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, 2022

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 or Organization)	**(I.R.S. 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:

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

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

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

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

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

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

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

Large Accelerated Filer	☐	Accelerated Filer	☐
Non-Accelerated Filer	☒	Smaller reporting company	☒
		Emerging Growth Company	☐

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

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

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

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

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

As of June 30, 2022, 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 $228,378,259, 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 6, 2023 there were 58,576,350 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 2023 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, 2022, 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, 2022
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our plans to develop and commercialize reproxalap, ADX-2191 and any other product candidates, if approved;
- delay in or failure to obtain regulatory approval of reproxalap, ADX-2191 or any of our other product candidates, including as a result of the U.S. Food and Drug Administration (FDA) not accepting our regulatory filings or requiring additional clinical trials or data prior to review or approval of such filings;
- the ability to maintain regulatory approval of reproxalap, ADX-2191 or any of our other our product candidates, if received, and the labeling for any approved products;
- uncertainty as to our ability to commercialize (alone or with others) and obtain reimbursement for reproxalap, ADX-2191 or any of our other product candidates following regulatory approval, if any;
- the size and growth of the potential markets and pricing for reproxalap, ADX-2191 or any of our other product candidates following regulatory approval, if any, and the ability to serve those markets;
- the rate and degree of market acceptance of any of reproxalap, ADX-2191 or any of our other product candidates following regulatory approval, if any;
- 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;
- 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;
- our expectations regarding our expenses and future revenue, the timing of future revenue, the sufficiency or use of our cash resources and needs for additional financing;
- our expectations regarding competition;
- our anticipated growth strategies;
- our ability to attract or retain key personnel;
- our commercialization, marketing and manufacturing capabilities and strategy;
- 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;

- political, economic, legal, social and health risks, including the ongoing COVID-19 pandemic and subsequent public health measures, and war or other military actions, that may affect our business, results of operations and financial position, or the global economy;
- 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 (SEC).

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

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

INDUSTRY AND MARKET DATA

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

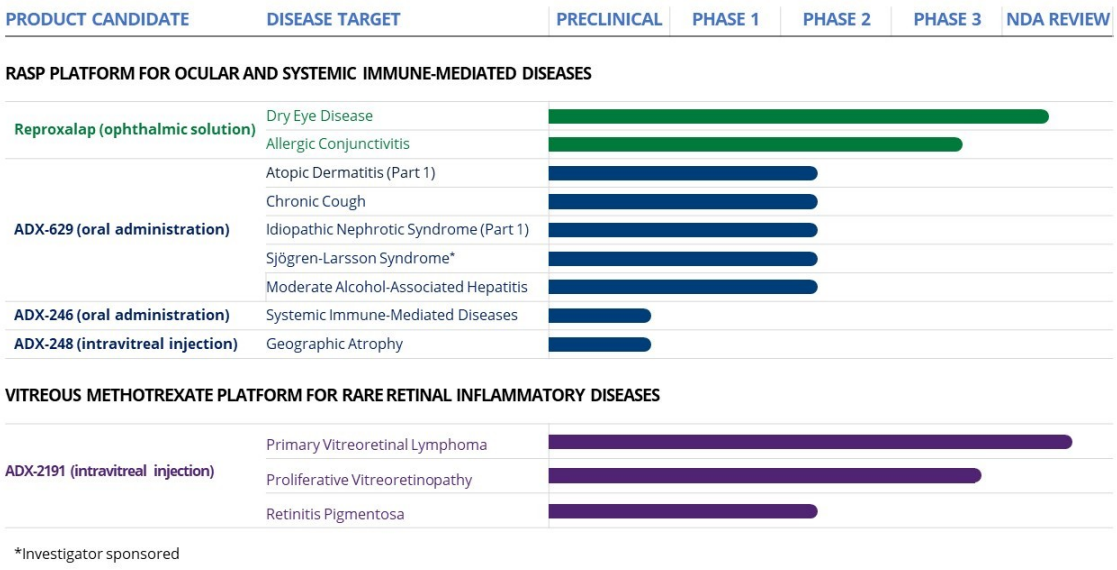
ITEM 1. *BUSINESS*

Overview

We are a biotechnology company devoted to discovering innovative therapies designed to treat immune-mediated diseases. We are developing a novel pharmaceutical platform targeting a class of pro-inflammatory mediators known as RASP (reactive aldehyde species) that exacerbate diseases characterized by inflammation. Our RASP modulator product pipeline includes ADX-629, a novel orally administered RASP modulator in clinical development for atopic dermatitis, idiopathic nephrotic syndrome, moderate alcohol-associated hepatitis, chronic cough, and Sjögren-Larsson Syndrome. Our preclinical RASP platform includes ADX-246, ADX-248, and other drug candidates in development for geographic atrophy and systemic inflammatory diseases. The validity of the RASP platform is supported by reproxalap, our first-in-class product candidate under New Drug Application (NDA) review by the United States Food and Drug Administration (FDA) for the treatment of dry eye disease. Reproxalap has demonstrated broad-based, rapid-onset activity and consistent safety across a number of Phase 2 and Phase 3 clinical trials. We have additional product candidates in development, including ADX-2191, which is under NDA review by the FDA for the treatment of a rare but fatal cancer known as primary vitreoretinal lymphoma. ADX-2191 is also in clinical development for the treatment of proliferative vitreoretinopathy and retinitis pigmentosa, two rare retinal diseases characterized by inflammation and vision loss. ADX-2191 has received Orphan Drug Designation for all three retinal diseases currently under development.

Our pipeline, as of the date of filing this annual report on Form 10-K is illustrated below.

Product Candidate Development Pipeline



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. As we continue to execute on our strategy of expanding our product candidate pipeline, we may license or acquire new immune-modulating approaches with novel therapeutic potential. In January 2019, we acquired from Helio Vision, Inc. and thereby obtained rights to ADX-2191.

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 more than 100 million 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 that 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.

We have no products approved for sale in the United States or elsewhere. We will not receive any revenue from any product candidates that we develop until we obtain regulatory approval. We intend to commercialize our products, if approved for sale, directly or through collaborations. Although we may receive commercial revenue in the future, we have to date primarily funded our operations through the sale of our common stock, convertible preferred 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. We have begun to incur commercialization expenses related to reproxalap and ADX-2191, including building a commercial infrastructure and expect to incur additional commercialization expenses in advance of potentially receiving marketing approval for reproxalap and ADX-2191. If we do obtain marketing approval for reproxalap, ADX-2191 or any other product candidate that we develop, we expect to incur significant additional commercialization expenses related to product sales, marketing, distribution and manufacturing. 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 products. 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 Science Supporting Our Product Candidates

RASP: Mediators of Inflammatory Diseases

In response to infection, injury, endogenous and exogenous chemical triggers, heat, and other stimuli, pro-inflammatory RASP (reactive aldehyde species) are generated through a variety of metabolic processes, including alcohol oxidation, enzymatic and non-enzymatic lipid oxidation, and polyamine and sphingosine metabolism. RASP appear to effect inflammation signaling via covalent binding to thiol (sulfur-containing) and amine (nitrogen-containing) residues on proteins, including receptors and enzymes. RASP-protein adducts directly influence the function of proteins, leading to activation of intracellular inflammatory factors, including NF-κB, an important mediator in the inflammatory response, and inflammasomes. 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, including the diseases represented in our RASP modulator pipeline, 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, for example, mutations in fatty aldehyde dehydrogenase are responsible for skin, neurological, and retinal disease.

Aside from the potentiation 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 modulators. Thus, pharmacotherapeutic RASP modulation is expected not to adversely affect normal physiologic processes. Consistent with the lack of accessibility of physiologic RASP, our most advanced RASP modulator, reproxalap, which has been administered as an ophthalmic solution to approximately 2,300 patients across a number of completed clinical trials for up to 12 months, has been observed to be generally well tolerated and has not been associated with any serious adverse events. Similarly, our most advanced orally administered RASP modulator, ADX-629, which has been administered to more than 100 patients across a number of Phase 1 and Phase 2 clinical trials for up to 90 days, has been observed to be generally well tolerated and has not been associated with any serious adverse events.

The RASP Modulator Platform

Because RASP affect many proteins simultaneously, the RASP modulator platform represents a unique and novel pharmacologic approach that, unlike almost all drugs in use today, is not designed to directly inhibit or activate a particular protein but instead targets a family of small molecules that in turn affect the activity and structure of many proteins at once. RASP modulation, therefore, has the potential to down-regulate pro-inflammatory systems or groups of proteins, and may lead to multiple beneficial clinical effects while avoiding toxicity associated with single-target inhibition or activation.

We are currently developing ADX-629, ADX-246, ADX-248, and other novel RASP modulators for the treatment of immune-mediated disease. RASP modulators are novel small molecules designed specifically to bind, and thereby allow for the degradation of, RASP. The validity of the RASP platform is supported by reproxalap, our first-in-class product candidate for the treatment of dry eye disease, which has demonstrated broad-based, rapid-onset activity and consistent safety across a number of Phase 2 and Phase 3 clinical trials and is under NDA review by the FDA. 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 modulators have the potential to substantially lower RASP levels.

We believe that we are the first biotechnology company to demonstrate the beneficial effects of RASP modulation in a variety of animal models relating to immune-mediated disease, suggesting that RASP modulators 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 TNFα, 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 & Immunology 2015 Annual Meeting)
- In a model of radiation mucositis (oral inflammation) in hamsters, chronic subcutaneous administration of reproxalap reduced healing time and decreased fibrosis (scarring). (Data presented at the Multinational Association of Supportive Care in Cancer – International Society of Oral Oncology 2015 Annual Meeting)
- In two different mouse models of inflammatory pain, intraperitoneally administered reproxalap dose-dependently reduced nociceptive behavior, suggesting that reproxalap down-regulates pain signaling in inflammation. (Data presented at The 2016 International Conference on Pain Research and Management)
- In rat cardiomyocyte culture, reproxalap prevented fibrotic transformation, and inhibited NF-κB activation and IL-1ß release. (Data presented at The American Society for Cell Biology® 2016 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 World Congress on Inflammation 2017 Annual Meeting)
- In a rat model of intraocular inflammation, a single intravitreal injection of the RASP modulator 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)
- In mice injected with endotoxin, orally administered ADX-629 statistically reduced a variety of inflammatory cytokines, including IL-5, Il-1ß, IL-17, IFNγ, and TNFα, while up-regulating the primary anti-inflammatory cytokine IL-10.

- In a mouse model of lung inflammation, oral administration of ADX-629 reduced infiltration of inflammatory cells in the lung.
- In a mouse model of ulcerative colitis, intraperitoneal administration of ADX-629 reduced the disease activity index, a composite score of histology, organ weights, and other indicators of disease severity.
- In a rat model of nephritis (kidney inflammation), oral administration of ADX-629 reduced proteinuria (protein in urine), an indicator of renal dysfunction.

Thus, we believe that the mechanism of action of RASP modulation 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, consistent with a systems-based pharmacologic approach.

In addition to the development of ADX-629, ADX-246, and ADX-248, we intend to continue the discovery and development of other novel RASP modulators, and we intend to continue to develop intellectual property around the molecules derived from our RASP modulator platform.

The Potential of ADX-2191 to Treat Primary Vitreoretinal Lymphoma, Prevent Proliferative Vitreoretinopathy, and Treat Retinitis Pigmentosa

ADX-2191 is a novel intravitreal formulation of methotrexate, a dihydrofolate reductase inhibitor that has been administered intravenously for decades to treat cancer and inflammatory diseases. Initially as an intravenous medication and subsequently as an intraocular injection, serial administration of methotrexate is the standard of care for the treatment of primary vitreoretinal lymphoma, also known as ocular lymphoma, a rare but often fatal cancer that originates in the eye. The goal of methotrexate therapy in ocular lymphoma is to prevent metastasis to the central nervous system, which can be difficult to treat and is ultimately fatal. ADX-2191 is a concentrated formulation of methotrexate that requires a small injection volume, thereby reducing injection site reflux and ensuing corneal toxicity relative to off-label ocular injections of methotrexate.

Proliferative vitreoretinopathy is a disease that occurs in a subset of patients with retinal detachments, and 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, as well as increased probability of subsequent retinal detachments. The anti-proliferative and anti-inflammatory properties of methotrexate are well described. In preclinical studies of primary cell cultures from proliferative vitreoretinopathy patients, methotrexate reduced pathological cell proliferation and scar-like collagen deposition. Thus, the observed clinical activity of ADX-2191 in proliferative vitreoretinopathy, described below, is believed to be the result of down-regulation of aberrant retinal cell proliferation and activity, thereby leading to reduced retinal scarring. ADX-2191 is denser than the vitreous, the fluid in the back of the eye, allowing for the concentration of methotrexate in the vicinity of retina.

Retinitis pigmentosa is a group of rare genetic eye diseases characterized by retinal cell death and loss of vision, for which there is no treatment. In vivo preclinical research has identified the activity of methotrexate in inducing misfolded rhodopsin (a visual cycle protein) clearance, suggesting the potential of ADX-2191 to treat genetic forms of retinitis pigmentosa that are characterized by misfolded rhodopsin.

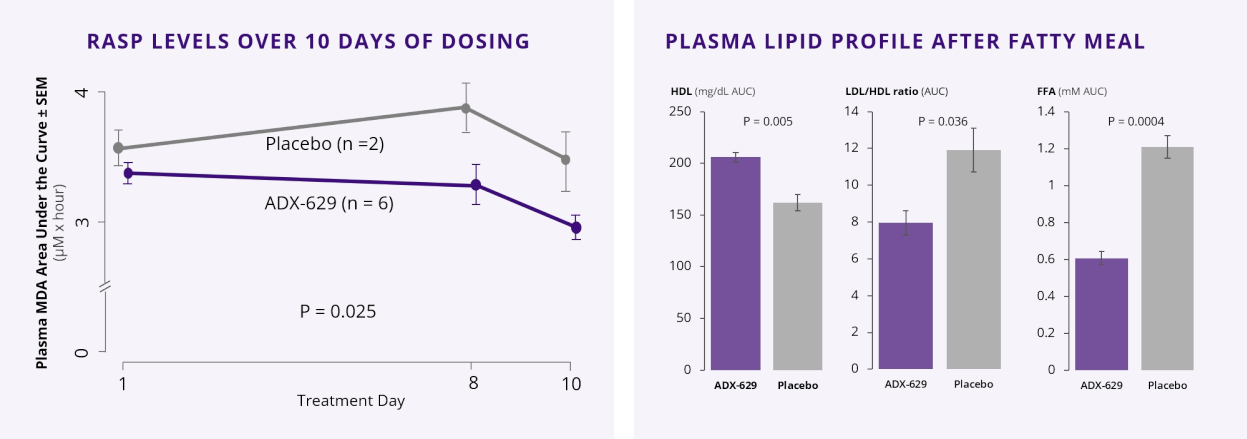
Clinical Trial Results and Development Plans

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 material clinical results have been previously disclosed elsewhere in detail, and we encourage review of all of our clinical trial disclosures in addition to this annual report on Form 10-K. 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. As a result of the COVID-19 pandemic, clinical site availability, staffing, patient recruitment, and patient retention have been negatively affected and the timelines to complete our clinical trials may be delayed.

Systemic RASP Modulation for the Treatment of Immune-Mediated Diseases

ADX-629 is a novel, orally administered RASP modulator in Phase 2 clinical development for the treatment of systemic immune-mediated diseases. In a Phase 1 clinical trial of ADX-629, no treatment-related adverse events were observed at any dose tested, and target engagement was evidenced by statistically lower levels of the RASP malondialdehyde in drug-treated subjects relative to controls (Figure 1). Additionally, following ingestion of a controlled high-fat meal, free fatty acids were statistically lower and HDL statistically higher in drug-treated subjects relative to placebo-treated subjects. The lipid results in the Phase 1 clinical trial suggested that ADX-629 diminished the inflammatory response that typically occurs following ingestion of a high-fat meal.

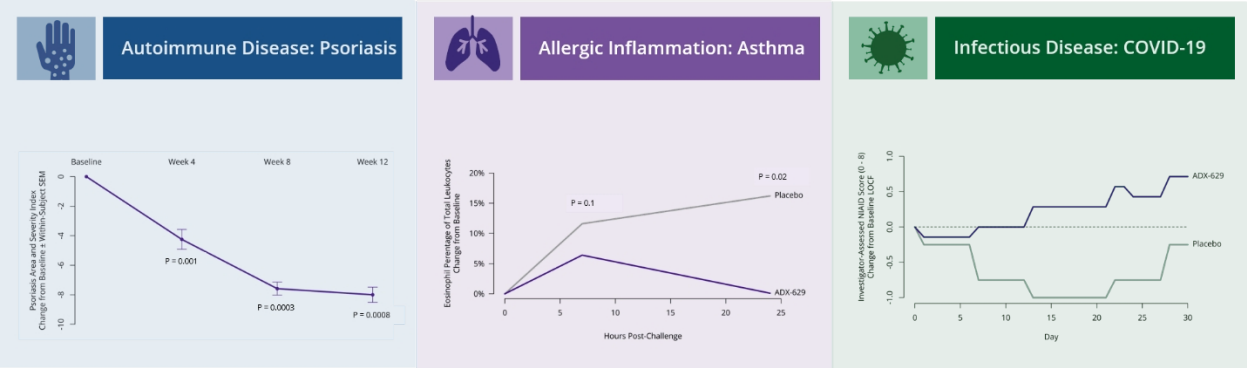
Figure 1: Phase 1 Clinical Trial of ADX-629



MDA = malondialdehyde; SEM = standard error of the mean; HDL= high-density lipoprotein; LDL = low-density lipoprotein; FFA = free fatty acids

In 2022, we announced results from Phase 2a clinical trials of ADX-629 in patients with psoriasis, atopic asthma, COVID-19, or alcohol intoxication, all of which suggested preliminary pharmacodynamic activity of ADX-629. The Phase 2a trials were performed as part of a systematic strategy to assess activity in different types of immunological diseases, including autoimmune disease, allergic inflammation, infectious disease, and toxin-induced inflammation. Across all Phase 2a clinical trials, in patients treated with ADX-629, no safety concerns were evident from adverse events and there were no treatment-related serious adverse events observed.

Figure 2: Phase 2a Clinical Trials of ADX-629 Psoriasis, Asthma, and COVID-19



SEM = standard error of the mean; NIAID = National Institute of Allergy and Infectious Diseases; LOCF = Last Observation Carried Forward

Autoimmune Disease: Psoriasis

Following treatment of 10 moderate psoriasis patients with ADX-629 for 12 weeks, psoriasis area and severity index (PASI) scores were statistically significantly decreased (P=0.0008 vs. baseline at Week 12), and peak PASI 50% and PASI 75% responder percentages were 57% (P=0.001) and 25% (P=0.051), respectively. Investigator global assessment scores decreased over the duration of treatment (P=0.01 vs. baseline at Week 12). Lesional pan-gene expression analysis suggested a trend toward normalization of global gene expression patterns; by Week 12 no gene expression pathways in lesional tissue were dysregulated compared to non-lesional skin. Plasma levels of the commonly described pro-inflammatory RASP malondialdehyde were reduced relative to baseline as soon as four weeks after initiation of treatment (P=0.02).

Allergic Inflammation: Asthma

In a placebo-controlled crossover trial of eight mild asthma patients treated for seven days, asthma symptom scores and sputum eosinophil cell counts were numerically reduced following treatment with ADX-629 relative to treatment with placebo. Compared to placebo treatment, treatment with ADX-629 led to statistically significant reductions in plasma levels of the pro-inflammatory cytokines IL-5 (P=0.02) and TNFα (P<0.0001), and numerical reductions in symptoms and in plasma levels of malondialdehyde.

Infectious Disease: COVID-19

Following treatment of 11 mild to moderate COVID-19 patients with ADX-629 or placebo for four weeks, change from baseline in the National Institute of Allergy and Infectious Diseases Score (1=death, 8=no activity limitation) was numerically higher in ADX-629-treated patients (n=7) than in placebo-treated patients (n=4) over all days assessed. Consistent with the clinical findings, relative to placebo-treated patients, reductions in plasma levels of the cytokines CXCL9 (P=0.0008), IFNγ (P=0.02), and TNFα (P=0.07) were observed in patients treated with ADX-629.

Toxin-Induced Inflammation: Alcohol Intoxication

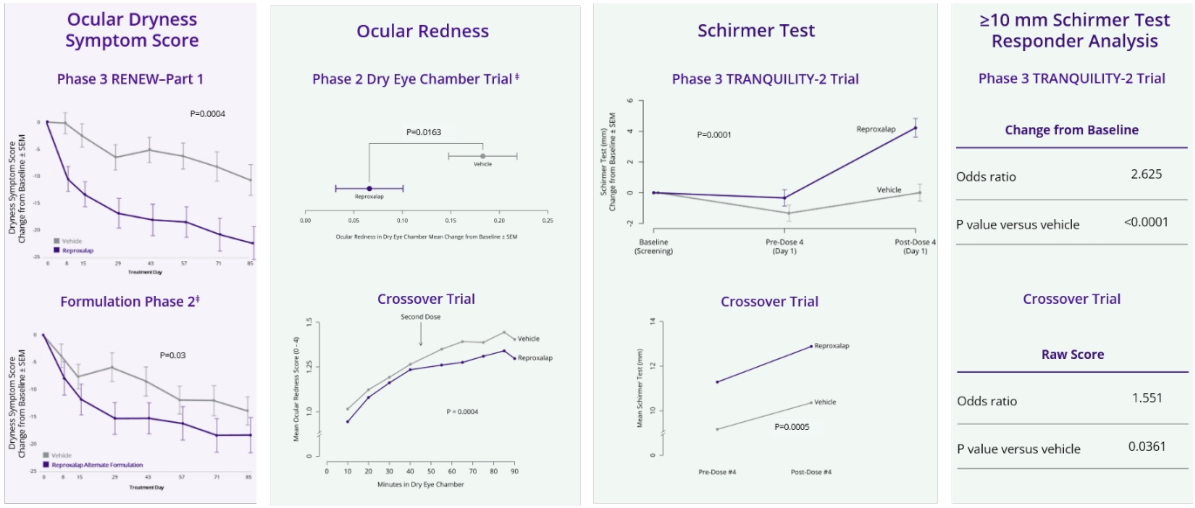
In a crossover trial of 23 healthy volunteers, where each subject received ADX-629 or placebo prior to ethanol ingestion, ADX-629 was statistically superior to placebo in improving Romberg test balance time (P=0.02); reducing facial flushing (P=0.0007); and lowering levels of the RASP acetaldehyde (P=0.03), total cholesterol (P=0.02), and LDL (P=0.047).

ADX-629 is currently in Phase 2 clinical trials for atopic dermatitis, chronic cough, idiopathic nephrotic syndrome, and Sjögren-Larsson Syndrome. In addition, a Phase 2 clinical trial of ADX-629 in moderate alcohol-associated hepatitis is expected to be initiated in 2023. Clinical trials of the RASP modulators ADX-246 in systemic immune-mediated disease and ADX-248 in geographic atrophy are expected to be initiated in the second half of 2023 or early 2024 pending completion of the FDA's Investigational New Drug (IND) requirements.

Dry Eye Disease

Reproxalap is a first-in-class, topically administered RASP modulator for the treatment of anterior segment ocular inflammation, and is currently under NDA review at the FDA for the treatment of dry eye disease. The NDA, which has been assigned a Prescription Drug User Fee Act (PDUFA) date of November 23, 2023, submission is supported by safety and efficacy data from five adequate and well-controlled clinical trials encompassing data for ocular dryness symptom score, ocular redness, Schirmer test (an objective measure of tear production), and Schirmer test ≥10 mm responder analysis (a measure of tear production that is correlated with symptomatic improvement) (Figure 3). The regulatory package includes activity ranging from within minutes of drug administration to up to 12 weeks of treatment (RENEW, Formulation Phase 2), crossover and parallel-group clinical trial designs, and assessment in dry eye chamber challenge (Phase 2 Dry Eye Chamber Trial, Crossover Trial, TRANQUILITY-2) and natural environment settings (RENEW, Formulation Phase 2). We believe that the NDA package for reproxalap, in aggregate, is the most comprehensive regulatory package ever submitted for a dry eye disease drug candidate.

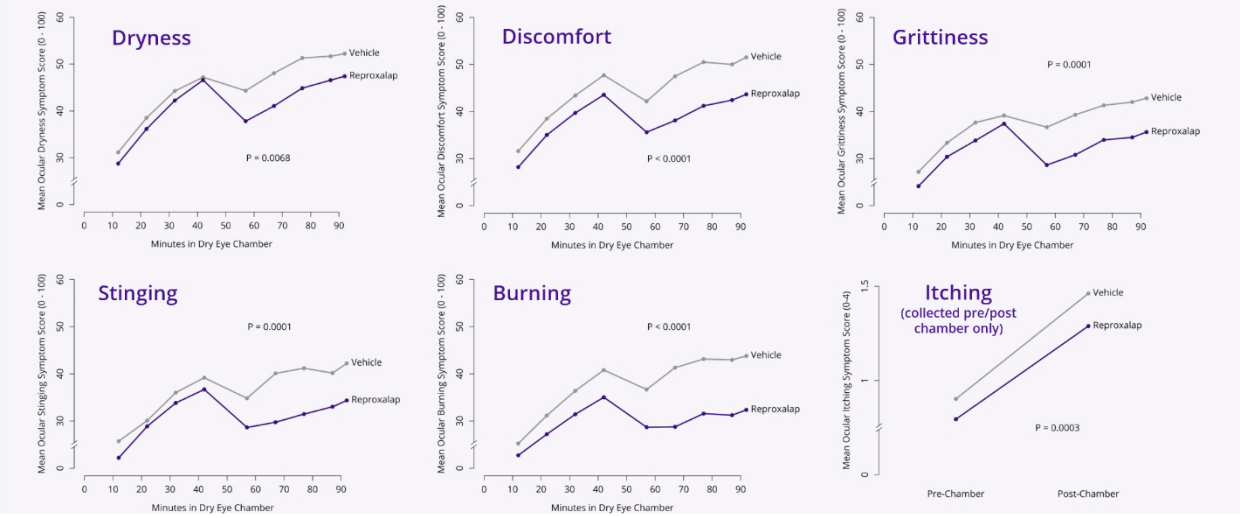
Figure 3: Pivotal Trial Results for Reproxalap in Dry Eye Disease



The NDA submission includes a combination of primary, secondary, multiplicity-adjusted, and nominal P-value endpoints. ‡Adequate and well-controlled Phase 2 or Phase 3 clinical trials can be submitted as pivotal. SEM = standard error of the mean.

In 12-week clinical trials, improvement in symptoms relative to vehicle was observed as soon as one week. In dry eye chamber trials, improvement in dry eye signs, including redness and the Schirmer test tear production assessment, was observed within minutes of dosing. The Schirmer test ≥10 mm responder analysis is correlated with symptomatic improvement, suggesting that a symptomatic benefit may be observed within minutes of dosing. Across all assessed symptoms, rapid symptomatic benefit was observed within dry eye chamber in the Crossover Trial (Figure 4), during which reproxalap or vehicle was administered prior to and 45 minutes after chamber entry.

Figure 4: Symptom Results from the Crossover Dry Eye Chamber Trial of Reproxalap in Dry Eye Disease



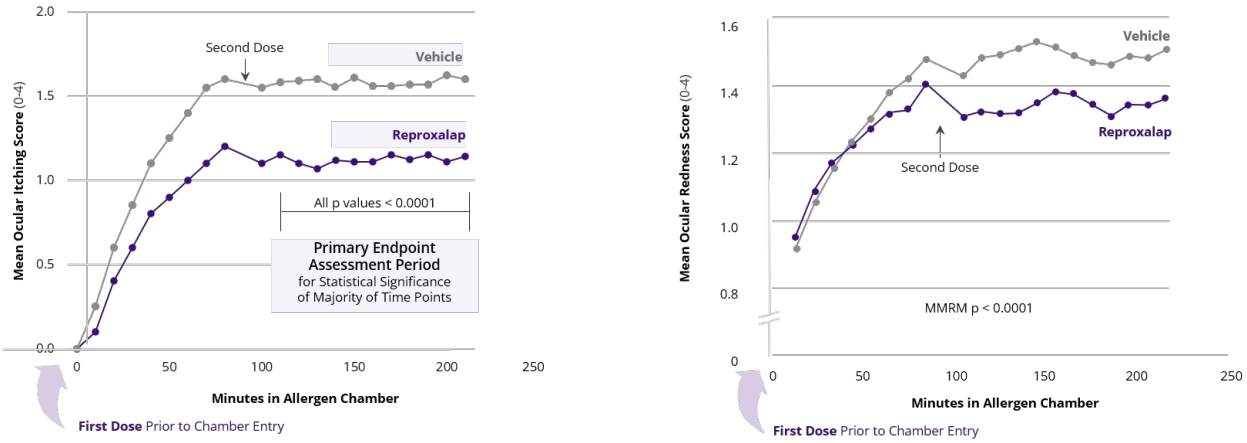
Topical ocular reproxalap has been studied in more than 2,300 patients with no observed clinically significant safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

Allergic Conjunctivitis

Allergic conjunctivitis is an anterior segment ocular inflammatory disease characterized by ocular itching and redness, and is often associated with dry eye disease. We estimate there to be 66 million patients with allergic conjunctivitis in the United States. In a number of Phase 2 and Phase 3 clinical trials in allergic conjunctivitis, reproxalap demonstrated consistent statistically significant and clinically relevant activity in improving ocular itching and redness. Thus, we believe reproxalap could offer differentiated efficacy relative to existing dry eye disease medications with regard to the potential treatment of the signs and symptoms of allergic conjunctivitis.

In 2021, we announced that the randomized, double-masked, vehicle-controlled allergen chamber Phase 3 INVIGORATE Trial of topically administered reproxalap in patients with allergic conjunctivitis (Figure 5) achieved the primary endpoint (patient-reported ocular itching score after the second dose of test article) and all secondary endpoints (investigator-assessed ocular redness score and patient-reported ocular tearing score).

Figure 5: Phase 3 INVIGORATE Trial Results for Reproxalap in Allergic Conjunctivitis



In 2022, we initiated the randomized, double-masked, vehicle-controlled allergen chamber Phase 3 INVIGORATE-2 Trial of reproxalap in patients with allergic conjunctivitis. Pending positive results from INVIGORATE-2, an allergic conjunctivitis safety trial, and regulatory input, we believe that we will have met NDA requirements for allergic conjunctivitis, although we expect that the NDA submission for allergic conjunctivitis would occur after marketing approval in dry eye disease.

