UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 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, 2019

OR

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

For transition period from _____ to _____

Commission File Number 001-36332

ALDEYRA THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**20-1968197**
(State or other jurisdiction of incorporation)	**(IRS Employer Identification No.)**

131 Hartwell Avenue, Suite 320
Lexington, MA 02421
(Address of principal executive offices)

(781) 761-4904
(Registrant's telephone number, including area code)

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

Common Stock, $0.001 par value per share	**ALDX**	**The Nasdaq Stock Market, LLC**
(Title of each class)	(Trading Symbol)	**(Name of each exchange on which registered)**

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 Section 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 a smaller reporting company or an emerging growth company. See the definitions of the "large accelerated filer," "accelerated filer," "non-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 is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

As of June 28, 2019, the last business day of the registrant's last completed second quarter, the aggregate market value of the registrant's Common Stock held by non-affiliates of the registrant was approximately $152,791,890, based on the closing price of the registrant's Common Stock, as reported by The Nasdaq Capital Market. Shares of Common Stock held by each executive officer, director and stockholders known by the registrant to be affiliated with such individuals based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 10, 2020 there were 29,662,125 shares of the registrant's Common Stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's proxy statement with respect to the registrant's 2020 Annual Meeting of Stockholders, which is to be filed pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2019, are incorporated by reference into Part III of this Annual Report on Form 10-K.

Aldeyra Therapeutics, Inc.
Annual Report on Form 10-K
For the Fiscal Year Ended December 31, 2019
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Various statements throughout this report are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this report regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. These statements are subject to risks and uncertainties and are based on information currently available to our management. Words such as, but not limited to, “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “contemplates,” “predict,” “project,” “target,” “likely,” “potential,” “continue,” “ongoing,” “design,” “might,” “objective,” “will,” “would,” “should,” “could,” or the negative of these terms and similar expressions or words, identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. The events and circumstances reflected in our forward-looking statements may not occur and actual results could differ materially from those projected in our forward-looking statements. Meaningful factors which could cause actual results to differ include, but are not limited to:

- the timing of enrollment, commencement, and completion of our clinical trials;
- the timing and success of preclinical studies and clinical trials conducted by us and our development partners;
- delay in or failure to obtain regulatory approval of our product candidates;
- the ability to maintain regulatory approval of our product candidates, and the labeling for any approved products;
- the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical or clinical trials, will not be replicated or will not continue in ongoing or future studies or trials involving our product candidates;
- the scope, progress, expansion, and costs of developing and commercializing our product candidates;
- uncertainty as to our ability to commercialize (alone or with others) our product candidates following regulatory approval, if any;
- the size and growth of the potential markets and pricing for our product candidates and the ability to serve those markets;
- our expectations regarding our expenses and revenue, the sufficiency or use of our cash resources and needs for additional financing;
- the rate and degree of market acceptance of any of our product candidates;
- our expectations regarding competition;
- our anticipated growth strategies;
- our ability to attract or retain key personnel;
- our limited sales and marketing infrastructure;
- our ability to establish and maintain development partnerships;
- our ability to successfully integrate acquisitions into our business;
- our expectations regarding federal, state and foreign regulatory requirements;
- regulatory developments in the United States and foreign countries;
- our ability to obtain and maintain intellectual property protection for our product candidates; and
- the anticipated trends and challenges in our business and the market in which we operate.

All written and verbal forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We caution investors not to rely too heavily on the forward-looking statements we make or that are made on our behalf. We undertake no obligation, and specifically decline any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosures we make on related subjects in any annual, quarterly or current reports that we may file with the Securities and Exchange Commission.

We encourage you to read the discussion and analysis of our financial condition and our financial statements contained in this annual report on Form 10-K. We also encourage you to read Item 1A of Part 1 of this annual report on Form 10-K, entitled “Risk Factors,” which contains a more complete discussion of the risks and uncertainties associated with our business. In addition to the risks described above and in Item 1A of this report, other unknown or unpredictable factors also could affect our results. Therefore, the information in this report should be read together with other reports and documents that we file with the SEC from time to time, including Forms 10-Q, 8-K and 10-K, which may supplement, modify, supersede or update those risk factors. There can be no assurance that the actual results or developments anticipated by us will be realized or, even if substantially realized, that our results will lead to the expected consequences to, or effects on, us. Therefore, no assurance can be given that the outcomes stated in such forward-looking statements and estimates will be achieved.

As used in this annual report on Form 10-K, the terms “Aldeyra,” “Registrant,” “the Company,” “we,” “us,” and “our” mean Aldeyra Therapeutics, Inc., together with its wholly-owned subsidiaries, unless the context indicates otherwise.

INDUSTRY AND MARKET DATA

We obtained the industry, market and certain other data used throughout this annual report on Form 10-K from our own internal estimates and research, as well as from industry and general publications, surveys and studies conducted by third parties. Internal estimates are derived from publicly-available information released by industry analysts and third-party sources, our internal research, and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In addition, while we believe the industry, market, and other data included in this annual report on Form 10-K are reliable and based on reasonable assumptions, such data involves risks and uncertainties and are subject to change based on various factors, including those discussed in "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

ITEM 1.*BUSINESS*

Overview

We are a biotechnology company devoted to developing and commercializing next-generation medicines to improve the lives of patients with immune-mediated diseases. Our lead product candidate, reproxalap, is a first-in-class treatment in late-stage development for dry eye disease ("DED") and allergic conjunctivitis ("AC"). We have additional product candidates in development for proliferative vitreoretinopathy ("PVR") and other retinal diseases, autoimmune disease, and cancer. We currently intend to commercialize our products directly or through collaborations. None of our product candidates have been approved for sale in the United States or elsewhere.

Immune-mediated diseases are conditions that result from an imbalance of inhibitory and stimulatory factors that regulate the immune system. Immunological dysregulation can lead to a broad array of conditions that include autoimmune disease, allergy, immunoproliferative disease, and cancer. Many ocular, cardiovascular, metabolic, neurological, and musculoskeletal diseases, affecting tens of millions of patients in the United States and hundreds of millions of patients worldwide, are at least partially immune-mediated. An estimated 7% of western society suffers from some form of immune-mediated disease, and incidence has been increasing. Given the complexity of immune dysregulation, which involves many mediators and signaling pathways, rarely is any single therapeutic approach effective, and today most immune-mediated diseases are generally considered to be inadequately treated. As such, we believe immune-mediated diseases represent considerable unmet medical need, and that demand for novel immune-modulating therapies is high. Consistent with large patient populations and high therapeutic demand, the current market for the treatment of immune-mediated diseases is considerable, representing an excess of $40 billion worldwide.

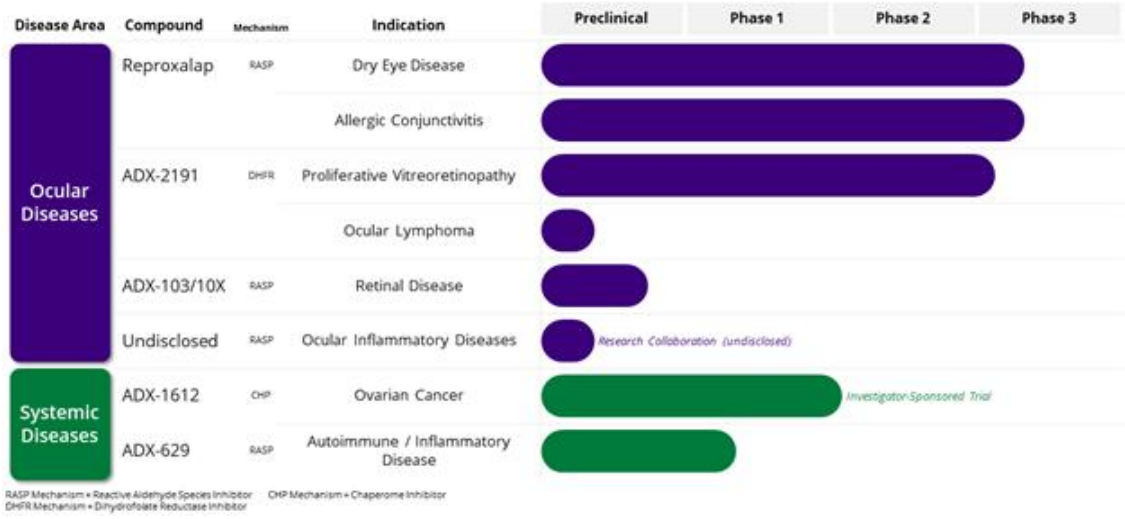
Our product development pipeline is focused on immune-mediated ocular diseases and select systemic diseases, and encompasses three distinct biological mechanisms of actions: reactive aldehyde species ("RASP") inhibition, dihydrofolate reductase ("DHFR") inhibition, and protein chaperome ("CHP") inhibition. The immunological activity of our product candidates generally leads to diminished levels of pathological inflammation via down-regulation of immune cell activation or proliferation.

Our lead product candidate reproxalap is a RASP inhibitor that has been shown to diminish ocular inflammation, and has demonstrated statistically significant and clinically relevant improvements across an aggregate of six Phase 2 clinical trials in DED and AC, a Phase 3 clinical trial in AC, and Part 1 of a Phase 3 clinical trial in DED, when administered topically to the eye as an ophthalmic solution. Administered to the skin as a topical dermatologic formulation in a Phase 2 clinical trial and in Part 1 of a Phase 3 clinical trial, reproxalap demonstrated statistically significant and clinically relevant improvements in ichthyosis (a severe skin disorder) caused by Sjögren-Larsson Syndrome, a rare RASP-mediated disease with no approved therapy. A growing body of clinical evidence supports the potential and relevance of RASP inhibition as a new and differentiated mechanism of action. We have discovered and are developing two additional RASP inhibitors, ADX-103 and ADX-629, for the treatment of retinal disease and autoimmune disease, respectively.

As we continue to execute on our strategy of expanding our product candidate pipeline, we intend to license or acquire new immune-modulating approaches with novel therapeutic potential. In January 2019, we acquired Helio Vision, Inc. and thereby obtained rights to ADX-2191, an intravitreal DHFR inhibitor (methotrexate) for the prevention of PVR, a serious sight-threatening retinal disease with no approved treatment. In addition, in December 2016, we in-licensed the clinical-stage product candidate ADX-1612 (investigated in oncology under the name ganetespib), which inhibits CHP, a mechanistically differentiated approach for the potential treatment of inflammatory diseases.

Our active clinical programs include four unique product candidates, representing three distinct mechanisms of action across a number of different potential indications. All of our development plans and timelines are subject to adjustment depending on recruitment rate, regulatory review, preclinical and clinical results, funding, and other factors that could delay the initiation, completion, or reporting of clinical trials. Our pipeline, as of the date of filing this annual report on Form 10-K is illustrated below.

Product Candidate Development Pipeline



We have no products approved for sale. We will not receive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize such products or until we potentially enter into agreements with third parties for the development and commercialization of product candidates. If our development efforts for any of our product candidates result in regulatory approval or we enter into collaboration agreements with third parties, we may generate revenue from product sales or from such third parties. We have primarily funded our operations through the sale of our convertible preferred stock, common stock, convertible promissory notes, warrants, and borrowings under debt facilities.

We will need to raise additional capital in the form of debt or equity or through partnerships to fund additional development of our product candidates, and we may in-license, acquire, or invest in complementary businesses or products. In addition, contingent on capital resources, we may augment, diminish, or otherwise modify the clinical development plan described herein.

Since our incorporation, we have devoted substantially all of our resources to the preclinical and clinical development of our product candidates. Our ability to generate revenues, if any, largely depends upon our ability, alone or with others, to complete development of and obtain regulatory approvals for our product candidates, and to successfully manufacture, market, and sell our product candidates. The results of our operations will vary significantly from year-to-year and quarter-to-quarter, and depend on a number of factors, including risks related to our business and industry, risks relating to intellectual property and other legal matters, risks related to our common stock, and other risks that are detailed in the section of this annual report on Form 10-K entitled “Risk Factors.”

The Markets for Our Product Candidates

Dry Eye Disease and Allergic Conjunctivitis – Two Prevalent Diseases with Significant Comorbidity

The symptoms of dry eye disease (“DED”) (ocular pain, dryness, gritty sensation) and allergic conjunctivitis (“AC”) (ocular itching and tearing) are chronic and persistently disturbing, impacting quality of life and leading to loss of work and substantial economic burden. DED and AC are two of the most common diseases treated by ophthalmologists and optometrists, and physicians and patients regard therapy as inadequate in a substantial number of cases.

There are approximately 20 million DED patients in the United States, yet only two drugs are approved for DED treatment, cyclosporine (0.05% as Restasis® or 0.09% as Cequa™) and lifitegrast (5% as Xiidra®). The activity of both drugs has been observed to be minimal or lacking in the majority of patients, and weeks or months of treatment may be required to achieve even modest clinical benefit. In addition, generic versions of Restasis® are also expected to become available in the U.S. in the near future.

There are approximately 100 million patients in the United States with AC, and we estimate that up to 30 million of such AC patients do not respond adequately to, or are dissatisfied with, topical antihistamines, the current standard of care. A primary reason for dissatisfaction with antihistamines appears to be lack of durable activity, which may be due to the fact that histamine is only one of the biological mediators of the disease, and the fact that increased histamine levels persist for only 10 to 20 minutes following allergen exposure.

Many patients manifest symptoms of both DED and AC, and differential diagnosis can be challenging for physicians. Approximately half of dry eye patients complain of itching, which is generally considered the result of allergy, and approximately half of AC patients complain of dryness, which is generally considered the result of DED. There are currently no United States Food and Drug Administration (“FDA”)-approved products that are indicated to treat both DED and AC. Neither cyclosporine nor lifitegrast have been approved for use in patients with AC, and antihistamines are known to exacerbate ocular dryness. Thus, with the possible exception of topical corticosteroids (discussed below), we believe that no currently available drug for DED or AC is likely to be effective for the treatment of patients who experience symptoms of both diseases.

By inhibiting RASP, which are elevated in a variety of inflammatory diseases, reproxalap represents a novel mechanism for diminishing ocular inflammation in DED and AC. In two Phase 2 clinical trials in DED, two Phase 2 clinical trials in AC, one Phase 3 trial in AC, and Part 1 of a Phase 3 trial in DED, reproxalap demonstrated consistent statistically significant and clinically relevant activity. We believe that reproxalap may have a commercially differentiated product profile versus currently approved drugs for each indication, having shown the potential for early and broad activity in DED, and durable activity in AC. Additionally, reproxalap also has added potential of being the only product able to effectively treat DED and AC, uniquely addressing the needs of the large underserved population that suffers from both diseases.

Based on the late-stage clinical trial results to date, discussed below, we believe reproxalap could offer superior efficacy relative to existing DED medications, particularly with regard to early onset of action and breadth of activity. Thus, our current expectation is that reproxalap could be priced similarly to, or at a premium to, currently marketed drugs for DED, which are generally priced in the range of $500 to $550 per month. The potential size of the DED market is substantial. Of the estimated 34 million patients with DED in the United States, approximately 20 million are diagnosed. Assuming approximately one-third of diagnosed patients are candidates for prescription medication, and assuming approximately six months of therapy per year, the potential total addressable market for reproxalap therapy in DED is greater than $21 billion in the United States.

Contingent on the results of current and planned clinical trials in DED and AC, in addition to regulatory authority approval, we intend to commercialize reproxalap ophthalmic solution directly or through marketing partnerships.

Proliferative Vitreoretinopathy and Other Retinal Diseases

Proliferative vitreoretinopathy (“PVR”) is a rare inflammatory disorder of the retina that leads to severe retinal scarring and blindness, and is the leading cause of failure of retinal reattachment surgery. Over 50% of PVR cases result in severe uncorrectable vision loss (visual acuity of 20/320 or worse), and 76% of PVR patients suffer from at least moderate uncorrectable vision loss. PVR occurs after up to 10% of surgeries for retinal detachment and 50% or more of surgeries for open globe injury. Based on the prevalence of primary retinal detachment, in addition to retinal detachment that occurs as a result of trauma, we estimate that there are, in aggregate, approximately 20,000 treatable cases of PVR in the United States, Europe, and Japan. By inhibiting cell growth and thereby diminishing scar formation, ADX-2191 has the potential to be the first FDA-approved drug for prevention of PVR. In April 2018, ADX-2191 received orphan drug designation from the FDA for the prevention of PVR. In September 2019, ADX-2191 received fast track designation from the FDA for the prevention of PVR. ADX-2191 has also been used to treat ocular lymphoma, a rare cancer with no approved therapy.

In addition to PVR, the retina is susceptible to a variety of immune-mediated diseases, many of which are mediated by RASP. Inflammatory retinal disorders that involve RASP include both posterior and pan-uveitis, uveitis-associated macular edema, diabetic macular edema, and diabetic retinopathy. Separately, RASP and RASP-adducts accumulate in dry age-related macular degeneration, Stargardt’s Disease (juvenile dry age-related macular degeneration-like disease), and Sjögren-Larsson Syndrome-associated maculopathy. We believe that the number of patients affected by immune-mediated retinal disorders is considerable. In 2010, the National Eye Institute estimated that diabetic retinopathy and age-related macular degeneration represent approximately 10 million patients in the United States, and is expected to grow to almost 14.5 million by 2030. In 2017, the global ophthalmic drugs market was valued at $23 billion, and the market for retinal diseases accounted 39%, or approximately $9 billion, one of the largest ocular segments. Therefore, we believe that the total market potential of RASP inhibitors for the treatment of retinal disease is substantial.

Immune-Mediated Systemic Diseases

Immune-mediated systemic diseases, such as autoimmune disease, are generally chronic conditions characterized by excessive and misdirected inflammatory responses. In aggregate, autoimmune diseases and related systemic inflammatory disorders represent tens of millions of patients in the United States, with aggregate drug sales expected to exceed $74 billion by 2022. In 2017, three of the top five highest-selling drugs, totaling more than $32 billion globally and $20 billion in United States sales, were prescribed for a variety of immune-mediated disorders, including Crohn’s disease, rheumatoid arthritis, psoriasis, ulcerative colitis, and ankylosing spondylitis.

The potential market for immune-modulating therapies could continue to expand as a result of growing evidence that excessive inflammation may be critical to the development and progression of cardiovascular disease, diabetes, Alzheimer's disease, and many other common conditions that are not typically defined as inflammatory or autoimmune diseases.

Given the complex pathophysiology of systemic immune-mediated disorders, many of which are caused by a variety of pro-inflammatory mediators, therapy often requires combinations of drugs with distinct mechanisms of action. As such, we believe novel product candidates for immune-mediated diseases are in high demand.

ADX-1612 (investigated in oncology under the name ganetespib) is a novel drug candidate that inhibits the protein chaperome (CHP). CHP is involved in the processing of a variety of proteins, and appears to be particularly important in cellular proliferation. Many immune-mediated diseases are at least in part the result of hyper-proliferation of immune cells, a phenomenon known as lymphoproliferation. Lymphoproliferative diseases include post-transplant lymphoproliferative disorder, systemic lupus erythematosus (lupus), autoimmune lymphoproliferative syndrome, Waldenstrom's macroglobulinemia, Wiskott-Aldrich syndrome, and myelodysplastic syndromes. We are not aware of any other company that is developing a CHP inhibitor for systemic immune-mediated disease. Similar to lymphoproliferative disease, cancer is also characterized by uncontrolled cellular replication, and ADX-1612 may represent a new therapeutic approach for the treatment of certain cancers in combination with other cancer drugs.

Additionally, our RASP inhibitor platform represents a potential novel therapeutic approach for a variety of common systemic immune-mediated conditions. Because RASP appear to be involved in the generation and potentiation of inflammation in general, we believe the potential therapeutic applicability of RASP inhibitors is broad. We are not aware of any other company actively developing RASP inhibitors. In 2019, we began Phase 1 clinical testing of ADX-629, a novel drug candidate that inhibits RASP. In 2020, we expect to begin Phase 2a clinical testing of ADX-629 in autoimmune or inflammatory diseases where RASP are implicated as pathologic mediators.

The Competitive Landscape of Our Product Candidates

The pharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies, academic institutions, government agencies, and research institutions. We believe that the key competitive factors that will affect the development and potential commercial success of our product candidates are efficacy, safety, tolerability, and the ability to reduce the dependence on, or the dose of, more toxic drug products.

Many of our potential competitors have substantially greater financial, technical, and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products, and in the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining regulatory approval for products and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed and sold, than any product that we may commercialize, and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. We anticipate that we will face intense and increasing competition as new products enter the market and advanced technologies become available. In addition, the development of new treatment methods for the diseases we are targeting could render our products non-competitive or obsolete.

While our product candidates may manifest efficacy, tolerability, or safety advantages, many marketed therapies are generic or may be priced considerably lower than the pricing we anticipate for our product candidates. Pricing factors may discourage the initial or prolonged use of our product candidates. In addition, the recent growth of Pharmacy Benefit Managers has diminished the profitability of drug commercialization for smaller companies, and may hamper our ability to support our operations or compete effectively in the marketplace following regulatory approval, if any.

RASP Inhibitor Platform

A number of academic groups have published on the concept of reducing RASP levels, primarily by using compounds with amines (certain nitrogen-containing molecules) that react with RASP through a chemical process known as the Schiff base reaction. Various RASP-binding amines have been described, particularly carnosine (a naturally occurring dipeptide), which has other potential mechanisms of action unrelated to RASP. At least one group has published on the use of certain nitrogen-containing marketed products to temporarily, in a reversible manner, bind retinaldehyde (a RASP) as a potential therapy for retinal disease. Schiff base reactions have also been mentioned as possible explanations for a portion of the activity of aminoguanidine, pyridoxamine, and possibly other non-proprietary amine-containing compounds that have been tested in clinical trials for diabetic nephropathy. However, the Schiff base reaction is reversible, and generally the substrates (precursors) and products of the reaction exist in equilibrium such that, at any point in time, the RASP substrate may be bound or unbound. In this way, Schiff base reactions alone represent reversible and temporary RASP binding, and likely lead to the relocation of RASP rather than the elimination of RASP. We believe that reproxalap and chemically related product candidates that we have discovered are differentiated from the above approaches in that the chemical structures of our product candidates are novel, and the reaction with RASP has been observed to be essentially irreversible *in vivo*, which, we believe, may result in a more effective means of diminishing RASP.

Other Immune-Modulating Pharmacotherapies

A myriad of new treatments have been or are being developed to treat inflammatory diseases, and have been used, or in theory could be used, for the treatment of the diseases that our product candidates are intended to target. Immune-modulating products include cytokine inhibitors, immune cell receptor inhibitors, complement inhibitors, and Janus kinase inhibitors. Companies that currently market such therapies include Abbvie, Inc., Johnson & Johnson, UCB Inc. and UCB S.A., Amgen, Inc., Bristol-Myers Squibb Co., and Pfizer, Inc. Currently marketed products may manifest efficacy and safety advantages over our product candidates, and may be used to treat the diseases for which we are developing our product candidates. In addition, CHP inhibitors other than ADX-1612 are in development for the treatment of cancer, and such compounds could theoretically be used for the treatment of immune-mediated diseases. Methotrexate, the active drug substance of ADX-2191, is generically available and has been used as a chemotherapeutic and immune modulating agent, and other formulations or application methods of methotrexate could be developed for the treatment of inflammatory retinal diseases.

Competitive Product Candidates by Indication

We believe the primary competitors by indication with respect to our current programs in late stage-clinical testing are as follows:

Competitive Pharmaceuticals by Indication

Indication	Competitive Products
Dry Eye Disease	Topical immunomodulators, such as cyclosporine (0.05% as Restasis® or 0.09% as Cequa™) and lifitegrast (5% as Xiidra®); topical corticosteroids; and artificial tear solutions
Allergic Conjunctivitis	Topical antihistamines and corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and mast cell stabilizers
Proliferative Vitreoretinopathy	None

We believe that there is significant unmet medical need for the diseases that we intend to target. If proven to be safe and effective, we believe that our product candidates could be used in place of, or in addition to, current therapies. Currently available therapies for the treatment of DED are generally considered by physicians and patients to be inadequate, may require weeks or months of treatment to achieve even moderate clinical benefit, and have not demonstrated clinical activity in AC, a common comorbidity. In addition, generic versions of Restasis® are also expected to become available in the U.S. in the near future. There is no approved therapy for PVR.

Many drugs are in development for AC and DED. We believe that there are currently no drugs in development for both DED and AC; or PVR. For the diseases we intend to study, there may be other developmental therapies of which we are not aware.

Our ability to compete successfully will depend in part on our ability to utilize our drug development expertise to identify, develop, secure rights to, and obtain regulatory approvals for promising pharmaceutical products before others are able to develop competitive products. Our ability to compete successfully will also depend on our ability to attract and retain skilled and experienced personnel. Additionally, our ability to compete may be diminished by insurers and other third-party payors, which generally encourage the use of cheaper, non-innovative, or generic products.

Clinical Trial Results and Development Plans

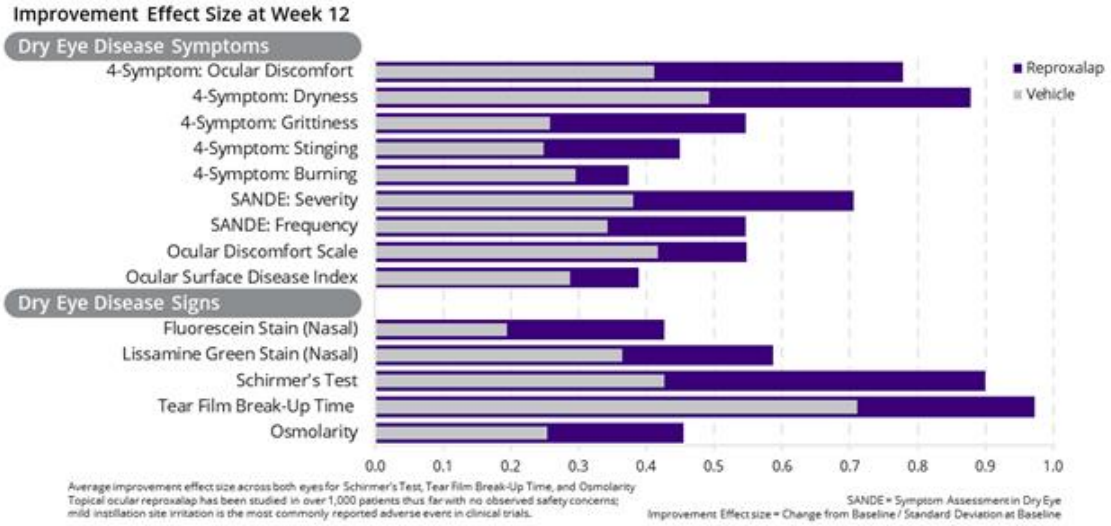
Prior to applying for marketing approval, our product candidates must satisfy regulatory authority requirements for safety and efficacy, including pivotal Phase 3 clinical assessment. Our active clinical programs with reproxalap have consistently demonstrated statistically and clinically significant efficacy, and have advanced to late-stage clinical testing. In addition, reproxalap has been observed to be well-tolerated and reported adverse events were generally mild in our clinical trials to date. Our material clinical results have been previously disclosed elsewhere in detail, and we encourage review of all of our clinical trial disclosures. All of our development plans and timelines are subject to adjustment depending on recruitment rate, regulatory review, preclinical and clinical results, funding, and other factors that could delay the initiation, completion, or reporting of clinical trials.

Dry Eye Disease

In September 2017, we announced that the results of a randomized, parallel-group, double-masked Phase 2a clinical trial of reproxalap ophthalmic solution demonstrated statistically and clinically relevant improvement from baseline in multiple signs and symptoms associated with dry eye disease. In September 2018, we announced that the results of a randomized, vehicle-controlled, parallel-group, multi-center, double-masked Phase 2b clinical trial of 0.1% and 0.25% concentrations of reproxalap topical ophthalmic solution demonstrated statistically significant improvement over vehicle in ocular signs and symptoms associated with DED (Figure 1). Relative to patients treated

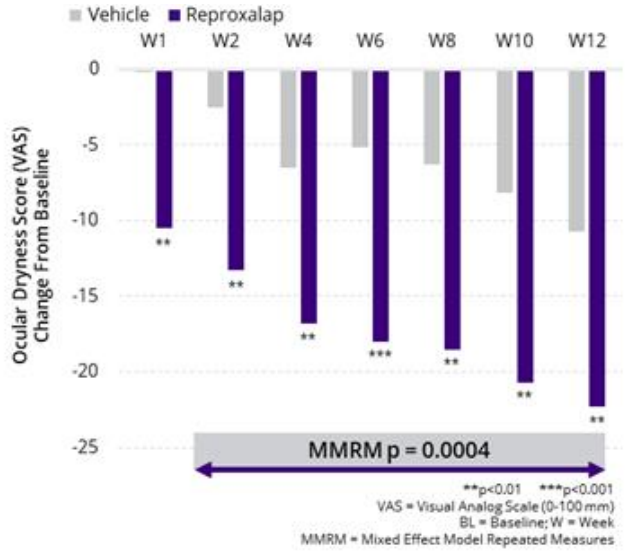
with vehicle, patients treated with the 0.25% concentration of reproxalap demonstrated statistically significant and clinically relevant reductions in the Four-Symptom Ocular Dryness Score and the Overall Ocular Discomfort Symptom Score. For drug-treated patients, improvement greater than that of vehicle was consistently observed across all symptoms, and activity versus vehicle was evident as early as two weeks, the first assessment following initiation of therapy. The early onset of symptomatic improvement is consistent with the Phase 2a clinical trial of topical ocular reproxalap in dry eye disease, and is supportive of a differentiated product profile relative to standard of care. Patients treated with the 0.25% concentration of reproxalap also demonstrated reductions in ocular fluorescein staining score that were statistically superior to those of patients treated with vehicle. Both 0.1% and 0.25% reproxalap concentrations demonstrated activity relative to vehicle, and a clear dose response was observed.

Figure 1: Phase 2b Dry Eye Disease Clinical Trial Results



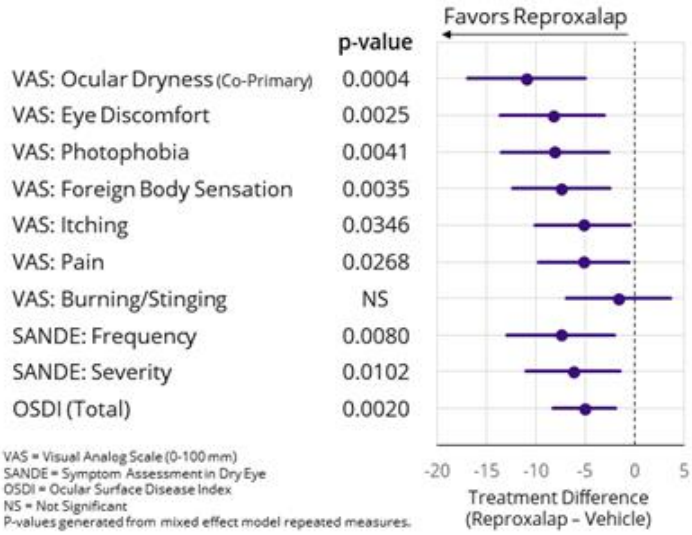
In April 2019, we initiated the RENEW Trial, an ongoing adaptive, two-part, multi-center, randomized, vehicle-controlled, double-masked, parallel-group Phase 3 trial of 0.25% topical ocular reproxalap compared to vehicle in patients with moderate to severe DED. The primary objective of RENEW Part 1 was to confirm dosing regimen, endpoints, and sample size for RENEW Part 2. In Part 1 of RENEW, 422 patients were randomized equally to receive either four-times-daily reproxalap or vehicle for twelve weeks (the constant dosing group) or four-times-daily reproxalap or vehicle for four weeks, followed by twice-daily reproxalap or vehicle for eight weeks (the induction-maintenance dosing group). In December 2019, we announced that, in the induction-maintenance dosing group, the RENEW co-primary endpoint of patient-reported visual analog scale ("VAS") ocular dryness from Weeks 2 to 12 was achieved (p=0.0004) (Figure 2), and activity was observed as early as one week after initiation of therapy (p=0.001) and was maintained until the end of the trial.

Figure 2: RENEW Part 1 Results – Co-Primary Symptom Endpoint



In the induction-maintenance dosing group from Weeks 2 to 12, reproxalap was statistically superior to vehicle in VAS ocular endpoints for itching (p=0.03), foreign body sensation (p=0.004), discomfort (p=0.003), photophobia (p=0.004), and pain (p=0.03) (Figure 3). In the induction-maintenance dosing group from Weeks 2 to 12, reproxalap was statistically superior to vehicle in Ocular Discomfort & 4-Symptom Questionnaire ocular endpoints for dryness (p=0.01), discomfort (p=0.03), burning (p=0.03), grittiness (p=0.003), and stinging (p=0.02). Although the improvement effect size of the co-primary endpoint of fluorescein nasal region ocular staining did not reach statistical significance, reproxalap was statistically superior to vehicle in reduction from baseline in the induction-maintenance dosing group from Weeks 1 to 4 of treatment (p=0.03), and statistical separation from vehicle was observed at Week 2 (p=0.04). Consistent with previous clinical trials, topical ocular reproxalap was well-tolerated, and reported adverse events were generally mild.

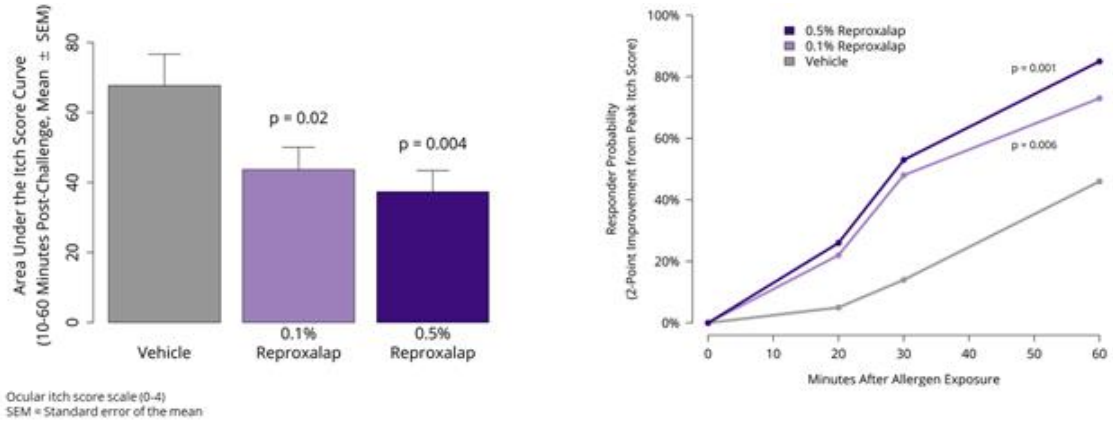
Figure 3: RENEW Part 1 Results – Symptom Treatment Differences Over Weeks 2 to 12



Allergic Conjunctivitis

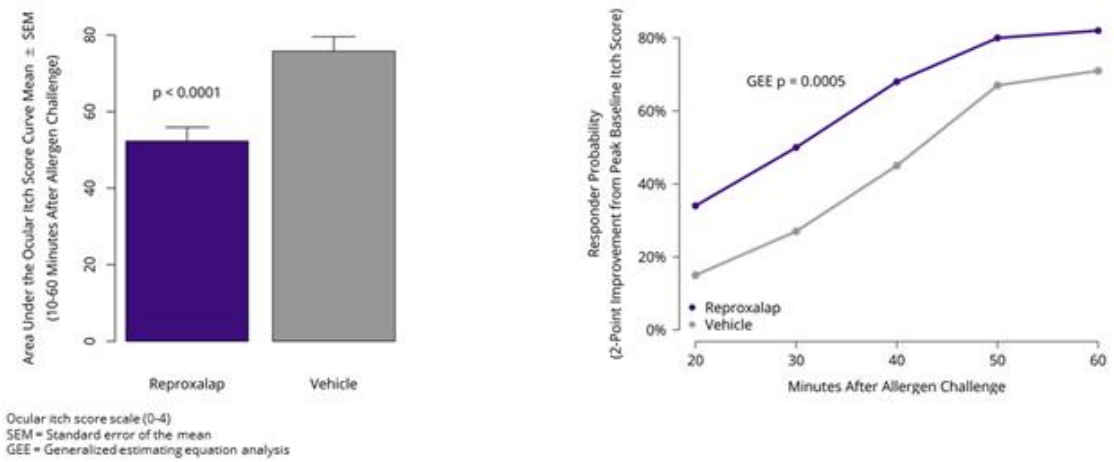
In February 2016, we announced that the results of a randomized, parallel-group, double-masked, vehicle-controlled Phase 2a clinical trial of reproxalap ophthalmic solution in patients with AC demonstrated statistically and clinically significant activity of reproxalap over vehicle in reducing ocular itching and tearing. In June 2017, we announced that the results of a randomized, parallel-group, double-masked, vehicle-controlled, multi-center Phase 2b clinical trial of 0.1% and 0.5% topical ocular reproxalap in patients with AC demonstrated statistically and clinically significant activity of reproxalap over vehicle in reducing ocular itching. In the Phase 2b clinical trial, which assessed ocular itching (scale 0 to 4) via a conjunctival allergen challenge model (allergen administered directly to the eye), the activity of reproxalap in subjects challenged with seasonal allergens was statistically significantly superior to activity in vehicle-treated subjects, as measured by area under the itch score curve from 10 to 60 minutes post-challenge. In addition, responder (two-point improvement from baseline itch score) probability in drug-treated patients was statistically superior to that of vehicle-treated patients for subjects challenged with seasonal allergens (Figure 4). A clear dose response was observed.

