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, 2018

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	**The Nasdaq Stock Market, LLC**
(Title of each class)	**(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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer 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 29, 2018, 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 $148,308,896, 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 8, 2019 there were 27,395,425 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 2019 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, 2018, 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, 2018
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Various statements in 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 they will have 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. 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 "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, allergic conjunctivitis, noninfectious anterior uveitis, and Sjögren-Larsson Syndrome. We have additional product candidates in development for proliferative vitreoretinopathy and other retinal diseases, post-transplant lymphoproliferative disease, autoimmune disease, metabolic 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 Heat Shock Protein 90 (Hsp90) 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 five Phase 2 clinical trials in dry eye disease, allergic conjunctivitis, and noninfectious anterior uveitis. In a sixth Phase 2 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. Additionally, in February 2018, we announced a partnership with Janssen, a Johnson & Johnson company, to develop RASP inhibitors for systemic inflammatory diseases. In the future, we may enter into additional partnerships that facilitate the development and commercialization of our product candidates.

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 proliferative vitreoretinopathy, 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) and ADX-1615 (an oral pro-drug of ADX-1612), both of which inhibit Hsp90, a mechanistically differentiated approach for the potential treatment of a number of inflammatory diseases.

As a result of the advancement of our product candidate pipeline, we expect to announce the results of a number of significant clinical trials in 2019:

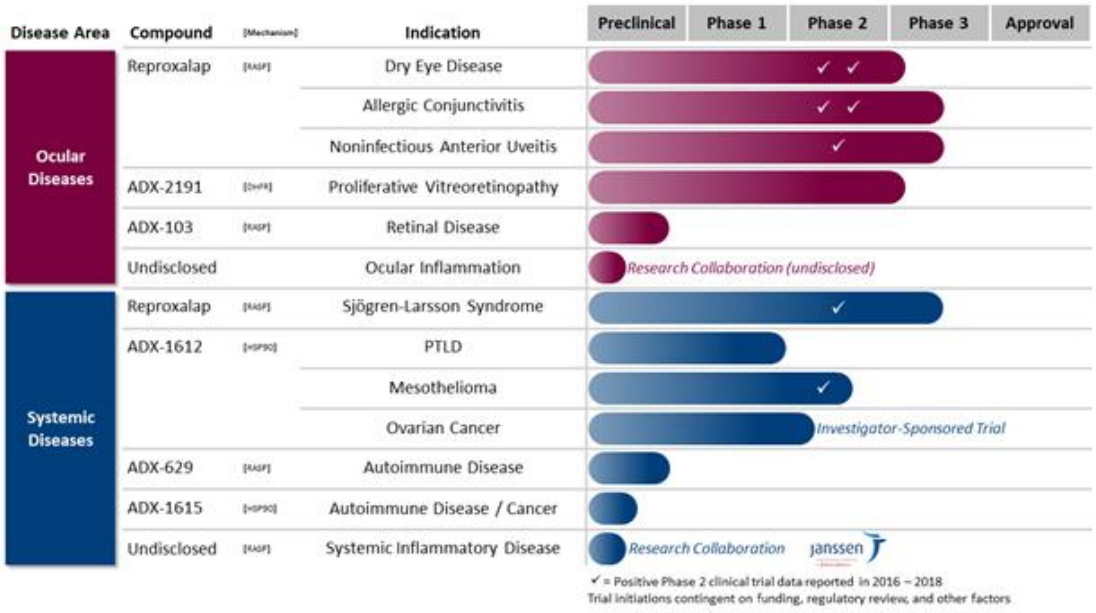
- The ALLEVIATE Phase 3 clinical trial of topical ocular reproxalap in allergic conjunctivitis;
- The SOLACE Phase 3 clinical trial of topical ocular reproxalap in noninfectious anterior uveitis; and
- Part 1 of the RESET Phase 3 clinical trial of topical dermatological reproxalap in Sjögren-Larsson Syndrome.

In addition, we expect to initiate a variety of important clinical programs in 2019:

- The RENEW Phase 3 clinical trial of topical ocular reproxalap in dry eye disease;
- A Phase 3 clinical trial of ADX-2191 in proliferative vitreoretinopathy;
- A Phase 2 clinical trial of ADX-1612 in post-transplant lymphoproliferative disorder;
- A Phase 2 clinical trial of ADX-1612 in mesothelioma; and
- A Phase 1 clinical trial of ADX-629 in autoimmune disease.

By the end of 2019, we expect that our active clinical programs will include six unique product candidates, representing three distinct mechanisms of action across ten 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 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 (ocular pain, dryness, gritty sensation) and allergic conjunctivitis (ocular itching and tearing) are chronic and persistently disturbing, impacting quality of life and leading to loss of work and substantial economic burden. Dry eye disease and allergic conjunctivitis are two of the most common diseases treated by ophthalmologists, and physicians and patients regard therapy as inadequate in a substantial number of cases.

There are approximately 20 million dry eye disease patients in the United States, yet only two drugs are approved for dry eye disease 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.

There are approximately 100 million patients in the United States with allergic conjunctivitis, and we estimate that up to 30 million of such allergic conjunctivitis 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 dry eye disease and allergic conjunctivitis, 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 allergic conjunctivitis patients complain of dryness, which is generally considered the result of dry eye disease. There are currently no United States Food and Drug Administration (FDA)-approved products that are indicated to treat both dry eye disease and allergic conjunctivitis. Neither cyclosporine nor lifitegrast have been approved for use in patients with allergic conjunctivitis, 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 dry eye disease or allergic conjunctivitis 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 dry eye disease and allergic conjunctivitis. In two Phase 2 clinical trials in dry eye disease and two Phase 2 clinical trials in allergic conjunctivitis, 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 dry eye disease, and durable activity in allergic conjunctivitis. Additionally, reproxalap also has added potential of being the only product able to effectively treat dry eye disease and allergic conjunctivitis, uniquely addressing the needs of the large underserved population that suffers from both diseases.

Based on Phase 2 clinical trial results to date, discussed below, we believe reproxalap could offer superior efficacy relative to existing dry eye disease medications, particularly relative 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 dry eye disease, which are generally priced in the range of $500-550 per month. The potential size of the dry eye disease market is substantial. There are approximately 20 million diagnosed dry eye disease patients in the United States. Assuming approximately one-third of diagnosed patients are candidates for prescription medication (roughly 5.3 million patients), and assuming approximately six months of therapy per year, the potential total addressable market for reproxalap therapy in dry eye disease is greater than $17 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. Based in part on similar proprietary topical ocular product launches, we expect that approximately 200-225 sales representatives will be required in the United States to launch reproxalap for ocular inflammation associated with dry eye disease and allergic conjunctivitis.

Noninfectious Anterior Uveitis

There are approximately 260,000 patients in the United States with noninfectious anterior uveitis, a potentially blinding disease that is currently treated with topical ocular corticosteroids. Topical ocular corticosteroid therapy is generally effective but can result in serious ocular toxicity. We estimate that about half of uveitis patients have recurrent (approximately between two to three flares per year) or chronic (four or more flares per year) forms of noninfectious anterior uveitis, requiring multiple consecutive courses of treatment. The known risks of ocular corticosteroid use, including increased intraocular pressure leading to glaucoma, cataract formation, secondary ocular infections, and corneal and scleral thinning, are elevated in recurrent and chronic patients. Given the risks associated with extended corticosteroid use, there is considerable demand for novel therapies that do not cause ocular toxicity following repeated administration.

In a Phase 2 clinical trial in which patients were treated with either reproxalap, topical corticosteroids, or a combination of reproxalap and low-dose topical corticosteroids, reproxalap monotherapy was statistically non-inferior to either corticosteroid monotherapy or combination therapy, suggesting that reproxalap treatment was as effective as corticosteroid treatment. Unlike corticosteroids, in the Phase 2 clinical trial, reproxalap did not induce elevations in intraocular pressure. Thus, reproxalap represents a potentially safer therapeutic option for patients suffering from noninfectious anterior uveitis. Given the fact that noninfectious anterior uveitis is a rare but potentially blinding disease, and given the potential safety advantage of reproxalap versus corticosteroids, we believe that a one-month treatment course of reproxalap therapy could be priced up to $1,500. On average, recurrent and relapsing noninfectious anterior uveitis patient populations require two to five months of treatment per year.

Contingent upon the current Phase 3 clinical program results and regulatory authority approval, we intend to commercialize reproxalap ophthalmic solution for the treatment of NAU. Because the recurrent and chronic forms of NAU are severe and require particular medical expertise, we intend to focus on the roughly 200 uveitis and ocular inflammation sub-specialists in the United States. Thus, we expect that a small number of sales representatives and medical science liaisons will be required for commercialization.

There are many ocular inflammatory diseases that are treated with topical ocular corticosteroids, including scleritis, post-operative inflammation, graft versus host disease, blepharitis, and cyclitis. In 2016, according to IMS data, total sales of topical ocular corticosteroids were approximately $800 million in the United States. Given the potential safety advantages over corticosteroids, reproxalap and similar product candidates have the potential to be first-line treatment options for corticosteroid-responsive ocular diseases in the United States, assuming FDA marketing approval.

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, more than 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 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 18 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 the total market potential of RASP inhibitors for the treatment of retinal disease is substantial.

Sjögren-Larsson Syndrome

Sjögren-Larsson Syndrome (SLS) is a rare systemic disease and inborn error of metabolism caused by mutations in an enzyme that metabolizes fatty (long-chain carbon) RASP, resulting in severe skin, neurological, and retinal disorders. Genetic mutation analysis suggests that there are approximately 1,300 SLS patients in the United States, and a greater number of SLS patients in Europe.

The primary day-to-day complaint of SLS patients and their caregivers is ichthyosis, a severe skin disorder characterized by thick, scaly, dry, flaking, wrinkled, pigmented, pruritic (itchy), inflamed skin. SLS patients are persistently disturbed by pruritus, and often excoriate skin by scratching. The scales that accumulate on the surface of the skin are subject to bacterial overgrowth, which results in an unpleasant odor that is associated with some SLS patients. The ichthyosis in SLS is usually present at birth and stabilizes within the first two years of life, affecting most of the body except the face, palms, and soles. SLS patients are often unable to care for themselves, and require constant monitoring, intensive daily patient care that includes extended bathing routines over multiple hours, and frequent doctor visits. The time required to attend to SLS patients often prevents caregivers from working outside the home. In addition, considerable social stigma and emotional burden is common, especially given scale odor, the flaking skin, and the external misperception that SLS patients suffer from diffuse cutaneous infectious disease. There is currently no therapy approved for the treatment of SLS, though some patients and their caregivers apply non-specific topical creams, including keratinolytics (acids that soften skin), moisturizers, and retinoids. We believe that the effects of keratinolytic and moisturizing creams are minimal or non-existent in treating SLS ichthyosis, and, due to toxicity, retinoids are not suitable for chronic use.

