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): July 12, 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 7.01. Regulation FD Disclosure.

As reported under Item 8.01 of this Current Report on Form 8-K, on July 12, 2022 Aldeyra Therapeutics, Inc. ("Aldeyra" or the "Company") issued a press release (the "Press Release") announcing the achievement of the primary endpoints in a crossover clinical trial of reproxalap, an investigational new drug candidate, for the treatment of dry eye disease. The Company is holding a conference call regarding this announcement on July 12, 2022. A copy of the supplemental presentation which will be referenced during the conference call is furnished herewith as Exhibit 99.1 and is incorporated by reference herein.

This information in this Item 7.01 of this Current Report on Form 8-K shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01. Other Events.

The Press Release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	**Description**
99.1	Aldeyra Therapeutics, Inc. Presentation dated July 12, 2022.
99.2	Aldeyra Therapeutics, Inc. Press Release dated July 12, 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.

ALDEYRA THERAPEUTICS, INC.

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

Dated: July 12, 2022

July 12, 2022

Top-Line Results from the Dry Eye Disease Chamber Crossover Trial of Reproxalap

NASDAQ: ALDX

Disclaimers and Forward-Looking Statements

This presentation and various remarks which may be made during this presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding Aldeyra's possible or assumed future results of operations, expenses and financing needs, business strategies and plans, expectations regarding the timing and results of the expected Type B Pre-NDA meeting, including the FDA's acceptance of Aldeyra's post-hoc review of data and the FDA's agreement with Aldeyra's methods of analyzing data, and Aldeyra's intention to submit the crossover clinical trial as part of its NDA, research, development and regulatory plans or expectations, political, economic, legal, social and health risks, including the COVID-19 pandemic and related public health measures and other responses to it, that may affect Aldeyra's business or the global economy, the structure, timing and success of Aldeyra's planned or pending clinical trials, expected milestones, market sizing, pricing and reimbursement, competitive position, regulatory matters, industry environment and potential growth opportunities, among other things. The results of earlier preclinical or clinical trials may not be predictive of future results. As a result of the COVID-19 pandemic, clinical site availability, staffing, and patient recruitment have been negatively affected and the timelines to complete Aldeyra's clinical trials may be delayed. Forward-looking statements include all statements that are not historical facts and, in some cases, can be identified by terms such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "anticipate," "project," "target," "design," "estimate," "predict," "potential," "plan" or similar expressions and the negatives of those terms.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause Aldeyra's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These statements reflect Aldeyra's current views with respect to future events and are based on assumptions and subject to risks and uncertainties, including the development, clinical and regulatory plans or expectations for Aldeyra's investigational new drugs (including reproxalap), and systems-based approaches, later developments with the FDA that may be inconsistent with Aldeyra's expectations and beliefs, including 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 for the same or different indications, inconsistent expectations regarding FDA acceptance and review of the company's filings and submitted data sets, and Aldeyra's continuing or post-hoc review and quality control analysis of clinical data. Important factors that could cause actual results to differ materially from those reflected in Aldeyra's forward-looking statements are described in Aldeyra's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as Aldeyra's subsequent filings with the Securities and Exchange Commission. All of Aldeyra's development plans and timelines may be subject to adjustment depending on funding, recruitment rate, regulatory review, preclinical and clinical results, and other factors any of which could result in changes to Aldeyra's development plans and programs or delay the initiation, enrollment, completion, or reporting of clinical trials.

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 presentation is provided only **as of July 12, 2022**, and Aldeyra undertakes no obligation to update any forward-looking statements contained in this presentation on account of new information, future events, or otherwise, except as required by law.

The Dry Eye Disease Crossover Trial Achieved Success for Three Dry Eye Disease Sign Endpoints and Six Secondary Symptom Endpoints

- The ocular redness primary endpoint was achieved (P=0.0004).
- The Schirmer test primary endpoint was achieved (P=0.0005).
- The multiplicity-controlled secondary endpoint of Schirmer test ≥10mm responder analysis was achieved (P=0.0361).
- Secondary endpoints for each assessed symptom (dryness, discomfort, grittiness, burning, stinging, and itching) were achieved.
- All endpoints were assessed over approximately a 24-hour period of dosing, suggesting rapid activity of reproxalap.
- The crossover trial design appeared to reduce the high degree of variability characteristic of dry eye disease clinical trials, at least for a drug with a potentially rapid mechanism of action.