Figure 4: Phase 2b Allergic Conjunctivitis Clinical Trial Results



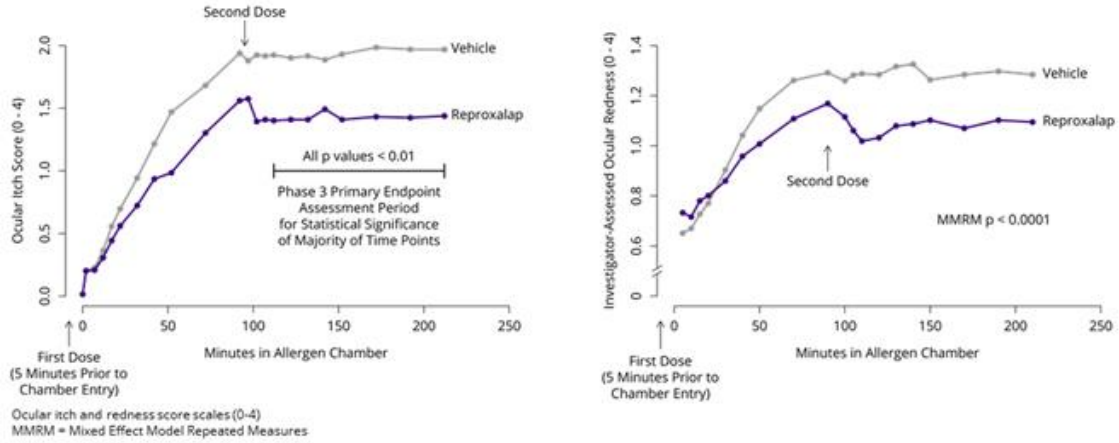
In March 2019, we announced that the Phase 3 ALLEVIATE clinical trial met the primary endpoint and the key secondary endpoint for both concentrations of reproxalap (Figure 5). The double-masked, randomized, vehicle-controlled, multi-center, parallel-group conjunctival allergen challenge Phase 3 ALLEVIATE trial assessed the efficacy and safety of 0.25% and 0.5% concentrations of reproxalap topical ophthalmic solutions compared to vehicle in 318 patients (approximately 100 per arm) with seasonal AC. The primary efficacy endpoint was the evaluation of ocular itch score (0 to 4 scale) area under the curve from 10 to 60 minutes after allergen challenge, and the key secondary endpoint was two-point responder rate, a measure of clinical relevance. Relative to patients treated with vehicle, patients treated with 0.25% and 0.5% reproxalap demonstrated statistically significant reduction in ocular itching ($p < 0.0001$ and $p = 0.0025$, respectively), as assessed by area under the ocular itch score curve. Two-point responder rates for 0.25% and 0.5% reproxalap were statistically greater than that of vehicle-treated patients ($p = 0.0005$ and $p = 0.0169$, respectively), confirming the clinical relevance of the observed primary endpoint improvements. Both concentrations of reproxalap exhibited an anti-inflammatory profile that is distinct from standard-of-care antihistamine therapy and support a differentiated mechanism of action for the treatment of AC.

Figure 5: Phase 3 ALLEVIATE Allergic Conjunctivitis Clinical Trial Results (0.25% Reproxalap)



In October 2019, we announced expanded results from our allergen chamber clinical methods trial of topical ocular reproxalap in patients with AC. The double-masked, randomized, vehicle-controlled, crossover allergen chamber clinical methods trial assessed the efficacy and safety of 0.25% and 0.5% concentrations of reproxalap topical ophthalmic solution compared with vehicle in 70 patients with ocular allergy to ragweed. Patient-reported ocular itching and tearing, and investigator-assessed ocular redness, were recorded at various intervals over approximately 3.5 hours during aerosolized exposure to a standardized amount of ragweed pollen. Test article was administered before chamber entry and at 90 minutes post-entry, near the peak of allergy symptoms and signs. Relative to patients treated with vehicle, patients treated with 0.25% or 0.5% reproxalap demonstrated statistically significant reduction in ocular itching ($p<0.0001$), redness ($p<0.0001$), and tearing ($p<0.0001$). The total ocular symptom score, a combination of itching, redness, and tearing, was also significantly lower in reproxalap-treated subjects than in vehicle-treated subjects ($p<0.0001$ for both concentrations) (Figure 6). Consistent with the positive results from the Phase 3 ALLEVIATE trial in AC, there was no statistical difference between the activity of 0.25% and 0.5% reproxalap. Consistent with prior clinical experience with topical ocular reproxalap in over 1,100 patients across 13 clinical trials, there were no observed safety or tolerability concerns, and the most common treatment-emergent adverse event was transient instillation site irritation.

Figure 6: Allergen Chamber Clinical Methods Allergic Conjunctivitis Trial Results (0.25% Reproxalap)



In 2020, based on the success of the Phase 3 ALLEVIATE trial and the allergen chamber clinical trial, we initiated the Phase 3 INVIGORATE trial of topical ocular reproxalap for the treatment of AC. The Phase 3 INVIGORATE trial will evaluate 0.25% reproxalap versus vehicle in an allergen chamber. The primary endpoint will be achieved if statistically significant reduction in ocular itching between drug and vehicle is demonstrated at the majority of eleven time points in a pre-specified range from 110 to 210 minutes following chamber entry. In the completed allergen chamber trial, reproxalap was statistically superior to vehicle at every time point to be pre-specified in the INVIGORATE trial.

Proliferative Vitreoretinopathy

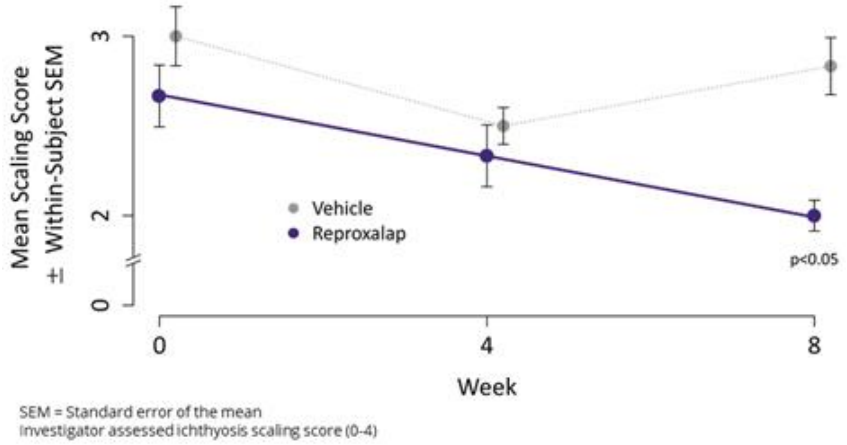
Standard of care treatment for proliferative vitreoretinopathy ("PVR") results in subsequent retinal detachment surgical rates that approximate 50%. In a single-arm, open-label, investigator-sponsored Phase 1b clinical trial performed at the Massachusetts Eye and Ear Infirmary, approximately 20% of patients with PVR treated with multiple injections of ADX-2191 required subsequent surgery for retinal detachment. Thus, relative to standard of care, ADX-2191 may reduce incidence of retinal detachment following the development of PVR, thereby increasing the probability of preservation of visual function.

In December 2019, we initiated the Phase 3 GUARD trial, a two-part, multi-center, randomized, controlled, adaptive Phase 3 clinical trial evaluating the efficacy of intravitreal injections of ADX-2191 versus standard-of-care for the prevention of PVR. GUARD will compare recurrent retinal detachment rates over a 24-week period following surgical repair of retinal detachment due to PVR or open globe injury. In September 2019, the FDA granted fast track designation to ADX-2191 for the prevention of PVR. ADX-2191 has also received orphan drug designation from the FDA for the prevention of PVR.

Sjögren-Larsson Syndrome

In August 2016, we announced that the results of a randomized, parallel-group, double-blind, vehicle-controlled clinical trial of a dermatologic formulation of 1% reproxalap for the treatment of the skin manifestations of Sjögren-Larsson Syndrome ("SLS") demonstrated clinically relevant activity of reproxalap in diminishing the severity of ichthyosis, a serious dermatologic disease characteristic of SLS. Twelve SLS patients with moderate to severe ichthyosis were randomized equally to receive reproxalap 1% dermatologic formulation or vehicle formulation administered once daily on a 4 x 10 inch area of skin for two months. Ichthyosis was graded by a blinded central review of digital photographs, as well as by clinical exam, using the Ichthyosis Severity Score, which is comprised of assessments of global impression, scaling, erythema (redness), lichenification (thickness) and excoriation (abrasion). As assessed by central review, five of six subjects (83%) treated with reproxalap achieved a rating of "almost clear" or "mild" on global assessment. Six of six (100%) subjects treated with reproxalap improved over the course of therapy as assessed by central review, and the improvement was statistically significantly greater than that observed with vehicle-treated patients. For reproxalap-treated subjects, mean reductions in ichthyosis severity were greater after eight weeks of therapy than after four weeks of therapy, suggesting a disease modifying effect of reproxalap (Figure 7). Topical dermal reproxalap was observed to be generally well tolerated, and there were no significant adverse events, serious adverse events, or discontinuations in the trial.

Figure 7: Sjögren-Larsson Syndrome Phase 2 Clinical Trial Results – Investigator Assessment of Ichthyosis



In August 2019, we announced the completion of Part 1 of the Phase 3 RESET trial, a two-part adaptive, randomized, multi-center, double-masked Phase 3 clinical trial of 1% topical dermal reproxalap for the treatment of ichthyosis, a severe skin disease associated with SLS. In Part 1 of the RESET trial, investigator-assessed dermal scaling scores in the six patients treated with 1% reproxalap topical dermatologic formulation were statistically lower than pre-treatment values over six months of therapy, an improvement that was numerically greater than that observed in the three patients treated with vehicle, when adjusted for baseline score. As a result of the strategic prioritization of late-stage ophthalmology programs announced in March 2020, further development in SLS was placed on hold.

Chaperome-Dependent Cancers

An open-label, multicenter, international, European-based, parallel-group, randomized investigator-sponsored Phase 2 clinical trial of ADX-1612 in combination with other chemotherapies in patients with ovarian cancer, carcinosarcoma, or fallopian tube or primary peritoneal cancer was initiated in November 2018. Approximately 120 patients are expected to be randomized equally to one of three treatment arms: carboplatin in combination with paclitaxel or gemcitabine followed by niraparib; ADX-1612 in combination with carboplatin followed by niraparib; or ADX-1612 in combination with carboplatin followed by niraparib plus ADX-1612.

In addition, in September 2018, we announced positive results from the MESO-2 investigator-sponsored Phase 1/2 clinical trial of ADX-1612 in patients with pleural malignant mesothelioma. ADX-1612, when combined with standard pemetrexed and platinum therapy, resulted in partial response rates that exceeded historical standard of care. Twenty-seven patients with pleural malignant mesothelioma were enrolled at a single site in the United Kingdom, and were divided into one of three cohorts receiving 100, 150, or 200 mg/m_2 of ADX-1612 on days 1 and 15 every 21 days. Of 23 evaluable patients, 22 patients (96%) manifested stable disease or clinical response, and one patient (4%) with non-epithelial histology progressed, as measured by via RECIST (Response Evaluation Criteria in Solid Tumors) criteria. The overall response rate was 61%, relative to historical standard of care response rates of 20% to 40%. The response rate in patients with epithelial histology was 76%. In seven patients, reduction of tumor burden was greater than 50%. One patient remained progression-free after 37 months. ADX-1612 was observed to be well-tolerated, and dose-limiting toxicity was observed in three patients, all of whom were enrolled in the highest dose group.

The Science Supporting Our Product Candidates

Reactive Aldehyde Species

In response to infection, injury, endogenous and exogenous chemical triggers, heat, and other stimuli, pro-inflammatory reactive aldehyde species ("RASP") are generated through a variety of metabolic processes, including alcohol oxidation, enzymatic and non-enzymatic lipid oxidation, and sphingosine metabolism. RASP appear to effect inflammation signaling via covalent binding to thiol (sulfur-containing) and amine (nitrogen-containing) residues on proteins, including receptors and enzymes. RASP-protein adducts directly influence the function of proteins, leading to activation of intracellular inflammatory factors, including NF-κB, an important mediator in the inflammatory response. In addition, RASP adducts bind to Scavenger Receptor A, which also initiates pro-inflammatory signaling and leads to the formation of antibodies against the adducted protein, at least in part explaining the presence of host-directed antibodies in autoimmune diseases such as rheumatoid arthritis. Levels of RASP are generally observed to be elevated in ocular and systemic inflammatory disease, and thus represent therapeutic targets for immune-modulation.

Because of the inherent toxicity of RASP, most, if not all, living organisms contain enzymes, such as aldehyde reductases and aldehyde dehydrogenases, that convert RASP into non-toxic molecules. Genetic mutations in the RASP-metabolizing enzymes cause disease. In SLS, mutations in fatty aldehyde dehydrogenase are responsible for skin, neurological, and retinal disease. In particular, ichthyosis, the severe skin disease associated with SLS, is thought to be due to RASP binding to epidermal fats that prevent moisture loss, leading to thick, scaly, dry, flaking, wrinkled, pigmented, pruritic (itchy), inflamed skin.

Aside from the stimulation of inflammation, there is no generally accepted biological role of high levels of RASP. Some physiologic molecules have RASP forms, including retinaldehyde (a form of Vitamin A) and pyridoxal and pyridoxal phosphate (forms of Vitamin B6), but the activity of physiological RASP is highly restricted by chaperone and other proteins that prevent reaction with other molecules, including our RASP inhibitors. Thus, pharmacotherapeutic RASP inhibition is expected not to adversely affect normal physiologic processes. Consistent with the lack of accessibility of physiologic RASP, our most advanced RASP inhibitor, reproxalap, which has been administered to over 450 patients across seven completed clinical trials, has been observed to be generally well tolerated and has not resulted in any serious adverse events.

The RASP Inhibitor Platform

We are currently developing reproxalap, a new chemical entity, and other novel RASP inhibitors for the treatment of immune-mediated disease. Reproxalap is a small molecule designed specifically to bind, and thereby allow for the degradation of, RASP. In *in vitro* and animal studies, reproxalap does not appear to affect most cellular components, including most receptors, enzymes, ion channels, or other proteins. Reproxalap has been shown to outcompete cellular constituents to covalently bind and trap RASP. Reproxalap-RASP adducts appear to be rapidly degraded in cellular environments, after which neither reproxalap nor RASP are detectable. Outside of biological systems, reproxalap-RASP adducts have shown to be remarkably non-reactive and stable, suggesting that reproxalap-RASP binding may be effectively irreversible. By forming covalent drug-RASP adducts that are then degraded, reproxalap and other RASP inhibitors have the potential to substantially lower RASP levels.

We believe we have been the first to demonstrate the beneficial effects of RASP inhibition in a variety of animal models relating to immune-mediated disease, suggesting that reproxalap and analogs may have potent anti-inflammatory effects that persist hours after administration at a variety of different doses relevant to clinical testing.

- In mouse models of ocular inflammation and post-surgical healing, topically applied reproxalap ophthalmic solution reduced ocular redness and inflammatory cytokines comparable to corticosteroid therapy and slowed the development of corneal haze (fibrosis). (Data presented at the Association for Research in Vision and Ophthalmology 2015 Annual Meeting)
- In mice injected with a pro-inflammatory agent known as endotoxin, intraperitoneally administered reproxalap statistically reduced a variety of inflammatory cytokines (protein inflammatory mediators), including IL-5, Il-1ß, IL-17, and TNF-α, while up-regulating the primary anti-inflammatory cytokine, IL-10. Additionally, in models of mouse contact dermatitis (induced by phorbol myristate acetate) and

allergic contact dermatitis (induced by sensitivity to oxazolone), reproxalap statistically reduced inflammation as measured by edema (swelling). (Data presented at the American Academy of Asthma Allergy and Immunology 2015 Annual Meeting)

- In a model of radiation mucositis (oral inflammation) in hamsters, chronic subcutaneous administration of reproxalap reduced healing time and decreased fibrosis (scarring). (Data presented at the Multinational Association of Supportive Care in Cancer – International Society of Oral Oncology 2015 Annual Meeting)
- In two different mouse models of inflammatory pain, intraperitoneally administered reproxalap dose-dependently reduced nociceptive behavior, suggesting that reproxalap down-regulates pain signaling in inflammation. (Data presented at the 2016 International Conference on Pain Research and Management)
- In rat cardiomyocyte culture, reproxalap prevented fibrotic transformation, and inhibited NF-κB activation and IL-1ß release. (Data presented at the 2016 American Society for Cell Biology Annual Meeting)
- In a mouse model of lung inflammation, intraperitoneal administration of reproxalap reduced infiltration of inflammatory cells and levels of pro-inflammatory cytokines in the lung. (Data presented at the 2017 World Congress on Inflammation Annual Meeting)
- In a rat model of intraocular inflammation, a single intravitreal injection of ADX-103 reduced the development of retinal pathology. (Data presented at the Association for Research in Vision and Ophthalmology 2018 Annual Meeting)
- In a rat model of diabetic macular edema, intravitreal injection of ADX-103 reduced retinal inflammatory cell infiltration. (Data presented at the Association for Research in Vision and Ophthalmology 2018 Annual Meeting)

Thus, we believe that the immune-modulating mechanism of action of RASP inhibition is potentially multifactorial – lowering inflammation, reducing healing time, diminishing scarring, and mitigating inflammatory pain – and may ameliorate inflammatory disease and deter disease progression in different ways simultaneously.

In addition to the development of reproxalap, we intend to continue the discovery and development of other novel RASP inhibitors, and we intend to continue to develop intellectual property around such molecules. We have identified, synthesized, and tested numerous molecules that may be more potent than reproxalap in inhibiting RASP. We are currently screening novel product candidates to address diseases where topical and systemic administration may reduce RASP-mediated pathology. We have nominated two new RASP inhibitors, ADX-103 and ADX-629, for clinical development. Development of ADX-103 for the treatment of inflammatory retinal disease may begin in 2021, depending on additional preclinical data, regulatory discussions, funding, and other factors. Development of ADX-629 for the treatment of autoimmune and other inflammatory diseases began in late 2019.

The Potential of ADX- 2191 to Prevent Proliferative Vitreoretinopathy

Proliferative vitreoretinopathy (“PVR”) is characterized by excessive replication and pro-inflammatory activity of retinal cells, at least a portion of which synthesize collagen, the principal component of scar tissue. Retinal scarring can lead to impairment of vision, including blindness. Methotrexate, the active component of ADX-2191 (intravitreal methotrexate), is a dihydrofolate reductase inhibitor, which has been used to treat cancer and autoimmune disease. The anti-proliferative and anti-inflammatory properties of dihydrofolate reductase inhibition are well described. In preclinical studies of primary cell cultures from PVR patients, dihydrofolate reductase inhibition reduced pathological cell proliferation and scar-like collagen deposition. Thus, the observed clinical activity of ADX-2191 in PVR is believed to be the result of down-regulation of aberrant retinal cell proliferation and activity, thereby leading to reduced retinal scarring.

The Immune Modulating and Anti-Proliferative Activity of Chaperome Inhibition

ADX-1612 is a novel, highly potent small molecule protein chaperome (“CHP”) inhibitor that has completed numerous clinical trials in oncologic diseases. The CHP system is involved in the processing of proteins that are

critical for physiologic cellular function. Inhibition of Hsp90 and potentially other members of the CHP system leads to diminished cellular replication. ADX-1612 appears to be reasonably well tolerated at doses that have been used in clinical testing.

CHP is elevated in autoimmune disease, and is believed to lead to broad activation of the immune system. Preclinical results have shown the potential of ADX-1612 to diminish inflammatory cytokines, immune cell numbers, autoantibody formation, and lymphadenopathy (pathologic swelling of the lymph glands, in part due to immune cell hyper-proliferation). In addition, ADX-1612 appears to preserve organ function in animal models of autoimmune disease. The immune-modulating potential of ADX-1612 was observed clinically in a patient treated for Chronic Myelocytic Leukemia, in whom resolution of vasculitis (a systemic autoimmune disease) occurred during treatment.

ADX-1612 in combination with DNA-damaging agents, may have utility in the treatment of certain cancers. CHP is required for DNA repair, and CHP inhibition in the setting of DNA damage could lead to cancer cell death. In ovarian cancer cell lines, preclinical studies have demonstrated the anti-proliferative synergy of ADX-1612 in combination with platinum-containing DNA damaging agents.

Intellectual Property and Proprietary Rights

Overview

In the United States and abroad, we are building an intellectual property portfolio for reproxalap and other RASP inhibitors, CHP inhibitors, and the therapeutic methods of use of DHFR inhibition. We currently seek, and intend to continue to seek, patent protection in the United States and internationally for our product candidates, methods of use, and processes for manufacture, and for other technologies, where appropriate. Our current policy is to actively seek to protect our proprietary position by, among other things, filing patent applications in the United States and abroad relating to proprietary technologies that are important to the development of our business. We also rely on, and will continue to rely on, trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our technology.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for the technologies that we consider important to our business, our ability to defend our patents, and our ability to preserve the confidentiality of our trade secrets and operate our business without infringing the patents and proprietary rights of third parties.

Patent Portfolio

Our patent portfolio currently includes patents and patent applications covering the composition, formulation, and uses of reproxalap, ADX-103, ADX-629, ADX-1612, and other novel compounds. As of December 31, 2019, we owned eleven United States patents and eight pending United States non-provisional patent applications, as well as numerous foreign counterparts to these patents and patent applications, relating to reproxalap, ADX-103, and ADX-629. Additionally, we have in-licensed certain patents and patent applications relating to ADX-1612, and retain an exclusive license to certain patents related to the use of ADX-2191 for the prevention of proliferative vitreoretinal disease.

We expect the issued reproxalap composition of matter patent in the United States, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2028. It is possible that the term of the composition of matter patent in the United States may be extended up to five additional years under the provisions of the Hatch-Waxman Act. We expect the foreign reproxalap composition of matter patents, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire in 2026. We expect other patent applications in the portfolio, if issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, to expire from 2026 to 2034. Reproxalap composition of matter patents have been issued in Australia, Canada, China, Europe (validated in approximately 14 member countries), Hong Kong, India, Japan, Mexico, Russia and South Korea. Reproxalap composition of matter patent claims are pending in Brazil.

Licenses and Agreements

Madrigal Agreement

We are developing ADX-1612 pursuant to a License Agreement with Madrigal Pharmaceuticals, Inc. (“Madrigal”), entered into on December 26, 2016 (the “Madrigal Agreement”). Pursuant to the Madrigal Agreement, we obtained an exclusive, worldwide license from Madrigal under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize CHP inhibitors, including ADX-1612 and other molecules (“Madrigal Agreement Products”). We have agreed to use our commercially reasonable efforts to develop Madrigal Agreement Products.

In consideration for the rights licensed under the Madrigal Agreement, we paid Madrigal an upfront license fee of $250,000 and are obligated to make future regulatory and development and sales-dependent milestone payments to Madrigal of less than $340 million in the aggregate (over 80% of such amount being tied to our achievement of increasingly greater annual worldwide net sales milestones), as well as royalty payments to Madrigal at a rate which, as a percentage of net sales, is in the high single digits for products containing ADX-1612 and mid-single digits for any other CHP inhibitor product. We are also obligated under the Madrigal Agreement to pay Madrigal a percentage of certain sublicense revenue that we receive in connection with entering into any sublicensing arrangements with any third parties, at a percentage rate which tiers downward from the mid-twenties to low-single digits based on the development stage of the product at the time of the sublicense.

The Madrigal Agreement will remain in effect until all payment obligations under the Madrigal Agreement expire. We may terminate the Madrigal Agreement in its entirety or on a Madrigal Agreement Product-by-Madrigal Agreement Product basis with timely notice to Madrigal. Either party may terminate the Madrigal Agreement for uncured material breach by the other party or upon certain insolvency or bankruptcy proceedings involving the other party, both with timely notice to the other party. In addition, Madrigal has the right to terminate the Madrigal Agreement if we, our affiliates, or sublicensees interfere with, challenge the validity or enforceability of, oppose the extension of, or grant of a supplementary protection certificate with respect to any of our licensed patents under the Madrigal Agreement. In the event of an early termination of the Madrigal Agreement, all rights licensed and developed by us under the Madrigal Agreement may revert back to Madrigal. Each party has agreed to indemnify the other party for certain third party claims arising under the Madrigal Agreement.

MEEI Agreement

We are developing ADX-2191 pursuant to an Exclusive License Agreement with Massachusetts Eye and Ear Infirmary ("MEEI") originally entered into in July 2016 between MEEI and Helio Vision, Inc. (as amended, the "MEEI Agreement"). We assumed the MEEI Agreement in connection with our 2019 acquisition of Helio Vision.

Pursuant and subject to the MEEI Agreement, we obtained an exclusive, worldwide license from MEEI to develop and commercialize ADX-2191 under certain patents and patent applications, and other licenses to intellectual property (the "MEEI Patent Rights"). We have agreed to use our commercially reasonable efforts to develop ADX-2191 and to meet certain specified effort and achievement benchmarks by certain dates.

In consideration for the rights licensed under the MEEI Agreement, Helio Vision issued MEEI a number of shares of its preferred stock and Helio Vision agreed to pay non-creditable non-refundable license maintenance fees to MEEI of $15,000 on each of the second and third anniversary of the MEEI Agreement, $25,000 on each of the fourth and fifth anniversary of the MEEI Agreement and $35,000 on the sixth and each subsequent anniversary of the MEEI Agreement during the term of such agreement. In addition, Helio Vision was obligated to make future sales-dependent milestone payments to MEEI of up to the low seven figures in the aggregate, as well as royalty payments to MEEI at a rate which, as a percentage of net sales, is in the low single digits for products that incorporate or use the MEEI Patent Rights in the United States and as a percentage in the low single digits for products that incorporate or use the MEEI Patent Rights outside the United States. We are also obligated under the MEEI Agreement to pay MEEI a percentage of certain sublicense revenue that we receive in connection with entering into any sublicensing arrangements with any third parties, at a percentage rate which tiers downward from low-double digits to mid-single digits based on the date of the sublicense. Following our acquisition of Helio Vision, we became obligated to make any future payments owed under the MEEI Agreement. There is no additional equity consideration issuable under the MEEI Agreement.

The MEEI Agreement will remain in effect until the expiration date of the last to expire patent licensed under the MEEI Agreement. We may terminate the MEEI Agreement with timely written notice to MEEI. MEEI has the right to terminate the MEEI Agreement if we, subject to certain specified cure periods, cease all business operations with respect to licensed products, fail to pay amounts due under the MEEI Agreement, fail to comply with certain due diligence obligations, default in our obligation to maintain insurance, one of our officers is convicted of a felony relating to the manufacture, use, sale or importation of licensed products, we materially breach any provisions of the MEEI Agreement or in the event of our insolvency or bankruptcy.

In the event of an early termination of the MEEI Agreement, all rights licensed and developed by us under the MEEI Agreement may revert back to MEEI. We have agreed to indemnify MEEI for certain claims that may arise under the MEEI Agreement.

Other Intellectual Property Rights

Our marks ALDEYRA THERAPEUTICS and our logo are registered with the United States Patent and Trademark Office.

Confidential Information and Inventions Assignment Agreements

We currently require and will continue to require each of our employees and consultants to execute confidentiality agreements upon the commencement of such individual's employment, consulting or collaborative relationships with us. These agreements provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions resulting from such individual's work performed for us, utilizing our property or relating to our business and conceived or completed by the individual during employment shall be our exclusive property to the extent permitted by applicable law. Our consulting agreements also provide for assignment to us of any intellectual property resulting from services performed by a consultant for us.

Manufacturing

We do not own or operate manufacturing facilities for the production of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently depend on third-party contract manufacturers for all of our required raw materials, drug substance and finished drug product for our preclinical research and clinical trials. We have no immediate plans to purchase, erect, or otherwise create any manufacturing facilities to be owned by us for any of these purposes, and intend to continue to depend on third-party contract manufacturers for the foreseeable future. We do not have any current contractual relationships for the manufacture of commercial supplies of our product candidates. If our product candidates are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production at such time. We may utilize third-party consultants to manage our manufacturing contractors. We believe that the active pharmaceutical ingredient and other materials needed for the formulation of our product candidates are relatively easy to manufacture, and that multiple suppliers and formulators could be employed for this purpose. Further, we believe the raw materials needed for manufacture of our product candidates, as well as other components of our formulations, are generally readily available currently from multiple sources.

Employees

As of December 31, 2019, we had 20 full-time employees and had engaged a number of consultants. We expect that a number of consultants previously engaged in development of our product candidates will participate in ongoing clinical and manufacturing activities. None of our employees is represented by a labor union. We have not experienced any work stoppages, and we consider our relations with our employees to be good.

Government Regulation

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Food Drug and Cosmetic Act ("FDCA") and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

FDA approval is required before any new drug, such as a new chemical entity, or a new dosage form, new use or new route of administration of a previously approved product, can be marketed in the United States. The process required by the FDA before a new drug product may be marketed in the United States generally involves:

- completion of preclinical laboratory and animal testing and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulation;
- submission to the FDA of an Investigational New Drug application ("IND") for human clinical testing which must become effective before human clinical trials may begin in the United States;
- approval by an independent institutional review board ("IRB") at each site where a clinical trial will be performed before the trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with current good clinical practices ("cGCP") to establish the safety and efficacy of the proposed product candidate for each intended use;
- submission to the FDA of a new drug application ("NDA") which must be accepted for filing by the FDA;
- satisfactory completion of an FDA pre-approval inspection(s) of the facility or facilities at which the product is manufactured to assess compliance with the FDA's current Good Manufacturing Practices ("cGMP") regulations;

- satisfactory completion of an FDA advisory committee review, if applicable;
- payment of user fees, if applicable; and
- FDA review and approval of the NDA.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources. Preclinical tests include laboratory evaluation of product chemistry, formulation, manufacturing and control procedures and stability, as well as animal studies to assess the toxicity and other safety characteristics of the product. The results of preclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Preclinical testing may continue even after the IND is submitted. The IND becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions and places the clinical trial on a partial or complete clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Even if the IND becomes effective and the trial proceeds without initial FDA objection, the FDA may stop the trial at a later time if it has concerns, such as if the potential for unacceptable safety risks arise.

Further, an independent IRB, covering each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and informed consent information for subjects before the trial commences at that site and it must monitor the study until completed. The FDA, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk or for failure to comply with the FDA's or IRB's requirements. Other conditions may also be imposed.

Clinical trials involve the administration of the investigational new product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Sponsors of clinical trials generally must register and report, at the NIH-maintained website ClinicalTrials.gov, key parameters of certain clinical trials. For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- *Phase 1:* The investigational drug product is initially introduced into healthy human subjects or patients and tested for safety, dose tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness.
- *Phase 2:* The investigational drug product is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive clinical trials.
- *Phase 3:* These are commonly referred to as pivotal studies. When Phase 2 evaluations suggest that certain dosing regimens may be efficacious and may have an acceptable safety profile, trials may be undertaken in larger patient populations to further evaluate dosage and to obtain evidence of potential clinical efficacy and safety. These studies may include multiple, geographically-dispersed clinical trial sites. Data generated from these studies may be used to establish the overall risk-benefit profile of the investigational drug product and to provide adequate information for the labeling of the product, if approved.
- *Phase 4:* In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor's commitment to conduct additional clinical trials to further assess the product's safety and/or effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase 4 studies.

The results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, chemistry, manufacturing and controls and proposed labeling, among other things.

For some products, the FDA may require a risk evaluation and mitigation strategy ("REMS") which could include measures imposed by the FDA such as prescribing restrictions, requirements for post-marketing studies and reporting or certain restrictions on distribution and use. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to prescription drug program fees. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information and is subject to payment of additional user fees. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission has been accepted for filing, the FDA begins an in-depth substantive review. Under the Prescription Drug User Fee Act ("PDUFA"), the FDA agrees to specific performance goals for NDA review time through a two-tiered classification system, Standard Review and Priority Review. Standard Review NDAs have a goal of being completed within a ten-month timeframe after acceptance of filing. A Priority Review designation is given to products that offer major advances in treatment or provide a treatment where no adequate therapy exists. The goal for completing a Priority Review is six months after acceptance of filing.

It is likely that our product candidates will be granted a Standard Review. The review process may be extended by the FDA for three additional months to consider certain information or obtain clarification regarding information already provided in the submission. The FDA may refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making decisions. In addition, for combination products, the FDA's review may include the participation of both the FDA's Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the FDA's Center for Devices and Radiological Health. This has the potential to complicate or prolong review of the application.

Before approving an NDA, the FDA may inspect the facility or facilities where the drug substance or drug product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP. FDA may also inspect sponsor facilities to determine if nonclinical and clinical studies were conducted in compliance with applicable regulations and guidelines.

After the FDA evaluates the NDA and, in some cases, the related manufacturing facilities, it may issue an approval letter or a Complete Response Letter ("CRL") to indicate that the review cycle for an application is complete and that the application is not ready for approval. CRLs generally outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when the deficiencies have been addressed to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications.

Once issued, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if potential adverse safety findings are identified after the product reaches the market. In addition, the FDA may require post-approval testing, including Phase 4 studies, and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Products may be promoted only for the approved labeled indications and in accordance with the provisions of the approved label, and, even if the FDA approves a product, it may limit the approved indications for use for the product or impose other conditions, including labeling or distribution restrictions or other risk-management mechanisms, such as a Black Box Warning, which highlights a specific warning. Further, if there are any modifications to the product, including changes in indications, labeling, or manufacturing processes or facilities, a company would be required to submit and obtain FDA approval of a new or supplemental NDA, which may require the company to develop additional data or conduct additional preclinical studies and clinical trials.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to product/facility listing, recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved 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. Changes to the manufacturing process are strictly regulated and may require prior FDA approval before being implemented. FDA regulations may also require investigation and correction of any deviations from cGMP and may impose reporting and documentation requirements upon us and any third-party manufacturers. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated seriousness, severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in, 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 pending applications or supplements to approved applications, or suspension or revocation of product license 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. The FDA does not regulate the practice of medicine. Physicians may prescribe for off-label uses; manufacturers may only promote for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability, both at the federal and state levels.

The Food and Drug Administration Amendments Act of 2007 gave the FDA the authority to require a Risk Evaluation and Mitigation Strategy, or REMS, from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks. In determining whether a REMS is necessary, FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. If the FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other measures that the FDA deems necessary to assure the safe use of the drug. In addition, the REMS must include a timetable to assess the strategy at 18 months, three years, and seven years after the strategy's approval. The FDA may also impose a REMS requirement on a drug already on the market if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits outweigh its risks.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition which is defined as one affecting fewer than 200,000 individuals in the United States or more than 200,000 individuals where there is no reasonable expectation that the product development cost will be recovered from product sales in the United States. Orphan drug designation must be requested before submitting an NDA and does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Reproxalap has received orphan designation for the treatment of congenital ichthyosis, and ADX-2191 has received orphan designation for the prevention of proliferative vitreoretinopathy.

If an orphan drug-designated product subsequently receives the first FDA approval for the disease for which it was studied, the sponsor will be entitled to seven years of product marketing exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited and rare circumstances, for seven years. If a competitor obtains approval of the same drug, as defined by the FDA, or if our product candidate is determined to be contained within the competitor's product for the same indication or disease, the competitor's exclusivity could block the approval of our product candidate in the designated orphan indication for seven years, unless superior safety or efficacy of our drug is demonstrated.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drug candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for extension must be made prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA) or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Manufacturing Requirements

We and our third-party manufacturers must comply with applicable FDA regulations relating to FDA's cGMP regulations and, if applicable, quality system regulation requirements for medical devices. The cGMP regulations

include requirements relating to, among other things, organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of the FDA and may be subject to a pre-approval inspection before we can use them to manufacture our products. We and our third-party manufacturers are also subject to periodic unannounced inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including, among other things, warning letters, voluntary corrective action, the seizure of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties.

Other Regulatory Requirements

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA has broad regulatory and enforcement powers, including, among other things, the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals, any one or more of which could have an adverse effect on our ability to operate our business and generate revenues. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, operating results and financial condition. There are evolving legal requirements and other statutory and regulatory regimes that will continue to affect our business.

Research and Development Expenses

Substantially all of our research and development expenses incurred to date have been related to the development of reproxalap and our other product candidates. Our research and development expenses totaled $44.4 million for the year ended December 31, 2019 and $29.8 million for the year ended December 31, 2018.

We anticipate that we will incur additional research and development expenses in the future as we evaluate and possibly pursue the development of our product candidates for additional indications, or develop additional product candidates.

We recognize research and development expenses as they are incurred. Our research and development expenses consist primarily of:

- salaries and related expenses for personnel;
- fees paid to consultants and contract research organizations in conjunction with independently monitoring clinical trials and acquiring and evaluating data in conjunction with clinical trials, including all related fees such as investigator grants, patient screening, lab work and data compilation and statistical analysis;
- costs incurred with third parties related to the establishment of a commercially viable manufacturing process for our product candidates;
- costs related to production of clinical materials, including fees paid to contract manufacturers;
- costs related to upfront, milestone payments under in-licensing agreements as well as costs for unapproved inventory for which there is no future alternative use;
- costs related to compliance with FDA regulatory requirements;
- consulting fees paid to third-parties involved in research and development activities; and
- costs related to stock options or other stock-based compensation granted to personnel in development functions.

We expense both internal and external development costs as they are incurred.

We expect that a large percentage of our research and development expenses in the future will be incurred in support of our current and future non-clinical, preclinical and clinical development programs. These expenditures are subject to numerous uncertainties in terms of both their timing and total cost to completion. We expect to continue to develop stable formulations of our product candidates, test such formulations in preclinical studies for toxicology, safety and efficacy and to conduct clinical trials for each product candidate. We anticipate funding clinical trials for our product candidates ourselves, but we may engage collaboration partners at certain stages of clinical development. As we obtain results from clinical trials, we may elect to discontinue or delay clinical trials for certain product candidates or programs in order to focus our resources on more promising product candidates or programs. Completion of clinical trials by us or our future collaborators may take several years or more, the length of time generally varying with the type, complexity, novelty and intended use of a product candidate. The costs of clinical trials may vary significantly over the life of a project owing to but not limited to the following:

- the number of sites included in the trials;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- the duration of patient follow-up;
- the phase of development the product candidate is in; and
- the efficacy and safety profile of the product candidate.