Topical ocular reproxalap has been studied in more than 2,300 patients with no observed clinically significant safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

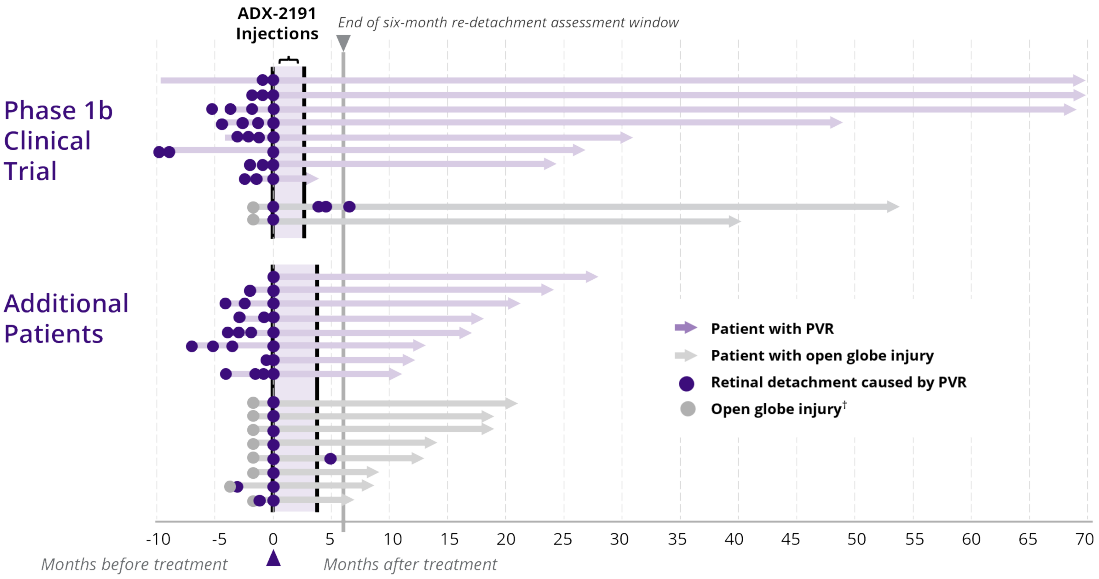
Primary Vitreoretinal Lymphoma

There is no approved treatment for primary vitreoretinal lymphoma. Given that intravitreal methotrexate, the active ingredient of ADX-2191, is the standard of care for the treatment of primary vitreoretinal lymphoma, and based on Pre-IND and Pre-NDA Type B meetings with the FDA, we submitted an NDA for ADX-2191 for the treatment of primary vitreoretinal lymphoma in the fourth quarter of 2022. The NDA submission, which received Priority Review designation and has been assigned a PDUFA date of June 21, 2023, is comprised in part of safety and efficacy evidence of methotrexate from the scientific literature, and safety data from our Phase 3 GUARD Trial in proliferative vitreoretinopathy, described below. The clinical efficacy literature search identified 32 published clinical trials encompassing a total of 406 treated eyes from 258 patients. The efficacy of intravitreal methotrexate for the treatment of primary vitreoretinal lymphoma has been demonstrated by clearance of lymphomatous cells from the vitreous, improvement in vision, clearance of retinal and subretinal lymphomatous infiltration, clearance or reduction in the number and/or size of lesions, decrease in cytokines, increase in overall survival, and increase in progression-free survival.

Proliferative Vitreoretinopathy

Proliferative vitreoretinopathy is a rare inflammatory disorder of the retina that leads to severe retinal scarring and blindness in a subset of patients with retinal detachments, and is the leading cause of failure of retinal reattachment surgery. Standard of care treatment for proliferative vitreoretinopathy results in subsequent retinal detachment surgical rates that approach 40%. In a single-arm, open-label, investigator-sponsored Phase 1b clinical trial performed at the Massachusetts Eye and Ear Infirmary, only approximately 20% of patients with proliferative vitreoretinopathy treated with multiple injections of ADX-2191 required subsequent surgery for retinal detachment (Figure 6).

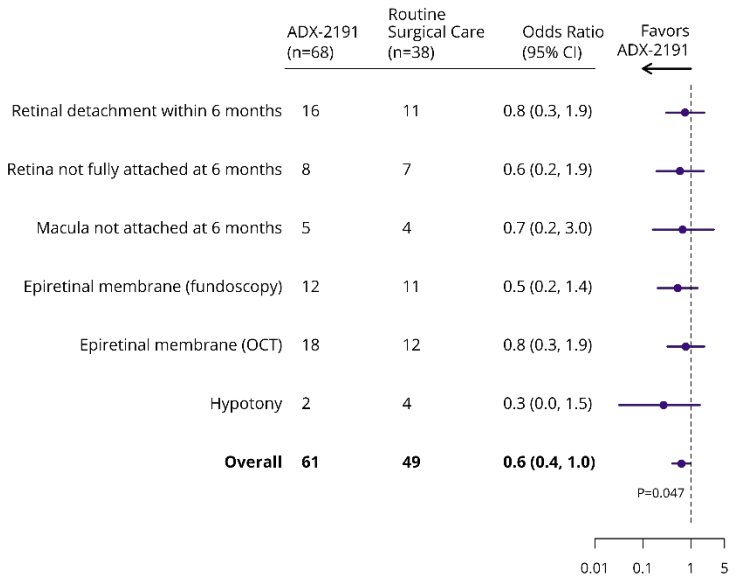
Figure 6: Phase 1b Investigator-Sponsored Clinical Trial of ADX-2191 in Proliferative Vitreoretinopathy



PVR= Proliferative Vitreoretinopathy

In October 2022, we announced results of Part 1 of the GUARD Trial, a two-part, multi-center Phase 3 clinical trial evaluating the efficacy of intravitreal injections of ADX-2191 versus standard-of-care for the prevention of proliferative vitreoretinopathy. The primary endpoint of GUARD Part 1, retinal detachment rate over six months following initiation of therapy relative to historical detachment rates, was achieved: relative to historical control, statistically significant reduction (P=0.024) in retinal detachment over six months was observed following serial intravitreal injection of ADX-2191. Although not statistically powered for secondary or exploratory endpoints, the results of the GUARD Trial demonstrated numerical superiority of ADX-2191 over routine surgical care in reducing the dichotomous endpoints of retinal detachment rate over six months, hypotony (low intraocular pressure), complete retinal attachment by six months, macular attachment by six months, and epiretinal membrane formation (overall P=0.047) (Figure 7). Visual acuity was similar between ADX-2191 treatment and routine surgical care groups. Central macular thickness was numerically lower in ADX-2191-treated patients.

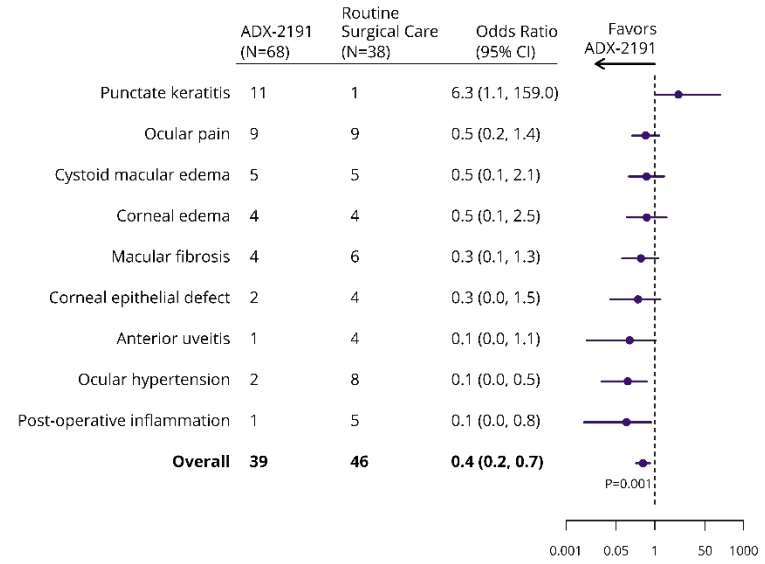
Figure 7: Dichotomous Secondary Endpoints in the Phase 3 GUARD Trial of ADX-2191 in Proliferative Vitreoretinopathy



OCT= optical coherence tomography; Ci= confidence interval

No safety signals were observed in the GUARD Trial, and ADX-2191 was well tolerated; there were no observed treatment-emergent serious adverse events. The most common adverse event associated with ADX-2191 treatment was punctate keratitis, a well-known side effect of intravitreal methotrexate, which was most commonly mild in severity. Across all other treatment-emergent adverse events occurring in at least 10% of patients in either treatment arm, relative to patients treated with routine surgical care, ADX-2191-treated patients had numerically fewer side effects, including pain, cystoid macular edema, corneal edema, macular fibrosis, corneal epithelial defects, anterior uveitis, ocular hypertension, and post-operative inflammation (overall P=0.001) (Figure 8).

Figure 8: All Treatment-Emergent Adverse Events Affecting at Least 10% of Patients in Either Treatment Group in the Phase 3 GUARD Trial of ADX-2191 in Proliferative Vitreoretinopathy



OCT= optical coherence tomography; Ci= confidence interval

The Markets for Our Product Candidates

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 afflicts in excess of 100 million individuals in the United States. In 2021, the top selling drugs for autoimmune conditions alone accounted for approximately $28 billion in sales.

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.

Our RASP modulator platform represents a potential novel therapeutic approach for a variety of common systemic immune-mediated conditions. We are not aware of any other company actively developing therapeutics that target RASP. Because RASP appear to be involved in the generation and potentiation of inflammation in general, we believe the potential therapeutic applicability of RASP modulators is broad. In 2022, we announced results from Phase 2a clinical trials of ADX-629, a first-in-class orally administered RASP modulator, in patients with COVID-19, atopic asthma, psoriasis, or alcohol intoxication, all of which suggested preliminary pharmacodynamic activity of ADX-629. The Phase 2 clinical trials followed a successful Phase 1 clinical trial of ADX-629, in which ADX-629 was well-tolerated; no treatment-related adverse events were observed; and, following ingestion of a fatty meal, levels of cholesterol and fatty acids were lower during ADX-629 treatment than with placebo.

Dry Eye Disease

The validity of the RASP platform is supported by reproxalap, our first-in-class product candidate for the treatment of dry eye disease, which has demonstrated broad-based, rapid-onset activity and consistent safety across a number of Phase 2 and Phase 3 clinical trials and is under NDA review by the FDA. Dry eye disease is an immune-mediated disease, the symptoms of which - ocular pain, dryness, burning, and stinging - are chronic and persistently disturbing, impacting quality of life and leading to loss of work and substantial economic burden. Dry eye disease is one of the most common diseases treated by ophthalmologists and optometrists, and healthcare providers and patients regard therapy as inadequate in a substantial number of cases.

There are approximately 18 million dry eye disease patients diagnosed in the United States, but only three topical ocular drugs are approved for dry eye disease treatment, cyclosporine (0.05% as Restasis®, 0.05% generic cyclosporine, or 0.09% as Cequa™), lifitegrast (5% as Xiidra®), and loteprednol (0.25% as Eysuvis®). The activity of cyclosporine and lifitegrast 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; over 60% of patients discontinue treatment within 12 months of initiation. Loteprednol, a generically available corticosteroid, is indicated only for short-term treatment (up to two weeks) due to corticosteroid-associated toxicity, which includes increases in intraocular pressure that may lead to glaucoma, the development of cataracts, ocular infection, and other ocular morbidities. Thus, there is considerable demand for a novel topical ocular drug that can be used chronically but that acts quickly.

By modulating RASP, which are elevated in a variety of inflammatory diseases, reproxalap represents a novel mechanism for diminishing ocular inflammation. In a number of Phase 2 and Phase 3 clinical trials in dry eye disease, reproxalap demonstrated consistent statistically significant and clinically relevant activity across a variety of symptoms and signs, occurring as early as within minutes of dosing. Given the broad activity and rapid onset of action observed in clinical trials, we believe that reproxalap may have a commercially differentiated product profile versus currently approved drugs for dry eye disease.

Based on the late-stage clinical trial results to date, discussed below, we believe reproxalap could offer differentiated efficacy relative to existing dry eye disease medications, particularly with regard to early onset of action and breadth of activity. The potential size of the dry eye disease market is substantial. We estimate there to be 39 million patients with dry eye disease in the United States, of which approximately 18 million are diagnosed. Assuming approximately one-half of diagnosed patients are candidates for prescription medication, and assuming

approximately four months of therapy per year, the potential total addressable market for reproxalap therapy in dry eye disease is greater than $23 billion in the United States.

Many patients with dry eye disease also manifest symptoms of allergic conjunctivitis, another common inflammatory disease that affects the front of the eye and is characterized by ocular itching and redness. Distinguishing between dry eye disease and allergic conjunctivitis can be challenging for healthcare providers. 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 FDA-approved products that are indicated for the chronic treatment of both dry eye disease and allergic conjunctivitis. Neither cyclosporine nor lifitegrast have been approved for use in patients with allergic conjunctivitis, and antihistamines, which are commonly used in allergic conjunctivitis, are known to exacerbate ocular dryness. In a number of Phase 2 and Phase 3 clinical trials in allergic conjunctivitis, reproxalap demonstrated consistent statistically significant and clinically relevant activity in improving ocular itching and redness. Thus, we believe reproxalap could offer differentiated efficacy relative to existing dry eye disease medications with regard to the potential treatment of the signs and symptoms of allergic conjunctivitis.

Primary Vitreoretinal Lymphoma, Proliferative Vitreoretinopathy, and Retinitis Pigmentosa

Primary vitreoretinal lymphoma is a rare, aggressive, high-grade cancer that arises in the vitreous and retina. An estimated 300-600 people in the United States are diagnosed annually and the median survival for newly diagnosed patients is less than five years. Although there is no approved treatment, the off-label standard of care is up to 25 serial ocular injections of methotrexate, the active ingredient of ADX-2191. ADX-2191 is a concentrated formulation of methotrexate that requires a small injection volume, thereby reducing injection site reflux and ensuing corneal toxicity relative to off-label ocular injections of methotrexate. ADX-2191, which is under NDA review by the FDA, has received Orphan Drug Designation from the FDA for the treatment of primary vitreoretinal lymphoma.

Proliferative vitreoretinopathy is a rare inflammatory disorder of the retina that leads to severe retinal scarring and blindness in a subset of patients with retinal detachments, and is the leading cause of failure of retinal reattachment surgery. Over 50% of proliferative vitreoretinopathy cases result in severe uncorrectable vision loss (visual acuity of 20/320 or worse), and 76% of proliferative vitreoretinopathy patients suffer from at least moderate uncorrectable vision loss. Proliferative vitreoretinopathy occurs after up to 10% of surgeries for retinal detachment and 50% or more of surgeries for open globe injury. Based on the prevalence of primary retinal detachment, in addition to retinal detachment that occurs as a result of trauma, we estimate that there are, in aggregate, approximately 4,000 treatable cases of proliferative vitreoretinopathy in the United States per year. By inhibiting cell growth and thereby diminishing scar formation, ADX-2191 has the potential to be the first FDA-approved drug for prevention of proliferative vitreoretinopathy. ADX-2191 has received Orphan Drug Designation and Fast-Track Designation from the FDA for the prevention of proliferative vitreoretinopathy, and ADX-2191 has been designated an Orphan Medicinal Product by the European Commission for the treatment of retinal detachment. A growing amount of scientific literature supports the use of methotrexate for the prevention of proliferative vitreoretinopathy. Unlike off-label ocular injections of methotrexate, ADX-2191 is denser than the vitreous, the fluid in the back of the eye, allowing for the concentration of methotrexate in the vicinity of retina.

Retinitis pigmentosa is a group of rare genetic eye diseases characterized by retinal cell death and loss of vision, for which there is no treatment. In vivo preclinical research has identified the activity of methotrexate in inducing misfolded rhodopsin clearance, suggesting the potential of ADX-2191 to treat genetic forms of retinitis pigmentosa that are characterized by misfolded rhodopsin. The prevalence of retinitis pigmentosa is more than one million people worldwide, and mutations leading to rhodopsin misfolding account for approximately one-third of cases. ADX-2191 has received Orphan Drug Designation from the FDA for the treatment of retinitis pigmentosa.

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, other 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. Further, competitors with numerous approved products may be able to negotiate pricing and reimbursement that is more favorable than that which we may be able to achieve. We anticipate that we will face intense and increasing competition as new products enter the market and advanced technologies become available. In addition, the development of new treatment methods for the diseases we are targeting could render our products non-competitive or obsolete.

While our product candidates may manifest efficacy, tolerability, or safety advantages, many marketed therapies are generic or may be priced considerably lower than the pricing we anticipate for our product candidates. Pricing, in addition to healthcare plan coverage, prior authorization requirements, step edits, co-pay amounts, and related factors, may discourage the initial or prolonged use of our product candidates. Further, 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 Modulator 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 bind the RASP retinaldehyde 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 temporary RASP binding, and likely lead to the relocation of RASP rather than the elimination or long-term modulation of RASP. We believe that our RASP modulator 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 modulating RASP levels.

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, phosphodiesterase 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., Eli Lilly and Company, Novartis AG, Regeneron Pharmaceuticals, Inc., Roche, Sanofi, Takeda, AstraZeneca, GlaxoSmithKline, Merck, 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.

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 retinal diseases. Though not approved by the FDA for the treatment of

retinal disease, intraocular injection of intravenous methotrexate formulations is the de facto standard of care for primary vitreoretinal lymphoma, and off-label methotrexate is now commonly administered for the treatment of proliferative vitreoretinopathy. The off-label intraocular injection of intravenous methotrexate for retinal diseases is an example of a practice known as compounding. The disadvantages of compounding are significant, and include a risk of microbial contamination that can lead to severe ocular infection resulting in vision loss or surgical removal of the eye. Unlike compounded intravenous formulations, ADX-2191 is specifically formulated for intraocular injection such that pH, viscosity, and tonicity have been designed to be compatible with the vitreous humor, the fluid in the back of the eye. Further, ADX-2191 is a concentrated formulation of methotrexate that requires a small injection volume, thereby reducing injection site reflux and ensuing corneal toxicity relative to off-label ocular injections of methotrexate. Unlike off-label ocular injections of methotrexate, ADX-2191 is denser than the vitreous, the fluid in the back of the eye, allowing for the concentration of methotrexate in the vicinity of retina.

Competitive Pharmaceuticals 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 for Reproxalap and ADX-2191

Indication	Competitive Products
Dry Eye Disease	Topical immunomodulators, such as cyclosporine (0.05% as Restasis® 0.09% as Cequa™ or 0.1% as CyclASol®) and lifitegrast (5% as Xiidra®); topical corticosteroids, such as loteprednol (0.25% as Eysuvis™); an intranasal spray, such as varenicline (0.03mg as Tyrvaya™), a lipid layer stabilizer, such as perfluorohexyloctane (100% as NOV03®), and other generic steroids; and artificial tear solutions
Primary Vitreoretinal Lymphoma, Proliferative Vitreoretinopathy	Off-label ocular injection of intravenous methotrexate

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. There is no approved therapy for primary vitreoretinal lymphoma or proliferative vitreoretinopathy.

Many drugs are in development for dry eye disease or related indications. In addition, generic versions of Restasis® became available in the United States in 2022. The competitive products for allergic conjunctivitis, which may be generic or sold over-the-counter, include topical antihistamines and corticosteroids, nonsteroidal anti-inflammatory drugs, and mast cell stabilizers. We believe that there are currently no drugs in development for primary vitreoretinal lymphoma or proliferative vitreoretinopathy. Many drugs, gene therapies, and cell therapies are in development for the treatment of retinitis pigmentosa. 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 often encourage the use of cheaper, non-innovative, or generic products.

Intellectual Property and Proprietary Rights

Overview

In the United States and abroad, we are building an intellectual property portfolio for reproxalap and other RASP modulators and for therapeutic methods of use of methotrexate for the treatment of retinal disease. 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-629, ADX-246, ADX-248, and other novel compounds. As of December 31, 2022, we owned twenty-five United States patents and twenty pending United States non-provisional patent applications, as well as numerous foreign counterparts to these patents and patent applications, relating to reproxalap and other RASP modulators. Additionally, we retain an exclusive license to certain patents covering the formulation of ADX-2191 and uses thereof in preventing and treating retinal indications including proliferative vitreoretinal disease and primary vitreoretinal lymphoma. As of December 31, 2022, our patent applications included one pending U.S. provisional application, four pending U.S. non-provisional patent applications, and approximately seven pending foreign counterparts to these patent applications, relating to ADX-2191.

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

MEEI Agreement

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

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

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

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

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

Other Intellectual Property Rights

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

Confidential Information and Inventions Assignment Agreements

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

Sales and Marketing

In light of our stage of development, we have not yet fully established a commercial organization or distribution capabilities. We have retained worldwide commercial rights for our product candidates. If our product candidates receive marketing approval, we plan to commercialize them in the United States with our own focused sales organization, a third-party sales force, or a combination of the two. We have begun to establish our commercial infrastructure, but do not expect to establish a complete sales force until approximately three months preceding marketing approval for our product candidates in the United States.

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, 2022, we had 15 full-time employees and had engaged a number of consultants. We expect that a number of consultants previously engaged in development of our product candidates will participate in ongoing clinical and manufacturing activities. None of our employees is represented by a labor union. We have not experienced any work stoppages, and we consider our relations with our employees to be good.

Human Capital

We recognize that attracting, motivating, and retaining talent at all levels is vital to our continued success. Our employees are a significant asset and we aim to create an equitable, inclusive, and empowering environment in which our employees can grow and advance their careers, with the overall goal of developing, expanding and retaining our workforce to support our current pipeline and future business goals. By focusing on employee retention and engagement, we also improve our ability to successfully commercialize our products following approval, if any, support our clinical trials, our pipeline, our platform technologies, business and operations, and also protect the long-term interests of our stockholders. Our success also depends on our ability to attract, engage and retain a diverse group of employees. Our efforts to recruit and retain a diverse and passionate workforce include providing competitive compensation and benefits packages and ensuring we listen to our employees.

We value innovation, passion, data-driven decision making, persistence and honesty, and are building a diverse environment where we believe that our employees thrive and are inspired to contribute to the development of novel therapies. We recognize and appreciate the importance of creating an environment where all team members feel valued, included, and empowered to do their best work and to bring great ideas to the table. We recognize that each team member's unique experiences, perspectives, and viewpoints add value to our ability to develop and deliver innovative diagnostic products and make a meaningful impact on patient care. We aim to foster and maintain a work culture that treats all employees fairly and with respect, promotes inclusivity, and provides equal opportunities for the professional growth and advancement based on merit. Our Code of Business Conduct and Ethics prohibits discrimination on the basis of race, color, religion, national origin, sex (including pregnancy), sexual orientation, age, disability, veteran status, or other characteristics protected by law.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, motivating, and integrating our existing and future employees. The principal purpose of our incentive plans is to increase shareholder value by attracting, retaining, and motivating employees, consultants, and directors through grants of stock-based compensation awards and payments of cash-based performance bonus awards. We are committed to providing a competitive and comprehensive benefits package to our employees. Our benefits package is designed to meet the individual health and wellness needs of our employees. We plan to continue to refine our efforts related to optimizing our use of human capital as we grow, including improvements in the way we hire, develop, motivate, and retain employees.

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, new dosage form, new therapeutic 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 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 an NDA which must be accepted for filing by the FDA;
- satisfactory completion of an FDA pre-approval inspection(s) of our office and 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;

- FDA may also inspect sponsor facilities to determine if nonclinical and clinical studies were conducted in compliance with applicable regulations and guidelines; 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, among other reasons, the potential for unacceptable safety risks arises.

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 informed consent in writing for participation in the clinical trial. Sponsors of clinical trials generally must register and report, at the NIH-maintained website ClinicalTrials.gov, key parameters and results 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.
- *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:* When Phase 2 evaluations suggest that certain dosing regimens may be efficacious and may have an acceptable safety profile, Phase 3 trials may be undertaken in larger patient populations to further evaluate dosage and to obtain evidence of potential clinical efficacy and safety. Phase 3 trials 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 trials.

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. In accordance with the FDAs guidance, the agency has 60 days from receipt of an NDA to determine whether the application will be accepted for filing 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.

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval, and priority review, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Under the fast track program, the sponsor of a new product candidate may request that the FDA designate the product candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the product candidate. To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat patients with a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. In September 2019, ADX-2191 received fast track designation from the FDA for the prevention of proliferative vitreoretinopathy. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

In addition, a sponsor can request breakthrough therapy designation for a drug if it is intended, alone or in combination with one or more other drugs, to treat patients with a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are eligible for intensive guidance from the FDA on an efficient drug development program, organizational commitment to the development and review of the product including involvement of senior managers, and, like fast track products, are also eligible for rolling review of the NDA. Both fast track and breakthrough product candidates may be eligible for accelerated approval and/or priority review, if relevant criteria are met.

Once the submission has been accepted for filing, the FDA begins an in-depth substantive review. Under the 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, with the exception of ADX-2191 which was designated by the FDA as Priority Review for the treatment of primary vitreoretinal lymphoma, and may also be designated Priority Review for other indications. 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. The participation of multiple distinct groups within the FDA has the potential to complicate or prolong review of the application. If the product is deemed a combination product, additional supporting studies may be required, and may delay an NDA submission.

Before approving an NDA, the FDA may inspect our offices and 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 may 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 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 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.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the biopharmaceutical industry has been a particular focus of these efforts and has been significantly affected by federal and state legislative initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing.

By way of example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was signed into law, intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the healthcare industry and impose additional health policy reforms.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will

remain in effect in its current form.

Other legislative changes have been proposed and adopted in the United States since the ACA. For example, through the process created by the Budget Control Act of 2011, there are automatic reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, following passage of the BBA and the Infrastructure Investment and Jobs Act, will remain in effect until 2031 unless additional Congressional action is taken. However, COVID-19 relief support legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics, also has resulted in executive orders, congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Further, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated.

At the state level, individual states in the United States have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some third-party payors also require pre-approval of coverage for new or innovative devices or therapies before they will reimburse healthcare providers that use such therapies.

We expect that these initiatives, as well as other healthcare reform measures that may be adopted in the future, as well as the trend toward managed healthcare and increasing influence of managed care organizations, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of current and future cost containment measures or other healthcare reforms may adversely affect our operations and prevent us from being able to generate revenue, attain profitability or commercialize our product candidate.

Orphan Drug Designation

The FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is defined as a disease or condition that affects 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 or approval process. ADX-2191 has received orphan designation for the prevention of proliferative vitreoretinopathy, and for the treatment of primary vitreoretinal lymphoma and retinitis pigmentosa.

If an orphan drug-designated product subsequently receives the first FDA approval for the disease specified in the orphan drug designation, 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. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of Orphan Drug Designation are tax credits for certain research and a waiver of the NDA application fee. If a competitor obtains approval of the same drug, as defined by the Orphan Drug Act, before we do 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.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

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 the 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 a 505(b)(1) NDA, 505(b)(2) NDA, or supplement to an approved NDA if new clinical investigations other than bioavailability studies (e.g., investigations that support new indications, dosages, or strengths of an existing drug) were conducted or sponsored by the applicant and are deemed by the FDA to be essential to the approval of the application. The 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 505(b)(1) NDA.

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 $47.3 million for the year ended December 31, 2022 and $44.9 million for the year ended December 31, 2021.

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.

Summary of Risks Related to our Business

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below and should be carefully considered, together with other information in this annual report on Form 10-K and our other filings with the Securities and Exchange Commission before making investment decisions regarding our common stock.

- Our business is dependent in large part on the successful commercialization of two product candidates, reproxalap and ADX-2191. If we are unable to successfully obtain marketing approvals for reproxalap or ADX-2191, or experience significant delays in doing so, or if, after obtaining marketing approvals, we fail to successfully commercialize these product candidates, our business will be materially harmed.
- To generate revenue, we will depend on FDA approval and successful commercialization of our product candidates, reproxalap and ADX-2191. If we are unable to successfully obtain FDA approval, or FDA approval is delayed or limited, our ability to generate revenue will be significantly delayed.
- If we fail to develop and commercialize other product candidates, we may be unable to grow our business.
- Reproxalap, ADX-2191, 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.
- 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 have incurred significant operating losses since inception and we expect to incur significant losses over the next several years. We may never become profitable or, if achieved, be able to sustain profitability.
- We will require substantial additional financing, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our product development, other operations or commercialization efforts.
- 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 successfully commercialize our product candidates when expected, or at all.
- Public health emergencies, epidemics or pandemics, such as the ongoing COVID-19 pandemic, may impact our business.

Risks Related to the Potential Development and Commercialization of Reproxalap, ADX-2191 and our Product Candidates

Our business is dependent in large part on the successful commercialization of two product candidates, reproxalap and ADX-2191. If we are unable to successfully obtain marketing approvals for reproxalap or ADX-2191, or experience significant delays in doing so, or if, after obtaining marketing approvals, we fail to successfully commercialize these product candidates, our business will be materially harmed.

We are dependent in large part on regulatory approval and successful commercialization of reproxalap and ADX-2191 for our future business success. There is a significant risk that we will fail to successfully obtain marketing approval and/or commercialize reproxalap and/or ADX-2191. Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of an NDA to the FDA, and even fewer are approved for commercialization.

Prior to and following potential NDA approval, we will invest a significant portion of our time and financial resources on the commercialization of reproxalap and ADX-2191. We cannot accurately predict when or if either of these product candidates will receive marketing approval. Our ability to generate product revenues will depend on our obtaining marketing approval for, and commercializing one or both of, reproxalap and ADX-2191. The future regulatory and commercial success of reproxalap, ADX-2191 and our other product candidates is subject to a number of risks, including the following:

- obtaining marketing approval for reproxalap and ADX-2191, for which the FDA has accepted our NDAs for filing, or any other product candidates;
- manufacturing at commercial scale, marketing, selling and distributing those products for which we obtain marketing approval;
- hiring and building a full commercial organization required for the marketing, selling and distributing for those products which we obtain marketing approval;
- achieving an adequate level of market acceptance of and obtaining and maintaining coverage and adequate reimbursement from third-party payors for any products we commercialize;
- obtaining, maintaining and protecting our intellectual property rights;
- we may not be able to provide sufficient evidence of safety and efficacy to obtain regulatory approval;
- 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 for which we seek approval;
- the FDA, or comparable foreign bodies, may require additional clinical data;
- we may not have sufficient financial and other resources to pursue our business plans, complete necessary clinical trials of our product candidates and commercialize our approved products, if any;
- if approved, reproxalap, ADX-2191 and our other 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;
- competitive products may be more effectively or comprehensively marketed to physicians or patients, or contracted with payors more successfully;
- the results of our clinical trials may not meet the endpoints, or level of statistical or clinical significance required by the FDA, or comparable foreign regulatory bodies, for marketing approval;
- the safety and efficacy results of our later phase or larger clinical trials may not confirm the results of our earlier trials;
- patients in our clinical trials may demonstrate greater response rates or improvements from vehicle or in the non-treatment arm then was expected when designing and powering our clinical trials;

- there may be variability in patients, adjustments to clinical trial procedures, and inclusion of additional clinical trial sites;
- the initial parts of adaptive clinical trials are not designed to be pivotal or definitive, and as such we may not satisfy the designated endpoints and also may need to revise the design or endpoints to achieve success in later parts of the trial or potentially abandon the trial;
- we may not be able to timely or adequately finalize the design or formulation of any product candidate or demonstrate that a formulation of our product candidate will be stable for commercially reasonable time periods;
- we may be adversely affected by legislative or regulatory reform of the health care system in the United States or other jurisdictions in which we may do business; and
- we may not be able to obtain, maintain, or enforce our patents and other intellectual property rights.

