission, upon its request, an unredacted copy of this exhibit.
◆	Certain of the exhibits and schedules to this exhibit have been omitted in accordance with Regulation S-K Item 601. The Registrant agrees to furnish a copy of all omitted exhibits and schedules to the SEC upon request.

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 14, 2023

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

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

Signature	Title	Date
/s/ George Lasezkay, Pharm.D., J.D. George Lasezkay, Pharm.D., J.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 14, 2023
/s/ Charles A. Deignan Charles A. Deignan	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 14, 2023
/s/ William D. Humphries William D. Humphries	Director	March 14, 2023
/s/ Richard Croarkin Richard Croarkin	Director	March 14, 2023
/s/ Jeffrey L. Edwards Jeffrey L. Edwards	Director	March 14, 2023
/s/ Nancy J. Hutson Nancy J. Hutson	Director	March 14, 2023
/s/ Christy L. Shaffer, Ph.D. Christy L. Shaffer, Ph.D.	Director	March 14, 2023
/s/Clay B. Thorp Clay B. Thorp	Director	March 14, 2023
/s/Benjamin R. Yerxa Benjamin R. Yerxa	Director	March 14, 2023

FIRST AMENDMENT TO OFFICE LEASE AGREEMENT

THIS FIRST AMENDMENT TO OFFICE LEASE AGREEMENT (this **"First Amendment")** is made and entered into effective as of the 1st day of November, 2022, by and between RADIANT-NORTH POINT PROPERTIES, LLLP, a Delaware limited liability limited partnership (as **"Landlord"),** and CLEARSIDE BIOMEDICAL, INC., a Delaware corporation (as **"Tenant").**

WITNESSETH:

WHEREAS, BRE/COH GA, LLC **("Original Landlord")** and Tenant entered into that certain Office Lease Agreement dated November 21, 2016 (the **"Original Lease"),** pursuant to which Tenant leases certain premises containing approximately 19,707 rentable square feet of space (the **"Existing Premises")** on the second (2^{nd}) floor of the building located at 900 North Point Parkway, Alpharetta, Georgia 30005 (the **"Building"),** as such space is more particularly described in the Lease; and

WHEREAS, Landlord (as successor-in-interest to Original Landlord) and Tenant (desire to modify and amend the Original Lease to extend the term of the Original Lease, to reduce the Existing Premises by returning to Landlord that approximately 5,659 rentable square foot portion of the Existing Premises shown on Exhibit A. attached hereto (the **"Reduction Premises"),** to clarify the suite designation of the Premises and to make certain changes hereinafter set forth.

NOW, THEREFORE, for and in consideration of the mutual premises, and for Ten and No/I 00 Dollars ($10.00) and other good and valuable consideration, paid by the parties hereto to one another, the receipt and sufficiency of which are acknowledged by the parties hereto, the parties for themselves and their successors and assigns hereto hereby covenant and agree as follows:

1. **Incorporation of Recitals.** The above recitals are true and correct and are incorporated herein as **if** set forth in full.

2. **Defined Terms.** All capitalized terms not defined in this First Amendment shall have the same meaning as set forth in the Original Lease. All references in the Original Lease and herein to the term **"Lease"** shall mean the Original Lease as amended by this First Amendment. Landlord and Tenant acknowledge and agree that, notwithstanding anything in the Original Lease to the contrary, the Premises shall be designated and referred to as Suite 200.

3. **Partial Reduction of Premises.**

(a) Effective as of November 1, 2022 (the **"Partial Reduction Date"),** the Lease shall expire as to the Reduction Premises, subject to the terms and conditions of this Section 3 and the other provisions of this First Amendment. Effective as of the Partial Reduction Date, Tenant releases, remises and forever quitclaims the Reduction Premises to Landlord, to have and hold so that neither Tenant nor any party claiming by, through or under Tenant shall thereafter have or claim any right thereto or any part thereof. On or before the Partial Reduction Date, Tenant shall surrender the Reduction Premises to Landlord in a broom clean condition and, except as expressly set forth in Section 3(b) below, with all of Tenant's personal property removed. Tenant acknowledges that TIME IS OF THE ESSENCE with respect to Tenant's surrender of the Reduction Premises as required herein. As a result of the partial reduction of the Existing Premises, effective as of the Partial Reduction Date, the **"Premises"** shall mean that certain area containing approximately 14,048 rentable square feet as shown on Exhibit A attached hereto.