The ichthyosis in SLS is thought to be caused by RASP-mediated modification of lipids (fats) that are generated in the epidermis (the most superficial layer of skin) to form a moisture barrier that holds water in the skin. Moisture barrier compromise leads to water loss, which in turn leads to the epidermal dryness and thickening that are characteristic of ichthyosis. We believe that by lowering levels of RASP and thereby preventing lipid modification and the ensuing moisture barrier dysfunction, reproxalap, when applied topically to the skin, has the potential to ameliorate the dermatologic symptoms of SLS. In April 2017, reproxalap received orphan drug designation from the FDA for the treatment of congenital ichthyosis, including the ichthyosis characteristic of SLS.

We have completed a payer survey to assess potential pricing of topical dermatologic reproxalap for the treatment of ichthyosis associated with SLS. During the survey, payers were informed that topical dermatologic reproxalap is unlikely to affect the neurological and retinal aspects of SLS, and that daily lifelong topical therapy covering 90% of the body surface could be required for disease control. Assuming genetic diagnosis of SLS, payers generally noted that coverage was possible within a range of $200,000 to $400,000 per patient per year.

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 Heat Shock Protein 90 (Hsp90). Hsp90 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 systemic lupus erythematosus (lupus), autoimmune lymphoproliferative syndrome, Waldenstrom’s macroglobulinemia, Wiskott-Aldrich syndrome, post-transplant lymphoproliferative disorder, and myelodysplastic syndromes. We are not aware of any other company that is developing an Hsp90 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, although we have partnered with Janssen, a Johnson & Johnson company, to develop novel RASP inhibiting agents for the treatment of systemic immune-mediated disease. In 2019, we expect to begin clinical testing of ADX-629, a novel drug candidate that inhibits RASP, in autoimmune disease.

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 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 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, Hsp90 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
Noninfectious Anterior Uveitis	Topical corticosteroids
Sjögren-Larsson Syndrome	Off-label use of retinoids, keratinolytics, and moisturizers
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 dry eye disease 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 allergic conjunctivitis, a common comorbidity. Topical antihistamines for the treatment of allergic conjunctivitis are not effective for all patients, in part due to lack of durable activity following exposure to allergen and, in addition, exacerbation of ocular dryness. Topical corticosteroids for noninfectious anterior uveitis and other ocular inflammatory diseases are associated with toxicity including glaucoma, cataracts, and ocular infection, and are not recommended for extended use. There is no approved therapy for Sjögren-Larsson Syndrome, and we believe that the current non-specific creams and medications for Sjögren-Larsson Syndrome are poorly effective, if effective at all. There is no approved therapy for proliferative vitreoretinopathy.

Many drugs are in development for allergic conjunctivitis and dry eye disease. Novartis/Alcon (ESBA105, LME636) and EyeGate Pharmaceuticals, Inc. (EGP-437) have conducted clinical trials in anterior uveitis. We believe that there are no drugs in development for both dry eye disease and allergic conjunctivitis, Sjögren-Larsson Syndrome, or proliferative vitreoretinopathy. 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

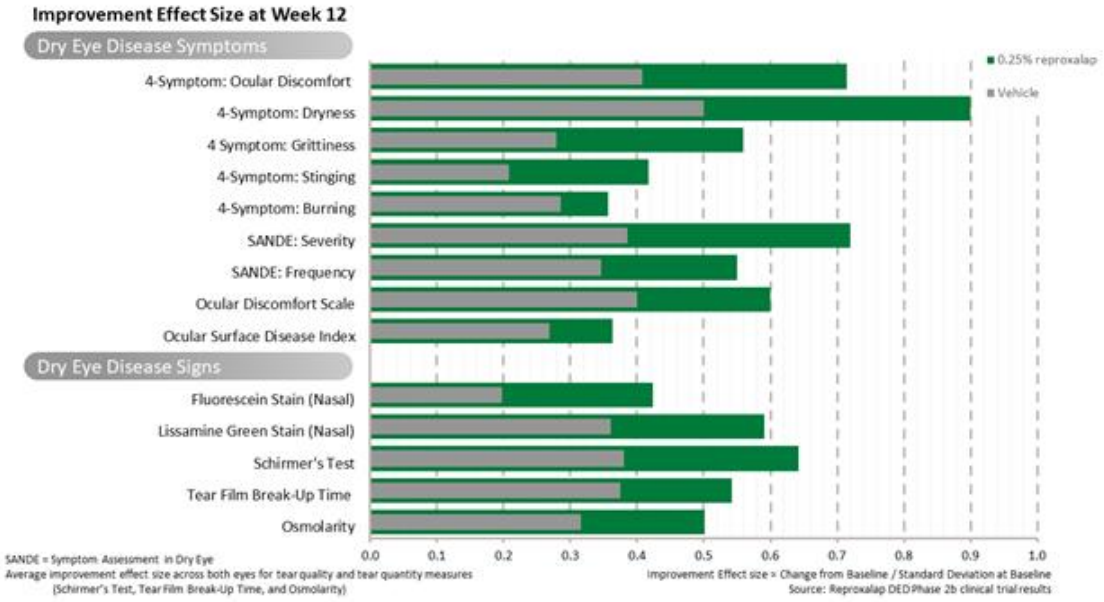
Prior to applying for marketing approval, our product candidates must satisfy regulatory authority requirements for safety and efficacy, including pivotal Phase 3 clinical assessment. Our active clinical programs with reproxalap have consistently demonstrated statistically and clinically significant 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 disclosed elsewhere in detail, and we encourage review of all clinical trial disclosures. Our programs in allergic conjunctivitis, noninfectious anterior uveitis, and Sjögren-Larsson Syndrome have begun Phase 3 clinical testing, and our programs

in dry eye disease and proliferative vitreoretinopathy are expected to begin Phase 3 clinical testing in 2019. 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 dry eye disease (see figure below). 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. Consistent with previous clinical trials, topical ocular reproxalap was well-tolerated, and reported adverse events were generally mild. Based on the success of the Phase 2 clinical trials we plan to initiate Part 1 of a two-part adaptive Phase 3 clinical trial in the first half of 2019. The clinical trial will evaluate the efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle in 400 patients with moderate-to-severe dry eye disease. Results from Part 1 will confirm dosing and size for Part 2 of the Phase 3 clinical trial. The co-primary endpoints of this trial will be ocular dryness, and fluorescein nasal region staining in pre-specified moderate to severe patient subsets analyzed over twelve weeks of therapy using Mixed effects Model Repeated Measures.

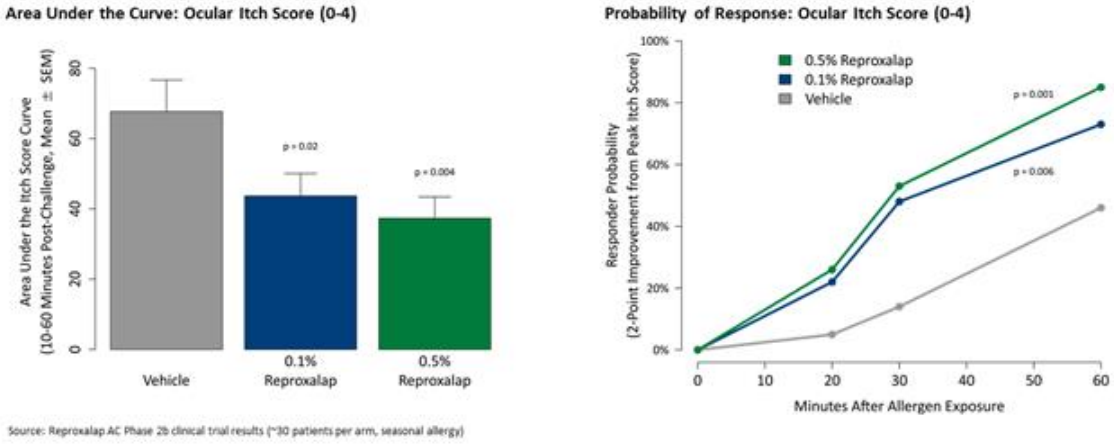
Phase 2b Dry Eye Disease Clinical Trial Results



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 allergic conjunctivitis 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 allergic conjunctivitis 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 (see figure below). A clear dose response was observed. Reproxalap was generally well tolerated and there were no safety concerns observed during the trial.

Phase 2b Allergic Conjunctivitis Clinical Trial Results



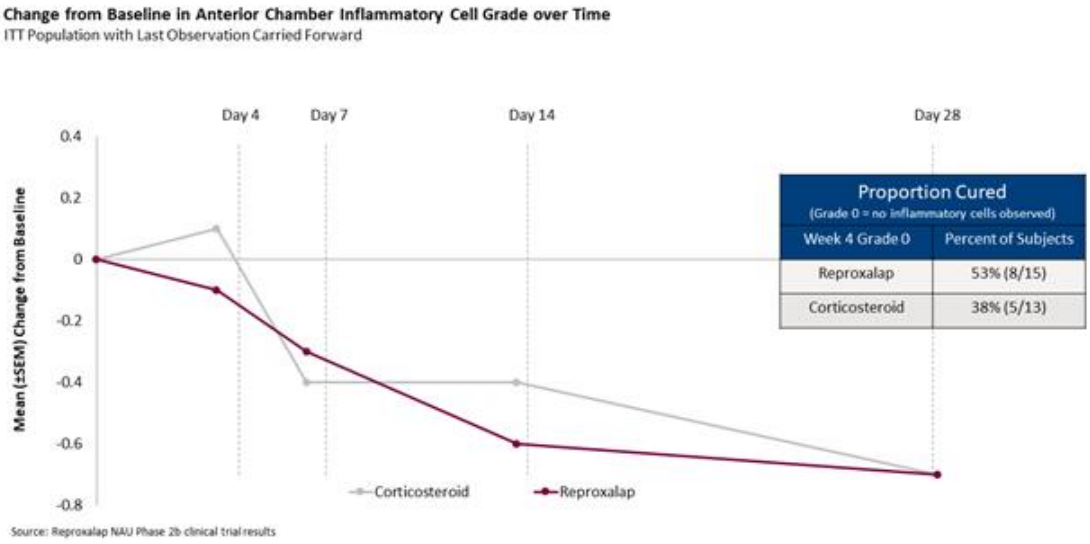
In 2018, based on the success of the Phase 2 clinical trials, we initiated the Phase 3 ALLEVIATE clinical trial of topical ocular reproxalap for the treatment of allergic conjunctivitis. The trial has enrolled over 300 patients, randomized equally to receive a single dose of either 0.25% topical ocular reproxalap, 0.5% topical ocular reproxalap, or vehicle. The primary endpoint is ocular itch score area under the curve 10 to 60 minutes post-challenge. Two-point responder probability is the key secondary endpoint. We expect to report the results of the Phase 3 trial in early 2019. In addition, in preparation for a subsequent Phase 3 clinical trial in allergic conjunctivitis, we have initiated two clinical methods development studies to assess the feasibility of measuring ocular itching following environmental exposure to allergen.