Our expenses related to clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation and vary from contract to contract and may result in uneven payment flows. Generally, these agreements set forth the scope of work to be performed at a fixed fee or unit price. Payments under the contracts depend on factors such as the successful enrollment of patients or the completion of clinical trial milestones. Expenses related to clinical trials generally are accrued based on contracted amounts applied to the level of patient enrollment and activity according to the protocol. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis.

None of our product candidates have received FDA or foreign regulatory marketing approval. In order to grant marketing approval, a health authority such as the FDA or foreign regulatory agencies must conclude that clinical and preclinical data establish the safety and efficacy of our product candidates with an appropriate benefit to risk profile relevant to a particular indication, and that the product can be manufactured under cGMP in a reproducible manner to deliver the product’s intended performance in terms of its stability, quality, purity and potency. Until our submission is reviewed by a health authority, there is no way to predict the outcome of their review. Even if the clinical studies meet their predetermined primary endpoints, and a registration dossier is accepted for filing, a health authority could still determine that an appropriate benefit to risk relationship does not exist for the indication that we are seeking.

We cannot forecast with any degree of certainty which of our product candidates will be subject to future collaborations or how such arrangements would affect our development plan or capital requirements.

As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our development projects or when and to what extent we will receive cash inflows from the commercialization and sale of an approved product candidate.

Corporate Information

We were incorporated in the state of Delaware on August 13, 2004 as Neuron Systems, Inc. On December 20, 2012, we changed our name to Aldexa Therapeutics, Inc. and on March 17, 2014, we changed our name to Aldeyra Therapeutics, Inc. Our principal executive offices are located at 131 Hartwell Avenue, Suite 320, Lexington, Massachusetts 02421. Our telephone number is (781) 761-4904. Our website address is www.aldeyra.com. Information contained on our website is not incorporated by reference into this annual report on Form 10-K, and you should not consider information contained on our website to be part of this annual report on Form 10-K or in deciding whether to purchase shares of our common stock. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge on the Investors portion of our website at http://ir.aldeyra.com/ as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

ITEM 1A.*RISK FACTORS*

Our business is subject to numerous risks. You should carefully consider the risks described below together with the other information set forth in this annual report on Form 10-K, which could materially affect our business, financial condition, and future results. The risks described below are not the only risks facing our company. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, prospects, financial condition, and operating results.

Risks Related to our Business, Financial Position and Capital Requirements

We have incurred significant operating losses since inception and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

We have incurred significant operating losses since we were founded in 2004 and expect to incur significant losses for the next several years as we continue our clinical trial and development programs for reproxalap and our other product candidates. Net loss for the year ended December 31, 2019 and 2018 was approximately $60.8 million and $38.9 million, respectively. As of December 31, 2019, we had total stockholders' equity of $48.1 million and an accumulated deficit of $199.4 million. Losses have resulted principally from costs incurred in our clinical trials, research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities, and, if reproxalap or any of our other product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in our incurring further significant losses for the next several years.

We currently generate no revenue from sales, and we may never be able to commercialize reproxalap or our other product candidates. We do not currently have the required approvals to market any of our product candidates and we may never receive them. We may not be profitable even if we or any of our future development partners succeed in obtaining regulatory approval and commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

Our business is dependent in large part on the success of a single product candidate, reproxalap, for which we are researching multiple indications. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, reproxalap.

Our product candidates, including reproxalap, will require additional preclinical studies, substantial clinical development and testing, and regulatory approval prior to commercialization. We have not yet completed development of any product candidate. We have only one product candidate that has been the focus of significant clinical development: reproxalap, a novel small molecule chemical entity that is believed inhibit RASP, toxic chemical species suspected to cause and exacerbate numerous diseases in humans and animals. We are in part dependent on successful continued development and ultimate regulatory approval of reproxalap for our future business success. Any negative results or perceived negative results in clinical trials for one indication may have an adverse effect on our ability to develop and potentially commercialize reproxalap for the treatment of another indication. We have invested, and will continue to invest, a significant portion of our time and financial resources in the development of reproxalap. We will need to raise sufficient funds for, and successfully enroll and complete, our current and planned clinical trials of reproxalap and our other product candidates. The future regulatory and commercial success of our product candidates is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to pursue our business plans and complete necessary clinical trials;
- we may not be able to provide sufficient evidence of safety and efficacy to continue a development program or obtain regulatory approval;

- the results of our clinical trials may not meet the endpoints, or level of statistical or clinical significance required by the FDA, or comparable foreign regulatory bodies, for marketing approval;
- the safety and efficacy results of our later phase or larger clinical trials may not confirm the results of our earlier trials;
- patients in our clinical trials may demonstrate greater response rates or improvements from vehicle or in the non-treatment arm then was expected when designing and powering our clinical trials;
- there may be variability in patients, adjustments to clinical trial procedures and inclusion of additional clinical trial sites;
- the initial parts of adaptive clinical trials are not designed to be pivotal or definitive, as such we may not satisfy the designated endpoints and also may need to revise the design or endpoints to achieve success in later parts of the trial or potentially abandon the trial;
- we may not be able to timely or adequately finalize the design or formulation of any product candidate or demonstrate that a formulation of our product candidate will be stable for commercially reasonable time periods;
- the FDA, or comparable foreign regulatory bodies, may implement new standards, or change the interpretation of existing standards or requirements for the regulatory approval, in general or with respect to the indications our product candidates are being developed to treat; the FDA, or comparable foreign bodies, may require clinical data in addition to the clinical trial programs we expect or may require changes to the designs and endpoints of the subsequent clinical trials;
- patients in clinical trials for our product candidates may suffer adverse effects or die for reasons that may or may not be related to our product candidates;
- if approved for certain diseases, our product candidates will compete with well-established and other products or therapeutic options already approved for marketing by the FDA, or comparable foreign regulatory bodies;
- we may be adversely affected by legislative or regulatory reform of the health care system in the United States or other jurisdictions in which we may do business; and
- we may not be able to obtain, maintain, or enforce our patents and other intellectual property rights.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a NDA to the FDA, and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market reproxalap and our other product candidates, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure that reproxalap and our other product candidates will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain regulatory approval for or, if approved, successfully commercialize, reproxalap and our other product candidates, we may not be able to generate sufficient revenue to continue our business.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our clinical trial and development programs;
- addition or termination of clinical trials or development programs;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting reproxalap and our other product candidates;

- our establishment of a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- our execution of any collaborative, licensing, or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- the number of administrative, clinical, regulatory and scientific personnel we engage;
- nature and terms of stock-based compensation grants; and

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

We will require substantial additional financing, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or commercialization efforts.

The development and commercialization of biopharmaceutical products is capital intensive. We are advancing reproxalap and our other product candidates through pre-clinical and clinical development, including our multiple ongoing and planned clinical trials for our product candidates. We expect our expenses to increase in connection with our ongoing activities as we continue the research and development of, and, if successful, seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to manufacturing, product sales, marketing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed on attractive terms, if at all, we will be forced to delay, reduce or eliminate certain of our clinical development plans, research and development programs or future commercialization efforts.

The development process for our product candidates is highly uncertain, and we cannot estimate with certainty the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of our product candidates. Our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than expected, through public or private equity, debt financings or other sources. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the type, number, scope, progress, expansion costs, results of, and timing of our planned clinical trials of reproxalap or any our other product candidates that we are pursuing or may choose to pursue in the future;
- the need for, and the progress, costs, and results of, any additional clinical trials of reproxalap and our other product candidates we may initiate based on the results of our planned clinical trials or discussions with the FDA, including any additional trials the FDA or other regulatory agencies may require evaluating the safety of reproxalap and our other product candidates;
- the costs of obtaining, maintaining, and enforcing our patents and other intellectual property rights;
- the costs and timing of obtaining or maintaining manufacturing for reproxalap and our other product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales and marketing capabilities and enhanced internal controls over financial reporting;
- the terms and timing of establishing collaborations, license agreements, and other partnerships on terms favorable to us;

- costs associated with any other product candidates that we may develop, in-license, or acquire, including potential milestone or royalty payments;
- the effect of competing technological and market developments;
- our ability to establish and maintain partnering arrangements for development; and
- the costs associated with being a public company.

Some of these factors are outside of our control. Our existing capital resources are not sufficient to enable us to fund the completion of our clinical trials and remaining development through commercial introduction. We expect that we will need to raise substantial additional funds in the near future.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through collaboration agreements and public or private financings, including debt financings. The state of the global economy and market instability has made the business climate volatile and more costly. Uncertain economic conditions, uncertainty as to the general direction of the macroeconomic environment and the price of our common stock, are beyond our control and may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Additional funding may not be available to us on acceptable terms, or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders or be excessively dilutive. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we will be unable to complete the planned clinical trials for reproxalap and our other product candidates and we may be required to significantly curtail, delay or discontinue one or more of our pre-clinical studies, clinical trials or other research or development programs, or the commercialization of any product candidate. We may also be unable to expand our operations or otherwise capitalize on our business opportunities, may need to restructure our organization, or may be required to relinquish rights to our candidates or other technologies, or otherwise agree to terms unfavorable to us. Any of these occurrences could materially affect our business, financial condition and results of operations.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and marketing and distribution arrangements. 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 its 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, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or 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 its product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market on our own.

We may allocate our cash and cash equivalents in ways that you and other stockholders may not approve.

Our management has broad discretion in the application of our cash and cash equivalents. Because of the number and variability of factors that will determine our use of our cash and cash equivalents, management's ultimate use of cash and cash equivalents may vary substantially from the currently intended use. Our management might not apply our cash and cash equivalents in ways that ultimately increase the value of your investment. We

expect to use our cash and cash equivalents to: fund our planned clinical trials of reproxalap and our other product candidates, develop other molecules that relate to immune-mediated disease, service our debt obligations, and provide working capital and capital for other general corporate purposes. The failure by our management to apply these funds effectively could harm our business. We may invest our cash and cash equivalents in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply our cash and cash equivalents in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

The United Kingdom's withdrawal from the European Union could result in increased regulatory and legal complexity, which may make it more difficult to for us to do business in Europe and impose additional challenges in securing regulatory approval of our product candidates in Europe.

The United Kingdom's exit from the European Union, or Brexit, and the related negotiations have caused political and economic uncertainty, including in the regulatory framework applicable to our operations and vaccine candidates in the United Kingdom and the European Union, and this uncertainty may persist for years. Brexit could, among other outcomes, disrupt the free movement of goods, services and people between the United Kingdom and the EU, and result in increased legal and regulatory complexities, as well as potential higher costs of conducting business in Europe. For instance, preparations for Brexit have resulted in the decision to move the European Medicines Agency from the United Kingdom to the Netherlands. This transition may cause disruption or delays in granting clinical trial authorization or opinions for marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supple chain for clinical trial product and final authorized formulations.

The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the European Union and/or the United Kingdom. It is possible that there will be increased regulatory complexities, which can disrupt the timing of our clinical trials and regulatory approvals. In addition, changes in, and legal uncertainty with regard to, national and international laws and regulations may present difficulties for our clinical and regulatory strategy. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenues and achieve and sustain profitability.

In addition, as a result of Brexit, other European countries may seek to conduct referenda with respect to their continuing membership with the European Union. Given these possibilities and others we may not anticipate, as well as the absence of comparable precedent, it is unclear what financial, regulatory and legal implications the withdrawal of the United Kingdom from the European Union will have and how such withdrawal will affect us, and the full extent to which our business could be adversely affected.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical

activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

The terms of our secured debt facility require us to meet certain operating covenants and place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

In March 2019, we entered into a credit facility with Hercules Capital that is secured by a lien covering all of our assets, other than our intellectual property. The loan agreement contains customary affirmative and negative covenants and events of default. Affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, and maintain insurance coverage. Negative covenants include, among others: restrictions on transferring any part of our business or intellectual property; incurring additional indebtedness; engaging in mergers or acquisitions; paying dividends or making other distributions; making investments; and creating other liens on our assets, in each case subject to customary exceptions. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility. These restrictions may include, among other things, limitations on borrowing and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem capital stock, or make investments. If we default under the terms of the Hercules Credit Facility or any future debt facility, the lender may accelerate all of our repayment obligations and take control of our pledged assets, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, the lender's right to repayment would be senior to the rights of the holders of our common stock. The lender could declare a default upon the occurrence of any event that they interpret as a material adverse effect as defined under the loan agreement. Any declaration by the lender of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

Our ability to use net operating loss carryforwards and tax credit carryforwards to offset future taxable income may be limited as a result of transactions involving our common stock.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses ("NOLs") and certain other tax assets ("tax attributes") to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period (generally three years). Transactions involving our common stock within the testing period, even those outside our control, such as purchases or sales by investors, could result in an ownership change. A limitation on our ability to utilize some or all of our NOLs or credits could have a material adverse effect on our results of operations and cash flows. Prior to December 31, 2018, we underwent three ownership changes and it is possible that additional ownership changes have occurred since. However, management believes that we have sufficient "Built-In-Gain" to offset any Section 382 limitation generated by such ownership changes. Any future ownership changes, including those resulting from our recent or future financing activities, may cause our existing tax attributes to have additional limitations. However, subject to annual limitations, NOLs generated in years 2018 and beyond will have an indefinite carryforward period and will not expire. Future changes in federal and state tax laws pertaining to NOLs carryforwards may also cause limitations or restrictions from us claiming such NOLs. If the NOLs carryforwards become unavailable to us or are fully utilized, our future taxable income will not be shielded from federal and state income taxation absent certain U.S. federal and state tax credits, and the funds otherwise available for general corporate purposes would be reduced.

Risks Related to the Development and Commercialization of our Product Candidates

Reproxalap and our other product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays, or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing, and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive and time-consuming, and can vary substantially based upon the type, complexity, and novelty of the products involved, as well as the target indication, and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit, or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval, and subsequent commercial success is uncertain and not guaranteed.

Reproxalap and our other product candidates, and the activities associated with development and potential commercialization, including testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other jurisdictions.

Our ongoing research and development activities and planned clinical development for our product candidates may be delayed, modified, or ceased for a variety of reasons, including:

- determining that a product candidate is ineffective or potentially causes harmful side effects during preclinical studies or clinical trials;
- difficulty establishing predictive preclinical models for demonstration of safety and efficacy of a product candidate in one or more potential therapeutic areas for clinical development;
- patients in our clinical trials may demonstrate greater response rates or improvements from vehicle or standard of care than was expected when designing and powering our clinical trials, such as was observed in the SOLACE Trial;
- lack of availability of, or difficulty recruiting, a sufficient number of patients to adequately power our clinical trials;

- difficulties in manufacturing a product candidate, including the inability to manufacture a product candidate in a sufficient quantity, suitable form, or in a cost-effective manner, or under processes acceptable to the FDA for marketing approval;
- the proprietary rights of third parties, which may preclude us from developing or commercializing a product candidate;
- determining that a product candidate may be uneconomical for us to develop or commercialize, or may fail to achieve market acceptance or adequate pricing or reimbursement;
- our expectations regarding our expenses and revenue, the sufficiency or use of our cash resources and needs for additional financing;
- our inability to secure strategic partners which may be necessary for advancement of a product candidate into clinical development or commercialization; or
- our prioritization of other indications or product candidates for advancement.

The FDA or comparable foreign regulatory authorities can delay, limit, or deny approval of a product candidate for many reasons, including but not limited to:

- such authorities may disagree with the design or implementation of our or any of our future development partners' clinical trials, including the endpoints of our clinical trials; such authorities may require clinical data in addition to clinical trial programs we expect, or may require changes to the designs and endpoints of subsequent clinical trials;
- we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;
- such authorities may not accept clinical data from trials if conducted at clinical facilities or in countries where the standard of care is potentially different from the United States;
- the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;
- we or any of our future development partners may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials or the design of such trials;
- changes in the leadership or operation of such authorities, which may result in, among other things, the implementation of new standards, or changes to the interpretation or enforcement of existing regulatory standards and requirements;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we or any of our future development partners contract for clinical and commercial supplies; or
- the approval policies, standards or regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the aforementioned risks, can involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates. Moreover, we cannot predict healthcare reform initiatives, including potential reductions in federal funding or insurance coverage, that may be adopted in the future and whether or not any such reforms would have an adverse effect on our business and

our ability to obtain regulatory approval for our current or future product candidates. There are evolving legal requirements and other statutory and regulatory regimes that will continue to affect our business.

Because the Company has no experience in commercializing pharmaceutical products, there is a limited amount of information about us upon which to evaluate our product candidates and business prospects.

We have not yet demonstrated an ability to successfully overcome many of the pre-commercial and commercial risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan we will need to successfully:

- execute our product candidate development activities, including successfully designing and completing our clinical trial programs and product design and formulation of future product candidates, in a cost- effective manner;
- file for and obtain required regulatory approvals for our product candidates;
- manage our spending as costs and expenses increase due to the performance and completion of clinical trials, attempting to obtain regulatory approvals, manufacturing and commercialization;
- secure substantial additional funding;
- develop and maintain successful strategic relationships;
- build and maintain a strong intellectual property portfolio;
- build and maintain appropriate clinical, regulatory, quality, manufacturing, compliance, sales, distribution, and marketing capabilities on our own or through third parties;
- implement and maintain operational, financial and management systems;
- price our product candidates, if approved, at expected levels and obtain and maintain sufficient insurance and reimbursement from insurers and other programs; and
- gain broad market acceptance for our product candidates.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop product candidates, raise capital, expand our business, or continue our operations. Further, even if we are successful in clinical trials of product candidates, we may choose to place further development or commercialization on hold given perceived marketing challenges or the relative differences in commercial attractiveness within our portfolio.

The results of preclinical studies and earlier clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials, including reproxalap, may not have favorable results in later clinical trials, if any, or receive regulatory approval.

Drug development has inherent risk. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Drug development is a long, expensive, and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials. In addition, as product candidates proceed through development, the trial designs may often be different and may need to evolve and change from phase to phase or within the same phase or same trial, in the case of an adaptive trial design; the vehicles or controls may be modified from trial to trial; and the product formulations or manufacturing process may differ due to the need to test product candidate samples that can be manufactured on a commercial scale. Success in earlier clinical trials or clinical trials focused on a different indication does not mean that later clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through other phases of clinical testing. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. For instance, in June 2019, we discontinued our noninfectious anterior uveitis program following the announcement of results from the SOLACE Trial. Moreover, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

Because we are developing novel product candidates for the treatment of diseases in a manner which there is little clinical drug development experience and, in some cases, are designing adaptive trials or using new endpoints or methodologies, the regulatory pathways for approval are not well defined, and, as a result, there is greater risk that our clinical trials will not result in our desired outcomes or require additional trials.

Our clinical focus is on the development of new products for inflammation and an inborn error of metabolism. Our Phase 3 vehicle-controlled clinical program in noninfectious anterior uveitis and our Phase 3 clinical program in SLS represent the first such clinical trials performed. In June 2019, we announced that statistical significance was not achieved for the primary or secondary endpoints in our SOLACE Trial in noninfectious anterior uveitis, due to high rates of disease resolution in vehicle-treated patients. We are performing adaptive trials in dry eye disease (“RENEW”) and proliferative vitreoretinopathy (“GUARD”), and may do so with other indications in the future. In an adaptive trial, the initial parts of the trial are not designed to be pivotal or definitive. Rather, the initial parts of adaptive trials are expected to provide data to guide subsequent parts of the trial, which could require design changes, including but not limited to, different endpoints. In addition, following the initial parts of adaptive trials, we may, among other things, determine to continue to the subsequent parts of the trial, conclude the trial based on its success or failure in such initial parts, or to discuss the trial results and regulatory pathway with regulatory authorities prior to determining next steps with respect to the trail and development program. For example, in August 2019, we announced that statistically significant improvement from baseline was observed in Part 1 of the Phase 3 RESET trial in SLS. However, due to the novel nature of reproxalap, the limited population of SLS patients, and the uncertain regulatory pathway in SLS, in connection with the strategic prioritization of late-stage ophthalmology programs announced in March 2020, further development in SLS was placed on hold. As such, the likelihood of success in our late-stage clinical programs cannot necessarily be predicted.

We could also face challenges in designing clinical trials and obtaining regulatory approval of our product candidates due to the lack of historical clinical trial experience for novel classes of therapeutics. Thus, it is difficult to determine whether regulatory agencies will be receptive to the approval of our product candidates, and to predict the time and costs associated with obtaining regulatory approvals. The clinical trial requirements of the FDA and other regulatory agencies and the criteria regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and require more time and trial data than for other, better known or more extensively studied classes of product candidates. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain regulatory approvals for our product candidates, would have an adverse impact on our business, prospects, financial condition, and results of operations.

To preserve trial integrity, clinical data from the initial parts of adaptive clinical trials may not be disclosed.

Adaptive clinical trials are often performed such that the initial parts of the trial are used to determine sample size and endpoints for subsequent, possibly pivotal parts of the trial. Results from the initial parts of adaptive trials are therefore not designed to be pivotal or definitive, and, in some cases, detailed trial data may not be disclosed so as not to positively or negatively bias investigators or patients involved in subsequent parts of the trial.

We are performing adaptive trials in dry eye disease ("RENEW") and proliferative vitreoretinopathy ("GUARD"). For the reasons stated above, detailed results from RENEW Part 1 have not, and from the initial part of GUARD may not, be disclosed until the completion of subsequent parts of the trials, or until the entire adaptive trial has completed. Further, the initial parts of adaptive trials may be performed in part to assess biomarkers or surrogate markers that may require substantial time to generate, analyze, and interpret. Thus, disclosure of clinical results from the initial parts of adaptive trials may also be delayed due to the time required for biomarker or surrogate marker assessment.

Because some of our product candidates are, to our knowledge, new chemical entities, it is difficult to predict the time and cost of development and our ability to successfully complete clinical development of these product candidates and obtain the necessary regulatory approvals for commercialization.

Some of our product candidates are, to our knowledge, new chemical entities, and unexpected problems related to new technologies may arise that can cause us to delay, suspend, or terminate our development efforts. As a result, short and long-term safety, as well as prospects for efficacy, are not fully understood and are difficult to predict. Regulatory approvals of new product candidates can be more expensive and take longer than approvals for well-characterized or more extensively studied pharmaceutical product candidates. Following discussions with the FDA and experts in the field, we may determine that it is not cost effective for us to develop one or more of our product in certain indications and we may decide to cease development in that area or seek a strategic partner.

Any termination or suspension of, or delays in the commencement or completion of, our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Delays in the commencement or completion of our planned clinical trials for reproxalap or other product candidates could significantly affect our product development costs and timeline. We do not know whether future trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA, or an institutional review board, or IRB, failing to grant permission to proceed or placing a clinical trial on hold;
- subjects failing to enroll or remain in our clinical trials at the rate we expect;
- subjects choosing an alternative treatment for the indication for which we are developing reproxalap or other product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe, serious, or unexpected drug-related adverse effects, whether drug-related or otherwise;
- a facility manufacturing reproxalap, any of our other product candidates or any of their components being ordered by the FDA or other government or regulatory authorities, to temporarily or permanently shut down due to violations of current Good Manufacturing Practices, or cGMP, or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- inability to timely manufacture sufficient quantities of the applicable product candidate for a clinical trial or expiration of materials intended for use in a clinical trial;

- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, current Good Clinical Practice or regulatory requirements, or other third parties not performing data collection or analysis in a timely or accurate manner;
- inspections of clinical trial sites by the FDA or the finding of regulatory violations by the FDA or IRB, that require us or others to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold in part or on the entire trial, or that prohibit us from using some or all of the data in support of our marketing applications;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial.

Product development costs will increase if we have delays in testing or approval of reproxalap or our other product candidates or if we need to perform more, larger, or longer clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur and we or our partners may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing, or successful completion of a clinical trial. If we experience delays in completion of, or if we, the FDA, or other regulatory authorities, the IRB, other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials, the commercial prospects for a product candidate may be harmed and our ability to generate product revenues, if any, will be delayed. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of reproxalap or other product candidates could be significantly reduced.

The novel coronavirus outbreak that began in China may affect our ability to recruit or retain patients for our clinical trials, disrupt our supply chains or have other adverse effects on our business and operations.

In December 2019, an outbreak of respiratory illness began in Wuhan, China. As of March 2020, that outbreak has led to thousands of confirmed cases worldwide, with many countries throughout the world confirming cases. The World Health Organization has declared the outbreak a global public health emergency. In addition to those who have been directly affected, millions more have been affected by government efforts around the world to slow the spread of the outbreak through quarantines, travel restrictions, heightened border scrutiny and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; the capital markets and the economy in general has been volatile; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the outbreak and its effects on our business and operations are uncertain. We may face difficulties recruiting or retaining patients in our ongoing and planned clinical trials if patients are affected by the virus or are fearful of traveling to our clinical trial sites because of the outbreak. We and our third-party contract manufacturers, contract research organizations and clinical sites may also face disruptions in procuring items that are essential for our research and development activities, including, for example, medical and laboratory supplies used in our clinical trials or preclinical studies, in each case, that are sourced from abroad or for which there are shortages because of ongoing efforts to address the outbreak.

We may find it difficult to enroll patients in our clinical trials or identify patients during commercialization (if our products are approved by regulatory agencies) for product candidates addressing orphan or rare diseases.

As part of our business strategy, we have and continue to evaluate the development and commercialization of product candidates for the treatment of orphan and other rare diseases, including PVR. We may not be able to

initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients willing and able to participate in the clinical trials required by the FDA or other non-United States regulatory agencies. In addition, if others develop products for the treatment of similar diseases, we would potentially compete with them for the enrollment in rare patient populations, which may adversely impact the rate of patient enrollment in and the timely completion of our current and planned clinical trials. Any negative results or perceived negative results in clinical trials of our product candidates may make it difficult or impossible to recruit or retain patients in other clinical trials of the same product candidate. Insufficient patient enrollment may be a function of other factors, including the size and nature of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the timing and magnitude of disease symptom presentation, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial. Our inability to identify and enroll a sufficient number of eligible patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials or development program. Delays in patient enrollment in the future as a result of these and other factors may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent us from completing these trials and adversely affect our ability to advance the development of our product candidates. For instance, in rare diseases such as PVR and SLS, lack of availability of, or difficulty recruiting a sufficient number of, patients may make it difficult or cost-prohibitive to sufficiently power our clinical trials, which may not enable us to continue development and seek regulatory approval for the applicable product candidate. Further, if our products are approved by regulatory agencies, we may not be able to identify sufficient number of patients to generate significant revenues.

Any product candidate we or any of our future development partners advance into clinical trials may cause unacceptable adverse events or have other properties that may delay or prevent its regulatory approval or commercialization or limit its commercial potential.

Unacceptable adverse events caused by any of our product candidates that we or others advance into clinical trials could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications and markets. This in turn could prevent us from completing development or commercializing the affected product candidate and generating revenue from its sale.

We have not yet completed testing of any of our product candidates in humans for the treatment of the indications for which we intend to seek approval, and we currently do not know the full extent of adverse events that will be observed in subjects that receive any of our product candidates. If any of our product candidates cause unacceptable adverse events in clinical trials, which may be larger or longer than those previously conducted, we may not be able to obtain regulatory approval or commercialize such product candidate.

Final marketing approval for reproxalap or our other product candidates by the FDA or other regulatory authorities may be delayed, limited, or denied, any of which would adversely affect our ability to generate operating revenues.

After the completion of our clinical trials, assuming the results of the trials are successful, and the submission of an NDA, we cannot predict whether or when we will obtain regulatory approval to commercialize reproxalap or our other product candidates and we cannot, therefore, predict the timing of any future revenue. We cannot commercialize reproxalap or our other product candidates until the appropriate regulatory authorities have reviewed and approved the applicable applications. We cannot assure you that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for reproxalap or our other product candidates. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials, and FDA regulatory review. If marketing approval for reproxalap or our other product candidates is delayed, limited or denied, our ability to market the product candidate, and our ability to generate product sales, would be adversely affected.

Even if we obtain marketing approval for reproxalap or any other product candidate, it could be subject to restrictions 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 are approved.

Even if United States regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance, or other potential additional clinical trials. Following approval, if any, of reproxalap or any other product candidate, such candidate will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping, and reporting of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements, including those relating to quality control, quality assurance, and corresponding maintenance of records and documents. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated seriousness, severity, or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for reproxalap or any other product candidate that may receive regulatory approval, if any, fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements or applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of product, or request us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue.

The FDA has the authority to require a risk evaluation and mitigation strategy ("REMS") plan as part of a NDA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria, and requiring treated patients to enroll in a registry.

In addition, if reproxalap or any of our other product candidates is approved, our product labeling, advertising, and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Even if we receive regulatory approval for reproxalap or any other product candidate, we still may not be able to successfully commercialize, and the revenue that we generate from its sales, if any, could be limited.

Even if our product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors, and the medical community. Coverage and reimbursement of our product candidates by third-party payors, including government payors, is also generally necessary for commercial success. In addition, we may not be able to price our products at the expected level or at levels that make successful commercialization viable. The pricing of our products will be subject to numerous factors, many of which are outside of our control, including the pricing of similar products. The degree of market acceptance of our product candidates will depend on a number of factors, including but not limited to:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the limitation of our targeted patient populations and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of a new formulations by health care providers and their patients;
- the prevalence, seriousness, and severity of any adverse effects;
- new procedures or methods of treatment that may be more effective in treating conditions for which our products are intended to treat;
- the safety of product candidates seen in a broader patient group, including their use outside the approved indications;
- pricing and cost-effectiveness, including the cost of treatment in relation to alternative treatments;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain and maintain sufficient and timely third-party coverage or reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- relative convenience and ease of administration;
- the prevalence and severity of adverse events;
- the effectiveness of our sales and marketing efforts;

- unfavorable publicity; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

Further, our ability to successfully commercialize ADX-2191, if approved, depends on a number of additional factors, including but not limited to, the level of enforcement by the FDA to ensure that compounded copies of commercially available FDA-approved products manufactured by compounding pharmacies, including compounded copies of ADX-2191, that may be in violation of the federal Drug Quality and Security Act ("DQSA") and other relevant provisions of the United States Federal Food, Drug, and Cosmetic Act, are not produced and dispensed to patients.

Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. Further federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms could have an adverse effect on the pricing of and anticipated revenues from our current or future product candidates for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop drug candidates.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors, or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payors on the benefits of reproxalap or any of our other product candidates may require significant resources and may never be successful. In addition, our ability to successfully commercialize our product candidate will depend on our ability to manufacture our products, differentiate our products from competing products and defend the intellectual property of our products.

Additionally, if any of our competitors' products are approved and are unable to gain market acceptance for any reason, there could be a market perception that products like reproxalap are not able to adequately meet an unmet medical need. If we are unable to demonstrate to physicians, hospitals, third-party payors, and patients that our products are better alternatives, we may not be able to gain market acceptance for our products at the levels we anticipate and our business may be materially harmed as a result.

If the market opportunities for reproxalap and our product candidates are smaller than we believe they are, and if we are not able to successfully identify patients and achieve significant market share, our revenues may be adversely affected and our business may suffer.

We focus our research and product development on treatments for immune-mediated diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower or more difficult to identify than expected. In addition, our product candidates may not achieve commercial success due to market conditions or regulatory challenges.

Any of these factors may negatively affect our ability to generate revenues from sales of our product and our ability to achieve and maintain profitability, and as a consequence, our business may suffer.

Reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate insurance coverage and reimbursement from third-party payors for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. The reimbursement levels may be significantly less than the currently anticipated pricing of our product candidates. As a result of negative trends in the general economy in the United States or other jurisdictions in which we may do business, these organizations may be unable to satisfy their reimbursement

obligations or may delay payment. Reimbursement by a third-party payor may depend upon a number of factors including the third-party payor's determination that use of a product candidate is:

- a covered benefit under its health plan;
- safe, effective, and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product candidate from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical, and cost effectiveness data for the use of the applicable product candidate to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Further, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only in limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved. In recent years, through legislative and regulatory actions, the federal government has made substantial changes to various payment systems under the Medicare program. Comprehensive reforms to the United States healthcare system were recently enacted, including changes to the methods for, and amounts of, Medicare reimbursement. More recently, the current presidential administration and many members of the United States Congress have attempted to repeal and replace the Patient Protection and Affordable Care Act ("PPACA"), but they have been unsuccessful in doing so as of the date of the filing of this report. We cannot predict the ultimate form or timing of any repeal or replacement of PPACA or the effect such repeal or replacement would have on our business. Regardless of the impact of repeal or replacement of PPACA on us, the government has shown significant interest in pursuing healthcare reform and reducing healthcare costs. These reforms could significantly reduce payments from Medicare and Medicaid over the next ten years. Reforms or other changes to these payment systems, including modifications to the conditions on qualification for payment, bundling of payments, or the imposition of enrollment limitations on new providers, may change the availability, methods, and rates of reimbursements from Medicare, private insurers, and other third-party payers for our current and future product candidates, if any, for which we are able to obtain regulatory approval. Some of these changes and proposed changes could result in reduced reimbursement rates for such product candidates, if approved, which would adversely affect our business strategy, operations, and financial results.

As a result of legislative proposals and the trend toward managed health care in the United States, third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also refuse to provide coverage of approved product candidates for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for use of newly approved drugs, which in turn could lower drug pricing. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations, and additional legislative proposals as well as country, regional, or local healthcare budget limitations.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

As part of our growth strategy, we plan to evaluate the development and commercialization of other therapies related to immune-mediated diseases. We will evaluate internal opportunities from our compound libraries, and also may choose to continue to in-license or acquire other product candidates, as well as commercial products, to treat patients suffering from immune-mediated disorders with high unmet medical needs and limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials, and approval by the FDA and/or applicable foreign regulatory authorities. In-licensed product candidates may have been unsuccessfully developed by others in indications similar to those that we may pursue. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be

sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, adequately priced, successfully commercialized, or widely accepted in the marketplace or be more effective than other commercially available alternatives.

Issues with product quality could have a material adverse effect upon our business, subject us to regulatory actions and cause a loss of customer confidence in us or our products.

Our success depends upon the quality of our products. Quality controls, assurance, and management plays an essential role in meeting customer requirements, preventing defects, improving our product candidates and services, and assuring the safety and efficacy of our product candidates. Our future success depends on our ability to maintain and continuously improve our quality management program. A quality or safety issue may result in adverse inspection reports, warning letters, product recalls or seizures, monetary sanctions, injunctions to halt manufacture and distribution of products, civil or criminal sanctions, costly litigation, refusal of a government to grant approvals and licenses, restrictions on operations, or withdrawal of existing approvals and licenses. An inability to address a quality or safety issue in an effective and timely manner may also cause negative publicity, a loss of customer confidence in us or our future products, which may result in difficulty in successfully launching product candidates and the loss of sales, which could have a material adverse effect on our business, financial condition, and results of operations.

Orphan drug designation, breakthrough therapy designation, or fast-track designation from the FDA may be difficult or impossible to obtain, and if we are unable to obtain such designations for reproxalap or our other product candidates, regulatory and commercial prospects may be negatively impacted.

The FDA designates orphan drug designation status to drugs that are intended to treat rare diseases with fewer than 200,000 patients in the United States or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug. Drugs that receive an orphan drug designation do not require prescription drug user fees at the time of marketing application, may qualify the drug development sponsor for certain tax credits, and can be marketed without generic competition for seven years. In April 2018, ADX-2191 received orphan drug designation from the FDA for the prevention of proliferative vitreoretinopathy. In addition, it may be difficult or impossible to obtain from the FDA orphan drug designation or a designation that facilitates and expedites development and review of certain new drugs, including breakthrough therapy designation, fast track designation, or any other expedited status that we may apply for in the future, for reproxalap or our other product candidates. We cannot guarantee that we will be able to receive breakthrough therapy or fast-track designation from the FDA for reproxalap or our other product candidates. If we are unable to secure breakthrough therapy designation or fast-track designation for reproxalap or our other product candidates, our regulatory and commercial prospects may be negatively impacted.

We rely and will continue to rely on outsourcing arrangements for many of our activities, including clinical development and supply of reproxalap and our other product candidates.

As of December 31, 2019, we had only 20 full-time employees and, as a result, we rely, and expect to continue to rely, on outsourcing arrangements for a significant portion of our activities, including clinical research, data collection and analysis, manufacturing, financial reporting and accounting, and human resources, as well as for certain functions required of publicly traded companies. We may have limited control over third parties and we cannot guarantee that any third party will perform its obligations in an effective and timely manner.

In addition, during challenging and uncertain economic environments and in tight credit markets, there may be a disruption or delay in the performance of our third party contractors, suppliers, or partners. If such third parties are unable to satisfy their commitments to us, our business and results of operations would be adversely affected.

We rely on third parties to conduct our clinical trials. If any third party does not meet our deadlines or otherwise conduct the trials as required and in accordance with regulations, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected, or at all.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. We are dependent on third parties to conduct the clinical trials for reproxalap and for our other product candidates and, therefore, the timing of the initiation and completion of these trials is controlled by such third parties and may occur on substantially different timing from our estimates. Specifically, we use Contract Research Organizations ("CRO") to conduct our clinical trials and we also rely on medical institutions, clinical investigators, and consultants to conduct our trials in accordance with our clinical protocols and regulatory requirements. Our CROs, investigators, and other third parties play a significant role in the conduct of these trials and subsequent collection and analysis of data.

There is no guarantee that CROs, investigators, or other third parties on which we rely for administration and conduct of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fails to meet expected deadlines, fails to adhere to our clinical protocols, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed, or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in our ongoing clinical trials unless we are able to transfer those subjects to another qualified clinical trial site. 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.