(b) Notwithstanding anything in the Original Lease to the contrary, Landlord and Tenant hereby acknowledge and agree that the furniture more particularly shown in the highlighted area

on Exhibit B attached hereto (collectively, the "Existing Furniture") shall be left in the Reduction Premises in the condition existing as of the date of this First Amendment and shall not be removed from the Reduction Premises by Tenant. Tenant hereby (i) represents and warrants to Landlord that Tenant owns the Existing Furniture free and clear of the interest of any party, and (ii) quitclaims unto Landlord all of Tenant's right, title and interest in and to the Existing Furniture for $1.00 and other valuable consideration, the receipt and sufficiency of which is hereby acknowledged.

4. **Demising Work** Landlord shall, in accordance with Landlord's standard build-out procedures at Landlord's sole cost and expense, demise the Reduction Premises from the remainder of the Existing Premises in accordance with mutually agreed upon plans and specifications (the **"Demising Work").** Landlord and Tenant shall cooperate in connection with the performance of the Demising Work in such a manner as to allow Landlord to complete such Demising Work in an efficient manner as soon as reasonably practicable after the Partial Reduction Date, including, without limitation, removing fixtures, furniture, equipment and other personal property from the portions of the Existing Premises adjacent thereto. Landlord shall provide Tenant with written notice (which notice may be provided via email) no less than ten (10) days prior to commencing the Demising Work. Landlord shall use commercially reasonable efforts to not unreasonably disturb Tenant's business operations in the Premises during the completion of the Demising Work; provided, however, that Tenant acknowledges and agrees that that noise, dust and other activities associated with such Demising Work may be disruptive to the business operations of Tenant in the Premises, or portions thereof. Notwithstanding anything herein to the contrary, Tenant hereby expressly acknowledges and agrees that between the Partial Reduction Date and the completion of the Demising Work, Tenant shall not use, occupy or otherwise encroach into all or any portion of the Reduction Premises and shall restrict its occupancy only to the remainder of the Existing Premises.

5. **Extension of Term.** Notwithstanding anything in the Original Lease to the contrary, Landlord and Tenant hereby agree to extend the Term of the Lease for a period of thirty-eight (38) months commencing on October 1, 2023 (the **"Extension Date")** and, unless sooner terminated, expiring on November 30, 2026 (the **"Termination Date").** The period from the Extension Date through the Termination Date is hereinafter referred to as the **"First Extension Term."**

6. **Base Rent.** Notwithstanding anything in the Lease to the contrary, commencing on the Partial Reduction Date and continuing until the expiration of the First Extension Term, Tenant shall pay Landlord the following sums as Base Rent for the Premises pursuant to the terms of the Lease:

Period	Annual Rent Per Square Foot	Monthly Installment of Rent
11/1/2022 - 10/31/2023	$26.00	$30,437.33 *
11/1/2023 - 10/31/2024	$26.78	$31,350.45
11/1/2024 - 10/31/2025	$27.58	$32,286.99
11/1/2025 - 10/31/2026	$28.41	$33,258.64
11/1/2026 - 11/30/2026	$29.26	$34,253.71

* Landlord agrees to provide Tenant a partial abatement of the Base Rent for the Premises (i) in the amount of $30,437.33 for the month of November 2022; (ii) in the amount of $30,437.33 for the month of December 2022; and (iii) in the amount of
$4,797.00 for the month of January 2023, for a total abatement of $65,671.66 (collectively, the **"Abated Rent").** Upon the occurrence of a Default by Tenant

under the Lease, the Abated Rent shall be revoked, null and void, and in addition to any other remedies under this Lease, the Abated Rent shall become immediately due and payable to Landlord.

7. **Additional Rent; Taxes and Expenses.** Tenant shall continue to pay Additional Rent for the Premises from the date hereof throughout the First Extension Term in accordance with the terms of the Lease, including, without limitation, the Tenant's Pro Rata Share of Expenses and Taxes in accordance with the terms and provisions of Exhibit B to the Original Lease; provided, however, that effective as of the Partial Reduction Date: (i) the **"Rentable Square Footage of the Building"** shall be deemed to be 130,381 rentable square feet, (ii) the **"Rentable Square Footage of the Premises"** shall be deemed to be 14,048 rentable square feet, and (iii) **"Tenant's Pro Rata Share"** shall be changed to l 0.7746%; and (iv) the **"Base Year"** shall be changed to calendar year 2022.