Noninfectious Anterior Uveitis

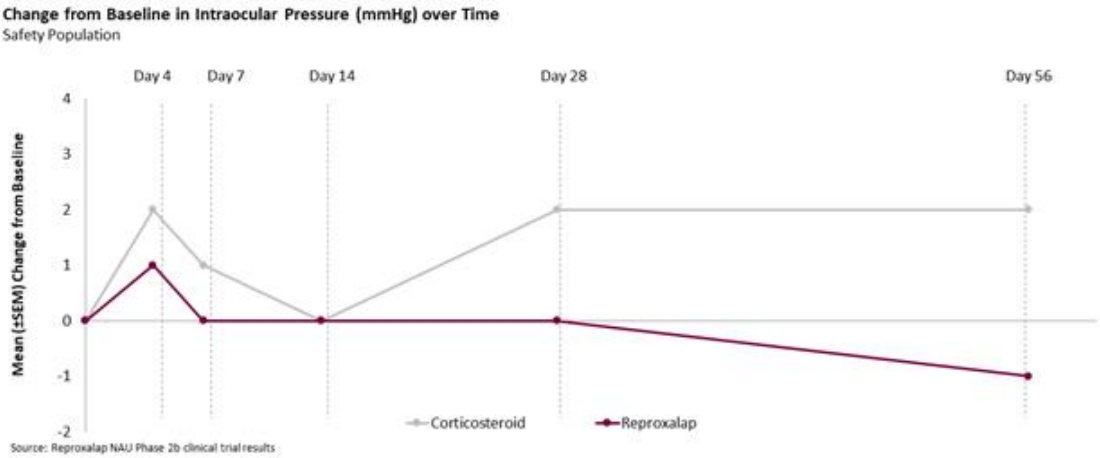
In May 2016, we announced that the results of our randomized, parallel-group, investigator-masked, active-controlled Phase 2 clinical trial of 0.5% reproxalap ophthalmic solution in patients with noninfectious anterior uveitis demonstrated that reproxalap reduced inflammatory cell count in the anterior chamber of the eye to a degree similar to that of standard-of-care corticosteroid therapy (which may lead to cataracts and glaucoma in some patients), but without the intraocular pressure elevations that were observed in subjects treated with corticosteroids. Forty-five subjects were randomized equally to receive six weeks of treatment with one of the following: 0.5% topical ocular reproxalap four times daily; Pred Forte® (1% prednisolone acetate, a corticosteroid) four times daily (tapered); or 0.5% topical ocular reproxalap four times daily and Pred Forte® two times daily (tapered). The results of the trial demonstrated that the activity of reproxalap was statistically non-inferior to Pred Forte® in reducing anterior chamber inflammatory cell count (see figure below). At the week 4 visit, grade 0 cell count (zero cells) was

observed in 53% of reproxalap-treated patients versus 38% of corticosteroid-treated patients. Elevations of intraocular pressure observed in corticosteroid-treated patients were not observed in reproxalap-treated patients (see figure below). Topical ocular reproxalap was observed to be generally well tolerated and there were no serious adverse events.

Noninfectious Anterior Uveitis Phase 2 Clinical Trial Results for Anterior Chamber Cell Count Grade



Noninfectious Anterior Uveitis Phase 2 Clinical Trial Results for Intraocular Pressure (mmHg)

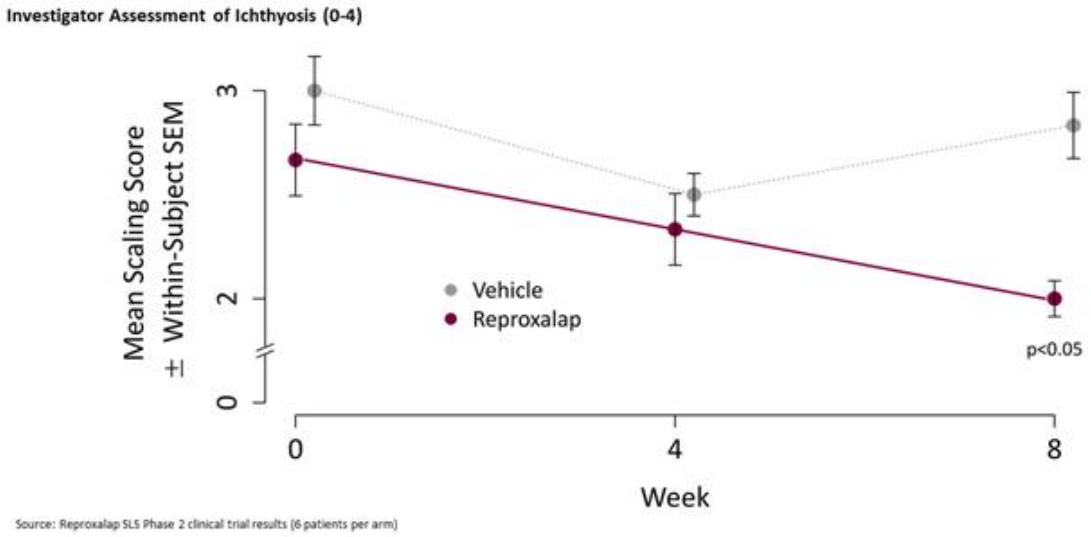


In 2017, based on the success of the Phase 2 clinical trial, we initiated the Phase 3 SOLACE clinical trial of 0.5% topical ocular reproxalap for the treatment of noninfectious anterior uveitis. The trial is expected to enroll approximately 100 patients, randomized equally to receive either topical ocular reproxalap 0.5% or vehicle for four weeks. The primary endpoint is time to zero inflammatory cells in the anterior chamber of the eye. We expect to report results of the Phase 3 clinical trial in the second half of 2019.

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 (see figure below). 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.

Sjögren-Larsson Syndrome Phase 2 Clinical Trial Results for Each Reproxalap-Treated Patient as Assessed by Clinical Exam



In 2018, based on the success of the Phase 2 clinical trial, we initiated the two-part Phase 3 RESET clinical trial of 1% topical dermatologic reproxalap for the treatment of ichthyosis associated with SLS. Part 1 of the trial is expected to enroll approximately nine patients, randomized 2:1 to receive either topical dermatologic reproxalap or vehicle, respectively, for six months. Body surface area coverage will escalate from 20% to 90% over the course of treatment. The primary endpoint will be ichthyosis scaling in drug-treated patients, as assessed by clinical exam using the Visual Index for Ichthyosis Severity, a scoring system similar to the Ichthyosis Severity Score. Part 2 of the RESET trial will be powered based on the results Part 1. The design of Part 2 is expected to be similar to that of Part 1, except that 90% of the body surface area will be treated for six months. We expect to report the results of Part 1 of the Phase 3 trial in the second half of 2019.

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.

We plan to begin a two-part, multi-center, non-masked, randomized, controlled, adaptive Phase 3 clinical trial of ADX-2191 in patients with PVR in the second half of 2019, following discussions with regulatory authorities. The trial is expected to compare patients treated with ADX-2191 to patients receiving standard of care. We expect to report results in 2020.

Mesothelioma and Other Cancers

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. Pending discussions with regulatory authorities, we plan to initiate a Phase 2 clinical trial of ADX-1612 in mesothelioma in 2019. In addition, a European-based investigator-sponsored trial (EUDARIO) of ADX-1612 in combination with either platinum therapy or a PARP (poly [ADP-ribose] polymerase) inhibitor has been initiated in ovarian cancer patients.

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-kB, 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 Sjögren-Larsson Syndrome, mutations in fatty aldehyde dehydrogenase are responsible for skin, neurological, and retinal disease. In particular, ichthyosis, the severe skin disease associated with Sjögren-Larsson Syndrome, 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-a, 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-kB 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, which may begin in 2019, depending on additional preclinical data, regulatory discussions, funding, and other factors.

The Immune Modulating and Anti-Proliferative Activity of Hsp90 Inhibition

ADX-1612 is a novel, highly potent small molecule Hsp90 inhibitor that has completed numerous clinical trials in oncologic diseases. Hsp90 is a protein involved in the processing of other proteins that are critical for physiologic cellular function. Inhibition of Hsp90 leads to diminished cellular replication. We intend to develop ADX-1612 for the treatment of one or more systemic lymphoproliferative inflammatory diseases where excessive immune cell replication leads to inflammation, organomegaly, and other pathologies. ADX-1612 appears to be reasonably well tolerated at doses that may be sufficient to diminish immune cell replication.

Hsp90 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, and an oral pro-drug of ADX-1612 (ADX-1615), in combination with DNA-damaging agents, may have utility in the treatment of certain cancers. Hsp90 is required for DNA repair, and Hsp90 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.

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.

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, Hsp90 inhibitors, and the therapeutic methods of use of dihydrofolate reductase 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, ADX-1615, and other novel compounds. As of December 31, 2018, 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 ADX-1615, 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

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 and ADX-1615 (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 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.

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, 2018, we had 19 full time employees and had engaged a number of consultants. We intend to increase our employee base in connection with the continuing clinical development of our product candidates. 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 $29.8 million for the year ended December 31, 2018 and $16.3 million for the year ended December 31, 2017.

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 and the Development and Commercialization of our Product Candidates

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 years ended December 31, 2018 and 2017 was approximately $38.9 million and $22.3 million, respectively. As of December 31, 2018, we had total stockholders' equity of $86.6 million and an accumulated deficit of $138.5 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 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. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, reproxalap.

Our product candidates, including reproxalap, are in the early stage of development and 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 to trap and allow for the degradation of 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. 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 complete necessary clinical trials;
- we may not be able to provide evidence of safety and efficacy;
- 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 safety and efficacy results of our later phase or larger clinical trials may not confirm the results of our earlier trials;

- there may be variability in patients, adjustments to clinical trial procedures and inclusion of additional clinical trial sites;
- 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 initial parts of adaptive clinical trials are not designed to be pivotal or definitive, as such we may need to revise the design or endpoints to achieve success in later parts of the trial or potentially abandon the trial;
- 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 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;
- 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;
- the effects of 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.

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;
- 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;
- 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.

