Aldeyra Therapeutics Announces Positive Top-Line Results from 12-Month Safety Clinical Trial of Reproxalap in Patients with Dry Eye Disease

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Primary Endpoints of Treatment-Related Serious Adverse Events in Ocular Safety Parameters Were Not Observed

Ocular Safety Events Were Similar Across Reproxalap and Vehicle Groups

In Post-Hoc Analysis, Reproxalap Potentially the First Chronically Administered Topical Ocular Therapy to Demonstrate Distance Visual Acuity Improvement in Adults

LEXINGTON, Mass.--(BUSINESS WIRE)--Feb. 28, 2023-- Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra) today announced top-line results from a 12-month, vehicle-controlled, multicenter, parallel-group safety clinical trial of reproxalap, an investigational new drug, in dry eye disease patients. The primary endpoints of treatment-related serious adverse events in ocular safety were not observed in any patient. Ocular safety events were similar across reproxalap and vehicle treatment groups. In a post-hoc analysis, reproxalap was statistically superior to vehicle in improvement from baseline in distance visual acuity, potentially representing the first demonstration of improvement in distance visual acuity with a topically administered therapy.

“The lack of treatment-related serious adverse events over 12 months confirms the safety profile of reproxalap observed in prior clinical trials, and the potentially landmark evidence of improvement in visual acuity may differentiate reproxalap, if approved for sale, from other therapeutic options for the treatment of dry eye disease,” stated Todd C. Brady, M.D., Ph.D., President and Chief Executive Officer of Aldeyra.

The 12-month safety clinical trial population was comprised of 447 dry eye disease patients; 299 patients were treated with reproxalap and 148 patients were treated with vehicle. Visual acuity and ocular safety assessments, including assessment of intraocular pressure, slit-lamp examination, corneal endothelial cell density, and dilated fundoscopy, were performed at baseline, and after 4 weeks, 6 weeks, 3 months, 6 months, and one year of treatment. The primary endpoints were the proportion of treatment-related ocular safety events related to visual acuity, intraocular pressure, slit-lamp examination, and dilated fundoscopy in reproxalap-treated patients compared to vehicle-treated patients. Change from baseline in visual acuity, as assessed by the logarithm of the minimum angle of resolution (logMAR, lower values indicate better visual acuity), was analyzed post-hoc over 12 months using a repeated measures analysis.

No serious adverse events related to treatment were observed in any patient. Ocular safety parameters were similar between treatment groups. Consistent with prior experience with reproxalap and other topical ocular medications, the most common adverse event in reproxalap-treated patients was mild and transient instillation site irritation.

Visual acuity improved over 12 months in both treatment groups, and improvement in patients treated with reproxalap was statistically superior ($P=0.018$) to that in patients treated with vehicle. In the reproxalap treatment group, logMAR improved by approximately 37% ($P<0.0001$), from 0.13 (Snellen 20/27) to 0.08 (Snellen 20/24).

Reproxalap has now been tested in more than 2,300 patients with no safety concerns identified. The detailed results of the clinical trial are expected to be presented at a major medical meeting.

“The long-term safety results announced today complement the broad activity of reproxalap evidenced across a number of late-stage clinical trials in dry eye disease,” stated John Sheppard, M.D., M.M.Sc., President of Virginia Eye Consultants and Professor of Ophthalmology, Microbiology, and Molecular Biology at Eastern Virginia Medical School. “The potential improvement in distance vision observed over one year of treatment is, in my experience, unprecedented for a topical ocular therapy and is consistent with reduction of the inflammation characteristic of dry eye disease.”

About Reproxalap

Reproxalap, an investigational new drug candidate, is a first-in-class small-molecule modulator of RASP (reactive aldehyde species), which are elevated in ocular and systemic inflammatory disease. The mechanism of action of reproxalap has been supported by the demonstration of statistically significant and clinically relevant activity in dry eye disease and other physiologically distinct late-phase clinical indications. Dry eye disease is a common inflammatory disease estimated to affect 39 million or more adults in the United States.[1] The disease is characterized by insufficient moisture and lubrication in the anterior surface of the eye, leading to dryness, inflammation, pain, discomfort, irritation, diminished quality of life, and in severe cases, permanent vision impairment. Among many physicians and patients, existing therapy for dry eye disease is generally regarded as inadequate and often requires weeks or months to demonstrate activity. In patients with dry eye disease, RASP may contribute to ocular inflammation, diminished tear production, ocular redness, and changes in tear lipid composition.[2] By diminishing RASP levels, reproxalap represents a novel and differentiated approach for the treatment of the symptoms and signs of dry eye disease.

About Aldeyra

Aldeyra Therapeutics is a clinical-stage biotechnology company developing innovative therapies designed to treat immune-mediated diseases. Our approach is to discover and develop pharmaceuticals that modulate immunological systems, instead of directly inhibiting or activating single protein targets, with the goal of optimizing multiple pathways at once while minimizing toxicity. Our product candidates include RASP (reactive aldehyde species) modulators ADX-629, ADX-246, ADX-248, and chemically related molecules for the potential treatment of systemic and retinal immune-mediated diseases. Our pre-commercial product candidates are reproxalap, a RASP modulator for the potential treatment of dry eye disease (under

U.S. Food and Drug Administration New Drug Application review) and allergic conjunctivitis, and ADX-2191, a novel formulation of intravitreal methotrexate for the potential treatment of primary vitreoretinal lymphoma (under U.S. Food and Drug Administration New Drug Application review), proliferative vitreoretinopathy, and other rare sight-threatening retinal diseases. For more information, visit https://www.aldeyra.com/ and follow us on LinkedIn, Facebook, and Twitter.