8. **Acceptance of Existing Premises.** Tenant is in possession of, and has accepted, the Existing Premises, and acknowledges that all the work to be performed by the Landlord in the Existing Premises as required by the terms of the Lease, if any, has been satisfactorily completed. Tenant further acknowledges and agrees that, except for the Demising Work, Landlord shall have no obligation to furnish, render or supply any work, labor, services, materials, improvements or other items to make the Premises (as reduced) ready or suitable for Tenant's continued occupancy.

9. **Parking;** Notwithstanding anything in the Original Lease to the contrary, Landlord and Tenant acknowledge and agree that, from and after the Partial Reduction Date, Tenant shall only be entitled to use three and one-half (3.5) unreserved parking spaces per 1,000 rentable square feet of the Premises (as reduced) and, except as amended hereby, the use of said parking spaces shall be subject to and in accordance with the terms and provisions of Additional Provision l (Parking) on Exhibit F to the Original Lease.

10. **Extension Option.** Effective as of the date hereof, any and all rights of extension options or rights to renew the Lease Term, without limitation, Additional Provision 2 (Extension Option) on Exhibit **F** to the Original Lease, shall be deleted in their entirety and shall be of no further force or effect. Notwithstanding the foregoing, provided no Default by Tenant has occurred which remains uncured either as of the date of Tenant's notice as set forth below or as of the first day of the Second Extension Term (as hereinafter defined), Tenant shall have the right (the **"Extension Option")** to extend the Term of the Lease for one (1) additional period of three (3) years (the **"Second Extension Term")** with respect to all, but not any lesser portion of the Premises, upon all of the following terms and conditions:

(a) Tenant must provide Landlord notice of its exercise of the option for the applicable Second Extension Term not less than nine (9) months prior, but not more than twelve (12) months prior, to the expiration of the First Extension Term. Time is of the essence with respect to the foregoing.

(b) The Base Rent for the Second Extension Term shall be one hundred percent (100%) of the then prevailing market rental rate, as of the date of Tenant's notice for the Second Extension Term **("Notice Date"),** for comparable leases during the Second Extension on a per ·rentable square foot basis in the Alpharetta, Georgia market area (the **"Market Area")** which market rental rate shall be determined by taking into account all relevant factors, including, without limitation, size of space, age, location and quality of building, length of term, credit standing of tenant, method of paying operating costs, services provided and other market terms such as tenant improvement allowances, commissions payable, free rent and/or other concessions then being provided in the market (the **"Market Rental Rate").**

(c) If Tenant exercises its option for the Second Extension Term by written notice to Landlord as provided above, Landlord and Tenant shall meet promptly and shall negotiate, in good faith, to reach agreement on the Market Rental Rate within thirty (30) days following the Notice Date. If Landlord and Tenant are unable to reach agreement within such thirty (30) day period, Tenant may, at its option, either (i) cancel its exercise of the option to extend the term of this Lease, or (ii) elect to have the Market Rental Rate determined as set forth below. Tenant shall notify Landlord, within five (5) business days after the expiration of the aforesaid thirty (30) day period, of its election either to cancel its exercise of the option to extend or to have the Market Rental Rate determined as set forth below. If Tenant elects to cancel its exercise of the option to extend, the Lease shall terminate upon the expiration of the First Extension Tenn. If Tenant does not notify Landlord of either of the options contained in subsentences (i) and (ii) above within said five (5) business day period, then Tenant shall be deemed to have elected the option contained in subsentence (ii) and to have the Market Rental Rate determined as set forth in subsection (d) below.

(d) If Tenant elects (or is deemed to have elected) to have the Market Rental Rate determined as described herein, then within fifteen (15) business days after the date of Tenant's election (or deemed election), Landlord and Tenant shall mutually agree upon a commercial real estate broker who has at least ten (10) years' experience, immediately prior to the date in question, evaluating Market Rental Rates for similar properties in the Market Area. If the parties are unable to agree on a broker the parties shall ask the commercial division of the Atlanta Board of Realtors to designate a broker. The broker agreed upon or so designated is hereinafter referred to as the **"Market Broker".** Within ten (10) business days after the Market Broker has been agreed upon or appointed, Landlord and Tenant shall each deliver to the Market Broker in writing their respective written determinations of the Market Rental Rate. Within thirty (30) days after receipt of the final written determinations, the Market Broker shall select Landlord's determination or Tenant's determination, but no other amount and no compromise between the two, as the Market Rental Rate. The fees and expenses of the Market Broker shall be borne equally by Landlord and Tenant. The determination of the Market Rental Rate as provided above shall be final, binding and conclusive on both Landlord and Tenant, shall be considered a final award pursuant to the rules of the American Arbitration Association and any applicable state or federal law and judgment may be had on the award in any court of competent jurisdiction.