Some of our product candidates may be studied in clinical trials co-sponsored by organizations or agencies other than us, or in investigator-initiated clinical trials, which means we have minimal or no control over the conduct of such trials.

We currently anticipate that part of our strategy for pursuing the wide range of indications potentially addressed by our product candidates, including ADX-1612, will involve investigator-initiated clinical trials. Investigator-initiated clinical trials pose similar risks as those set forth elsewhere in this "Risk Factor" section relating to our internal clinical trials. While investigator-initiated trials may provide us with clinical data that can inform our future development strategy, we generally have less control over the conduct and design of the trials. Because we are not the sponsors of investigator-initiated trials, we do not control the protocols, administration, or conduct of the trials, including follow-up with patients and ongoing collection of data after treatment. As a result, we are subject to risks associated with the way investigator-initiated trials are conducted. In particular, we may be named in lawsuits that would lead to increased costs associated with legal defense. Additional risks include difficulties or delays in communicating with investigators or administrators, procedural delays and other timing issues, and difficulties or differences in interpreting data. Third-party investigators may design clinical trials with clinical endpoints that are more difficult to achieve, or in other ways that increase the risk of negative clinical trial results compared to clinical trials that we may design on our own. Negative results in investigator-initiated clinical trials could have a material adverse effect on our prospects and the perception of our product candidates. As a result, our lack of control over the conduct and timing of, and communications with the FDA regarding, investigator-sponsored trials expose us to additional risks and uncertainties, many of which are outside our control, and the occurrence of which could adversely affect the commercial prospects for our product candidates.

We rely completely on third parties to supply drug substance and manufacture drug product for our clinical trials and preclinical studies. We intend to rely on other third parties to produce commercial supplies of product candidates, and our dependence on third parties could adversely impact our business.

We are completely dependent on third-party suppliers of the drug substance and drug product for our product candidates. If third-party suppliers do not supply sufficient quantities of materials to us on a timely basis and in accordance with applicable specifications and other regulatory requirements, there could be a significant interruption of our supplies, which would adversely affect clinical development. Furthermore, if any of our contract manufacturers cannot successfully manufacture material that conforms to our specifications within regulatory requirements, we will not be able to secure and/or maintain regulatory approval, if any, for our product candidates.

We also rely on our contract manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our anticipated clinical trials. We do not have any control over the process or timing of the acquisition of raw materials by our contract manufacturers. Moreover, we currently do not have agreements in place for the commercial production of these raw materials. Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial could considerably delay completion of that clinical trial, product candidate testing, and potential regulatory approval of that product candidate.

We do not expect to have the resources or capacity to commercially manufacture any of our proposed product candidates if approved and will likely continue to be dependent on third-party manufacturers. Our dependence on third parties to manufacture and supply clinical trial materials and any approved product candidates may adversely affect our ability to develop and commercialize our product candidates on a timely basis.

We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit supply of our products.

The process of manufacturing our products is complex, highly regulated, and subject to several risks, including:

- The manufacturing of compounds is extremely susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our products or in the manufacturing facilities in which our products are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facilities in which our products are made could be adversely affected by equipment failures, labor shortages, natural disasters, power failures, and numerous other factors.
- We and our contract manufacturers must comply with the FDA's cGMP regulations and guidelines. We and our contract manufacturers may encounter difficulties in achieving quality control and quality assurance, and may experience shortages in qualified personnel. We and our contract manufacturers are subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or any delay, interruption, or other issues that arise in the manufacture, fill-finish, packaging, or storage of our products as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our products, including leading to significant delays in the availability of products for our clinical studies, the termination or hold on a clinical study, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions, and criminal prosecutions, any of which could damage our reputation. If we are

not able to maintain regulatory compliance, we may not be permitted to market our products and/or may be subject to product recalls, seizures, injunctions, or criminal prosecution.

Any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to account for inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

We may not be successful in establishing and maintaining development, commercial, or other strategic partnerships, which could adversely affect our ability to develop and commercialize product candidates.

We have in the past, and may in the future, choose to enter into development or other strategic partnerships, including collaborations with major biotechnology or pharmaceutical companies. We face significant competition in seeking appropriate partners and the negotiation process is time consuming and complex. Moreover, we may not be successful in our efforts to establish other development partnerships or other alternative arrangements for any of our product candidates or programs because our research and development pipeline may be insufficient, our product candidates or programs may be deemed to be at too early a stage of development for collaborative effort, and/or third parties may not view our product candidates or programs as having the requisite commercial or technical potential. Even if we are successful in our efforts to establish development or commercial partnerships, the terms that we agree upon may not be favorable to us and we may not be able to maintain such partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product candidate are below expectations. Any delay in entering into development partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce competitiveness, if approved.

Moreover, if we fail to maintain partnerships related to our product candidates:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development and commercialization of certain of our current or future product candidates would increase significantly and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and
- we will bear all of the risk related to the development and commercialization of any such product candidates.

We may not realize the benefits of our current or future strategic alliances.

We have in the past, and may in the future, form strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including the continued development or commercialization of reproxalap or our other product candidates. Strategic alliances may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for reproxalap or our other product candidates because third parties may view the risk of development failure as too significant or the commercial opportunity for our product candidate as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction.

If our competitors develop treatments for the target indications of our product candidates that are approved more quickly than ours, marketed more successfully, or demonstrated to be safer or more effective than our product candidates, our commercial opportunity will be reduced or eliminated.

We operate in highly competitive segments of the biotechnology market. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions,

government agencies, and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies (including generic and over-the-counter drugs) as well as with new treatments that may be introduced by our competitors. With the exception of SLS and PVR, there are a variety of approved drugs and drug candidates in development for the indications that we intend to test. While there are no drugs currently approved in the United States for the temporary relief of the signs and symptoms of dry eye disease, current treatments that are used in the United States for dry eye disease include over the counter artificial tears, Restasis®, Xiidra®, Cequa TM and off label use of corticosteroids. Generic versions of Restasis® are also expected to become available in the U.S. in the near future. Many of our competitors have significantly greater financial, product candidate development, manufacturing, and marketing resources than we do. Large pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. In addition, universities and private and public research institutes could be in direct competition with us. We also may compete with these organizations to recruit management, scientists, and clinical development personnel. We will also face competition from these third parties in establishing clinical trial sites, registering subjects for clinical trials, and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

New developments, including the development of other pharmaceutical technologies and methods of treating disease, occur in the pharmaceutical and life sciences industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. Other parties may discover and patent treatment approaches and compositions that are similar to or different from ours. Competition in drug development is intense. We anticipate that we will face intense and increasing competition as new treatments enter the market and advanced technologies become available.

Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development, and commercialization of reproxalap or our other product candidates. Inflammatory diseases may be treated with general immune suppressing therapies, including corticosteroids, some of which are generic. Our potential competitors in inflammatory diseases may be developing novel immune modulating therapies that may be safer or more effective than our product candidates.

We may not be successful in executing our sales and marketing strategy for the commercialization of our product candidates. We have no sales, marketing, or distribution capabilities and expect to invest significant financial and management resources to develop these capabilities. If we are unable to establish sales, distribution, and marketing capabilities or enter into agreements with third parties to market, sell, and distribute our product candidates, we may be unable to generate any revenues.

We have no internal sales, marketing, or distribution capabilities. If reproxalap or any of our other product candidates ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We will have to invest significant amounts of financial and management resources to develop internal sales, distribution, and marketing capabilities, some of which will be committed prior to any confirmation that reproxalap or any of our other product candidates will be approved. We may not be able to hire consultants or external service providers to assist us in sales, marketing, and distribution functions on acceptable financial terms or at all. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without a significant internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies. Even if we determine to perform sales, marketing, and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenues generated by reproxalap or any other product candidates that we may develop, in-license, or acquire; and
- our direct sales and marketing efforts may not be successful.

If we are unable to successfully implement our commercialization plans and drive adoption by patients of our approved product candidates, if any, through our sales, marketing, and commercialization efforts, then we will not be able to generate significant revenue, which will have a material adverse effect on our business, results of operations, financial condition, and prospects.

We are highly dependent on the services of our senior management team and certain key consultants.

As a company with a limited number of personnel, we are highly dependent on the development, regulatory, commercial, and financial expertise of our senior management team composed of five individuals and certain other employees: Todd C. Brady, M.D., Ph.D., our President and Chief Executive Officer; Joshua Reed, M.B.A., our Chief Financial Officer; David B. McMullin, M.B.A., our Chief Commercial Officer; James A. Gow, M.D., our Senior Vice President, Clinical Development; and Stephen G. Machatha, Ph.D., our Senior Vice President, Technical Operations. Our current management team has only been working together for a relatively short period of time. Our future performance will depend significantly on our ability to successfully integrate our management team, and on those officers' ability to develop and maintain an effective working relationship. Our failure to integrate these recently hired executive officers with other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates, and our results of operations. In addition, we rely on the services of a number of key consultants, including IP, pharmacokinetic, chemistry, toxicology, and drug development consultants. The loss of such individuals or the services of future members of our management team could delay or prevent the further development and potential commercialization of our product candidates and, if we are not successful in finding suitable replacements, could harm our business.

If we fail to attract and retain senior management and key commercial personnel, we may be unable to successfully develop or commercialize our product candidates.

We will need to expand and effectively manage our managerial, operational, financial, and other resources in order to successfully pursue our clinical development and commercialization efforts. Our success also depends on our continued ability to attract, retain, and motivate highly qualified management and scientific personnel, and we may not be able to do so in the future due to intense competition among biotechnology and pharmaceutical companies, universities, and research organizations for qualified personnel. If we are unable to attract and retain the necessary personnel, we may experience significant impediments to our ability to implement our business strategy.

We expect to expand our management team. Our future performance will depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, adversely affecting future regulatory approvals, sales of our product candidates, and our results of operations.

In order to commercialize our product candidates, we will need to substantially grow the size of our organization. We may encounter difficulties in managing our growth and expanding our operations successfully.

Because, as of December 31, 2019, we only had 20 full-time employees, we will need to grow our organization to continue development and pursue the potential commercialization of reproxalap and our other product candidates, as well as function as a public company. As we seek to advance reproxalap and other product candidates towards potential commercialization, increase the number of ongoing product development programs, and advance our future product candidates through preclinical studies and clinical trials, we will need to expand our financial, development, regulatory, manufacturing, marketing, and sales capabilities, or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers, and other third parties. Future growth will impose significant added responsibilities on members of management and require us to retain additional internal capabilities. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train, and integrate additional management, clinical and regulatory, financial, administrative and sales, and marketing personnel. We may not be able to accomplish these tasks, and our failure to so accomplish could prevent us from successfully growing our company.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain regulatory and marketing approval of and commercialize our product candidates, and may 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 healthcare systems that could prevent or delay marketing approval for our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell our product candidates.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. In addition, increased scrutiny by the United States 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. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of reproxalap or any future product candidates. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance, or interpretations will be changed, or what effect changes in regulations, statutes, legal interpretation, or policies, when and if promulgated, enacted, or adopted may have on our business in the future. Such changes could, among other things, require:

- changes to manufacturing methods;
- additional studies, including clinical studies;
- recall, replacement, or discontinuance of one or more of our products;
- the payment of additional taxes; or
- additional record keeping.

Each of these requirements would likely entail substantial time and cost and could adversely harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory approvals for any future products would harm our business, financial condition, and results of operations. We intend to seek approval to market our product candidates in both the United States and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to such product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In the United States, the Medical Modernization Act of 2003 ("MMA") changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for drugs. In addition, this legislation authorized Medicare Part D prescription drug plans to use formulas where they can limit the number of

drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, we expect that there will be additional pressure to contain and reduce costs. These cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products and could seriously harm our business. 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.

In early 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (together, "PPACA"), 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 healthcare and health insurance industries, impose new taxes and fees on the health industry, and impose additional health policy reforms. Effective October 1, 2010, the PPACA's definition of "average manufacturer price" was revised for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, beginning in 2011, the PPACA imposed a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. The law appears likely to continue the pressure on pharmaceutical pricing, especially under Medicare, and may also increase our regulatory burdens and operating costs.

More recently, the current presidential administration and many members of the United States Congress have attempted to repeal and replace PPACA, but have been unsuccessful in doing so as of the date of the filing of this report. We cannot predict the ultimate form or timing of any repeal or replacement of PPACA or the effect such repeal or replacement would have on our business. Regardless of the impact of repeal or replacement of PPACA on us, the government has shown significant interest in pursuing healthcare reform and reducing healthcare costs.

In addition, a federal court in Texas ruled in December 2018 that the PPACA is unconstitutional. That decision currently is being appealed and may result in an opinion by appellate courts, including potentially the Supreme Court of the United States, on the constitutionality of the PPACA as revised. We cannot predict the ultimate content, timing, or effect of any such reform activities, litigation, or court decisions on our operations. Additionally, the pricing and reimbursement of pharmaceutical products continues to receive significant attention from U.S. policymakers, the Trump Administration, and others. For example, on January 31, 2019, the Department of Health and Human Services issued a proposed rule that removes from existing anti-kickback statute safe harbor protection certain reductions in price paid by pharmaceutical manufacturers to Medicare Part D plan sponsors, Medicaid MCOs, and those entities' pharmacy benefit managers ("PBMs"), and adds two new safe harbors that protect certain point-of-sale price reductions by pharmaceutical manufacturers as well as certain service fee payments from pharmaceutical manufacturer to PBMs. At this time, we cannot predict the impact of this increased scrutiny would have on our business.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures, and may adversely affect our operating results.

The continuing efforts of the government, insurance companies, managed care organizations, and other payors of healthcare services to contain or reduce costs of health care may adversely affect:

- the demand for any product candidates for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our product candidates;
- our ability to generate revenue and achieve or maintain profitability;
- our ability to identify and establish strategic partnerships;
- the level of taxes that we are required to pay; and
- the availability of capital.

If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting laws, we may be subject to civil or criminal penalties.

In addition to FDA restrictions on the marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include false claims statutes and anti-kickback statutes. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce, or in return for, purchasing, leasing, ordering, or arranging for the purchase, lease, or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers, and formula managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing, or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability.

Over the past few years, several pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as: allegedly providing free trips, free goods, sham consulting fees and grants, and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion that caused claims to be submitted to Medicaid for non-covered, off-label uses; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Most states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer’s products from reimbursement under government programs, criminal fines, and imprisonment.

Governments may impose price controls, which may adversely affect our future profitability.

We intend to seek approval to market our product candidates in both the United States and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product candidates. In some foreign countries, particularly in 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 candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

The FDA’s ability to review and approve new products may be hindered by a variety of factors, including budget and funding levels, ability to hire and retain key personnel, and statutory, regulatory, and policy changes.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including budget and funding levels, ability to hire and retain key personnel, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

The ability of the FDA and other government agencies to properly administer their functions is highly dependent on the levels of government funding and the ability to fill key leadership appointments, among various factors. Currently, the FDA is managed by an Acting Commissioner, pending the appointment of a new Commissioner. The confirmation process for a new commissioner may not occur efficiently. Delays in filling or

replacing key positions could significantly impact the ability of the FDA and other agencies to fulfill their functions, and could greatly impact healthcare and the pharmaceutical industry.

In December 2016, the 21st Century Cures Act was signed into law, and was designed to advance medical innovation and empower the FDA with the authority to directly hire positions related to drug and device development and review. In the past, the FDA was often unable to offer key leadership candidates (including scientists) competitive compensation packages as compared to those offered by private industry. The 21st Century Cures Act is designed to streamline the agency's hiring process and enable the FDA to compete for leadership talent by expanding the narrow ranges that are provided in the existing compensation structures.

Disruptions at the FDA and other governmental agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our operating results and business.

U.S. federal income tax reform could adversely affect us.

In December 2017, U.S. federal tax legislation, commonly referred to as the Tax Cuts and Jobs Act ("TCJA"), was signed into law, significantly reforming the Internal Revenue Code of 1986, as amended ("IRC"). The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest, allows for the expensing of capital expenditures, puts into effect the migration from a "worldwide" system of taxation to a territorial system, and modifies or repeals many business deductions and credits.

We continue to examine the impact the TCJA may have on our business. The TCJA is a far-reaching and complex revision to the U.S. federal income tax laws with disparate and, in some cases, countervailing impacts on different categories of taxpayers and industries, and will require subsequent rulemaking and interpretation in a number of areas. The long-term impact of the TCJA on the overall economy, the industries in which we operate, and our and our partners' businesses cannot be reliably predicted at this early stage of the new law's implementation. There can be no assurance that the TCJA will not negatively impact our operating results, financial condition, and future business operations. The estimated impact of the TCJA is based on our management's current knowledge and assumptions, following consultation with our tax advisors. Because of our valuation allowance in the U.S., ongoing tax effects of the Act are not expected to materially change our effective tax rate in future periods. The impact of the TCJA on holders of common stock is uncertain and could be materially adverse. This report does not discuss any such tax legislation or the manner in which it might affect investors in common stock. Investors should consult with their own tax advisors with respect to such legislation and the potential tax consequences of investing in common stock.

New legislation or regulation which could affect our tax burden could be enacted by any governmental authority. We cannot predict the timing or extent of such tax-related developments which could have a negative impact on our financial results. Additionally, we use our best judgment in attempting to quantify and reserve for these tax obligations. However, a challenge by a taxing authority, our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax-related assumptions could have a material adverse effect on our business, results of operations, or financial conditions.

Failure to obtain regulatory approval in foreign jurisdictions would prevent us from marketing our products abroad.

We intend to market our product candidates internationally. In order to market our products in foreign jurisdictions, we will be required to obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and jurisdictions and can involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Additionally, the foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we may not obtain foreign regulatory approvals 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 foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market. The failure to obtain these approvals could harm our business materially.

Our business is subject to political, economic, legal, and social risks in those markets, which could adversely affect our business.

There are significant regulatory, economic and legal barriers in markets in the United States and outside the United States that we must overcome. We may be subject to the burden of complying with a wide variety of national and local laws, including multiple and possibly overlapping and conflicting laws. We also may experience difficulties adapting to new cultures, business customs, and legal systems. Any sales and operations would be subject to political, economic, and social uncertainties including, among others:

- changes and limits in import and export controls;
- increases in custom duties and tariffs;
- changes in currency exchange rates;
- economic and political instability, such as Brexit in the United Kingdom or “trade wars”;
- the impact of public health epidemics on employees, suppliers, customers and the global economy, such as the recent outbreak of a novel strain of coronavirus first identified in Wuhan, China;
- changes in government regulations and laws;
- absence in some jurisdictions of effective laws to protect our intellectual property rights; and
- currency transfer and other restrictions and regulations that may limit our ability to sell certain products or repatriate profits to the United States.

The current presidential administration has expressed antipathy towards existing trade agreements such as the North American Free Trade Agreement, greater restrictions on free trade generally, and significant increases on tariffs on goods imported into the United States, particularly from China and Mexico. Changes in United States social, political, regulatory, and economic conditions or in laws and policies governing foreign trade, manufacturing, development, and investment, and any negative sentiments towards the United States as a result of such changes, could adversely affect our business.

Any changes related to these and other factors could adversely affect any business operations that we conduct outside the United States**.**

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of reproxalap or our other product candidates.

We face an inherent risk of product liability as a result of the clinical testing of reproxalap and our other product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if reproxalap or our other product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing, or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for reproxalap or our other product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to continue to develop or commercialize reproxalap or our other product candidates; and
- a decline in our stock price.

We maintain product liability insurance with $5.0 million in coverage. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of reproxalap or our other product candidates. Although we will maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

We are subject to litigation risks.

From time to time, we may become involved in various litigation matters and claims, including regulatory proceedings, administrative proceedings, governmental investigations, and contract disputes. We may face potential claims or liability for, among other things, breach of contract, defamation, libel, fraud, or negligence. We may also face employment-related litigation, including claims of age discrimination, sexual harassment, gender discrimination, immigration violations, or other local, state, and federal labor law violations. Because of the uncertain nature of litigation and insurance coverage decisions, the outcome of such actions and proceedings cannot be predicted with certainty and an unfavorable resolution of one or more of them could have a material adverse effect on our business, financial condition, results of operations, cash flows, and the trading price of our securities. In addition, legal fees and costs associated with prosecuting and defending litigation matters could have a material adverse effect on our business, financial condition, results of operations, and the trading price of our securities.

We and our development partners, third-party manufacturers, and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage, or disposal of these materials could be time consuming or costly.

We and our development partners, third-party manufacturers, and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our development partner, third-party manufacturers, and suppliers also produce hazardous waste products. Federal, state, and local laws and regulations govern the use, generation, manufacture, storage, handling, and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

We and any of our future development partners will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

If we and any of our future development partners are successful in commercializing our products, the FDA and foreign regulatory authorities will require that we and any of our future development partners report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our future development partners may fail to report adverse events we become aware of within the prescribed timeframe or to perform inadequate investigations of their causes. We and any of our future development partners may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we and any of our future development partners fail to comply with our reporting obligations, the FDA or a foreign regulatory authority could take action including criminal prosecution, the imposition of civil monetary penalties, seizure of our products, or delay in approval or clearance of future products.

Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, product and clinical trial liability, workers' compensation, and directors' and officers' insurance. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant, uninsured liability may require us to pay substantial amounts, which would adversely affect our working capital and results of operations.

If we engage in an acquisition, reorganization, or business combination, we will incur a variety of risks that could adversely affect our business operations or our stockholders.

From time to time, we have entered into, and we will continue to consider in the future, strategic business initiatives intended to further the development of our business. These initiatives may include acquiring businesses, technologies, or products, or entering into a business combination with another company. For example, in January 2019 we acquired Helio Vision, Inc. and obtained the rights to ADX-2191, an intravitreal DHFR inhibitor (methotrexate) for the prevention of proliferative vitreoretinopathy. Any acquisitions we undertake or have recently completed will likely be accompanied by business risks which may include, among other things:

- the effect of the acquisition on our financial and strategic position and reputation;

- the failure of an acquisition to result in expected benefits, which may include benefits relating to new product candidates, human resources, costs savings, operating efficiencies, goodwill, and other synergies;
- the difficulty, cost, and management effort required to integrate the acquired businesses, including costs and delays in implementing common systems and procedures and costs and delays caused by communication difficulties;
- the assumption of certain known or unknown liabilities of the acquired business, including litigation-related liabilities;
- the reduction of our cash available for operations and other uses, the increase in amortization expense related to identifiable assets acquired, potentially dilutive issuances of equity securities, or the incurrence of debt;
- the possibility that we will pay more than the value we derive from the acquisition;
- the impairment of relationships with our partners, consultants, or suppliers, or those of the acquired business; and
- the potential loss of key employees of the acquired business.

These factors could harm our business, results of operations, or financial condition.

In addition to the risks commonly encountered in the acquisition of a business or assets as described above, we may also experience risks relating to the challenges and costs of closing a transaction. The risks described above may be exacerbated as a result of managing multiple acquisitions at once.

Security breaches, loss of data and other disruptions to us or our third-party service providers could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business and our reputation.

In the ordinary course of our business, we and our third-party service providers collect and store sensitive data, including legally protected health information, personally identifiable information about patients, intellectual property, and our proprietary business and financial information. We manage and maintain our applications and data utilizing a combination of on-site systems, managed data center systems and cloud-based data center systems. We face a number of risks related to our protection of, and our service providers' protection of, this critical information, including loss of access, inappropriate disclosure and inappropriate access, as well as risks associated with our ability to identify and audit such events.

The secure processing, storage, maintenance and transmission of this critical information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure may be vulnerable to attacks by hackers or viruses or otherwise breached due to employee error, malfeasance or other activities. While we are not aware of any such attack or breach, if such event would occur and cause interruptions in our operations, our networks would be compromised and the information we store on those networks could be accessed by unauthorized parties, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under federal, state, and international laws that protect the privacy of personal information, such as HIPAA, and regulatory penalties. Unauthorized access, loss or dissemination could also disrupt our ability to conduct our clinical trials, conduct research and development activities, collect, process and prepare company financial information, provide information about our product candidates and other patient and physician education and outreach efforts through our website, manage the administrative aspects of our business and damage our reputation, any of which could adversely affect our business.

In addition, the interpretation and application of consumer, health-related and data protection laws in the United States, Europe and elsewhere are often uncertain, contradictory and in flux. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. If so, this could result in government-

imposed fines or orders requiring that we change our practices, which could adversely affect our business. In addition, we are subject to various state laws, including the California Consumer Privacy Act, or CCPA, which was enacted in California in 2018 and components of which were scheduled to go into effect on January 1, 2020. The CCPA will, among other things, require covered companies to provide disclosures to California consumers concerning the collection and sale of personal information, and will give such consumers the right to opt-out of certain sales of personal information. Amendments to the CCPA have been made since its enactment, and it remains unclear what, if any, further amendments will be made to this legislation or how it will be interpreted. We cannot yet predict the impact of the CCPA on our business or operations, but it may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply.

Recent developments in Europe have created compliance uncertainty regarding the processing of personal data from Europe. For example, the General Data Protection Regulation, or GDPR, which became effective in the E.U. on May 25, 2018, applies to our activities conducted from an establishment in the EU or related to products and services that we offer to E.U. users. The GDPR creates new compliance obligations applicable to our business, which could cause us to change our business practices, and increases financial penalties for noncompliance (including possible fines of up to 4% of global annual turnover for the preceding financial year or €20 million (whichever is higher) for the most serious infringements). As a result, we may need to modify the way we treat such information.

Our internal computer systems, or those of our development partners, third-party clinical research organizations, or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants, and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. While to our knowledge we have not experienced any such material system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed.

We rely on email and other messaging services in connection with our operations. We may be targeted by parties using fraudulent spoofing and phishing emails to misappropriate passwords, payment information, or other personal information, or to introduce viruses through Trojan horse programs or otherwise through our networks, computers, smartphones, tablets, or other devices. Despite our efforts to mitigate the effectiveness of such malicious email campaigns through a variety of control and non-electronic checks, spoofing and phishing may damage our business and increase our costs. Any of these events or circumstances could materially adversely affect our business, financial condition, and operating results.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition, and increase our costs and expenses. We rely on third-party manufacturers to produce reproxalap and our other product candidates. Our ability to obtain clinical supplies of reproxalap or our other product candidates could be disrupted, if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Our employees or others may engage in misconduct or other improper activities, including noncompliance with regulatory standards, regulatory requirements, and insider trading.

We are exposed to the risk of employee and non-employee, fraud or other misconduct. Misconduct by employees, consultants, or agents could include intentional failures to comply with FDA regulations, provide accurate information to regulatory authorities, comply with manufacturing standards we have established, comply with federal and state health care fraud and abuse laws and regulations, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Our current and former employees, consultants or sub-contractors may also become subject to allegations of sexual harassment, racial and gender discrimination, or other similar misconduct, which, regardless of the ultimate outcome, may result in adverse publicity that could significantly harm our company's brand, reputation and operations. Employee misconduct could also involve improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

In addition, during the course of our operations, our directors, executives, employees, consultants, and other third parties may have access to material, nonpublic information regarding our business, our results of operations, or potential transactions we are considering. We may not be able to prevent trading in our common stock on the basis of, or while having access to, material, nonpublic information. If any such person was to be investigated or an action were to be brought against them for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

Risks Relating to Our Intellectual Property

Our success depends on our and our licensors ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies, and the use of our product candidates or proprietary technologies as well as our ability to operate without infringing upon the proprietary rights of others. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around, or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to these product candidates could have a material adverse effect on our financial condition and results of operations.

Composition-of-matter patents on the active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. While we have issued composition-of-matter patents in the United States and other countries for reproxalap and other product candidates, we cannot be certain that the claims in our patent applications covering composition-of-matter of early stage candidates will be considered patentable by the United States Patent and Trademark Office ("USPTO") and courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute. In addition, there are possibly treatment compositions and methods that we have not conceived of or attempted to patent, and other parties may discover and patent approaches and compositions that are similar to or different from ours.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential product candidates;
- there may be significant pressure on the United States government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop, and market competing product candidates.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants, and advisors, third parties may still obtain this information or may come upon this or similar information independently. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of our trade secrets or proprietary know-how may be greatly reduced.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of reproxalap or our other product candidates. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases, and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could likely:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing reproxalap or our other product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology; or
- require us to enter into royalty or licensing agreements.

Although no third party has asserted a claim of patent infringement against us, others may hold proprietary rights that could prevent reproxalap or our other product candidates from being marketed. Any patent-related legal

action against us claiming damages and seeking to enjoin commercial activities relating to our product candidate or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market reproxalap or our other product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing reproxalap or our other product candidates, which could harm our business, financial condition, and operating results.

Any such claims against us could also be deemed to constitute an event of default under our loan and security agreement with Hercules Capital, Inc. ("Hercules"). In the case of a continuing event of default under the loan, Hercules, could, among other remedies, elect to declare all amounts outstanding to be immediately due and payable and terminate all commitments to extend further credit. In the event we do not or are not able to repay the obligations at the time a default occurred, Hercules may elect to commence and prosecute bankruptcy and/or other insolvency proceedings, or proceed against the collateral granted to Hercules under the loan.

Our issued patents could be found invalid or unenforceable if challenged in court.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

We may fail to comply with any of our obligations under existing or future agreements pursuant to which we license rights or technology, which could result in the loss of rights or technology that are material to our business.

We are a party to technology licenses, including the in-license agreement for ADX-1612 and an in-license agreement for ADX-2191, and we may enter into additional licenses in the future. Such licenses do, and may in the future, impose commercial, contingent payment, royalty, insurance, indemnification, and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we could lose valuable rights under our collaboration agreements and our ability to develop product candidates could be impaired. Additionally, should such a license agreement be terminated for any reason, there may be a limited number of replacement licensors, and a significant amount of time may be required to transition to a replacement licensor.

Our rights to develop and commercialize ADX-1612 and ADX-2191 are each subject in part to the terms and conditions of a third party license, pursuant to which we have acquired exclusive rights to ADX-1612 and ADX-2191 and other intellectual property. Our rights with respect to the intellectual property to develop and commercialize ADX-1612 and ADX-2191 may terminate, in whole or in part, if we fail to meet certain milestones contained in each of our license agreements relating to the development and commercialization of ADX-1612 and ADX-2191. We may also lose our rights to develop and commercialize either of ADX-1612 or ADX-2191 if we fail to pay required milestones or royalties. In the event of an early termination of our license agreement, all rights licensed and developed by us under this agreement may be extinguished, which may have an adverse effect on our business and results of operations.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees, consultants, or agents have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants and our employees were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that our company or an employee, consultant, or agent inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

If we do not obtain protection under the Hatch-Waxman Amendments by extending the patent terms and obtaining data exclusivity for our product candidate, our business may be materially harmed.

Depending upon the timing, duration, and specifics of FDA marketing approval of reproxalap or other product candidates, one or more of our United States patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest, and our business may be adversely affected. Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights, or other intellectual property may be ineffective and could result in substantial costs and diversion of resources, and could adversely impact our financial condition or results of operations.

Changes in United States patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves technological and legal complexity. Therefore, obtaining and enforcing biotechnology patents is costly, time consuming, and inherently uncertain. In addition, Congress may pass patent reform legislation. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available or weakening the rights of patent owners. 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 decisions by the United States 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 our existing patents and patents we might obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

While we have issued composition-of-matter patents covering reproxalap and certain of our other product candidates in the United States and other countries, filing, prosecuting, and defending patents on reproxalap and our other product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and, further, may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Our Common Stock

An active trading market for our common stock may not develop or be sustained and investors may not be able to resell their shares at or above the price at which they purchased them.

We have a limited history as a public company. An active trading market for our shares may never develop or be sustained. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the price they paid or at the time that they would like to sell. In addition, an inactive market may impair our ability to raise capital by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration, which, in turn, could harm our business.

The trading price of the shares of our common stock has been and is likely to continue to be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has been and will likely continue to be volatile for the foreseeable future. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price they paid. The market price for our common stock may be influenced by many factors, including:

- results of clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- the expectations of investors or securities analysts regarding our business and clinical development program, including interim or final top-line results that we may announce;
- regulatory developments in the United States and foreign countries;
- our ability to enroll patients in our clinical trials;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the United States healthcare system;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, or capital commitments;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of securities analysts' reports or recommendations;
- sales of our stock by insiders and 5% stockholders;
- trading volume of our common stock;
- general economic, industry, and market conditions other events or factors, many of which are beyond our control;
- additions or departures of key personnel; and
- intellectual property, product liability, or other litigation against us.

In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical 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, which could have a material adverse effect on our business, financial condition, and results of operations.

Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of The Nasdaq Capital Market ("Nasdaq"), such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to de-list our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we would expect to take actions to restore our compliance with Nasdaq's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement, or prevent future non-compliance with Nasdaq's listing requirements.

If our shares become subject to the penny stock rules, it would become more difficult to trade our shares.

The SEC has adopted rules that regulate broker-dealer practices in connection with transactions in penny stocks. Penny stocks are generally equity securities with a price of less than $5.00, other than securities registered on certain national securities exchanges or authorized for quotation on certain automated quotation systems, provided that current price and volume information with respect to transactions in such securities is provided by the exchange or system. If we do not retain a listing on The Nasdaq Capital Market and if the price of our common stock is less than $5.00, our common stock will be deemed a penny stock. The penny stock rules require a broker-dealer, before a transaction in a penny stock not otherwise exempt from those rules, to deliver a standardized risk disclosure document containing specified information. In addition, the penny stock rules require that before effecting any transaction in a penny stock not otherwise exempt from those rules, a broker-dealer must make a special written determination that the penny stock is a suitable investment for the purchaser and receive (i) the purchaser's written acknowledgment of the receipt of a risk disclosure statement; (ii) a written agreement to transactions involving penny stocks; and (iii) a signed and dated copy of a written suitability statement. These disclosure requirements may have the effect of reducing the trading activity in the secondary market for our common stock, and therefore stockholders may have difficulty selling their shares.

Because a small number of our existing stockholders own a majority of our voting stock, your ability to influence corporate matters will be limited.

As of December 31, 2019, our executive officers, directors, and greater than 5% stockholders, in the aggregate, own approximately 35% of our outstanding common stock. As a result, such persons, acting together, will have the ability to control our management and business affairs and substantially all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction. This concentration of ownership may have the effect of delaying, deferring, or preventing a change in control, impeding a merger, consolidation, takeover, or other business combination involving us, or discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividend on our common stock, and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, the Hercules Credit Facility currently prohibits, and any future debt financing arrangements may contain terms prohibiting or limiting the amount of, dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in the value of our common stock. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased shares.

A substantial number of shares of our common stock could be sold into the public market in the near future, which could depress our stock price.

Sales of substantial amounts of our common stock in the public market could reduce the prevailing market prices for our common stock. Substantially all of our outstanding common stock is eligible for sale as is common stock issuable under vested and exercisable stock options. If our existing stockholders sell a large number of shares of our common stock, or the public market perceives that existing stockholders might sell shares of common stock, the market price of our common stock could decline significantly. Existing stockholder sales might also make it more difficult for us to sell additional equity securities at a time and price that we deem appropriate.

We are a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to smaller reporting companies will make our common stock less attractive to investors.

We are a smaller reporting company under Rule 12b-2 of the Securities Exchange Act of 1934. For as long as we continue to be a smaller reporting company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not smaller reporting companies, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements However, our status as a smaller reporting company will not exempt us from the requirement to provide the annual attestation report from our independent registered public accounting firm regarding the effectiveness of our internal control over financial reporting. We cannot predict if investors will find our common stock less attractive because we may rely on smaller reporting company exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile.

We are incurring significant increased costs and demands upon management as a result of operating as a public company.

As a public company, and particularly if and after we cease to be a "smaller reporting company," we incur significant legal, accounting, and other expenses that we did not incur as a private company. We ceased to be an "emerging growth company," as defined in the JOBS Act, on December 31, 2019. As a result, we expect to incur additional expenses and to devote increased management time toward ensuring compliance with those requirements applicable to companies that are not emerging growth companies. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which require, among other things, that we file with the Securities and Exchange Commission, or the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Capital Market to implement provisions of the Sarbanes-Oxley Act, imposes significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may result in substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to continue to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If public company rules and regulations divert the attention of our management and personnel from other business concerns, our business, financial condition, and results of operations could be adversely affected. Increased costs associated with public company expenses will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, public company rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements, the impact of which could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees, or as executive officers.

If we fail to maintain proper and effective internal control over financial reporting in the future, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to Section 404 of the Sarbanes-Oxley Act, our management is required to report upon the effectiveness of our internal control over financial reporting. In addition, as a result of our ceasing to be an emerging growth company as of December 31, 2019, our independent registered public accounting firm is required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we will be required to continue to upgrade and maintain our systems including information technology; implement additional financial and management controls, reporting systems, and procedures; and hire additional accounting and finance staff.

As we grow, we plan to hire additional personnel and engage in external temporary resources and may implement, document, and modify policies and procedures to maintain effective internal controls. However, we may identify deficiencies and weaknesses or fail to remediate previously identified deficiencies in our internal controls. If material weaknesses or deficiencies in our internal controls exist and go undetected or unremediated, our financial statements could contain material misstatements that, when discovered in the future, could cause us to fail to meet our future reporting obligations and cause the price of our common stock to decline. In addition, we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market, or our competitors. We currently have limited research coverage by securities and industry analysts. If other securities or industry analysts do not commence coverage of our company, the trading price for our stock could be negatively impacted. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. The risk of securities class action litigation is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- permitting our board of directors to accelerate the vesting of outstanding option grants upon certain transactions that result in a change of control; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, the provisions would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Our business could be negatively affected as a result of the actions of activist stockholders.