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Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

Aldeyra Intends to Submit Symptom and Three Sign Endpoints to Support Dry Eye Disease NDA Efficacy Requirements†

- Based on previously announced clinical trials, the dry eye disease New Drug Application (NDA) package for 0.25% reproxalap ophthalmic solution is expected to include two clinical trials for each of the following endpoints:
  - Symptoms (ocular dryness symptom score) over 12 weeks,
  - Ocular redness in a dry eye chamber,
  - Schirmer test following a single day of dosing, and
  - Schirmer test ≥10mm responder analysis following a single day of dosing.

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†NDA submission requirements depend, in part, on clinical safety results and regulatory feedback. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

The Crossover Trial Represents a Unique Clinical Paradigm in Dry Eye Disease and Was Designed to Serve as a Pivotal Trial

- The dry eye disease crossover trial was designed to eliminate inter-patient variability by testing all interventions on each patient.
- To our knowledge, an adequate and well-controlled crossover trial has not been previously performed with an investigational drug candidate in dry eye disease patients.
- The dry eye disease crossover clinical trial was intended to support the objective sign results from previously completed clinical trials.
- Because the crossover trial was designed to be adequate and well-controlled, and because the endpoints were multiplicity-controlled, the trial was intended to be submitted as pivotal, assuming success, for one or more of the following objective sign endpoints: ocular redness, Schirmer test, and ≥10mm Schirmer test responder analysis.

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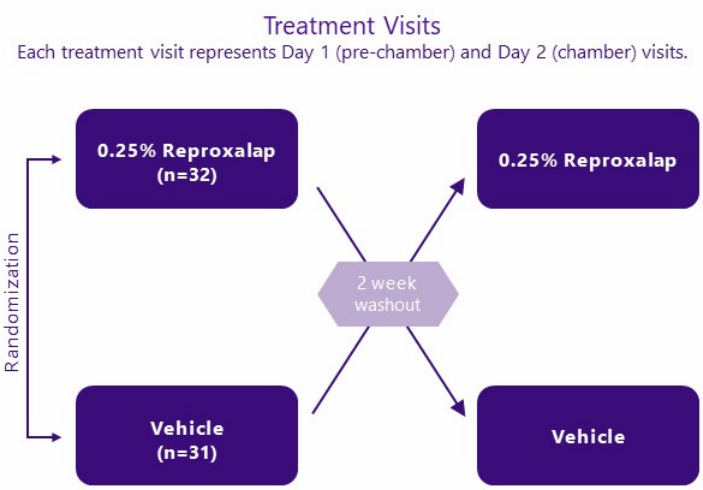
†NDA submission requirements depend, in part, on clinical safety results and regulatory feedback. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

The Crossover Trial Was Designed to Serve as a Pivotal Trial in Support of NDA Submission for Dry Eye Disease

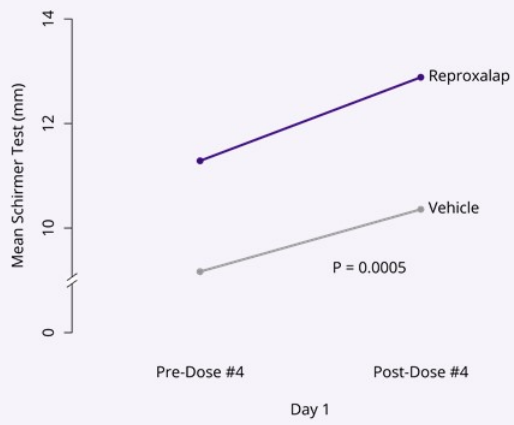
Design	Randomized, double-masked, crossover, vehicle-controlled, single-center
Dosing	0.25% reproxalap or vehicle, two-week washout Day 1: four doses Day 2: one dose before 90-minute dry eye chamber, one dose 45 minutes after chamber entry
Size	63 patients
Primary Endpoints[†]	• Schirmer test on Day 1 (pre/post fourth dose) • Ocular redness in dry eye disease chamber
Secondary Endpoints	• Schirmer test ≥10mm responder analysis • Dry eye disease symptoms