(e) Except for Base Rent at the new rate determined pursuant to the terms and provisions set forth above, all of the terms and conditions of the Lease shall remain the same and shall remain in full force and effect throughout the Second Extension Term; provided, however, that any construction provisions requiring Landlord to construct improvements, free rent, improvement allowances, moving allowances, lease assumption payments, plan design allowances (or payments) or other similar concessions provided for in the Lease shall not apply during the Second Extension Tenn. During the Second Extension Term, Tenant shall continue to pay the Tenant's Pro Rata Share of Expenses and Taxes as provided in the Lease.

This Extension Option is personal to Clearside Biomedical, Inc., a Delaware corporation, may not be exercised by any party other than Clearside Biomedical, Inc., a Delaware corporation (or an assignee pursuant to a Business Transfer (as defined in Section 11.04 of the Original Lease), and shall become null and void upon the occurrence of an assignment of the Lease (by operation of law or otherwise) or a sublet of all or a part of the Premises other than in connection with a Business Transfer.

11. **Right of First Refusal.** Additional Provision 3 (Right of First Refusal) on Exhibit F to the Original Lease is hereby deleted in its entirety and shall be of no further force or effect.

12. **Monument Signage.** Landlord Tenant hereby acknowledge and agree that, notwithstanding the fact that Tenant will not be leasing and occupying over 18,500 rentable square feet in

the Building after the Partial Reduction Date, Tenant shall continue to have its rights and obligations with respect to the Monument Sign pursuant to and in accordance with the terms and provisions of Additional Provision 4 (Monument Signage) on Exhibit F to the Original Lease.

13. **Letter of Credit.** Notwithstanding anything in the Original Lease to the contrary, Landlord and Tenant acknowledge and agree that, at any time after the Partial Reduction Date, so long as no uncured Default under the Lease exists as of such date, Tenant may replace the Letter of Credit outlined in Additional Provision 5 (Letter of Credit) with a cash Security Deposit in the amount of $30,437.33 and such cash Security Deposit shall thereafter be held by Landlord pursuant to and in accordance with the terms and provisions of Section 6 of the Original Lease.

14. **Access.** Tenant shall have access to the Premises and Building twenty-four (24) hours per day, seven (7) days per week, fifty-two (52) weeks per year, subject to Landlord's right to close the Building in the event of an emergency or casualty or due to other reasons outside of Landlord's reasonable control.

15. **Notice Address.** Landlord's address for notice set forth in Section 1.12 of the Original Lease is hereby deleted in its entirety and the following is substituted therefor:

Radiant-North Point Properties, LLLP 1170 Peachtree Street, Suite 2000
Atlanta, Georgia 30309 Attn: A. Boyd Simpson

16. **Brokers.** Lincoln Property Company Commercial, Inc. **("Landlord's Broker")** acted as agent for Landlord in connection with this First Amendment and Lavista Associates, Inc. **("Tenant's Broker")** has acted as agent for Tenant in connection with this First Amendment. Both Landlord's Broker and Tenant's Broker are to be paid a commission by Landlord pursuant to separate agreements. Landlord represents that it has dealt with no broker other than Landlord's Broker and Tenant's Broker in connection with this First Amendment. Landlord agrees that, if any other broker makes a claim for a commission based upon the actions of Landlord, Landlord shall indemnify, defend and hold Tenant harmless from any such claim. Tenant represents that it has dealt with no broker other than Landlord's Broker and Tenant's Broker in connection with this First Amendment. Tenant agrees that, if any other broker makes a claim for a commission based upon the actions of Tenant, Tenant shall indemnify, defend and hold Landlord harmless from any such claim.

17. **Counterparts.** This First Amendment may be executed in multiple counterparts, each of which shall constitute an original, but all of which shall constitute one document. This First Amendment may be executed by each party upon a separate copy, and one or more execution pages may be detached from one copy of this First Amendment and attached to another copy in order to form one or more counterparts. Each of the parties agree that the delivery of an executed copy of this First Amendment by facsimile or email shall be legal and binding and shall have the same full force and effect as if an original executed copy of this First Amendment had been delivered, and neither party will have the right to object to the manner (i.e., electronic signatures, via DocuSign, via .pdf, via fax, or scanned images of signature pages) in which the First Amendment was executed as a defense to the enforcement of this First Amendment or the Lease.