Proxy contests have been waged against many companies in the biotechnology industry over the last few years. We may be particularly vulnerable to activist stockholders due to the highly concentrated ownership of our common stock. If faced with a proxy contest or other type of shareholder activism, we may not be able to respond successfully to the contest or dispute, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest or shareholder dispute involving us or our partners because:

- responding to proxy contests and other actions by activist stockholders can be costly and time-consuming, disrupting operations and diverting the attention of management and employees;
- perceived uncertainties as to future direction may result in the loss of potential acquisitions, collaborations, or in-licensing opportunities, and may make it more difficult to attract and retain qualified personnel and business partners; and
- if individuals are elected to a board of directors with a specific agenda, it may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

These actions could cause our stock price to experience periods of volatility.

ITEM 1B.*UNRESOLVED STAFF COMMENTS*

Not applicable.

ITEM 2.*PROPERTIES*

Our offices are located in Lexington, Massachusetts. As of December 31, 2019, we had leased approximately 9,351 square feet of office space pursuant to leases that expire in 2020. Management believes that this office space is suitable and adequate to meet our anticipated near-term needs. We anticipate that following the expiration of the leases, additional or alternative space will be available at commercially reasonable terms.

ITEM 3.*LEGAL PROCEEDINGS*

From time to time, we may become subject to legal proceedings, claims and litigation arising in the ordinary course of business. We currently are not a party to any threatened or pending material litigation and do not have contingency reserves established for any litigation liabilities. However, third parties might allege that we are infringing their patent rights or that we are otherwise violating their intellectual property rights, including trade names and trademarks. Such third parties may resort to litigation. We accrue contingent liabilities when it is probable that future expenditures will be made and such expenditures can be reasonably estimated.

ITEM 4.*MINE SAFETY DISCLOSURES*

Not applicable.

PART II

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

Holders of Record

As of December 31, 2019, there were 45 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have not declared or paid any cash dividends on our common stock since our inception. We do not plan to pay dividends in the foreseeable future. Under our credit facility, we have agreed not to pay any dividends so long as it has any outstanding obligations thereunder. We currently intend to retain all available funds and any future earnings, if any, for use in the operation of our business. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to applicable laws, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors may deem relevant, and subject to the restrictions contained in future financing instruments. Consequently, stockholders will need to sell shares of our common stock to realize a return on their investment, if any.

ITEM 6.*SELECTED FINANCIAL DATA*

As a smaller reporting company, we are not required to provide this information.

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 together with our financial statements and the related notes appearing at the end of this annual report on Form 10-K. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks, uncertainties and assumptions. You should read the "Risk Factors" and "Special Note Regarding Forward-Looking Statements" sections of this annual report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biotechnology company devoted to developing and commercializing next-generation medicines to improve the lives of patients with immune-mediated diseases. Our lead product candidate, reproxalap, is a first-in-class treatment in late-stage development for dry eye disease ("DED") and allergic conjunctivitis ("AC"). We have additional product candidates in development for proliferative vitreoretinopathy ("PVR") and other retinal diseases, autoimmune disease, and cancer. We currently intend to commercialize our products directly or through collaborations. None of our product candidates have been approved for sale in the United States or elsewhere.

Our lead product candidate reproxalap is a reactive aldehyde species ("RASP") inhibitor that has been shown to diminish ocular inflammation, and has demonstrated statistically significant and clinically relevant improvements across an aggregate of six Phase 2 clinical trials in DED and AC, a Phase 3 clinical trial in AC, and Part 1 of a Phase 3 clinical trial in DED, when administered topically to the eye as an ophthalmic solution. Administered to the skin as a topical dermatologic formulation in a Phase 2 clinical trial and in Part 1 of a Phase 3 clinical trial, reproxalap demonstrated statistically significant and clinically relevant improvements in ichthyosis (a severe skin disorder) caused by Sjögren-Larsson Syndrome ("SLS"), a rare RASP-mediated disease with no approved therapy. A growing body of clinical evidence supports the potential and relevance of RASP inhibition as a new and differentiated mechanism of action. We have discovered and are developing two additional RASP inhibitors, ADX-103 and ADX-629, for the treatment of retinal disease and autoimmune disease, respectively.

Since our incorporation, we have devoted substantially all of our resources to the preclinical and clinical development of our product candidates. Our ability to generate revenues largely depends upon our ability, alone or with others, to complete development of our product candidates to obtain regulatory approvals for and to manufacture, market, and sell our product candidates. The results of our operations will vary significantly from year-to-year and quarter-to-quarter, and depend on a number of factors, including risks related to our business and industry, risks relating to intellectual property and other legal matters, risks related to our common stock, and other risks that are detailed in the section of this annual report on Form 10-K entitled "Risk Factors."

In June 2017, we entered into a Controlled Equity Offering SM Sales Agreement ("Cantor Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor"), as sales agent, pursuant to which we could offer and sell, from time to time through Cantor, shares of our common stock, providing for aggregate sales proceeds of up to $20,000,000. For the year ended, December 31, 2018, we sold an aggregate of 1,796,306 shares of common stock and received $14.2 million after deducting commissions related to the Cantor Sales Agreement and other offering costs. In October 2018, we closed an underwritten public offering in which we sold an aggregate of 5,250,000 shares of common stock. The net proceeds of the offering were approximately $67.6 million, after deducting underwriting discounts, commissions, and other offering expenses payable by us.

In December 2018, we entered into an Open Market Sale Agreement SM ("Jefferies Sales Agreement") with Jefferies LLC ("Jefferies"), as sales agent, pursuant to which we could offer and sell, from time to time through Jefferies, shares of our common stock, par value $0.001 per share, providing for aggregate sales proceeds of up to $50,000,000. Under the Jefferies Sales Agreement, Jefferies may sell such shares of common stock in privately negotiated transactions with our consent; as block transactions; or by any other method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, including sales made directly on The Nasdaq Capital Market or sales made into any other existing trading

market for our common stock, with us setting the parameters for the sale of shares thereunder, including the number of shares to be issued, the time period during which sales are requested to be made, any limits on the number of shares that may be sold in any one trading day, and any minimum price below which sales may not be made. The Jefferies Sales Agreement provides that Jefferies will be entitled to a commission rate of up to 3.0% of the aggregate gross proceeds from each sale of shares. We have no obligation to sell any shares under the Sales Agreement, and may at any time suspend solicitations and offers under the Jefferies Sales Agreement. During the year ended December 31, 2019, we sold, at a volume-weighted average price of $9.73, an aggregate of 1.3 million shares of common stock and received $8.0 million after deducting commissions related to the Jefferies Sales Agreement and other offering costs. From January 1, 2020 through March 12, 2020, we sold at a volume-weighted average price of $5.79 an aggregate of 562,669 shares of common stock and received $3.2 million after deducting commissions related to the Jefferies Sales Agreement and other offering costs.

In March 2019, we entered into the Hercules Credit Facility, pursuant to which a term loan of up to an aggregate principal amount of $60.0 million may be made available to us. The Loan Agreement provides for an initial term loan advance of up to $5.0 million at our option, commencing on March 25, 2019 through and including April 15, 2019, which expired unutilized; three additional term loan advances of up to $15.0 million each, at our option, available to us upon the occurrence of certain funding conditions prior to September 30, 2019, March 31, 2020, and March 31, 2021, respectively, the first of tranche of which was drawn down in full by the Company in September 2019; and a final additional term loan advance of up to $10.0 million prior to December 31, 2020, at our option, subject to approval by Lender's investment committee. The loan agreement contains customary affirmative and negative covenants and events of default. Affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, and maintain insurance coverage. Negative covenants include, among others: restrictions on transferring any part of our business or intellectual property; incurring additional indebtedness; engaging in mergers or acquisitions; paying dividends or making other distributions; making investments; and creating other liens on our assets, in each case subject to customary exceptions. As of December 31, 2019, $15.0 million was outstanding under the Hercules Credit Facility.

We will need to raise additional capital in the form of debt or equity or through partnerships to fund additional development of our product candidates, and we may in-license, acquire, or invest in complementary businesses or products. In addition, as capital resources permit, we may augment or otherwise modify the clinical development plans described herein.

Our Agreement with Madrigal

We are developing ADX-1612 pursuant to a License Agreement with Madrigal Pharmaceuticals, Inc. ("Madrigal"), entered into on December 26, 2016 (the "Madrigal Agreement"). Pursuant to the Madrigal Agreement, we obtained an exclusive, worldwide license from Madrigal under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize Hsp90 inhibitors, including ADX-1612 (investigated in oncology under the name ganetespib) ("Madrigal Agreement Products"). We have agreed to use our commercially reasonable efforts to develop Madrigal Agreement Products.

In consideration for the rights licensed under the Madrigal Agreement, we paid Madrigal an upfront license fee of $250,000 and are obligated to make future regulatory and development and sales-dependent milestone payments to Madrigal of less than $340 million in the aggregate (over 80% of such amount being tied to our achievement of increasingly greater annual worldwide net sales milestones), as well as royalty payments to Madrigal at a rate which, as a percentage of net sales, is in the high single digits for products containing ADX-1612 and mid-single digits for any other Hsp90 inhibitor product. We are also obligated under the Madrigal Agreement to pay Madrigal a percentage of certain sublicense revenue that we receive in connection with entering into any sublicensing arrangements with any third parties, at a percentage rate which tiers downward from the mid-twenties to low-single digits based on the development stage of the product at the time of the sublicense.

The Madrigal Agreement will remain in effect until all payment obligations under the Madrigal Agreement expire. We may terminate the Madrigal Agreement in its entirety or on a Madrigal Agreement Product-by Madrigal Agreement Product basis with timely notice to Madrigal. Either party may terminate the Madrigal Agreement for uncured material breach by the other party or upon certain insolvency or bankruptcy proceedings involving the other party, both with timely notice to the other party. In addition, Madrigal has the right to terminate the Madrigal

Agreement if we, our affiliates, or sublicensees interferes with, challenges the validity or enforceability of, opposes the extension of, or grant of a supplementary protection certificate with respect to any of our licensed patents under the Madrigal Agreement. In the event of an early termination of the Madrigal Agreement, all rights licensed and developed by us under the Madrigal Agreement may revert back to Madrigal. Each party has agreed to indemnify the other party for certain third party claims arising under the Madrigal Agreement.

Our Agreement with MEEI

We are developing ADX-2191 pursuant to an Exclusive License Agreement with Massachusetts Eye and Ear Infirmary ("MEEI") originally entered into in July 2016 between MEEI and Helio Vision, Inc. (as amended, the "MEEI Agreement"). We assumed the MEEI Agreement in connection with our 2019 acquisition of Helio Vision.

Pursuant and subject to the MEEI Agreement, we obtained an exclusive, worldwide license from MEEI to develop and commercialize ADX-2191 under certain patents and patent applications, and other licenses to intellectual property (the "MEEI Patent Rights"). We have agreed to use our commercially reasonable efforts to develop ADX-2191 and to meet certain specified effort and achievement benchmarks by certain dates.

In consideration for the rights licensed under the MEEI Agreement, Helio Vision issued MEEI a number of shares of its preferred stock and Helio Vision agreed to pay non-creditable non-refundable license maintenance fees to MEEI of $15,000 on each of the second and third anniversary of the MEEI Agreement, $25,000 on each of the fourth and fifth anniversary of the MEEI Agreement and $35,000 on the sixth and each subsequent anniversary of the MEEI Agreement during the term of such agreement. In addition, Helio Vision was obligated to make future sales-dependent milestone payments to MEEI of up to the low seven figures in the aggregate, as well as royalty payments to MEEI at a rate which, as a percentage of net sales, is in the low single digits for products that incorporate or use the MEEI Patent Rights in the United States and as a percentage in the low single digits for products that incorporate or use the MEEI Patent Rights outside the United States. We are also obligated under the MEEI Agreement to pay MEEI a percentage of certain sublicense revenue that we receive in connection with entering into any sublicensing arrangements with any third parties, at a percentage rate which tiers downward from low-double digits to mid-single digits based on the date of the sublicense. Following our acquisition of Helio Vision, we became obligated to make any future payments owed under the MEEI Agreement. There is no additional equity consideration issuable under the MEEI Agreement.

The MEEI Agreement will remain in effect until the expiration date of the last to expire patent licensed under the MEEI Agreement. We may terminate the MEEI Agreement with timely written notice to MEEI. MEEI has the right to terminate the MEEI Agreement if we, subject to certain specified cure periods, cease all business operations with respect to licensed products, fail to pay amounts due under the MEEI Agreement, fail to comply with certain due diligence obligations, default in our obligation to maintain insurance, one of our officers is convicted of a felony relating to the manufacture, use, sale or importation of licensed products, we materially breach any provisions of the MEEI Agreement or in the event of our insolvency or bankruptcy.

In the event of an early termination of the MEEI Agreement, all rights licensed and developed by us under the MEEI Agreement may revert back to MEEI. We have agreed to indemnify MEEI for certain claims that may arise under the MEEI Agreement.

Our Acquisition of Helio Vision, Inc.

On January 28, 2019, we acquired Helio Vision, Inc., a Delaware corporation ("Helio"). As a result of the acquisition, we issued an aggregate of 1,160,444 shares of common stock to the former securityholders and an advisor of Helio. We, subject to the conditions of the acquisition agreement, will be obligated to make additional payments to the former securityholders of Helio as follows: (a) $2.5 million of common stock on the date that is 24 months following the closing date; (b) $10.0 million of common stock following approval by the FDA of a new drug approval application for the prevention and/or treatment of proliferative vitreoretinopathy or a substantially similar label ("PVR") prior to the 10th anniversary of the closing date; and (c) $2.5 million of common stock following FDA of a new drug approval application for an indication (other than PVR) prior to the 12th anniversary of the closing date, provided that in no event shall we be obligated to issue more than 5,248,885 shares of Common Stock.

Additionally, in the event of certain change of control or divestitures by us, certain former convertible noteholders of Helio will be entitled to a tax gross-up payment in an amount not to exceed $1.0 million.

The founders were issued 568,627 shares and non-founders were issued 591,817 shares. The Company recognizes the expense associated with the founders' restricted shares as compensation expense on a straight-line basis as the shares vest over the three-year period. For the year ended December 31, 2019, the Company recorded $2.2 million of research and development compensation expense for the founders' restricted shares. During the year ended December 31, 2019, the Company recorded $6.6 million of IPR&D expense related to the fair value of consideration given which includes transaction costs and the deferred tax impact of the Helio acquisition.

Research and development expenses

We expense all of our research and development expenses as they are incurred. Research and development costs that are paid in advance of performance are capitalized as a prepaid expense until incurred. Research and development expenses primarily include:

- non-clinical development, preclinical research, and clinical trial and regulatory-related costs;
- expenses incurred under agreements with sites and consultants that conduct our clinical trials; and
- employee-related expenses, including salaries, benefits, travel, and stock-based compensation expense.

Substantially all of our research and development expenses to date have been incurred in connection with reproxalap. We expect our research and development expenses to increase for the foreseeable future as we advance reproxalap and other compounds through preclinical and clinical development. The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. We are unable to estimate with any certainty the costs we will incur in the continued development of reproxalap and our other product candidates. Clinical development timelines, the probability of success, and development costs can differ materially from expectations. We may never succeed in achieving marketing approval for our product candidates.

The costs of clinical trials may vary significantly over the life of a project owing to, but not limited to, the following:

- per patient trial costs;
- 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 design of the trials;
- the cost of manufacturing the drug;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the cost of vehicle or active comparative agents used in trials;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up;
- the phase of development the product candidate is in; and
- the efficacy and safety profile of the product candidate.

We do not expect reproxalap and our other product candidates to be commercially available, if at all, for the next several years.

General and administrative expenses

Our general and administrative expenses consisted primarily of payroll expenses and related benefits, including stock-based compensation for our full-time employees during the years ended December 31, 2019 and 2018. Other general and administrative expenses include professional fees for auditing, tax, and legal services, including patent related costs. We expect that general and administrative expenses will increase in the future as we expand our operating activities, continue to incur additional costs associated with being a publicly-traded company, and maintain compliance with exchange listing and SEC requirements. These increases will likely include higher consulting costs, legal fees, accounting fees, directors' and officers' liability insurance premiums, and fees associated with investor relations.

Total other income (expense)

Total other income (expense) consists primarily of interest income we earn on interest-bearing accounts, and interest expense incurred on our outstanding debt.

Comprehensive loss

Comprehensive loss is defined as the change in equity during a period from transactions and other events and/or circumstances from non-owner sources. For the year ended December 31, 2019, comprehensive loss is equal to our net loss of $60.8 million and an unrealized gain on marketable securities of $15,000. For the year ended December 31, 2018, comprehensive loss is equal to our net loss of $38.9 million and an unrealized gain on marketable securities of $9,000.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States ("US GAAP"). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the expenses during the reported periods. We evaluate these estimates and judgments on an ongoing basis. 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. Our actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 to our financial statements appearing elsewhere in this annual report on Form 10-K, we believe that the following accounting policies are the most critical in order to fully understand and evaluate our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing financial statements, we are required to estimate and accrue research and development expenses. This process involves the following:

- communicating with our applicable 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;
- estimating and accruing expenses in our financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with selected service providers and making adjustments, if necessary.

Examples of estimated research and development expenses that we accrue include:

- fees paid to investigative sites in connection with clinical studies;
- fees paid to contract manufacturing organizations in connection with non-clinical development, preclinical research, and the production of clinical study materials; and
- professional service fees for consulting and related services.

In-process research and development

Assets purchased in an asset acquisition transaction are expensed as in-process research and development unless the assets acquired are deemed to have an alternative future use, provided that the acquired asset did not also include processes or activities that would constitute a "business" as defined under GAAP, the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no established alternative future use. Acquired in-process research and development payments are immediately expensed in the period in which they are incurred and include upfront payments, as well as transaction fees and subsequent pre-commercial milestone payments. Research and development costs incurred after the acquisition are expensed as incurred.

We base our expense accruals related to non-clinical development, preclinical studies, and clinical trials on our estimates of the services received and efforts expended pursuant to contracts with organizations/consultants that conduct and manage clinical studies on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts may depend on many factors, such as the successful enrollment of patients, site initiation, and the completion of clinical study milestones. Our service providers invoice us monthly in arrears for services performed. 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 we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, we have not experienced significant changes in our estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research activities.

Other Information

Net Operating Loss Carryforwards

As of December 31, 2019, the Company had federal and state income tax net operating loss ("NOL") carryforwards of approximately $139.5 million and $133.9 million, respectively. Federal NOL carryforwards generated through December 31, 2017 and state NOL carryforwards will expire at various dates through 2037. Federal NOLs generated during the years ended December 31, 2018 and thereafter will carry forward indefinitely. As of December 31, 2019, we have federal and state research and development tax credit carryforwards of approximately $4.2 million and $0.8 million, respectively, which will expire at various dates through 2039.

Under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs and certain other tax assets ("tax attributes") to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period (generally three years). Transactions involving our common stock within the testing period, even those outside our control such as purchases or sales by investors, could result in an ownership change. A limitation on our ability to utilize some or all our NOLs or credits could have a material adverse effect on our results of operations and cash flows. Prior to December 31, 2018, we underwent three ownership changes and it is possible that additional ownership changes have occurred since. However, Management believes that we have sufficient "Built-In-Gain" to offset any Section 382 limitation generated by such ownership changes. Any future ownership changes, including those resulting from our recent or future financing activities, may cause our existing tax attributes to have additional limitations.

Subject to annual limitations, net operating losses generated in years 2018 and beyond will have an indefinite carryforward period and will not expire. Future changes in federal and state tax laws pertaining to net operating loss carryforwards may also cause limitations or restrictions from us claiming such net operating losses. If the net operating loss carryforwards become unavailable to us or are fully utilized, our future taxable income will not be shielded from federal and state income taxation absent certain U.S. federal and state tax credits, and the funds otherwise available for general corporate purposes would be reduced.

Recent Accounting Pronouncements

Recent accounting pronouncements which may be applicable to us are described in Note 2 to our Consolidated Financial Statements included in the Annual Report on Form 10-K.

Results of Operations

We anticipate that our results of operations will fluctuate for the foreseeable future due to several factors, including the progress of our research and development efforts, the timing and outcome of clinical trials, and regulatory requirements. Our limited operating history makes predictions of future operations difficult or impossible. Since our inception, we have incurred significant losses.

Comparison of Years Ended December 31, 2019 and 2018

Net loss. Net loss for the years ended December 31, 2019 and 2018 was approximately $60.8 million and $38.9 million, respectively. As of December 31, 2019, we had total stockholders' equity of $48.1 million. Losses have resulted principally from costs incurred in our clinical trials and other research and development programs, IPR&D and amortization costs of founders' stock related to the acquisition of Helio in January 2019, and from our general and administrative expenses.

Research and development expenses. Research and development expenses were $44.4 million for the year ended December 31, 2019 compared to $29.8 million for the same period in 2018. The increase of $14.6 million is primarily related to the increase in our external research and development expenditures, including clinical, manufacturing, and pre-clinical activities; an increase in personnel costs; and non-cash compensation costs related to a portion of the upfront consideration paid to the founders of Helio, which is subject to vesting based on continuous service.

General and administrative expenses. General and administrative expenses were $12.2 million for the year ended December 31, 2019, compared to $9.9 million for the year ended December 31, 2018. The increase of approximately $2.3 million is primarily related to an increase in personnel costs, including stock-based compensation and public company costs primarily related to continuing compliance with the Sarbanes-Oxley Act of 2002.

Acquired in-process research and development expenses. Acquired in-process research and development expenses were $6.6 million for the year ended December 31, 2019. We did not have acquired in-process research and development expense for the year ended December 31, 2018. The $6.6 million increase is related to the in-process research and development expenses associated with the January 2019 acquisition of Helio. We determined that the assets acquired from Helio did not constitute a business since substantially all of the assets acquired were related to ADX-2191, and that the transaction would be accounted for as an asset acquisition. As the asset and development program acquired from Helio are at an early stage of development and determining the future economic benefit of the acquired assets at the date of acquisition is highly uncertain, the fair value of the assets was fully expensed as in-process research and development. During the year ended December 31, 2019, we recorded $6.6 million of acquired in-process research and development expense related to the fair value of consideration given, which includes transaction costs.

Other income (expense). Total other income (expense) was approximately $938,000 for the year ended December 31, 2019, compared to $806,000 for the year ended December 31, 2018, and consisted of interest income, partially offset by interest expense related to our credit facility.

Liquidity and Capital Resources

We have funded our operations primarily from the sale of equity securities and convertible equity securities and borrowed under credit facilities. Since inception, we have incurred operating losses and negative cash flows from operating activities and have devoted substantially all our efforts to research and development. At December 31, 2019, we had total stockholders' equity of approximately $48.1 million and cash, cash equivalents, and marketable securities of $73.4 million. During the year ended December 31, 2019, we had net loss of approximately $60.8 million. We expect to generate operating losses for the foreseeable future.

We were a party to a loan and security agreement ("the Credit Facility") with Pacific Western Bank (Pacific Western, formerly Square 1 Bank), which was originally entered into in April 2012 and was subsequently amended. Pursuant to the Credit Facility, Pacific Western made term loans in a principal amount of up to $5.0 million available to us to fund expenses related to our clinical trials and general working capital purposes. As of December 31, 2017, approximately $1.4 million of principal was outstanding on the Credit Facility which was repaid and extinguished during the year ended December 31, 2018.

In June 2017, we entered into a Controlled Equity Offering SM Sales Agreement ("Cantor Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor"), as sales agent, pursuant to which we may offer and sell, from time to time through Cantor, shares of our common stock, par value $0.001 per share, providing for aggregate sales proceeds of up to $20,000,000. For the year ended December 31, 2018, we sold an aggregate of 1,796,306 shares of common stock and received $14.2 million after deducting commissions related to the Cantor Sales Agreement and other offering costs.

In October 2018, we closed an underwritten public offering in which we sold an aggregate of 5,250,000 shares of common stock. The net proceeds of the offering were approximately $67.6 million, after deducting underwriting discounts, commissions, and other offering expenses payable by us.

In December 2018, we entered into an Open Market Sale Agreement SM ("Jefferies Sales Agreement") with Jefferies LLC ("Jefferies"), as sales agent, pursuant to which we could offer and sell, from time to time through Jefferies, shares of our common stock, par value $0.001 per share, providing for aggregate sales proceeds of up to $50,000,000. Under the Jefferies Sales Agreement, Jefferies may sell such shares of common stock in privately negotiated transactions with our consent; as block transactions; or by any other method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, including sales made directly on The Nasdaq Capital Market or sales made into any other existing trading market for our common stock, with us setting the parameters for the sale of shares thereunder, including the number of shares to be issued, the time period during which sales are requested to be made, any limits on the number of shares that may be sold in any one trading day, and any minimum price below which sales may not be made. The Jefferies Sales Agreement provides that Jefferies will be entitled to a commission rate of up to 3.0% of the aggregate gross proceeds from each sale of shares. We have no obligation to sell any shares under the Sales Agreement and may at any time suspend solicitations and offers under the Jefferies Sales Agreement. During the year ended December 31, 2019, we sold, at a volume-weighted average price of $9.73, an aggregate of 1.3 million shares of common stock and received $8.0 million after deducting commissions related to the Jefferies Sales Agreement and other offering costs. From January 1, 2020 through March 12, 2020, we sold at a volume-weighted average price of $5.79 an aggregate of 562,669 shares of common stock and received $3.2 million after deducting commissions related to the Jefferies Sales Agreement and other offering costs.

In March 2019, we entered into the Hercules Credit Facility, pursuant to which a term loan of up to an aggregate principal amount of $60.0 million may be made available to us. The Loan Agreement provides for an initial term loan advance of up to $5.0 million at our option, commencing on March 25, 2019 through and including April 15, 2019, which expired unutilized; three additional term loan advances of up to $15.0 million each, at our option, available to us upon the occurrence of certain funding conditions prior to September 30, 2019, March 31, 2020, and March 31, 2021, respectively, the first of tranche of which was drawn down in full by the Company in September 2019; and a final additional term loan advance of up to $10.0 million prior to December 31, 2020, at our option, subject to approval by Lender's investment committee. The loan agreement contains customary affirmative and negative covenants and events of default. Affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, and maintain insurance

coverage. Negative covenants include, among others: restrictions on transferring any part of our business or intellectual property; incurring additional indebtedness; engaging in mergers or acquisitions; paying dividends or making other distributions; making investments; and creating other liens on our assets, in each case subject to customary exceptions. As of December 31, 2019, $15.0 million was outstanding under the Hercules Credit Facility.

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of December 31, 2019, together with the proceeds of the sales of common stock under the Jefferies Sales Agreement through the date of this filing will be adequate to fund our currently anticipated operating expenses through the end of 2021, including the currently planned Part 2 of the Phase 3 clinical trial in dry eye disease (the RENEW trial, pending FDA feedback), the initial part of the adaptive Phase 3 clinical trial in proliferative vitreoretinopathy (the GUARD trial), and the Phase 3 trial in allergic conjunctivitis (the INVIGORATE trial). We will need to secure additional funding in the future, from one or more equity or debt financings, collaborations, or other sources, in order to carry out all of our planned research and development activities, commercialize our product candidates, or conduct any substantial additional development requirements requested by the FDA. At this time, due to the risks inherent in the drug development process, we are unable to estimate with any certainty the costs we will incur in the continued clinical development of reproxalap and our other product candidates. Subsequent trials initiated at a later date will cost considerably more, depending on the results of our prior clinical trials, and feedback from the FDA or other third parties. Accordingly, we will continue to require substantial additional capital to continue our clinical development and potential commercialization activities. The amount and timing of our future funding requirements will depend on many factors, including but not limited to:

- the progress, costs, results of, and timing of our clinical development program for reproxalap and our other product candidates, including our current and planned clinical trials;
- the need for, and the progress, costs, and results of any additional clinical trials of reproxalap or our other product candidates that we may initiate based on the results of our planned clinical trials or discussions with the FDA, including any additional trials the FDA or other regulatory agencies may require evaluating the safety of reproxalap and our other product candidates;
- the outcome, costs, and timing of seeking and obtaining regulatory approvals from the FDA, and any similar regulatory agencies;
- the timing and costs associated with manufacturing reproxalap and our other product candidates for clinical trials and other studies and, if approved, for commercial sale;
- our need and ability to hire additional management, development, and scientific personnel;
- the cost to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, filing, prosecuting, defending, and enforcing of any patents or other intellectual property rights;
- the timing and costs associated with establishing sales and marketing infrastructure;
- market acceptance of reproxalap and our other product candidates;
- the costs of acquiring, licensing, or investing in additional businesses, products, product candidates, and technologies; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

We may need or desire to obtain additional capital to finance our operations through debt, equity, or alternative financing arrangements. We may also seek capital through collaborations or partnerships with other companies. The issuance of debt could require us to grant additional liens on certain of our assets that may limit our flexibility. If we raise additional capital by issuing equity securities, the terms and prices for these financings may be much more favorable to the new investors than the terms obtained by our existing stockholders. These financings also may significantly dilute the ownership of our existing stockholders. If we are unable to obtain additional financing, we may be required to reduce the scope of our future activities, which could harm our business, financial

condition, and operating results. There can be no assurance that any additional financing required in the future will be available on acceptable terms, if at all.

We will continue to incur costs as a public company including, but not limited to, costs and expenses for directors fees; increased directors and officers insurance; investor relations fees; expenses for compliance with the Sarbanes-Oxley Act of 2002 and rules implemented by the SEC and Nasdaq, on which our common stock is listed; and various other costs. The Sarbanes-Oxley Act of 2002 requires that we maintain effective disclosure controls and procedures and internal controls. The following table summarizes our cash flows for the years ended December 31, 2019 and 2018:

	Years Ended December 31,	
	2019	2018
Net cash used in operating activities	$ (44,984,226)	$ (29,857,131)
Net cash provided by (used in) investing activities	18,476,851	(23,335,576)
Net cash provided by financing activities	23,575,733	80,526,842
Net (decrease) increase in cash and cash equivalents	$ (2,931,642)	$ 27,334,135

Operating Activities. Net cash used in operating activities was $45.0 million in 2019, compared to net cash used in operating activities of $29.9 million in 2018. The primary use of cash was to fund our operations. The increase in the amount of cash used in operating activities for 2019 as compared to 2018 was due to an increase in research and development expenses, including clinical, manufacturing, and preclinical activities.

Investing Activities. Net cash provided by investing activities in 2019 was $18.5 million, related primarily to the sales and maturities of marketable securities partially offset by the purchase of marketable securities, compared to net cash used in investing activities in 2018 of $23.3 million, related primarily to the purchase of marketable securities partially offset by sales and maturities of marketable securities.

Financing Activities. Net cash provided by financing activities was $23.6 million for the year ended December 31, 2019, related primarily to our Hercules Credit Facility, under which $15.0 million is currently outstanding, the Jefferies Sales Agreement, under which we sold an aggregate of 1.3 million shares of our common stock resulting in $8.0 million in proceeds after deducting commissions and other offering costs, and proceeds from the exercise of stock options. Net cash provided by financing activities of $80.5 million for year ended 2018, primarily related to our underwritten public offering and sales of common stock under the Cantor Sales Agreement.

Off-Balance Sheet Arrangements

Through December 31, 2019, we have not entered into and did not have any relationships with unconsolidated entities or financial collaborations, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purpose.

Contractual Obligations and Commitments

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934 and are not required to provide the information under this item.

ITEM 7A.*QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK*

Interest rates

Our exposure to market risk is currently confined to our cash, our cash equivalents, our marketable securities and our Hercules Credit Facility. We have not used derivative financial instruments for speculation or trading purposes. Because of the short-term maturities of our cash, cash equivalents and marketable securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our investments. Our Hercules Credit Facility accrues interest from its date of issue at a variable annual interest rate equal to the greater of (i) 9.10% and (ii) the prime rate (as reported in the Wall Street Journal or any successor publication thereto) plus 3.10%. As of December 31, 2019, $15.0 million was outstanding under the Hercules Credit Facility.

Effects of inflation

Inflation has not had a material impact on our results of operations.

ITEM 8.*FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA*

The information required by this Item 8 is contained on pages 94 through 119 of this annual report on Form 10-K and is incorporated herein by reference.

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

None.

ITEM 9A.*CONTROLS AND PROCEDURES*

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

As of the end of the period covered by this annual report on Form 10-K, we carried out an evaluation under the supervision and with the participation of our Disclosure Committee and our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rules 13a-15(e) and 15d-15(e). Disclosure controls are procedures that are designed to ensure that information required to be disclosed in our reports filed under the Securities Exchange Act of 1934, or the Exchange Act, such as this annual report on Form 10-K, is recorded, processed, summarized, and reported within the time periods specified by the United States Securities and Exchange Commission. Disclosure controls are also designed to ensure that such information is accumulated and communicated to our management, including our Chief Executive Officer and our Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure. Our quarterly evaluation of disclosure controls includes an evaluation of some components of our internal control over financial reporting. We also perform a separate annual evaluation of internal control over financial reporting for the purpose of providing the management report below.

The evaluation of our disclosure controls included a review of their objectives and design, our implementation of the controls and the effect of the controls on the information generated for use in this annual report on Form 10-K. In the course of the control evaluations, we reviewed data errors or control problems identified and sought to confirm that appropriate corrective actions, including process improvements, were being undertaken. This type of evaluation is performed on a quarterly basis so that the conclusions of management, including our Chief Executive Officer and our Chief Financial Officer, concerning the effectiveness of the disclosure controls can be reported in our periodic reports on Form 10-Q and Form 10-K. The overall goals of our evaluation activities are to monitor our disclosure controls and to modify them as necessary. We intend to maintain our disclosure controls as dynamic processes and procedures that we adjust as circumstances merit.

Based on our management’s evaluation (with the participation of our Chief Executive Officer and our Chief Financial Officer), as of the end of the period covered by this report, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures were effective.

Management’s Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed 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. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management utilized the criteria established in the Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") to conduct an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2019. Based on the assessment, our management has concluded that, as of December 31, 2019, our internal control over financial reporting was effective. The attestation report concerning the effectiveness of our internal control over financial reporting as of December 31, 2019 issued by BDO USA, LLP, an independent registered public accounting firm, appears in Item 8 of this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act) during the fourth quarter of 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B.*OTHER INFORMATION*

None.

PART III

ITEM 10.Directors, Executive Officers and Corporate Governance

Except as set forth below, the information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with our 2020 Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2019 (the "Proxy Statement"), and is incorporated in this annual report on Form 10-K by reference.

Code of Conduct

Our board of directors adopted a code of ethics and business conduct that applies to each of our directors, officers and employees. The full text of our code of business conduct is posted on the Investors portion of our website at http://ir.aldeyra.com. Any waiver of the code of ethics and business conduct for an executive officer or director may be granted only by our board of directors or a committee thereof and must be timely disclosed as required by applicable law. We have implemented whistleblower procedures that establish format protocols for receiving and handling complaints from employees. Any concerns regarding accounting or auditing matters reported under these procedures will be communicated promptly to the audit committee.

ITEM 11.Executive Compensation

Other than with respect to the Securities Authorized for Issuance under Equity Incentive Plans contained below, the information required by this item will be contained in the Proxy Statement and is incorporated in this annual report on Form 10-K by reference.

ITEM 12.Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Securities Authorized for Issuance under Equity Incentive Plans

The following table provides information as of December 31, 2019, with respect to shares of our common stock that may be issued, subject to certain vesting requirements, under our existing equity compensation plans, including our 2013 Equity Incentive Plan ("2013 Plan"), 2010 Employee, Director and Consultant Equity Incentive Plan ("2010 Plan"), 2004 Employee, Director and Consultant Stock Plan ("2004 Plan") and our 2016 Employee Stock Purchase Plan ("2016 ESPP").

	A		B		C	
Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants, and Rights		Weighted-Average Exercise Price of Outstanding Options, Warrants, and Rights		Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (A))	
Equity compensation plans approved by security holders	4,624,239	(1)	$ 6.62	(2)	1,369,016	(3)
Equity compensation plans not approved by security holders	—		—		—	
Total	4,624,239	(1)	6.62	(2)	1,369,016	(3)

(1) Of these shares, 430,425 were underlying then outstanding restricted stock unit awards and 3,780,684 were subject to options then outstanding under the 2013 Plan, 413,130 were subject to options then outstanding under the 2010 Plan and none were subject to options then outstanding under the 2004 Plan.

(2) Does not take into account restricted stock units, which have no exercise price.

(3) Represents 772,323 shares of common stock available for issuance under our 2013 Plan and 596,693 shares of common stock available for issuance under our 2016 ESPP. No shares are available for future issuance under the 2010 Plan or 2004 Plan. Our 2013 Plan provides for annual increases in the number of shares available for issuance thereunder on the first day of each fiscal year equal to the lower of: (1) 6% of the total number of shares of common stock outstanding at that time; or (2) such other amount as our board of directors may determine. Our 2016 ESPP provides for annual increases in the number of shares available for issuance thereunder on the first day of each fiscal year equal to the lesser of: (1) 1% of the shares of common stock outstanding at that time; and (2) such other amount as our board of directors may determine. On January 1, 2020, an additional 1,744,998 shares became available for future issuance under the 2013 Plan and an additional 290,833 shares became available for future issuance under the 2016 ESPP. The additional shares from the annual increase on January 1, 2020 are not included in the table above.

ITEM 13.Certain Relationships and Related Party Transactions, and Director Independence

The information required by this item will be contained in the Proxy Statement and is incorporated in this annual report on Form 10-K by reference.

ITEM 14.Principal Accounting Fees and Services

The information required by this item will be contained in the Proxy Statement and is incorporated in this annual report on Form 10-K by reference.

PART IV

ITEM 15.Exhibits and Financial Statements Schedules

The financial statements filed as part of this annual report on Form 10-K are listed in the Index to Financial Statements. Certain schedules are omitted because they are not applicable, or not required, or because the required information is included in the financial statements or notes thereto. The Exhibits are listed in the Exhibit Index below.

