Aldeyra Therapeutics Announces Achievement of Statistical Significance for Primary Endpoint and All Secondary Endpoints in Phase 3 INVIGORATE-2 Trial of Reproxalap in Allergic Conjunctivitis

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- **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=0.004)**
- **Statistical Significance Achieved for Secondary Endpoints of Ocular Tearing (P<0.0001) and Total Ocular Severity Score (P<0.0001)**
- **Results Consistent with Previous Phase 2 and Phase 3 Clinical Trials in Allergic Conjunctivitis**
- **Activity in Allergic Conjunctivitis Complements Commercial Potential in Dry Eye Disease**
- **Company to Discuss Results in Conference Call and Webcast at 8:00 a.m. ET Today**

LEXINGTON, Mass.--(BUSINESS WIRE)--Jun. 15, 2023-- Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra), a biotechnology company devoted to discovering and developing innovative therapies designed to treat immune-mediated diseases, today announced positive top-line results from the Phase 3 INVIGORATE-2 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.

“Consistent with the results of the Phase 3 INVIGORATE Trial and in conjunction with a number of successful Phase 2 and Phase 3 clinical trials in dry eye disease, achievement of the primary endpoint and all secondary endpoints in INVIGORATE-2 supports the potential of reproxalap as a treatment for inflammatory diseases of the ocular surface,” stated Todd C. Brady, M.D., Ph.D., President and CEO of Aldeyra. “We believe that the rapid-onset activity of reproxalap evidenced in the INVIGORATE clinical trials may offer hope to allergic conjunctivitis patients who are today not adequately treated, and also to dry eye disease patients, up to 50% of whom suffer from ocular allergy.”

The randomized, double-masked, vehicle-controlled, two-way crossover design allergen chamber Phase 3 INVIGORATE-2 Trial enrolled 131 allergic conjunctivitis patients. The primary efficacy endpoint was change from baseline in patient-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 across 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=0.004) 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).

“The co-morbidity of allergic conjunctivitis and dry eye disease poses diagnostic and treatment challenges to patients and healthcare providers,” stated William B. Trattler, MD., Vice Chair of Research and Associate Professor of Ophthalmology at Herbert Wertheim College of Medicine. “For patients who have had a poor response to over-the-counter ocular allergy medications, the data announced today may suggest that reproxalap could satisfy a substantial unmet need in patients who suffer from allergic conjunctivitis and dry eye disease.”

Reproxalap ophthalmic solution has now been administered to more than 2,400 patients across 21 clinical trials. Consistent with prior clinical experience with reproxalap, there were no observed safety or tolerability concerns in the INVIGORATE-2 Trial; the most common adverse event was mild and transient instillation site irritation. No patients discontinued due to adverse events, and 130 of 131 randomized patients completed the clinical trial. A New Drug Application (NDA) of reproxalap for the treatment of dry eye disease is under review at the U.S. Food and Drug Administration. The NDA Prescription Drug User Fee Act (PDUFA) date for reproxalap for the treatment of dry eye disease is November 23, 2023.

Conference Call & Webcast Information

Aldeyra will host a conference call at 8:00 a.m. ET today to discuss results of the INVIGORATE-2 Trial. The dial-in numbers are (833) 470-1428 for domestic callers and (404) 975-4839 for international callers. The access code is 349573. A live audio webcast of the conference call also will be accessible from the “Investors & Media” section of Aldeyra's website at ir.aldeyra.com. 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 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 multiple physiologically distinct late-phase clinical indications. Reproxalap has been studied in more than 2,400 patients with no observed safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

About Aldeyra

Aldeyra Therapeutics is a biotechnology company devoted to discovering innovative therapies designed to treat immune-mediated diseases. Our approach is to 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 Priority 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 regarding the likelihood and timing of the FDA's potential approval of the NDA for reproxalap by the PDUFA date, or at any other time, and the adequacy of the data included in the NDA submission, and the commercial potential of reproxalap. 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,” “contemplates,” “likely,” “potential,” “continue,” “ongoing,” “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, 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, 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; delay in or failure to obtain regulatory approval of Aldeyra's product candidates, including as a result of the FDA not accepting Aldeyra’s regulatory filings, requiring additional clinical trials or data prior to review or approval of such filings; 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 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; 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; 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; 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 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, 2022, and Aldeyra’s Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, expected to be filed with the SEC in the third 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.

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