18. **No Claims, Offsets or Breaches.** Tenant acknowledges, certifies, affirms, and represents that there are no claims, offsets, or breaches of the Lease, or any action or causes of action by Tenant against Landlord directly or indirectly relating to the Lease.

19. **No Other Modifications.** Except as expressly modified herein, the Lease shall remain in full force and effect and, as modified herein, is expressly ratified and confirmed by the parties hereto. In the event of a conflict between the terms of the Lease and the terms of this First Amendment, the terms of this First Amendment shall control.

[Signatures Begin on Following Page]

IN WITNESS WHEREOF, the parties below have caused this First Amendment to be executed under seal as of the date and year first above written.

LANDLORD:

RADIANT-NORTH POINT PROPERTIES, LLLP,
a Delaware limited liabiltiy limited partnership

By: TSO RNP GP, LP, A Georgia limited partnership,
Its: General Partner

By: TSO RNP General Partner, LP,
a Georgia limited partnership,
Its: General Partner

By: TSO RNP GP SPE, Inc.,
a Georgia corporation
Its: General Partner

By: /s/ A. Boyd Simpson
Name: A. Boyd Simpson
Title: President

[Signatures Continue on Following Page]

TENANT:

CLEARSIDE BIOMEDICAL, INC.,
a Delaware Corporation

By: /s/ Charles A. Deignan
Name: Charles A. Deignan
Title: CFO

EXHIBIT A

PREMISES/REDUCTION PREMISES

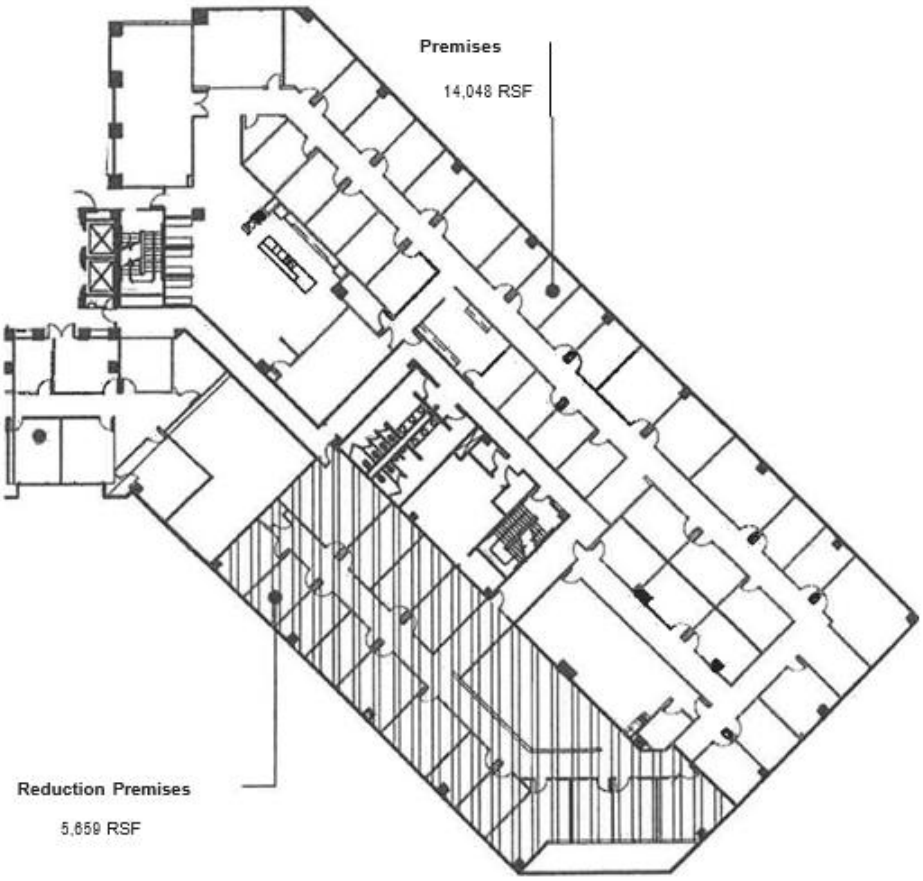
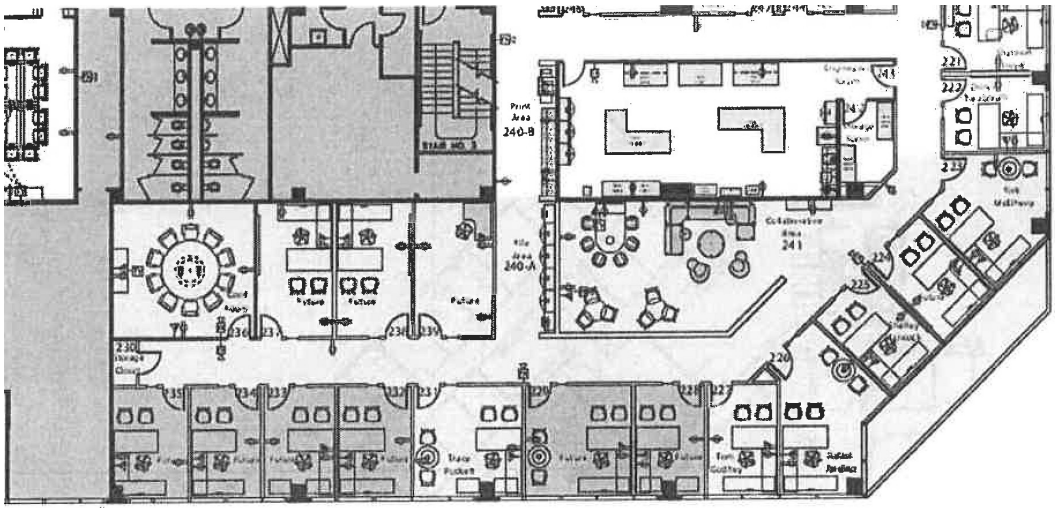


