Aldeyra Therapeutics Achieves Primary Endpoint in Part 1 of Phase 3 GUARD Trial of ADX-2191 in Proliferative Vitreoretinopathy

October 6, 2022

- *ADX-2191 Statistically Superior to Historical Control for Primary Endpoint of Prevention of Retinal Detachment (P=0.024)*
- *Numerical Superiority of ADX-2191 over Routine Surgical Care Achieved for Majority of Secondary, Exploratory, and Safety Endpoints*
- *ADX-2191 Observed to be Well Tolerated with No Safety Concerns Noted*
- *Company Plans to Discuss Completion of Clinical Development in Proliferative Vitreoretinopathy with the U.S. Food and Drug Administration in the First Half of 2023*
- *Company to Host Conference Call at 8:00 a.m. ET Today*

LEXINGTON, Mass.--(BUSINESS WIRE)--Oct. 6, 2022-- Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra or the Company) today announced the achievement of the primary endpoint in Part 1 of the Phase 3 GUARD Trial of ADX-2191 (methotrexate injection, USP[1]) for intravitreal administration, an investigational drug candidate, for the prevention of proliferative vitreoretinopathy (PVR), a rare sight-threatening retinal disease with no approved therapy. ADX-2191 was statistically superior to historical control[2] for the prevention of retinal detachment due to PVR over six months (P=0.024).

“Proliferative vitreoretinopathy represents a major unmet medical need and is particularly difficult to treat, highlighting the need for an effective therapy,” stated Marco Zarbin, M.D., Ph.D., Professor and Chair of the Institute of Ophthalmology and Visual Science, Rutgers New Jersey Medical School. “The recent reports describing the activity of methotrexate in preventing PVR, in conjunction with the results of the GUARD Trial, offer hope to many patients and physicians that today have few options for treatment.”

Part 1 of the GUARD Trial was designed to assess the preliminary activity of ADX-2191, a novel vitreous-compatible formulation of methotrexate, versus historical control and routine surgical care without therapy in patients with PVR. Sixty-eight patients received ADX-2191, and 38 patients received routine surgical care. Relative to historical control, statistically significant reduction (P=0.024) in retinal detachment over six months was observed following serial intravitreal injection of ADX-2191. Although not statistically powered for secondary or exploratory endpoints, the results of the GUARD Trial demonstrated numerical superiority of ADX-2191 over routine surgical care in reducing the dichotomous endpoints of retinal detachment rate over six months, hypotony (low intraocular pressure), complete retinal attachment by six months, macular attachment by six months, and epiretinal membrane formation (overall P=0.047). Visual acuity was similar between ADX-2191 treatment and routine surgical care groups. Central macular thickness was numerically lower in ADX-2191-treated patients.

No safety signals were observed in the trial, and ADX-2191 was well tolerated; there were no observed treatment-emergent serious adverse events. The most common adverse event associated with ADX-2191 treatment was punctate keratitis, a well-known side effect of intravitreal methotrexate, that was most commonly mild in severity. Across all other treatment-emergent adverse events occurring in at least 10% of patients in either treatment arm, relative to patients treated with routine surgical care, ADX-2191-treated patients had numerically fewer side effects, including pain, cystoid macular edema, corneal edema, macular fibrosis, corneal epithelial defects, anterior uveitis, ocular hypertension, and post-operative inflammation (overall P=0.0002). In the ADX-2191 group, there was one discontinuation, which was due to scheduling difficulties.

Aldeyra intends to discuss completion of clinical development of ADX-2191 for the prevention of PVR in a Type C meeting with the U.S. Food and Drug Administration (FDA) in the first half of 2023. ADX-2191 has received FDA Orphan Drug Designation and FDA Fast Track Designation for the prevention of PVR, and EU Orphan Medicinal Product Designation for the treatment of retinal detachment. ADX-2191 has also received FDA Orphan Drug Designation for the treatment of primary vitreoretinal lymphoma and retinitis pigmentosa.