Furthermore, even if we do receive regulatory approval to market reproxalap, ADX-2191, or any of 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 commercialize our product candidates or continue to fund our development programs, we cannot assure that reproxalap and/or ADX-2191 will be successfully commercialized, or our other product candidates will be successfully developed or commercialized. If we are unable to obtain regulatory approval for or, if approved, we or any of our future partners are unable to successfully commercialize reproxalap and/or ADX-2191, and our other product candidates, we may not be able to generate sufficient revenue to continue our business.

To generate revenue, we will depend on FDA approval and successful commercialization of our product candidates, reproxalap and ADX-2191. If we are unable to successfully obtain FDA approval, or FDA approval is delayed or limited, our ability to generate revenue will be significantly delayed.

Our ability to generate revenue will depend on the successful development, regulatory approval and commercialization of reproxalap and ADX-2191. We submitted an NDA for reproxalap for the treatment of the signs and symptoms of dry eye disease in December 2022. In February 2023, the FDA accepted the reproxalap NDA for filing and set a PDUFA date of November 23, 2023. We submitted an NDA for ADX-2191 for the treatment of primary vitreoretinal lymphoma in December 2022. In March 2023, we announced that the FDA accepted the ADX-2191 NDA for filing with priority review and set a PDUFA date of June 21, 2023. However, the FDA's decision to accept the NDAs for filing and set PDUFA dates does not indicate that it has made any decision regarding approval nor does it guarantee approval by such dates, if at all. The FDA has substantial discretion in the approval process and may disagree with our interpretation of or the sufficiency of the data from our clinical trials. Clinical trial results frequently are susceptible to varying interpretations and regulatory authorities may disagree on what are appropriate methods for analyzing data, which may delay, limit or prevent regulatory approvals. The FDA could also require that we conduct additional studies or clinical trials and submit the results of those studies or clinical trials before the application will be reconsidered, which would require us to expend more resources than we planned or that are available to us, and could substantially delay any approval of our application. If marketing approval for reproxalap, ADX-2191, 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. Such a delay could occur because a competitor product is approved before our product and secures patent protection, market exclusivity, or both, and thereby precludes our product approval for a number of years. It is also possible that additional studies or clinical trials may not suffice to make our application approvable. There can be no assurance that NDAs accepted for filing by the FDA will be approved in a timely manner or at all.

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.

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 ongoing or planned clinical trials for our 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:

- public health epidemics or pandemics, including the COVID-19 pandemic or responses thereto;
- 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 our 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 our product candidates, or drug product components being ordered by the FDA or other government or regulatory authorities to temporarily or permanently shut down due to violations of 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, cGMP, 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;
- delays in shipment of clinical trial material reaching clinical sites;
- 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 our 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 our product candidates could be significantly reduced.

Reproxalap, ADX-2191, and our other product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays, or prevent the receipt of the required approvals to commercialize our product candidates.

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

Reproxalap, ADX-2191, and our other product candidates, and the activities associated with development and 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 and commercialization 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;
- adverse events which had initially been considered unrelated to the product candidate may later, even following approval and/or commercialization, be found to be caused by the product candidate;
- difficulty establishing predictive preclinical models for demonstration of safety and efficacy of a product candidate in one or more potential therapeutic areas for clinical development;
- patients in our clinical trials may demonstrate greater response rates or improvements from vehicle or standard of care than was expected when designing and powering our clinical trials;
- delays resulting from or additional protocols being required as result of the COVID-19 pandemic;
- lack of availability of, or difficulty recruiting and retaining, a sufficient number of patients to adequately power our clinical trials;
- difficulties in manufacturing a product candidate, including the inability to manufacture a product candidate in a sufficient quantity, suitable form, or in a cost-effective manner, or under processes acceptable to the FDA for marketing approval or commercial sale;
- the proprietary rights of third parties, which may preclude us from developing or commercializing a product candidate;

- determining that a product candidate may be uneconomical for us to develop or commercialize, or may fail to achieve market acceptance or adequate pricing or reimbursement;
- our expectations regarding our expenses and revenue, the sufficiency or use of our cash resources, and needs for additional financing;
- a safety concern or signal may arise that triggers a clinical hold;
- any negative results or perceived negative results in clinical trials for one indication may have an adverse effect on our ability to develop and potentially commercialize reproxalap, ADX-2191, or our other product candidates for the treatment of another indication;
- our inability to secure strategic partners which may be necessary for advancement of a product candidate into clinical development or commercialization; or
- our prioritization of other indications or product candidates for advancement.

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

- such authorities may disagree with the design, conduct, 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;
- a competitor product may have patent protection or another type of market exclusivity that delays approval of our product;
- 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 or require additional trials and data;
- 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 that will continue to affect our business.

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

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

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

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

The results of preclinical studies and earlier clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials 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. Any negative results or perceived negative results in clinical trials for one indication may have an adverse effect on our ability to develop and potentially commercialize reproxalap, ADX-2191, or our other product candidates for the treatment of another indication. 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, as is the case for adaptive trials; 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 run-in cohorts, 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. In

addition, discussions with regulatory bodies, such as the FDA, may lead to changes in trial designs or programs. Companies frequently suffer significant setbacks in advanced clinical trials, even after run-in cohorts or earlier clinical trials have shown promising results. For example, the results of the TRANQUILITY Trial did not reflect the results of the TRANQUILITY run-in cohort. 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 immune-mediated diseases. We performed an adaptive trial in proliferative vitreoretinopathy, the GUARD trial, and may do so with other indications in the future. In an adaptive trial, the initial parts of the trial are not designed to be pivotal or definitive. Rather, the initial parts of adaptive trials are expected to provide data to guide subsequent parts of the trial, which could require design changes, including but not limited to, different endpoints. In addition, following the initial parts of adaptive trials, we may, among other things, decide to continue to the subsequent parts of the trial, conclude the trial based on its success or failure in such initial parts, or discuss the trial results and regulatory pathway with regulatory authorities prior to determining next steps with respect to the trial and development program. As such, the likelihood of success in our late-stage clinical programs cannot necessarily be predicted.

We could also face challenges in designing clinical trials and obtaining regulatory approval of our product candidates due to the lack of historical clinical trial experience for novel classes of therapeutics. Thus, it is difficult to determine whether regulatory agencies will be receptive to the approval of our product candidates, and to predict the time and costs associated with obtaining regulatory approvals. The clinical trial requirements of the FDA and other regulatory agencies and the criteria regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and require more time and trial data than for other, better known, or more extensively studied classes of product candidates. In addition, it is possible that, as regulatory bodies gain more familiarity with our type of product candidates by reviewing competitor candidates, those agencies could impose new conditions on our product candidates that we did not expect. Any inability to design clinical trials with protocols, methodology, 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 some of our product candidates are, to our knowledge, new chemical entities, it is difficult to predict the time and cost of development and our ability to successfully complete clinical development of these product candidates and obtain the necessary regulatory approvals for commercialization.

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

We may not be able to qualify for or obtain various designations from regulators that would have the potential to expedite the review process of one or more of our product candidates, and even if we do receive one or more of such designations there is no guarantee that they will ultimately expedite the process, or aid in our obtaining marketing approval or provide market exclusivity.

There exist several designations that we can apply for from the FDA and other regulators that would provide us with various combinations of the potential for expedited regulatory review, certain financial incentives as well as the potential for post-approval exclusivity for a period of time. These designations include but are not limited to orphan drug designation, breakthrough therapy designation, accelerated approval, fast track status, and priority

review for our product candidates. We may seek one or more of these designations for our current and future product candidates. In April 2018, ADX-2191 received orphan drug designation from the FDA for the prevention of proliferative vitreoretinopathy and, in June 2020, ADX-2191 was designated an orphan medicinal product by the European Commission for the treatment of retinal detachment. In September 2019, ADX-2191 received fast track designation from the FDA for the prevention of proliferative vitreoretinopathy. There can be no assurance that any of our other product candidates will qualify for any of these designations. There can also be no assurance that any of our product candidates, that do qualify for these designations, will be granted such designations or that the FDA will not revoke such a designation it grants at a later date. Further, there can be no assurance that any of our product candidates that are granted such designations will ever benefit from such designations or that the FDA would not withdraw such designations once granted. Were we to receive a designation that promised a period of market exclusivity, such as orphan drug exclusivity, such exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Further, with respect to orphan drug status, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective, or makes a major contribution to patient care.

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

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

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

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

As part of our business strategy, we have and continue to evaluate the development and commercialization of product candidates for the treatment of orphan and other rare diseases, including proliferative vitreoretinopathy and retinitis pigmentosa. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients willing and able to participate in the clinical trials required by the FDA or other non-United States regulatory agencies. In addition, if others develop products for the treatment of similar diseases, we would potentially compete with them for the enrollment in rare patient populations, which may adversely impact the rate of patient enrollment in and the timely completion of our current and planned clinical trials. Any negative results or perceived negative results in clinical trials of our product candidates may make it difficult or impossible to recruit or retain patients in other clinical trials of the same product candidate. Insufficient patient enrollment may be a function of other factors, including the size and nature of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the timing and magnitude of disease symptom presentation, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial. Our inability to identify and enroll a sufficient number of eligible patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials or development program. The ongoing COVID-19 pandemic has and may have an impact on our ability to enroll and retain patients in our clinical trials. For instance, patient enrollment in our GUARD trial of ADX-2191 and our 12-month safety trial of reproxalap were negatively impacted as a result of limited clinical trial staffing at trial sites and some patients electing to delay surgery. Delays in patient enrollment in the future as a result of these and other factors may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent us from completing these trials and adversely affect our ability to advance the development of our product candidates. For instance, in rare diseases such as proliferative vitreoretinopathy, lack of availability of, or difficulty recruiting or retaining a sufficient number of, patients may make it difficult or cost-prohibitive to sufficiently power our clinical trials, which may not enable us to

continue development and seek regulatory approval for the applicable product candidate. Further, if our products are approved by regulatory agencies, we may not be able to identify sufficient number of patients to generate significant revenues.

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

Unacceptable adverse events caused by any of our product candidates that we or others advance into clinical trials could cause us or regulatory authorities to interrupt, delay, or halt clinical trials, or impose a clinical hold, potentially resulting 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 continue to develop our product candidates 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.

Even if we obtain marketing approval for reproxalap, ADX-2191, 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 or clinical trials, post-market surveillance, or other potential additional clinical trials. Following approval, if any, of reproxalap, ADX-2191, 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, ADX-2191, 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 an 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, ADX-2191, or any of our other product candidates is approved, our product labeling, advertising, and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The government has also entered into consent decrees and Corporate Integrity Agreements under which specified promotional conduct is changed or curtailed.

Even if we receive regulatory approval for reproxalap, ADX-2191, 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, or 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 secure advantageous contracts with payors or 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, commercially advantageous, 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.

In addition, because the active ingredient of ADX-2191 (methotrexate) is a generic drug, a generic manufacturer may be able to develop and market a competitive intravitreal formulation of methotrexate following expiration of commercial exclusivity mandated via certain orphan drug designations. Generic drug competition would have a material and adverse effect on the commercial potential of ADX-2191. 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 (FDCA), 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 that ongoing initiatives in the United States will 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, ADX-2191, 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. Competitors with numerous approved products may be able to negotiate pricing and reimbursement that is substantially more advantageous than that which we will be able to negotiate.

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 and ADX-2191 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, ADX-2191, and our other 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 estimated addressable markets and market opportunities for our drug candidates are based on a variety of inputs, including data published by third parties, our own market insights and internal market intelligence, and internally generated data and assumptions. We have not independently verified any third-party information and cannot be assured of its accuracy or completeness. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower or more difficult to identify than expected. In addition, our product candidates may not achieve commercial success due to market conditions or regulatory challenges.

Any of these factors may negatively affect our ability to generate revenues from sales of our product and our ability to achieve and maintain profitability, and as a consequence, our business may suffer. In addition, these inaccuracies or errors may cause us to misallocate capital and other critical business resources, which could harm our business.

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, including cost effectiveness relative to existing contracts with other pharmaceutical companies; 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 the United States healthcare system, including changes to the methods for, and amounts of, Medicare reimbursement. 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. Payors 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, larger companies contracting with payors to diminish reimbursement for competitive products, and additional legislative proposals as well as country, regional, or local healthcare budget limitations.

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 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 trials, the termination or hold on a clinical trial, 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 or impair our ability to develop and commercialize our products. 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.

In order to conduct clinical trials of our drug candidates, we will need to manufacture them in large quantities. Quality issues may arise during scale-up activities. Our reliance on a limited number of Contract Manufacturing Organizations (CMOs), the complexity of drug manufacturing and the difficulty of scaling up a manufacturing process could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our drug candidates, and cause us to incur higher costs and prevent us from commercializing our drug candidates successfully. Furthermore, if our CMOs fail to deliver the required commercial quality and quantities of materials on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement CMOs capable of production in a timely manner at a substantially equivalent cost, then testing and clinical trials of that drug candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. In addition, failure of CMOs to comply with regulatory and quality requirements could delay manufacturing or the review of our marketing applications.

Any adverse developments affecting manufacturing operations for our products, including as a result of the COVID-19 pandemic or responses taken thereto, may result in shipment delays; inventory shortages; lot failures; product withdrawals, recalls, approvals; 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.

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

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

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

We operate in highly competitive segments of the biotechnology market. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies, and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies (including generic and over-the-counter drugs) as well as with new treatments that may be introduced by our competitors. With the exception of proliferative vitreoretinopathy, primary vitreoretinal lymphoma, and retinitis pigmentosa, there are a variety of approved drugs and drug candidates in development for the indications that we intend to test. Current treatments that are used in the United States for dry eye disease include over the counter artificial tears, Restasis®, Xiidra®, Cequa™, Eysuvis®, and Tyrvaya™ . In February 2022, the FDA approved the first generic version of Restasis®, which is now available for sale in the U.S. 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 commercial 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, ADX-2191, 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.

If we are unable to successfully establish and maintain 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 only recently begun to establish a sales or marketing infrastructure and have no experience as a Company in the sale, marketing or distribution of biopharmaceutical products. If reproxalap, ADX-2191, 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 and maintain internal sales, distribution, and marketing capabilities, some of which will be committed prior to any confirmation that reproxalap, ADX-2191, or any of our other product candidates will be approved.

We currently expect that we may build our own sales and marketing organization to support the commercialization in the United States of product candidates for which we receive marketing approval. In advance of receiving marketing approval for reproxalap and ADX-2191, we have begun to build our commercial infrastructure. There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of reproxalap, ADX-2191 or any product candidate for which we establish a commercial infrastructure is delayed or does not occur for any reason, including if we do not receive marketing approval on the timeframe we expect, we would have incurred these commercialization expenses prematurely or unnecessarily. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

If we are unable to establish our own sales and marketing capabilities and enter into arrangements with third parties to perform these services, our revenue from product sales and our profitability, if any, are likely to be lower than if we ourselves were to market and sell any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to market and sell our drug candidates or may be unable to do so on terms that are acceptable to us. Any of these third parties may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our product candidates that receive marketing approval, or such authorities do not grant our product candidates appropriate periods of data or market exclusivity before approving generic versions of our product candidates, the sales of our product candidates could be adversely affected.

Once an NDA is approved, the drug covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations." Manufacturers may seek marketing approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications (ANDAs) in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials demonstrating safety and efficacy. Rather, the applicant generally must show that its drug is pharmaceutically equivalent to the reference listed drug, in that it has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug, and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic drugs may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic drugs are generally able to offer drug products at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug is typically lost to the generic drug.

The FDA may not approve an ANDA for a generic drug until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such product candidate 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, enforceability or non-infringement. The FDCA also provides three years of marketing exclusivity for a 505(b)(1) NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations other than bioavailability studies (e.g., investigations

that support new indications, dosages, or strengths of an existing drug) were conducted or sponsored by the applicant and are deemed by the FDA to be essential to the approval of the application. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving competitor products for product candidates containing the original active agent for other conditions of use. Five-year and three-year exclusivity will not delay the submission or approval of a full 505(b)(1) NDA. Manufacturers may seek to launch these generic drugs following the expiration of the marketing exclusivity period, even if we still have patent protection for our drug.

In the EU and the UK, innovative medicinal products are authorized based on a full marketing authorization application (as opposed to an application for marketing authorization that relies on data in the marketing authorization dossier for another, previously approved medicinal product). Applications for marketing authorization for innovative medicinal products must contain the results of pharmaceutical tests, preclinical tests, and clinical trials conducted with the medicinal product for which marketing authorization is sought (and where applicable the result of the pediatric studies unless a waiver or a deferral has been obtained - as described further below). In the EU, these applications must be made pursuant to either Directive 2001/83/EC (for the decentralized procedure or the mutual recognition procedure) or Regulation 726/2004 (for the centralized procedure). In the UK, there are various procedures available under the new regulatory legal framework to pharmaceutical products, including the possibility of a recognized assessment conducted by the European authorities under certain circumstance or by applying directly to the UK regulatory authority (MHRA).

Where an applicant for a marketing authorization submits a full dossier containing its own pharmaceutical, pre-clinical tests and clinical trials data, and where the application does not fall within the "global marketing authorization" of an existing medicinal product, the applicant is entitled to eight years of regulatory data protection upon grant of the marketing authorization (the period starts to run from the first marketing authorization in the EU/ European Economic Area (EEA)). During this period, applicants for approval of generics or biosimilars cannot rely on data contained in the marketing authorization dossier submitted for the already authorized, or reference, medicinal product to support their application. After the expiration of the eight-year period of regulatory data protection, the reference medicinal product benefits from a further two-year period of marketing protection. During these two years of marketing protection, no generic or biosimilar medicinal product that relies upon the reference medicinal product’s dossier may be placed on the EU market, but a generic or biosimilar marketing authorization application can be submitted to the competent regulatory authorities in the EU Member States during this time. The two-year period of marketing protection can further be extended by one year if, during the first eight years of the grant of the first marketing authorization, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, even if a compound is considered to be a new active substance and the innovator is able to gain the period of regulatory data protection and marketing protection, provided that no other IP or regulatory exclusivities applied, another unrelated company could also apply for a marketing authorization and market another competing medicinal product for the same therapeutic indication if such company obtained its own marketing authorization based on a separate marketing authorization application based on a full self-standing scientific data package supporting the application. The period of regulatory data protection and marketing protection applies in the UK (running from the date of the first authorization in Great Britain).

In the EU, pursuant to Regulation 1901/2006, and in the UK pursuant to the Human Medicines Regulations 2012 (as amended), marketing authorization applications must include pediatric data based on pediatric investigation plans agreed with the EMA if the MAA concerns (i) a new active substance, or (ii) a new indication, pharmacological form, or route of administration (where the product is protected by a supplementary protection certificate or a patent qualifying for a supplementary certificate). Applicants may obtain waivers or deferrals to these requirements in certain circumstances (for example a waiver may be obtained if the condition only occurs in adult populations). Where required, pediatric studies must cover all sub-sets of the pediatric population for both existing and new indications, pharmacological forms and route of administrations. Limited further exclusions apply, including in relation to generic or biosimilar applications. Certain rewards may be available for completion of pediatric studies. For example, where MAAs include the results of all studies conducted in compliance with an agreed pediatric investigation plan, the holder of the patent or supplementary protection certificate may be entitled to a six-month extension to the supplementary protection certificate.

In order to obtain orphan designation in the EEA, the product must fulfill certain challenging criteria. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as an orphan medicinal product if it meets the following criteria: (1) is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; and (2) either the prevalence of such condition must not be more than five in 10,000 persons in the EU when the application is made, or without the benefits derived from orphan status, it must be unlikely that the marketing of the medicine would generate sufficient return in the EU to justify the investment needed for its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000.

Products receiving orphan designation in the EU may receive 10 years of orphan market exclusivity, which can be further extended by two years if pediatric studies have been conducted in accordance with an agreed pediatric investigational plan. Applications must first satisfy the orphan designation criteria and apply for orphan designation before making the application for marketing authorization. The applicant must then successfully maintain the orphan designation at the time of the marketing authorization application in order to qualify for 10 years of orphan market exclusivity. During this 10-year period, the competent authorities of the EU Member States and European Commission may not accept applications or grant marketing authorization for other similar medicinal products for the same orphan therapeutic indication. The protection afforded by orphan market exclusivity in the EU may, in some circumstances, be circumvented by competitor products which are demonstrated not to be "similar" or which are authorized for different therapeutic indications. There may be a risk that products may be prescribed "off-label" for the orphan therapeutic indication by healthcare professions in some EU Member States.

There are also three exceptions to the orphan market exclusivity principle. Marketing authorization may be granted to a similar medicinal product for the same orphan therapeutic indication if:

- The second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective, or otherwise clinically superior;
- The holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- The holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

An orphan product can also obtain an additional two years of orphan market exclusivity in the EU if the marketing authorization application contains the results of all pediatric studies conducted in accordance with and agreed pediatric investigation plan. The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation; for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity.

The UK’s regulatory legal framework provides for similar periods of protection, namely regulatory data protection, marketing protection and market exclusivity.

It is important to note that the regulatory protection afforded to medicinal product such as data exclusivity, marketing protection, market exclusivity for orphan indications, and pediatric extension are currently under review at EU level. It is expected that the protection currently afforded in the EU will be reduced in the years to come.

Competition that our product candidates may face from generic versions of our product candidates could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates. Our future revenues, profitability, and cash flows could also be materially and adversely affected and our ability to obtain a return on the investments we have made in those product candidates may be substantially limited if our product candidates, if and when approved, are not afforded the appropriate periods of non-patent exclusivity.

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. 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 was 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.

Failure to obtain regulatory approval in foreign jurisdictions would prevent us from marketing and commercializing our products abroad and may limit our ability to generate revenue from product sales.

We intend to market and commercialize our product candidates internationally. To market and sell our drug candidates in jurisdictions outside the United States, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Failure to obtain foreign regulatory approvals on a timely basis or non-compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs for us and could delay or prevent the introduction of our drug candidates in certain countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any jurisdiction, which would materially impair our ability to generate revenue.

The UK's exit from the EU continues to create political and economic uncertainty, particularly in the UK and the EU. The UK is now being treated as a "third country" by the EU and new UK legislation has taken effect. This means that some regulatory activities, such as batch testing and Qualified Person certification conducted in Great Britain is no longer recognized in the EU. However, the UK and EU have concluded a Trade and Cooperation Agreement (TCA), which has been approved by the UK Parliament, European Council and European Parliament and has limited the disruption to the supply of medicines, particularly by enabling tariff and quota-free trade between the UK and the EU (provided that the rules of origin requirements are met), and has streamlined some issues, for example by enabling mutual recognition of cGMP inspections and certificates. The regulatory framework for medicines that existed before the end of the transition period has also effectively been preserved in UK domestic legislation as "retained EU law." By retaining a snapshot of EU legislation at its core, the UK has prevented substantial divergence to the regulation of medicines (although divergence has appeared in some areas). However, some changes to the UK legislation have been immediately necessary, including the implementation of the Northern Ireland Protocol (NIP), pursuant to which, the EU pharmaceutical legal framework acquis continues to apply in

Northern Ireland (subject to periodic consent of the Northern Ireland Legislative Assembly), and only products compliant with EU law can be placed in the Northern Ireland market - adding an extra layer of regulatory complexity. As companies now need to comply with a separate UK regulatory legal framework in order to commercialize medicinal products in Great Britain (namely, England, Wales and Scotland, as EU law continues to apply in Northern Ireland). The UK government is currently trying to renegotiate fundamental aspects of the NIP so this is an unpredictable area for companies in the near future. The TCA allows for future deviation from the current regulatory framework and it is not known if and/or when any deviations may occur, which may have an impact on development, manufacture, marketing authorization, commercial sales and distribution of pharmaceutical products. It is also important to note that obtaining a marketing authorization is not sufficient to gain effective access to the market in the EU and in the UK; companies still need to agree to a reimbursement price for the products and in some jurisdictions, such as the UK and Germany, a further positive recommendation from health technology on cost-effectiveness is required for the products to be actually prescribed and reimbursed by the respective national health systems (see below). If we fail to comply with the regulatory requirements in international markets and thus receive applicable marketing approvals, our target market will be reduced, our ability to realize the full market potential of our drug candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all. Our failure to obtain approval of any of our drug candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that drug candidate and our business prospects could decline.

Risks Related to our Financial Position and Capital Requirements

We have incurred significant operating losses since inception and we expect to incur significant losses over the next several years. 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, development programs, and commercial activities for reproxalap, ADX-2191, and our other product candidates. Net loss for the year ended December 31, 2022 and 2021 was approximately $62.0 million and $57.8 million, respectively. As of December 31, 2022, we had total stockholders' equity of $151.0 million and an accumulated deficit of $356.7 million. Losses have resulted principally from costs incurred in our clinical trials, research and development programs and from general and administrative expenses. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities, pre-commercial activities, and, if reproxalap, ADX-2191, or any of our other product candidates is approved, commercialization efforts, including 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. Our net losses may fluctuate significantly from quarter to quarter and year to year.

We anticipate that our expenses will increase substantially as compared to prior periods as we prepare for commercialization of reproxalap and ADX-2191, as a result of increased headcount, including management personnel to support our clinical, manufacturing and commercialization activities, expanded infrastructure, increased legal, compliance, accounting and investor and public relations expenses associated with being a public company and increased insurance premiums, among other factors. Our license agreement with Massachusetts Eye and Ear Infirmary, or MEEI, under which we license certain of our patent rights and a significant portion of the technology for ADX-2191, imposes royalty and other financial obligations on us, and we may enter into additional licensing and funding arrangements with third parties that may impose milestone payment, royalty, insurance and other obligations on us.

Our expenses will also increase if and as we:

- seek marketing approval for reproxalap and ADX-2191 and establish our sales, marketing and distribution capabilities for reproxalap and ADX-2191 in advance of and upon any such approval;
- conduct any necessary clinical trials and other development activities and/or seek marketing approvals for ADX-629, ADX-246, ADX-248 and any other product candidates;
- pursue the clinical development of reproxalap or ADX-2191 for the treatment of other additional indications or for use in other patient populations or, if approved, seek to broaden the label of reproxalap or ADX-2191;

- scale up our manufacturing processes and capabilities to support commercialization of reproxalap and ADX-2191, and any of our other product candidates for which we seek and/or obtain marketing approval;
- leverage our RASP-modulator discovery platform to advance additional therapeutics into preclinical and clinical development;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, scientific, manufacturing, commercial and management personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- increase our product liability insurance coverage as we initiate and expand our commercialization efforts; and
- expand our sales, marketing and distribution capabilities for our other product candidates, prior to or upon receiving marketing approval;

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase from what we anticipate if:

- we are required by the FDA or non-U.S. regulatory agencies to perform clinical trials or studies in addition to those expected;
- there are any delays in enrollment of patients in or completing our clinical trials or the development of our product candidates; or
- there are any third-party challenges to our intellectual property portfolio, or the need arises to defend against intellectual property-related claims.

Our ability to become and remain profitable depends on our ability to generate revenue. We currently generate no revenue from sales, and we may never be able to commercialize reproxalap, ADX-2191, 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 do not expect to generate revenue that is sufficient to achieve profitability unless and until we obtain marketing approval for and commercialize one or more of our product candidates. We do not expect to commercialize reproxalap and ADX-2191 or any of our other product candidates before late 2023, if ever. Achieving profitability will require us to be successful in a range of challenging activities, including:

- obtaining marketing approval for reproxalap and ADX-2191, for which the FDA has accepted our NDAs for filing, or any other product candidates;
- manufacturing at commercial scale, marketing, selling and distributing those products for which we obtain marketing approval;
- hiring and building a full commercial organization required for the marketing, selling and distributing for those products which we obtain marketing approval;
- achieving an adequate level of market acceptance of and obtaining and maintaining coverage and adequate reimbursement from third-party payors for any products we commercialize; and
- obtaining, maintaining and protecting our intellectual property rights.

We may never succeed in these activities and may never generate revenue that is sufficient to achieve profitability. 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. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations.

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

The development and commercialization of biopharmaceutical products is capital intensive. We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we seek marketing approval and prepare for commercialization of reproxalap and ADX-2191, and continue the development of our product candidates through preclinical and clinical development, including multiple ongoing and planned clinical trials for our product candidates. We expect our expenses to increase in connection with our ongoing activities, particularly as we commercialize reproxalap and ADX-2191, if approved, and we continue the research and development of, and, if successful, seek marketing approval for, our product candidates.

We have begun to incur commercialization expenses related to reproxalap and ADX-2191, including beginning to build a commercial infrastructure and expect to incur additional commercialization expenses in advance of potentially receiving marketing approval for reproxalap and ADX-2191. If we do obtain marketing approval for reproxalap, ADX-2191 or any other product candidate that we develop, we expect to incur significant additional commercialization expenses related to product sales, marketing, distribution and manufacturing. We may also need to raise additional funds sooner if we choose to pursue additional indications for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed on attractive terms, if at all, we will be forced to delay, reduce, or eliminate certain of our clinical development plans, research and development programs or future commercialization efforts. In addition, there can be no assurance that we will be able to obtain such financing on commercially reasonable terms or at all. The development process for our product candidates is highly uncertain, and we cannot estimate with certainty the actual amounts necessary to successfully complete the development, regulatory approval, and commercialization of our product candidates. Our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than expected, through public or private equity, debt financings, or other sources. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the costs, timing and outcome of regulatory review of reproxalap and ADX-2191, including any additional trials the FDA or other regulatory agencies may require for approval or label expansion;
- the progress, costs and results of any clinical activities for regulatory review of reproxalap and ADX-2191 outside of the United States;
- the costs and timing of process development and manufacturing scale-up activities associated with reproxalap and ADX-2191;
- the costs of commercialization activities for reproxalap and/or ADX-2191 if we receive marketing approval and pre-commercialization costs for reproxalap and/or ADX-2191 incurred prior to receiving, any such marketing approval, including the costs and timing of establishing product sales, marketing, distribution and outsourced manufacturing capabilities;
- assuming receipt of marketing approval, the amount of revenue received from commercial sales of reproxalap and ADX-2191 or any other product candidates;
- the terms and timing of establishing collaborations, license agreements, and other partnerships on terms favorable to us;
- the type, number, scope, progress, expansion costs, results, and timing of our clinical trials of any product candidates that we are pursuing or may choose to pursue in the future;

- costs associated with any other product candidates that we may develop, in-license, or acquire, including potential milestone or royalty payments; and
- the costs of obtaining, maintaining, and enforcing our patents and other intellectual property rights.

Some of these factors are outside of our control. Our existing capital resources are not sufficient to enable us to fund the commercialization of reproxalap and ADX-2191 and completion of our clinical trials and remaining development through commercial introduction for our product candidates. We expect that we will need to raise substantial additional funds in the near future.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through collaboration agreements and public or private financings, including debt financings. The state of the global economy and market instability has made the business climate volatile and more costly. Uncertain economic conditions, uncertainty as to the general direction of the macroeconomic environment, and the price of our common stock, are beyond our control and may make any necessary debt or equity financing more difficult, more costly, and more dilutive. For example, the capital and credit markets may be adversely affected by the ongoing conflict between Russia and Ukraine, and the possibility of a wider European or global conflict, and global sanctions imposed in response thereto. A severe or prolonged economic downturn, such as a global financial crisis, could affect our ability to raise additional capital. 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 may be required to significantly curtail, delay, reduce or discontinue our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates or curtail, delay, or discontinue one or more of our preclinical studies, clinical trials or other research or development programs. We may also be unable to expand our operations or otherwise capitalize on our business opportunities, may need to restructure our organization, or may be required to relinquish rights to our product candidates or other technologies, or otherwise agree to terms unfavorable to us. Any of these occurrences could materially affect our business, financial condition, and results of operations.