EXHIBIT B

EXISTING FURNITURE



Existing Furniture in this area to remain with Landlord

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

Exhibit 10.30

AMENDMENT NO. 1
TO THE
OPTION AND LICENSE AGREEMENT

This Amendment No. 1 (the "**Amendment**") dated January 14, 2023 ("**Amendment Effective Date**") is made by and between Clearside Biomedical, Inc., a Delaware corporation ("**Clearside**") and REGENXBIO Inc., a Delaware corporation ("**REGENXBIO**"). Clearside and REGENXBIO may each be referred to herein individually as a "**Party**" and collectively as the "**Parties**."

WHEREAS, the Parties have entered into that certain Option and License Agreement, dated August 29, 2019, as amended, supplemented or otherwise modified to the date hereof (the "**Agreement**");

WHEREAS, REGENXBIO has entered into an agreement related to a Covered Product known as RGX-314 ("**RGX-314**") with AbbVie Global Enterprises Ltd., a Bermuda company and its Affiliates (collectively, "**AbbVie**") in particular the License and Collaboration Agreement, dated September 10, 2021 by and between REGENXBIO and AbbVie (the "**AbbVie Collaboration**");

WHEREAS, Clearside has been informed by REGENXBIO that AbbVie is a Collaboration Partner of REGENXBIO with respect to RGX-314, as defined in and pursuant to the AbbVie Collaboration; and

WHEREAS, the Parties hereto desire to amend the Agreement, as described below, on the terms and subject to the conditions set forth herein.

NOW, THEREFORE, in consideration of the foregoing and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, hereby agree as follows:

1. **Definitions**. Capitalized terms used and not defined in this Amendment have the respective meanings ascribed to them in the Agreement.

2. **Amendments**. As of the Amendment Effective Date, the Agreement is hereby amended as follows:

(a) The first sentence of Section 1.78.1 of the Agreement is deleted in its entirety and replaced with the following: "**Net Sales**" means, with respect to Covered Product for any period, the gross amount billed or invoiced by REGENXBIO, its Affiliates and/or its or their Sublicensees and their Affiliates, Collaboration Partner(s) (including but not limited to AbbVie Global Enterprises Ltd., a Bermuda company and its Affiliates ("**AbbVie**")) and their Affiliates, or its or their Sublicensees (collectively, the "**Covered Product Sellers**") for the final sale of Covered Product to Third Parties in bona fide transactions, less deductions for the following, consistent with GAAP and the standard accounting practices of each Covered Product Seller with respect to Net Sales made by each Covered Product Seller:"

(b)The following language is added to the Agreement as a new Section 1.78.7:

"1.78.7 For the avoidance of doubt, no sales between or among REGENXBIO and/or its Covered Product Sellers shall be considered a sale for determining Net Sales under the Agreement."