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. 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. Our Phase 3 clinical trial in SLS is an adaptive trial, where Part 1 is not designed to be pivotal or definitive. Rather, Part 1 is expected to provide data to allow us to design Part 2 of the trial, which could require design changes, including but not limited to, different end points. Further, we have proposed to the FDA a novel assessment methodology for our Phase 3 clinical program in allergic conjunctivitis, which may require changes to the design of subsequent Phase 3 clinical trials. As we prepare for a subsequent Phase 3 clinical trial in allergic conjunctivitis, we have initiated two clinical methods development studies to assess the feasibility of measuring ocular itching following environmental exposure to allergen. If neither clinical methods study yields favorable results, subsequent Phase 3 testing may not be feasible or cost-effective, and it may be difficult or impossible for us to complete clinical testing of reproxalap for the treatment of allergic conjunctivitis. 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 these 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, take longer and require more 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.

Because 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.

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.

Our dermatologic topical formulation of reproxalap is unlikely to affect other clinical manifestations of Sjögren-Larsson Syndrome, which may decrease the likelihood of regulatory and commercial acceptance.

While the primary day-to-day complaint of SLS patients and their caregivers are symptoms associated with severe skin disease, SLS patients also manifest varying degrees of delay in mental development, spasticity, seizures, and retinal disease. In August 2016, we announced that the results of our randomized, parallel-group, double-masked, vehicle-controlled clinical trial of a dermatologic formulation of reproxalap for the treatment of the skin manifestations of SLS demonstrated clinically relevant activity of reproxalap in diminishing the severity of ichthyosis, a serious dermatologic disease characteristic of SLS. Given the expected low systemic exposure of reproxalap when administered topically to the skin, it is not possible to anticipate the effect of reproxalap on the non-dermatologic conditions of SLS. Lack of effect in neurologic and ocular manifestations of SLS may negatively impact the potential market for reproxalap in SLS, and may also negatively impact reimbursement, pricing, and commercial acceptance of reproxalap, if approved.

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, often takes many years, and can vary substantially based upon the type, complexity, and novelty of the products involved, as well as the target indications, 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 never 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 in the non-treatment arm than was expected when designing and powering 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 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 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.

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.

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. Given that we are in the early stages of clinical trials for reproxalap and our other product candidates, 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 these rare patient populations, which may adversely impact the rate of patient enrollment in and the timely completion of our current and planned clinical trials. Additionally, insufficient patient enrollment, may be a function of many 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. 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 their 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.

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 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 one or both 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 2017, we announced that the FDA granted reproxalap orphan drug designation for the treatment of congenital ichthyosis, a severe skin disease characteristic of SLS. In addition, it may be difficult or not possible 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 believe that reproxalap and certain of our other product candidates may qualify as an orphan drug for noninfectious anterior uveitis, and possibly other diseases that we may test. However, we cannot guarantee that we will be able to receive orphan drug designation for indications other than treatment of ichthyosis or breakthrough therapy designation from the FDA for reproxalap or our other product candidates. If we are unable to secure orphan drug designation, 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, 2018, we had only 19 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 CROs 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 any 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 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 potential to demonstrate safety and efficacy. Even if we are successful in our efforts to establish development partnerships, the terms that we agree upon may not be favorable to us and we may not be able to maintain such development 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 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 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 as well as with new treatments that may be introduced by our competitors. With the exception of SLS, there are a variety of drug candidates in development for the indications that we intend to test. 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 four 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 J. Clark, M.D., our Chief Medical Officer; and David B. McMullin, M.B.A., our Chief Commercial Officer. 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 candidate, 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, 2018, we only had 19 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;

- 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 Commissioner position is vacant, pending the appointment of a new Commissioner by the new presidential administration. 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 Annual 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.

To the extent that we enter markets outside the United States, our business will be subject to political, economic, legal and social risks in those markets, which could adversely affect our business.

There are significant regulatory and legal barriers in markets outside the United States that we must overcome to the extent we enter or attempt to enter markets in countries other than the United States. We will 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 outside the United States 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;
- 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, as they relate to our services and business. 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 operation 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. For example, we recently acquired Helio Vision, Inc. and obtained the rights to ADX-2191, an intravitreal DHFR inhibitor (methotrexate) for the prevention of PVR. These initiatives may include acquiring businesses, technologies, or products, or entering into a business combination with another company. 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.

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 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 others, 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, we cannot be certain that the claims in our patent applications covering composition-of-matter of our other product 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.

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 Financial Position and Need for Capital

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize reproxalap and our other product candidates.

We will require substantial future capital in order to complete the remaining clinical development for reproxalap and our other product candidates, and to potentially commercialize these product candidates, if approved. We expect our spending levels to increase in connection with our clinical trials of reproxalap and our other product candidates, as well as other corporate activities. 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 which 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, and uncertainty as to the general direction of the macroeconomic environment, 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 some or all of our activities. We also could be required to seek funds through arrangements with collaborative partners that may require us to relinquish rights to our product candidates or other technologies, or otherwise agree to terms unfavorable to us.

If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

On November 20, 2018, we repaid in full all outstanding indebtedness and terminated all commitments under the $5.0 million Credit Facility with Pacific Western Bank. 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 a 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 (Code), 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, even those outside our control, such as purchases or sales by investors, within the testing period 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. We have undergone three ownership changes through the year ended December 31, 2018. However, our management believes that we had sufficient "Built-In-Gain" to offset the Section 382 limitation generated by such ownership changes. Any future

ownership changes may cause our existing tax attributes to have additional limitations. In addition, we may not be able to have sufficient future taxable income prior to their expiration because net operating losses have carryforward periods. 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 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:

- our ability to enroll patients in our planned clinical trials;
- results of clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory developments in the United States and foreign countries;
- 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 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;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting reproxalap and our other product candidates;
- our execution of any collaborative, licensing, or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- nature and terms of stock-based compensation grants; and
- derivative instruments recorded at fair value.

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.

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.

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 of our cash and cash equivalents to fund our planned clinical trials of reproxalap and our other product candidates, development of other molecules that relate to immune-mediated disease, service our debt obligations and the remainder for working capital and 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.

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, 2018, 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.

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.

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, future debt financing arrangements, if any 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 are eligible for sale as are 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 an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding nonbinding advisory votes on executive compensation, and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company until December 31, 2019, although circumstances could cause us to lose that status earlier, including: if we become a large accelerated filer; if we have total annual gross revenue of $1.07 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31; or, if we issue more than $1.0 billion in non-convertible debt during any three year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on emerging growth 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, we are incurring significant legal, accounting, and other expenses that we did not incur as a private company. 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. Recent legislation permits smaller "emerging growth companies" to implement many of these requirements over a longer period up to five years from our Initial Public Offering. We intend to continue to take advantage of this new legislation, but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned, incurring unexpected expenses. 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. When and if we are a "large accelerated filer" or an "accelerated filer" and are no longer an "emerging growth company," each as defined in the Exchange Act, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls 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 upgrade our systems including information technology; implement additional financial and management controls, reporting systems, and procedures; and hire additional accounting and finance staff.

Historically, we have not had sufficient accounting and supervisory personnel with the appropriate level of technical accounting experience and training necessary, or adequate formally documented accounting policies and procedures to support, effective internal controls. As we grow, we will 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.

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.

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, 2018, 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*

Recent Sales of Unregistered Securities

During the year ended December 31, 2018, we issued 5,133 shares of our common stock upon the cashless net exercise of previously issued warrants. The issuance was made in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act as the transactions did not involve a public offering. The holders provided representation letters pursuant to Rule 144 promulgated under Section 4(a)(1) of the Securities Act.

Holders of Record

As of December 31, 2018, there were 10 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. 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 inflammatory diseases. Our lead product candidate, reproxalap, is a first-in-class treatment in late-stage development for dry eye disease, allergic conjunctivitis, noninfectious anterior uveitis and Sjögren-Larsson Syndrome. We have additional product candidates in development for proliferative vitreoretinopathy and other retinal diseases, post-transplant lymphoproliferative disease, autoimmune disease, metabolic 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 RASP inhibitor that has been shown to diminish ocular inflammation, and has demonstrated statistically significant and clinically relevant improvements across an aggregate of five Phase 2 clinical trials in DED, AC, and NAU. In a sixth Phase 2 clinical trial, reproxalap demonstrated statistically significant and clinically relevant improvements in ichthyosis caused by SLS, a rare systemic disease with no approved therapy where RASP accumulate due to genetic mutations in a RASP-metabolizing enzyme. There is a growing body of clinical evidence supporting 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. Additionally, in February 2018, we announced a partnership with Janssen, a Johnson & Johnson company, to develop RASP inhibitors for systemic inflammatory diseases. In the future, we may enter into additional partnerships that facilitate the development and commercialization of our product candidates. All of our development timelines may be subject to adjustment depending on recruitment rate, regulatory review, preclinical and clinical results, and other factors that could delay the initiation, completion, or reporting of clinical trials.

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 February 2017, we closed an underwritten public offering in which we sold 2,555,555 shares of our common stock, including 333,333 shares sold in connection with the exercise in full by the underwriters of their option to purchase additional shares. The net proceeds of the offering, including the full exercise of the option, were approximately $10.6 million, after deducting the underwriting discounts and commissions and the other estimated offering expenses payable by us. 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 Sales Agreement and other offering costs. In September 2017, we closed an underwritten public offering in which we sold an aggregate of 3,967,500 shares of common stock, including 517,500 shares sold in connection with the exercise in full by the underwriters of their option to purchase additional shares. The net proceeds of the offering, including the full exercise of the option, were approximately $26.9 million, after deducting underwriting discounts, commissions, and other offering expenses payable by us. 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. No sales had been made pursuant to the Jefferies Sales Agreement as of December 31, 2018.

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 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 initially issued an aggregate of 1,150,990 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.

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

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation. Our general and administrative expenses consisted primarily of payroll expenses for our full-time employees during the years ended December 31, 2018 and 2017. 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, 2018, comprehensive loss is equal to our net loss of $38.9 million and an unrealized gain on marketable securities of $9,000. For the year ended December 31, 2017, comprehensive loss is equal to our net loss of $22.3 million and an unrealized loss on marketable securities of $18,000.

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.

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.

Stock-Based Compensation

Stock-based compensation expense represents the grant date fair value of restricted stock awards and stock option grants, which are being recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis, net of estimated forfeitures. In the quarter ended September 30, 2018, we adopted provisions of ASU 2018-07. With this adoption, we changed the expense recognition for share-based payments to non-employees to an amount determined at grant or modification date instead of a variable amount to be valued at each reporting period. This aligns the accounting for share-based payments of non-employees with that of employees.

The Black-Scholes option pricing model requires the input of highly subjective assumptions, including the risk-free interest rate, the expected volatility of our stock, the expected term of the award, and the expected dividend yield. We have computed the historical volatility of our own stock price and have determined that a volatility range of 76.52%-78.38% is reasonable. We have 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. 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.