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:

- regulatory developments affecting reproxalap, ADX-2191, and our other product candidates;
- our establishment and maintenance of a sales, marketing and distribution infrastructure and outsourced manufacturing capabilities to commercialize any product candidate for which we may obtain marketing approval;
- variations in the level of expenses related to our clinical trial and development programs;
- addition or termination of clinical trials or development programs;
- any intellectual property infringement lawsuit in which we may become involved;
- the impact of the COVID-19 pandemic on our business, results of operations, and financial position;
- our establishment and maintenance of a sales, marketing and distribution infrastructure and outsourced manufacturing capabilities to commercialize any product candidate for which we may obtain marketing approval;
- our execution of any collaborative, licensing, or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- the number of administrative, clinical, regulatory, and scientific personnel we engage;
- nature and terms of stock-based compensation grants; and

- 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.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and marketing and distribution arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting its ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

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

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

Our management has broad discretion in the application of our cash, cash equivalents, and marketable securities. Because of the number and variability of factors that will determine our use of our cash, cash equivalents, and marketable securities, management's ultimate use of cash, cash equivalents, and marketable securities may vary substantially from the currently intended use. Our management might not apply our cash, cash equivalents, and marketable securities in ways that ultimately increase the value of your investment. We expect to use our cash, cash equivalents, and marketable securities to: fund our planned clinical trials of a number of product candidates; continue to fund the NDA approval process for reproxalap and ADX-2191, including conducting any additional clinical trials or other activities that the FDA may require for approval of reproxalap or ADX-2191; fund an initial commercialization and launch of reproxalap and ADX-2191, if approved; develop other molecules that relate to immune-mediated disease; pursue regulatory approval for our product candidates; service our debt obligations; and provide working capital and capital for other general corporate purposes. The failure by our management to apply these funds effectively could harm our business. We may invest our cash, cash equivalents, and marketable securities 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, cash equivalents, and marketable securities in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

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

In March 2019, we entered into a credit facility with Hercules Capital, which was subsequently amended in April 2021 and December 2022, that is secured by a lien covering all of our assets, other than our intellectual property. The loan agreement contains customary affirmative and negative covenants and events of default. Affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, and maintain insurance coverage. Negative covenants

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

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

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses (NOLs) and certain other tax assets (tax attributes) to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period (generally three years). Transactions involving our common stock within the testing period, even those outside our control, such as purchases or sales by investors, could result in an ownership change. A limitation on our ability to utilize some or all of our NOLs or credits could have a material adverse effect on our results of operations and cash flows. We believe, prior to December 31, 2021 that four ownership changes occurred since inception. Management believes that its aggregate Section 382 limitation (including the additional limitation for recognized "built-in gains") is sufficient so that no current impairment of its pre-ownership change tax attributes is required. There were no ownership changes in 2022. Any future ownership changes, including those resulting from our recent or future financing activities, may cause our existing tax attributes to have additional limitations. However, subject to annual limitations, Federal 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 NOL carryforwards may also cause limitations or restrictions from us claiming such NOLs. If the NOL 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.

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 the United States, we will be subject to the recently enacted Inflation Reduction Act (IRA), which, among other things, will allow Department of Health and Human Services (HHS) to negotiate the selling price of certain drugs and biologics that Centers for Medicare & Medicaid Services (CMS) reimburses under Medicare Part B and Part D. 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 EU, 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. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. Furthermore, in some European countries, the authorities conduct a Health Technology Appraisal to assess the cost-effectiveness of the product, which may significantly impact effective access to the

market. 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.

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

Our operations could be subject to business disruptions such as earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, public health epidemics (including the COVID-19 pandemic), regional or larger scale conflicts or geo-political actions, war or other military conflict, including an escalation of the conflict between Russia and Ukraine, trade policies, sanctions, treaties and tariffs and other natural or man-made disasters or other 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, ADX-2191, and our other product candidates. Our ability to obtain clinical and commercial supplies of reproxalap, ADX-2191, or our other product candidates could be disrupted, if the operations of these suppliers are affected by these business disruptions.

We are in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability due to the ongoing military conflict between Russia and Ukraine and the COVID-19 pandemic. Our business, financial condition, and results of operations may be materially adversely affected by the negative impact on the global economy and capital markets resulting from the conflict in Ukraine or any other geopolitical tensions or the COVID-19 pandemic.

U.S. and global markets are experiencing volatility and disruption following the escalation of geopolitical tensions and the military conflict between Russia and Ukraine. In February 2022, a full-scale military invasion of Ukraine by Russian troops began. Although the length and impact of the ongoing military conflict is highly unpredictable, the conflict in Ukraine has led to market disruptions, including significant volatility in commodity prices, credit, and capital markets, as well as supply chain disruptions.

Additionally, various of Russia's actions have led to sanctions and other penalties being levied by the U.S., the European Union, and other countries, as well as other public and private actors and companies, against Russia and certain other geographic areas, including agreement to remove certain Russian financial institutions from the SWIFT payment system and restrictions on imports of Russian oil, liquefied natural gas, and coal. Additional potential sanctions and penalties have also been proposed and/or threatened. Russian military actions and the resulting sanctions could further adversely affect the global economy and financial markets and lead to instability and lack of liquidity in capital markets, potentially making it more difficult for us to obtain additional funds.

The global spread of COVID-19, and variants thereof, has created significant volatility, uncertainty, and economic disruption. Our business has been and will continue to be adversely affected by the COVID-19 pandemic. For instance, we have experienced operational interruptions as a result of the COVID-19 pandemic and we may also incur additional costs to remedy damages caused by business disruptions, including clinical trial delays or interruptions. The extent to which the COVID-19 pandemic impacts our business, operations, and financial results will depend on numerous evolving factors that we may not be able to accurately predict, including: the duration and scope of the pandemic; governmental, business and individuals' actions that have been and continue to be taken in response to the pandemic; the impact of the pandemic on economic activity and actions taken in response; the effect on our ongoing or planned clinical trials; and any closures of our offices or clinical trial facilities.

Any of the above-mentioned factors could affect our business, prospects, financial condition, and operating results. The extent and duration of the military action, sanctions, as well as the COVID-19 pandemic, and resulting market disruptions are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described in this annual report.

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

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

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

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

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

Risks Related to our Reliance on Third Parties

We rely and will continue to rely on outsourcing arrangements for many of our activities, including clinical development, commercial readiness preparations, and supply of reproxalap, ADX-2191, and our other product candidates.

As of December 31, 2022, we had only 15 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, commercial readiness preparations, 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, in tight credit markets and during public health epidemics, such as the COVID-19 pandemic, and with the political uncertainty involving Russia and Ukraine, 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 successfully 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 our 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 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. The COVID-19 pandemic or any worsening of the global business and economic environment may have the effect of heightening or exacerbating these risks.

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 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 and commercialization. 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, including as a result of the COVID-19 pandemic or the conflict between Russia and Ukraine, 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 may not be successful in establishing and maintaining development, commercial, or other strategic partnerships, which could adversely affect our ability to develop and commercialize product candidates.

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

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

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

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

We have in the past, and may in the future, form strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including the continued development or commercialization of reproxalap, ADX-2191, 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, ADX-2191, 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.

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 or other military conflict, including an escalation of the conflict between Russia and Ukraine, and telecommunication and electrical failures. While to our knowledge we have not experienced any such material system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed.

We rely on email and other messaging services in connection with our operations. We may be targeted by parties using fraudulent spoofing and phishing emails to misappropriate passwords, payment information, or other personal information, or to introduce viruses through Trojan horse programs or otherwise through our networks, computers, smartphones, tablets, or other devices. Despite our efforts to mitigate the effectiveness of such malicious email campaigns through a variety of control and non-electronic checks, spoofing and phishing may damage our business and increase our costs. These risks may be heightened during the ongoing COVID-19 pandemic, should any of our employees voluntarily choose to work remotely. In addition, due to the political uncertainty involving Russia and Ukraine, there is an increased likelihood that escalation of tensions could result in cyberattacks that could either directly or indirectly impact our operations. Any of these events or circumstances could materially adversely affect our business, financial condition, and operating results.

Risks Relating to Our Intellectual Property

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

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

Composition-of-matter patents on the active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. While we have issued composition-of-matter patents in the United States and other countries for reproxalap, and other product candidates, we cannot be certain that the claims in our patent applications covering composition-of-matter of early stage candidates will be considered patentable by the United States Patent and Trademark Office (USPTO) and courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found

invalid or unenforceable if challenged. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products off-label. Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute. In addition, there are possibly treatment compositions and methods that we have not conceived of or attempted to patent, and other parties may discover and patent approaches and compositions that are similar to or different from ours.

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

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

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

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

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third-party patents that may be infringed by commercialization of reproxalap, ADX-2191, 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 or commercialization delays;
- prevent us from commercializing reproxalap, ADX-2191, 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, ADX-2191, 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, ADX-2191, 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, ADX-2191, or our other product candidates, which could harm our business, financial condition, and operating results.

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

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

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

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

We are a party to technology licenses, including an in-license agreement for ADX-2191 (in-license program), 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 our in-license program are each subject in part to the terms and conditions of a third-party license, pursuant to which we have acquired exclusive rights and other intellectual property. Our rights with respect to the intellectual property to develop and commercialize the in-license program may terminate, in whole or in part, if we fail to meet certain milestones contained in each of our license agreements relating to their development and commercialization. We may also lose our rights to develop and commercialize either in-license agreement 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, ADX-2191, 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 and of significantly shorter duration 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 Employee Matters and Managing Growth

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 comprised of: Todd C. Brady, M.D., Ph.D., our President and Chief Executive Officer, and Stephen G. Machatha, Ph.D., our Chief Development Officer, and Bruce Greenberg, our Interim Chief Financial Officer, as well as certain other employees. In addition, we rely on the services of a number of key consultants, including IP, pharmacokinetic, chemistry, toxicology, drug development, and commercialization consultants. Effective May 2022, our board of directors appointed our current Vice President and Controller, Bruce Greenberg as Interim Chief Financial Officer until a permanent successor can be named. Leadership transitions can be inherently difficult to manage, and an inadequate transition to a permanent Chief Financial Officer may cause disruption within our company. In addition, if we are unable to identify a qualified candidate to become the permanent Chief Financial Officer in a timely manner, our ability to meet operational goals

and strategic plans could be adversely impacted. The loss of such individuals or the services of future members of our management team could delay or prevent the further development and 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, including by identifying a permanent Chief Financial Officer. 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 results of our operations.

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

As of December 31, 2022, we only had 15 full-time employees. Accordingly, we will need to grow our organization to continue development and pursue the potential commercialization of reproxalap, ADX-2191, and our other product candidates, as well as function as a public company. As we seek to advance reproxalap, ADX-2191, 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.

Risks Related to Other Legal or Regulatory Matters

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

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

- changes and limits in import and export controls;
- increases in custom duties and tariffs;
- changes in currency exchange rates;

- economic weakness, including inflation, and political instability, including effects of the ongoing conflict between Russia and Ukraine, and the possibility of a wider European or global conflict, and global sanctions imposed in response thereto;
- the impact on employees, suppliers, customers, and the global economy related to public health epidemics or pandemics, such as the COVID-19 pandemic, and actions taken in response to such events;
- 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.

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. Concerns over economic recession, the COVID-19 pandemic, interest rate increases and inflation, supply chain delays and disruptions, policy priorities of the U.S. presidential administration, trade wars, unemployment, or prolonged government shutdown may contribute to increased volatility and diminished expectations for the economy and markets. Additionally, concern over geopolitical issues may also contribute to prolonged market volatility and instability. For example, the conflict between Russia and Ukraine could lead to disruption, instability, and volatility in global markets and industries. The U.S. government and other governments in jurisdictions have imposed severe economic sanctions and export controls against Russia and Russian interests, have removed Russia from the Society for Worldwide Interbank Financial Telecommunication payment (SWIFT) system, and have threatened additional sanctions and controls. The impact of these measures, as well as potential responses to them by Russia, is unknown.

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

Security breaches , cyberattacks, loss of data, and other disruptions impacting our information technology systems or those of our third-party collaborators, service providers, contractors or consultants could compromise the privacy, security, integrity or confidentiality of sensitive information related to our business or prevent us from accessing critical information and expose us to adverse consequences, including but not limited to regulatory investigations or actions, litigation, and significant fines and penalties, which could adversely affect our business, financial condition, and reputation.

In the ordinary course of our business, we and our current or future third-party collaborators, service providers, contractors, and consultants collect, may store and transmit sensitive data, including legally protected health information, personal data (also referred to as personal information or personally identifiable information under certain data privacy laws) about patients and employees, intellectual property, and our proprietary business and financial information (collectively, sensitive information). We manage and maintain data, including sensitive information, utilizing a combination of on-site systems, managed data center systems, and cloud-based data center systems. We face a number of risks related to our protection of, and our third-party collaborators', service providers', contractors', and consultants' protection of, this sensitive information, including loss of access, inappropriate disclosure and inappropriate or unauthorized access, as well as risks associated with our ability to identify and audit such events.

The secure processing, storage, maintenance, and transmission of sensitive information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure, and those of our third-party collaborators, service providers, contractors, and consultants, may be vulnerable to breakdown or other damage or interruption from service interruptions, system malfunctions, natural disasters, terrorism, war and telecommunications and electrical failures, as well as from cyberattacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity and availability of

information) or viruses or otherwise breached due to employee or third-party error, malfeasance, or other activities. These risks may be heightened during the ongoing COVID-19 pandemic, if any of our employees work remotely.

While we are not aware of any such attack, breach or system failure, we cannot guarantee that our data protection efforts and our investment in information technology, or those of our third-party collaborators, service providers, contractors, and consultants will prevent significant breakdowns, data leakages, and breaches in the relevant systems or other cyber incidents. If such event were to occur and cause interruptions in our operations, our networks could be compromised and the sensitive information we store on those networks could be accessed by unauthorized parties, publicly disclosed, lost, or stolen. Any such unauthorized access, disclosure or other loss of information, or the perception that any of these has occurred, could result in legal claims or proceedings, liability under federal, state, and international laws that protect the privacy of personal data, including but not limited to private lawsuits or class actions under the California Consumer Privacy Act, as amended by the California Privacy Rights Act of 2020 (CPRA), and regulatory penalties, which could result in significant legal or financial exposure. In addition, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal data, which is a broader class of information than the health information protected by the Health Insurance Portability and Accountability Act (HIPAA). Unauthorized access, loss, or dissemination of sensitive information could also disrupt our ability to conduct research and development activities; collect, process, and prepare company financial information; provide information about our product candidates and other patient and physician education or outreach efforts through our website; manage the administrative aspects of our business; or prevent damage to our reputation, any of which could adversely affect our business.

We are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies, and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; significant fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; loss of customers or sales; and other adverse business consequences.

In the ordinary course of our business, we process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) personal data (also referred to as personal information or personally identifiable information under certain data privacy laws) and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, sensitive third-party data, and patient information. Our data processing activities may subject us to numerous data privacy and security obligations, such as various federal, state, and foreign laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts, and other obligations that govern the processing of personal data by us and on our behalf. We strive to comply with applicable data privacy and security obligations to the extent possible. However, it is possible that these obligations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other rules and/or our practices. Any failure or perceived failure by us to comply with applicable privacy and data security laws and regulations, our privacy policies, or our privacy-related obligations to third parties, or any compromise of security that results in the unauthorized access, release or transfer of personal data or other sensitive information, may result in governmental enforcement actions and fines or orders requiring that we change our practices, private litigation (including class action lawsuits), or public statements against us by consumer advocacy groups or others and could cause a loss of trust in us, which could result in significant legal or financial exposure and reputational damage that could potentially have an adverse effect on our business.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, and consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act). For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. In addition, we may be subject to various state data privacy and security laws and regulations, including the California Consumer Privacy Act, as amended by the CPRA, which, among other things, requires covered "businesses" to provide specific disclosures to California consumers concerning the collection, sale, and sharing of their personal data, and gives such consumers the right to opt-out of certain sales of personal information. The CPRA provides for civil penalties for violations, as well as a private right of action for certain security breaches that may increase the likelihood of, and the risks associated with, security breach litigation. Additionally, the CPRA created a new state agency to oversee implementation and

enforcement efforts, potentially resulting in further uncertainty and requiring us to incur additional costs and expenses in an effort to comply. Many of the CPRA's provisions became effective on January 1, 2023. Further, Virginia enacted its own comprehensive state privacy law, the Virginia Consumer Data Protection Act (VCDPA), which also went into effect on January 1, 2023. Three additional comprehensive state privacy laws will go into effect later in 2023: the Colorado Privacy Act (CPA) and Connecticut Data Privacy Act (CTDPA), will both go into effect on July 1, 2023, and the Utah Consumer Privacy Act (UCPA) will go into effect on December 31, 2023. The CPRA, VCDPA, CPA, CTDPA, and UCPA may, to the extent they apply, increase our compliance costs and potential liability, particularly in the event of a data breach, and could have a material adverse effect on our business, including how we process personal data, our financial condition, and the results of our operations. These laws have also prompted a number of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs, and adversely affect our business.

Recent developments in Europe have created compliance uncertainty regarding the processing of personal data from Europe. For example, the European Union's General Data Protection Regulation (EU GDPR), the United Kingdom's GDPR (UK GDPR), and the Swiss Federal Act on Data Protection extend the geographical scope of European data protection laws to non-European entities and impose strict requirements for processing personal data. For example, under the EU GDPR and/or the UK GDPR, government regulators may impose temporary or definitive bans on data processing, as well as possible fines of up to 4% of global annual turnover for the preceding financial year or €20 million, whichever is higher, for the most serious infringements. This exposes us to two parallel sets of regulations, each of which potentially authorizes similar fines and other potentially divergent enforcement actions for certain violations. Further, individuals or consumer protection organizations authorized at law to represent their interests may initiate litigation related to the processing of individuals' personal data.

In the ordinary course of our business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. The EU GDPR and UK GDPR prohibit the transfer of personal data to countries outside of the EEA, or the UK including the United States, that have not been deemed adequate by the European Commission or by the UK data protection regulator, respectively. Switzerland has adopted similar restrictions. Although there are legal mechanisms that allow for the transfer of personal data from the EEA, UK, and Switzerland to the United States, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. For example, recent legal developments in the EU have created complexity and uncertainty regarding such transfers and data protection authorities from the different EU Member States may interpret the EU GDPR differently. Additionally, guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data in the EU. These transfer mechanisms have also been subject to various legal challenges. In particular, on July 16, 2020, the Court of Justice of the European Union, in the case of Data Protection Commissioner v. Facebook Ireland Limited, Maximillian Schrems (Case C-311/18) (Schrems II), invalidated the EU-U.S. Privacy Shield Program for transfers of personal data from the EU to the U.S., and added further uncertainty and complexity to the use of standard contractual clauses as a compliance mechanism for transfers of personal data outside the EU.

If there is no lawful manner for us to transfer personal data from the EEA, UK, or Switzerland to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third-parties, which could limit our ability to conduct clinical trial activities in Europe or elsewhere, and injunctions against our processing or transferring of personal data necessary to operate our business.

In addition to the EU, UK, and Switzerland, a growing number of other global jurisdictions are considering or have passed legislation implementing data protection requirements or requiring local storage and processing of data or similar requirements that could increase the cost and complexity of our business. Some of these laws, such as the General Data Protection Law in Brazil, or the Act on the Protection of Personal Information in Japan, impose similar obligations as those under the EU GDPR and UK GDPR. Others, such as those in Russia, India, and China, could potentially impose more stringent obligations, including data localization requirements. If we are unable to meet these evolving legal requirements or if we violate or are perceived to violate any laws, regulations, or other obligations relating to privacy, data protection, or information security, we may experience harm to our reputation

and become subject to investigations, claims, and other remedies, which could expose us to significant fines, penalties, and other damages, all of which would harm our business.

Current 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 any product candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product.

Healthcare reform measures that may be adopted in the future, may result in reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies, and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation and regulation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient support programs, reduce the costs of drugs under Medicare, and reform government program reimbursement methodologies for drug products. For example, included in the Consolidated Appropriations Act, 2021 were several drug price reporting and transparency measures, such as a new requirement for certain Medicare plans to develop tools to display Medicare Part D prescription drug benefit information in real time and for group and health insurance issuers to report information on pharmacy benefit and drug costs to the Secretaries of the HHS, the Department of Labor, and the Treasury. Additionally, both Congress and the Biden administration have each indicated willingness to continue to seek new legislative and/or administrative measures to address prescription drug costs. For example, on July 9, 2021, President Biden issued an Executive Order to promote competition in the U.S. economy that included several initiatives addressing prescription drugs. Among other provisions, the Executive Order stated that the Biden administration will "support aggressive legislative reforms that would lower prescription drug prices, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and through other related reforms." In response to the Executive Order, on September 9, 2021, the HHS issued a Comprehensive Plan for Addressing High Drug Prices that identified potential legislative policies and administrative tools that Congress and the agency can pursue in order to make drug prices more affordable and equitable, improve and promote competition throughout the prescription drug industry, and foster scientific innovation. Congress has also continued to conduct inquiries into the prescription drug industry's pricing practices.

These initiatives recently culminated in the enactment of the IRA, in August 2022, which, among other things, will allow HHS to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although this will only apply to high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics). The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price representing a significant discount from average prices to wholesalers and direct purchasers. The law will also, beginning in October 2023, penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. In addition, the law eliminates the "donut hole" under Medicare Part D beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. These provisions will take effect progressively starting in 2023, although they may be subject to

legal challenges. Thus, it is unclear how the IRA will be implemented, but will likely have a significant impact on our business and the pharmaceutical industry as a whole.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing. These include legislation and regulations regarding price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, legislative action designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, if approved, or put pressure on our product pricing.

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

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

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

Our operations and relationships with actual and potential customers, providers and third-party payors will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to penalties including criminal sanctions, civil penalties, exclusions from government programs, contractual damages, and reputational harm, and could diminish our future profits and earnings.

Our arrangements with third-party payors, physicians, and other potential customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drug candidates for which we obtain marketing approval.

Applicable U.S. federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, a criminal law, which prohibits, among other things, persons and entities from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, in cash or in kind, to induce or reward purchasing, leasing, ordering, or arranging for, referring, or recommending the purchase, lease, or order of any good or service for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations of the federal Anti-Kickback Statute can result in significant civil monetary penalties and criminal fines, as well as imprisonment and exclusion from participation in federal healthcare programs;
- the federal civil False Claims Act, which may be enforced through civil whistleblower or qui tam actions and imposes significant civil penalties, treble damages, and potential exclusion from federal

healthcare programs against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or for making a false record or statement material to an obligation to pay the federal government or for knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. Further, a violation of the federal Anti-Kickback Statute can serve as a basis for liability under the federal civil False Claims Act. There is also the federal Criminal False Claims Act, which is similar to the federal Civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious, or fraudulent claim to the federal government;

- the federal Civil Monetary Penalties Law, which authorizes the imposition of substantial civil monetary penalties against an entity that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal health care programs to provide items or services reimbursable by a federal health care program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;
- federal criminal statutes created by the Health Insurance Portability and Accountability Act (HIPAA), which impose criminal liability for, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program, including private insurance plans, or, in any matter involving a healthcare benefit program, for knowingly and willfully making materially false, fictitious, or fraudulent statements in connection with the delivery of or payment for health care benefits;
- HIPAA, as amended by HITECH, and its implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the FDCA which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing such products for off-label use or misbranding or adulterating their products, and regulates the distribution of samples;
- the federal and state laws that require pharmaceutical manufacturers to report certain calculated product pricing metrics to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of product coverage and reimbursement under federal healthcare programs
- the federal Physician Payment Sunshine Act, which requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, among others, to annually track and report payments and other transfers of value provided to U.S.-licensed physicians and teaching hospitals, and for reports submitted on or after January 1, 2022, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants, and certified nurse-midwives, as well as certain ownership and investment interests held by physicians and their immediate families;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to our business practices, including sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers;
- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and relevant compliance guidance promulgated by the federal government;
- state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures;
- other state laws that prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals; require the reporting of certain pricing information, including information pertaining

to and justifying price increases, or prohibit prescription drug price gouging; and certain state and local laws that require the registration of pharmaceutical sales representatives; and

- state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties; damages; fines; imprisonment; exclusion of drug candidates from government-funded healthcare programs, such as Medicare and Medicaid; disgorgement; contractual damages; reputational harm; diminished profits and future earnings; and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may also be subject to criminal, civil, or administrative sanctions, including exclusions from government-funded healthcare programs. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause us to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

Providing benefits or advantages to induce or reward improper performance generally to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the EU. The provision of benefits or advantages to induce or reward improper performance is governed by the national anti-bribery laws of EU Member States, and in respect of the U.K., the Bribery Act 2010. Infringement of these laws may result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, provides that, where medicinal products are being promoted to healthcare professionals, no gifts, pecuniary advantages, or benefits in kind may be supplied, offered or promised to such individuals unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision was transposed into the Human Medicines Regulations 2012 and as such remains applicable in the UK.

Payments made to physicians in certain EU Member States must be publicly disclosed. In addition, agreements with healthcare professionals must often be the subject of prior notification and approval by the healthcare professional's employer, his or her competent professional organization, and/or the regulatory authorities of individual EU Member States. These requirements are set out in national laws, industry codes, or professional codes of conduct, applicable in the EU Member States and in the UK. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

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.

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

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

Disruptions at the FDA and other agencies, including as a result of or in response to the COVID-19 pandemic, may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC, and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of reproxalap, ADX-2191, or our other product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if reproxalap, ADX-2191, 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, ADX-2191, 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, ADX-2191, or our other product candidates; or
- a decline in our stock price.

We maintain product liability insurance with $5.0 million in coverage. We anticipate that we will need to increase our insurance coverage if we commercialize any product candidate. 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, ADX-2191, 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 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 enforcement action including the issuance of a Warning Letter, the requirement of a labeling change, the initiation of a criminal prosecution, the imposition of civil monetary penalties, the seizure of our products, or delay in approval or clearance of future products.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws, and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, or other remedial measures and legal expenses, any of which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the Foreign Corrupt Practices Act (FCPA), the Bribery Act and other anticorruption laws that apply in countries where we do business and may do business in the future. The FCPA, the Bribery Act, and other laws generally prohibit us, our officers, and our employees, and intermediaries from bribing, being bribed, or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, the Bribery Act, or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We also are subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, UK, and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements, and currency exchange regulations, which we collectively refer to as Trade Control Laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act, or other legal requirements including Trade Control Laws. If we are not in compliance with the FCPA, the Bribery Act, and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, legal expenses, disgorgement, and other sanctions and remedial measures, which could have an adverse impact on our business, financial condition, results of operations, or liquidity. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Likewise, any investigation of any potential violations of the FCPA; the Bribery Act; or other anti-corruption laws or Trade Control Laws by U.S., U.K., or other authorities also could have an adverse impact on our reputation, our business, results of operations, or financial condition.

Our employees, independent contractors, vendors, principal investigators, contract research organizations (CROs), and consultants may engage in misconduct or other improper activities, including noncompliance with regulatory standards, regulatory requirements, and insider trading.

We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include:

- intentional, reckless, or negligent conduct or disclosure to us of unauthorized activities that violate the regulations of the FDA or similar foreign regulatory authorities;
- healthcare fraud and abuse in violation of U.S. and foreign laws and regulations;
- violations of U.S. federal securities laws relating to trading in our common stock; and
- failures to report financial information or data accurately.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations govern a wide range of pricing, discounting, marketing and promotion, sales

commission, customer incentive programs and other business arrangements. While we have adopted a code of conduct and implemented other internal controls applicable to all our employees, it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective. Additionally, we are subject to the risk that a person could allege fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business or cause reputational harm, including the imposition of civil, criminal and administrative penalties, and damages; possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs; and diminished profits and future earnings.

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.

We are subject to litigation risks.

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

We 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 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.

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

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.

Risks Related to Our Common Stock

In the absence of an active trading market for our common stock, investors may not be able to resell their shares at or above the price at which they purchased them.

In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the price they paid or at the time that they would like to sell. In addition, an inactive market may impair our ability to raise capital by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration, which, in turn, could harm our business.

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

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

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

Concerns over economic recession, the COVID-19 pandemic, interest rate increases and inflation, supply chain delays and disruptions, policy priorities of the U.S. presidential administration, trade wars, unemployment, or prolonged government shutdown may contribute to increased volatility and diminished expectations for the economy and markets. Additionally, concern over geopolitical issues may also contribute to prolonged market volatility and instability. For example, the conflict between Russia and Ukraine could lead to disruption, instability

and volatility in global markets and industries. The U.S. government and other governments in jurisdictions have imposed severe economic sanctions and export controls against Russia and Russian interests, have removed Russia from the SWIFT system, and have threatened additional sanctions and controls. The impact of these measures, as well as potential responses to them by Russia, is unknown.

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

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

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

Because a small number of our existing stockholders own a substantial percentage of our outstanding common stock, your ability to influence corporate matters will be limited.

As of December 31, 2022, our executive officers, directors, and greater than 5% stockholders, in the aggregate, own approximately 21% of our outstanding common stock. As a result, such persons, acting together, may 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.

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

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

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

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

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

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

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

As a public company, and particularly if and after we cease to be a "smaller reporting company," we incur significant legal, accounting, and other expenses that we did not incur as a private company. We 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 Nasdaq to implement provisions of the Sarbanes-Oxley Act, imposes significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may result in substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to continue to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If public company rules and regulations divert the attention of our management and personnel from other business concerns,

our business, financial condition, and results of operations could be adversely affected. Increased costs associated with public company expenses will increase our net loss. For example, public company rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, the cost of which has continued to rise in recent years, and thus 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. 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 continue to comply with the requirements of being a reporting company under the Exchange Act, we will be required to continue to upgrade and maintain our systems including information technology; implement and maintain additional financial and management controls, reporting systems, and procedures; and hire additional accounting and finance staff. Furthermore, we rely on third-parties, including software and system providers, for ensuring our reporting obligations and effective internal controls, and to the extent these third parties fail to provide adequate service including as a result of any inability to scale to handle our growth and the imposition of these increased reporting and internal controls and procedures, we could incur material costs for upgrading or switching systems and our business could be materially affected.

However, as a smaller reporting company and a non-accelerated filer, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 for as long as we are not deemed an "accelerated filer" or "large accelerated filer."

If we are unable to establish and maintain effective internal controls it could have a material adverse effect on our business, financial condition, results of operations or cash flows.

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

If securities or industry analysts do not continue to 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. If one or more of the analysts who covers us downgrades our stock or publish unfavorable research or reports about our business, 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.

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 and other awards upon certain transactions that result in a change of control; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

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

Our restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine. This provision would not apply to claims brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Our amended and restated bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. These choices of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees and may discourage these types of lawsuits. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation or bylaws has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive-forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. If a court were to find the exclusive-forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could 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 fluctuations in our stock price. If faced with a proxy contest or other type of stockholder 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 stockholder 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*

None.

