UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 18, 2022

ALDEYRA THERAPEUTICS, INC.
(Exact name of Registrant as specified in its charter)

Delaware	001-36332	20-1968197
(State or other jurisdiction of incorporation)	(Commission File No.)	(IRS Employer Identification No.)

131 Hartwell Avenue, Suite 320
Lexington, MA 02421
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: (781) 761-4904

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	**ALDX**	**The Nasdaq Stock Market, LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

On May 18, 2022, Aldeyra Therapeutics, Inc. (the "Company") issued a press release (the "Press Release") to announce that post-hoc analysis using computer automated grading of digital photography from the completed Phase 3 TRANQUILITY Trial demonstrated statistical significance in favor of reproxalap over vehicle for the primary endpoint of ocular redness. The Press Release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

In addition, the Company is supplementing the risk factors previously disclosed in the Company's Annual Report on Form 10-K for the year ended December 31, 2021 and its subsequent Quarterly Reports on Form 10-Q and Current Reports on From 8-K, with the following risk factor:

To generate revenue, we will depend on FDA approval and successful commercialization of our lead product candidate, reproxalap, for the treatment of dry eye disease. If we are unable to successfully conduct the TRANQUILITY-2 trial, prepare and timely submit the planned NDA, and obtain FDA approval, our ability to generate revenue will be significantly delayed.

Our ability to generate revenue will depend on the successful development, regulatory approval and commercialization of reproxalap. Based on our discussions with and our interpretation of feedback from the FDA, as well as data from our previously completed clinical trials in dry eye disease and the TRANQUILITY-2 trial, we currently plan to submit an NDA to the FDA for reproxalap for the potential treatment of dry eye disease in mid-2022, subject to positive clinical trial results, including results from a dry eye disease safety trial. There can be no assurance that we can prepare and submit an NDA in a timely manner or at all. We have limited experience in preparing, filing, and pursuing applications necessary to gain regulatory approvals. The preparation of an NDA requires a great deal of effort and expertise, and if we do not secure the necessary resources and hire and retain personnel having the requisite expertise to prepare and submit the NDA, the filing of the NDA would be delayed. Further, if an NDA is submitted by the company, there can be no assurance that it will be accepted for filing by the FDA. If the FDA determines after an initial review of the NDA that the data included in the application is insufficient and not ready for formal consideration, we could receive a "refuse to file" notice. The FDA has substantial discretion in the approval process and may disagree with our interpretation of or the sufficiency of the data from our clinical trials. Clinical trial results frequently are susceptible to varying interpretations and regulatory authorities may disagree on what are appropriate methods for analyzing data, which may delay, limit or prevent regulatory approvals. For instance, pending discussion with the FDA, for satisfaction of the sign efficacy requirements for regulatory approval per draft FDA guidance, we intend to submit the ocular redness results from post-hoc analysis using computer automated grading of digital photography from the completed the Phase 3 TRANQUILITY and Phase 2 dry eye chamber trials. However, given that this is a novel method of analyzing data and we have not discussed this method with the FDA, and we cannot be sure that the FDA will accept the data derived from this method of analysis. In addition, regulatory authorities typically give greater weight to results from pre-specified analyses and less weight to results from post-hoc, retrospective analyses. The FDA could also require that we conduct additional studies and submit the results of those studies before the application will be reconsidered, which would require us to expend more resources than we planned or that are available to us, and could substantially delay any approval of our application. It is also possible that additional studies may not suffice to make our application approvable. Even if the NDA is accepted for filing by the FDA, there can be no assurance that it would be approved in a timely manner or at all.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	**Description**
99.1	Aldeyra Therapeutics, Inc. Press Release dated May 18, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated May 18, 2022

ALDEYRA THERAPEUTICS, INC.