(c)The following language is added to the Agreement as a new Section 3.8:

(d) "3.8. **No Implied Licenses or Sub-licenses**. Except as set forth herein, neither Party nor its Affiliates or Collaboration Partners shall acquire any license, sub-license or other intellectual property interest, by implication or otherwise, under any Intellectual Property of the other Party. For the avoidance of doubt, the Parties agree that no sub-licenses under any Intellectual Property of Clearside are needed for REGENXBIO to supply Clearside Devices to Collaboration Partners."

(e) The following revisions are hereby added to the Agreement in Section 4.1:

(i) The words ", itself or through its Collaboration Partners," are hereby inserted immediately after the occurrence of "REGENXBIO" in the first sentence of Section 4.1.

(ii) The words ", itself or through its Collaboration Partners" are hereby inserted after the occurrence of "REGENXBIO" in the second sentence of Section 4.1.

(iii) The words "or such Collaboration Partner's" is hereby inserted in the second sentence of Section 4.1 immediately after the occurrence of "REGENXBIO's".

(iv) The words ", itself or through its Collaboration Partners" is hereby inserted immediately after the occurrence of "REGENXBIO" in the third sentence of Section 4.1.

(f) The following revisions are hereby added to the Agreement in Section 4.3:

(i) The words "As between the Parties, REGENXBIO (itself or through its Affiliates or its or their Sublicensees)" are hereby deleted in the first sentence of Section 4.3 and the following words are hereby inserted in their place: "REGENXBIO (itself or through its Sublicensees, its Affiliates or their Sublicensees, or its Collaboration Partners or their Sublicensees)" .

(ii) The words, "REGENXBIO is" are hereby deleted in the second sentence of Section 4.3, and the words "REGENXBIO and its Collaboration Partners are" are hereby inserted in their place, and the words "and its Collaboration Partners" are hereby inserted immediately after "… imposing on REGENXBIO" and before "the duty…".

(g) The following revisions are hereby added to the Agreement in Section 4.4:

(i) The words "and its Collaboration Partners" are hereby inserted immediately after each occurrence of "REGENXBIO" in this Section 4.4.

(h) The following language is hereby added to the Agreement as new Section 4.5:

"4.5. **Sharing of Information and Cooperation**. Pursuant to Section 3.2, REGENXBIO shall identify to Clearside collaboration partners that have been granted rights by REGENXBIO related to the Development or Commercialization of Covered Products and their Affiliates and Sublicensees (collectively, "**Collaboration Partners**"). Clearside hereby acknowledges that it has been informed by REGENXBIO that AbbVie is a Collaboration Partner of REGENXBIO, as it relates to the Development and/or Commercialization of that certain Covered Product known as RGX-314 or other Covered Products resulting from that certain License and Collaboration Agreement, dated September 10, 2021 by and between REGENXBIO and AbbVie ("**AbbVie Collaboration**"). Clearside agrees to engage in 3-way discussions between Clearside,

REGENXBIO, and AbbVie as reasonably requested by REGENXBIO, and to disclose the same information in such 3-way discussions that Clearside would otherwise share or disclose directly to REGENXBIO under this Agreement, including any Quality Agreement or Pharmacovigilance Agreement entered into pursuant to this Agreement, provided that AbbVie is bound by a confidentiality agreement containing terms of confidentiality and non-use at least as stringent as the applicable terms set forth in this Agreement. Further, REGENXBIO may share any information with AbbVie that Clearside has shared or disclosed directly to REGENXBIO under this Agreement, including any Quality Agreement or Pharmacovigilance Agreement entered into pursuant to this Agreement, and including but not limited to information related to obtaining Regulatory Approvals pursuant to Section 4.2.1(a), provided that AbbVie is bound by a confidentiality agreement containing terms of confidentiality and non-use at least as stringent as the applicable terms set forth in this Agreement."

(i) In the first sentence of Section 5.1.1 of the Agreement the words "and REGENXBIO's Collaboration Partners'" are hereby added after "REGENXBIO's" and before "requirements".

(j) In the first sentence of Section 5.2.1 of the Agreement the words "and any Collaboration Partner" are hereby added after "REGENXBIO" and before "for".

(k) In the first sentence of Section 5.3 of the Agreement the words "and a Collaboration Partner, if requested by REGENXBIO" are hereby added after "Parties" and before ", together".