ITEM 2. *PROPERTIES*

Our offices are located in Lexington, Massachusetts. As of December 31, 2022, we had leased approximately 9,351 square feet of office space pursuant to leases that expire in 2023. 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 lease, 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*

Market Information

Our common stock has been publicly traded on the Nasdaq Capital Market under the symbol "ALDX" since our initial public offering in May of 2014. Prior to our initial public offering, there was no public market for our common stock.

Holders of Record

As of December 31, 2022, there were 21 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

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

Securities Authorized for Issuance under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this annual report on Form 10-K.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. *[RESERVED]*

ITEM 7. *MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS*

You should read the following discussion and analysis of our financial condition and results of operations 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 discovering innovative therapies designed to treat immune-mediated diseases. We are developing a novel pharmaceutical platform targeting a class of pro-inflammatory mediators known as RASP (reactive aldehyde species) that exacerbate diseases characterized by inflammation. Our RASP modulator product pipeline includes ADX-629, a novel orally administered RASP modulator in clinical development for atopic dermatitis, idiopathic nephrotic syndrome, moderate alcohol-associated hepatitis, chronic cough, and Sjögren-Larsson Syndrome. Our preclinical RASP platform includes ADX-246, ADX-248, and other drug candidates in development for geographic atrophy and systemic inflammatory diseases. The validity of the RASP platform is supported by reproxalap, our first-in-class product candidate under New Drug Application (NDA) review by the United States Food and Drug Administration (FDA) for the treatment of dry eye disease. Reproxalap has demonstrated broad-based, rapid-onset activity and consistent safety across a number of Phase 2 and Phase 3 clinical trials. We have additional product candidates in development, including ADX-2191, which is under NDA priority review by the FDA for the treatment of a rare but fatal cancer known as primary vitreoretinal lymphoma. ADX-2191 is also in clinical development for the treatment of proliferative vitreoretinopathy and retinitis pigmentosa, two rare retinal diseases characterized by inflammation and vision loss. ADX-2191 has received Orphan Drug Designation for all three retinal diseases currently under development.

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 March 2019, we entered into the Hercules Credit Facility, which provided for a term loan of up to $60.0 million, $15.0 million of which has been drawn-down as of December 31, 2022. In April 2021, the Hercules Credit Facility was amended to, among other things, increase the amount which may become available for draw-down prior to May 2023, subject to the satisfaction of certain conditions contained therein, from $10.0 million to $20.0 million. In December 2022, the Hercules Credit Facility was further amended to, among other things, (i) extend the expiration of the period in which interest-only payments on borrowings from May 1, 2023 to May 1, 2024; (ii) extend the Maturity Date from October 1, 2023 to October 1, 2024; and (iii) extend the availability of the $20.0 million draw-down from May 2023 to May 2024, subject to the satisfaction of certain conditions contained therein. The Hercules Credit Facility contains customary affirmative and negative covenants and events of default. Affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, and maintain insurance coverage. Negative covenants include, among others: restrictions on transferring any part of our business or intellectual property; incurring additional indebtedness; engaging in mergers or acquisitions; paying dividends or making other distributions; making investments; and creating other liens on our assets, in each case subject to customary exceptions. The Hercules Credit Facility, as amended, is described in Note 9 to the notes to the consolidated financial statements contained in this annual report on Form 10-K. As of December 31, 2022, $15.0 million was outstanding under the Hercules Credit Facility, and an additional $20.0 million may be available under the Loan and Security Agreement at our option through May 1, 2024, subject to approval of the Lender's investment committee.

In January 2021, we sold 7.9 million shares of our common stock in an underwritten public offering at $9.50 per share, for an aggregate gross cash purchase price of $74.7 million or proceeds of $70.0 million after underwriters' discount, commissions, and other offering expenses.

In March 2021, we entered into an Open Market Sales Agreement SM (2021 Jefferies Sales Agreement) with Jefferies LLC (Jefferies), as sales agent, pursuant to which we may offer and sell, from time to time through Jefferies, shares of common stock providing for aggregate sales proceeds of up to $100.0 million. We have no obligation to sell any shares under the 2021 Jefferies Sales Agreement, and could at any time suspend solicitations and offers under the 2021 Jefferies Sales Agreement. No sales had been made pursuant to the 2021 Jefferies Sales Agreement as of December 31, 2022.

In May and June 2021, we sold an aggregate of 10.2 million shares of our common stock at a public offering price of $12.50 per share, in an underwritten public offering, for an aggregate gross cash purchase price of $127.8 million or proceeds of approximately $119.8 million after underwriters' discount, commissions, and other offering expenses, which included the partial exercise of the underwriters' option to purchase additional shares.

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, subject to regulatory approval, if any, the commercialization 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. However, any disruption in the capital markets caused by the COVID-19 pandemic could make any financing more challenging, and there can be no assurance that we will be able to raise capital on commercially reasonable terms or at all.

Our Agreement with MEEI

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

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

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

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

relating to the manufacture, use, sale or importation of licensed products, we materially breach any provisions of the MEEI Agreement or in the event of our insolvency or bankruptcy.

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

Our Acquisition of Helio Vision, Inc.

On January 28, 2019, we acquired Helio. Upon the closing of the acquisition, we issued an aggregate of 1,160,444 shares of common stock to the former securityholders and an advisor of Helio. In January 2021, pursuant to the terms of the acquisition agreement, we issued an additional 246,562 shares of common stock to the former securityholders of Helio. Subject to the conditions of the acquisition agreement, we are contingently obligated to make additional payments to the former securityholders of Helio as follows: (a) $10.0 million of common stock following approval by the FDA of a new drug approval application for the prevention and/or treatment of proliferative vitreoretinopathy or a substantially similar label prior to the 10th anniversary of the closing date; and (b) $2.5 million of common stock following FDA of a new drug approval application for an indication (other than proliferative vitreoretinopathy or a substantially similar label) 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 in the aggregate. 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 and ADX-2191. We expect our research and development expenses to increase for the foreseeable future as we advance ADX-629 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 our 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;
- delays of, or other effects on, clinical trials resulting from the ongoing COVID-19 pandemic and subsequent public health measures, and war or other military actions, or for other reasons;
- the length of time required to enroll eligible patients;
- the design of the trials;
- the cost of drug manufacturing;

- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the costs of assay development, assays, or other assessment of clinical trial endpoints;
- 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 our product candidates.

Included in research and development are expenses associated with asset acquisitions. Assets purchased in an asset acquisition transaction are expensed as in-process research and development unless the assets acquired are deemed to have an alternative future use. Acquired in-process research and development payments are immediately expensed, and include upfront payments, as well as transaction fees and subsequent milestone payments. Development costs incurred after the asset acquisition are expensed as incurred.

We do not expect reproxalap, ADX-2191, or any of our other product candidates to be commercially available, if at all, before at least the second half of 2023.

General and administrative expenses

Our general and administrative expenses consisted primarily of pre-commercial costs for reproxalap and ADX-2191, as well as employee-related expenses, including benefits and stock-based compensation for our full-time employees during the years ended December 31, 2022 and 2021. Other general and administrative expenses include insurance premiums, consulting, and professional fees for auditing, tax, investor relations, 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 maintaining compliance with exchange listing and SEC requirements. These increases will likely include higher consulting costs, fees for commercializing our product candidates, legal fees, accounting fees, insurance premiums, and fees associated with investor relations.

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, 2022, comprehensive loss is equal to our net loss of $62.0 million and $0.1 million of unrealized loss on marketable securities. For the year ended December 31, 2021, comprehensive loss is equal to our net loss of $57.8 million and no unrealized loss on marketable securities.

Critical Accounting 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.

Other Information

Net Operating Loss Carryforwards

As of December 31, 2022, we had federal and state income tax net operating loss (NOL) carryforwards of approximately $239.2 million and $231.3 million, respectively. Federal NOL carryforwards generated through December 31, 2017 and state NOL carryforwards will expire at various dates through 2042. Federal NOLs generated during the years ended December 31, 2018 and thereafter will carry forward indefinitely. As of December 31, 2022, we had federal and state research and development tax credit carryforwards of approximately $8.7 million and $2.1 million, respectively, which will expire at various dates through 2042. Additionally, as of December 31, 2022, we had a federal orphan drug tax credit carryforward of approximately $1.7 million that expires in 2042.

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.

Under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs and certain other tax assets (tax attributes) to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period (generally three years). Transactions involving our common stock within the testing period, even those outside our control such as purchases or sales by investors, could result in an ownership change. A limitation on our ability to utilize some or all our NOLs or credits could have a material adverse effect on our results of operations and cash flows. We believe, prior to December 31, 2021 that four ownership changes occurred since inception. Management believes that its aggregate Section 382 limitation (including the additional limitation for recognized "built-in gains") is sufficient so that no current impairment of its pre-ownership change tax attributes is required. There were no ownership changes in 2022. Any future ownership changes, including those resulting from our recent or future financing activities, may cause our existing tax attributes to have additional limitations.

Recent Accounting Pronouncements

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

Results of Operations

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

Comparison of Years Ended December 31, 2022 and 2021

Net loss. Net loss for the years ended December 31, 2022 and 2021 was approximately $62.0 million and $57.8 million, respectively. As of December 31, 2022, we had total stockholders' equity of $151.0 million. Losses have resulted principally from costs incurred in our clinical trials and other research and development programs, amortization costs of founders' stock related to the acquisition of Helio in January 2019, and from our general and administrative expenses.

Research and development expenses. Research and development expenses were $47.3 million for the year ended December 31, 2022 compared to $44.9 million for the same period in 2021. The increase of $2.4 million is primarily related to an increase in our drug product manufacturing expenditures, personnel costs, consulting expenditures, and external preclinical development costs, partially offset by a decrease in our external clinical development costs.

General and administrative expenses. General and administrative expenses were $15.4 million for the year ended December 31, 2022, compared to $11.3 million for the year ended December 31, 2021. The increase of approximately $4.1 million is primarily related to higher consulting expenditures and personnel costs.

Other income (expense). Total other income (expense) was approximately $0.7 million for the year ended December 31, 2022, compared to ($1.6) million for the year ended December 31, 2021. The increase in total other income (expense), was principally due to an increase in interest income as a result of increased interest rates on our investments.

Liquidity and Capital Resources

We have funded our operations primarily from the sale of equity securities and convertible equity securities and borrowings under credit facilities. Since inception, we have incurred operating losses and negative cash flows from operating activities and have devoted substantially all our efforts to research and development. At December 31, 2022, we had total stockholders' equity of approximately $151.0 million and cash, cash equivalents, and marketable securities of $174.3 million. During the year ended December 31, 2022, we had net loss of approximately $62.0 million. We expect to generate operating losses for the foreseeable future.

In January 2021, we closed an underwritten public offering in which we sold an aggregate of 7.9 million shares of common stock at $9.50 per share. The net proceeds of the offering were approximately $70.0 million, after deducting underwriting discounts, commissions, and other offering expenses.

In March 2021, we entered into an Open Market Sales Agreement SM (2021 Jefferies Sales Agreement) with Jefferies LLC (Jefferies), as sales agent, pursuant to which we may offer and sell, from time to time through Jefferies, shares of common stock providing for aggregate sales proceeds of up to $100.0 million. We have no obligation to sell any shares under the 2021 Jefferies Sales Agreement, and could at any time suspend solicitations and offers under the 2021 Jefferies Sales Agreement. No sales had been made pursuant to the 2021 Jefferies Sales Agreement as of December 31, 2022.

In May and June 2021, we sold an aggregate of 10.2 million shares of our common stock at a public offering price of $12.50 per share, in an underwritten public offering, for an aggregate gross cash purchase price of $127.8 million or proceeds of approximately $119.8 million after underwriters' discount, commissions, and other offering expenses, which included the partial exercise of the underwriters' option to purchase additional shares.

In March 2019, we entered into the Hercules Credit Facility (the Loan and Security Agreement), pursuant to which a term loan of up to an aggregate principal amount of $60.0 million may be made available to us. The Loan and Security Agreement provides for (i) an initial term loan advance of up to $5.0 million at our option, which expired unutilized on April 15, 2019; (ii) three additional term loan advances of up to $15.0 million each, at our option, available to us upon the occurrence of certain funding conditions prior to September 30, 2019 (2019 Tranche), March 31, 2020 (2020 Tranche), and March 31, 2021 (2021 Tranche); and (iii) a final additional term loan advance (Fourth Loan Tranche) of up to $10.0 million prior to December 31, 2021, at our option, subject to approval by Lender's investment committee. We drew down the 2019 Tranche in full in September 2019 and the 2020 Tranche and the 2021 Tranche expired unutilized prior to us satisfying the funding conditions for such tranche. On April 20, 2021, we entered into the First Amendment (First Amendment) to Loan and Security Agreement with Hercules. The First Amendment, among other things, (i) increased the Fourth Loan Tranche from $10.0 million to $20.0 million and extended the deadline for drawing down the Fourth Loan Tranche to July 1, 2022; (ii) lowered the variable per annum rate of interest on borrowings under the Loan and Security Agreement to the greater of (a) the Prime Rate plus 3.10% or (b) 8.60%; (iii) extended the expiration of the period in which interest-only payments on borrowings under the Loan and Security Agreement are required from May 1, 2021 to July 1, 2022; and (iv) following the satisfaction of certain conditions, which conditions were satisfied in April 2021, further extended the expiration of the interest-only period and the deadline for drawing down the Fourth Loan Tranche to May 1, 2023. On December 22, 2022, we entered into the Second Amendment (Second Amendment) to the Loan and Security Agreement with Hercules, which became effective as of December 31, 2022 (Second Amendment Effective Date). The Second Amendment, among other things, (i) extended the expiration of the period in which interest-only payments on borrowings under the Loan and Security Agreement are made from May 1, 2023 to May 1, 2024; (ii) extended the Maturity Date from October 1, 2023 to October 1, 2024 (Maturity Date); (iii) extended the availability of the Fourth Loan Tranche commitment of $20 million from May 1, 2023 to May 1, 2024; and (iv) amended the Prepayment Charge (as defined therein) to equal 0.75% of the amount prepaid during the 12-month period following the Second Amendment Effective Date, and 0% thereafter. The ability to draw the Fourth Loan Tranche remains conditioned on approval by the Lenders' investment committee. In addition, a supplemental end of term charge of $292,500 (Supplemental End of Term Charge) shall be due on the earlier of (A) the Maturity Date, as amended, or (B) repayment of the aggregate amount of advances under the Loan and Security Agreement. The existing end of term charge of $1,042,500 (End of Term Charge) remains due on the earlier of (A) October 1, 2023 or (B) repayment of the aggregate amount of advances under the Loan and Security Agreement. Repayment of the

aggregate outstanding principal balance of the term loan, in monthly installments, commences upon expiration of the interest-only period and continues through the Maturity Date.

The Loan and Security Agreement contains customary affirmative and negative covenants and events of default. Affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, and maintain insurance coverage. Negative covenants include, among others: restrictions on transferring any part of our business or intellectual property; incurring additional indebtedness; engaging in mergers or acquisitions; paying dividends or making other distributions; making investments; and creating other liens on our assets, in each case subject to customary exceptions. As of December 31, 2022, $15.0 million was outstanding under the Loan and Security Agreement, and an additional $20.0 million under the Fourth Loan Tranche at our option through May 1, 2024, subject to approval of the Lender's investment committee.

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities, as of December 31, 2022, will be sufficient to fund our currently projected operating expenses into the second half of 2024, including the initial commercialization and launch plans for reproxalap and ADX-2191, if approved; and continued early and late-stage development of our product candidates in ocular and systemic immune-mediated diseases. We base our projections of operating capital requirements on our current operating plan, which includes several assumptions that may prove to be incorrect, and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount of our working capital requirements. 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 and regulatory activities, commence or continue ongoing commercialization, including manufacturing, sales, marketing and distribution for 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, ADX-2191, 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 costs, timing, and outcome of regulatory review of reproxalap and ADX-2191, including any additional trials the FDA or other regulatory agencies may require for approval or label expansion;
- the progress, costs, and results of any clinical activities for regulatory review of reproxalap and ADX-2191 outside of the United States;
- the costs and timing of process development and manufacturing scale-up activities associated with reproxalap and ADX-2191;
- the costs of commercialization activities for reproxalap and/or ADX-2191 if we receive marketing approval and pre-commercialization costs for reproxalap and/or ADX-2191 incurred prior to receiving, any such marketing approval, including the costs and timing of establishing product sales, marketing, distribution and outsourced manufacturing capabilities;
- assuming receipt of marketing approval, the amount of revenue received from commercial sales of reproxalap and ADX-2191 or any other product candidates;

- the terms and timing of establishing collaborations, license agreements, and other partnerships on terms favorable to us;
- the type, number, scope, progress, expansion costs, results, and timing of our clinical trials of any product candidates that we are pursuing or may choose to pursue in the future;
- costs associated with any other product candidates that we may develop, in-license, or acquire, including potential milestone or royalty payments; and
- costs of obtaining, maintaining, and enforcing our patents and other intellectual property rights.

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. In addition, the disruption in the capital markets could make any financing more challenging, and there can be no assurance that we will be able to obtain such financing on commercially reasonable terms or at all. 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 related to 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.

Cash Flows. The following table summarizes our cash flows for the years ended December 31, 2022 and 2021:

	Years Ended December 31,	
	2022	2021
Net cash used in operating activities	$ (56,637,187)	$ (42,555,907)
Net cash used in investing activities	(29,954,530)	(7,806)
Net cash provided by financing activities	1,220,092	194,496,391
Net increase (decrease) in cash and cash equivalents	$ (85,371,625)	$ 151,932,678

Operating Activities. Net cash used in operating activities was $56.6 million in 2022, compared to net cash used in operating activities of $42.6 million in 2021. The primary use of cash was to fund our operations. The increase in the amount of cash used in operating activities for 2022 as compared to 2021 was primarily due to an increase in our net loss, primarily from our loss from operations, and also comprised of changes in prepaid expenses and accrued expenses, due to the amount and timing of payments for research and development activities.

Investing Activities. Net cash used in investing activities in 2022 was $30.0 million compared to net cash used in investing activities in 2021 of $7.8 thousand. Net cash used in investing activities primarily related to the purchases of marketable securities, offset by maturities of marketable securities in 2022. There were no significant investing activities in 2021.

Financing Activities. Net cash provided by financing activities was $1.2 million for the year ended December 31, 2022, consisted of proceeds from stock option exercises. Net cash provided by financing activities of $194.5 million for year ended 2021, primarily related to the January and May 2021 public offerings, under which we sold an aggregate of 18.1 million shares of our common stock with net proceeds of $189.8 million after deducting underwriting discounts, commissions, and other offering related costs, along with proceeds from stock option exercises.

Off-Balance Sheet Arrangements. Through December 31, 2022, 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.

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

Interest rates

Our exposure to market risk is currently confined to our cash, our cash equivalents, our marketable securities (if any) and our Hercules Credit Facility. We have not used derivative financial instruments for speculation or trading purposes. Because of the short-term maturities of our cash, cash equivalents and marketable securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our investments. Our Hercules Credit Facility accrues interest from its date of issue at a variable annual interest rate equal to the greater of (i) 8.60% and (ii) the prime rate (as reported in the Wall Street Journal or any successor publication thereto) plus 3.10%. As of December 31, 2022, $15.0 million was outstanding under the Hercules Credit Facility.

Effects of inflation

Inflation has increased during the periods covered by this annual report on Form 10-K, and is expected to continue to increase for the near future. Inflationary factors, such as increases in the cost of our product candidates (and components thereof), interest rates, overhead costs, and transportation costs may adversely affect our operating results. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience some effect in the near future (especially if inflation rates continue to rise) due to supply chain constraints, consequences associated with COVID-19, the ongoing conflict between Russia and Ukraine, employee availability and wage increases, trade tariffs imposed on certain products from China, and increased product pricing.

ITEM 8. *FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA*

The information required by this Item 8 is contained on pages 105 through 129 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 Interim 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 Interim Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure. Our quarterly evaluation of disclosure controls includes an evaluation of some components of our internal control over financial reporting. We also perform a separate annual evaluation of internal control over financial reporting for the purpose of providing the management report below.

The evaluation of our disclosure controls included a review of their objectives and design, our implementation of the controls and the effect of the controls on the information generated for use in this annual report on Form 10-K. In the course of the control evaluations, we reviewed data errors or control problems identified and sought to confirm that appropriate corrective actions, including process improvements, were being undertaken. This type of evaluation is performed on a quarterly basis so that the conclusions of management, including our Chief Executive Officer and our Interim 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 Interim Chief Financial Officer), as of the end of the period covered by this report, our Chief Executive Officer and our Interim 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, 2022. Based on the assessment, our management has concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

Attestation Report on Internal Control over Financial Reporting

This annual report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to the deferral allowed given we are neither an accelerated or large accelerated filer.

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 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. *OTHER INFORMATION*

None.

ITEM 9C. *DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS*

Not applicable.

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 2023 Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2022 (Proxy Statement), and is incorporated in this annual report on Form 10-K by reference.

Code of Ethics and Business 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 Corporate Governance portion of our website at http://ir.aldeyra.com/corporate-governance. 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 in Item 12 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, 2022, 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), 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	6,588,585 (1)	$ 5.90 (2)	6,411,874 (3)
Equity compensation plans not approved by security holders	—	—	—
Total	6,588,585 (1)	$ 5.90 (2)	6,411,874 (3)

(1) Of these shares, 1,184,603 were underlying then outstanding restricted stock unit awards, 5,005,435 were subject to options then outstanding under the 2013 Plan, and 398,547 were subject to options then outstanding under the 2010 Plan.

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

(3) Represents 4,625,881 shares of common stock available for issuance under our 2013 Plan and 1,785,993 shares of common stock available for issuance under our 2016 ESPP. No shares are available for future issuance under the 2010 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 3, 2023, an additional 3,513,605 shares became available for future issuance under the 2013 Plan and an additional 585,601 shares became available for future issuance under the 2016 ESPP. The additional shares from the annual increase on January 3, 2023 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	Description of Securities (filed as Exhibit 4.6 to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 (as filed on March 12, 2020, 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)
10.3†	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)
10.3(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)
10.4†	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)
10.5†	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)
10.5(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)
10.5(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)

10.6	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))
10.7	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))
10.8†	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)
10.9†	Aldeyra Therapeutics, Inc. Amended and Restated Change in Control Plan (filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 (as filed on August 5, 2021, and incorporated herein by reference))
10.10	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))
10.11	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)).
10.12	Second Amendment to Lease between WLC Three VI, L.L.C. and the Registrant, dated as of October 7, 2020 (filed as Exhibit 10.33 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 (as filed on November 5, 2020 and incorporated herein by reference)).
10.13	Third Amendment to Lease between WLC Three VI, L.L.C. and the Registrant, dated as of August 12, 2021 (filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 (as filed on October 26, 2021 and incorporated herein by reference)).
10.14†	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))
10.15†	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))
10.16†	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))
10.17	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))
10.18†	Offer Letter, effective as of October 21, 2015, between the Registrant and Stephen Machatha, Ph.D.(filed as Exhibit 10.19 to the Registrant's Annual Report on Form 10-K (as filed on March 17, 2022, and incorporated herein by reference))
10.18(a)†	Offer Letter Amendment No. 1, effective as of January 1, 2018, between the Registrant and Stephen Machatha, Ph.D. (filed as Exhibit 10.19(a) to the Registrant's Annual Report on Form 10-K (as filed on March 17, 2022, and incorporated herein by reference))
10.18(b)†	Offer Letter Amendment No. 2, effective as of March 23, 2021, between the Registrant and Stephen Machatha, Ph.D. (filed as Exhibit 10.19(b) to the Registrant's Annual Report on Form 10-K (as filed on March 17, 2022, and incorporated herein by reference))
10.19	

	Loan and Security Agreement, dated as of March 25, 2019, by and among the Registrant, certain subsidiaries of the Registrant from time to time party thereto, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc. (filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K (as filed on March 26, 2019, and incorporated herein by reference))
10.20	First Amendment to Loan and Security Agreement, dated April 20, 2021, by and among the Registrant, Helio Vision, LLC, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc. (filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K as filed on April 21, 2021, and incorporated herein by reference).
10.21	Second Amendment to Loan and Security Agreement, dated December 22, 2022 and effective as of December 31, 2022, by and among the Registrant, Helio Vision, LLC, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc. (filed as Exhibit 10.2 to the Registrant's Current Report on Form 8-K as filed on December 27, 2022, and incorporated herein by reference).
10.22**	Exclusive License Agreement, effective as of July 7, 2016, between the Massachusetts Eye and Ear Infirmary and Helio Vision, Inc. (filed as Exhibit 10.39 to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 (as filed on March 12, 2020, and incorporated herein by reference))
10.23**	Amendment Number 1 and Waiver Agreement dated December 20, 2018 by and between Helio Vision, Inc. and the Massachusetts Eye and Ear Infirmary (filed as Exhibit 10.40 to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 (as filed on March 12, 2020, and incorporated herein by reference))
10.24†*	Offer Letter, effective as of November 27, 2019, between the Registrant and Bruce Greenberg.
21.1*	Subsidiaries of Aldeyra Therapeutics, Inc.
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*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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

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

ITEM 16. Form 10-K Summary

None.

Signatures

Pursuant to the requirements of Section 13 and 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this annual report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the Commonwealth of Massachusetts, on March 9, 2023.

ALDEYRA THERAPEUTICS, INC.

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

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Todd C. Brady and Bruce Greenberg, and each of them, as his or her true and lawful attorneys-in-fact, proxies, and agents, each with full power of substitution, for him in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, proxies, and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, proxies, and agents, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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 9, 2023
/s/ Bruce Greenberg Bruce Greenberg	Vice President of Finance, Interim Chief Financial Officer (principal financial and accounting officer)	March 9, 2023
/s/ Richard H. Douglas, Ph. D. Richard H. Douglas, Ph.D.	Chairman of the Board of Directors	March 9, 2023
/s/ Ben Bronstein, M.D. Ben Bronstein, M.D.	Director	March 9, 2023
/s/ Martin J. Joyce Martin J. Joyce	Director	March 9, 2023
/s/ Nancy Miller-Rich Nancy Miller-Rich	Director	March 9, 2023
/s/ Gary Phillips, M.D. Gary Phillips, M.D.	Director	March 9, 2023
/s/ Neal Walker, D.O. Neal Walker, D.O.	Director	March 9, 2023

ALDEYRA THERAPEUTICS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Aldeyra Therapeutics, Inc. and subsidiaries (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of their operations and their cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the 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 consolidated 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 consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

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

not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Estimation of Accrued Clinical Trial Expenses

As described in Note 8 to the consolidated financial statements, the Company's accrued research and development expenses totaled $8.5 million as of December 31, 2022. As described in Note 2 to the consolidated financial statements, a portion of the accrued expenses relate to clinical trial activities. Clinical trial activities pertain to third-party services, including subject-related fees at the sites where the Company's clinical trials are being conducted and investigator fees, amongst other costs. Costs associated with these clinical trial expenses are generally payable on the passage of time or when certain milestones are achieved. Accrued liabilities are recorded related to those expenses for which vendors have not yet billed the Company with respect to services provided that the Company has received. The determination of accrued liabilities for clinical trial expenses requires management to make assumptions related to expected total cost, number of subjects in the study and clinical trial sites, and study length.

We identified the estimation of accrued clinical trial expenses for certain contracts as a critical audit matter. Significant judgment is required by management in estimating completion of clinical trial activities and the associated costs incurred used to determine the accrued liabilities for clinical trial expenses. Auditing these elements involved especially challenging and subjective auditor judgment due to the nature and extent of auditor effort required to address the matter.

The primary procedures we performed to address this critical audit matter included:

- Testing the process used by management for developing the estimate of accrued clinical trial expenses for certain contracts, including estimating the completion of the clinical trial activities and the associated cost incurred, by (i) reviewing Company press releases and other public information and communications with vendors relating to the Company's clinical trial studies, (ii) interviewing respective project leads to obtain information related to the status of the projects, and (iii) examining original clinical vendor contract terms and change orders, including the expected timeline for the related study.
- Testing management's estimates of completion of the clinical trial activities and the associated cost incurred for certain contracts by, (i) confirming clinical costs, contracted fees and total amounts billed with the clinical vendors to evaluate the completeness of costs in the estimates and, (ii) examining certain subsequent invoices and payments related to the accruals.
- Testing the completeness and accuracy of the data used in the development of the estimate of accrued clinical trial expenses for certain contracts, by (i) examining reporting data detailing patient site visit information for trials in patient enrollment process, and (ii) inspecting on a sample basis invoices received from and payments made by the Company to clinical vendors throughout the year and comparing invoice and payment amounts to the related contract details.

