Aldeyra Therapeutics Receives Complete Response Letter from the U.S. Food and Drug Administration for the Reproxalap New Drug Application for the Treatment of Signs and Symptoms of Dry Eye Disease

April 3, 2025

- **Top-Line Data from Dry Eye Chamber Trial and Field Trial Expected in Q2 2025**
- **Pending Positive Results and Discussions with the FDA, New Drug Application Resubmission Expected Mid-Year 2025**

LEXINGTON, Mass.--(BUSINESS WIRE)--Apr. 3, 2025-- Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra), a biotechnology company devoted to discovering and developing innovative therapies designed to treat immune-mediated and metabolic diseases, today announced receipt of a Complete Response Letter from the U.S. Food and Drug Administration (FDA) for the resubmission of the New Drug Application (NDA) of reproxalap, an investigational drug candidate, for the treatment of dry eye disease. Although no manufacturing or safety issues with reproxalap were identified, the FDA stated in the letter that the NDA "failed to demonstrate efficacy in adequate and well controlled studies in treating ocular symptoms associated with dry eyes" and that "at least one additional adequate and well controlled study to demonstrate a positive effect on the treatment of ocular symptoms of dry eye" should be conducted. The letter identified concerns with the data from the trial submitted to the NDA that may have affected interpretation of the results, which the FDA stated may be related to methodological issues, including a difference in baseline scores across treatment arms.

Per draft FDA dry eye disease guidance, to be considered for regulatory approval in the United States, efficacy in dry eye disease may be demonstrated with two symptom trials and two sign trials. Among other clinical trials of reproxalap, Aldeyra previously conducted two trials for ocular redness (a dry eye disease sign) in a dry eye chamber, and two dry eye disease symptom field (environmental exposure) trials, which were submitted as part of an initial NDA in November 2022. In November 2023, the FDA issued a Complete Response Letter to the initial NDA stating that at least one additional symptom trial was required. Following discussions with the FDA, and as part of a comprehensive strategy designed to account for disease heterogeneity and potential differences in clinical sites and environment, Aldeyra initiated three clinical trials assessing dry eye disease symptoms: a dry eye chamber trial, a clinical trial in a different dry eye chamber, and a six-week field trial. In August 2024, Aldeyra announced the achievement of the primary endpoint in the first dry eye chamber clinical trial of reproxalap, and the NDA was resubmitted in October 2024. A Type A meeting is expected to be held within approximately 30 days to discuss the Complete Response Letter for the resubmitted NDA and the ongoing clinical trials of reproxalap in dry eye disease.

In the second quarter of 2025, Aldeyra expects to announce top-line results from the ongoing dry eye disease field trial and the ongoing chamber clinical trial. Subject to positive results and discussions with the FDA, Aldeyra intends to resubmit the NDA mid-year 2025. The review period for the potential NDA resubmission is expected to be six months.

As of December 31, 2024, Aldeyra reported cash, cash equivalents, and marketable securities of $101 million. With a majority of costs for the ongoing dry eye clinical trials having occurred in 2024, the full-year 2025 costs of the trials are expected to be approximately $6 million.

"Pending positive results from the ongoing clinical trials and discussions with the FDA, we look forward to a potential NDA resubmission mid-year 2025," stated Todd C. Brady, M.D., Ph.D., President and Chief Executive Officer of Aldeyra Therapeutics. "Reproxalap remains the only late-stage topical ocular therapy suitable for chronic administration to have potentially demonstrated acute reduction in ocular redness, as well as reduction in ocular discomfort, highlighting rapid and broad activity for both the signs and symptoms of dry eye disease."

Conference Call & Webcast Information
Aldeyra will host a conference call at 5:00 p.m. ET today, April 3, 2025, to provide a regulatory update on reproxalap. The dial-in numbers are (833) 470-1428 for domestic callers and (404) 975-4839 for international callers. The access code is 287309. 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. 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 is an investigational new drug candidate in development for the treatment of dry eye disease and allergic conjunctivitis, two of the largest markets in ophthalmology. Reproxalap is a first-in-class small-molecule modulator of RASP, which are elevated in ocular and systemic inflammatory diseases. 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 2,500 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 and metabolic diseases. Our approach is to develop pharmaceuticals that modulate protein 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-248, ADX-743, ADX-631, ADX-246, and chemically related molecules for the potential treatment of systemic and retinal immune-mediated and metabolic diseases. Our late-stage product candidates are reproxalap, a RASP modulator for the potential treatment of dry eye disease and allergic conjunctivitis, and ADX-2191, a novel formulation of intravitreal methotrexate for the potential treatment of retinitis pigmentosa.

For additional information, please visit www.aldeyra.com.

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 Aldeyra's future expectations, plans, and prospects, including without limitation statements regarding: the goals, opportunity, and potential for reproxalap; the costs, outcome and expected timing and the results of the ongoing dry eye disease clinical trials; the outcome and expected timing of discussions with the FDA the potential and the timing of a potential NDA resubmission; the outcome and timing of the FDA's acceptance, review, or approval of the potential NDA resubmission for reproxalap and the adequacy of the data included in the initial NDA and resubmitted NDA, and expected to be included in the potential resubmitted NDA; the likelihood and timing of the exercise of the Option; and Aldeyra's expectations regarding the labeling for reproxalap, if approved. 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, issuing a complete response letter, or requiring additional clinical trials or data prior to review or approval of such filings or in connection with resubmissions 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; 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, 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, 2024, 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, 2025, expected to be filed with the SEC in the second quarter of 2025, and Aldeyra's other filings with the SEC.

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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