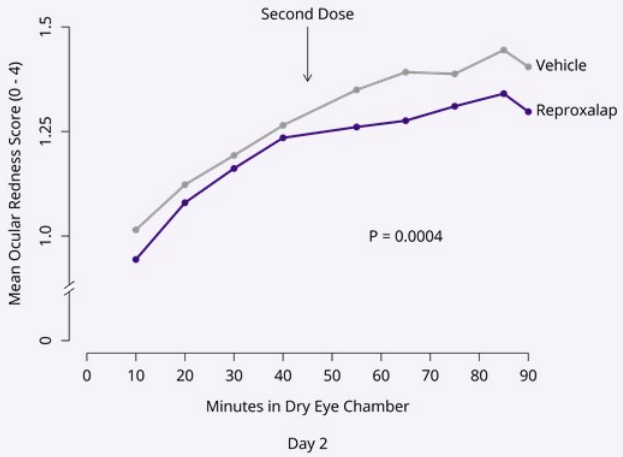
[†] The Hochberg procedure was used to control for multiplicity. Unused alpha from the Hochberg procedure was passed to a fixed sequence of secondaries, the first of which was the Schirmer responder analysis. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

In the Dry Eye Disease Crossover Trial, Both Primary Endpoints Were Statistically Significant in Favor of Reproxalap over Vehicle

Tear Production
(Higher scores favor reproxalap.)



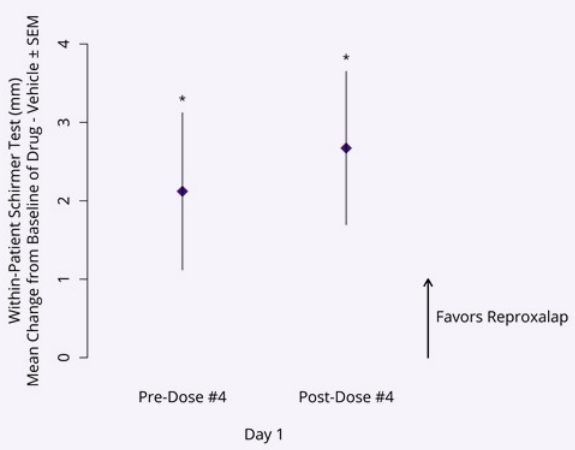
Ocular Redness
(Lower scores favor reproxalap.)



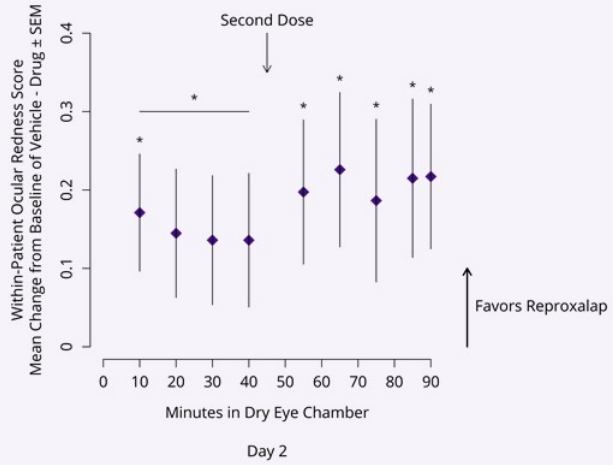
P values derived from mixed effect model of repeated measures of change from baseline. **Source:** Dry eye disease crossover clinical trial results on file. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

In the Dry Eye Disease Crossover Trial, Within-Patient Clinical Relevance Assessments Demonstrated Reproxalap Superiority

Tear Production



Ocular Redness



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*P < 0.05. **SEM** = standard error of the mean. **mm** = millimeter. **Source:** Dry eye disease crossover clinical trial results on file. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