/s/ BDO USA, LLP

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

Boston, Massachusetts

March 9, 2023

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

	December 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 144,419,364	$ 104,790,989
Cash equivalent - reverse repurchase agreements	—	125,000,000
Marketable securities	29,881,520	—
Prepaid expenses and other current assets	6,722,229	2,961,781
Total current assets	181,023,113	232,752,770
Fixed assets, net	19,279	32,487
Right-of-use assets	249,265	351,863
Total assets	$ 181,291,657	$ 233,137,120
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 133,625	$ 1,019,702
Accrued expenses	14,065,885	10,523,353
Current portion of long-term debt	911,763	—
Current portion of operating lease liabilities	249,265	229,607
Total current liabilities	15,360,538	11,772,662
Operating lease liabilities, long-term	—	125,232
Long-term debt	14,923,090	15,503,703
Total liabilities	30,283,628	27,401,597
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 15,000,000 shares authorized, none issued and outstanding	—	—
Common stock, voting, $0.001 par value; 150,000,000 authorized and 58,560,078 and 58,081,215 shares issued and outstanding, respectively	58,560	58,081
Additional paid-in capital	507,770,045	500,369,444
Accumulated other comprehensive loss	(103,938)	—
Accumulated deficit	(356,716,638)	(294,692,002)
Total stockholders’ equity	151,008,029	205,735,523
Total liabilities and stockholders’ equity	$ 181,291,657	$ 233,137,120

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

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Years ended December 31,	
	2022	2021
Operating expenses:		
Research and development	$ 47,306,066	$ 44,936,532
General and administrative	15,373,921	11,283,004
Loss from operations	(62,679,987)	(56,219,536)
Other income (expense):		
Interest income	2,349,449	185,363
Interest expense	(1,694,098)	(1,742,101)
Total other income (expense), net	655,351	(1,556,738)
Net loss	$ (62,024,636)	$ (57,776,274)
Net loss per share - basic and diluted	$ (1.06)	$ (1.07)
Weighted average common shares outstanding - basic and diluted	58,405,897	54,042,103

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

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

	Years ended December 31,	
	2022	2021
Net loss	$ (62,024,636)	$ (57,776,274)
Other comprehensive loss:		
Unrealized loss on marketable securities	(103,938)	—
Total other comprehensive loss	$ (103,938)	$ —
Comprehensive loss	$ (62,128,574)	$ (57,776,274)

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

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Stockholders' Equity					
	Common Voting Stock					
	Shares	Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Income/(Loss), net of tax	Accumulated Deficit	Total Stockholders' Equity
Balance, December 31, 2020	38,667,491	$ 38,667	$ 296,385,619	$ —	$ (236,915,728)	59,508,558
Stock-based compensation	—	—	7,006,857	—	—	7,006,857
Release of restrictions on Helio founders' shares	141,965	142	(142)	—	—	—
Issuance of common stock, net of issuance costs	18,091,947	18,092	189,793,519	—	—	189,811,611
Issuance of common stock, exercise of stock options	634,214	634	4,622,617	—	—	4,623,251
Issuance of common stock, employee stock purchase plan	12,092	12	61,517	—	—	61,529
Issuance of common stock, vested restricted stock awards	286,944	287	(287)	—	—	—
Issuance of common stock in connection with Helio Vision, Inc. acquisition milestone	246,562	247	2,499,744	—	—	2,499,991
Other comprehensive loss	—	—	—	—	—	—
Net loss	—	—	—	—	(57,776,274)	(57,776,274)
Balance, December 31, 2021	58,081,215	58,081	500,369,444	—	(294,692,002)	205,735,523
Stock-based compensation	—	—	6,180,988	—	—	6,180,988
Release of restrictions on Helio founders' shares	10,890	11	(11)	—	—	—
Issuance of common stock, exercise of stock options	236,962	237	1,123,190	—	—	1,123,427
Issuance of common stock, employee stock purchase plan	28,485	29	96,636	—	—	96,665
Issuance of common stock, vested restricted stock awards	202,526	202	(202)	—	—	—
Other comprehensive loss	—	—	—	(103,938)	—	(103,938)
Net loss	—	—	—	—	(62,024,636)	(62,024,636)
Balance, December 31, 2022	58,560,078	$ 58,560	$ 507,770,045	$ (103,938)	$ (356,716,638)	$ 151,008,029

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

ALDEYRA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years ended December 31,	
	2022	2021
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (62,024,636)	$ (57,776,274)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	8,288,976	7,108,027
Non-cash interest expense	331,150	409,471
Net amortization of premium on marketable securities	(47,245)	—
Depreciation and amortization expense	258,707	264,180
Change in operating assets and liabilities:		
Prepaid expenses and other current assets	(3,760,448)	2,239,176
Accounts payable	(886,077)	638,064
Accrued expenses and other liabilities	1,202,386	4,561,449
Net cash used in operating activities	(56,637,187)	(42,555,907)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Acquisitions of fixed assets	(16,317)	(7,806)
Purchases of marketable securities	(92,938,213)	—
Maturities of marketable securities	63,000,000	—
Net cash used in investing activities	(29,954,530)	(7,806)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock, net of issuance costs	—	189,811,611
Proceeds from exercise of stock options	1,123,427	4,623,251
Proceeds from employee stock purchase plan	96,665	61,529
Net cash provided by financing activities	1,220,092	194,496,391
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	(85,371,625)	151,932,678
CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD	229,790,989	77,858,311
CASH AND CASH EQUIVALENTS, END OF PERIOD	$ 144,419,364	$ 229,790,989
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Cash paid during the period for interest	$ 1,338,542	$ 1,337,083
SUPPLEMENTAL INFORMATION AND DISCLOSURES OF NONCASH ACTIVITIES:		
Common stock issued in connection with Helio Vision, Inc. acquisition milestone	$ —	$ 2,499,991

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

ALDEYRA THERAPEUTICS, INC.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

1. NATURE OF BUSINESS

Aldeyra Therapeutics, Inc. (Aldeyra, Company, we, us and our) was incorporated in the state of Delaware on August 13, 2004 as Neuron Systems, Inc. On December 20, 2012, the Company changed its name to Aldexa Therapeutics, Inc. and, on March 17, 2014, the Company changed its name to Aldeyra Therapeutics, Inc. Aldeyra, together with its wholly-owned subsidiaries, is a clinical-stage biotechnology company discovering and developing innovative therapies designed to treat immune-mediated diseases.

The Company's principal activities to date include research and development activities along with related general business planning, including raising capital.

2. BASIS OF PRESENTATION AND SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Consolidation – The accompanying consolidated financial statements were prepared in conformity with accounting principles generally accepted in the United States of America (US GAAP) and pursuant to the rules and regulations of the Securities and Exchange Commission (SEC). The Company's consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated.

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, 2022, will be sufficient to fund the Company's currently projected operating expenses into the second half of 2024. As a result of the COVID-19 pandemic, clinical site availability, staffing, and patient recruitment have been negatively affected and the timelines to complete the Company's clinical trials may be delayed. The Company's assessment of its liquidity and capital resources includes an estimate of the financial impacts of these changes. The Company has based its projections of operating capital requirements on its current operating plan, which includes several assumptions that may prove to be incorrect, and Company may use all of its available capital resources sooner than the Company expects. 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 and regulatory activities; commence or continue ongoing commercialization activities, including manufacturing, sales, marketing and distribution, for any of our product candidates for which the Company may receive marketing approval; or conduct any substantial, additional development requirements requested by the 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 funding, it will be required to significantly decrease the amount of planned expenditures and may be required to cease operations.

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

Use of Estimates – The preparation of consolidated financial statements in conformity with US GAAP requires management to make estimates and assumptions, including fair value estimates for investments, that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. The Company evaluates its estimates and assumptions on an ongoing basis. The most significant estimates in the Company's consolidated financial statements include, but are not limited to, clinical trial accruals, deferred and accrued research and development costs, stock-based compensation, and accounting for income taxes and related valuation allowance. Although these estimates and assumptions are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may ultimately 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 the requirement that collateral received is maintained at 102% of the value of the RRAs on a daily basis.

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

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

Concentration of Credit Risk – Financial instruments that potentially subject the Company to significant concentrations of credit risk principally consist of cash, cash equivalents and marketable securities, if any. The Company places its cash and cash equivalents and marketable securities with financial institutions which management believes have high credit ratings and may hold some amounts exceed federally insured limits. 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, 2022 and 2021, 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, 2022 and 2021 were $1.0 million and $1.3 million, respectively.

Income Taxes – The Company follows the provisions of Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) 740, *Income Taxes (ASC 740)*, in reporting deferred income taxes. ASC 740 requires a company to recognize deferred tax liabilities and assets for expected future income tax consequences of events that have been recognized in the Company's financial statements. Under this method, deferred tax assets and liabilities are determined based on temporary differences between financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates in the years in which the temporary differences are expected to reverse. Valuation allowances are provided if based on the weight of available evidence, it is more likely than not that some or all the deferred tax assets will not be realized.

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

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

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

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

Stock-Based Compensation – Stock-based payments are accounted for in accordance with the provisions of ASC 718, *Compensation – Stock Compensation*. For options, the fair value of stock-based payments is estimated, on the date of grant, using the Black-Scholes option pricing model. For restricted stock units, fair value is based on the fair value of the stock on the date of grant. The resulting fair value for restricted stock units 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 units or option. The Company records the effect of forfeitures and cancellations when they occur.

For performance-based awards, at each reporting period we assess the probability that the performance condition(s) will be achieved. We use the accelerated attribution method to expense the awards over the continuous

service period based on the probability of achieving the performance conditions. We estimate the continuous service period based on our best estimate of the period over which an award's vesting condition(s) will be achieved. We review and evaluate these estimates on a quarterly basis.

The Company has cash awards and performance cash settled bonus awards, which are awards that will be settled in cash on their vesting dates (Liability Awards), rather than in equity units. The fair value of Liability Awards is updated at each balance sheet date and changes in the fair value of the vested portions of the Liability Awards are recorded as increases or decreases to compensation expense. The Company recognizes forfeitures as 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, 2022, comprehensive loss is equal to the Company's net loss of $62.0 million and an unrealized loss on marketable securities of $0.1 million. For December 31, 2021, comprehensive loss is equal to the Company's net loss of $57.8 million.

Net Loss Per Share – The Company computes net loss per share in accordance with the two-class method. Under the two-class method, net loss is allocated between common stock and other participating securities based on their participation rights. The Company has determined that the nonvested shares issued to the Helio founders represents a participating security and as such the nonvested shares are excluded from basic earnings per share. Net losses are not allocated to the nonvested stockholders for computing net loss per share under the two-class method because nonvested stockholders do not have contractual obligations to share in the losses of the Company. Basic earnings per share is calculated by dividing net loss allocable to common stockholders by the weighted average number of common stock outstanding during the period, excluding the effects of any potentially dilutive instruments.

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

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

3. HELIO VISION ACQUISITION

On January 28, 2019 (Closing Date), the Company acquired Helio Vision, Inc. (Helio). As a result of the acquisition, the Company initially issued an aggregate of 1,160,444 shares of common stock to the former securityholders and an advisor of Helio. The founders of Helio were issued 568,627 shares and non-founders were issued 591,817 shares. The Helio founders' shares were subject to vesting based on continued service to the Company through January 28, 2022. The Company recognized the expense associated with the founders' restricted shares as research and development compensation expense on a straight-line basis as the shares vested over the three-year period. For the year ended December 31, 2022 and 2021, the Company recorded $0.1 million and $1.2 million of research and development compensation expense, respectively, for the founders' restricted shares.

In January 2021, pursuant to the terms of the acquisition agreement, the Company issued 246,562 shares of its common stock to the former securityholders of Helio (January Shares). In addition, the Company, subject to the conditions of the acquisition agreement, is contingently obligated to make additional payments to the former securityholders of Helio as follows: (a) $10.0 million of common stock following approval by the FDA of an NDA for the prevention and/or treatment of proliferative vitreoretinopathy or a substantially similar label prior to the 10th

anniversary of the Closing Date; and (b) $2.5 million of common stock following FDA approval of an NDA for an indication (other than proliferative vitreoretinopathy or a substantially similar label) prior to the 12th anniversary of the Closing Date (the shares of common stock issuable pursuant to the preceding clauses (a) and (b) are referred to herein as the Milestone Shares), provided that in no event shall the Company be obligated to issue more than an aggregate of 5,248,885 shares of common stock in connection with the Helio acquisition. 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 in the aggregate.

The Company determined that liability accounting is not required for the Milestone Shares under FASB ASC Topic 480, *Distinguishing Liabilities from Equity* (ASC 480). The Company also determined that the Milestone Shares meet the scope exception as a derivative under FASB ASC Topic 815, *Derivatives and Hedging* (ASC 815), from inception of the Milestone Shares through December 31, 2022. Accordingly, the Milestone Shares are evaluated under FASB ASC Topic 450, *Contingencies* (ASC 450) and the Company will record a liability related to the Milestone Shares if the milestones are achieved, and the obligation to issue the Milestone Shares becomes probable. At such time, the Company will record the cost of the Milestone Shares issued to the founders as compensation expense and to the Helio non-founders as an in-process research and development (IPR&D) expense if there is no alternative future use. At December 31, 2020, the issuance of the January Shares was considered probable and $2.5 million was accrued as contingent consideration payable in stock and the Company recorded $1.8 million to IPR&D (Milestone IPR&D), which included a $0.5 million income tax benefit, and $1.2 million of compensation expense related to the January Shares, which amounted to 246,562 shares and were issued during the quarter ended March 31, 2021. No other milestones related to the remaining Milestone Shares are considered probable of being achieved as of December 31, 2022.

4. NET LOSS PER SHARE

For the years ended December 31, 2022 and 2021, 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,	
	2022	2021
Options to purchase common stock	5,403,982	4,622,870
Nonvested restricted stock units	1,184,603	501,255
Nonvested founder shares [(1)]	—	10,891
Total of common stock equivalents	6,588,585	5,135,016

(1) Represents 10,891 shares of common stock that are issued and outstanding but that were subject to vesting based on service requirements at December 31, 2021, and were not included in stockholders' equity at such date.

5. CASH, CASH EQUIVALENTS, AND MARKETABLE SECURITIES

At December 31, 2022, 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	$ 135,151,081	$ —	$ —	$ 135,151,081	$ 135,151,081	$ —
Money market funds	9,268,283	—	—	9,268,283	9,268,283	—
Total cash and cash equivalents	$ 144,419,364	$ —	$ —	$ 144,419,364	$ 144,419,364	—
U.S. government agency securities	$ 29,985,458	$ —	$ (103,938)	$ 29,881,520	$ —	$ 29,881,520
Available for sale [1]	29,985,458	—	(103,938)	29,881,520	—	29,881,520
Total cash, cash equivalents, and current marketable securities					$ 144,419,364	$ 29,881,520

At December 31, 2021, 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	$ 100,364,523	$ —	$ —	$ 100,364,523	$ 100,364,523	$ —
Money market funds	4,426,466	—	—	4,426,466	4,426,466	—
Reverse repurchase agreements	125,000,000	—	—	125,000,000	125,000,000	—
Total cash and cash equivalents	$ 229,790,989	$ —	$ —	$ 229,790,989	$ 229,790,989	$ —
Available for sale [1]	—	—	—	—	—	—
Total cash, cash equivalents, and current marketable securities					$ 229,790,989	$ —

There were no marketable securities held at December 31, 2021.

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

The contractual maturities of all available for sale securities were less than one year at December 31, 2022

6. FAIR VALUE MEASUREMENTS

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

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

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

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

The following table presents information about the Company's assets measured at fair value at December 31, 2022 and December 31, 2021:

	December 31, 2022			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds (a)	$ 9,268,283	$ —	$ —	$ 9,268,283
U.S government agency securities (b)	—	29,881,520	—	29,881,520
Total assets at fair value	$ 9,268,283	$ 29,881,520	$ —	$ 39,149,803

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds (a)	$ 4,426,466	$ —	$ —	$ 4,426,466
Reverse repurchase agreements (b)	—	125,000,000	—	125,000,000
Total assets at fair value	$ 4,426,466	$ 125,000,000	$ —	$ 129,426,466

(a) Money market funds included in cash and cash equivalents in the consolidated balance sheets, are valued at quoted market prices in active markets.

(b) Reverse repurchase agreements and U.S. government agency securities, are recorded at fair market value, which are determined based on the most recent observable inputs for similar instruments in active markets or quoted prices for identical or similar instruments in markets that are not active or are directly or indirectly observable.

7. PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets at December 31, 2022 and 2021 were:

	December 31, 2022	December 31, 2021
Deferred research and development expenses	$ 2,605,252	$ 2,404,145
Prepaid insurance expenses	432,230	435,410
Other current receivables	3,242,026	28,770
Miscellaneous prepaid expenses	442,721	93,456
Total prepaid expenses and other current assets	$ 6,722,229	$ 2,961,781

8. ACCRUED EXPENSES

Accrued expenses at December 31, 2022 and 2021 were:

	December 31, 2022	December 31, 2021
Accrued compensation	$ 3,821,904	$ 1,512,885
Accrued research and development expenses	8,476,422	8,415,560
Accrued other expenses	1,767,559	594,908
Total accrued expenses	$ 14,065,885	$ 10,523,353

9. CREDIT FACILITY

The Company's long-term debt obligation consists of amounts the Company is obligated to repay under its credit facility with Hercules Capital, Inc. (Hercules). In March 2019, the Company entered into a Loan and Security Agreement (Loan and Security Agreement or Hercules Credit Facility) with Hercules and several banks and other financial institutions or entities, from time-to-time parties thereto (collectively, referred to herein as Lender), providing for a term loan of up to $60.0 million, subject to the satisfaction of certain conditions contained therein, that is secured by a lien covering all of the Company's assets, other than the Company's intellectual property. The Loan and Security Agreement provided for (i) an initial term loan advance of up to $5.0 million at the Company's option, which expired unutilized on April 15, 2019; (ii) three additional term loan advances of up to $15.0 million each, at the Company's option, available to the Company upon the occurrence of certain pre-specified funding conditions prior to September 30, 2019 (2019 Tranche), March 31, 2020 (2020 Tranche), and March 31, 2021 (2021 Tranche); and (iii) a final additional term loan advance (Fourth Loan Tranche) of up to $10.0 million prior to December 31, 2021, at the Company's option, subject to approval by the Lender's investment committee. The 2019 Tranche was drawn down in full by the Company in September 2019 and the 2020 Tranche and 2021 Tranche expired unutilized prior to the Company satisfying the funding conditions for such tranche. On April 20, 2021, the Company entered into the First Amendment to the Loan and Security Agreement (First Amendment). The First Amendment, among other things, (i) increased the Fourth Loan Tranche from $10.0 million to $20.0 million and extended the deadline for drawing down the Fourth Loan Tranche to July 1, 2022; (ii) lowered the variable per annum rate of interest on borrowings under the Loan and Security Agreement from the greater of (a) 9.10% and (b) the prime rate (as reported in the Wall Street Journal or any successor publication thereto) plus 3.10% to the greater of (x) the Prime Rate (as defined therein) plus 3.10% or (y) 8.60%; (iii) extended the expiration of the period in which interest-only payments on borrowings under the Loan and Security Agreement are required from May 1, 2021 to July 1, 2022; and (iv) following the satisfaction of certain conditions, which conditions were satisfied in April 2021, further extended the expiration of the interest-only period and the deadline for drawing down the Fourth Loan Tranche to May 1, 2023. Repayment of the aggregate outstanding principal balance of the term loan, in monthly installments, commences upon expiration of the interest-only period and continues through October 1, 2023 (Maturity Date). The First Amendment was determined to be a modification in accordance with FASB ASC Topic 470, *Debt* and did not result in extinguishment.

On December 22, 2022, the Company entered into the Second Amendment to the Loan and Security Agreement (Second Amendment), which became effective as of December 31, 2022 (Second Amendment Effective Date). The Second Amendment, among other things, (i) extended the expiration of the period in which interest-only payments on borrowings under the Loan and Security Agreement are made from May 1, 2023 to May 1, 2024; (ii) extended the Maturity Date from October 1, 2023 to October 1, 2024; (iii) extended the availability of the Fourth Loan Tranche commitment of $20 million from May 1, 2023 to May 1, 2024; and (iv) amended the Prepayment Charge (as defined therein) to equal 0.75% of the amount prepaid during the 12-month period following the Second Amendment Effective Date, and 0% thereafter. The ability to draw the Fourth Loan Tranche remains conditioned on approval by the Lenders' investment committee. In addition, a supplemental end of term charge of $292,500 (Supplemental End of Term Charge) shall be due on the earlier of (A) the Maturity Date, as amended, or (B) repayment of the aggregate amount of advances under the Loan and Security Agreement. The existing end of term charge of $1,042,500 (End of Term Charge) remains due on the earlier of (A) October 1, 2023 or (B) repayment of the aggregate amount of advances under the Loan and Security Agreement. The Second Amendment was determined to be a modification in accordance with FASB ASC Topic, Debt and did not result in extinguishment.

In connection with the Hercules Credit Facility, the Company incurred a commitment charge of $25,000, transaction costs of $273,186, a fee of $375,000 upon closing, and will be required to pay the End of Term Charge and Supplemental End of Term Charge. The fees and transaction costs are amortized to interest expense from 2019 through the Maturity Date using the effective interest method. The End of Term Charge is amortized to interest expense from 2019 through October 2023, and the Supplemental End of Term Charge is amortized to interest expense from December 2022 through the Maturity Date, both using the effective interest method. The effective interest rate was 13.2% at December 31, 2022. At the Company's option, the Company may elect to prepay all, but not less than all, of the outstanding term loan by paying the entire principal balance and all accrued and unpaid interest thereon plus all fees and other amounts due under the Loan and Security Agreement as of the date of such prepayment, including a prepayment charge equal to 0.75% of the principal amount being prepaid during the 12-month period following the Second Amendment Effective Date, and 0% thereafter.

Following the effective time of the First Amendment and the Second Amendment and as of December 31, 2022, an aggregate of $35 million, subject to the terms and conditions of the Loan and Security Agreement, may be made available to the Company for borrowing, $15 million of which was funded prior to the date of the First Amendment.

Long-term debt consisted of the following:

	December 31, 2022	December 31, 2021
Term loan payable	$ 15,000,000	$ 15,000,000
End of term charge	911,763	703,269
Unamortized debt issuance costs	(76,910)	(199,566)
Less: current portion	(911,763)	—
Total long-term debt	$ 14,923,090	$ 15,503,703

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

2023	$ 1,042,500
2024	15,292,500
Total	$ 16,335,000

The Loan and Security Agreement also contains certain events of default, representations, warranties and non-financial covenants of the Company. As of December 31, 2022, the Company was in compliance with all covenants of the Hercules Credit Facility in all material respects. In addition, subject to the terms of the Loan and Security Agreement, the Company granted the Lender the right to purchase up to an aggregate of $2.0 million of the

Company's equity securities, or instruments exercisable for or convertible into equity securities, sold to investors in financings upon the same terms and conditions afforded to such other investors.

10. 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, 2022, a total of 5,403,982, 4,625,881, and 1,785,993, shares of common stock were reserved for issuance upon (i) the exercise of outstanding stock options, (ii) the issuance of stock awards under the Company's Amended 2013 Plan, and (iii) the issuance of shares under the 2016 ESPP, respectively.

2021 Jefferies Sales Agreement

In March 2021, the Company entered into an Open Market Sales Agreement SM with Jefferies LLC (Jefferies), as sales agent (2021 Jefferies Sales Agreement), pursuant to the 2021 Jefferies Sales Agreement, the Company may offer and sell, from time to time through Jefferies, shares of common stock providing for aggregate sales proceeds of up to $100.0 million. The Company has no obligation to sell any shares under the 2021 Jefferies Sales Agreement, and could at any time suspend solicitations and offers under the 2021 Jefferies Sales Agreement. No sales had been made pursuant to the 2021 Jefferies Sales Agreement as of December 31, 2022.

Underwritten Public Offerings

In January 2021, the Company sold 7.9 million shares of its common stock in an underwritten public offering at $9.50 per share, for an aggregate gross cash purchase price of $74.7 million or proceeds of $70.0 million after deducting underwriters' discount, commissions, and other offering expenses.

In May and June 2021, the Company sold an aggregate of 10.2 million shares of its common stock at a public offering price of $12.50 per share, in an underwritten public offering, for an aggregate gross cash purchase price of $127.8 million or proceeds of $119.8 million after deducting underwriters' discount, commissions, and other offering expenses, which included the partial exercise of the underwriters' option to purchase additional shares.

11. INCOME TAXES

No current or deferred tax provision expenses for federal and state income taxes have 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 Accounting Standards Codification (ASC) 740, Income Taxes (ASC 740), the Company considers whether it is more likely than not that some portion or all the deferred tax assets will not be realized. Based on the weight of available evidence, primarily the incurrence of net losses since inception, anticipated net losses in the near future, reversals of existing temporary differences and expiration of various federal and state attributes, the Company does not consider it more likely than not that some or all of the net deferred taxes will be realized. Accordingly, a 100% valuation allowance has been applied against net deferred tax assets. Effective January 1, 2021, the Company adopted ASU No. 2019-12, Income Taxes (Topic 740), which did not have a material impact to the Company's financial statements.

As of December 31, 2022, the Company had federal and state income tax net operating loss (NOL) carryforwards of approximately $239.2 million and $231.3 million, respectively. Federal NOL carryforwards generated through December 31, 2017 and state NOL carryforwards will expire at various dates through 2041. The federal NOL carryforwards generated during the year ended December 31, 2018 and thereafter will carryforward indefinitely. As of December 31, 2022, the Company had federal and state research and development tax credit carryforwards of approximately $8.7 million and $2.1 million, respectively, which will expire at various dates through 2041. Additionally, as of December 31, 2022, the Company had a federal orphan drug tax credit carryforward of approximately $1.7 million that expires in 2042.

On August 16, 2022 President Biden signed into law the Inflation Reduction Act (IRA). From a tax perspective, the IRA provisions includes a new corporate alternative minimum tax (CAMT) of 15% on adjusted financial statement income (AFSI) for corporations with over $1 billion in profits, a new excise tax on corporate stock buybacks and increased funding for IRS enforcement. A company's AFSI can be reduced by net operating losses, foreign tax credits, general business credits and depreciation for property under Section 197. To determine its US federal income tax liability, a company will need to compute taxes under both systems — the regular tax system and the CAMT system. The company then will pay the larger amount as its tax liability in any given year. The Company does not expect to fall into the CAMT system. The IRA provisions have no impact on the Company's financial statements for the period ended December 31, 2022.

Significant components of the Company's deferred tax assets and liabilities at December 31, 2022 and 2021 are as follows:

	Years ended December 31,	
	2022	2021
Deferred Tax Assets		
Federal & state NOL carryforward	$ 64,840,595	$ 61,308,787
Federal & state R&D credit carryforward	12,110,003	9,200,758
Deferred costs	342,210	—
Intangibles – net	78,378	78,378
Accounts payable and accrued expenses	2,004,737	2,301,117
Reserves	28,396	—
Stock options	4,042,117	3,906,501
Capitalized R&D expenses	11,151,910	—
Other items	98,552	127,791
Gross deferred tax assets	94,696,898	76,923,332
Valuation allowance	(94,628,799)	(76,827,203)
Deferred tax assets, net	$ 68,099	$ 96,129
Deferred Tax Liabilities		
Right of use asset	(68,099)	(96,129)
TOTAL	$ —	$ —

The change in valuation allowance of $17.8 million from December 31, 2021 to December 31, 2022 was primarily the result of an increase in capitalized R&D expenses, net operating losses, and tax credits.

The components of the income tax benefit for the years ended December 31, 2022 and 2021, are as follows:

	Years ended December 31,	
	2022	2021
Deferred Taxes		
Federal	$ —	$ —
State	—	—
Total income tax benefit	$ —	$ —

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.

Under Section 382 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs and certain other tax assets to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders' lowest percentage ownership during the testing period (generally three years). Transactions involving the Company's common stock within the testing period, even those outside the Company's control such as purchases or sales by investors, could result in an ownership change. A limitation on the Company's ability to utilize some or all its NOLs or credits could have a material adverse effect on the Company's results of operations and cash flows. The Company believes, prior to December 31, 2021 that four ownership changes occurred since inception. Management believes that its aggregate Section 382 limitation (including the additional limitation for recognized "built-in gains") is sufficient so that no current impairment of its pre-ownership change tax attributes is required. There were no ownership changes in 2022. Any future ownership changes, including those resulting from any recent or future financing activities, may cause our existing tax attributes to have additional limitations.

As of December 31, 2022, the Company is subject to tax in the U.S. (Federal and Massachusetts). The Company is open to examination for the tax years ended December 31, 2022, 2021, 2020, and 2019. In addition, any loss years remain open to the extent that losses are available for carryover to future years.

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,	
	2022	2021
Statutory tax rate	21.00 %	21.00 %
State taxes, net of federal benefits	6.05 %	6.65 %
Federal research and development credits	4.12 %	4.29 %
Change in valuation allowance	(28.66)%	(31.35)%
Stock-based compensation	(2.53)%	(0.73)%
Other	0.02 %	0.14 %
Effective tax rate	0.00 %	(0.00)%

12. STOCK INCENTIVE PLAN

The Company approved the 2010 Employee, Director and Consultant Equity Incentive Plan (2010 Plan) in September 2010 to replace the 2004 Employee, Director and Consultant Equity Incentive 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, 2022, options to purchase 398,547 shares of common stock at a weighted average exercise price of $1.52 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. The 2013 Equity Incentive Plan was amended in June 2016 and June 2018, (Amended 2013 Plan). The Amended 2013 Plan provides for the granting of stock options, restricted stock units (RSU), stock appreciation rights, and stock units to certain employees, members of the board of directors and consultants of the Company. On first business day 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, 2022, options to purchase 5,005,435 shares of common stock at a weighted average exercise price of $6.25 per share and 1,184,603 shares of common stock underlying restricted stock units remained outstanding under the Amended 2013 Plan. As of December 31, 2022, there were 4,625,881 shares of common stock available for grant under the Amended 2013 Plan. As of January 3, 2023, the number of shares of common stock that may be issued under the Amended 2013 Plan was automatically increased by 3,513,605 shares, increasing the number of shares of common stock available for issuance under the Amended 2013 Plan to 8,139,486.

In 2019, 2020, and 2022 the Company granted cash awards under its Management Cash Incentive Plan, as amended. The cash awards vest in four annual installments from the date of grant and entitle the employees to receive a cash payment, on the earlier of (i) four years from the date of grant or (ii) a change of control, equal in value to the amount by which the then value of the Company's common stock exceeds the base value. As of December 31, 2022, $1.4 million was accrued as compensation expense for vested cash awards. There was no unrecognized expense as of December 31, 2022.

In 2022, the Company granted performance cash settled bonus awards (CSBUs) under its Management Cash Incentive Plan, as amended. Subject to and conditioned upon the acceptance by the FDA of the Company's submission of an NDA for reproxalap (Performance Criteria), the awards will vest in four annual installments from the date of grant and entitle the employees to receive a cash payment for each vested CSBU, on the earlier of (i) four years from the date of grant or (ii) a change of control, equal in value of the closing price per share of the Company's common stock on the Nasdaq Capital Market on the payment date. As of December 31, 2022, $1.1 million was accrued as compensation expense for CSBUs as the Performance Criteria was deemed probable and was subsequently met in February 2023. There was no unrecognized expense as of December 31, 2022.

The Company recognizes stock-based compensation expense over the requisite service period. The Company's share-based awards are accounted for as equity instruments, except for cash awards and CSBUs, which are accounted for as liabilities. The amounts included in the consolidated statements of operations relating to stock-based compensation associated with the two equity incentive plans, cash awards, CSBUs, and Helio founders' shares are as follows:

	Years ended December 31,	
	2022	2021
Research and development expenses	$ 4,087,073	$ 3,562,181
General and administrative expenses	4,201,903	3,545,846
Total stock-based compensation expense	$ 8,288,976	$ 7,108,027

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 from which 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, 2022:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value(a)
Outstanding at December 31, 2021	4,622,870	$ 6.73		$ 1,268,089
Granted	1,756,297	4.05		—
Cancelled/Forfeited	(738,223)	7.09		—
Exercised	(236,962)	4.74		414,682
Outstanding at December 31, 2022	5,403,982	$ 5.90	6.56	$10,506,953
Exercisable at December 31, 2022	3,528,792	$ 6.13	5.33	$ 6,098,269

(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, 2022 of $6.96 and the per share exercise price of the underlying options. The total intrinsic value of stock options exercised was $0.4 million and $2.5 million for the years ended December 31, 2022 and 2021, respectively.

The Company records stock-based compensation related to stock options granted at fair value. During the years ended December 31, 2022 and 2021, 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 $2.92 and $7.95 for the years ended December 31, 2022 and 2021, respectively. The assumptions used in determining fair value of the employee stock options for the years ended December 31, 2022 and 2021, are as follows:

	December 31, 2022	December 31, 2021
Expected dividend yield	0%	0%
Anticipated volatility	84.82% - 85.21%	81.73% - 83.50%
Stock price	$3.49 - $4.52	$8.33 - $12.97
Exercise price	$3.49 - $4.52	$8.33 - $12.97
Expected life (years)	5.50 - 6.08	5.50 - 6.08
Risk free interest rate	1.47% - 3.26%	0.88% - 1.67%

The dividend yield of zero is based on the fact that the Company has never paid cash dividends and have no present intention to pay cash dividends. Expected volatility is estimated using the historical volatility of the Company. The Company has estimated the expected life of its 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, 2022, there is approximately $6.1 million of unrecognized compensation cost relating to stock options outstanding, which the Company expects to recognize over a weighted average period of 2.31 years. Total unrecognized compensation cost will be adjusted for future forfeitures, if necessary.