By: /s/ Todd C. Brady
Name: Todd C. Brady M.D., Ph.D.
Title: Chief Executive Officer

Exhibit 99.1

Aldeyra Therapeutics Announces that Post-Hoc Analysis Using Computer Automated Grading of Phase 3 TRANQUILITY Trial Digital Photography Demonstrated Statistical Significance in Favor of Reproxalap Over Vehicle for Primary Endpoint of Ocular Redness

- ***Post-Hoc Analysis Using Computer Automated Grading Indicated that Reproxalap is Statistically Superior to Vehicle (p=0.020) in Reducing Dry-Eye Associated Ocular Redness, the Primary Endpoint of Phase 3 TRANQUILITY Trial***
- ***Statistical Superiority of Reproxalap over Vehicle (p=0.003) for the Primary Endpoint of Ocular Redness in the Previously Announced Phase 2 Dry Eye Chamber Trial Confirmed Using Post-Hoc Computer Automated Grading***
- ***Pending Discussion with the U.S. Food & Drug Administration (FDA), Aldeyra Intends to Include Ocular Redness as an Objective Sign of Dry Eye Disease for New Drug Application (NDA), Expected to be Submitted Mid-2022***
- ***TRANQUILITY-2 Top-Line Results Expected in the Second Quarter of 2022***

LEXINGTON, Mass.--(BUSINESS WIRE)--May 18, 2022--Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra) today reported that a post-hoc analysis using computer automated grading of digital photography from the completed Phase 3 TRANQUILITY dry eye chamber trial demonstrated statistical significance (p=0.020) in favor of reproxalap over vehicle for the primary endpoint of reduction of ocular redness. As previously announced, the Phase 3 TRANQUILITY trial failed to meet the primary endpoint of ocular redness as assessed by independent central reviewers.

When applied to Aldeyra's Phase 2 dry eye chamber trial, which was completed in late 2021, the computer automated grading assessment (p=0.003) confirmed the previously announced achievement of the primary endpoint of ocular redness (p=0.016), which, similar to the Phase 3 TRANQUILITY trial, was originally assessed by independent central reviewers. Aldeyra intends to discuss the results of the post-hoc analyses, as well as the algorithm used for the computer automated assessment of ocular redness,[1] with the FDA prior to NDA submission.

The computer automated grading of redness in the completed Phase 3 TRANQUILITY and Phase 2 clinical trials of reproxalap is based on digital images captured by portable cameras fitted with eye cups to standardize distance, lighting, focus, hue, and contrast. The assessment consisted of automated selection of temporal conjunctiva from images of subjects focusing on nasal targets in the eye cup. Redness intensity was averaged across all pixels in the selected region, and combined with vessel geometry to generate a theoretical maximum score of 255. The average baseline score from the post-hoc analyses of the Phase 3 TRANQUILITY and Phase 2 clinical trials was approximately 18.

Per draft FDA guidance, to be considered for regulatory approval in the United States, a product candidate for the treatment of dry eye disease must, with certain exceptions, demonstrate efficacy in an objective sign in at least two clinical trials and efficacy in a subjective symptom in at least two clinical trials. Statistical significance versus vehicle is generally considered sufficient for demonstration of efficacy.

For satisfaction of symptom efficacy requirements, Aldeyra intends to submit two previously completed adequate and well-controlled 12-week symptom trials that pre-specified patient-reported ocular dryness score as a primary endpoint, the Phase 3 RENEW-Part 1 and Formulation Phase 2 clinical trials. Pending discussion with the FDA, for satisfaction of the sign efficacy requirements, Aldeyra intends to submit the ocular redness results from the Phase 3 TRANQUILITY and Phase 2 dry eye chamber trials. If the primary endpoint of Schirmer test is achieved in the Phase 3 TRANQUILITY-2 trial, and pending discussion with the FDA, Aldeyra intends to submit Schirmer test results from both TRANQUILITY trials as evidence for achievement of an additional objective sign of dry eye disease.

Top-line results from TRANQUILITY-2 are expected in the second quarter of 2022. Pending discussion with the FDA and enrollment of the ongoing 12-month safety trial in dry eye disease patients, NDA submission for dry eye disease is expected to occur mid-2022.

About Aldeyra

Aldeyra develops 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 Phase 3 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 (intravitreal methotrexate 0.8%), 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 submission of a potential New Drug Application; the anticipated timing of results from Aldeyra's clinical trials; expectations regarding the FDA's acceptance of Aldeyra's post-hoc review of data and agreement with Aldeyra's methods of analyzing data; and Aldeyra's projected cash runway. 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 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 March 31, 2022, which are on file with the Securities and Exchange Commission (SEC) and available on the SEC's website at https://www.sec.gov/.

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] Rodriguez JD et al. Automated grading system for evaluation of ocular redness associated with dry eye. Clin Ophthalmol. 2013;7:1197-1204.

Contacts

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