(l) In the preamble of Section 6.2.1 of the Agreement, the phrase ", or by a Collaboration Partner," is hereby added after "REGENXBIO, an Affiliate, or a Sublicensee".

(m) In the preamble of Section 6.3 of the Agreement, the phrase ", or a Sublicensee, and/or by a Collaboration Partner," is hereby added after "whether such milestone is achieved by REGENXBIO, an Affiliate".

(n) Section 6.4.1 is hereby deleted in its entirety and replaced with the following:

"6.4.1. **Royalty Rates.** As further consideration for the rights granted to REGENXBIO hereunder and subject to the terms and conditions of this Agreement, during the Royalty Term, REGENXBIO will pay to Clearside a royalty in the amount of [***] of Net Sales of Covered Products by REGENXBIO or its Affiliates or any Covered Product Seller (including but not limited to AbbVie pursuant to the AbbVie Collaboration), subject to the royalty reductions set forth below. For the avoidance of doubt, in no case shall REGENXBIO owe to Clearside more than one such royalty on a sale of a Covered Product. REGENXBIO will have no obligation to pay any royalty with respect to Net Sales of Covered Product in any country after the Royalty Term for such Covered Product in such country has expired. Following the expiration of the Royalty Term for Covered Product in a country, the grants in Section 3.1 will become full-paid, royalty-free, perpetual and irrevocable for such Covered Product in such country, and no further royalties will be payable. REGENXBIO will include any Covered Product Sellers' sales in the reports described in Section 6.5 of the Agreement and use reasonable efforts to ensure that each Covered Product Seller retains accurate financial books and records as set forth in Section 6.8 of the Agreement."

(o) In the last sentence of Section 6.5, the phrase "… attributable to its Affiliates and Sublicensees." is hereby deleted in its entirety and replaced with the following phrase "attributable to its Affiliates, Sublicensees and other Covered Product Sellers."

(p)The follow language is hereby added after the last sentence in Section 6.9:

(q)"Upon Clearside's or EGT Licensors' written request, REGENXBIO shall provide Clearside or EGT Licensors with the portions relevant to the Net Sales of Covered Product of any audit report that REGENXBIO has received from an independent public accounting firm in connection with such firm's audit of a Collaboration Partner, consistent with the audit rights afforded to REGENXBIO pursuant to its agreement with such Collaboration Partner (and, in the case of AbbVie, pursuant to the AbbVie Collaboration).In Section 9.4.3 of the Agreement, "and its Collaboration Partners" is hereby added after "(and with respect to REGENXBIO, its Sublicensees… ".

3. **Conflicting Terms**. In the event of a conflict between the terms of this Amendment and the terms of the Agreement, the terms of this Amendment shall prevail as to the subject matter hereof.

4. **Continuation**. Except as expressly provided or modified in this Amendment, all of the terms and provisions of the Agreement are and will remain in full force and effect, shall not be modified and are hereby ratified and confirmed by the Parties.

5. **Counterparts**. This Amendment may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

[Signatures follow on next page]

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

IN WITNESS WHEREOF, the Parties by their authorized representatives have executed this Amendment as of the Amendment Effective Date.

Clearside Biomedical, Inc.	**REGENXBIO Inc.**
/s/ George Lasezkay	/s/ Patrick Christmas
Signature	Signature
George Lasezkay	Patrick Christmas
By: Name	By: Name
President and Chief Executive Officer	Chief Legal Officer
Title	Title
January 14, 2023	January 17, 2023
Date	Date

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. 333-238128) of Clearside Biomedical, Inc.,
4. Registration Statement (Form S-3 No. 333-235880) of Clearside Biomedical, Inc.,
5. 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.,
6. Registration Statement (Form S-8 No. 333-231383) pertaining to the 2016 Equity Incentive Plan of Clearside Biomedical, Inc.,
7. Registration Statement (Form S-8 No. 333-238133) pertaining to the 2016 Equity Incentive Plan of Clearside Biomedical, Inc.,
8. Registration Statement (Form S-8 No. 333-256212) pertaining to the 2016 Equity Incentive Plan of Clearside Biomedical, Inc., and
9. Registration Statement (Form S-8 No. 333-264885) pertaining to the 2016 Equity Incentive Plan of Clearside Biomedical, Inc.

of our report dated March 14, 2023, 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, 2022.

/s/Ernst & Young LLP

Atlanta, Georgia
March 14, 2023

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, 2022 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 14, 2023

/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, 2022 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 14, 2023

/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, 2022, 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 14th day of March, 2023.

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