Restricted Stock Units

Terms of 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. RSUs 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, 2022 :

	Number of Shares	Weighted-Average Grant Date Fair Value
Outstanding at December 31, 2021	501,255	$ 5.94
Granted	1,055,460	4.64
Cancelled/Forfeited	(169,586)	4.37
Vested/released	(202,526)	6.28
Outstanding at December 31, 2022	1,184,603	$ 4.95

The weighted-average fair value of RSUs granted was $4.64 and $11.71 per share for the years ended December 31, 2022 and December 31, 2021, respectively. The total fair value of RSUs vested was $1.3 million and $1.5 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, the outstanding RSUs had unamortized stock-based compensation of $4.3 million with a weighted-average remaining recognition period of 3.16 years and an aggregate intrinsic value of $8.2 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 initially authorized 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, 2022	December 31, 2021
Expected dividend yield	0%	0%
Anticipated volatility	84.04% - 84.99%	81.76% - 82.87%
Stock price	$3.80 - $4.27	$6.53 - $11.31
Exercise price	$3.80 - $4.27	$6.53 - $11.31
Expected life (years)	0.50	0.50
Risk free interest rate	0.22% - 4.76%	0.05% - 0.09%

At December 31, 2022, the Company has 1,785,993 shares available for issuance under the 2016 ESPP. The number of shares available for issuance under the 2016 ESPP was increased as of January 3, 2023 by 585,601 shares. 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, 2022 and 2021 are as follows:

	December 31, 2022	December 31, 2021
Weighted-average grant-date fair value per share	$ 1.57	$ 2.98
Total shares issued	28,485	12,092
Total stock-based compensation expense	$ 57,413	$ 45,190

13. COMMITMENTS AND CONTINGENCIES

Guarantees and Indemnifications

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The term of the indemnification is for the officer's or director's lifetime. Through December 31, 2022, 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

MEEI Agreement

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

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

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

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

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

Litigation

From time to time, the Company is party to legal proceedings. There are none deemed to be material at this time. Accordingly, the Company has not accrued any liabilities in its consolidated financial statements related to proceedings.

14. LEASES

The Company currently leases an office used to conduct business. The exercise of lease renewal options is at the Company's discretion and the renewal to extend the lease terms are not included in the Company's Right-Of-Use assets and lease liabilities as they are not reasonably certain of exercise. The Company regularly evaluates the renewal options and when they are reasonably certain of exercise, the Company includes the renewal period in its lease term. As the Company's lease does not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of the lease payments. In August 2021, the Company entered into a lease amendment extending the lease by 18 months through June 30, 2023, which had an immaterial impact to the balance sheet as of December 31, 2021. In December 2022, the Company exercised its option to extend the lease for an additional 6 months through December 31, 2023, which had an immaterial impact on the balance sheet as of December 31, 2022. For the years ended December 31, 2022 and 2021, right of use assets obtained in exchange for lease obligations were $0.2 million and $0.3 million, respectively.

As of December 31, 2022, the Company maintained an unamortized Right-Of-Use asset with a corresponding operating lease liability of approximately $0.2 million based on the present value of the minimum rental payments in accordance with ASC Topic 842, *Leases*. The weighted average discount rate used for leases as of December 31, 2022 is 9.1%. The weighted average lease term as of December 31, 2022 is 1.0 years. The operating lease expense for the year ended December 31, 2022 was $0.2 million. Maturities and balance sheet presentation of our lease liabilities for all operating leases as of December 31, 2022 is as follows:

2023 remaining total lease payments	$ 261,828
Less: effect of discounting	(12,563)
Present value of lease liabilities	$ 249,265
Current operating lease liabilities	$ 249,265
Total	$ 249,265

The Company's gross future minimum payments under all non-cancelable operating leases as of December 31, 2022 are:

	Total	2023	2024	2025	2026
Operating lease obligations	$ 261,828	$ 261,828	$ —	$ —	$ —

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K
(Amendment No. 1)

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

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

For 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 or Organization)	**(I.R.S. 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:

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

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

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

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

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

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

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

Large Accelerated Filer	☐	Accelerated Filer	☐
Non-Accelerated Filer	☒	Smaller reporting company	☒
		Emerging Growth Company	☐

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

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

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

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

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

As of June 30, 2022, 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 $228,378,259, 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 April 21, 2023, there were 58,576,350 shares of the registrant's Common Stock issued and outstanding.

Audit Firm ID: 243 Auditor Name: BDO USA, LLP Auditor Location: Boston, Massachusetts

EXPLANATORY NOTE

This Amendment No. 1 to Form 10-K (this "Form 10-K/A") amends the Annual Report on Form 10-K of Aldeyra Therapeutics, Inc., a Delaware corporation ("Aldeyra," "we," "us," the "registrant" or the "Company," including our subsidiaries, as applicable), for the year ended December 31, 2022 that we originally filed with the Securities and Exchange Commission (the "SEC") on March 9, 2023 (the "Original Filing"). We are filing this Form 10-K/A to provide the information required by Items 10, 11, 12, 13, and 14 of Part III of Form 10-K. We previously omitted this information from the Original Filing in reliance on General Instruction G(3) to Form 10-K, which permits that information to be incorporated by reference from a registrant's definitive proxy statement if the proxy statement is filed within 120 days after fiscal year-end. The reference on the cover page of the Original Filing to such incorporation by reference has been deleted, and this Form 10-K/A amends and restates in their entirety the cover page and Part III of the Original Filing. Capitalized terms not otherwise defined in Part III of this Form 10-K/A shall have the same meanings assigned to those terms in Parts I and II of the Original Filing.

Pursuant to the rules of the SEC, Part IV, Item 15 (Exhibit Index) has also been amended to contain the currently dated certifications from our principal executive officer and principal financial officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. The certifications of our principal executive officer and principal financial officer are attached to this Form 10-K/A as Exhibits 31.3 and 31.4, respectively. Because no financial statements have been included in this Form 10-K/A and this Form 10-K/A does not contain or amend any disclosure with respect to Items 307 and 308 of Regulation S-K, we have omitted paragraphs 3, 4 and 5 of the certifications filed with this Form 10-K/A. Additionally, we are not including the certifications under Section 906 of the Sarbanes-Oxley Act of 2002, because we are not filing any financial statements with this Form 10-K/A.

Except as set forth in this Form 10-K/A, this Form 10-K/A does not amend or otherwise update any other information in the Original Filing. Other than the information specifically amended and restated herein, this Form 10-K/A does not reflect events occurring after March 9, 2023, the date of the Original Filing, or modify or update those disclosures that may have been affected by subsequent events. Accordingly, this Form 10-K/A should be read in conjunction with the Original Filing and with our filings with the SEC after the Original Filing.

Aldeyra Therapeutics, Inc.
Form 10-K/A
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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 ("SEC").

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

PART III

ITEM 10. Directors, Executive Officers and Corporate Governance

Directors

The table below lists the name, age and certain other information of each member of our Board of Directors (the "Board") as of April 21, 2023. We have also included below a summary of the business experience; public company director positions held currently or at any time during the last five years; involvement in certain legal or administrative proceedings, if applicable; and the experiences, qualifications, attributes or skills that led our nominating and corporate governance committee and our Board to the conclusion that each of our directors should serve as a member of our Board.

				Committee Membership		
Name	Age	Director Class	Term Expires	Audit	Compensation	Nominating/Corporate Governance
Todd C. Brady, M.D., Ph.D.	51	III	2023	—	—	—
Martin J. Joyce, M.B.A.	69	III	2023	Chair	—	✓
Ben R. Bronstein, M.D.	73	I	2024	✓	—	Chair
Nancy B. Miller-Rich	64	I	2024	—	✓	—
Richard H. Douglas, Ph.D.	70	II	2025	—	—	✓
Gary M. Phillips, M.D.	57	II	2025	✓	Chair	—
Neal S. Walker, D.O.	52	II	2025	—	✓	—

Name	Principal Occupation and Business Experience
Todd C. Brady, M.D., Ph.D.	Dr. Brady has served as our President and Chief Executive Officer since January of 2012 and as a member of our Board since 2005. Prior to Aldeyra, Dr. Brady served as Entrepreneur in Residence at Domain Associates, LLC, a leading healthcare venture capital firm, where he was a Principal from 2004 to 2013. Dr. Brady currently serves on the board of directors of Evoke Pharma, Inc., a publicly traded healthcare company. Dr. Brady holds a Ph.D. in pathology from Duke University Graduate School, a M.D. from Duke University Medical School, and an A.B. from Dartmouth College in Philosophy and Psychology. Dr. Brady's extensive knowledge of our business, as well as his years of experience in the biotechnology industry, including executive leadership in several biotechnology companies, contributed to our conclusion that he should serve as a director of our company.

Martin J. Joyce, M.B.A.	Mr. Joyce has served as member of our Board since October 2013. Mr. Joyce's professional background includes leadership roles in public and private, medical device, biotechnology, and pharmaceutical companies from start-up stage to over $500 million in annual revenue. He has experience in public equity financings, business development, SEC reporting, strategic planning, mergers, acquisitions, investor relations, and biotechnology operations. Since 2012, Mr. Joyce has served as a consultant to the life science industry assisting biotechnology and pharmaceutical companies in strategic planning, fund raising, and operations. From March 2011 to July 2012, Mr. Joyce was Chief Financial Officer at Lucid Inc., an early stage skin cancer diagnostic company. Previously, Mr. Joyce served as Executive Vice President and Chief Financial Officer of BioSphere Medical from January 2006 through September 2010 and as BioSphere's Chief Financial Officer and Vice President from September 2004 to January 2006. From January 2001 to September 2004, Mr. Joyce served as Managing Partner of Stratex Group LLC, a provider of biopharmaceutical executive services to early-stage companies and venture investors. From 1996 to January 2001, Mr. Joyce was North American Chief Financial Officer for Serono Inc. a biotechnology company. From April 1987 to 1996, Mr. Joyce held a variety of senior level positions within Serono in finance, sales, marketing and manufacturing. Mr. Joyce was previously employed at Millipore Corporation, a high technology bioscience company. Mr. Joyce received a B.S. in finance from Northeastern University and a M.B.A. from Suffolk University, Boston, Massachusetts. Mr. Joyce's extensive knowledge of our business and history, experience in multiple publicly traded and privately-held companies, and expertise in developing and financing numerous biopharmaceutical companies contributed to our conclusion that he should serve as a director of our company.

Ben R. Bronstein, M.D.	Dr. Bronstein has served as a member of our Board since 2010. Since 1999, Dr. Bronstein has been an independent consultant providing advisory services to companies in the life sciences industry. From 2017 to 2018, Dr. Bronstein served as Executive Vice President, Clinical Development at Aclaris Therapeutics, Inc. Prior to his time at Aclaris, Dr. Bronstein served as the interim Chief Medical Officer at Sentien Biotechnologies, Inc. from 2016 to 2017. Dr. Bronstein is a board-certified pathologist and dermatopathologist, with over 20 publications. Dr. Bronstein began his professional career on the staff of the Massachusetts General Hospital and on the faculty of Harvard Medical School. He has spent the past 33 years in entrepreneurial and management roles in life science companies and venture capital firms. Dr. Bronstein has founded or held senior management positions at several venture-backed life science companies including: Aldeyra; BioSurface Technology, Inc., a regenerative medicine company; Peptimmune, Inc., an immunotherapeutics company (a spinout from Harvard and MIT); and Vidus Ocular, Inc., a Yale University spinout developing an implantable device for the treatment of glaucoma. Dr. Bronstein has served as Chief Medical Officer of Stealth BioTherapeutics, Inc., as a Visiting Scholar at the Wyss Institute of Biologically Inspired Engineering at Harvard Medical School, and as a founder and Senior Vice President of Access BridgeGap Ventures, the life science investment unit of Access Industries, Inc. Dr. Bronstein serves on the board of directors of Cleveland Diagnostics, Inc. where he is non-executive chair. Dr. Bronstein received his M.D. and M.B.A. from Boston University. Dr. Bronstein's extensive knowledge of our business and history, experience as a board member and executive of biotechnology companies, and expertise in developing and financing numerous biopharmaceutical companies contributed to our conclusion that he should serve as a director of our company.

Nancy B. Miller-Rich	Ms. Miller-Rich has been a member of our Board since January 2020. She is Chief Executive of Miller-Rich Associates, a pharmaceutical industry consultancy she founded in 2017. Previously, she served as Senior Vice-President, Global Human Health Business Development & Licensing, Strategy and Commercial Support at Merck Pharmaceuticals. At Merck, Ms. Miller-Rich had direct P&L involvement in the $38 billion pharmaceutical division and closed approximately 300 deals producing $10 billion of value creation. Prior to Merck, she worked for Schering-Plough Corporation, where she was Senior Vice President, Global Human Health Business Development & Licensing, Strategy and Commercial Support from 2013 to 2017 and Group Vice President, Consumer Care Global New Ventures and Strategic Commercial Development from 2007 to 2013. Prior to joining Schering-Plough in 1990, Ms. Miller-Rich served in a variety of commercial and marketing roles at Sandoz Pharmaceuticals and Sterling Drug, Inc. She is a director of Intercept Pharmaceuticals, Inc. and 4D Molecular Therapeutics, Inc., and previously served as a director of Kadmon Holdings. Ms. Miller-Rich also serves as a board member of a number of private and not-for-profit entities. Ms. Miller-Rich received her B.S. in Business Administration, Marketing from Ithaca College in Ithaca, New York. Ms. Miller-Rich's public company experience and strong background in areas such as licensing, joint ventures, and global commercial development contributed to our conclusion that she should serve as a director of our company.

Richard H. Douglas, Ph.D.	Dr. Douglas has served on our Board since September 2016. Dr. Douglas was formerly Senior Vice President, Corporate Development of Genzyme Corporation. From 1989 to 2011, he led Genzyme Corporation's Corporate Development team, and was involved in numerous acquisitions, licenses, financings, joint ventures, and strategic alliances. From 1982 until its merger with Genzyme Corporation in 1989 (now Sanofi Genzyme), Dr. Douglas served in science and corporate development capacities at Integrated Genetics. Currently, Dr. Douglas is on the board of directors of Novavax, Inc., a publicly-traded clinical-stage vaccine company; MaxCyte, Inc., a publicly traded instrument and immunotherapeutic company; and the University of Michigan Technology Transfer National Advisory Board. Dr. Douglas received a B.S. in chemistry from the University of Michigan and a Ph.D. in biochemistry from the University of California, Berkeley, and he was a postdoctoral fellow in Leroy Hood's laboratory at the California Institute of Technology. Dr. Douglas's extensive knowledge of our business; experience as a board member of publicly-traded biotechnology companies; substantial scientific background; and expertise in developing, financing and providing strong executive leadership within the pharmaceutical industry contributed to our conclusion that he should serve as a director of our company.

Gary M. Phillips, M.D.	Dr. Phillips has served as a member of our Board since May 2009. Dr. Phillips has served as Chief Business Officer of Anaveon AG since May 2022. Prior to that, he was President & CEO of OrphoMed, Inc. from 2018 to 2022 and Executive Vice President & Chief Strategy Officer at Mallinckrodt Pharmaceuticals plc from 2013 to 2018. Previously, Dr. Phillips held the dual roles of president, U.S. surgical and pharmaceuticals and global head of pharmaceuticals at Bausch & Lomb. Additionally, he has served as the head of global health at the World Economic Forum in Geneva and was president of Reckitt Benckiser Pharmaceuticals, Inc. (now Indivior). He has also held executive roles at Merck KGaA, Novartis, and Wyeth (now Pfizer). He was a healthcare strategy managing consultant at Towers Perrin (now Willis Towers Watson) and a medical officer with the United States Navy, from which he was honorably discharged as a lieutenant commander. Dr. Phillips was educated at the University of Pennsylvania, where he received an M.D. (Alpha Omega Alpha) from the School of Medicine, an M.B.A. from the Wharton School, and B.A. (summa cum laude, Phi Beta Kappa) in biochemistry from the College of Arts and Sciences. He completed postgraduate medical education at Naval Medical Center San Diego and maintains an active medical license. Dr. Phillips' extensive knowledge of our business and history, and his experience in pharmaceutical strategy at multiple multinational companies, contributed to our conclusion that he should serve as a director of our company.

Neal S. Walker, D.O. — Dr. Walker has served on our Board since June 2013. Dr. Walker is the Chair of the board of directors at Aclaris Therapeutics, Inc., a publicly-traded drug development company, having previously served as President and Chief Executive Officer until December 2022. He is a board certified dermatologist and serial entrepreneur with over 25 years of experience in the biopharmaceutical industry. Prior to founding Aclaris Therapeutics, Inc. in 2012, he was co-founder, President and CEO of Vicept Therapeutics, Inc. (acquired by Allergan, Inc.) from 2009 to 2012. Dr. Walker has co-founded and led a number of life science companies: Octagon Research Solutions, Inc., a software and services provider to biopharmaceutical companies (acquired by Accenture plc); Trigenesis Therapeutics, Inc., a specialty dermatology company where he served as Chief Medical Officer (acquired by Dr. Reddy's Laboratories Ltd); and Cutix Inc., a commercial dermatology company that markets PreSun®, a sunscreen brand acquired from Bristol-Myers Squibb Co. He began his pharmaceutical industry career at Johnson & Johnson, Inc. In addition to Aclaris, Dr. Walker currently is also on the board of directors of Zoomi, Inc, and Myota, Inc. Dr. Walker previously served on the board of directors for Octagon, a contract research organization. He is also on the Advisory Board of Flexible Medical Systems LLC, a privately held medical device company. Dr. Walker received his M.B.A. from The Wharton School of the University of Pennsylvania, his D.O. from Philadelphia College of Osteopathic Medicine, and a B.A. in Biology from Lehigh University. Dr. Walker's experience as a founder of a number of healthcare companies, strong background in clinical and product development, and substantial knowledge of the pharmaceutical industry contributed to our conclusion that he should serve as a director of our company.

Executive Officers

The following table provides information concerning our executive officers as of April 21, 2023:

Name	Age	Position(s)
Todd C. Brady, M.D., Ph.D.	51	Chief Executive Officer and Director
Bruce Greenberg, M.B.A.	55	Vice President of Finance, Interim Chief Financial Officer
Stephen G. Machatha, Ph.D.	46	Chief Development Officer

Todd C. Brady, M.D., Ph.D. See biographical information set forth above under "Directors."

Bruce Greenberg, M.B.A. joined Aldeyra in December 2019 as Vice President, Controller, and has served as our Interim Chief Financial Officer since May 2022. Mr. Greenberg has more than 25 years of accounting and financial operations experience. Prior to Aldeyra, from May 2017 to December 2019, he served as the Corporate Controller for Karyopharm Therapeutics Inc., which develops and commercializes drugs for use in oncological treatments. Previously, he held positions of increasing responsibility at KVH Industries, Inc., Berklee College of Music, Harvard Bioscience, Inc., and MKS Instruments, Inc. He began his career as a member of the audit practice of Ernst & Young LLP, where he focused on life science and technology clients. Mr. Greenberg, a certified public accountant, received his B.A. in Economics from Clark University and his M.B.A. in Accounting from Northeastern University's D'Amore-McKim School of Business.

Stephen G. Machatha, Ph.D. joined Aldeyra in January 2016 as Vice President of Chemistry Manufacturing and Controls, was later appointed as Senior Vice President of Technical Operations in January 2019, and subsequently, Chief Development Officer in January 2021. Prior to joining Aldeyra, Dr. Machatha held scientific

and product development roles of increasing responsibilities at Synageva Biopharmaceuticals (acquired by Alexion Pharmaceuticals), Cubist Pharmaceuticals (acquired by Merck & Co.), and CyDex Pharmaceuticals (acquired by Ligand Pharmaceuticals). Dr. Machatha attended the University of Arizona, where he received a Ph.D. in Pharmaceutical Sciences, an M.A. in Chemistry, and a B.Sc. in Chemistry.

CORPORATE GOVERNANCE

Code of Ethics and Business Conduct

Our Board 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 Corporate Governance portion of our website at http://ir.aldeyra.com/corporate-governance. Any waiver of the code of ethics and business conduct for an executive officer or director may be granted only by our Board 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.

Board Committees

Our Board has established an audit committee, a compensation committee, a nominating/corporate governance committee, and a stock option committee. The Board and its committees set schedules to meet throughout the year and also can hold special meetings and act by written consent from time to time as appropriate. The Board has delegated various responsibilities and authority to its committees. The committees regularly report on their activities and actions to the full Board. Each committee has a written charter that has been approved by the full Board. The composition of these committees meets the criteria for independence under, and the functioning of these committees comply with, the applicable requirements of the Sarbanes-Oxley Act of 2002, the current rules of The Nasdaq Capital Market, and SEC rules and regulations. We intend to comply with future requirements as they become applicable to us.

Audit Committee

The current members of our audit committee are Martin J. Joyce, M.B.A.; Ben R. Bronstein, M.D.; and Gary M. Phillips, M.D.; each of whom is a non-employee member of our Board. Mr. Joyce serves as the chair of the audit committee.

The audit committee's main function is to oversee our accounting and financial reporting processes, internal systems of control, independent registered public accounting firm relationships, and the audits of our financial statements. The full text of the audit committee's charter is posted on the corporate governance section of our website at https://ir.aldeyra.com/corporate-governance. Pursuant to the audit committee charter, the functions of the committee include, among other things:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting and our disclosure controls and procedures;
- meeting independently with our registered public accounting firm and management;
- preparing the audit committee report required by SEC rules;
- reviewing and approving or ratifying any related person transactions; and
- overseeing our risk assessment and risk management policies.

All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and The Nasdaq Capital Market. Our Board has determined that Mr. Joyce is an "audit committee financial expert" as defined by applicable SEC rules and has the financial sophistication required by applicable Nasdaq listing standards.

Board Oversight of Risk

Our Board has responsibility for the oversight of our risk management processes and, either as a whole or through its committees, regularly discusses with management our major risk exposures, their potential impact on our business, and the steps we take to manage them. The risk oversight process includes receiving regular reports from board committees and members of senior management to enable our Board to understand our risk identification, risk management, and risk mitigation strategies with respect to areas of potential material risk, including operations, finance, legal, regulatory, strategic, and reputational risk. The audit committee reviews information regarding liquidity and operations, and oversees our management of financial risks. Periodically, the audit committee reviews our policies with respect to risk assessment, risk management, loss prevention, and regulatory compliance. Oversight by the audit committee includes direct communication with our external auditors, and discussions with management regarding significant risk exposures and the actions management has taken to limit, monitor, or control such exposures. The compensation committee is responsible for assessing whether any of our compensation policies or programs has the potential to encourage excessive risk-taking. The nominating/corporate governance committee manages risks associated with the independence of the Board, corporate disclosure practices, and potential conflicts of interest. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire board is regularly informed through committee reports about such risks. Matters of significant strategic risk are considered by our Board as a whole.

ITEM 11. Executive Compensation

Compensation Committee

The current members of our compensation committee are Neal S. Walker, D.O.; Gary M. Phillips, M.D.; and Nancy B. Miller-Rich. Gary M. Phillips, M.D. serves as the chair of the compensation committee. Our compensation committee reviews and recommends policies relating to compensation and benefits of our officers and employees.

The full text of the compensation committee's charter is posted on the corporate governance section of our website at https://ir.aldeyra.com/corporate-governance. Pursuant to the compensation committee charter, the functions of this committee include:

- evaluating the salary and performance-based compensation of our executive officers;
- identifying the corporate and individual objectives governing compensation of our executive officers;
- making recommendations to our Board with respect to director compensation;
- reviewing and approving the terms of material agreements with our executive officers;
- overseeing and administering our equity incentive plans and employee benefit plans;
- reviewing and approving policies and procedures relating to the perquisites and expense accounts of our executive officers;
- if and as applicable, furnishing the annual compensation committee report required by SEC rules; and
- conducting a review of executive officer succession planning, as necessary; reporting its findings and recommendations to our Board; and working with the Board in evaluating potential successors to executive officer positions.

Our Board has determined that each of Neal S. Walker, D.O.; Gary M. Phillips, M.D.; and Nancy B. Miller-Rich is independent under the applicable rules and regulations of Nasdaq and is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act.

Our Chief Executive Officer and Interim Chief Financial Officer assist our compensation committee in carrying out its functions, although they do not participate in deliberations or decisions with respect to their own compensation. Since January 2015, our compensation committee has engaged the services of Pearl Meyer & Partners, LLC (Pearl Meyer), a nationally recognized compensation consulting firm, to advise the compensation committee regarding the amount and types of compensation that we provide to our executives and directors, and compare our compensation practices to the compensation practices of other companies. Pearl Meyer reports directly to the compensation committee. Pearl Meyer does not provide any services to us other than the services provided to the compensation committee. The compensation committee believes that, under applicable SEC rules or Nasdaq listing standards, Pearl Meyer does not have any conflicts of interest in advising the compensation committee.

Summary Compensation Table

The following table provides information concerning the compensation paid to our Chief Executive Officer and our next two most highly compensated executive officers for our year ended December 31, 2022. We refer to these individuals as our named executive officers.

Name and Principal Position	Year	Salary ($)	Stock Awards ($)(1)	Option Awards ($)(1)	Non-Equity Incentive Plan		All Other Compensation		Total ($)
Todd C. Brady, M.D., Ph.D.	2022	559,357	1,130,000	818,523	338,410	(2)	12,200	(3)	2,858,490
President and Chief Executive Officer	2021	547,097	545,908	2,050,361	300,903		11,400		3,455,670
Bruce Greenberg	2022	285,340	595,131	490,385	99,000	(2)	12,200	(3)	1,482,055
Vice President of Finance, Interim Chief Financial Officer(4)									
Stephen G. Machatha, Ph.D.	2022	359,287	1,167,121	818,523	208,086	(5)	12,200	(3)	2,565,216
Chief Development Officer	2021	333,572	—	953,016	133,429		11,400		1,431,416

(1) Reflects the aggregate grant date fair value of stock awards and option awards granted during the applicable year calculated in accordance with FASB ASC Topic 718. For a discussion of valuation assumptions, see Note 12 to our audited financial statements included in the Original Filing. In accordance with SEC rules, the grant date fair value of an award subject to performance conditions is based on the probable outcome of the conditions.

(2) Represents amounts paid under our 2022 performance bonus plan in March 2023.
(3) Consists of annual matching contributions to the executives 401(k) plan account.
(4) Mr. Greenberg was appointed as our Interim Chief Financial Officer in May 2022.
(5) Represents amounts paid under our 2022 performance bonus plan in March 2023 and a one-time $50,000 bonus paid to Dr. Machatha in December 2022.

Narrative Explanation of Certain Aspects of the Summary Compensation Table

Employment Letter Agreements and Offer Letters

We currently maintain letter agreements and offer letters with each of Dr. Brady, Mr. Greenberg, and Dr. Machatha. The letter agreements and offer letters provide for the initial base salary for our executive officers and eligibility to receive an annual cash target bonus as determined by our Board or compensation committee, subject to his attainment of one or more pre-established performance goals established by our Board or compensation committee.

The table below sets for the 2023 base salary and target bonus as a percentage of base salary for Dr. Brady, Mr. Greenberg and Dr. Machatha.

Name	Base Salary ($)	Target Cash Incentive Award (% of Base Salary)
Todd C. Brady, M.D., Ph.D.	581,170	55
Bruce Greenberg	330,000	35
Stephen G. Machatha, Ph.D.	377,250	40

The letter agreements and offer letters provide for at-will employment and, other than as set forth below under “Severance and Change in Control Benefits”, may be terminated at any time.

Equity Compensation

We offer stock options, restricted stock units and performance based cash units to our named executive officers as the long-term incentive component of our compensation program. We typically grant equity awards to new hires upon their commencing employment with us and provide additional grants annually.

In March 2022, Drs. Brady and Machatha and Mr. Greenberg were each granted an option to purchase shares of our common stock. The table below provides details regarding the foregoing grants.

Name	Number of Shares Underlying Option Grants		Exercise Price for Option Grants ($)(2)
Todd C. Brady, M.D., Ph.D.	250,000	(1)	4.52
Bruce Greenberg	73,156	(1)	4.52
Bruce Greenberg	100,000	(3)	3.50
Stephen G. Machatha, Ph.D.	250,000	(1)	4.52

(1) Option vests in equal monthly installments over four years of service following January 1, 2022 provided the optionee remains in continuous service to us through each such vesting date.
(2) The exercise price is equal to the closing price per share of our common stock on The Nasdaq Capital Market on the date of grant.
(3) Option vests in equal monthly installments over four years of service following January 1, 2021 provided the optionee remains in continuous service to us through each such vesting date.

In addition, in March 2022, the compensation committee of our Board also awarded restricted stock units representing 250,000 shares of our common stock to Dr. Brady, and 64,395 shares of our common stock to Dr. Machatha. These awards vest in equal annual installments over four years of service following January 1, 2022. In March 2022, Dr. Brady was also granted 207,758 performance based cash units. The performance based cash units vest in four annual installments from the date of grant and entitle Dr. Brady to receive a cash payment, on the earlier of (i) four years from the date of grant or (ii) a change of control, equal in value to the amount by which the then value of our common stock exceeds the base value of $4.52.

In July 2022, the compensation committee of our Board granted Dr. Brady 604,308 cash based bonus units and Dr. Machatha 69,473 cash based bonus units. Subject to and conditioned upon the acceptance by the U.S. Food and Drug Administration of our submission of a New Drug Application for reproxalap, the cash based bonus units vest in four annual installments from the date of grant and entitle Drs. Brady and Machatha to receive a cash payment for each vested bonus unit, on the earlier of (i) four years from the date of grant or (ii) a change of control, equal in value to the closing price per share of the our common stock on The Nasdaq Capital Market on the payment date. In addition, in July 2022, the compensation committee of our Board also awarded restricted stock units representing 185,605 shares of our common stock to Dr. Machatha and 126,087 shares of our common stock to Mr. Greenberg. These awards vest in equal annual installments over four years of service following July 15, 2022.

In February 2023, the compensation committee of our Board approved the grant of options to purchase 250,000 shares of our common stock to Dr. Brady; 110,028 shares of our common stock to Mr. Greenberg; and 220,258 shares of our common stock to Dr. Machatha. The exercise price for each of the options was $6.76 per share, which was the closing price of our common stock on The Nasdaq Capital Market on February 28, 2023. The options vest in equal monthly installments over four years of service following January 1, 2023 provided the named executive officer provides continuous service to us through such vesting dates. In addition, in February 2023, the compensation committee of our Board also awarded restricted stock units representing 238,750 shares of our common stock to Dr. Brady. The award vests in equal annual installments over four years of service following January 1, 2023.

As discussed below under “Severance and Change in Control Benefits,” stock options, restricted stock units and performance based cash units granted or awarded to our named executive officers are generally subject to accelerated vesting in the event such officer is subject to an involuntary termination or if we experience a change in control.