The assumptions used in the Black-Scholes option pricing model to determine the fair value of employee stock option grants in 2018 and 2017 were as follows:

	December 31, 2018	December 31, 2017
Expected dividend yield	0%	0%
Anticipated volatility	76.52% - 78.38%	76.52% - 88.57%
Stock price	$6.80 - $11.83	$4.90 - $6.10
Exercise price	$6.80 - $11.83	$4.90 - $6.10
Expected life (years)	5.50 - 6.25	5.50 - 6.25
Risk free interest rate	2.32% - 3.10%	1.87% - 2.26%

Other Information

Net Operating Loss Carryforwards

As of December 31, 2018, the Company had Federal and State income tax net operating loss ("NOL") carryforwards of approximately $93.5 million and $89.7 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 carry forward indefinitely. As of December 31, 2018, we have Federal and State research and development tax credit carryforwards of approximately $3.3 million and $0.6 million, respectively, which will expire at various dates through 2038.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended (Code), 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, even those outside our control, such as purchases or sales by investors, within the testing period 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. We have undergone three ownership changes through the year ended December 31, 2018. However, our management believes that we had sufficient "Built-In-Gain" to offset the Section 382 limitation generated by such ownership changes. Any future ownership changes may cause our existing tax attributes to have additional limitations. In addition, we may not be able to have sufficient future taxable income prior to their expiration because net operating losses have carryforward periods. However, 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 –

In June 2018, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2018-07, Compensation — Stock Compensation (Topic 718) (ASU 2018-07). The amendments in ASU 2018-07 expand the scope of the employee share-based payments guidance to include share-based payments issued to non-employees. The amendments specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards to non-employees. We adopted the provisions of ASU 2018-07 in the quarter ended September 30, 2018 and it did not have a material impact on our financial statements. When adopting the provisions of ASU 2018-07, we changed the expense recognition for share-based payments to non-employees to an amount determined at grant or modification date instead of a variable amount to be valued at each reporting period.

In August 2016, the FASB issued ASU No. 2016-15 (ASU 2016-15), Statement of Cash Flows. The standard is intended to reduce the diversity in practice around how certain transactions are classified within the statement of cash flows. We adopted ASU 2016-15 in the quarter ended March 31, 2018, and it did not have a material impact on our financial statements.

In February 2016, the FASB issued ASU No. 2016-02 (ASU 2016-02), Leases. 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. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018. We are currently evaluating the impact of the guidance on our condensed financial statements and related processes and internal controls. While we expect the implementation to result in the recognition of right-of-use assets and lease liabilities for the lease of our occupied office space, the right-of-use assets and lease liabilities will not have a material impact on our financial statements. There is no material uncertainty of cash flows arising from our lease.

In January 2016, the FASB issued ASU No. 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities (ASU 2016-01). ASU 2016-01 amends the guidance on the classification and measurement of financial instruments. Although ASU 2016-01 retains many current requirements, it significantly revises accounting related to the classification and measurement of investments in equity securities and the presentation of certain fair value changes for financial liabilities measured at fair value. ASU 2016-01 also amends certain disclosure requirements associated with the fair value of financial instruments. We adopted ASU 2016-01 in the quarter ended March 31, 2018, and it did not have a material impact on our financial statements.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606), which supersedes the revenue recognition requirements in ASC 605, Revenue Recognition. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The ASU also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. We adopted ASU 2014-09 on January 1, 2018, and it did not have a material impact on our financial statements.

JOBS Act

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and are eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including, but not limited to, only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy or information statements, exemptions from the requirements of holding a non-binding advisory vote on executive compensation and seeking stockholder approval of any golden parachute payments not previously approved and not being required to adopt certain accounting standards until those standards would otherwise apply to private companies.

As an emerging growth company, we have irrevocably elected to not take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards and, as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

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, 2018 and 2017

Net loss. Net loss for the years ended December 31, 2018 and 2017 was approximately $38.9 million and $22.3 million, respectively. As of December 31, 2018, we had total stockholders' equity of $86.6 million. Losses have resulted principally from costs incurred in our clinical trials and other research and development programs, as well as from our general and administrative expenses.

Research and development expenses. Research and development expenses were $29.8 million for the year ended December 31, 2018 compared to $16.3 million for the same period in 2017. The increase of $13.5 million is primarily related to the increase in our external research and development expenditures, including clinical and manufacturing costs, personnel, and preclinical costs.

General and administrative expenses. General and administrative expenses were $9.9 million for the year ended December 31, 2018, compared to $6.2 million for the year ended December 31, 2017. The increase of approximately $3.7 million is primarily related to an increase in personnel, patent-related legal, and professional service costs.

Other income (expense). Total other income (expense) was approximately $806,000 for the year ended December 31, 2018 compared to $148,000 for the year ended December 31, 2017 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 borrowings under our Credit Facility, discussed below. We have incurred operating losses since inception and negative cash flows from operating activities in devoting substantially all of our efforts towards research and development. At December 31, 2018, we had total stockholders' equity of approximately $86.6 million, and cash, cash equivalents, and marketable securities of $93.6 million. During the year ended December 31, 2018, we had net loss of approximately $38.9 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 February 2017, we closed an underwritten public offering in which we sold 2,555,555 shares of our common stock, including 333,333 shares sold in connection with the exercise in full by the underwriters of their option to purchase additional shares. The net proceeds of the offering, including the full exercise of the option, were approximately $10.6 million, after deducting the underwriting discounts and commissions and the other estimated offering expenses payable by us.

In June 2017, we entered into a Controlled Equity Offering SM Sales Agreement (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 Sales Agreement and other offering costs.

In September 2017, we closed an underwritten public offering in which we sold an aggregate of 3,967,500 shares of common stock, including 517,500 shares sold in connection with the exercise in full by the underwriters of their option to purchase additional shares. The net proceeds of the offering, including the full exercise of the option, were approximately $26.9 million, after deducting underwriting discounts, commissions, and other offering expenses payable by us.

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. No sales had been made pursuant to the Jefferies Sales Agreement as of December 31, 2018.

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of December 31, 2018, will be adequate to fund our currently anticipated operating expenses through the end of 2020, including the currently planned announcements of top-line data from Phase 3 clinical trials in allergic conjunctivitis, noninfectious anterior uveitis, SLS (Part 1) and dry eye disease. 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 remediate any material weaknesses and 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, 2018 and 2017:

	Years ended December 31,	
	2018	2017
Net cash used in operating activities	$ (29,857,131)	$ (19,222,862)
Net cash used in investing activities	(23,335,576)	(10,197,842)
Net cash provided by financing activities	80,526,842	37,428,980
Net increase in cash and cash equivalents	$ 27,334,135	$ 8,008,276

Operating Activities. Net cash used in operating activities was $29.9 million in 2018, compared to net cash used in operating activities of $19.2 million in 2017. The primary use of cash was to fund our operations. The increase in the amount of cash used in operating activities for 2018 as compared to 2017 was due to an increase in research and development expenses, in addition to general and administrative expenses.

Investing Activities. Net cash used in investing activities in 2018 were $23.3 million, related primarily to the purchase of marketable securities partially offset by sales and maturities of marketable securities, compared to net cash used in investing activities in 2017 of $10.2 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 $80.5 million for the year ended December 31, 2018, related to our underwritten public offering and sales of common stock under the Cantor Sales Agreement, compared to net cash provided by financing activities of $37.4 million for year ended 2017, related to our underwritten public offerings.

Off-Balance Sheet Arrangements

Through December 31, 2018, 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

The following table summarizes our contractual obligations at December 31, 2018:

	Total	Less than 1 Year	Years 1 - 3	Years 3 - 5	More than 5 Years
Operating lease obligations	$ 465,991	$ 228,320	$ 237,671	$ —	$ —

The table above detailing contractual commitments and obligations does not include severance pay obligations to certain of our executive officers in the event of a not-for-cause termination under existing employment contracts, or any contingent obligations under licensing agreements. The cash amount for which we might be liable upon any such termination, based on current executive pay and bonus levels, could be up to approximately $1.9 million.

In December 2016, we entered into the Madrigal Agreement providing us with exclusive, worldwide license from Madrigal under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize the Madrigal Agreement Products. Under the terms of the Madrigal Agreement, we 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. The amounts payable pursuant to the Madrigal Agreement are not included in the table above as the timing of the payments is uncertain.

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

Interest rates

Our exposure to market risk is currently confined to our cash and our cash equivalents. 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.

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 [86] through [106] 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 controls evaluation, 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, 2018. Based on the assessment, our management has concluded that, as of December 31, 2018, our internal control over financial reporting was effective.

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 2018 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 2019 Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2018 (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, 2018, 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	3,837,056	(1)	$ 6.22	(2)	727,178	(3)
Equity compensation plans not approved by security holders	—		—		—	
Total	3,837,056	(1)	$ 6.22	(2)	727,178	(3)

(1) Of these shares, 212,297 were underlying then outstanding restricted stock unit awards and 3,135,079 were subject to options then outstanding under the 2013 Plan, 413,130 were subject to options then outstanding under the 2010 Plan and 21,871 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 358,406 shares of common stock available for issuance under our 2013 Plan and 368,772 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, 2019, an additional 1,574,666 shares became available for future issuance under the 2013 Plan and an additional 262,444 shares became available for future issuance under the 2016 ESPP. The additional shares from the annual increase on January 1, 2019 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)
4.3	Form of Representative's Warrant Agreement (filed as Exhibit 4.3 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)
4.4	Form of Warrant to Purchase Common Stock of Aldeyra Therapeutics, Inc. (filed as Exhibit 4.4 to the Registrant's Current Report on Form 8-K as filed on January 15, 2015, and incorporated herein by reference)
4.5	Form of Warrant to Purchase Common Stock of Aldeyra Therapeutics, Inc. (filed as Exhibit 4.5 to the Registrant's Current Report on Form 8-K as filed on January 22, 2015, and incorporated herein by reference)
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)

Exhibit Number	Exhibit Title
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)
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)
10.9	Loan and Security Agreement, dated as of April 12, 2012, between Square 1 Bank and the Registrant (filed as Exhibit 10.11 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)
10.10	Amendment No. 1 to Loan and Security Agreement, dated as of November 20, 2013 between Square 1 Bank and the Registrant (filed as Exhibit 10.12 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)
10.11	Amended and Restated Intellectual Property Security Agreement, dated as of November 20, 2013 between Square 1 Bank and the Registrant (filed as Exhibit 10.13 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)
10.12†	Offer Letter dated June 13, 2014 between the Registrant and Stephen Tulipano (filed as Exhibit 10.14 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2014 (as filed on August 7, 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))
10.14	Second Amendment to Loan and Security Agreement, dated as of November 7, 2014, between Square 1 Bank and the Registrant (filed as Exhibit 10.2 to the Registrant's Current Report on Form 8-K as filed on November 12, 2014, and incorporated herein by reference)
10.16	Form of Registration Rights Agreement, dated as of January 14, 2015 (filed as Exhibit 10.43 to the Registrant's Current Report on Form 8-K as filed on January 15, 2015, and incorporated herein by reference)
10.18	Form of Registration Rights Agreement, dated as of January 21, 2015 (filed as Exhibit 10.45 to the Registrant's Current Report on Form 8-K as filed on January 22, 2015, and incorporated herein by reference)
10.19	Third Amendment to Loan and Security Agreement, dated as of March 18, 2015, between Pacific Western Bank and the Registrant. (filed as Exhibit 10.21 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 (as filed on May 14, 2015, and incorporated herein by reference))
10.20	Fourth Amendment to Loan and Security Agreement, dated as of November 9, 2015, between Pacific Western Bank and the Registrant. (filed as Exhibit 10.21 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2015 (as filed on November 13, 2015, and incorporated herein by reference))

Exhibit Number	Exhibit Title
10.21	Fifth Amendment to Loan and Security Agreement, dated as of December 1, 2016, between Pacific Western Bank and the Registrant (filed as Exhibit 10.21 to the Registrant's Annual Report on Form 10-K (as filed on March 30, 2017, 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))
10.26	Controlled Equity Offering℠ Sales Agreement by and between Cantor Fitzgerald & Co. and the Registrant (filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K as filed on June 2, 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))
10.31†	Separation and Consulting Letter Agreement, effective as of July 27, 2018, between the Registrant and Stephen Tulipano (filed as Exhibit 10.31 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

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))
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.