“The ADX-2191 platform for the prevention and treatment of rare retinal disease continues to advance towards commercialization, and is a critical late-stage pipeline program with the potential to address a number of diseases with no FDA-approved therapies,” stated Todd C. Brady, M.D., Ph.D., President and Chief Executive Officer of Aldeyra.

Conference Call Information

Aldeyra will host a conference call to discuss this announcement at 8:00 a.m. ET today, October 6, 2022. The dial-in numbers are (844) 200-6205 for domestic callers and (646) 904-5544 for international callers. The access code is 005042. A live webcast of the conference call will also be available on the “Investors & Media” section of the Aldeyra website at https://ir.aldeyra.com. Presentation slides, which contain material information and should be reviewed in conjunction with this press release, will be available on the investor relations page prior to the start of the conference call and webcast.

After the live webcast, the event will remain archived on the Aldeyra website for 90 days.

About ADX-2191

ADX-2191 (methotrexate injection, USP) is a sterile, non-compounded intravitreal formulation of methotrexate for the potential prevention or treatment of specific rare retinal diseases, including primary vitreoretinal lymphoma, proliferative vitreoretinopathy, and retinitis pigmentosa. The ADX-2191 intravitreal formulation is preservative-free, designed to be vitreous-compatible, and optimized for excipient composition, viscosity, density, tonicity, pH, concentration, and volume of administration. ADX-2191 has received FDA Orphan Drug Designation for the prevention of proliferative vitreoretinopathy, and the treatment of primary vitreoretinal lymphoma and retinitis pigmentosa.

About Proliferative Vitreoretinopathy

Proliferative vitreoretinopathy (PVR) is a rare inflammatory fibroproliferative disorder that leads to severe retinal scarring and blindness, and is the leading cause of failure of retinal reattachment surgery. Left untreated, retinal detachment due to PVR can progress to permanent blindness. PVR affects approximately 4,000 patients per year in the U.S. There is currently no approved therapy for the treatment of PVR.

About Aldeyra

Aldeyra is a clinical-stage biotechnology company developing innovative therapies designed to treat immune-mediated diseases. Our approach is to discover 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. Two of our lead product candidates, reproxalap and ADX-629, target pre-cytokine, systems-based mediators of inflammation known as RASP (reactive aldehyde species). Reproxalap is in late-stage clinical trials in patients with dry eye disease and allergic conjunctivitis. ADX-629, an orally administered RASP modulator, is in Phase 2 clinical testing for the treatment of systemic immune-mediated diseases. Our pipeline also includes ADX-2191 (methotrexate injection) for intravitreal administration, in development for the prevention of proliferative vitreoretinopathy and the treatment of retinitis pigmentosa and primary vitreoretinal lymphoma. 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 Aldeyra's future expectations, plans, and prospects, including without limitation statements regarding: the potential regulatory approval of ADX-2191 and Aldeyra's goals as to timing; the potential profile and benefit of ADX-2191; and other statements regarding the goals, opportunity and potential for ADX-2191, anticipated clinical or regulatory milestones for ADX-2191, including expectations regarding timing and results of meetings with the FDA, including scheduled Type C and pre-NDA meetings, and submissions to the FDA. 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, 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; updated or refined data based on Aldeyra's continuing or post-hoc review and quality control analysis of clinical data, Aldeyra's ability to design clinical trials with protocols, data analysis methodologies, 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 earlier clinical trials, portions of clinical trials, or pooled clinical data may not accurately predict results of subsequent 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) 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 revenue, the sufficiency or use of Aldeyra's cash resources and needs for additional financing; 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; 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, 2021, and Aldeyra's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, 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 set forth in those sections of Aldeyra's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, expected to be filed with the SEC in the fourth quarter of 2022.

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] United States Pharmacopeia

[2] Ophthalmology 124(6):757-767, 2017; Archives of Ophthalmology 25(9):1161-7, 2007.

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Source: Aldeyra Therapeutics, Inc.