EXHIBIT INDEX

Exhibit Number	Exhibit Title
3.1	Restated Certificate of Incorporation of Registrant, (filed as Exhibit 3.1 to the Registrant's Current Report on Form 8-K as filed on May 7, 2014, and incorporated herein by reference)
3.2	Amended and Restated Bylaws of the Registrant (filed as Exhibit 3.2 to the Registrant's Current Report on Form 8-K as filed on May 7, 2014, and incorporated herein by reference)
4.1	Specimen stock certificate evidencing the shares of common stock (filed as Exhibit 4.1 to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on March 17, 2014, and incorporated herein by reference)
4.2	Amended & Restated Investor Rights Agreement dated as of December 20, 2012 (filed as Exhibit 4.2 to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on March 17, 2014, and incorporated herein by reference)
4.6*	Description of Securities
10.1	Form of Indemnity Agreement for Directors and Officers (filed as Exhibit 10.1 to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on March 17, 2014, and incorporated herein by reference)
10.2†	Offer Letter, effective as of August 1, 2013, between the Registrant and Todd C. Brady, M.D., Ph.D. (filed as Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on January 6, 2014, and incorporated herein by reference)
10.4†	Offer Letter, effective November 29, 2013 between the Registrant and Todd C. Brady, M.D., Ph.D. (filed as Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on January 6, 2014, and incorporated herein by reference)
10.4(a)†	Offer Letter Amendment, effective February 19, 2014 between the Registrant and Todd C. Brady, M.D., Ph.D. (filed as Exhibit 10.4(a) to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on March 17, 2014, and incorporated herein by reference)
10.6†	2004 Employee, Director and Consultant Stock Plan, as amended, and form of option agreement thereunder (filed as Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on January 6, 2014, and incorporated herein by reference)
10.7†	2010 Employee, Director and Consultant Equity Incentive Plan, as amended, and form of option agreement thereunder (filed as Exhibit 10.7 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on January 6, 2014, and incorporated herein by reference)
10.8†	2013 Equity Incentive Plan and form of option agreement thereunder (filed as Exhibit 10.8 to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on March 17, 2014, and incorporated herein by reference)
10.8.(a)†	Form Notice of Stock Option Grant under the 2013 Equity Incentive Plan (filed as Exhibit 10.8(a) to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on March 17, 2014, and incorporated herein by reference)

Exhibit Number	Exhibit Title
10.8(b)†	Form Notice of Stock Unit Award under the 2013 Equity Incentive Plan (filed as Exhibit 10.8(b) to Amendment No. 2 to the Registrant's Registration Statement on Form S-1 (SEC File No. 333-193204), as filed on March 17, 2014, and incorporated herein by reference)
10.13	Sublease dated September 12, 2014 between the Registrant and MacLean Power L.L.C. (filed as Exhibit 10.15 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2014 (as filed on November 12, 2014, and incorporated herein by reference))
10.22†	Offer Letter between the Registrant and David J. Clark, M.D. dated December 15, 2015 (filed as Exhibit 10.23 to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2015 (as filed on March 30, 2016, and incorporated herein by reference))
10.23	Sublease dated as of March 7, 2016 between Planck, LLC and the Registrant and Master Lease dated June 3, 2014 between WLC Three VI, L.L.C. and Plank, LLC (filed as Exhibit 10.24 to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2015 (as filed on March 30, 2016, and incorporated herein by reference))
10.24†	Aldeyra Management Cash Incentive Plan (filed as Exhibit 10.25 to the Registrant's Current Report on Form 8-K as filed on March 18, 2016, and incorporated herein by reference)
10.25†	Aldeyra Therapeutics, Inc. Change in Control Plan (filed as Exhibit 10.25 to the Registrant's Annual Report on Form 10-K (as filed on March 30, 2017, and incorporated herein by reference))
10.27	Lease Agreement by and between WLC Three VI, L.L.C. and the Registrant, dated as of September 11, 2017 (filed as Exhibit 10.27 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 (as filed on November 9, 2017, and incorporated herein by reference))
10.28	First Amendment to Lease between WLC Three VI, L.L.C. and the Registrant, dated as of November 27, 2017 (filed as Exhibit 10.28 to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (as filed on March 29, 2018, and incorporated herein by reference)).
10.29†	Amendment No. 2 to the Aldeyra Therapeutics, Inc. 2013 Equity Incentive Plan (filed as Exhibit 10.29 to the Registrant's Quarterly Form 10-Q (as filed on August 9, 2018, and incorporated herein by reference))
10.30†	Offer Letter, effective as of July 30, 2018, between the Registrant and Joshua Reed (filed as Exhibit 10.30 to the Registrant's Quarterly Form 10-Q (as filed on November 14, 2018, and incorporated herein by reference))
10.32†	Amendment No. 1 to the Aldeyra Therapeutics, Inc. 2013 Equity Incentive Plan (filed as Exhibit 10.26 to the Registrant's Quarterly Report on Form 10-Q (as filed on August 10, 2016, and incorporated herein by reference))
10.33†	Aldeyra Therapeutics, Inc. 2016 Employee Stock Purchase Plan (filed as Exhibit 10.27 to the Registrant's Quarterly Report on Form 10-Q (as filed on August 10, 2016, and incorporated herein by reference))
10.34	Agreement and Plan of Merger, dated as of January 24, 2019, by and among Aldeyra Therapeutics, Inc., Helio Vision, Inc., Halo Merger Sub, Inc., Halo Merger Sub, LLC and Josef von Rickenbach, as the Securityholder Representative (filed as Exhibit 2.1 to the Registrant's Current Report on Form 8-K (as filed on January 29, 2019, and incorporated herein by reference))
10.35†	Offer Letter, effective as of April 19, 2018, between the Registrant and David McMullin (filed as Exhibit 10.35 to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (as filed on March 8, 2019, and incorporated herein by reference))

Exhibit Number	Exhibit Title
10.36‡	License Agreement, dated as of December 26, 2016, by and between Registrant and Madrigal Pharmaceuticals, Inc. (filed as Exhibit 99.2 to the Registrant's Current Report on Form 8-K (as filed on September 25, 2018, and incorporated herein by reference))
10.37	Open Market Sale Agreement℠, dated December 28, 2018, by and between the Registrant and Jefferies LLC (filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K (as filed on December 28, 2018, and incorporated herein by reference))
10.38	Loan and Security Agreement, dated as of March 25, 2019, by and among the Registrant, certain subsidiaries of the Registrant from time to time party thereto, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc. (filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K (as filed on March 26, 2019, and incorporated herein by reference))
10.39*, **	Exclusive License Agreement, effective as of July 7, 2016, between the Massachusetts Eye and Ear Infirmary and Helio Vision, Inc.
10.40*,**	Amendment Number 1 and Waiver Agreement dated December 20, 2018 by and between Helio Vision, Inc. and the Massachusetts Eye and Ear Infirmary
23.1*	Consent of BDO USA, LLP, independent registered public accounting firm
31.1*	Certification of the Chief Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of the Chief Financial Officer as required by Section 302 of the Sarbanes-Oxley Act of 2002
32.1*	Certifications of the Chief Executive Officer and Chief Financial Officer as required by 18 U.S.C. 1350
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

† Compensation Arrangement.
‡ Confidential treatment has been granted with respect to certain portions of this document.
* Filed herewith.
** In accordance with Item 601(b)(2)(ii) of Regulation S-K, certain information (indicated by "*****") has been excluded from this exhibit because it is both not material and would likely cause competitive harm to the Company if publicly disclosed.

The Exhibits listed in the Exhibit Index are filed as part of this annual report on Form 10-K.

ITEM 16.Form 10-K Summary

None.

Signatures

Pursuant to the requirements of Section 13 and 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this annual report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the Commonwealth of Massachusetts, on March 12, 2020.

ALDEYRA THERAPEUTICS, INC.

By: /s/ Todd C. Brady, M.D., Ph.D.
Todd C. Brady, M.D., Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1934, this annual report on Form 10-K 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/ Todd C. Brady, M.D., Ph.D. Todd C. Brady, M.D., Ph.D.	Chief Executive Officer and Director (principal executive officer)	March 12, 2020
/s/ Joshua Reed Joshua Reed	Chief Financial Officer (principal financial and accounting officer)	March 12, 2020
/s/ Richard H. Douglas, Ph. D. Richard H. Douglas, Ph.D.	Chairman of the Board of Directors	March 12, 2020
/s/ Ben Bronstein, M.D. Ben Bronstein, M.D.	Director	March 12, 2020
/s/ Martin J. Joyce Martin J. Joyce	Director	March 12, 2020
/s/ Nancy Miller-Rich Nancy Miller-Rich	Director	March 12, 2020
/s/ Gary Phillips, M.D. Gary Phillips, M.D.	Director	March 12, 2020
/s/ Jesse Treu, Ph.D. Jesse Treu, Ph.D.	Director	March 12, 2020
/s/ Neal Walker, D.O. Neal Walker, D.O.	Director	March 12, 2020

ALDEYRA THERAPEUTICS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
Aldeyra Therapeutics, Inc.
Lexington, Massachusetts

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Aldeyra Therapeutics, Inc. (the "Company") and subsidiaries as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company and its subsidiaries at December 31, 2019 and 2018, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated March 12, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the 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 consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts

March 12, 2020

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
Aldeyra Therapeutics, Inc.
Lexington, Massachusetts

Opinion on Internal Control over Financial Reporting

We have audited Aldeyra Therapeutics, Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019 based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2019, and the related notes and our report dated March 12, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Item 9A, Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of internal control over financial reporting in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ BDO USA, LLP

Boston, MA

March 12, 2020

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

	December 31, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 16,425,830	$ 3,357,472
Cash equivalent - reverse repurchase agreements	28,000,000	44,000,000
Marketable securities	28,938,545	46,242,220
Prepaid expenses and other current assets	1,804,450	1,169,594
Total current assets	75,168,825	94,769,286
Deferred offering costs	—	86,644
Property and equipment, net	148,449	235,225
Right-of-use assets	201,007	—
Total assets	$ 75,518,281	$ 95,091,155
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 808,302	$ 3,051,678
Accrued expenses	11,873,122	5,421,498
Current portion of operating lease liabilities	226,328	—
Total current liabilities	12,907,752	8,473,176
Long-term debt	14,528,212	—
Total liabilities	27,435,964	8,473,176
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 15,000,000 shares authorized, none issued and outstanding	—	—
Common stock, voting, $0.001 par value; 150,000,000 authorized and 28,656,832 and 26,244,435 shares issued and outstanding, respectively	28,657	26,244
Additional paid-in capital	247,409,793	225,136,127
Accumulated other comprehensive income (loss)	5,866	(9,224)
Accumulated deficit	(199,361,999)	(138,535,168)
Total stockholders’ equity	48,082,317	86,617,979
Total liabilities and stockholders’ equity	$ 75,518,281	$ 95,091,155

The accompanying notes are an integral part of these consolidated financial statements.

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Years ended December 31,	
	2019	**2018**
Operating expenses:		
Research and development	$ 44,351,851	$ 29,823,007
Acquired in-process research and development	6,567,754	—
General and administrative	12,154,702	9,876,144
Loss from operations	(63,074,307)	(39,699,151)
Other income (expense):		
Interest income	1,541,349	952,698
Interest expense	(603,846)	(146,792)
Total other income (expense), net	937,503	805,906
Loss before income taxes	(62,136,804)	(38,893,245)
Income tax benefit	1,309,973	—
Net loss	$ (60,826,831)	$ (38,893,245)
Net loss per share - basic and diluted	$ (2.24)	$ (1.79)
Weighted average common shares outstanding - basic and diluted	27,111,840	21,685,642

The accompanying notes are an integral part of these consolidated financial statements.

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

	Years ended December 31,	
	2019	**2018**
Net loss	$ (60,826,831)	$ (38,893,245)
Other comprehensive income/(loss):		
Unrealized gain/(loss) on marketable securities	15,090	8,607
Total other comprehensive income/(loss)	$ 15,090	$ 8,607
Comprehensive loss	$ (60,811,741)	$ (38,884,638)

The accompanying notes are an integral part of these consolidated financial statements.

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Stockholders' Equity					
	Common Voting Stock			Accumulated Other Comprehensive Income/(Loss), net of tax		
	Shares	Amount	Additional Paid-in Capital		Accumulated Deficit	Total Stockholders' Equity
Balance, December 31, 2017	19,137,639	$ 19,138	$ 139,241,635	$ (17,831)	$ (99,641,923)	$ 39,601,019
Stock-based compensation	—	—	4,144,853	—	—	4,144,853
Issuance of common stock, net of issuance costs	7,046,306	7,046	81,664,126	—	—	81,671,172
Issuance of common stock, ESPP	14,382	14	85,559	—	—	85,573
Issuance of common stock, vested restricted stock awards	40,975	41	(41)	—	—	—
Issuance of common stock, warrants exercised	5,133	5	(5)	—	—	—
Other comprehensive income	—	—	—	8,607	—	8,607
Net loss	—	—	—	—	(38,893,245)	(38,893,245)
Balance, December 31, 2018	26,244,435	26,244	225,136,127	(9,224)	(138,535,168)	86,617,979
Stock-based compensation	—	—	8,082,751	—	—	8,082,751
Issuance of common stock, acquisition of Helio Vision, Inc.	733,972	733	4,943,676	—	—	4,944,409
Issuance of common stock, net of issuance costs	1,347,156	1,348	7,890,330	—	—	7,891,678
Issuance of common stock, exercise of stock options	232,004	232	1,162,160	—	—	1,162,392
Issuance of common stock, ESPP	34,253	35	194,814	—	—	194,849
Issuance of common stock, vested restricted stock awards	65,012	65	(65)	—	—	—
Other comprehensive income	—	—	—	15,090	—	15,090
Net loss	—	—	—	—	(60,826,831)	(60,826,831)
Balance, December 31, 2019	28,656,832	$ 28,657	$ 247,409,793	$ 5,866	$ (199,361,999)	$ 48,082,317

The accompanying notes are an integral part of these consolidated financial statements.

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years ended December 31,	
	2019	**2018**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (60,826,831)	$ (38,893,245)
Adjustments to reconcile net loss to net cash used in operating activities:		
Acquired in-process research and development	6,567,754	—
Deferred taxes	(1,309,973)	—
Stock-based compensation	8,082,751	4,144,853
Amortization of debt discount – non-cash interest expense	248,567	59,322
Net amortization of premium on debt securities available for sale	(583,701)	(237,541)
Depreciation	96,305	71,003
Change in assets and liabilities:		
Prepaid expenses and other current assets	(454,429)	(150,627)
Accounts payable	(2,846,142)	2,049,582
Accrued expenses	6,041,473	3,099,522
Net cash used in operating activities	(44,984,226)	(29,857,131)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Acquisitions of property and equipment	(9,529)	(262,966)
Cash acquired in Helio asset acquisition	609,464	—
Purchases of marketable securities	(57,768,084)	(59,731,610)
Sales of marketable securities	75,645,000	36,659,000
Net cash provided by (used in) investing activities	18,476,851	(23,335,576)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock	7,891,678	81,837,102
Proceeds from exercise of stock options	1,162,392	—
Proceeds from employee stock purchase plan	194,849	85,573
Extinguishment of long-term debt	—	(1,395,833)
Proceeds from long-term debt	14,450,000	—
Debt issuance costs paid in cash	(123,186)	—
Net cash provided by financing activities	23,575,733	80,526,842
NET (DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS	(2,931,642)	27,334,135
CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD	47,357,472	20,023,337
CASH AND CASH EQUIVALENTS, END OF PERIOD	$ 44,425,830	$ 47,357,472
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Cash paid during the period for:		
Interest	$ 238,491	$ 88,963
SUPPLEMENTAL DISCLOSURES OF NONCASH ACTIVITIES:		
Helio acquisition:		
Assets acquired	$ 75,632	$ —
Liabilities acquired	$ 637,994	$ —
Fair value of securities issued	$ 4,944,409	$ —

The accompanying notes are an integral part of these consolidated financial statements.

1. NATURE OF BUSINESS

Aldeyra Therapeutics, Inc. ("Aldeyra", "Company", "we", "us" and "our") was incorporated in the state of Delaware on August 13, 2004 as Neuron Systems, Inc. On December 20, 2012, the Company changed its name to Aldexa Therapeutics, Inc. and, on March 17, 2014, the Company changed its name to Aldeyra Therapeutics, Inc. Aldeyra, together with its wholly-owned subsidiaries, is developing next-generation medicines to improve the lives of patients with immune-mediated diseases.

The Company's principal activities to date include raising capital and research and development activities.

2. BASIS OF PRESENTATION AND SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation – The accompanying consolidated financial statements were prepared in conformity with accounting principles generally accepted in the United States of America ("US GAAP").

Risks and Uncertainties –The ongoing research and development activities will be subject to extensive regulation by numerous governmental authorities in the United States. Prior to marketing in the United States, any drug developed by the Company must undergo rigorous preclinical and clinical testing and an extensive regulatory approval process implemented by the United States Food and Drug Administration ("FDA") under the Food, Drug and Cosmetic Act. The Company has limited experience in conducting and managing the preclinical and clinical testing necessary to obtain regulatory approval. There can be no assurance that the Company will not encounter problems in the clinical trials that will cause the Company or the FDA to delay or suspend clinical trials.

The Company's success will depend in part on its ability to obtain patents and product license rights, maintain trade secrets, and operate without infringing on the property rights of others, both in the United States and other countries. There can be no assurance that patents issued to or licensed by the Company will not be challenged, invalidated, circumvented, or that the rights granted thereunder will provide proprietary protection or competitive advantages to the Company.

Based on its current operating plan, the Company believes that its cash, cash equivalents, and marketable securities as of December 31, 2019, together with the proceeds of the sales of common stock under the Jefferies Sales Agreement through the date of this filing will be adequate to fund our currently anticipated operating expenses through the end of 2021, including the currently planned Part 2 of the Phase 3 clinical trial in dry eye disease (the RENEW trial, pending FDA feedback), the initial part of the adaptive Phase 3 clinical trial in proliferative vitreoretinopathy (the GUARD trial), and the Phase 3 trial in allergic conjunctivitis (the INVIGORATE trial). The Company will need to secure additional funding in the future, from one or more equity or debt financings, collaborations, or other sources, in order to carry out all of the Company's planned research and development activities; commercialize its product candidates; or conduct any substantial, additional development requirements requested by the FDA. Additional funding may not be available to the Company on acceptable terms, or at all. If the Company is unable to secure additional capital, it will be required to significantly decrease the amount of planned expenditures, and may be required to cease operations.

Curtailment of operations would cause significant delays in the Company's efforts to develop and introduce its products to market, which is critical to the realization of its business plan and the future operations of the Company.

Use of Estimates – The preparation of consolidated financial statements in conformity with US GAAP requires management to make estimates and assumptions, including fair value estimates for investments that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. The Company evaluates its estimates and assumptions on an ongoing basis. The most significant estimates in the Company's financial statements include, but are not limited to, estimates related to clinical trial accruals, estimates related to

prepaid and accrued research and development costs, acquired in-process research and development ("IPR&D") expense, and accounting for income taxes and the related valuation allowance. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may materially differ from these estimates and assumptions.

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 segment, which is the identification and development of next-generation medicines to improve the lives of patients with immune-mediated diseases.

Cash and Cash Equivalents – The Company classifies all highly liquid investments with original maturities of three months or less as cash equivalents and all highly liquid investments with original maturities of greater than three months but less than 12 months as current marketable securities. The Company has a policy of making investments only with commercial institutions that have at least an investment grade credit rating. The Company invests its cash primarily in reverse repurchase agreements ("RRAs"), government securities and obligations, and money market funds.

RRAs are collateralized by deposits in the form of 'Government Securities and Obligations' for an amount not less than 102% of their value. The Company does not record an asset or liability related to the collateral as the Company is not permitted to sell or repledge the associated collateral. The Company has a policy that the collateral has at least an A (or equivalent) credit rating. The Company utilizes a third-party custodian to manage the exchange of funds as well as requirement that collateral received is maintained at 102% of the value of the RRAs on a daily basis.

Marketable Securities – Marketable securities consist of government securities and obligations with original maturities of more than 90 days. Investments are classified as available-for-sale and are recorded on the balance sheet at fair value with unrealized gains or losses reported as a separate component of other comprehensive income/(loss). Management determines the appropriate classification of its investments at the time of purchase and re-evaluates such determination at each balance sheet date.

Fair Value of Financial Instruments – Financial instruments including cash equivalents and accounts payable are carried in the financial statements at amounts that approximate their fair value based on the short maturities of those instruments. Marketable securities are carried at fair value and are more fully described in Note 6. The carrying amount of the Company's credit facility with Hercules Capital, Inc. approximates fair value since the effective interest rate approximates market rates currently available to the Company.

Concentration of Credit Risk – Financial instruments that potentially subject the Company to significant concentrations of credit risk principally consist of cash, cash equivalents and marketable securities. The Company places its cash and cash equivalents and marketable securities with financial institutions which management believes have high credit ratings. As part of its cash and investment management processes, the Company performs periodic evaluations of the credit standing of the financial institutions with whom it maintains deposits.

Intellectual Property – The legal and professional costs incurred by the Company to acquire its patent rights are expensed as incurred and included in general and administrative expenses. At December 31, 2019 and 2018, the Company has determined that these expenses have not met the criteria to be capitalized since the future benefits to be derived from the patents is uncertain. Intellectual property related expenses for the years ended December 31, 2019 and 2018 were $1.4 million and $1.3 million, respectively.

Income Taxes – The Company follows the provisions of Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 740, *Income Taxes ("ASC 740")*, in reporting deferred income taxes. ASC 740 requires a company to recognize deferred tax liabilities and assets for expected future income tax consequences of events that have been recognized in the Company's financial statements. Under this method, deferred tax assets and liabilities are determined based on temporary differences between financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates in the years in which the

temporary differences are expected to reverse. Valuation allowances are provided if based on the weight of available evidence, it is more likely than not that some or all the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions pursuant to ASC 740 which prescribes a recognition threshold and measurement process for financial statement recognition of uncertain tax positions taken or expected to be taken in a tax return. If the tax position meets this threshold, the benefit to be recognized is measured as the tax benefit having the highest likelihood of being realized upon ultimate settlement with the taxing authority. The Company recognizes interest accrued related to unrecognized tax benefits and penalties in the provision for income taxes. Management is not aware of any uncertain tax positions.

Research and Development Costs – Research and development ("R&D") costs are charged to expense as incurred and relate to salaries, employee benefits, stock-based compensation related to employees, consulting services, other operating costs and expenses associated with preclinical and clinical trial activities. Payments made by the Company in advance for research and development services not yet provided and/or for materials not yet received are recorded as prepaid expenses. Accrued liabilities are recorded related to those expenses for which vendors have not yet billed us with respect to services provided and/or materials that we have received.

Preclinical and clinical trial expenses relate to third-party services, subject-related fees at the sites where the Company's clinical trials are being conducted, laboratory costs, analysis costs, toxicology studies and investigator fees. Costs associated with these expenses are generally payable on the passage of time or when certain milestones are achieved. Expense is recorded during the period incurred or in the period in which a milestone is achieved. In order to ensure that the Company has adequately provided for preclinical and clinical expenses during the proper period, the Company maintains an accrual to cover these expenses. These accruals are assessed on a quarterly basis and are based on such assumptions as expected total cost, the number of subjects and clinical trial sites and length of the study. Actual results may differ from these estimates and could have a material impact on the Company's reported results. The Company's historical accrual estimates have not been materially different from actual costs.

In-process research and development – Assets purchased in an asset acquisition transaction are expensed as in-process research and development unless the assets acquired are deemed to have an alternative future use, provided that the acquired asset did not also include processes or activities that would constitute a "business" as defined under GAAP, the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no established alternative future use. Acquired IPR&D payments are immediately expensed in the period in which they are incurred and include upfront payments, as well as transaction fees and subsequent pre-commercial milestone payments. Research and development costs incurred after the acquisition are expensed as incurred.

Stock-Based Compensation – Stock-based payments are accounted for in accordance with the provisions of ASC 718, *Compensation – Stock Compensation*. For options, the fair value of stock-based payments is estimated, on the date of grant, using the Black-Scholes option pricing model. For restricted stock, fair value is based on the fair value of the stock on the date of grant. The resulting fair value for restricted stock and options expected to vest is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the applicable restricted stock or option. The Company records the effect of forfeitures and cancellations when they occur.

Comprehensive Loss – Comprehensive loss is defined as the change in equity during a period from transactions and other events and/or circumstances from non-owner sources. For December 31, 2019, comprehensive loss is equal to the Company's net loss of $60.8 million and an unrealized gain on marketable securities of $15,000. For December 31, 2018, comprehensive loss is equal to our net loss of $38.9 million and an unrealized gain on marketable securities of $9,000.

Net Loss Per Share – The Company computes net loss per share in accordance with the two-class method. Under the two-class method, net loss is allocated between common stock and other participating securities based on their participation rights. The Company has determined that the nonvested shares issued to the Helio founders represents a participating security and as such the nonvested shares are excluded from basic earnings per share. Net losses are not allocated to the nonvested shareholders for computing net loss per share under the two-class method because nonvested shareholders do not have contractual obligations to share in the losses of the Company. Basic

earnings per share is calculated by dividing net loss allocable to common stockholders by the weighted average number of common stock outstanding.

Diluted net loss per share is computed using the more dilutive of (a) the two-class method, or (b) treasury stock method, as applicable, to the potentially dilutive instruments. The weighted-average number of common shares outstanding gives effect to all potentially dilutive common equivalent shares, including outstanding stock options and restricted stock, warrants, and nonvested shares.

Recent Accounting Pronouncements – In February 2016, the FASB issued Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which supersedes the lease guidance under FASB ASC Topic 840, *Leases* ("ASC 840"), resulting in the creation of FASB ASC Topic 842, *Leases* ("ASC 842"). ASU 2016-02 requires lessees to recognize on the balance sheet a right-of-use asset, representing its right to use the underlying asset for the lease term, and a lease liability for all leases with terms greater than 12 months. The guidance also requires qualitative and quantitative disclosures designed to assess the amount, timing, and uncertainty of cash flows arising from leases. The standard requires the use of a modified retrospective transition approach, which includes a number of optional practical expedients that entities may elect to apply. The Company adopted the new standard on January 1, 2019. The Company elected to utilize the available practical expedients. Upon adoption, the Company recorded a ROU asset and a lease liability that were immaterial. There was no impact to opening retained earnings as a result of the adoption of the new guidance. The impact of applying ASC 842 on the results for reporting periods and balance sheet beginning after January 1, 2019 is presented under ASC 842, while prior amounts are not adjusted and continue to be reported in accordance with the Company's historic accounting under ASC 840, Leases. Refer to Note 14 for further information.

In June 2016, the FASB issued ("ASU") No. 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"). ASU 2016-13 requires that credit losses be reported as an allowance using an expected losses model, representing the entity's current estimate of credit losses expected to be incurred. The accounting guidance currently in effect is based on an incurred loss model. For available-for-sale debt securities with unrealized losses, this standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. The amendments under ASU 2016-13 are effective for interim and annual fiscal periods beginning after December 15, 2022. We do not expect the adoption of ASU 2016-13 to have a material impact on our consolidated financial statements.

3. HELIO VISION ACQUISITION

On January 28, 2019 (the "Closing Date"), the Company acquired Helio Vision, Inc. ("Helio"). As a result of the acquisition, the Company initially issued an aggregate of 1,160,444 shares of common stock to the former securityholders and an advisor of Helio. The founders of Helio were issued 568,627 shares and non-founders were issued 591,817 shares. The Helio founders' shares are subject to vesting based on continued service to the Company over three years from the Closing Date of which 25% are vested as of December 31, 2019. The Company recognizes the expense associated with the founders' restricted shares as compensation expense on a straight-line basis as the shares vest over the three-year period. For the year ended December 31, 2019, the Company recorded $2.2 million of research and development compensation expense for the founders' restricted shares.

The Company, subject to the conditions of the acquisition agreement, is contingently obligated to make additional payments to the former securityholders of Helio as follows: (a) $2.5 million of common stock on the date that is 24 months following the Closing Date (assuming certain technical milestones are met); (b) $10.0 million of common stock following approval by the FDA of a new drug approval application for the prevention and/or treatment of proliferative vitreoretinopathy or a substantially similar label prior to the 10th anniversary of the Closing Date; and (c) $2.5 million of common stock following FDA approval of a new drug application for an indication (other than proliferative vitreoretinopathy) prior to the 12th anniversary of the Closing Date (the shares of common stock issuable pursuant to the preceding clauses (a) – (c) are referred to herein as the Milestone Shares), provided that in no event shall the Company be obligated to issue more than an aggregate of 5,248,885 shares of common stock. Additionally, in the event of certain change of control or divestitures by the Company, certain former convertible noteholders of Helio will be entitled to a tax gross-up payment in an amount not to exceed $1.0 million.

The Company determined that liability accounting is not required for the Milestone Shares under FASB ASC Topic 480, *Distinguishing Liabilities from Equity* ("ASC 480"). The Company also determined that the Milestone Shares meet the scope exception as a derivative under FASB ASC Topic 815, *Derivatives and Hedging* ("ASC 815"), from inception of the Milestone Shares through December 31, 2019. Accordingly, the Milestone Shares are evaluated under FASB ASC Topic 450, *Contingencies* ("ASC 450") and the Company will record a liability related to the Milestone Shares if the milestones are achieved, and the obligation to make additional payment(s) becomes probable. At that time, the Company will record the cost of the Milestone Shares issued to the founders as compensation expense and to the Helio non-founders as in-process research and development expense if there is no alternative future use. No milestones related to the Milestone Shares are probable of being achieved as of December 31, 2019.

The Company assessed the acquisition of Helio under the FASB ASC Topic 805, *Business Combinations* ("ASC 805"). Under ASC 805, the Company determined that the acquired assets did not constitute a business since substantially all the assets acquired were related to ADX-2191 and that the transaction would be accounted for as an asset acquisition. The asset and development program acquired from Helio are at an early stage of development and will require a significant investment of time and capital for development. There is no assurance that the Company will be successful in developing such asset, and a failure to successfully develop such asset could diminish the Company's prospects. Under ASC 805, the asset acquired is considered to have no alternative future uses, since the future economic benefit of the acquired asset at the date of acquisition is highly uncertain. The fair value of the assets was determined using the quoted market price of the Company's common stock on the closing date and was fully expensed as in-process research and development. Additionally, the Company assessed the Helio acquisition under ASC 740. The acquisition resulted in an income tax benefit of $1.3 million and a corresponding increase to acquired IPR&D expense. The expense resulted from the reduction in the Company's valuation allowance due to the deferred tax liability created as a result of the book and tax basis difference. During the year ended December 31, 2019, the Company recorded $6.6 million of IPR&D expense related to the fair value of consideration given which includes transaction costs and the deferred tax impact of the Helio acquisition.

4. NET LOSS PER SHARE

For the years ended December 31, 2019 and 2018, diluted weighted-average common shares outstanding is equal to basic weighted-average common shares due to the Company's net loss position.

The following potentially dilutive securities outstanding have been excluded from the computation of diluted weighted-average shares outstanding, because such securities had an antidilutive impact:

	Years ended December 31,	
	2019	2018
Options to purchase common stock	4,193,814	3,383,047
Warrants to purchase common stock	—	40,300
Restricted stock units	430,425	212,297
Unvested restricted shares (1)	426,472	—
Total of common stock equivalents	5,050,711	3,635,644

(1) Represents 426,472 shares of common stock that are issued and outstanding but that were subject to a right of repurchase by the Company at December 31, 2019 and are not included in stockholders' equity pursuant to US GAAP.

5. CASH, CASH EQUIVALENTS AND MARKETABLE SECURITIES

At December 31, 2019, cash, cash equivalents and marketable securities were comprised of:

	Carrying Amount	Unrecognized Gain	Unrecognized Loss	Estimated Fair Value	Cash and Cash Equivalents	Current Marketable Securities
Cash	$15,363,462	$ —	$ —	$15,363,462	$15,363,462	$ —
Money market funds	1,062,368	—	—	1,062,368	1,062,368	—
Reverse repurchase agreements	28,000,000	—	—	28,000,000	28,000,000	—
Total Cash and cash equivalents	44,425,830	—	—	44,425,830	44,425,830	—
U.S. government agency securities	28,932,679	5,866	—	28,938,545	—	28,938,545
Available for Sale (1)	28,932,679	5,866	—	28,938,545	—	28,938,545
Total Cash, cash equivalents and current marketable securities					$44,425,830	$28,938,545

(1) Available for sale securities are reported at fair value with unrealized gains and losses reported net of taxes, if material, in other comprehensive income.

The contractual maturities of all available for sale securities are less than one year at December 31, 2019.

At December 31, 2018, cash, cash equivalents and marketable securities were comprised of:

	Carrying Amount	Unrecognized Gain	Unrecognized Loss	Estimated Fair Value	Cash and Cash Equivalents	Current Marketable Securities
Cash	$ 2,127,175	$ —	$ —	$ 2,127,175	$ 2,127,175	$ —
Money market funds	1,230,297	—	—	1,230,297	1,230,297	—
Reverse repurchase agreements	44,000,000	—	—	44,000,000	44,000,000	—
Total Cash and cash equivalents	47,357,472	—	—	47,357,472	47,357,472	—
U.S. government agency securities	46,251,444	—	(9,224)	46,242,220	—	46,242,220
Available for Sale (1)	46,251,444	—	(9,224)	46,242,220	—	46,242,220
Total Cash, cash equivalents and current marketable securities					$47,357,472	$46,242,220

(1) Available for sale securities are reported at fair value with unrealized gains and losses reported net of taxes, if material, in other comprehensive income.

6. FAIR VALUE MEASUREMENTS

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value are performed in a manner to maximize the use of observable inputs and minimize the use of unobservable inputs. ASC 820, *Fair Value Measurements*, establishes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, which are the following:

Level 1 – Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

Level 2 – Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 – Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

There were no liabilities measured at fair value at December 31, 2019 or 2018, respectively.

The following table presents information about the Company's assets measured at fair value at December 31, 2019 and December 31, 2018:

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds (a)	$ 1,062,368	$ —	$ —	$ 1,062,368
Reverse repurchase agreements (b)	—	28,000,000	—	28,000,000
U.S. government agency securities (b)	—	28,938,545	—	28,938,545
Total assets at fair value	$ 1,062,368	$ 56,938,545	$ —	$ 58,000,913

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds (a)	$ 1,230,297	$ —	$ —	$ 1,230,297
Reverse repurchase agreements (b)	—	44,000,000	—	44,000,000
U.S. government agency securities (b)	—	46,242,220	—	46,242,220
Total assets at fair value	$ 1,230,297	$ 90,242,220	$ —	$ 91,472,517

(a) Money market funds included in cash and cash equivalents in the consolidated balance sheets, are valued at quoted market prices in active markets.
(b) Reverse repurchase agreements and U.S. government agency securities are recorded at fair market values, which are determined based on the most recent observable inputs for similar instruments in active markets or quoted prices for identical or similar instruments in markets that are not active or are directly or indirectly observable.

7. ACCRUED EXPENSES

Accrued expenses at December 31, 2019 and 2018 were:

	December 31, 2019	December 31, 2018
Accrued compensation	$ 1,489,475	$ 1,172,880
Accrued research and development	9,493,093	3,882,313
Accrued general and administrative	890,554	366,305
Accrued expenses	$ 11,873,122	$ 5,421,498

8. CREDIT FACILITY

The Company's long-term debt obligation consists of amounts the Company is obligated to repay under its credit facility with Hercules Capital, Inc. ("Hercules"). In March 2019, the Company entered into a Loan and Security Agreement with Hercules and the several banks and other financial institutions or entities, from time-to-time parties thereto (collectively, referred to as "Lender"), providing for a term loan of up to $60.0 million that is secured by a lien covering all of the Company's assets, other than the Company's intellectual property (the "Loan and Security Agreement" or the "Hercules Credit Facility"). The Loan and Security Agreement provides for an initial term loan advance of up to $5.0 million at the Company's option, commencing on March 25, 2019 through and including April 15, 2019, which expired unutilized; three additional term loan advances of up to $15.0 million each, at the Company's option, available to the Company upon the occurrence of certain funding conditions prior to September 30, 2019, March 31, 2020, and March 31, 2021, respectively, the first of which tranche was drawn down in full by the Company in September 2019; and a final additional term loan advance of up to $10.0 million prior to December 31, 2021, at the Company's option, subject to approval by the Lender's investment committee. As of December 31, 2019, $15.0 million was outstanding under the Hercules Credit Facility. As of December 31, 2019, the Company was in material compliance with all covenants of the Hercules Credit Facility.

The term loan bears interest at an annual rate equal to the greater of (i) 9.10% and (ii) the prime rate (as reported in the Wall Street Journal or any successor publication thereto) plus 3.10%. The Loan and Security Agreement provides for interest-only payments until May 1, 2021, with an option to extend the interest-only period to May 1, 2022 based upon the achievement of certain milestones. Repayment of the aggregate outstanding principal balance of the term loan, in monthly installments, starts upon expiration of the interest-only period and continues through October 1, 2023 (the "Maturity Date"). Associated with this debt facility, the Company incurred a commitment charge of $25,000, transaction costs of $273,186, a fee of $375,000 upon closing, and is required to pay a fee ("End of Term Charge") of 6.95% multiplied by the aggregate amount of advances under the Loan and Security Agreement at maturity. The fees, transaction costs and end of term charge are amortized to interest expense through the Maturity Date using the effective interest method. The effective interest rate was 12.9% at December 31, 2019. At the Company's option, the Company may elect to prepay all, but not less than all, of the outstanding term

loan by paying the entire principal balance and all accrued and unpaid interest thereon plus all fees and other amounts due under the Loan and Security Agreement, including a prepayment charge equal to the following percentage of the principal amount being prepaid: 3% if the term loan is prepaid prior to March 25, 2021 and 1.5% if the term loan is prepaid any time thereafter, but prior to March 25, 2022.

