Aldeyra Therapeutics Achieves Statistical Significance for Primary Endpoint and All Secondary Endpoints in Phase 3 INVIGORATE Clinical Trial of Reproxalap in Allergic Conjunctivitis

April 27, 2021

- *Statistical Significance Achieved for Primary Endpoint of Ocular Itching at All Prespecified Timepoints (p<0.0001)*
- *Statistical Significance Achieved for Key Secondary Endpoint of Ocular Redness (p<0.0001)*
- *Statistical Significance Achieved for Secondary Endpoints of Ocular Tearing (p<0.0001) and Total Ocular Severity Score (p<0.0001)*
- *Results Consistent with Phase 3 ALLEVIATE Allergic Conjunctivitis Clinical Trial and Previous Chamber Results in Phase 2 Allergic Conjunctivitis Trial and Run-In Cohort of Phase 3 TRANQUILITY Dry Eye Disease Trial*
- *Reproxalap Potentially Represents the First New Allergic Conjunctivitis Therapeutic Mechanism in Decades*
- *Company to Discuss Results in Conference Call and Webcast at 8:00 a.m. ET Today*

LEXINGTON, Mass.--(BUSINESS WIRE)--Apr. 27, 2021-- Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra), a clinical-stage biotechnology company focused on the development of novel therapies with the potential to improve the lives of patients with immune-mediated diseases, today announced positive top-line results from the Phase 3 INVIGORATE Clinical Trial of 0.25% reproxalap ophthalmic solution (reproxalap), an investigational new drug, in patients with allergic conjunctivitis. The clinical trial successfully achieved statistical significance for the primary endpoint and all secondary endpoints.

“The statistically significant superiority of reproxalap over vehicle across all allergic conjunctivitis symptoms and signs assessed in INVIGORATE is remarkable, and suggests utility in one of the world’s most common ocular surface diseases,” stated Todd C. Brady, M.D., Ph.D., President and CEO of Aldeyra. “We believe the consistent activity observed across chamber models in allergic conjunctivitis and dry eye disease bodes well for the commercial positioning of reproxalap as potentially the only broadly applicable topical anterior segment immune-modulating drug that may be used for chronic treatment, if approved for marketing.”

The randomized, double-masked, vehicle-controlled, two-way crossover design allergen chamber Phase 3 INVIGORATE Trial enrolled 95 allergic conjunctivitis patients. The primary efficacy endpoint was change from baseline in subject-reported ocular itching score on a 0-4 point scale over a majority of 11 timepoints from 110 to 210 minutes after allergen chamber entry. The key secondary endpoint was change from baseline in ocular redness on a 0-4 point scale over the duration of the allergen chamber (approximately 3.5 hours).

Relative to patients treated with vehicle, patients treated with reproxalap reported statistically significant ocular itching score reduction over all 11 prespecified primary endpoint comparisons (p<0.0001 for each comparison) from 110 to 210 minutes in the allergen chamber. The reproxalap-treated patients demonstrated statistically significant reduction from baseline compared to vehicle (p<0.0001) for the key secondary endpoint of investigator-assessed ocular redness over the duration of the allergen chamber. Statistical significance was also achieved for the two secondary endpoints of change from baseline in patient-reported ocular tearing score on a 0-3 point scale over the duration of the allergen chamber (p<0.0001) and change from baseline in total ocular severity score (11-point composite of the itching, redness, and tearing scores) over the duration of the allergen chamber (p<0.0001).

“Ocular allergy is a market that is ripe for innovation, and allergic conjunctivitis sufferers know it,” said Milton Hom, OD, of Canyon City Eyecare in Azusa, CA. “Exacerbated by the rise in global temperatures, seasonal pollen counts are exploding, leading to escalations in the prevalence of allergic conjunctivitis and dry eye disease that are growing unchecked. Even with the availability of treatments over the counter, many patients are using more than one prescription to manage ocular symptoms and redness. Based on my review of the INVIGORATE data, reproxalap, as one of the first new therapeutic mechanisms of action in years, would be a meaningful complement to the current treatment paradigm for moderate-to-severe allergic conjunctivitis patients.”

In the Phase 3 ALLEVIATE Trial, 0.25% reproxalap demonstrated statistically significant reductions from vehicle in patient-reported ocular itching over one hour following direct topical conjunctival allergen challenge. In Aldeyra’s Phase 2 allergen chamber trial, 0.25% reproxalap demonstrated statistically significant reductions from vehicle in patient-reported ocular itching and investigator-assessed ocular redness. In the run-in cohort of the Phase 3 TRANQUILITY Trial in dry eye disease patients, 0.25% reproxalap demonstrated statistically significant reductions from vehicle in patient-reported ocular dryness scores and investigator-assessed ocular redness in the dry eye chamber. The primary endpoint of the Phase 3 TRANQUILITY and TRANQUILITY-2 trials is ocular redness over the duration of the chamber. Results from the TRANQUILITY trials in dry eye disease are expected in the second half of 2021.