Safe Harbor Statement

This release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements relating to the expectations regarding the clinical data from its 12-month safety clinical trial of reproxalap in patients with dry eye disease, the post-hoc analysis of the 12-month safety clinical trial and the potential to demonstrate distance visual acuity improvement in adults, expectations regarding evidence of acuity improvements and differentiation of reproxalap, if approved for sale, from other therapeutic options. Aldeyra intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by terms such as, but not limited to, “may,” “might,” “will,” “objective,” “intend,” “should,” "could," “can,” “would,” “expect,” “believe,” “anticipate,” “project,” “on track,” “on schedule,” “target,” “design,” “estimate,” “predict,” “potential,” “aim,” “plan,” or the negative of these terms, and similar expressions intended to identify forward-looking statements. Such forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions, and uncertainties. Aldeyra is at an early stage of development and may not ever have any products that generate significant revenue. All of Aldeyra's development timelines are subject to adjustment depending on recruitment rate, regulatory review, which regulatory review timeline may be flexible and subject to change based on the regulator’s workload and other potential review issues, preclinical and clinical results, funding, and other factors that could delay the initiation, enrollment or completion of clinical trials. Important factors that could cause actual results to differ materially from those reflected in Aldeyra's forward-looking statements include, among others, Aldeyra’s plans to develop and commercialize product candidates, if they are approved; delay in or failure to obtain regulatory approval of Aldeyra's product candidates; the ability to maintain regulatory approval of Aldeyra's product candidates, and the labeling for any approved products; uncertainty as to Aldeyra’s ability to commercialize (alone or with others) and obtain reimbursement for Aldeyra's product candidates following regulatory approval, if any; the size and growth of the potential markets and pricing for Aldeyra's product candidates and the ability to serve those markets; the rate and degree of market acceptance of any of Aldeyra's product candidates; the rate and degree of market acceptance of any of Aldeyra’s product candidates, following regulatory approval, if any; the timing of enrollment, commencement and completion of Aldeyra's clinical trials; the timing and success of preclinical studies and clinical trials conducted by Aldeyra and its 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 clinical trials involving Aldeyra's product candidates in clinical trials focused on the same or on different indications; the scope, progress, expansion, and costs of developing and commercializing Aldeyra's product candidates; the current and potential future impact of the COVID-19 pandemic on Aldeyra’s business, results of operations and financial position; Aldeyra's expectations regarding Aldeyra's expenses and future revenue, the timing of future revenue, the sufficiency or use of Aldeyra's cash resources and needs for additional financing; Aldeyra's expectations regarding competition; Aldeyra's anticipated growth strategies; Aldeyra's ability to attract or retain key personnel; Aldeyra’s commercialization, marketing and manufacturing capabilities and strategy; Aldeyra's ability to establish and maintain development partnerships; Aldeyra’s ability to successfully integrate acquisitions into its business; Aldeyra's expectations regarding federal, state, and foreign regulatory requirements; political, economic, legal, social, and health risks, including the COVID-19 pandemic and subsequent public health measures, and war or other military actions, that may affect Aldeyra’s business or the global economy; regulatory developments in the United States and foreign countries; Aldeyra's ability to obtain and maintain intellectual property protection for its product candidates; the anticipated trends and challenges in Aldeyra's business and the market in which it operates; and other factors that are described in the “Risk Factors” and “Management's Discussion and Analysis of Financial Condition and Results of Operations” sections of Aldeyra's Annual Report on Form 10-K for the year ended December 31, 2021, and Aldeyra’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, which are on file with the Securities and Exchange Commission (SEC) and available on the SEC's website at https://www.sec.gov/. Additional factors may be described in those sections of Aldeyra's Annual Report on Form 10-K for the year ended December 31, 2022, expected to be filed with the SEC in the first quarter of 2023.

In addition to the risks described above and in Aldeyra's other filings with the SEC, other unknown or unpredictable factors also could affect Aldeyra's results. No forward-looking statements can be guaranteed, and actual results may differ materially from such statements. The information in this release is provided only as of the date of this release, and Aldeyra undertakes no obligation to update any forward-looking statements contained in this release on account of new information, future events, or otherwise, except as required by law.

[1] Company estimates and Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014;157(4):799-806.

[2] Choi W, Lian C, Ying L, Kim GE, You IC, Park SH, Yoon KC. Expression of Lipid Peroxidation Markers in the Tear Film and Ocular Surface of Patients with Non-Sjogren Syndrome: Potential Biomarkers for Dry Eye Disease. Curr Eye Res. 2016 Sep;41(9):1143-9. doi: 10.3109/02713683.2015.1098707. Epub 2016 Jan 5. PMID: 26731289.

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