Future principal payments, including the End of Term Charge, are as follows for the years ending December 31:

2020	$ —
2021	3,659,776
2022	5,931,718
2023	6,451,006
Total	$ 16,042,500

The Loan and Security Agreement also contains certain events of default, representations, warranties and non-financial covenants of the Company. In addition, the Company granted the Lender the right to purchase up to an aggregate of $2.0 million of the Company's equity securities, or instruments exercisable for or convertible into equity securities, sold to investors in financings upon the same terms and conditions afforded to such other investors.

9. STOCKHOLDERS' EQUITY

Common Stock

Each share of common stock is entitled to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and when declared by the board of directors, subject to the prior rights of holders of all classes of stock outstanding. As of December 31, 2019, a total of 4,193,814, 772,323, and 596,693, shares of common stock were reserved for issuance upon (i) the exercise of outstanding stock options, (ii) the issuance of stock awards under the Company's Amended 2013 Plan, and (iii) the issuance of shares under the 2016 ESPP, respectively.

Underwritten Public Offerings

In October 2018, the Company sold 5,250,000 shares of its common stock in an underwritten public offering at $13.75 per share, for an aggregate gross cash purchase price of $72.2 million or proceeds of $67.6 million after underwriters discount and expenses.

Cantor Sales Agreement

In June 2017, the Company entered into a Controlled Equity Offering SM Sales Agreement ("Cantor Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor"), as sales agent, pursuant to which the Company could offer and sell, from time to time through Cantor, shares common stock providing for aggregate sales proceeds of up to $20.0 million. For the year ended, December 31, 2018, the Company sold an aggregate of 1,796,306 shares of common stock and received $14.2 million after deducting commissions related to the Cantor Sales Agreement and other offering costs.

Jefferies Sales Agreement

In December 2018, the Company entered into an Open Market Sales Agreement SM ("Jefferies Sales Agreement") with Jefferies LLC ("Jefferies"), as sales agent, pursuant to which the Company could offer and sell, from time to time through Jefferies, shares common stock providing for aggregate sales proceeds of up to $50.0 million. During the year ended December 2019, the Company sold, at a volume-weighted average price of $9.73, an aggregate of 1.3 million shares of common stock and received $8.0 million after deducting commissions related to the Jefferies Sales Agreement and other offering costs. From January 1, 2020 through March 12, 2020, the Company sold at a volume-weighted average price of $5.79 an aggregate of 562,669 shares of common stock and received $3.2 million after deducting commissions related to the Jefferies Sales Agreement and other offering costs.

10. INCOME TAXES

No current provision for federal and state income taxes has been recorded as the Company has incurred losses since inception for tax purposes. 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.

In assessing the realizability of net deferred taxes in accordance with ASC 740 the Company considers whether it is more likely than not that some portion or all the deferred tax assets will not be realized. Based on the weight of available evidence, primarily the incurrence of net losses since inception, anticipated net losses in the near future, reversals of existing temporary differences and expiration of various federal and state attributes, the Company does not consider it more likely than not that some or all of the net deferred taxes will be realized. Accordingly, a 100% valuation allowance has been applied against net deferred taxes. Effective January 1, 2019, the Company adopted ASU 2016-02 which resulted in the recognition of lease liabilities and right-of-use assets. The Company has adjusted its deferred tax assets and liabilities as a result of the adoption.

As of December 31, 2019, the Company had federal and state income tax net operating loss ("NOL") carryforwards of approximately $139.5 million and $133.9 million, respectively. Federal NOL carryforwards generated through December 31, 2017 and state NOL carryforwards will expire at various dates through 2037. The federal NOL generated during the year ended December 31, 2018 will carryforward indefinitely. As of December 31, 2019, the Company had federal and state research and development tax credit carryforwards of approximately $4.2 million and $0.8 million, respectively, which will expire at various dates through 2039.

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 ("Tax Act") was enacted into law making significant changes to the Internal Revenue Code. The main provision impacting the Company is the reduction in the U.S. statutory corporate tax rate to 21% for years beginning after December 31, 2017. On the same day, the SEC staff issued Staff Accounting Bulletin No. 118, or SAB 118, which provides guidance for companies that have not completed their accounting for the income tax effects of the Tax Act in the period of enactment, allowing for a measurement period of up to one year after the enactment date to finalize the recording of the related tax impacts. The net impact of the change in tax rate was zero due to the Company's full valuation allowance.

Significant components of the Company's deferred tax assets and liabilities at December 31, 2019 and 2018 are as follows:

	Years ended December 31,	
	2019	2018
Deferred Tax Assets		
Federal & state NOL carryforward	$ 37,752,925	$ 25,311,547
Federal & state R&D credit carryforward	4,840,115	3,781,160
Intangibles – net	120,318	164,508
Accounts payable and accrued expenses	2,898,710	1,958,174
Stock options	4,527,462	3,146,034
Other items	80,812	10,173
Gross deferred tax assets	50,220,342	34,371,596
Valuation allowance	(50,165,427)	(34,371,596)
Deferred tax assets, net	$ 54,915	$ —
Deferred Tax Liabilities		
Lease liability	(54,915)	—
TOTAL	$ —	$ —

The change in valuation allowance of $15.8 million from December 31, 2018 to December 31, 2019 was primarily the result of an increase in net operating losses and tax credits during the current year.

The components of the incomes tax benefit for the years ended December 31, 2019 and 2018, are as follows:

	Years ended December 31,	
	2019	2018
Deferred Taxes		
Federal	$ (1,205,175)	$ —
State	(104,798)	—
Total income tax benefit	$ (1,309,973)	$ —

Under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs and certain other tax assets to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period (generally three years). Transactions involving the Company's common stock within the testing period, even those outside the Company's control such as purchases or sales by investors, could result in an ownership change. A limitation on the Company's ability to utilize some or all its NOLs or credits could have a material adverse effect on the Company's results of operations and cash flows. Prior to December 31, 2018, we underwent three ownership changes and it is possible that additional ownership changes have occurred since. However, management believes that we have sufficient "Built-In-Gain" to offset any Section 382 limitation generated by such ownership changes. Any future ownership changes, including those resulting from our recent or future financing activities, may cause our existing tax attributes to have additional limitations.

Subject to annual limitations, net operating losses generated in years 2018 and beyond will have an indefinite carryforward period and will not expire. Future changes in federal and state tax laws pertaining to net operating loss carryforwards may also cause limitations or restrictions from us claiming such net operating losses. If the net operating loss carryforwards become unavailable to us or are fully utilized, our future taxable income will not be shielded from federal and state income taxation absent certain U.S. federal and state tax credits, and the funds otherwise available for general corporate purposes would be reduced.

All tax years are open for examination by the taxing authorities for both federal and state purposes.

A reconciliation of the federal statutory tax rate of 21% to the Company's effective income tax rates are as follows:

	Years ended December 31,	
	2019	2018
Statutory tax rate	21.00 %	21.00 %
State taxes, net of federal benefits	5.62 %	6.83 %
Federal research and development credits	1.44 %	3.81 %
Change in valuation allowance	(25.44)%	(31.51)%
Stock-based compensation	(0.81)%	(0.20)%
Other	0.30 %	0.07 %
Effective tax rate	2.11 %	— %

11. STOCK INCENTIVE PLAN

The Company approved the 2010 Employee, Director and Consultant Equity Incentive Plan ("2010 Plan") in September 2010 to replace the 2004 Plan. The 2010 Plan provided for the granting of stock options and restricted stock awards. The 2010 Plan terminated upon the Company's initial public offering in May 2014. However, grants made under the 2010 Plan are still governed by that plan. As of December 31, 2019, options to purchase 413,130 shares of common stock at a weighted average exercise price of $1.58 per share remained outstanding under the 2010 Plan.

The Company approved the 2013 Equity Incentive Plan in October 2013. The 2013 Equity Incentive Plan became effective immediately on adoption although no awards were to be made under it until the effective date of the registration statement for the Company's initial public offering. The 2013 Equity Incentive Plan was amended in June 2016 and June 2018, (the "Amended 2013 Plan"). The Amended 2013 Plan provides for the granting of stock options, restricted stock, stock appreciation rights, stock units, and performance cash awards to certain employees, members of the board of directors and consultants of the Company. On January 1 of each year the aggregate number of common shares that may be issued under the Amended 2013 Plan shall automatically increase by a number of shares equal to the lower of (a) 6% of the total number of shares of common stock outstanding on the last calendar day of the prior fiscal year, or (b) a number of shares of common stock determined by the Company's board of directors. As of December 31, 2019, options to purchase 3,780,684 shares of common stock at a weighted average exercise price of $7.17 per share and 430,425 shares of common stock underlying restricted stock units remained outstanding under the Amended 2013 Plan. As of December 31, 2019, there were 772,323 shares of common stock available for grant under the Amended 2013 Plan. As of January 1, 2020, the number of shares of common stock that may be issued under the Amended 2013 Plan was automatically increased by 1,744,998 shares, increasing the number of shares of common stock available for issuance under the Amended 2013 Plan to 2,517,321.

The Company recognizes stock-based compensation expense over the requisite service period. The Company's share-based awards are accounted for as equity instruments. The amounts included in the consolidated statements of operations relating to stock-based compensation, employee incentive plan and Helio founder shares as are as follows:

	Years ended December 31,	
	2019	2018
Research and development expenses	$ 2,441,542	$ 1,541,915
General and administrative expenses	$ 3,446,887	$ 2,602,938
Helio founders' shares (Note 3)	$ 2,194,322	$ —
Total stock-based compensation expense	$ 8,082,751	$ 4,144,853

Stock Options

Terms of stock option agreements, including vesting requirements, are determined by the board of directors or its compensation committee, subject to the provisions of the respective plan they were granted. Options granted by the Company typically vest over a four year period. The options are subject to acceleration of vesting in the event of certain change of control transactions. The options may be granted for a term of up to ten years from the date of grant. The exercise price for options granted under the Amended 2013 Plan must be at a price no less than 100% of the fair market value of a common share on the date of grant.

The following table summarizes option activity under the incentive plans for the year ended December 31, 2019:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term	Aggregate Intrinsic Value(a)
Outstanding at December 31, 2018	3,383,047	$ 6.17		
Granted	1,447,255	7.71		
Cancelled/Forfeited	(404,484)	7.66		
Exercised	(232,004)	5.01		
Outstanding at December 31, 2019	4,193,814	$ 6.62	7.34	$ 2,615,717
Exercisable at December 31, 2019	2,514,720	$ 5.91	6.38	$ 2,471,702

(a) The aggregate intrinsic value in this table was calculated on the positive difference, if any, between the closing price per share of the Company's common stock on December 31, 2019 of $5.81 and the per share exercise price of the underlying options.

The Company records stock-based compensation related to stock options granted at fair value. During the years ended December 31, 2019 and 2018, the Company used the Black-Scholes option-pricing model to estimate the fair value of stock option grants and to determine the related compensation expense. The assumptions used in calculating the fair value of stock-based payment awards represent management's best estimates. The weighted-average fair value of options granted was $5.23 and $5.79 for the years ended December 31, 2019 and 2018, respectively. The assumptions used in determining fair value of the employee stock options for the years ended December 2019 and 2018, are as follows:

	December 31, 2019	December 31, 2018
Expected dividend yield	0%	0%
Anticipated volatility	74.65% - 77.12%	76.52% - 78.38%
Stock price	$5.16 - $8.76	$6.80 - $11.83
Exercise price	$5.16 - $8.76	$6.80 - $11.83
Expected life (years)	5.50 - 6.08	5.50 - 6.25
Risk free interest rate	1.59% - 2.62%	2.32% - 3.10%

The dividend yield of zero is based on the fact that the Company has never paid cash dividends and have no present intention to pay cash dividends. Expected volatility is estimated using the historical volatility of the Company. The Company has estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option for service-based awards since the Company doesn't have sufficient historical or implied data of its own. The risk-free interest rates for periods within the expected life of the option are based on the yields of zero-coupon United States Treasury securities.

At December 31, 2019, there is approximately $8.1 million of unrecognized compensation cost relating to stock options outstanding, which the Company expects to recognize over a weighted average period of 2.54 years. Total unrecognized compensation cost will be adjusted for future forfeitures, if necessary.

Restricted Stock Units

Terms of restricted stock unit ("RSUs") agreements, including vesting requirements, are determined by the board of directors or its compensation committee, subject to the provisions of the Amended 2013 Plan. RSUs granted by the Company typically vest over a four year period. In the event that the employees' employment with the Company terminates any unvested shares are forfeited and revert to the Company. Restricted stock units are not included in issued and outstanding common stock until the shares are vested and released. The table below summarizes activity relating to RSUs for the year ended December 31, 2019:

	Number of Shares
Outstanding at December 31, 2018	212,297
Granted	283,140
Vested/released	(65,012)
Outstanding at December 31, 2019	430,425

The weighted-average fair value of RSUs granted was $8.05 and $8.60 per share for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, the outstanding restricted stock units had unamortized stock-based compensation of $2.3 million with a weighted-average remaining recognition period of 2.65 years and an aggregate intrinsic value of $2.5 million.

Employee Stock Purchase Plan

In March 2016, the Company's board of directors approved the 2016 Employee Stock Purchase Plan ("2016 ESPP"), which became effective in June 2016 following the approval of the Company's stockholders. The 2016 ESPP authorizes the issuance of up to a total of 414,639 shares of the Company's common stock to participating employees. The number of shares reserved for issuance under the 2016 ESPP automatically increases on the first business day of each fiscal year, commencing in 2017, by a number equal to the lower of (i) 1% of the shares of common stock outstanding on the last business day of the prior fiscal year; or (ii) the number of shares determined by the Company's Board of Directors. Unless otherwise determined by the administrator of the 2016 ESPP, two offering periods of six months' duration will begin each year on January 1 and July 1. Participating employees purchase stock under the 2016 ESPP at a price equal to the lower of 85% of the closing price on the applicable offering commencement date or 85% of the closing price on the applicable offering termination date. The fair value of the purchase rights granted under this plan was estimated on the date of grant using the Black-Scholes option-pricing model using assumptions as shown below:

	December 31, 2019	December 31, 2018
Expected dividend yield	0%	0%
Anticipated volatility	70.55% - 76.02%	77.49% - 80.59%
Stock price	$6.12 - $8.51	$7.00 - $8.05
Exercise price	$6.12 - $8.51	$7.00 - $8.05
Expected life (years)	0.50	0.50
Risk free interest rate	2.10% - 2.56%	1.61% - 2.11%

At December 31, 2019, the Company has 596,693 shares available for issuance under the 2016 ESPP. A summary of the weighted-average grant-date fair value, shares issued and total stock-based compensation expense recognized related to the 2016 ESPP for the years ended December 31, 2019 and 2018 are as follows:

	December 31, 2019	December 31, 2018
Weighted-average grant-date fair value per share	$ 2.79	$ 2.21
Total shares issued	34,253	14,382
Total stock-based compensation expense	$ 91,790	$ 75,141

12. STOCK PURCHASE WARRANTS

In connection with the Initial Public Offering, the Company issued the underwriters of the offering warrants to purchase up to 60,000 shares of common stock. The warrants were exercisable beginning on May 1, 2015 for cash, or on a cashless basis, at a per share price of $10.00. Unexercised warrants to purchase up to 40,300 shares of common stock expired on May 1, 2019 pursuant to their terms and as of December 31, 2019, none of these warrants were outstanding.

13. COMMITMENTS AND CONTINGENCIES

Guarantees and Indemnifications

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The term of the indemnification is for the officer's or director's lifetime. Through December 31, 2019, the Company had not experienced any losses related to these indemnification obligations and no material claims were outstanding. The Company does not expect significant claims related to these indemnification obligations, and consequently, concluded that the fair value of these obligations is negligible, and no related reserves were established.

In-License Agreements

Madrigal Agreement

The Company is developing ADX-1612 pursuant to a License Agreement with Madrigal Pharmaceuticals, Inc. (Madrigal), entered into on December 26, 2016 (the "Madrigal Agreement"). Pursuant to the Madrigal Agreement, the Company obtained an exclusive, worldwide license from Madrigal under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize Hsp90 inhibitors, including ADX-1612 and ADX-1615 ("Madrigal Agreement Products"). The Company has agreed to use its commercially reasonable efforts to develop Madrigal Agreement Products.

In consideration for the rights licensed under the Madrigal Agreement, the Company paid Madrigal an upfront license fee of $250,000 and are obligated to make future regulatory and development and sales-dependent milestone payments to Madrigal of less than $340 million in the aggregate (over 80% of such amount being tied to the Company's achievement of increasingly greater annual worldwide net sales milestones), as well as royalty payments to Madrigal at a rate which, as a percentage of net sales, is in the high single digits for products containing ADX-1612 and mid-single digits for any other Hsp90 inhibitor product. The Company is also obligated under the Madrigal Agreement to pay Madrigal a percentage of certain sublicense revenue that the Company receives in connection with entering into any sublicensing arrangements with any third parties, at a percentage rate which tiers downward from the mid-twenties to low-single digits based on the development stage of the product at the time of the sublicense.

The Madrigal Agreement will remain in effect until all payment obligations under the Madrigal Agreement expire. The Company may terminate the Madrigal Agreement in its entirety or on a Madrigal Agreement Product-by Madrigal Agreement Product basis with timely notice to Madrigal. Either party may terminate the Madrigal Agreement for uncured material breach by the other party or upon certain insolvency or bankruptcy proceedings involving the other party, both with timely notice to the other party. In addition, Madrigal has the right to terminate

the Madrigal Agreement if the Company, its affiliates, or sublicensees interfere with, challenge the validity or enforceability of, oppose the extension of, or grant of a supplementary protection certificate with respect to any of the Company's licensed patents under the Madrigal Agreement. In the event of an early termination of the Madrigal Agreement, all rights licensed and developed by the Company under the Madrigal Agreement may revert back to Madrigal. Each party has agreed to indemnify the other party for certain third party claims arising under the Madrigal Agreement.

MEEI Agreement

The Company is developing ADX-2191 pursuant to an Exclusive License Agreement with Massachusetts Eye and Ear Infirmary ("MEEI") originally entered into in July 2016 between MEEI and Helio Vision, Inc. (as amended, the "MEEI Agreement"). The Company assumed the MEEI Agreement in connection with its 2019 acquisition of Helio Vision.

Pursuant and subject to the MEEI Agreement, the Company obtained an exclusive, worldwide license from MEEI to develop and commercialize ADX-2191 under certain patents and patent applications, and other licenses to intellectual property (the "MEEI Patent Rights"). The Company has agreed to use our commercially reasonable efforts to develop ADX-2191 and to meet certain specified effort and achievement benchmarks by certain dates.

In consideration for the rights licensed under the MEEI Agreement, Helio Vision issued MEEI a number of shares of its preferred stock and Helio Vision agreed to pay non-creditable non-refundable license maintenance fees to MEEI of $15,000 on each of the second and third anniversary of the MEEI Agreement, $25,000 on each of the fourth and fifth anniversary of the MEEI Agreement and $35,000 on the sixth and each subsequent anniversary of the MEEI Agreement during the term of such agreement. In addition, Helio Vision was obligated to make future sales-dependent milestone payments to MEEI of up to the low seven figures in the aggregate, as well as royalty payments to MEEI at a rate which, as a percentage of net sales, is in the low single digits for products that incorporate or use the MEEI Patent Rights in the United States and as a percentage in the low single digits for products that incorporate or use the MEEI Patent Rights outside the United States. The Company is also obligated under the MEEI Agreement to pay MEEI a percentage of certain sublicense revenue that it receives in connection with entering into any sublicensing arrangements with any third parties, at a percentage rate which tiers downward from low-double digits to mid-single digits based on the date of the sublicense. Following the Company's acquisition of Helio Vision, the Company became obligated to make any future payments owed under the MEEI Agreement. There is no additional equity consideration issuable under the MEEI Agreement.

The MEEI Agreement will remain in effect until the expiration date of the last to expire patent licensed under the MEEI Agreement. The Company may terminate the MEEI Agreement with timely written notice to MEEI. MEEI has the right to terminate the MEEI Agreement if it, subject to certain specified cure periods, ceases all business operations with respect to licensed products, fails to pay amounts due under the MEEI Agreement, fail to comply with certain due diligence obligations, defaults in our obligation to maintain insurance, one of our officers is convicted of a felony relating to the manufacture, use, sale or importation of licensed products, we materially breach any provisions of the MEEI Agreement or in the event of its insolvency or bankruptcy.

In the event of an early termination of the MEEI Agreement, all rights licensed and developed by the Company under the MEEI Agreement may revert back to MEEI. The Company has agreed to indemnify MEEI for certain claims that may arise under the MEEI Agreement.

14. LEASES

The Company currently leases an office used to conduct business. The exercise of lease renewal options is at our discretion and the renewal to extend the lease terms are not included in the Company's Right-Of-Use assets and lease liabilities as they are not reasonably certain of exercise. The Company regularly evaluates the renewal options and when they are reasonably certain of exercise, the Company includes the renewal period in its lease term. As the Company's lease does not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of the lease payments.

As of December 31, 2019, the Company maintained an unamortized Right-Of-Use asset with a corresponding operating lease liability of approximately $0.2 million based on the present value of the minimum rental payments as a result of adoption of ASC Topic 842, *Leases*. The weighted average discount rate used for leases as of December 31, 2019 is 9.1%. The weighted average lease term as of December 31, 2019 is 1.0 years. The operating lease expense for the year ended December 31, 2019 was $210,753. Maturities and balance sheet presentation of our lease liabilities for all operating leases as of December 31, 2019 is as follows:

2020 total lease payments	$ 237,671
Less: effect of discounting	(11,343)
Present value of lease liabilities	$ 226,328
Current operating lease liabilities	$ 226,328
Non-current operating lease liabilities	—
Total	$ 226,328

The Company's gross future minimum payments under all non-cancelable operating leases as of December 31, 2019 are:

	Total	2020	2021	2022	2023
Operating lease obligations	$ 237,671	$ 237,671	$ —	$ —	$ —

15. SUBSEQUENT EVENTS

None.

Exhibit 4.6

DESCRIPTION OF REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 13 OF THE SECURITIES EXCHANGE ACT

DESCRIPTION OF COMMON STOCK

The following description of the common stock of Aldeyra Therapeutics, Inc. ("Aldeyra" or the "Company") is based upon the Company's restated certificate of incorporation, as amended ("Restated Certificate of Incorporation"), the Company's Amended and Restated Bylaws ("Bylaws") and applicable provisions of law. The summary below is not complete and is subject to, and is qualified in its entirety by express reference to, the provisions of the Restated Certificate of Incorporation and Bylaws, each of which is filed as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.6 is a part.

Authorized Capital Stock

Under the Restated Certificate of Incorporation, Aldeyra's authorized capital stock consists of 150,000,000 shares of common stock, par value $0.001 per share, and 15,000,000 shares of preferred stock, par value $0.001 per share.

Common Stock

Aldeyra Common Stock Outstanding. The outstanding shares of the Company's common stock are duly authorized, validly issued, fully paid and nonassessable. The Company's common stock is listed and principally traded on The Nasdaq Capital Market under the ticker symbol "ALDX."

Voting Rights. Each holder of the Company's common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of the stockholders, including the election of directors. Except as otherwise provided by law or the Restated Certificate of Incorporation or Bylaws, all matters other than the election of directors submitted to the stockholders at any meeting shall be decided by the affirmative vote of a majority of the outstanding shares of common stock present in person or represented by proxy at the meeting and entitled to vote thereon. Directors are elected by a plurality of the votes cast at the meeting. The Restated Certificate of Incorporation and Bylaws do not provide for cumulative voting rights. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, the holders of the Company's outstanding shares of common stock are entitled to receive dividends, if any, as may be declared from time to time by the Company's board of directors out of legally available funds.

Liquidation. In the event of the Company's liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of the Company's debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Other Rights and Preferences. Holders of the Company's common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to the Company's common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of the Company's preferred stock that it may designate and issue in the future.

Transfer Agent and Registrar. The transfer agent and registrar for the Company's common stock is American Stock Transfer & Trust Company.

Preferred Stock

The Company's board of directors is authorized to issue preferred stock in one or more series, to establish the number of shares to be included in each such series and to fix the designation, powers, preferences and rights of such shares and any qualifications, limitations or restrictions thereof. The issuance of preferred stock may have the effect of delaying, deferring or preventing a change in control of the Company without further action by the stockholders and may adversely affect the voting and other rights of the holders of common stock. The issuance of preferred stock with voting and conversion rights may adversely affect the voting power of the holders of common stock, including the loss of voting control to others.

Certain Anti-Takeover Effects of Delaware Law

Some provisions of Delaware law and the Restated Certificate of Incorporation and Bylaws could make the following transactions more difficult: the Company's acquisition by means of a tender offer; the Company's acquisition by means of a proxy contest or otherwise; or removal of the Company's incumbent officers and directors.

Section 203 of the Delaware General Corporation Law is applicable to takeovers of Delaware corporations. Subject to exceptions enumerated in Section 203, Section 203 provides that a corporation shall not engage in any business combination with any "interested stockholder" for a three-year period following the date that the stockholder becomes an interested stockholder unless:

- prior to that date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, though some shares may be excluded from the calculation; and
- on or subsequent to that date, the business combination is approved by the board of directors of the corporation and by the affirmative votes of holders of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

Except as specified in Section 203, an interested stockholder is generally defined to include any person who, together with any affiliates or associates of that person, beneficially owns, directly or indirectly, 15% or more of the outstanding voting stock of the corporation, or is an affiliate or associate of the corporation and was the owner of 15% or more of the outstanding voting stock of the corporation, any time within three years immediately prior to the relevant date. Under certain circumstances, Section 203 makes it more difficult for an interested stockholder to effect various business combinations with a

corporation for a three-year period, although the stockholders may elect not to be governed by this section, by adopting an amendment to the certificate of incorporation or bylaws, effective 12 months after adoption. The Restated Certificate of Incorporation and Bylaws do not opt out from the restrictions imposed under Section 203

Certain Provisions of the Company's Restated Certificate of Incorporation and Bylaws

In addition to the Company's board of directors' ability to issue shares of preferred stock, the Restated Certificate of Incorporation and Bylaws contain provisions that may discourage, delay or prevent a change in the Company's management or control over the Company that stockholders may consider favorable. The Restated Certificate of Incorporation and Bylaws:

- authorize the issuance of "blank check" preferred stock that could be issued by the Company's board of directors to thwart a takeover attempt;
- do not provide for cumulative voting in the election of directors, which would allow holders of less than a majority of the stock to elect some directors;
- establish a classified board of directors, as a result of which the successors to the directors whose terms have expired will be elected to serve from the time of election and qualification until the third annual meeting following their election;
- require that directors only be removed from office for cause;
- provide that vacancies on the board of directors, including newly-created directorships, may be filled only by a majority vote of directors then in office;
- limit who may call special meetings of stockholders;
- prohibit stockholder action by written consent, requiring all actions to be taken at a meeting of the stockholders; and
- establish advance notice requirements for nominating candidates for election to the board of directors or for proposing matters that can be acted upon by stockholders at stockholder meetings.

Exhibit 10.39

In accordance with Item 601(b)(2)(ii) of Regulation S-K, certain information (indicated by "***") has been excluded from this exhibit because it is both not material and would likely cause competitive harm to the registrant if publicly disclosed.**

EXCLUSIVE LICENSE AGREEMENT

This Exclusive License Agreement, effective as of July 7, 2016 ("Effective Date"), is between the Massachusetts Eye and Ear Infirmary, a Massachusetts non-profit organization having a principal place of business at 243 Charles Street, Boston, Massachusetts 02114 ("MEEI") and Helio Vision, Inc., a Delaware corporation having a principal place of business at 28 Brent Road, Lexington, MA 02420 ("Licensee").

Background

MEEI is the owner of certain rights in technology as later defined, subject only to a royalty-free, nonexclusive license previously granted to the United States Government; and

MEEI desires to have the rights used to promote the public interest by granting a license;

Licensee has represented to MEEI that it has the capabilities and/or experience to develop, produce, market and sell products utilizing technology that is similar to the technology that is the subject of this Agreement and has the financial capacity and the strategic commitment to facilitate the transfer of the technology for the public interest; and

Licensee desires to obtain a license to MEEI's rights and MEEI is willing to grant a license upon the terms and conditions of this Agreement.

MEEI and Licensee therefore agree as follows.

Article 1 – Definitions

1.1 "Agreement" means this Exclusive License Agreement, including all attached schedules.

1.2 "Affiliate" means any company, corporation or other business entity that is controlled by, controlling, or under common control with Licensee. For this purpose "control" means direct or indirect beneficial ownership of at least fifty percent (50%) interest in the voting stock (or the equivalent) of the company, corporation or other business or having the right to direct, appoint or remove a majority of members of its board of directors (or their equivalents) or having the power to control the general management of the company, corporation or other business, by law or contract.

1.3 "Field of Use" means all fields.

1.4 "First Commercial Sale" means the initial transfer of Licensed Product by or on behalf of Licensee, an Affiliate or Sublicensee for cash or non-cash consideration to which a fair market value can be assigned for purposes of determining Net Sales.

1.5 "Licensed Process" means any process covered in whole or in part by an issued, unexpired claim or a pending claim in Patent Rights.

1.6 "Licensed Products" means any product covered in whole or in part by an issued, unexpired claim or a pending claim in the Patent Rights or products manufactured or services or methods of use provided according to a Licensed Process

1.7 "Net Sales" means the ***** by an entity licensed under this Agreement from the sales of Licensed Products to independent third party customers in bona-fide arms-length transactions less the following deductions, which may not exceed reasonable and customary amounts in the country in which the transaction occurs:

(a) *****;

(b) *****;

(c) *****;

(d) *****.

Net Sales includes the fair market value of any non-cash consideration from sale of Licensed Products received by Licensee, its Affiliates or Sublicenses.

Licensed Products are considered "sold" *****.

1.8 "Patent Rights" means *****, and any conversion, continuation, division, or substitution thereof, any patents issuing thereon, any reissues, reexaminations or extensions of the patents and any foreign counterparts of the patent applications and patents.

1.9 "Sale" or "Sold" means any grant, sale, lease, assignment, transfer, conveyance or other disposition of Licensed Products for value by or on behalf of Licensee, any Affiliate(s) or Sublicensee(s).

1.10 "Sublicensee" means any natural person or legal entity, which is not an Affiliate, to which Licensee grants a sublicense of some or all of the rights granted to Licensee under this Agreement.

1.11 "Territory" means worldwide.

Article 2 – Grant of Licenses, Reserved Rights and Sublicensing

2.1 **License Grants.** Subject to all of the terms and conditions of this Agreement and the non-exclusive license granted to the United States government, MEEI grants to Licensee an exclusive license under Patent Rights, with the right to grant sublicenses, to make, have made, use, offer to sell, sell, export and import Licensed Products and to practice Licensed Processes in the Territory for the Field of Use for the term of this Agreement; and

The license will continue for the term of this Agreement unless the grant is sooner terminated according to Article 8.

2.2 **Affiliates**. Licensee is entitled to extend its licenses under this Article 2 to its Affiliates, consistent with all of the terms and conditions of this Agreement. If Licensee does extend its license and an Affiliate assumes obligations under the Agreement, Licensee remains responsible for performance by the Affiliate. If MEEI has a claim arising under this Agreement against an Affiliate, MEEI may seek a remedy directly against Licensee and may, but is not required to, seek a remedy against the Affiliate. Any termination of the Agreement under Article 8 as to Licensee also constitutes termination as to any Affiliates.

2.3 **No Implied Licenses.** This Agreement confers no license or rights by implication, estoppel or otherwise under any other patent applications or patents owned in whole or in part by MEEI.

2.4 **Reserved Rights.** The licenses granted by MEEI are subject to the following reserved rights.

2.4.1 The rights of the United States of America, as set forth in Public laws 96-517 and 98-620, the regulations promulgated thereunder, and the policy of any funding agencies. Any rights granted hereunder, which are greater than permitted by Public Laws 96-517 and 98-620, are subject to modification as required to conform to the provisions of those statutes.

2.4.2 MEEI's right to make and use the Patent Rights in the Field of Use for teaching, education and research purposes, both laboratory and clinical.

2.4.3 MEEI's right to grant non-exclusive, non-transferable licenses under Patent Rights to other organizations academic, governmental or not-for-profit organizations to make and use the Patent Rights for non-commercial (i) research purposes in the Field of Use and not for use in human subjects, (ii) clinical trials or (iii) diagnostic purposes involving human subjects.

2.5 **Sublicensing.** Licensee has the right to grant sublicenses under this Agreement consistent with the terms and conditions of this Agreement. Licensee remains responsible for the operations of any Sublicensee under this Agreement, as if the operations were carried out by Licensee.

2.5.1 **Notice and Approval**. Licensee shall promptly notify MEEI in writing of the identity of any prospective Sublicensee.

2.5.2 **Form and Content of Sublicenses.** Licensee shall issue any sublicense(s) granted by it under this Agreement in writing and shall attach a copy of this Agreement to all sublicenses.

Licensee shall include the equivalent of at least the following provisions in all sublicenses.

(a) Sublicensee shall use ***** and shall report ***** to Licensee on its operations under the sublicense.

(b) Sublicensee shall make payments due to Licensee in relation to Net Sales of Licensed Products in a timely manner, so that Licensee may comply with its obligations to make payments to MEEI as set forth in Articles 3 and 4 of this Agreement.

(c) The terms and conditions of Section 2.4 (**Reserved Rights.**), Paragraphs 4.2.1 (**Books and Records**) and 4.2.2 (**Inspections)**, Sections 5.2 – 5.6 (**U.S. Manufacture**, **Other Government Laws, Patent Marking, Publicity, and Confidentiality)**, Article 6 (**Patent Preparation, Filing, Prosecution and Maintenance**), Article 7 **(Patent Infringement and Enforcement**), Paragraph 8.4.4 **(Termination- Sublicenses)**, Article 9 (**Indemnification, Defense and Insurance)**, Article 10 (**Disclaimer of Warranties**) and Article 12 **(Dispute Resolution)** of this Agreement are binding on the Sublicensee.

(d) Sublicensees do not have the right to grant further sublicenses.

2.5.3 **Copies of Sublicenses to MEEI.** Licensee shall forward to MEEI a copy of any and all fully executed sublicenses. Such copy shall be postmarked within ***** of the execution of the sublicense. Licensee shall also forward to MEEI ***** a copy of the reports received by Licensee from its Sublicensee during the preceding ***** period under the sublicenses as shall be pertinent to (1) its operations under the sublicense and (2) a royalty accounting under the sublicense agreement.

2.5.4 **Licensee's Continuing Obligations.** Nothing is Section 2.5 may be construed to relieve Licensee of its obligations to MEEI under this Agreement, including but not limited to Licensee's obligations under Article 9.

Article 3 – Consideration - Amounts and Time for Payment

In partial consideration of the rights granted by MEEI to Licensee under this Agreement, Licensee shall make the following payments to MEEI according to this Article 3 and Article 4, on behalf of itself, any Affiliate(s) or Sublicensee(s).

3.1 Reimbursements and Other Financial Consideration

3.1.1 **Past Patent Expenses**. MEEI shall waive the payment of all out-of-pocket expenses incurred and paid by MEEI before the Effective Date for filing, prosecuting, maintaining and enforcing Patent Rights.

3.1.2 **Future Patent Expenses.** Licensee shall pay all reasonable out-of-pocket patent expenses incurred or paid by MEEI on or after the Effective Date for filing, prosecuting, and maintaining Patent Rights according to Article 6. Licensee shall pay MEEI within ***** after MEEI mails Licensee an invoice that documents the out-of-pocket expenses incurred or paid by MEEI during the period being invoiced and states the total amount owed to MEEI.

3.1.3 **Issuance of Shares.** In lieu of an upfront licensing fee, upon the closing of Licensee's first Series A equity financing (the "Financing"), Licensee shall issue to MEEI or its designees a number of shares of Licensee's stock being offered in the Financing having an aggregate value of $25,000.00 based on the value of the Company at the time of the Financing, and subject to the execution by MEEI or its designee of such agreements as are executed by the other investors in the Financing.

3.1.4 **License Maintenance Fees.** Licensee shall pay MEEI a non-creditable, non-refundable license maintenance royalty as follows:

(a) Fifteen thousand dollars ($15,000) due upon the second (2nd) and third (3rd) anniversary of the Effective Date of the Agreement;

(b) Twenty-five thousand dollars ($25,000) due upon the fourth (4th) and fifth (5th) anniversary of the Effective Date of the Agreement; and

(c) Thirty-five thousand dollars ($35,000) due upon the sixth (6th) anniversary of the Effective Date of the Agreement and every anniversary thereafter for the Term of the Agreement.

3.1.5 **Milestone Payments.** With respect to each Licensed Product, Licensee shall make the following milestone payments to MEEI within ***** of the occurrence of the following events, whether Licensee, an Affiliate or Sublicensee achieves the events:

(a) ***** upon cumulative Net Sales of

Licensed Product of *****;

(b) ***** upon cumulative Net Sales of Licensed Product of *****; and

(c) ***** upon cumulative Net Sales of Licensed Product of *****.

3.1.6 **Royalties**. Licensee shall pay MEEI the following royalties on Net Sales by Licensee and its Affiliates as follows:

(a) ***** of Net Sales of Licensed Products that incorporate or use the Patent Rights in the United States.

(b) ***** of Net Sales of Licensed Products that incorporate or use the Patent Rights or related know-how in all countries other than the United States.

3.1.7 **Sublicensing Royalties.** With respect to sales by Sublicensees, Licensee shall pay MEEI an amount equivalent to the sum MEEI would otherwise have received in royalties if Licensed Products were sold directly by Licensee. Recording and payment of these royalties by Licensee must be made according to the provisions of Article 4.

