Aldeyra Therapeutics Receives Orphan Designation from the European Medicines Agency for ADX-2191 for the Treatment of Primary Large B-Cell Lymphomas of Immune-Privileged Sites, including Primary Vitreoretinal Lymphoma

August 28, 2025

LEXINGTON, Mass.--(BUSINESS WIRE)--Aug. 28, 2025-- Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra) today announced that the European Medicines Agency (EMA) has granted Orphan Designation for ADX-2191 (methotrexate intravitreal injection, USP) for the treatment of primary large B-Cell lymphomas of immune-privileged sites, including primary vitreoretinal lymphoma. There is currently no approved treatment for patients with primary vitreoretinal lymphoma, a rare, aggressive, high-grade cancer that affects approximately 100 to 200 people per year in the European Union.

“Primary vitreoretinal lymphoma is a potentially fatal cancer that today is treated with off-label compounded formulations of methotrexate that are injected into the eye,” stated Todd C. Brady, M.D., Ph.D., President and CEO of Aldeyra. “The receipt of Orphan Designation from the EMA, in conjunction with the previously announced Orphan Drug Designation from the U.S. Food and Drug Administration, is another important step forward for our retinal disease program, complementing our ongoing clinical development of ADX-2191, a novel, vitreous-compatible formulation of methotrexate that is specifically designed for intraocular injection.”

A proposed clinical trial, which received Special Protocol Assessment agreement from the U.S. Food and Drug Administration, is designed to compare cancer cell clearance after 30 days of therapy in up to 20 patients following 1:1 randomization to receive either a single intraocular injection or eight intraocular injections of ADX-2191. The frequency of methotrexate injections has been linked to cancer cell clearance in patients with primary vitreoretinal lymphoma,[1] and approximately five injections on average has been observed to achieve cancer cell clearance.[2] The clinical trial is expected to begin in the second half of 2025 and conclude in 2026.

The EMA grants orphan designation to drugs and biologics intended for the treatment, diagnosis, or prevention of rare, life-threatening, or chronically debilitating diseases or conditions that affect fewer than five in 10,000 people in the European Union. Orphan designation allows companies certain benefits, including reduced regulatory fees, clinical protocol assistance, research grants, and up to 10 years of market exclusivity in the European Union.

About ADX-2191

ADX-2191 (methotrexate intravitreal injection, USP) is a sterile, non-compounded intravitreal formulation of methotrexate for the potential treatment of specific rare retinal diseases, including primary vitreoretinal lymphoma and retinitis pigmentosa. The ADX-2191 intravitreal formulation is preservative-free, is designed to be vitreous-compatible, and is optimized for excipient composition, viscosity, density, tonicity, pH, concentration, and volume of administration. ADX-2191 received FDA Orphan Drug Designation for the treatment of primary vitreoretinal lymphoma and retinitis pigmentosa, and EMA Orphan Designation for the treatment of inherited retinal dystrophies of the rod-dominant phenotype, including retinitis pigmentosa, and the treatment of primary large B-cell lymphomas of immune-privileged sites, including primary vitreoretinal lymphoma.

About Primary Vitreoretinal Lymphoma

Primary vitreoretinal lymphoma is a rare, aggressive, and potentially fatal retinal cancer that is diagnosed in approximately 200 to 600 patients in the United States and 100 to 200 patients in the European Union per year. The median survival for newly diagnosed patients is less than five years. No approved treatments are currently available, though intravitreal injection of compounded methotrexate represents the current standard of care.

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 primary vitreoretinal lymphoma and retinitis pigmentosa.

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 ADX-2191; and the outcome and timing of any clinical trials of ADX-2191. 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, and Aldeyra's Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, which are on file with the Securities and Exchange Commission (SEC) and available on the SEC 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 September 30, 2025, expected to be filed with the SEC in the fourth 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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[1] Am J Ophthalmol 251: 189–196, 2023

[2] Br J Haematol, 194, 92–100, 2021; Cancer Sci. 107:1458-1464, 2016

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