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 8, 2019.

ALDEYRA THERAPEUTICS, INC.

By: /s/ Todd Brady, M.D., Ph.D.
Todd 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 8, 2019
/s/ Joshua Reed Joshua Reed	Chief Financial Officer (principal financial and accounting officer)	March 8, 2019
/s/ Richard H. Douglas, Ph. D. Richard H. Douglas, Ph.D.	Chairman of the Board of Directors	March 8, 2019
/s/ Ben Bronstein, M.D. Ben Bronstein, M.D.	Director	March 8, 2019
/s/ Martin J. Joyce Martin J. Joyce	Director	March 8, 2019
/s/ Gary Phillips, M.D. Gary Phillips, M.D.	Director	March 8, 2019
/s/ Jesse Treu, Ph.D. Jesse Treu, Ph.D.	Director	March 8, 2019
/s/ Neal Walker, D.O. Neal Walker, D.O.	Director	March 8, 2019

ALDEYRA THERAPEUTICS, INC.
INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Aldeyra Therapeutics, Inc. (the "Company") as of December 31, 2018 and 2017, the related statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2018, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2018**,** in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ BDO USA, LLP

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

Boston, Massachusetts

March 8, 2019

ALDEYRA THERAPEUTICS, INC.

BALANCE SHEETS

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$ 3,357,472	$ 2,023,337
Cash equivalent - Reverse Repurchase Agreements	44,000,000	18,000,000
Marketable securities	46,242,220	22,923,462
Prepaid expenses and other current assets	1,169,594	1,018,967
Total current assets	94,769,286	43,965,766
Deferred offering costs	86,644	165,930
Fixed assets, net	235,225	43,262
Total assets	$ 95,091,155	$ 44,174,958
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 3,051,678	$ 1,000,963
Accrued expenses	5,421,498	2,236,465
Current portion of credit facility	-	116,319
Total current liabilities	8,473,176	3,353,747
Credit facility, net of current portion and debt discount	-	1,220,192
Total liabilities	8,473,176	4,573,939
Commitments and contingencies (Note 12)		
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 26,244,435 and 19,137,639 shares issued and outstanding, respectively	26,244	19,138
Additional paid-in capital	225,136,127	139,241,635
Accumulated other comprehensive loss	(9,224)	(17,831)
Accumulated deficit	(138,535,168)	(99,641,923)
Total stockholders’ equity	86,617,979	39,601,019
Total liabilities and stockholders’ equity	$ 95,091,155	$ 44,174,958

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

ALDEYRA THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS

	Years ended December 31,	
	2018	**2017**
Operating expenses:		
Research and development	$ 29,823,007	$ 16,302,568
General and administrative	9,876,144	6,185,820
Loss from operations	(39,699,151)	(22,488,388)
Other income (expense):		
Interest income	952,698	261,252
Interest expense	(146,792)	(113,453)
Total other income (expense), net	805,906	147,799
Net loss	$ (38,893,245)	$ (22,340,589)
Net loss per share - basic and diluted	$ (1.79)	$ (1.40)
Weighted average common shares outstanding - basic and diluted	21,685,642	15,921,884

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

ALDEYRA THERAPEUTICS, INC.

STATEMENTS OF COMPREHENSIVE LOSS

	Years ended December 31,	
	2018	**2017**
Net loss	$ (38,893,245)	$ (22,340,589)
Other comprehensive income/(loss):		
Unrealized gain/(loss) on marketable securities	8,607	(17,960)
Total other comprehensive income/(loss)	$ 8,607	$ (17,960)
Comprehensive loss	$ (38,884,638)	$ (22,358,549)

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

ALDEYRA THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

	Stockholders' Equity					
	Common Voting Stock					
	Shares	Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Income/(Loss), net of tax	Accumulated Deficit	Total Stockholders' Equity
Balance, December 31, 2016	12,576,325	$ 12,576	$ 98,938,446	$ 129	$ (77,301,334)	$ 21,649,817
Stock-based compensation	—	—	2,714,841	—	—	2,714,841
Issuance of common stock, net of issuance costs	6,523,055	6,524	37,463,087	—	—	37,469,611
Issuance of common stock, ESPP	31,485	31	125,261	—	—	125,292
Issuance of common stock, RSUs	6,774	7	—	—	—	7
Other comprehensive loss	—	—	—	(17,960)	—	(17,960)
Net loss	—	—	—	—	(22,340,589)	(22,340,589)
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, RSUs	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

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

ALDEYRA THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS

	Years ended December 31,	
	2018	**2017**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (38,893,245)	$ (22,340,589)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	4,144,853	2,714,841
Amortization of debt discount – non-cash interest expense	59,322	20,341
Net amortization of premium on debt securities available for sale	(237,541)	129,245
Depreciation	71,003	37,849
Change in assets and liabilities:		
Prepaid expenses and other current assets	(150,627)	(800,285)
Accounts payable	2,049,582	725,522
Accrued expenses	3,099,522	290,214
Net cash used in operating activities	(29,857,131)	(19,222,862)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Acquisitions of property and equipment	(262,966)	(24,759)
Purchases of marketable securities	(59,731,610)	(35,095,083)
Sales of marketable securities	36,659,000	24,922,000
Net cash used in investing activities	(23,335,576)	(10,197,842)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock	81,837,102	37,469,611
Proceeds from issuance of common stock in employee plans	85,573	125,299
Deferred offering costs paid in cash	—	(165,930)
Extinguishment of long term debt	(1,395,833)	—
Net cash provided by financing activities	80,526,842	37,428,980
NET INCREASE IN CASH	27,334,135	8,008,276
CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD	20,023,337	12,015,061
CASH AND CASH EQUIVALENTS, END OF PERIOD	$ 47,357,472	$ 20,023,337
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Cash paid during the period for:		
Interest	$ 88,963	$ 91,633

The accompanying notes are an integral part of these 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 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 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, 2018, will be adequate to fund operations through the end of 2020, including the currently planned announcements of top-line data from Phase 3 clinical trials in allergic conjunctivitis, noninfectious anterior uveitis, SLS (Part 1) and dry eye disease. 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 U.S. Food and Drug Administration (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 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 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 relate to accruals, including research and development costs, accounting for income taxes and the related valuation allowance and accounting for stock based compensation and the related fair value. 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 5.

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 has 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, 2018 and 2017, 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, 2018 and 2017 were $1,337,000 and $768,000, 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 of 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.

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, 2018, comprehensive loss is equal to the Company's net loss of $38.9 million and an unrealized gain on marketable securities of $9,000. For December 31, 2017, comprehensive loss is equal to our net loss of $22.3 million and an unrealized loss on marketable securities of $18,000.

Net Loss Per Share – Basic net loss per share available to common stockholders is calculated by dividing the net loss available to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share available to common stockholders is computed by dividing the net loss available to common stockholders by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, stock options, restricted stock units and common stock warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share available to common stockholders when their effect is dilutive.

Recent Accounting Pronouncements **–** In June 2018, the FASB issued ASU 2018-07, Compensation — Stock Compensation (Topic 718) (ASU 2018-07). The amendments in ASU 2018-07 expand the scope of the employee share-based payments guidance to include share-based payments issued to non-employees. The amendments specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards to non-employees. The Company has adopted the provisions of ASU 2018-07 in the quarter ended September 30, 2018 and it did not have a material impact on the Company's financial statements. When adopting the provisions of ASU 2018-07, the Company changed the expense recognition for share-based payments to non-employees to an amount determined at grant or modification date instead of a variable amount to be valued at each reporting period.

In August 2016, the FASB issued ASU No. 2016-15 (ASU 2016-15), Statement of Cash Flows. The standard is intended to reduce the diversity in practice around how certain transactions are classified within the statement of cash flows. The Company adopted ASU 2016-15 in the quarter ended March 31, 2018, and it did not have a material impact on the Company's financial statements.

In February 2016, the FASB issued ASU No. 2016-02 (ASU 2016-02), Leases. 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. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018. The Company is currently evaluating the impact of the guidance on its condensed financial statements and related processes and internal controls. While the Company expects the implementation to result in the recognition of right-of-use assets and lease liabilities for the lease of its occupied office space, the right-of-use assets and lease liabilities will not have a material impact on its financial statements. There is no material uncertainty of cash flows arising from the Company's lease.

In January 2016, the FASB issued ASU No. 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities (ASU 2016-01). ASU 2016-01 amends the guidance on the classification and measurement of financial instruments. Although ASU 2016-01 retains many current requirements, it significantly revises accounting related to the classification and measurement of investments in equity securities and the presentation of certain fair value changes for financial liabilities measured at fair value. ASU 2016-01 also amends certain disclosure requirements associated with the fair value of financial instruments. The Company adopted ASU 2016-01 in the quarter ended March 31, 2018, and it did not have a material impact on the Company's financial statements.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606), which supersedes the revenue recognition requirements in ASC 605, Revenue Recognition. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The ASU also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. The Company adopted ASU 2014-09 on January 1, 2018, and it did not have a material impact on the Company's financial statements.

Reclassifications - Certain reclassifications have been made to prior period financial statements to conform to the current period presentation, specifically cash equivalents and reverse repurchase agreements are disclosed separately on the balance sheet for current and prior periods presented.