3.1.8 **Royalty Sublicensing or Partnering Income.** Licensee shall pay MEEI a percentage of sublicense issue fees, sublicense milestone payments (to the extent that Licensee receives payments for achieving milestones other than the milestones provided for in paragraph 3.1.7 above), sublicense maintenance fees, technology access fees, and any similar payments made by Sublicensees to Licensee or an Affiliate (collectively, "Sublicense Fees") on account of sublicenses granted under this Agreement as follows:

(a) ***** of Sublicense Fees received by Licensee or Affiliate on the Effective Date to before or on ***** of the Agreement;

(b) ***** of Sublicense Fees received by Licensee or Affiliate after the ***** of the Agreement to before or on ***** of the Agreement; and

(c) ***** of Sublicense Fees received by Licensee or Affiliate during year beginning on the ***** of the Agreement.

Excluded from these royalty obligations are payments that are fees for services or payments for equity. Further, Sublicense Fees do not include any amounts paid by a Sublicensee to Licensee that are equivalent to the sum MEEI would otherwise have received in Milestone Payments from Licensee if Licensed Products were sold directly by Licensee. For example, if all Sales are through a Sublicensee and Sublicensee is required to pay Licensee a royalty of ***** upon cumulative Net Sales of *****, the Sublicense Fee for purposes of the above royalty calculation will be *****, which is the difference between the Milestone Payment owed to MEEI under Section 3.1.5 and the aggregate royalty paid to Licensee. Licensee shall pay these royalties to MEEI within ***** days of each calendar quarter in which the Sublicense Fees are received by Licensee or its Affiliate.

3.2 **Waiver or Deferral.** Waiver or deferral by MEEI of any payment owed under any paragraph under Section 3.1 may not be construed as a waiver or deferral of any subsequent payment owed by Licensee to MEEI.

3.3 **Combination Packages.** If a Licensed Product is sold in a combination package or kit containing other active products or processes, then Net Sales for purposes of determining royalty payments on, or milestone payments with respect to the combination package will be calculated using one of the following methods, but (i) the royalties payable to MEEI may not be reduced to less than ***** of that provided for in paragraph 3.1.6 of this Agreement, and (ii) the Net Sale amount of a Licensed Product for purposes of calculating milestone payments under paragraph 3.1.5 may not be reduced to less than ***** of the Net Sale amount of the combination package or kit containing the Licensed Product :

(a) By multiplying the net selling price of the combination by *****; or

(b) If no separate sales are made of the Licensed Product or any of the active products in such combination package during the royalty-paying period in question, Net Sales for the purposes of determining royalty payments and milestone payments, must be calculated by dividing the *****.

3.4 **Third Party Royalty Offsets.** Licensee may reduce the amount of royalties payable under Section 3.1.6 with respect to any Licensed Product on a country-by-country basis by ***** of the amounts payable by Licensee or any Affiliate or Sublicensee to any third party in consideration for a license, granted after the Effective Date, to any rights under any third party patent, patent application which is necessary in order to have freedom of operation under the Patent Rights in such country; provided, however, that the royalties payable under Section 3.1.6 with respect to such Licensed Product on a country-by-country basis for any Calendar Quarter shall not be reduced below ***** of the amounts set forth in Section 3.1.6 by applying the reduction set forth in this Section 3.4.

3.5 **Reduced Rate after Expiration of Patents**. Licensee's obligation to pay royalties to MEEI under paragraphs 3.1.6, 3.1.7 and 3.1.8 terminate on a country-by-country basis upon expiration of the last-to-expire Patent Right in the applicable country. Licensee's obligation to pay royalties under Section 3.1.6(b) with respect to sales in foreign countries in which Patent Rights are not obtained will terminate upon termination of the U.S. Patent Rights.

Article 4 – Royalty Reports, Payments and Financial Records

4.1 **Royalty Reports**. Within ***** after *****, *****, ***** and *****, of each year in which this Agreement is in effect, Licensee shall deliver to MEEI full, true and accurate reports of its activities and those of its Affiliates or Sublicensee(s), if any, relating to this Agreement during the preceding ***** period. These reports must include at least the following:

(a) Number of Licensed Products manufactured and sold by Licensee, and any Affiliates or Sublicensees, in each country of the Territory;

(b) Total billings for the Licensed Products sold;

(c) Deductions applicable to determining Net Sales;

(d) The nature and amount of Sublicense Fees received by Licensee;

(e) Total royalties due to MEEI;

With each report, Licensee shall pay to MEEI the royalties due and payable. If no royalties are due, Licensee shall so report. If multiple Licensed Products are covered by the license granted under this Agreement, Licensee shall separately identify each Licensed Product in the royalty report and specify which patents/application within Patent Rights are used for each Licensed Product.

4.2 **Record Keeping.**

4.2.1 **Books and Records.** Licensee shall keep, and shall require its Affiliates and Sublicensees to keep, true books of account containing an accurate record (together with supporting documentation) of all data necessary for determining the amounts payable to MEEI. Licensee shall keep it records at its principal place of business or the principal place of business of the appropriate division of Licensee to which this Agreement relates and shall require its Affiliates and Sublicenses to keep their books and records in the same manner.

4.2.2 **Inspections.** In order for MEEI to determine the correctness of any report or payment made under this Agreement, Licensee shall make its records available to MEEI for inspection, for a period of ***** following the end of the calendar year to which they pertain. Licensee shall also require any Affiliates or Sublicensees to make their records available for inspection by MEEI, in the same manner as provided in this paragraph 4.2.2.

MEEI may inspect the records during regular business hours and upon reasonable notice by a certified public accountant selected by MEEI and reasonably acceptable to the licensed entity whose records are being inspected. In conducting inspections under this paragraph 4.2.2, Licensee agrees that MEEI's accountant may have access to all records which MEEI reasonably believes to be relevant to calculating royalties owed to MEEI under Article 3.

MEEI is responsible for the cost of any inspection, unless the examination shows an underreporting or underpayment by any entity in excess of ***** for any ***** period, in which case Licensee shall pay the cost of the inspection as well as any additional sum that would have been payable to MEEI had the Licensee reported correctly, plus interest as set forth in Section 4.5.

4.3 **Form of Payments and Taxes.** Licensee must make all payments to be made to MEEI in Boston, Massachusetts, or at such other place or in such other way as MEEI may reasonably designate. Payments must be paid by check made payable to Massachusetts Eye and Ear and sent to:

Director
Intellectual Property & Commercial Ventures
Massachusetts Eye and Ear
243 Charles Street
Boston, MA 02114

Licensee shall pay all amounts payable to MEEI under this Agreement in United States funds without deduction for taxes, exchange, collection or other charges that may be imposed by any country or political subdivision with respect to any amounts payable to MEEI under this Agreement. Licensee is responsible for paying, or ensuring payment of, such taxes, exchange, collection or other charges.

4.4 **Currency Conversion.** If any currency conversion is required in connection with any payment owed to MEEI, the conversion will be made at the buying rate for the transfer of such other currency as quoted by the Wall Street Journal on the last business day of the applicable accounting period in the case of any payment payable with respect to a specified accounting period or, in the case of any other payment, the last business day before the date the payment is due.

4.5 **Interest.** Any payment owed to MEEI under this Agreement that is not made when due will accrue interest beginning on the first day following the due date specified in Article 3. The interest will be calculated at the annual rate of the sum of (a) ***** plus (b), the prime interest rate quoted by Bank of America on the date the payment is due, the interest being compounded on the last day of each calendar quarter. However, the annual rate may not exceed the maximum legal interest rate allowed in Massachusetts. The payment of interest as required by this Section does not foreclose MEEI from exercising any other rights or remedies it has as a consequence of the lateness of any payment.

Article 5 – Operations under the License

5.1 Due Diligence.

5.1.1 General Obligations. Licensee shall use ***** to bring one or more Licensed Products to the marketplace *****, through a *****. Such efforts must not be less than *****. After commercialization, Licensee shall continue ***** efforts to keep Licensed Products *****.

5.1.2 Development Plan. Within ninety (90) days after the Effective Date, Licensee shall provide MEEI with a bona fide written development plan that describes Licensee's plan for bringing the subject matter of the Patent Rights to practical application ("Development Plan"). The Development Plan must set forth the particular Licensed Product(s) and practical application(s) of Licensed Product(s) that Licensee initially intends to develop, cite Licensee's specific goals and objectives for the ensuing year for developing or commercializing the Patent Rights and outline Licensee's plan for achieving the specific due diligence obligations set forth in Section 5.1.3 below. The outline must include actual or projected financial resources or strategic alliances that will be required to meet such objectives.

5.1.3 Specific Diligence Benchmarks. Licensee shall use its commercially reasonable efforts to meet the following specific effort and achievement benchmarks ("Diligence Benchmarks") by the dates specified in this paragraph. For purposes of this paragraph 5.1.3, MEEI will consider efforts of an Affiliate or Sublicensee as efforts of Licensee:

(a) Within one year of the Effective Date of the Agreement Licensee will obtain orphan drug designation for Licensed Product and identify the path for registration of a Licensed Product; and

(b) Licensee will have a First Commercial Sale of a Licensed Product no later than the ***** after the Effective Date.

5.1.4 Adjustments. The Diligence Benchmarks or dates set forth above may be adjusted by mutual agreement by the parties. If Licensee anticipates any material delays in its ability to achieve the foregoing benchmarks it will provide MEEI written notice together with an explanation of the basis for the delay.

5.1.5 **Development and Commercialization Reports.** On or before *****, Licensee shall provide to MEEI a written report describing the efforts by Licensee, or any Affiliates or Sublicensees, to bring one or more Licensed Products to the marketplace. The report must be in sufficient detail to permit MEEI to monitor Licensee's compliance with the due diligence provisions of this Agreement.

Licensee shall include at least the following in these reports: (a) a summary of Licensee's progress toward meeting the goals and objectives that had been established for the previous year; (b) a summary of Licensees goals and objectives for the ensuing year for developing and commercializing Patent Rights including an identification of additional Licensed Products that Licensee intends to develop, if any; and (c) to the extent not covered by the foregoing, a summary of Licensee's progress in meeting the Diligence Benchmarks of Section 5.1.3.

If multiple technologies are covered by this Agreement, the progress report must provide the information set forth above for each Licensed Product.

5.1.6 **Failure to Perform.** Licensee's failure to perform with any due diligence requirement provided in any paragraph in this Section 5.1 is grounds for MEEI to terminate this Agreement according to Section 8.2.3.

5.2 **U.S. Manufacture.** Licensee shall manufacture Licensed Products leased, used or sold in the United States substantially in the United States as required by 35 U.S.C. 204 and 37 C.F.R. 401 et. seq., as amended. Licensee shall also require any Affiliate(s) or Sublicensee(s) to comply with this U.S. manufacture requirement.

5.3 **Other Government Laws**. Licensee shall comply with, and ensure that its' Affiliates and Sublicensees comply with, all government statutes and regulations that relate to Licensed Products. These include but are not limited to FDA statutes and regulations, the Export Administration Act of 1979, as amended, codified in 50 App. U.S.C. 2041 et seq. and the regulations promulgated thereunder or other applicable export statutes or regulations.

5.4 **Patent Marking**. Licensee shall mark, and shall require its Sublicensees and Affiliates to mark, all Licensed Products sold in the United States with the word "Patent" and the number or numbers of Patent Rights applicable to the Licensed Product.

5.5 **Publicity - Use of Name.** Licensee, its' Affiliate and Sublicensees are not permitted to use the name of "Massachusetts Eye and Ear Infirmary" or any variation, adaptation, or abbreviation thereof, its related entities or its employees, or any adaptations thereof, in any advertising, promotional or sales literature, or in any securities report required by the Securities and Exchange Commission (except as required by law), without the prior written consent of MEEI in each case. However Licensee may (a) refer to publications in the scientific literature by employees of MEEI or (b) state that a license from MEEI has been granted as provided in this Agreement.

5.6 **Confidentiality.** Information that is provided to Licensee in connection with patent prosecution under the terms of Section 6 below is deemed to be MEEI Confidential Information, and information provided by Licensee to MEEI regarding the development, distribution, sales and marketing of the Licensed Products by Licensee, its Affiliates and Sublicensees is deemed to be Licensee Confidential Information. Each party, as a recipient (the "Recipient") of the other party's Confidential Information agrees that, during the term of this Agreement, and for ***** thereafter, to employ all reasonable efforts to maintain the information secret and confidential, such efforts to be no less than the degree of care employed by the Recipient to preserve and safeguard its own confidential information. The information shall not be disclosed or revealed to anyone except employees or agents of or consultants to the Recipient who have a need to know the information and who have entered into a confidentiality agreement with the Recipient under which such employees, agents, or consultants are required to maintain confidential the disclosing party's Confidential Information and such employees, agents, or consultants shall be advised by the Recipient of the confidential nature of the information and that the information shall be treated accordingly. The Recipient's obligations under this Section shall not extend to any part of the information:

(a) that can be demonstrated to have been in the public domain or publicly known and readily available to the trade or the public prior to the date of the disclosure; or

(b) that can be demonstrated, from written records to have been in the Recipient's possession or readily available to the recipient from another source not under obligation of secrecy to the disclosing party prior to the disclosure; or

(c) that becomes part of the public domain or publicly known by publication or otherwise, not due to any unauthorized act by the Recipient; or

(d) that is demonstrated from written records to have been developed by or for the Recipient without reference to confidential information disclosed by the disclosing party; or

(e) that is required to be disclosed by law, government regulation or court order.

Licensee may publish manuscripts, abstracts or the like describing the Patent Rights and inventions contained therein, provided MEEI Confidential Information as defined in this Section, is not included without first obtaining written approval from MEEI to include such MEEI Confidential Information, such approval not to be unreasonably withheld.

Article 6 – Patent Preparation, Filing, Prosecution and Maintenance

6.1 **Responsibility.** MEEI, in its sole discretion, is responsible for preparing, filing, prosecuting and maintaining the patent applications and patents included within Patent Rights. For purposes of this Agreement, patent prosecution includes ex parte prosecution, interference proceedings, reissues, reexaminations and oppositions. In the event that during the term of this Agreement, MEEI elects to abandon the maintenance of any Patent Rights within the Territory, it shall give not less than *****-notice thereof to Licensee and Licensee shall thereupon have the right (i) to file on behalf of MEEI, but at Licensee's expense, all filings, documents, instruments and notices with the appropriate governmental patent office within the appropriate jurisdiction to keep the Patent Rights in full force and effect, and (2) to offset against royalties thereafter payable to MEEI hereunder the reasonable, and substantiated, costs of doing so. As long as the license remains exclusive, MEEI shall provide, or cause its agent to provide, copies of relevant correspondence between MEEI and the United States Patent Office or the various foreign patent offices and give Licensee reasonable opportunity to advise MEEI or MEEI's counsel on such matters. Licensee designates the following individual or department for receiving the patent-related correspondence**.**

Helio Vision, Inc.
28 Brent Road
Lexington, MA 02420

Upon Licensee's request, MEEI shall be available to consult with Licensee on matters relating to preparing, filing, prosecuting or maintaining any of the applications or patents within Patent Rights, which matters may be of particular interest to Licensee. MEEI, shall consider the legitimate interests of Licensee in performing its responsibility under this Section 6.1. MEEI designates the following individual or department to receive such requests by Licensee.

Director
Intellectual Property & Commercial Ventures
Massachusetts Eye and Ear
243 Charles Street
Boston, MA 02114

Cooperation. Licensee shall cooperate with MEEI in preparing, filing, prosecuting and maintaining the patent applications and patents within Patent Rights. Licensee shall provide prompt notice to MEEI of any matter that comes to its attention that may affect the patentability, validity or enforceability of any patent application or patent within Patent Rights.

6.2 **Relinquishing Rights.** Licensee may surrender its licenses under any, of the patents or patent applications within Patent Rights in any country of the licensed Territory by giving ***** advance written notice to MEEI. However, if Licensee is surrendering any patent or application within Patent Rights on which an interference proceeding or opposition has been declared or filed, the notice period is *****. If Licensee so surrenders its rights, it will remain responsible for all patent-related expenses incurred by MEEI during the applicable notice period. Thereafter, Licensee will have no further obligation to pay any patent expenses for the patents or patent applications that it surrendered. Not withstanding the foregoing, if such surrender results in termination of all rights under this agreement, then the termination notice provision in Section 8.3, below, shall apply.

Article 7 - Patent Infringement and Enforcement

7.1 **Notice.** If at any time during the term of this Agreement, Licensee becomes aware of an apparent Substantial Infringement (as defined in Section 7.2) in a particular country of a patent within Patent Rights, it will promptly notify MEEI.

7.2 **Action by MEEI.**

7.2.1 **Procedure.** MEEI is responsible for enforcing its Patent Rights and prosecuting apparent infringers when, in its judgment, such action may be reasonably necessary and justified. Licensee may request MEEI to take steps to protect the Patent Rights from an apparent infringement. However, before MEEI must respond to the request, Licensee shall supply MEEI (i) an opinion of qualified legal counsel demonstrating to MEEI's reasonable satisfaction that an infringement of the Patent Rights exists in a particular country and (ii) with written evidence demonstrating to MEEI's reasonable satisfaction that a Substantial Infringement of the Patent Rights exists in a particular country ("Substantial Infringer").

7.2.2 MEEI has ***** from the date of receiving satisfactory written evidence from Licensee of a Substantial Infringement to decide whether it will seek to terminate the Substantial Infringement. MEEI shall give Licensee notice of its decision by the end of this three-month period. If MEEI notifies Licensee that it intends to prosecute the alleged infringer, then MEEI has ***** from the date of its notice to Licensee to either (a) cause the Substantial Infringement to terminate or (b) initiate legal proceedings against the infringer. If any such suit is brought by MEEI in its own name, or jointly with licensee if required by law, it will be at MEEI's expense and on its own behalf, but MEEI shall not be obligated to bring more than one such suit at a time.

7.2.3 **Licensee's Right to Join.** Licensee independently has the right to join any legal proceeding brought by MEEI under this Section 7.2 and fund up to ***** of the cost of the legal proceeding from the date of joining. If Licensee elects to join as a party plaintiff pursuant to this paragraph 7.2.2, Licensee may jointly participate in the action with MEEI, but MEEI's counsel will be lead counsel.

7.3 Action by Licensee.

7.3.1 Procedure. If MEEI notifies Licensee within the first three-month period that it does not intend to prosecute the Substantial Infringement or, if MEEI fails to cause the Substantial Infringement to terminate or bring legal proceeding to compel termination within ***** of the date of its notice to Licensee, then Licensee may initiate legal proceedings against the alleged infringer, at Licensee's expense according to the terms of this Section 7.3. Before Licensee commences any legal proceeding with respect to the Substantial Infringement, Licensee shall consider in good faith the views of MEEI, particularly as they relate to the potential effects on the public interest. Licensee has the right to join MEEI as a party-plaintiff if required by law, at Licensee's expense.

7.3.2 MEEI's Right To Join. MEEI independently has the right to join any legal proceeding brought by Licensee under this Section 7.3 and fund up to ***** of the cost of the legal proceeding from the date of joining. If MEEI elects to join as a party plaintiff pursuant to this paragraph 7.3, MEEI may jointly participate in the action with Licensee, but Licensee's counsel will be lead counsel.

7.3.3 Reduction of Royalties. If Licensee initiates legal proceedings under this Section 7.3 in any country and MEEI does not independently join the proceeding, License may deduct up to ***** of Licensee's documented costs and expenses of the proceeding (including reasonable attorney fees) from royalties payable to MEEI under paragraphs 3.1.6 and 3.1.7 of this Agreement from sales of Licensed Products covered by the patent(s)-in suit. However, Licensee may not reduce MEEI's royalty payments by more than ***** of the amount otherwise due under Article 3. If ***** of Licensee's costs and expenses exceed the amount of royalties deducted by Licensee for any calendar year, Licensee may, to that extent, reduce the royalties due to MEEI in succeeding calendar quarters for so long as Licensee is actively engaged in legal proceedings to terminate the Substantial Infringement. However, Licensee may not reduce total royalties due to MEEI in a given calendar quarter by more than *****. Licensee's right to reduce royalty payments to MEEI under this paragraph 7.3.3 applies only for so long as the Substantial Infringement continues.

7.3.4 Settlement. Regardless of whether MEEI is joined or joins any legal proceeding initiated by Licensee, no settlement, consent judgment or other voluntary final disposition of the legal proceeding may be entered into without the consent of MEEI.

7.4 Cooperation. If one party initiates legal proceedings to enforce the Patent Rights pursuant to this Article 7, the other party shall cooperate with and supply all assistance reasonably requested by the party initiating the proceedings, at the initiating party's request and expense.

7.5 **Distribution of Amounts Paid by Third Parties.** In any legal proceeding brought by MEEI under Section 7.2 and funded solely by MEEI, any damages or other amounts recovered as a result of the proceeding will be retained by MEEI. In any other legal proceeding, any damages or other amounts will be distributed as follows. The damages or other amounts will first be used to reimburse Licensee and MEEI for litigation costs not paid from royalties and then to reimburse MEEI a sum equivalent to the total amount of royalties and minimum royalties deducted by Licensee under paragraph 7.3.3. The balance, if any, will be divided equally between the parties.

7.6 **Declaratory Judgment Actions.** In the event that any third party initiates a declaratory judgment action alleging the invalidity or unenforceability of the Patent Rights, or if any third party brings an infringement action against Licensee or its Affiliates or Sublicensees because of the exercise of the rights granted Licensee under this Agreement, then Licensee shall have the right to defend such action under its own control and at its own expense; provided, however, that MEEI shall have the right to intervene and assume sole control of such defense, at its own expense. Licensee shall not enter into any settlement, consent judgment or other voluntary final disposition of any action under this Section 7.6 without the consent of the other party, which consent shall not be unreasonably withheld unless the settlement includes any express or implied admission of liability or wrongdoing on MEEI's part, in which case MEEI's right to grant or deny consent is absolute and at its sole discretion. Any recovery shall be first applied to reimburse each party pro rata for any out-of pocket expenses it may have incurred with respect to defense of such action and the remainder shall be retained entirely by the party controlling the action; provided, however, that any recovery for infringement will be distributed as described in Section 7.5.

Article 8 – Term and Termination

8.1 **Term.** Unless terminated earlier under the provisions of this Agreement, this Agreement will terminate on the expiration date of the last to expire of patents within Patent Rights.

8.2 **Termination by Licensor.** MEEI has the right to immediately terminate this Agreement and all licenses granted hereunder by providing Licensee with written notice of termination, upon the occurrence of any of the following events.

8.2.1 Licensee ceases all business operations with respect to Licensed Products.

8.2.2 Licensee fails to pay on schedule any royalty or other payment that has become due and is payable under Articles 3 or 4 of this Agreement and has not cured the default by making the required payment, together with interest due, within ***** of receiving a written notice of default from MEEI requesting such payment.

8.2.3 Licensee fails to comply with any due diligence obligation provided for in Section 5.1, unless Licensee has cured the default by meeting the obligation within ***** of receiving written notice of default from MEEI.

8.2.4 Licensee defaults in its obligations to procure and maintain insurance under Section 9.2.

8.2.5 An officer of the Licensee is convicted of a felony relating to the manufacture, use, sale or importation of Licensed Products.

8.2.6 Licensee materially breaches any other provision of this Agreement, unless Licensee has cured the breach within ***** of receiving written notice from MEEI specifying the nature of the breach.

8.2.7 Termination for Insurance and Insolvency. MEEI may terminate this Agreement immediately upon written notice, with no further notice obligation or opportunity to cure, if Licensee fails to obtain and maintain the insurance required by Section 9. MEEI or Licensee may terminate this Agreement immediately upon written notice, with no further notice obligation or opportunity to cure, if MEEI or Licensee shall become insolvent, shall make an assignment for the benefit of creditors, or shall have a petition in bankruptcy filed for or against it that is not dismissed within ***** of filing.

8.3 **Termination by Licensee.** Licensee has the right to terminate this Agreement without cause by giving MEEI ***** prior written notice.

8.4 **Effect of Termination.**

8.4.1 **No release.** Upon termination of this Agreement for any reason, nothing in this Agreement may be construed to release either party from any obligation that matured prior to the effective date of the termination.

8.4.2 **Survival.** The provisions of Section 3.1 (Patent Expenses), Article 4 (Royalty Reports, Payments and Financial Records), Section 5.5 (Publicity – Use of Name), Section 5.6 (Confidentiality), paragraph 8.4.3 (Inventory), Article 9 (Indemnification, Defense and Insurance), Article 10 (Disclaimer of Warranties) and Article 12 (Dispute Resolution) survive termination or expiration of this Agreement.

8.4.3 **Inventory.** Licensee, any Affiliate(s) and any Sublicensees whose sublicenses are not converted as provided in paragraph 8.4.4, may, after the effective date of termination, sell all Licensed Products that are in inventory as of the date of written notice of termination, and complete and sell Licensed Products which the licensed entity(ies) can clearly demonstrate were in the process of manufacture as of the date of written notice of termination, provided that Licensee shall pay to MEEI the royalties thereon as required by Article 3 and shall submit the reports required by Article 4 on the sales of Licensed Products.

8.4.4 **Sublicenses.** Any sublicenses will terminate contemporaneously with this Agreement. However, any Sublicensee not in default under its sublicense may request conversion of the sublicense to a license directly between MEEI and Sublicensee. MEEI shall not unreasonably withhold its acceptance of such conversion, however, as a condition of MEEI's acceptance, the Sublicensee must first agree to be bound by all of the provisions of this Agreement.

Article 9 – Indemnification, Defense and Insurance

Indemnification and Defense.

9.1 Licensee shall indemnify, defend and hold harmless the Institution and its trustees, officers, medical and professional staff, employees and agents and their respective successors, heirs and assigns (the "Indemnitees"), against any liability, damage, loss or expense (including reasonable attorney's fees and expenses of litigation) incurred by or imposed upon the Indemnitees or any one of them in connection with any claims, suits, actions, demands or judgments: arising out of *****.

9.2 Licensee's indemnification under this Section 9 shall not apply to *****.

9.3 Licensee agrees, at its own expense, to provide attorneys reasonably acceptable to the Institution to defend against any actions brought or filed against any party indemnified hereunder with respect to the subject of indemnity contained herein, whether or not such actions are rightfully brought.

9.4 This Section 9 shall survive expiration or termination of this Agreement.

Insurance.

9.5 Beginning no later than the time any such product, process or service is being commercially distributed or sold (other than for the purpose of obtaining regulatory approvals) by Licensee or by a sub-licensee, affiliate or agent of Licensee, Licensee shall, at its own cost and expense procure and maintain Commercial General Liability (CGL) insurance or other coverage acceptable to the Institution in amounts not less than ***** and naming the Indemnitees as additional insureds. Such CGL or other insurance shall provide:

a. Product liability coverage, and

b. Contractual liability coverage for Licensee's indemnification under Section 9 of this Agreement.

If Licensee elects to self-insure all or parts of the limits described above (including deductibles or retentions which are in excess of *****) such self-insurance program must be acceptable to the Institution and CRICO. The minimum amount of insurance coverage required under this Section 9.5 shall not be construed to create a limit of Licensee's liability with respect to its indemnification under Section 9.1 of this Agreement. Licensee shall provide the MEEI with written evidence of such insurance upon request of MEEI. Licensee shall provide MEEI with written notice at least ***** prior to the cancellation, non-renewal or material change in such insurance, if:

(a) Licensee does not obtain replacement insurance providing comparable coverage within such ***** period, the MEEI shall have the right to terminate this Agreement effective at the end of such ***** without notice of any additional waiting period.

(b) Licensee shall maintain such CGL or other insurance during

(i) the period that any such product, process or service is being commercially distributed or sold (other than for the purpose of obtaining regulatory approvals) by Licensee or by a Sublicensee, Affiliate or agent of Licensee;

(ii) a reasonable period after the period referred to in (iii) (a) above, which in no event shall be less than *****.

(c) This Section 9.5 shall survive expiration or termination of this Agreement.

Article 10 – Disclaimer of Warranties

10.1 MEEI MAKES NO WARRANTY, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR OF FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO ANY PATENT, TRADEMARK, SOFTWARE, NON-PUBLIC OR OTHER INFORMATION, OR TANGIBLE RESEARCH PROPERTY, LICENSED OR OTHERWISE PROVIDED TO LICENSEE HEREUNDER AND HEREBY DISCLAIMS THE SAME.

10.2 MEEI DOES NOT WARRANT THE VALIDITY OF THE PATENT RIGHTS LICENSED HEREUNDER AND MAKES NO REPRESENTATION WHATSOEVER WITH REGARD TO THE SCOPE OF THE LICENSED PATENT RIGHTS OR THAT SUCH PATENT RIGHTS MAY BE EXPLOITED BY LICENSEE, AFFILIATE OR SUBLICENSEE WITHOUT INFRINGING OTHER PATENTS. IF BIOLOGICAL MATERIALS ARE LICENSED HEREUNDER, MEEI MAKES NO REPRESENTATION THAT SUCH MATERIALS OR THE METHODS USED IN MAKING OR USING SUCH MATERIALS ARE FREE FROM LIABILITY FOR PATENT INFRINGEMENT.

Article 11 – Notices

11.1 **Notices to MEEI.** Unless otherwise specified in this Agreement, reports, notices and other communications from Licensee to MEEI as provided hereunder must be sent to:

Director, Intellectual Property & Commercial Ventures
Massachusetts Eye and Ear
243 Charles Street
Boston, MA 02114

or other individuals or addresses as MEEI subsequently furnish by written notice to Licensee.

11.2 **Notices to Licensee.** Unless otherwise specified in this Agreement, reports, notices and other communications from MEEI to Licensee as provided hereunder must be sent to:

Josef von Rikenbach
Helio Vision, Inc.
28 Brent Road
Lexington, MA 02420

or other individuals or addresses as Licensee subsequently furnish by written notice to MEEI.

Article 12 – Dispute Resolution

12.1 **Negotiation between the Parties.** The parties shall first attempt to resolve any controversy that arises from this Agreement, or claim for breach of the Agreement, by good faith negotiations, first between their respective business development representatives and then, if necessary, between senior representatives for the parties, such as the Vice President, Research & Academic Affairs of MEEI and the President of Licensee.

12.2 **Non-Binding Mediation.** If the controversy or claim cannot be settled through good faith negotiation between the parties, the parties agree first to try in good faith to settle their dispute by non-binding mediation under the Mediation Rules of the American Arbitration Association, before resorting to arbitration, litigation or other dispute resolution procedure.

Article 13 - Independent Contractor

13.1 For the purpose of this Agreement and all services to be provided hereunder, both parties are and will be deemed to be, independent contractors and not agents or employees of the other. Neither party has authority to make any statements, representations or commitments of any kind, or to take any action, that will be binding on the other party.

Article 14- Severability

14.1 If any one or more of the provisions of this Agreement is held to be invalid, illegal or unenforceable, the validity, legality or enforceability of the remaining provisions of this Agreement will not in any way be affected or impaired thereby.

Article 15 – Force Majeure

15.1 Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party, including without limitation, fire, floods, embargoes, war, acts of war (whether war is declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, acts of God or acts, omissions or delays in acting by any governmental authority or the other party. Performance shall be excused only to the extent of and during the reasonable continuance of such disability

Article 16 - Non-Assignability

16.1 Neither this Agreement nor any part of the Agreement is assignable by either party without the express written consent of the other, which consent a party will not unreasonably withhold. However, Licensee may assign this agreement in conjunction with the sale of essentially all of its related business assets. Any attempted assignment without such consent is void.

Article 17 - Entire Agreement

17.1 This instrument contains the entire Agreement between the parties. No verbal agreement, conversation or representation between any officers, agents, or employees of the parties either before or after the execution of this Agreement may affect or modify any of the terms or obligations herein contained.

Article 18 - Modifications in Writing

18.1 No change, modification, extension, or waiver of this Agreement, or any of the provisions herein contained is valid unless made in writing and signed by a duly authorized representative of each party.

Article 19 - Governing Law

19.1 The validity and interpretation of this Agreement and the legal relations of the parties to it are governed by the laws of the Commonwealth of Massachusetts without regard to any choice of law principle that would dictate the application of the law of another jurisdiction.

Article 20 – Captions

20.1 The captions are provided for convenience and are not to be used in construing this Agreement.

Article 21 – Construction

21.1 The parties agree that they have participated equally in the formation of this Agreement and that the language herein should not be presumptively construed against either of them.

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed by their duly authorized representatives as of the date first above written.

MASSACHUSETTS EYE AND EAR INFIRMARY	**HELIO VISION, INC.**
By: /s/ Ojas P. Mehta, JD	By: /s/ Tomasz P. Stryjewski MD, MPP
Name: Ojas P. Mehta, JD	Name: Tomasz P. Stryjewski MD, MPP
Title: Director, Intellectual Property & Commercial Ventures	Title: President, Helio Vision, Inc.
Date: July 6, 2016	Date: 7/7/2016

Exhibit 10.40

In accordance with Item 601(b)(2)(ii) of Regulation S-K, certain information (indicated by "***") has been excluded from this exhibit because it is both not material and would likely cause competitive harm to the registrant if publicly disclosed.**

AMENDMENT NUMBER 1 AND WAIVER AGREEMENT TO EXCLUSIVE LICENSE AGREEMENT

THIS AMENDMENT NUMBER 1 AND WAIVER AGREEMENT (this "Amendment"), dated as of December 20, 2018, is entered into by and between Helio Vision, Inc., a Delaware corporation ("Licensee"), and Massachusetts Eye and Ear Infirmary, a Massachusetts non-profit organization ("MEEI"). Licensee and MEEI are the sole parties to that certain Exclusive License Agreement, dated as of July 7, 2017, (the "Agreement"). Capitalized terms used herein and not defined herein have the meanings ascribed to them in the Agreement.

Licensee and MEEI hereby agree as follows:

1. Subsection (b) of Section 5.1.3 of the Agreement is hereby amended by deleting the text "***** after the Effective Date" and replacing it with "*****".

2. MEEI hereby acknowledges that it received, on or about August 29, 2018, a letter (the "2018 Update Letter") from the Licensee's Chief Financial Officer summarizing Licensee's then current royalty payment obligations to MEEI (which were $0.00 as of such date) and containing the Company's Development Plan and information intended to be responsive to Licensee's obligation to provide a progress report pursuant to Section 5.1.5 of the Agreement (a "Progress Report"). MEEI also acknowledges that Licensee obtained the orphan drug designation for Licensed Product contemplated by Section 5.1.3(a) of the Agreement by April of 2018 (and did not receive it within one year of the Effective Date) and that the 2018 Update Letter included a description of the path for registration of Licensed Product that was sufficient to satisfy the Licensee's requirements under Section 5.1.3(a). MEEI hereby waives any breach of the Agreement by Licensee resulting from any failure of Licensee to have delivered the Development Plan within 90 days after the Effective Date, or to have delivered a Progress Report or royalty report pursuant to Section 4.1 of the Agreement prior to delivery of the 2018 Update Letter. MEEI hereby accepts the 2018 Update Letter as satisfying for all purposes of the Agreement the Licensee's obligations pursuant to Sections 4.1, 5.1.3 and 5.1.5 of the Agreement from the Effective Date through the date of the 2018 Update Letter.

3. Except as expressly set forth herein, nothing contained herein shall be deemed to amend, modify or waive any other terms of the Agreement.

4. This Amendment may be executed in any number of counterparts, including by electronic or .PDF format, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Amendment shall be governed by and construed under the laws of the Commonwealth of Massachusetts, exclusive of the provisions thereof governing conflict of laws.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the undersigned have executed this Amendment as an instrument under seal.

HELIO VISION, INC.

By: /s/Josef von Rickenbach
Name: Josef von Rickenbach
Title: President

MASSACHUSETTS EYE AND EAR INFIRMARY

By: /s/John Fernandez
Name: John Fernandez
Title: President

GDSVF&H\4918295.1

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

Aldeyra Therapeutics, Inc.
Lexington, Massachusetts

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-226266) and Form S-8 (Nos. 333-196674, 333-203076, 333-210492, 333-213045, 333-217043, 333-224019, and 333-230161) of Aldeyra Therapeutics, Inc. of our report dated March 12, 2020, relating to the consolidated financial statements and the effectiveness of Aldeyra Therapeutics, Inc.'s internal control over financial reporting, which appears in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ BDO USA, LLP
Boston, Massachusetts

March 12, 2020

Exhibit 31.1

CERTIFICATION

I, Todd C. Brady, certify that:

1. I have reviewed this annual report on Form 10-K of Aldeyra Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statements 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 consolidated 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 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.

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 12, 2020

/s/ Todd C. Brady, M.D., Ph.D.
Todd C. Brady, M.D., Ph.D.
Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Joshua Reed, certify that:

1. I have reviewed this annual report on Form 10-K of Aldeyra Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statements 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 consolidated 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 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.

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 12, 2020

/s/ Joshua Reed
Joshua Reed
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION

In connection with the Annual Report of Aldeyra Therapeutics, Inc. (the "Registrant") on Form 10-K for the annual period ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Todd C. Brady, M.D., Ph.D., Chief Executive Officer and Director of the Registrant, and Joshua Reed, Chief Financial Officer, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to their respective knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: March 12, 2020

/s/ Todd C. Brady, M.D., Ph.D.
Todd C. Brady, M.D., Ph.D.
Chief Executive Officer and Director
(Principal Executive Officer)

Date: March 12, 2020

/s/ Joshua Reed
Joshua Reed
Chief Financial Officer
(Principal Financial and Accounting Officer)

This certification is made solely for the purposes of 18 U.S.C. Section 1350, subject to the knowledge standard contained therein, and not for any other purpose. A signed original of this written statement required by Section 906 has been provided to the Registrant and will be retained by the Registrant and furnished to the United States Securities and Exchange Commission or its staff upon request.

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 Registrant under the Securities Act of 1933 or the Securities Exchange Act of 1934 (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.