Severance and Change in Control Benefits

Pursuant to their letter agreements and offer letters, in addition to any equity acceleration provided for in our Change in Control Plan, as amended and restated, (the “CIC Plan”) discussed below, if we terminate the employment of any of our current named executive officers without cause or in the case of Dr. Brady, if Dr. Brady resigns for good reason, then such named executive will be eligible to receive:

- continued payment of base salary for 9 months (12 months in the case of Dr. Brady);
- a lump-sum cash payment equal to the greater of such executive’s target bonus for the year in which such termination occurs or the actual bonus paid to the executive with respect to our most recently completed fiscal year; and
- payment by us of the monthly premiums under COBRA for such executive and their eligible dependents for up to 9 months (12 months in the case of Dr. Brady) following the termination of such executive’s employment.

Such payments are contingent on the officer’s executing and not revoking a release of claims against us. “Cause” means an officer’s:

- unauthorized use or disclosure of our confidential information or trade secrets;

- material breach of any agreement with us;
- material failure to comply with our written policies or rules;
- conviction of, or plea of "guilty" or "no contest" to, a felony;
- gross negligence or willful misconduct;
- continuing failure to perform assigned duties after receiving written notification of such failure from our Board; or
- failure to cooperate in good faith with a governmental or internal investigation of us or our directors, officers, or employees if such cooperation has been requested.

"Good Reason" means a resignation within 12 months after one of the following conditions has come into existence without the officer's consent, but only if such officer has provided us with written notice of such condition within 90 days after it has come into existence and we have failed to cure such condition within 30 days after we receive such notice:

- a reduction in such executive officer's base salary or target bonus by more than 10%;
- a material reduction of such executive officer's authority, duties, or responsibilities, including reporting relationships; or
- a relocation of such executive officer's principal workplace by more than 50 miles.

In March 2017, the compensation committee of our Board approved and established the CIC Plan and in August 2021, the compensation committee of our Board amended and restated the CIC Plan. The CIC Plan provides for the accelerated vesting for outstanding (i) unvested equity awards and/or (ii) unvested performance based cash unit awards issued under our Management Cash Incentive Plan (the Management Plan) held by our eligible employees who are subject to a qualifying employment termination in connection with a change in control, including our executive officers. The CIC Plan provides for acceleration of 100% of the unvested equity and/or performance based cash unit awards issued under the Management Plan held by our executive officers in the event the officer's employment is terminated without cause, or the officer resigns for good reason, in each case within 3 months before or 12 months following a change in control. In connection with the adoption of the CIC Plan, Dr. Brady waived the "single trigger" acceleration of his equity awards on consummation of a change in control provided for in his offer letter. In addition, the CIC Plan shall replace any and all change of control provisions provided for in the equity or equity based awards granted to Dr. Brady prior to the establishment of the CIC Plan.

For the purpose of the CIC Plan, the following terms have the definitions set forth below:

A termination for "cause" means termination by us of the executive officer's employment by reason of the occurrence of any one or more of the following: (i) an act or acts of personal dishonesty taken by the executive officer and intended to result in substantial personal enrichment of the executive officer at our expense; (ii) repeated violations by the executive officer of the executive officer's duties and obligations (other than as a result of incapacity due to physical or mental illness) that are demonstrably willful and deliberate on the executive officer's part, that are committed in bad faith or without reasonable belief that such violations are in our best interests, and that are not remedied in a reasonable period of time after receipt of written notice from us; (iii) indictment or plea of nolo contendere of the executive officer of a felony involving moral turpitude; or (iv) the material breach of the executive's proprietary information and inventions agreement.

"Change in Control" means the occurrence of any of the following: (i) any "person" (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the "beneficial owner" (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of our securities representing more than fifty percent (50%) of the total voting power represented by our then-outstanding voting securities; (ii) the consummation of the sale or disposition by us of all or substantially all of our assets; (iii) the consummation of a merger or consolidation of our company with or into any other entity, other than a merger or consolidation which would result in our voting securities outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its parent) more than fifty percent (50%) of the

total voting power of the voting securities of our company or such surviving entity or its parent outstanding immediately after such merger or consolidation; or the Incumbent Board ceases for any reason to constitute a majority of the members of our Board over a period of 12 months; provided, however, that if the appointment or election (or nomination for election) of any new member of our Board was approved or recommended by a majority vote of the members of the Incumbent Board then still in office, such new member shall, for purposes of the CIC Plan, be considered as a member of the Incumbent Board. A transaction shall not constitute a Change in Control under the definition set forth in the preceding sentence if its sole purpose is to change the state of our incorporation or to create a holding company that will be owned in substantially the same proportions by the persons who held our securities immediately before such transaction.

"Good reason" means (i) a material diminution in the executive officer's base salary or target bonus by more than 10%, except in connection with company-wide cost reduction; (ii) a material diminution in the executive officer's authority, duties, or responsibilities with respect to our company or any successor or acquiring entity, including, without limitation, any requirement that an officer who is our chief executive officer report to anyone other than to the board of directors of our ultimate parent entity (the "Ultimate Parent") or that an executive officer (other than our chief executive officer) report to anyone other than the chief executive officer of the Ultimate Parent; (iii) a breach of a material provision of the executive officer's employment or other written agreement governing employment with us (it being understand that a change in title without the executive officer's consent shall be a material breach); or (iv) a relocation of the executive officer's principal workplace by more than 50 miles from where the executive officer performed services prior to the relocation, without the executive officer's prior consent. However, good reason shall not exist unless (i) the executive officer has given written notice to us within 90 days of the initial existence of the good reason event or condition(s) giving specific details regarding the event or condition; (ii) we have failed to cure such event or condition within 30-days of receiving such notice; and (iii) the executive officer resigns within 30 days of the expiration of the 30-day cure period provided for in clause (ii) provided that we have not cured the event or condition.

We do not offer any tax gross-up payments to our executive team for any change-of-control payments, although we may decide to do so in the future.

Employee Benefits and Perquisites

Our named executive officers are eligible to participate in our health and welfare plans to the same extent as all other full-time employees. We do not provide our named executive officers with perquisites or other personal benefits.

Stockholder Engagement

At our 2022 annual meeting of stockholders, our annual say-on-pay proposal for our 2022 compensation program received support from 88.0% of the votes cast by our stockholders on the matter. To confirm the majority affirmative outcome of the advisory vote, we continued with our proactive stockholder engagement program to seek stockholder input on our executive compensation program. In 2022 and 2023, our management and the Chair of our compensation committee communicated with several of our largest stockholders, and solicited their feedback on our executive compensation policies.

As part of our stockholder engagement effort, we provided further detail on our compensation decision process, beginning with selecting a group of peer companies at a similar size and stage of development, benchmarking against the peer group to determine a competitive range, and targeting our compensation within that range in order to attract, retain, and motivate the personnel to achieve our goals.

From this stockholder engagement effort, along with feedback we received during investor meetings throughout the year and input from our professional advisers concerning executive compensation trends, our major stockholders have not expressed significant concerns about the general design of our equity incentive program, which consists of grants of stock options and restricted stock units as the primary incentive vehicles. We encourage stockholders to take into account the feedback we received during meetings meeting with stockholders as part of our annual stockholder outreach program.

Restrictions on Trading

Our Company Policy Regarding Insider Trading prohibits our employees (including officers) and directors, or any of their designees, from purchasing financial instruments (including prepaid variable forward contracts, equity swaps, collars, and exchange funds), or otherwise engaging in transactions, that hedge or offset, or are designed to hedge or offset, any decrease in the market value of our equity securities (i) granted to the employee or director as part of the compensation of the employee or director; or (ii) held, directly or indirectly, by the employee or director. In addition, our employees (including officers) and directors may not pledge our equity securities held by them without the prior clearance of our securities compliance officer.

Outstanding Equity Awards at Fiscal 2022 Year-End

The following tables show certain information regarding outstanding equity awards, including, but not limited to, restricted stock unit awards, held by our named executive officers as of December 31, 2022. For information regarding the vesting acceleration provisions applicable to the options held by our named executive officers, please see "Severance and Change in Control Benefits" above.

	Option Awards						Stock Awards			
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Vested	Number of Securities Underlying Unexercised Options (3) Unvested	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price ($)	Option Expiration Date	Number of shares or unit of stock that have not vested (#)	Market value of shares or units of stock that have not vested ($)(1)	Equity Incentive Plan Awards: number of unearned shares units or other rights that have not vested (#)	Equity Incentive Plan Awards: market or payout value of unearned shares, units or other rights that have not yet vested ($)
Todd C Brady, M.D., Ph.D.	9/8/2013	192,084	—	—	0.552	9/7/2023				
	9/8/2013	48,021	—	—	0.552	9/7/2023				
	9/8/2013	32,953	—	—	0.552	9/7/2023				
	10/30/2013	96,042	—	—	4.56	10/29/2023				
	5/7/2014	76,068	—	—	8.00	5/6/2024				
	6/3/2015	90,000	—	—	7.85	6/2/2025				
	3/16/2016	250,000	—	—	4.59	3/15/2026				
	3/3/2017	250,000	—	—	5.10	3/2/2027				
	3/6/2018	217,293	—	—	8.60	3/5/2028				
	3/5/2019	244,791 (2)	5,209		8.05	3/4/2029				
	3/5/2019						62,500 (3)	435,000		
	3/2/2020	182,291 (4)	67,709		3.78	3/1/2030				
	3/2/2020						125,000 (5)	870,000		
	4/12/2021	119,791 (6)	130,209		11.71	4/11/2031				
	4/12/2021						34,965 (7)	243,356		
	3/30/2022	57,291 (8)	192,709		4.52	3/29/2032				
	3/30/2022						250,000 (9)	1,740,000		
Bruce Greenberg	12/12/2019	33,738 (10)	11,262		5.32	12/11/2029				
	3/5/2020	14,583 (4)	5,417		3.57	3/4/2030				
	3/22/2021	28,020 (6)	30,457		12.24	3/21/2031				
	4/18/2021	14,010 (6)	15,229		11.28	4/17/2031				
	3/4/2022	22,916 (8)	77,084		3.50	3/3/2032				
	3/30/2022	16,764 (8)	56,392		4.52	3/29/2032				
	7/15/2022						126,087 (11)	877,566		
Stephen G. Machatha, Ph.D.	4/5/2016	35,000	—		4.60	4/4/2026				
	3/10/2017	26,200	—		5.25	3/9/2027				
	3/1/2018	45,573	—		8.35	2/28/2028				
	3/5/2019	61,687 (2)	1,313		8.05	3/4/2029				
	3/2/2020	98,845 (4)	36,715		3.78	3/1/2030				
	4/12/2021	55,679 (6)	60,522		11.71	4/11/2031				
	3/30/2022	57,291 (8)	192,709		4.52	3/29/2032				
	3/30/2022						64,395 (9)	448,189		
	7/15/2022						185,605 (11)	1,291,811		

(1) Computed in accordance with SEC rules as the number of unvested shares multiplied by the closing market price of our Common Stock on December 31, 2022, which was $6.96. The actual value (if any) to be realized by the officer depends on whether the shares vest and the future performance of our Common Stock.

(2) Option vests in equal monthly installments over four years following January 1, 2019.
(3) Restricted stock unit award vests in equal annual installments over four years of service following January 1, 2019 provided the grantee provides continuous service to us through each such vesting date.
(4) Option vests in equal monthly installments over four years following January 1, 2020.
(5) Restricted stock unit award vests in equal annual installments over four years of service following January 1, 2020 provided the grantee provides continuous service to us through each such vesting date.
(6) Option vests in equal monthly installments over four years following January 1, 2021.
(7) Restricted stock unit award vests in equal annual installments over four years of service following January 1, 2021 provided the grantee provides continuous service to us through each such vesting date.
(8) Option vests with respect to 25% of the shares after 12 months of continuous service with us following January 1, 2022, with the balance becoming exercisable in equal monthly installments over the next 36 months of continuous service provided thereafter.
(9) Restricted stock unit award vests in equal annual installments over four years of service following January 1, 2022 provided the grantee provides continuous service to us through each such vesting date.
(10) Option vests with respect to 25% of the shares after 12 months of continuous service with us following December 12, 2019, with the balance becoming exercisable in equal monthly installments over the next 36 months of continuous service provided thereafter.
(11) Restricted stock unit award vests in equal annual installments over four years of service following July 15, 2022 provided the grantee provides continuous service to us through each such vesting date.

In addition to the amounts set forth in the table above, on March 5, 2019, Dr. Brady was granted 45,329 performance based cash units (the "March 2019 Performance Units"). The March 2019 Performance Units vested in four annual installments from the date of grant and entitle Dr. Brady to receive a cash payment, on the earlier of (i) four years from the date of grant or (ii) a change of control, equal in value to the amount by which the then value of our common stock exceeds the base value of $8.05. Upon the completion of vesting of the March 2019 Performance Units, the value of our common stock had not exceeded the March 2019 Performance Units base value of $8.05. Accordingly, Dr. Brady did not receive a cash payment in connection with the completion of vesting of the March 2019 Performance Units. On March 2, 2020, Dr. Brady was granted 450,865 performance based cash units. The performance based cash units vest in four annual installments from the date of grant and entitle Dr. Brady to receive a cash payment, on the earlier of (i) four years from the date of grant or (ii) a change of control, equal in value to the amount by which the then value of our common stock exceeds the base value of $3.78. On March 15, 2022, Dr. Brady was granted 207,758 performance based cash units. The performance based cash units vest in four annual installments from the date of grant and entitle Dr. Brady to receive a cash payment, on the earlier of (i) four years from the date of grant or (ii) a change of control, equal in value to the amount by which the then value of our common stock exceeds the base value of $4.52. On July 15, 2022, Dr. Brady was granted 604,308 cash based bonus units and Dr. Machatha was granted 69,473 cash based bonus units. Subject to and conditioned upon the acceptance by the U.S. Food and Drug Administration of our submission of a New Drug Application for reproxalap, the cash based bonus units vest in four annual installments from the date of grant and entitle Drs. Brady and Machatha to receive a cash payment for each vested bonus unit, on the earlier of (i) four (4) years from the date of grant or (ii) a change of control, equal in value to the closing price per share of the our common stock on The Nasdaq Capital Market on the payment date.

Director Compensation

The following table sets forth information about the compensation of the non-employee members of our Board who served as a director during our year ended December 31, 2022. Other than as set forth in the table and described more fully below, during our year ended December 31, 2022, we did not pay any fees to, make any equity awards or non-equity awards to, or pay any other compensation to the non-employee members of our Board. Dr. Brady, our Chief Executive Officer, receives no compensation for his service as a director, and is not included in the table below. Dr. Douglas currently serves as chair of our Board.

	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)(2)	Total ($)
Ben R. Bronstein, M.D.	$ 37,250	$ 155,406(3)	$192,656
Richard H. Douglas, Ph.D.	$ 49,250	$ 176,681(4)	$225,931
Martin J. Joyce, M.B.A.	$ 39,250	$ 158,952(5)	$198,202
Nancy B. Miller-Rich	$ 32,500	$ 142,997(6)	$175,497
Gary M. Phillips, M.D.	$ 38,750	$ 157,770(7)	$196,520
Neal S. Walker, D.O.	$ 32,500	$ 142,997(8)	$175,497

(1) The amounts in this column represent the aggregate grant date fair value of option awards granted to the director during our fiscal year ended December 31, 2022, computed in accordance with FASB ASC Topic 718. See Note 12 to our financial statements included in the 2022 Annual Report for a discussion of our assumptions in determining the ASC 718 values of our option awards.

(2) As of December 31, 2022, our non-employee directors held outstanding stock options as follows: Dr. Bronstein, 201,603 options; Dr. Walker, 187,967 options; Mr. Joyce 199,773 options; Dr. Phillips, 196,085 options; Dr. Douglas, 211,396 options; and Ms. Miller-Rich, 121,015 options. All of these options granted were made pursuant to our non-employee director compensation program.

(3) On June 7, 2022, Dr. Bronstein was granted options to purchase an aggregate of 61,002 shares of our common stock at an exercise price per share of $3.60.

(4) On June 7, 2022, Dr. Douglas was granted options to purchase an aggregate of 69,353 shares of our common stock at an exercise price per share of $3.60.

(5) On June 7, 2022, Mr. Joyce was granted options to purchase an aggregate of 62,394 shares of our common stock at an exercise price per share of $3.60.

(6) On June 7, 2022, Ms. Miller-Rich was granted options to purchase an aggregate of 56,131 shares of our common stock at an exercise price per share of $3.60.

(7) On June 7, 2022, Dr. Phillips was granted options to purchase an aggregate of 61,930 shares of our common stock at an exercise price per share of $3.60.

(8) On June 7, 2022, Dr. Walker was granted options to purchase an aggregate of 56,131 shares of our common stock at an exercise price per share of $3.60.

Non-Employee Director Compensation

For the year ended December 31, 2022, pursuant to our non-employee director compensation plan, each non-employee member of our Board received the following cash and equity compensation for board services, as applicable:

	Role	Annual Cash Retainer (1)	Initial Equity Grant (2)	Annual Equity Grant (5)
Board of Directors	Director	$ 30,000	Option to purchase $120,000 worth of shares of Common Stock (3)	Option to purchase $116,000 worth of shares of Common Stock
	Chair	$ 17,500	Option to purchase $30,000 worth of shares of Common Stock (4)	Option to purchase $30,000 worth of shares of Common Stock (increased to $40,000 in February, 2023)
Audit Committee	Chair	$ 7,500	Option to purchase $15,000 worth of shares of Common Stock (4)	Option to purchase $15,000 worth of shares of Common Stock
	Other Member	$ 3,750	Option to purchase $7,500 worth of shares of Common Stock (4)	Option to purchase $7,500 worth of shares of Common Stock
Compensation Committee	Chair	$ 5,000	Option to purchase $10,000 worth of shares of Common Stock (4)	Option to purchase $10,000 worth of shares of Common Stock
	Other Member	$ 2,500	Option to purchase $5,000 worth of shares of Common Stock (4)	Option to purchase $5,000 worth of shares of Common Stock
Nominating/Corporate Governance Committee	Chair	$ 3,500	Option to purchase $8,000 worth of shares of Common Stock (4)	Option to purchase $8,000 worth of shares of Common Stock
	Other Member	$ 1,750	Option to purchase $3,500 worth of shares of Common Stock (4)	Option to purchase $3,500 worth of shares of Common Stock

(1) Annual cash retainers are payable quarterly.
(2) Initial equity grants are automatically granted on the date the director is elected or appointed as a director, chair, member of a committee, or chair of a committee, as applicable.
(3) The initial equity grant upon election or appointment as a director shall vest in three equal annual installments following the grant date.
(4) Each initial equity grant shall be pro-rated for the number of whole months remaining until the anniversary of the prior year's stockholders' meeting, rounded down to the nearest whole share, and shall vest on the anniversary of the prior year's stockholders' meeting provided the director provides continuous service as a director through such date.
(5) Annual equity grants are automatically granted on the date of each annual meeting of our stockholders and shall vest on the 1-year anniversary of the grant date provided the director provides continuous service as a director, member of the applicable committee, or chair, as applicable, through such date.

In addition, the following rules apply to initial and annual equity awards:

- All of the awards will be automatically granted to each non-employee director in the form of non-statutory stock options issued under our 2013 Equity Incentive Plan;
- The number of shares subject to a stock option is determined by using the Black-Scholes option valuation method to determine the value per option on the valuation date (the exercise price shall be the closing price of our common stock on the third trading day prior to the grant date);
- All of the non-employee directors' equity awards will become fully vested upon a Change in Control (as defined below) of our company; and
- All such automatic director option grants to non-employee directors shall have a maximum term of ten years.

For purposes of our non-employee director compensation plans or programs, a non-employee director is a director who is not employed by us and who does not receive compensation from us, or have a business relationship with us that would require disclosure under certain rules of the SEC.

We also reimburse our non-employee directors for their reasonable out-of-pocket expenses incurred in attending Board and committee meetings.

Change in Control means the occurrence of any of the following: (a) any "person" (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the "beneficial owner" (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of our securities representing more than fifty percent (50%) of the total voting power represented by our then-outstanding voting securities; (b) the consummation of the sale or disposition by us of all or substantially all of our assets; (c) the consummation of a merger or consolidation of our company with or into any other entity, other than a merger or consolidation that would result in the voting securities of our company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its parent) more than fifty percent (50%) of the total voting power of the voting securities of our company or such surviving entity or its parent outstanding immediately after such merger or consolidation; or (d) individuals who are members of our Board (the Incumbent Board) cease for any reason to constitute a majority of the members of our Board over a period of 12 months; provided, however, that if the appointment or election (or nomination for election) of any new member of our Board was approved or recommended by a majority vote of the members of the Incumbent Board then still in office, such new member shall, for purposes hereof, be considered as a member of the Incumbent Board. A transaction shall not constitute a Change in Control under the definition set forth in the preceding sentence if its sole purpose is to change the state of our incorporation or to create a holding company that will be owned in substantially the same proportions by the persons who held our securities immediately before such transaction. In addition, if a Change in Control constitutes a payment event with respect to any equity or other benefit that provides for a deferral of compensation and which is subject to Section 409A of the Internal Revenue Code of 1986, as amended (the Code), then notwithstanding anything to the contrary in this letter agreement or in any document governing such award, the transaction with respect to such equity or other benefit must also constitute a "change in control event" as defined in Treasury Regulation Section 1.409A-3(i)(5) to the extent required by Section 409A of the Code.

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

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of April 21, 2023 for:

- each of our named executive officers;
- each of our directors;
- all of our current executive officers and directors as a group; and

- each stockholder known by us to be the beneficial owner of more than 5% of our outstanding shares of common stock.

The table below is based upon information supplied by officers, directors and principal stockholders and Schedule 13Gs and 13Ds filed with the SEC through April 21, 2023.

The percentage ownership is based upon 58,576,350 shares of common stock outstanding as of April 21, 2023. For purposes of the table below, we deem shares of common stock subject to options that are currently exercisable or exercisable within sixty (60) days of April 21, 2023 and common stock subject to restricted stock unit awards that will vest within sixty (60) days of April 21, 2023 to be outstanding and to be beneficially owned by the person holding the options or restricted stock unit award for the purpose of computing the percentage ownership of that person, but we do not treat them as outstanding for the purpose of computing the percentage ownership of any other person. Except as otherwise noted, the persons or entities in this table have sole voting and investing power with respect to all of the shares of common stock beneficially owned by them, subject to community property laws, where applicable. Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Aldeyra Therapeutics, Inc., 131 Hartwell Avenue, Suite 320, Lexington, Massachusetts 02421.

Name of Beneficial Owner	Number of Shares	Percentage
5% or Greater Stockholders		
Perceptive Advisors LLC	11,350,085 (1)	19.4%
Named Executive Officers and Directors		
Todd C. Brady, M.D., Ph.D.	2,883,186 (2)	4.8%
Bruce Greenberg	171,876 (3)	*
Stephen G. Machatha, Ph.D.	476,741 (4)	*
Ben R. Bronstein, M.D.	159,245 (5)	*
Richard H. Douglas, Ph.D.	267,043 (6)	*
Martin J. Joyce, M.B.A.	161,346 (7)	*
Nancy B. Miller-Rich	64,884 (8)	*
Gary M. Phillips, M.D.	143,530 (9)	*
Neal S. Walker, D.O.	138,086 (10)	*
All current executive officers and directors as a group (9 persons)	4,465,937 (11)	7.2%

* Less than 1% of the outstanding shares of common stock.

(1) Perceptive Advisors LLC and Joseph Edelman beneficially own 11,350,085 shares of common stock, all of which are held by Perceptive Life Sciences Master Fund Ltd, a private investment fund to which Perceptive Advisors LLC serves as the investment manager. Mr. Edelman is the managing member of Perceptive Advisors LLC. The address for Perceptive Advisors LLC, Perceptive Life Sciences Master Fund Ltd and Joseph Edelman is 51 Astor Place, 10th Floor, New York, NY 10003. The foregoing information in this footnote is based on a Schedule 13G/A filed by Perceptive Advisors LLC, Perceptive Life Sciences Master Fund Ltd and Joseph Edelman on February 14, 2023.

(2) Includes options to purchase 1,939,961 shares of common stock that may be exercised within 60 days of April 11, 2023.

(3) Includes options to purchase 164,063 shares of common stock that may be exercised within 60 days of April 11, 2023.

(4) Includes options to purchase 437,169 shares of common stock that may be exercised within 60 days of April 11, 2023 and 211 shares of common stock held by his spouse.

(5) Includes options to purchase 140,601 shares of common stock that may be exercised within 60 days of April 11, 2023.

(6) Includes options to purchase 142,043 shares of common stock that may be exercised within 60 days of April 11, 2023

(7) Includes options to purchase 137,379 shares of common stock that may be exercised within 60 days of April 11, 2023.

(8) Includes options to purchase 64,884 shares of common stock that may be exercised within 60 days of April 11, 2023.

(9) Includes options to purchase 134,155 shares of common stock that may be exercised within 60 days of April 11, 2023.
(10) Includes options to purchase 131,836 shares of common stock that may be exercised within 60 days of April 11, 2023.
(11) Includes options to purchase 3,292,091 shares of common stock that may be exercised within 60 days of April 11, 2023.

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

In addition to the compensation arrangements with our directors and executive officers described elsewhere in this Form 10-K/A, the following is a description of each transaction since January 1, 2022 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amount involved exceeds the lesser of $120,000 or one percent of the average of our total assets at yearend for the last two completed fiscal years; and
- any of our directors, executive officers, or holders of more than 5% of our capital stock, or any immediate family member of or person sharing the household with any of these individuals (other than tenants or employees), had or will have a direct or indirect material interest.

Employment Agreements

We have entered into offer letters with our named executive officers. For more information regarding these agreements, see the section of this Form 10-K/A entitled “Executive Compensation.”

Indemnification Agreements

We have entered into separate indemnification agreements with our directors and executive officers, in addition to indemnification provided for in our amended and restated certificate of incorporation and amended and restated bylaws. These agreements, among other things, provide for indemnification of our directors and executive officers for certain expenses, judgments, fines, and settlement amounts, among others, incurred by this person in any action or proceeding arising out of this person’s services as a director or executive officer in any capacity with respect to any employee benefit plan or as a director, partner, trustee, or agent of another entity at our request. We believe that these provisions in our amended and restated certificate of incorporation and amended and restated bylaws and indemnification agreements are necessary to attract and retain qualified persons as directors and executive officers.

Equity Grants and Awards to Executive Officers and Directors

We have granted equity to our executive officers and certain of our directors as more fully described in the sections entitled “Director Compensation” and “Executive Compensation.”

Policies and Procedures for Related Party Transactions

Pursuant to our code of conduct and audit committee charter, any related party transaction or series of transactions with an executive officer, director, or any of such persons’ immediate family members or affiliates, in which the amount, either individually or in the aggregate, involved exceeds $120,000 must be presented to our audit committee for review, consideration, and approval. All of our directors and executive officers are required to report to our audit committee any such related party transaction. In approving or rejecting the proposed transactions, our audit committee shall consider the relevant facts and circumstances available and deemed relevant to the audit committee, including, but not limited to, the risks, costs, and benefits to us; the terms of the transaction; the availability of other sources for comparable services or products; and, if applicable, the impact on a director’s independence. Our audit committee shall approve only those transactions that, in light of known circumstances, are consistent with Aldeyra’s and our stockholders’ interests, as our audit committee determines in the good faith exercise of its discretion.

Director Independence

Our common stock is listed on The Nasdaq Capital Market. The listing rules of this stock exchange generally require that a majority of the members of a listed company's board of directors be independent. In addition, the rules of Nasdaq require that, subject to specified exceptions, each member of a listed company's audit, compensation, and nominating/corporate governance committees be independent. The Nasdaq director independence definition includes a series of objective tests, such as that the director is not also one of our employees and has not engaged in various types of business dealings with us. In addition, as further required by Nasdaq rules, our Board has made a subjective determination as to each independent director that no relationships exist which, in the opinion of our Board, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities as they may relate to us and our management.

Our Board has determined that none of our non-employee directors has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of Nasdaq. The independent members of our Board hold separate regularly scheduled executive session meetings at which only independent directors are present.

Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the Board or any other board committee: accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or be an affiliated person of the listed company or any of its subsidiaries. Each of Martin J. Joyce, M.B.A., Gary M. Phillips, M.D. and Ben R. Bronstein, M.D. qualify as an independent director pursuant to Rule 10A-3.

ITEM 14. Principal Accounting Fees and Services

The following table sets forth all fees paid or accrued by us for professional audit services and other services rendered by BDO USA, LLP during the years ended December 31, 2022 and 2021:

	2022	2021
Audit Fees(1)	$391,850	$565,936
Audit-Related Fees	—	—
Tax Fees	—	—
All Other Fees	—	—
Total Fees	$391,850	$565,936

(1) Audit Fees: This category represents fees for professional services provided in connection with the audit of our financial statements; review of our quarterly financial statements; and audit services provided in connection with other regulatory or statutory filings for which we have engaged BDO USA, LLP, including the consents issued for our registration statements, and securities offerings. The decrease in audit fees in 2022 compared to 2021 was due to, among other things, a decrease in financing activity.

Pre-Approval of Audit and Non-Audit Services

Consistent with requirements of the SEC and the Public Company Accounting Oversight Board regarding auditor independence, our audit committee is responsible for the appointment, compensation, and oversight of the work of our independent registered public accounting firm. In recognition of this responsibility, our audit committee (or the chair if such approval if needed on a time urgent basis) generally pre-approves of all audit and permissible non-audit services provided by the independent registered public accounting firm. These services may include audit services, audit-related services, tax services, and other services.

PART IV

ITEM 15. Exhibits and Financial Statements Schedules

(a) The following documents were filed as part of the Original Filing:

1. *Financial Statements*. We are not filing any financial statements with this Form 10-K/A because they were included in the Original Filing.

2. *Financial Statement Schedules.* We are not filing any schedules with this Form 10-K/A, which were either appropriately omitted from the Original Filing or the information required to be presented in them was shown in the financial statements or related notes at Part II, Item 8 of the Original Filing.

3. *Exhibits.* The exhibits required to be filed by Item 15 are set forth in, and filed with or incorporated by reference in, the "Exhibit Index" of the Original Filing. The attached list of exhibits in the "Exhibit Index" sets forth the additional exhibits required to be filed with this Form 10-K/A and are incorporated herein by reference in response to this item.

(b) *Exhibits.* See Item 15(a)(3) above.

(c) *Financial Statement Schedules.* See Item 15(a)(2) above.

EXHIBIT INDEX

Exhibit Number	Exhibit Title
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 Interim Chief Financial Officer as required by Section 302 of the Sarbanes-Oxley Act of 2002
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

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

Signatures

Pursuant to the requirements of Section 13 and 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the Commonwealth of Massachusetts, on April 28, 2023.

ALDEYRA THERAPEUTICS, INC.

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

Exhibit 31.1

CERTIFICATION

I, Todd C. Brady, M.D., Ph.D., certify that:

1. I have reviewed this Amendment No. 1 to the annual report on Form 10-K of Aldeyra Therapeutics, Inc.; and

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.

Date: April 28, 2023

/s/ Todd C. Brady, M.D., Ph.D.

Todd C. Brady, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Bruce Greenberg, certify that:

1. I have reviewed this Amendment No.1 to the annual report on Form 10-K of Aldeyra Therapeutics, Inc.; and

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.

Date: April 23, 2023

/s/ Bruce Greenberg

Bruce Greenberg
Vice President of Finance, Interim Chief Financial Officer
(Principal Financial and Accounting Officer)