Reproxalap ophthalmic solution has now been administered to more than 1,200 patients across 14 clinical trials. Consistent with prior clinical experience with reproxalap, there were no observed safety or tolerability concerns in the INVIGORATE Trial and no observed adverse events other than mild and transient instillation site discomfort typical of many prescribed topical ophthalmic medications for anterior segment inflammation.

Aldeyra plans to meet with the U.S. Food and Drug Administration (FDA) in the second half of 2021 to discuss the INVIGORATE results and the potential submission of a New Drug Application.

Conference Call & Webcast Information

Aldeyra will host a conference call at 8:00 a.m. ET today to discuss results of the INVIGORATE Trial. The dial-in numbers are (844) 940-4939 for domestic callers and (639) 380-0129 for international callers. The Conference ID is 7578367. Due to the expected high demand on our conference provider, please plan to dial in to the call at least 15 minutes prior to the start time.

A live webcast of the conference call will be available on the Investor Relations page of the company's website at https://ir.aldeyra.com. After the live webcast, the event will remain archived on the Aldeyra Therapeutics website for 90 days.

About Reproxalap

Reproxalap, an investigational new drug, is a novel small-molecule immune-modulating covalent inhibitor of RASP (reactive aldehyde species), which are elevated in ocular and systemic inflammatory disease. Reproxalap's mechanism of action has been validated with the demonstration of statistically significant and clinically relevant activity in multiple physiologically distinct late-phase clinical indications. Reproxalap is currently in Phase 3 clinical development as a 0.25% ophthalmic solution for the treatment of dry eye disease and allergic conjunctivitis, two ocular inflammatory diseases that often occur together.

About Allergic Conjunctivitis

Allergic conjunctivitis affects more than 1 billion people worldwide,[1] including more than 66 million in the U.S.[2] The disease is thought to be mediated in part by reactive aldehyde species (RASP), leading to activation of intracellular inflammatory factors, including NF-κB, inflammasomes, and Scavenger Receptor A. The symptoms of allergic conjunctivitis – ocular itching and tearing – are chronic, painful, and persistent, affecting quality of life and leading to loss of work that can create a substantial economic burden for patients and their families.[3] Although allergic conjunctivitis is one of the most common diseases treated by ophthalmologists and optometrists, in many cases physicians and patients report that currently available therapy is inadequate. Today, nearly one in five allergic conjunctivitis patients utilizes corticosteroids or other adjunctive therapy in addition to antihistamines.

About Aldeyra Therapeutics

Aldeyra Therapeutics is a clinical-stage biotechnology company focused on the development of novel therapies with the potential to improve the lives of patients with immune-mediated diseases. Two of the company's lead investigational compounds, reproxalap and ADX-629, target RASP (reactive aldehyde species), which are elevated in ocular and systemic inflammatory disease and result in cytokine release via activation of a broad array of inflammatory factors, including NF-κB, inflammasomes, and Scavenger Receptor A. Reproxalap is being evaluated in Phase 3 clinical trials in patients with dry eye disease and allergic conjunctivitis. The company's clinical pipeline also includes ADX-2191, a dihydrofolate reductase inhibitor in Phase 3 testing for proliferative vitreoretinopathy. 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 regarding the planned NDA submission of reproxalap in allergic conjunctivitis and the commercial potential thereof. 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," "scheduled," "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 may be subject to adjustment depending on recruitment rate, regulatory review, preclinical and clinical results, and other factors that could delay the initiation 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, 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; updated or refined data based on Aldeyra's continuing review and quality control analysis of clinical data, Aldeyra's ability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities; 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; 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 risk that the results from smaller clinical trials or portions of clinical trials may not accurately predict results of larger scale trials or the remainder of a clinical trial; the scope, progress, expansion, and costs of developing and commercializing Aldeyra's product candidates; uncertainty as to Aldeyra's ability to commercialize (alone or with others) 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; Aldeyra's expectations regarding Aldeyra's expenses and revenue, the sufficiency or use of Aldeyra's cash resources and needs for additional financing; political, economic, legal, social and health risks, including the recent COVID-19 outbreak and subsequent public health measures, that may affect Aldeyra's business or the global economy; the rate and degree of market acceptance of any of Aldeyra's product candidates; Aldeyra's expectations regarding competition; Aldeyra's anticipated growth strategies; Aldeyra's ability to attract or retain key personnel; Aldeyra's limited sales and marketing infrastructure; 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; 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, 2020, which is 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, expected to be filed with the SEC in the second quarter of 2021.

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] White Book on Allergy (2013 Update)

[2] Singh K, Axelrod S, Bielory L. The epidemiology of ocular and nasal allergy in the United States, 1988-1994. J Allergy ClinImmunol. 2010;126(4):778-783.e6

[3] Andrew D. Pitt, Andrew F. Smith, Lynda Lindsell, Li Wern Voon, Peter W. Rose & Anthony J. Bron (2004) Economic and quality-of-life impact of seasonal allergic conjunctivitis in Oxfordshire, Ophthalmic Epidemiology, 11:1, 17-33, DOI: 10.1076/opep.11.1.17.26437

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