3. NET LOSS PER SHARE

For the years ended December 31, 2018 and 2017, 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,	
	2018	2017
Options to purchase common stock	3,570,080	2,246,857
Warrants to purchase common stock	40,300	1,384,608
Restricted stock units	212,297	157,128
Total of common stock equivalents	3,822,677	3,788,593

4. CASH, CASH EQUIVALENTS AND MARKETABLE SECURITIES

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	—
U.S. government agency securities	46,251,444	—	(9,224)	46,242,220	—	46,242,220
Available for Sale(1)	90,251,444	—	(9,224)	90,242,220	44,000,000	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.

The contractual maturities of all available for sale securities are less than one year at December 31, 2018.

At December 31, 2017, 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	$ 979,485	$ —	$ —	$ 979,485	$ 979,485	$ —
Money market funds	1,043,852	—	—	1,043,852	1,043,852	—
Reverse repurchase agreements	18,000,000	—	—	18,000,000	18,000,000	—
U.S. government agency securities	22,941,293	—	(17,831)	22,923,462	—	22,923,462
Available for Sale(1)	40,941,293	—	(17,831)	40,923,462	18,000,000	22,923,462
Total Cash, cash equivalents and current marketable securities					$20,023,337	$22,923,462

(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.

5. 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, 2018 or 2017, respectively.

The following table presents information about the Company's assets measured at fair value at December 31, 2018 and December 31, 2017:

	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

	December 31, 2017			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds(a)	$ 1,043,852	$ —	$ —	$ 1,043,852
Reverse repurchase agreements(b)	—	18,000,000	—	18,000,000
U.S. government agency securities(b)	—	22,923,462	—	22,923,462
Total assets at fair value	$ 1,043,852	$ 40,923,462	$ —	$ 41,967,314

(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) U.S. 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.

6. ACCRUED EXPENSES

Accrued expenses at December 31, 2018 and 2017 were:

	December 31, 2018	December 31, 2017
Accrued compensation	$ 1,172,880	$ 788,570
Accrued research and development	3,882,313	1,327,103
Accrued general & administrative	366,305	120,792
Accrued expenses	$ 5,421,498	$ 2,236,465

7. CREDIT FACILITY

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 connection with the extinguishment of the debt, all unamortized discounts were written off.

8. 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, 2018, a total of 3,570,080, 40,300, 358,406, and 368,772, shares of common stock were reserved for issuance upon (i) the exercise of outstanding stock options, (ii) the exercise of outstanding warrants, (iii) the issuance of stock awards under the Company's Amended 2013 Plan, and (iv) the issuance of shares under the 2016 ESPP, respectively.

Underwritten Public Offerings

In February 2017, the Company sold 2,555,555 shares of its common stock in an underwritten public offering at $4.50 per share, for an aggregate gross cash purchase price of $11.5 million, or proceeds of $10.6 million after underwriters discount and expenses. In September 2017, the Company sold 3,967,500 shares of its common stock in an underwritten public offering at $7.25 per share, for an aggregate gross cash purchase price of $28.8 million, or proceeds of $26.9 million after underwriters discount and expenses. 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 (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. As of December 31, 2018, no shares were sold under the Jefferies Sales Agreement.

9. INCOME TAXES

No 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, *Income Taxes*, the Company considers whether it is more likely than not that some portion or all of 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.

As of December 31, 2018, the Company had Federal and State income tax net operating loss ("NOL") carryforwards of approximately $93.5 million and $89.7 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, 2018, the Company had Federal and State research and development tax credit carryforwards of approximately $3.3 million and $0.6 million, respectively, which will expire at various dates through 2038.

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, 2018 and 2017 are as follows:

	Years ended December 31,	
	2018	2017
Deferred Tax Assets		
Federal & State NOL carryforward	$ 25,311,547	$ 16,935,101
Federal & State R&D credit carryforward	3,781,160	2,058,771
Intangibles – net	164,508	325,744
Accounts payable and accrued expenses	1,958,174	615,490
Stock options	3,146,034	2,197,983
Fixed assets – net	10,173	6,409
Gross deferred tax assets	34,371,596	22,139,498
Valuation Allowance	(34,371,596)	(22,123,292)
Net Deferred Tax Assets	-	16,206
Deferred Tax Liabilities		
Note discounts	-	(16,206)
Gross deferred tax liabilities	-	(16,206)
TOTAL	$ —	$ —

The change in valuation allowance of $12.2 million from December 31, 2017 to December 31, 2018 is driven by no tax benefit being recorded on the current year loss from operations

Under Section 382 of the Internal Revenue Code of 1986, as amended (Code), 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 the Company’s common stock, even those outside the Company’s control, such as purchases or sales by investors, within the testing period could result in an ownership change. A limitation on the Company’s ability to utilize some or all of its NOLs or credits could have a material adverse effect on the Company’s results of operations and cash flows. Aldeyra has undergone three ownership changes through the year ended December 31, 2018. However, the Company’s management believes that it had sufficient “Built-In-Gain” to offset any Section 382 limitation generated by such ownership changes. Any future ownership changes may cause the Company’s existing tax attributes to have additional limitations.

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,	
	2018	2017
Statutory tax rate	21.00%	34.00%
State taxes, net of federal benefits	6.83%	5.37%
Federal research and development credits	3.81%	3.00%
Change in valuation allowance	(31.51)%	(1.51)%
Stock-based compensation	(0.20)%	(1.11)%
Federal rate change	—	(39.75)%
Other	0.07%	—
Effective tax rate	0.00%	0.00%

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.

10. STOCK INCENTIVE PLAN

The Company has three equity incentive plans. One was adopted in 2004 (2004 Plan) and provided for the granting of stock options and restricted stock awards and generally prescribed a contractual term of seven years. The 2004 Plan terminated in August 2010. However, grants made under the 2004 Plan are still governed by that plan. As of December 31, 2018, options to purchase 21,871 shares of common stock at a weighted average exercise price of $3.24 per share remained outstanding under the 2004 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, 2018, 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, 2018, options to purchase 3,135,079 shares of common stock at a weighted average exercise price of $6.80 per share and 212,297 shares of common stock underlying restricted stock units remained outstanding under the Amended 2013 Plan. As of December 31, 2018, there were 358,406 shares of common stock available for grant under the Amended 2013 Plan. As of January 1, 2019, the number of shares of common stock that may be issued under the Amended 2013 Plan was automatically increased by 1,574,666 shares, increasing the number of shares of common stock available for issuance under the Amended 2013 Plan to 1,933,072.

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 are as follows:

	Years ended December 31,	
	2018	2017
Research and development expenses	$ 1,541,915	$ 896,339
General and administrative expenses	$ 2,602,938	1,818,502
Total stock-based compensation expense	$ 4,144,853	$ 2,714,841

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, 2018:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term	Aggregate Intrinsic Value(a)
Outstanding at December 31, 2017	2,246,857	$ 4.87		
Granted	1,325,306	8.38		
Cancelled/Forfeited	(2,083)	3.24		
Exercised	—	—		
Outstanding at December 31, 2018	3,570,080	$ 6.18	7.73	$ 7,909,697
Exercisable at December 31, 2018	1,857,645	$ 5.10	6.69	$ 5,977,280

(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, 2018 of $8.30 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, 2018 and 2017, 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 $5.79 and $3.76 for the years ended December 31, 2018 and 2017, respectively. The assumptions used in determining fair value of the employee stock options for the years ended December 2018 and 2017, are as follows:

	December 31, 2018	December 31, 2017
Expected dividend yield	0%	0%
Anticipated volatility	76.52% - 78.38%	76.52% - 88.57%
Stock price	$6.80 - $11.83	$4.90 - $6.10
Exercise price	$6.80 - $11.83	$4.90 - $6.10
Expected life (years)	5.50 - 6.25	5.50 - 6.25
Risk free interest rate	2.32% - 3.10%	1.87% - 2.26%

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 both the historical volatility of the Company and the historical volatility from a group of similar companies 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, 2018, there is approximately $7.9 million of unrecognized compensation cost relating to stock options outstanding, which the Company expects to recognize over a weighted average period of 2.73 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, 2018:

	Number of Shares
Outstanding at December 31, 2017	157,128
Granted	96,144
Vested/released	(40,975)
Outstanding at December 31, 2018	212,297

The weighted-average fair value of RSUs granted was $8.60 and $5.10 per share for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, the outstanding restricted stock units had unamortized stock-based compensation of $1.1 million with a weighted-average remaining recognition period of 2.74 years and an aggregate intrinsic value of $1.8 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, 2018	December 31, 2017
Expected dividend yield	0%	0%
Anticipated volatility	77.49% - 80.59%	75.46% - 76.14%
Stock price	$8.05 - $8.51	$4.70 - $4.90
Exercise price	$8.05 - $8.51	$4.70 - $4.90
Expected life (years)	1.00	0.70
Risk free interest rate	1.61% - 2.11%	1.13% - 0.97%

At December 31, 2018, the Company has 368,772 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, 2018 and 2017 are as follows:

	December 31, 2018	December 31, 2017
Weighted-average grant-date fair value per share	$ 2.21	$ 2.03
Total shares issued	14,382	31,485
Total stock-based compensation expense	$ 75,141	$ 64,033

11. STOCK PURCHASE WARRANTS

As of December 31, 2018, there were 40,300 warrants to purchase shares of common stock of the Company outstanding with a weighted-average exercise price of $10.00 per share and weighted-average remaining life of 0.3 years. During the year ended December 31, 2018, there was a net exercise of 19,700 warrants which resulted in 5,133 shares of common stock issued by the Company and there were 1,324,608 warrants to purchase shares of common stock of the Company that expired unexercised. For the year ended December 31, 2017 there were no exercises, issuances or expirations of warrants to purchase shares of common stock of the Company. A summary of the common share purchase warrants outstanding and exercisable at December 31, 2018 is as follows:

Exercise Price	Number Outstanding	Expiry Date
$ 10.00	40,300	May 1, 2019

12. 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, 2018, 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 **–** 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.

Other Contractual Arrangements **–** In September 2017, the Company executed a Lease Agreement (the "Office Lease"), which was amended in November 2017. The amended lease as of December 31, 2017, consisted of approximately 9,351 square feet of office space of office space located in Lexington, Massachusetts (the "Premises"). The Company intends to use the Premises as our corporate headquarters. The term of the Office Lease is through December 31, 2020, or as extended under our option to extend in the Office Lease. The Office Lease provides for a monthly base rent of $13,559, commencing on December 1, 2017. In addition to the base rent, the Company is required to pay the landlord certain operating expenses, taxes and other fees in accordance with the terms of the Office Lease. Rent expense for the years ended December 31, 2018 and 2017 was $238,532 and $157,682, respectively.

