Aldeyra Therapeutics Announces Phase 3 TRANQUILITY Dry Eye Disease Trial Design

February 4, 2021

- TRANQUILITY to Utilize Two-Day Treatment and Challenge Design
- Consistent with Previously Announced Top-Line TRANQUILITY Run-In Cohort Results, Ocular Redness Selected as Primary Endpoint
- Tear RASP Levels Reduced After Single Doses of Reproxalap in Run-In Cohort of TRANQUILITY and Selected as Secondary Endpoint for Confirmation of Mechanism of Action

LEXINGTON, Mass.--(BUSINESS WIRE)--Feb. 4, 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 the finalization of the design of the Phase 3 TRANQUILITY Trial of 0.25% reproxalap ophthalmic solution for the treatment of dry eye disease. Consistent with previously announced results from the run-in cohort of TRANQUILITY, ocular redness over 90 minutes in a dry eye chamber will be the primary endpoint. Approximately 150 dry eye disease patients are expected to be enrolled per arm. The TRANQUILITY protocol will utilize the two-day dosing paradigm, dry eye challenge design, and enrollment criteria of the run-in cohort.

Tear RASP levels from the TRANQUILITY run-in cohort were reduced after single doses of the novel RASP inhibitor reproxalap, as assessed by enzyme-linked immunosorbent assay (ELISA) of 4-hydroxynonenal protein adducts (HNE), a RASP selected based on results from a natural history study of dry eye patients conducted by Aldeyra. For subjects with sufficient tear volumes for analysis, across the two doses where tear RASP levels were assessed before and after drug administration, HNE levels declined by an average of 1018 picograms/milliliter (pg/mL) in reproxalap-treated patients (n=9) versus an increase of 32 pg/mL in vehicle-treated patients (n=7). Accordingly, tear RASP levels have been selected as a secondary endpoint for confirmation of mechanism of action. HNE is well-characterized in the scientific literature as a critical pro-inflammatory RASP,[1] and ocular levels of HNE correlate with the signs and symptoms of dry eye disease.[2]

“The rapid activity of reproxalap demonstrated in the run-in cohort of TRANQUILITY in improving ocular redness, potentially the only dry eye disease sign of interest to patients, allows for the use of a two-day challenge design — a time and cost-efficient model for Phase 3 clinical testing,” statedTodd C. Brady, M.D., Ph.D., President and Chief Executive Officer of Aldeyra. “Consistent with the observed rapid improvement in dry eye disease signs and symptoms, the reduction of tear RASP levels was evident after single doses of reproxalap, representing, to our knowledge, the first confirmation of drug mechanism in clinical trials of a topical ocular dry eye disease drug.”

TRANQUILITY and the confirmatory Phase 3 TRANQUILITY-2 Trial are expected to initiate in the first half of 2021. Results from both trials are expected in the second half of 2021.

About Reproxalap

Reproxalap 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 Dry Eye Disease

Dry eye disease is a common inflammatory disease estimated to affect 34 million or more adults in the United States.[3] 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, pro-inflammatory RASP may contribute to ocular inflammation and changes in tear lipid composition. By diminishing RASP levels, Aldeyra’s lead RASP inhibitor reproxalap represents a novel and differentiated approach for the treatment of the symptoms and signs of dry eye disease.

About Aldeyra Therapeutics, Inc.

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, and ADX-1612, a chaperome inhibitor in development for COVID-19 and ovarian cancer. 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 statements regarding expectations regarding the main cohort of TRANQUILITY and the Phase 3 TRANQUILITY-2 Trial. 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; 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, 2019 and Aldeyra's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, 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, 2020, expected to be filed with the SEC in the first 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]Ayala A, Muñoz MF, Argüelles S. Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. Oxid Med Cell Longev. 2014;2014:360438. doi: 10.1155/2014/360438. Epub 2014 May 8. PMID: 24999379; PMCID: PMC4066722.

[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.

[3]Paulsen AJ, Cruickshanks KJ, Fischer ME, Huang GH, Klein BE, Klein R, Dalton DS. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014 Apr;157(4):799-806. doi: 10.1016/j.ajo.2013.12.023. Epub 2014 Jan 2. PMID: 24388838; PMCID: PMC3995164.

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