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

November 27, 2023

- **Additional Trial Required to Demonstrate Positive Effect on the Treatment of Ocular Symptoms in Dry Eye Disease**
- **Special Protocol Assessment Submitted on November 16, 2023 for Dry Eye Disease Chamber Crossover Clinical Trial**
- **Proposed Trial Top-Line Results and Potential NDA Resubmission Anticipated in First Half of 2024**
- **Cash Runway Extended into Late 2025**

LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 27, 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 receipt of a Complete Response Letter from the U.S. Food and Drug Administration (FDA) for the New Drug Application (NDA) of reproxalap, an investigational drug candidate, for the treatment of dry eye disease. Although no safety or manufacturing issues with reproxalap were identified, the FDA stated in the letter that the NDA did not demonstrate "efficacy 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.

Per draft FDA dry eye disease guidance, efficacy in dry eye disease may be demonstrated with two symptom trials and two sign trials. Among other clinical trials, Aldeyra previously conducted two trials for ocular redness (a dry eye disease sign) as well as a dry eye disease symptom trial. On November 16, 2023, Aldeyra submitted to the FDA a Special Protocol Assessment (SPA) for a dry eye disease chamber crossover clinical trial (the proposed trial) similar to the crossover chamber trial from which Aldeyra announced results on July 12, 2022. The SPA review cycle is anticipated to be 45 days, and Aldeyra expects FDA feedback from the SPA in December of 2023. The proposed trial is expected to cost less than $2 million, and top-line results are anticipated in the first half of 2024, subject to FDA feedback on the SPA.

The potential NDA resubmission is anticipated in the first half of 2024, pending FDA SPA feedback and positive results from the proposed trial. Aldeyra intends to include in the potential NDA resubmission a draft label describing chronic and acute symptomatic benefit, in addition to acute reduction in ocular redness of reproxalap. The review period for the potential NDA resubmission is expected to be six months.

"With $143 million in cash, cash equivalents, and marketable securities as of September 30, 2023, we are well positioned to conduct another symptom trial of reproxalap in patients with dry eye disease, with a potential NDA resubmission in the first half of 2024," stated Todd C. Brady, M.D., Ph.D., President and Chief Executive Officer of Aldeyra Therapeutics. "If the SPA and proposed trial results are successful, and the potential resubmitted NDA is approved, the drug label may be the first label in dry eye disease to contain acute reduction in ocular redness, as well as a combination of chronic and acute symptomatic benefit, potentially highlighting the rapid activity of reproxalap on both signs and symptoms of dry eye disease."

Reproxalap is also under development for the treatment of allergic conjunctivitis, a common inflammatory disease that affects an estimated 20% of the worldwide population. Results from the third positive Phase 3 clinical trial of reproxalap in allergic conjunctivitis, the INVIGORATE-2 Trial, were announced on June 15, 2023. Aldeyra plans to conduct a Type C meeting with the FDA in the first half of 2024 to discuss the potential NDA submission of reproxalap for the treatment of allergic conjunctivitis.

Aldeyra is extending previous cash runway guidance into late 2025, including clinical trial costs associated with the proposed trial and potential NDA resubmission; the initial commercialization and launch plans for reproxalap, if approved in late 2024; and continued early and late-stage development of its product candidates in ocular and systemic immune-mediated diseases. The extended cash runway guidance is based on Aldeyra's current operating plan, which excludes any potential licensing or product revenue associated with reproxalap.

Conference Call & Webcast Information

Aldeyra will host a conference call at 8:00 a.m. ET tomorrow, November 28, 2023, 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 334884. 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 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 and allergic conjunctivitis, and ADX-2191, a novel formulation of intravitreal methotrexate for the potential treatment of proliferative vitreoretinopathy and retinitis pigmentosa.

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 (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.

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 outcome and timing of the FDA's potential feedback on the SPA; the outcome and expected timing and the results of the proposed trial (as defined above); the outcome and timing of the FDA's review, acceptance and/or approval of a potential NDA resubmission for reproxalap and the adequacy of the data included in the original NDA and the potential NDA resubmission; Aldeyra's expectations regarding the labeling for reproxalap, if approved; Aldeyra's projected cash runway; Aldeyra's ability to successfully commercialize (alone or with others) reproxalap; Aldeyra's expectations regarding the development of reproxalap for the treatment of allergic conjunctivitis; and Aldeyra's expectations regarding timing and results of potential or scheduled FDA meetings, including the planned Type C meeting with the FDA to discuss the development of reproxalap for the treatment of allergic conjunctivitis. 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 reproxalap or Aldeyra's other product candidates, including as a result of the FDA not accepting Aldeyra's regulatory filings, issuing a complete response letter, providing feedback and/or rejecting the SPA, 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, 2022, and Aldeyra's Quarterly Report on Form 10-Q for the quarter ended September 30, 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 Annual Report on Form 10-K for the year ended December 31, 2023, expected to be filed with the SEC in the first quarter of 2024, 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20231127889140/en/

Investors & Media:
David Burke
Tel: (917) 618-2651
investorrelations@aldeyra.com

Source: Aldeyra Therapeutics, Inc.