The Company's gross future minimum payments under all non-cancelable operating leases as of December 31, 2018, are:

	Total	2019	2020	2020	2021
Operating lease obligations	$ 465,991	$ 228,320	$ 237,671	$ —	$ —

13. SUBSEQUENT EVENTS

On January 28, 2019, the Company acquired Helio Vision, Inc., a Delaware corporation (“Helio”). As a result of the acquisition, the Company initially issued an aggregate of 1,150,990 shares of common stock to the former securityholders and an advisor of Helio. The Company, 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 the Company 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 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.

Exhibit 10.35

ALDEYRA THERAPEUTICS, INC.
131 HARTWELL AVENUE, SUITE 320
LEXINGTON, MA 02421

April 19, 2018

Mr. David B. McMullin
xxx xxxxxxx xxxx xxxx
xxxxxxx, xx xxxxx

Dear Dave,

Aldeyra Therapeutics, Inc. (the "Company") is pleased to offer you employment on the following terms:

1. **Position**. Your initial title will be Senior Vice President, Corporate Development and Strategy and you will initially report to the Company's Chief Executive Officer, Todd C. Brady, M.D., Ph.D. This is a full-time position. While you render services to the Company, you will not engage in any other employment, consulting or other business activity (whether full-time or part-time) that would create a conflict of interest with the Company. By signing this letter agreement, you confirm to the Company that you have no contractual commitments or other legal obligations that would prohibit you from performing your duties for the Company.

2. **Cash Compensation**. The Company will pay you a starting salary at the rate of $14,583.34 per pay period (twenty four pay periods per year), payable in accordance with the Company's standard payroll schedule. This salary will be subject to adjustment pursuant to the Company's employee compensation policies in effect from time to time**.** In addition, you will be eligible to be considered for an incentive bonus for each fiscal year of the Company. The bonus (if any) will be awarded based on objective or subjective criteria established by your supervisor and approved by the Company's Chief Executive Officer. Your target bonus will be equal to 30% of your annual base salary. Any bonus for the fiscal year in which your employment begins will be prorated, based on the number of days you are employed by the Company during that fiscal year. Any bonus for a fiscal year is expected to be paid within 2.5 months after the close of that fiscal year, but only if you are still employed by the Company at the time of payment. The determinations of the Company's Board of Directors or its Compensation Committee with respect to your bonus will be final and binding.

3. **Employee Benefits**. As a regular employee of the Company, you will be eligible to participate in a number of Company-sponsored benefits. In addition, you will be entitled to 4 weeks paid time off in accordance with the Company's time off policy, as in effect from time to time. The Company performs annual employee evaluations and reviews, during which the potential for promotions, employee compensation adjustments, and other employment modifications is assessed.

4. **Stock Options**. Subject to the approval of the Company's Board of Directors or its Compensation Committee, you will be granted an option to purchase 225,000 shares of the Company's Common Stock (the "Option"). The exercise price per share of the Option will be determined by the Board of Directors or the Compensation Committee when the Option is granted. The Option will be subject to the terms and conditions applicable to options granted under the Company's 2013 Stock Plan (the "Plan") and the applicable Stock Option Agreement. You will vest in 25% of the Option shares after 12 months of continuous service with the Company, and the balance will vest in equal monthly installments over the next 36 months of continuous service, as described in the applicable Stock Option Agreement.

   The Option will be subject to acceleration in connection with a change of control, subject to the terms and conditions of the Company's Change in Control Plan effective as of March 28, 2017, as such plan may be amended or restated from time to time.

5. Severance Benefits.

   a. **General.** If you are subject to an Involuntary Termination, then you will be entitled to the benefits described in this Section 5. However, this Section 5 will not apply unless you (i) have returned all Company property in your possession, (ii) have resigned as a member of the Boards of Directors of the Company and all of its subsidiaries, to the extent applicable, and (iii) have executed a general release of all claims that you may have against the Company or persons affiliated with the Company. The release must be in the form prescribed by the Company, without alterations. You must execute and return the release on or before the date specified by the Company in the prescribed form (the "Release Deadline"). The Release Deadline will in no event be later than 50 days after your Separation. If you fail to return the release on or before the Release Deadline, or if you revoke the release, then you will not be entitled to the benefits described in this Section 5.

   b. **Salary Continuation.** If you are subject to an Involuntary Termination, then the Company will continue to pay your base salary for a period of 6 months after your Separation. Your base salary will be paid at the rate in effect at the time of your Separation and in accordance with the Company's standard payroll procedures. The salary continuation payments will commence within 60 days after your Separation and, once they commence, will include any unpaid amounts accrued from the date of your Separation. However, if the 60-day period described in the preceding sentence spans two calendar years, then the payments will in any event begin in the second calendar year.

   c. **Cash Bonus.** If you are subject to an Involuntary Termination, then the Company will pay you a lump-sum in cash equal to the greater of (i) your target bonus for the year in which the Involuntary Termination occurs or (ii) the actual bonus paid to you with respect to the Company's most recently completed fiscal year. Such payment will be made within 60 days after your Separation; however, if such 60-day period spans two calendar years, then the payment will in any event be made in the second calendar year.

d. **COBRA.** If you are subject to an Involuntary Termination and you elect to continue your health insurance coverage under the Consolidated Omnibus Budget Reconciliation Act ("COBRA") following your Separation, then the Company will pay the same portion of your monthly premium under COBRA as it pays for active employees and their eligible dependents until the earliest of (i) the close of the 6-month period following your Separation, (ii) the expiration of your continuation coverage under COBRA or (iii) the date when you become eligible for substantially equivalent health insurance coverage in connection with new employment or self-employment. Such payments will be treated as taxable compensation income to you if required or advisable, in the Company's sole discretion, to avoid adverse consequences to you, the Company or the Company's other employees.

6. **Confidentiality, Non-Competition and Work Product Agreement**. Like all Company employees, you will be required, as a condition of your employment with the Company, to sign the Company's standard "Confidentiality, Non-Competition and Work Product Agreement", a copy of which is attached hereto as **Exhibit A**.

7. **Employment Relationship**. Employment with the Company is for no specific period of time. Your employment with the Company will be "at will," meaning that either you or the Company may terminate your employment at any time and for any reason, with or without Cause, subject to the severance benefits you may be entitled to under this letter. Any contrary representations that may have been made to you are superseded by this letter agreement. This is the full and complete agreement between you and the Company on this term. Although your job duties, title, compensation and benefits, as well as the Company's personnel policies and procedures, may change from time to time, the "at will" nature of your employment may only be changed in an express written agreement signed by you and a duly authorized officer of the Company (other than you).

8. **Tax Matters**.

a. Withholdings. All forms of compensation referred to in this letter agreement are subject to applicable with holding and payroll taxes and other deductions required by law.

b. Section 409A. To the extent that any payment or benefit described in this letter agreement constitutes "non-qualified deferred compensation" under Section 409A of the Internal Revenue Code (the "Code"), and to the extent that such payment or benefit is payable upon your termination of employment, then such payments or benefits shall be payable only upon your "separation from service." It is intended that payments under this letter satisfy, to the greatest extent possible, the exemption from the application of Section 409A of the Code (the (and any state law of similar effect) provided under Treasury Regulation Section 1.409A-1(b)(4) (as a "short-term deferral"). The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A 1(h). The parties intend that this letter shall be administered in accordance with Section 409A of the Code. To the extent that any

provision of this letter is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. Each payment pursuant to this letter is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A 2(b)(2). The parties agree that this letter may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

c. Tax Advice. You are encouraged to obtain your own tax advice regarding your compensation from the Company. You agree that the Company does not have a duty to design its compensation policies in a manner that minimizes your tax liabilities, and you will not make any claim against the Company, its Board of Directors or its Compensation Committee related to tax liabilities arising from your compensation.

9. **Interpretation, Amendment and Enforcement**. This letter agreement and Exhibit A supersede and replace any prior agreements, representations or understandings (whether written, oral, implied or otherwise) between you and the Company and constitute the complete agreement between you and the Company regarding the subject matter set forth herein. This letter agreement may not be amended or modified, except by an express written agreement signed by both you and a duly authorized officer of the Company. The terms of this letter agreement and the resolution of any disputes as to the meaning, effect, performance or validity of this letter agreement or arising out of, related to, or in any way connected with, this letter agreement, your employment with the Company or any other relationship between you and the Company (the "Disputes") will be governed by Massachusetts law, excluding laws relating to conflicts or choice of law. You and the Company submit to the exclusive personal jurisdiction of the federal and state courts located in Massachusetts in connection with any Dispute or any claim related to any Dispute.

Definitions. The following terms have the meaning set forth below wherever they are used in this letter agreement:

"Cause" means (a) your unauthorized use or disclosure of the Company's confidential information or trade secrets, which use or disclosure causes material harm to the Company, (b) your material breach of any written agreement between you and the Company, (c) your material failure to comply with the Company's written policies or rules, (d) your conviction of, or your plea of "guilty" or "no contest" to, a felony under the laws of the United States or any State, (e) your gross negligence or willful misconduct in performance of your duties, (f) your continuing failure to perform assigned duties after receiving written notification of the failure from the Company's Board of Directors or (g) your failure to cooperate in good faith with a governmental or internal investigation of the Company or its directors, officers or employees, if the Company has requested your cooperation.

"Involuntary Termination" means your Termination Without Cause.

“Separation” means a “separation from service,” as defined in the regulations under Section 409A of the Code.

“Termination Without Cause” means a Separation as a result of a termination of your employment by the Company without Cause.”

* * * * *

GDSVF&H\

We hope that you will accept our offer to join the Company. You may indicate your agreement with these terms and accept this offer by signing and dating both the enclosed duplicate original of this letter agreement and the enclosed Confidentiality, Non-Competition and Work Product Agreement and returning them to me. This offer, if not accepted, will expire at the close of business on Friday, April 20, 2018. As required by law, your employment with the Company is contingent upon your providing legal proof of your identity and authorization to work in the United States. Your employment is also contingent upon (i) your starting work with the Company on or before Monday, May 7, 2018, (ii) your completing an employment application and (iii) a background and/or reference check to the Company's satisfaction.

Very truly yours,

ALDEYRA THERAPEUTICS, INC.

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

I have read and accept this employment offer:

/s/ David B. McMullin
Signature of David B. McMullin

Dated: 4/20/2018

Attachment

Exhibit A: Confidentiality, Non-Competition and Work Product Agreement

GDSVF&H\

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 and 333-224019) of Aldeyra Therapeutics, Inc. of our report dated March 8, 2019, relating to the financial statements of Aldeyra Therapeutics, Inc., which appears in this Annual Report on Form 10-K for the year ended December 31, 2018.

/s/ BDO USA, LLP
Boston, Massachusetts

March 8, 2019

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 8, 2019

/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 8, 2019

/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, 2018 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 8, 2019

/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 8, 2019

/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.