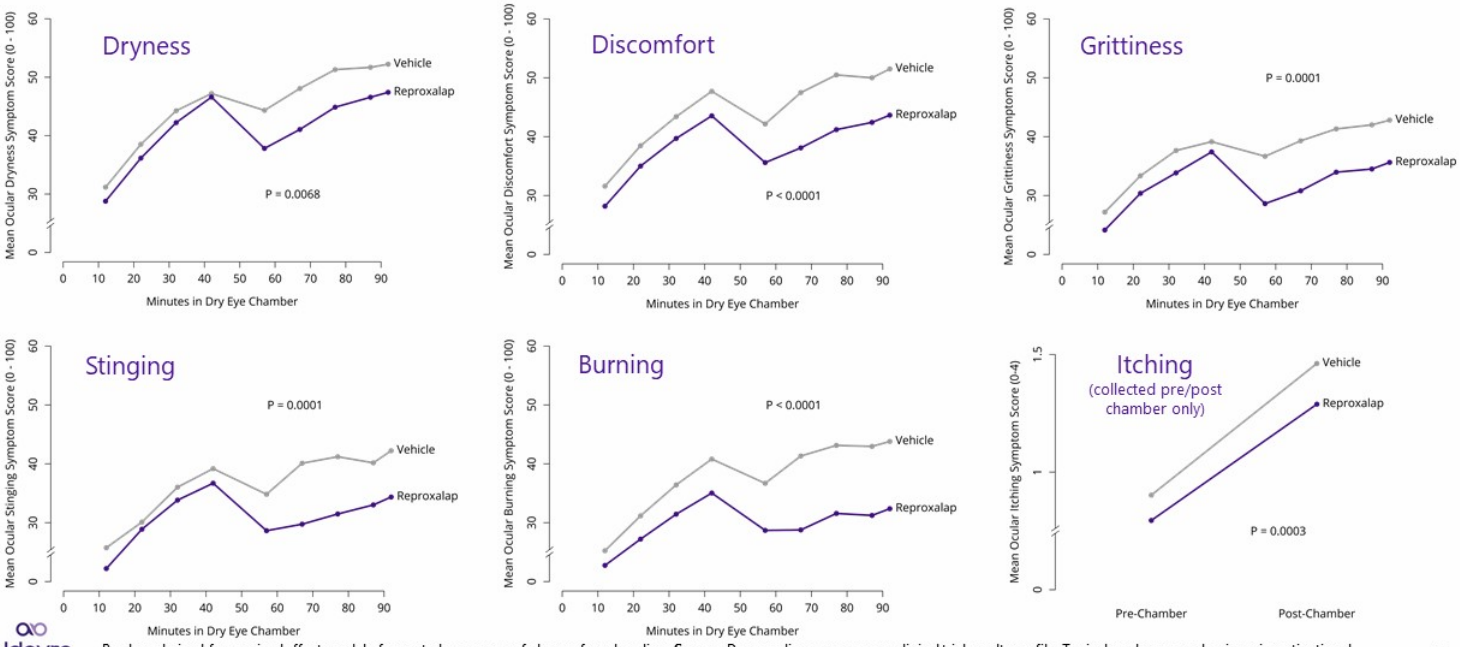
In the Dry Eye Disease Crossover Trial, the Multiplicity-Controlled Schirmer Test ≥10mm Responder Secondary Endpoint Was Achieved

Schirmer Test Responder Analysis

	Reproxalap	Vehicle
≥10 mm tear production post-Dose #4 on Day 1	48%	41%
Odds ratio (95% confidence interval)†	1.551 (1.029, 2.338)	
P value versus vehicle†	0.0361	

† Generalized estimating equation analysis of Schirmer test score ≥10mm pre- and post-Dose #4 on Day 1. **Source**: Dry eye disease crossover clinical trial results on file. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

In the Dry Eye Disease Crossover Trial, Secondary Endpoints for All Assessed Symptoms Were Achieved



P values derived from mixed effect model of repeated measures of change from baseline. **Source:** Dry eye disease crossover clinical trial results on file. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

The Dry Eye Disease Crossover Trial Met Each of the Sign Endpoints Intended to be Submitted to Support a Potential NDA

- The results suggest that a crossover design may reduce the high degree of variability characteristic of dry eye disease clinical trials.
- The primary endpoints of ocular redness and Schirmer test were achieved.
- The Schirmer test ≥10mm responder analysis, which was also achieved, correlates with symptomatic improvement[†], consistent with the achievement of secondary endpoints for each of the assessed symptoms (dryness, discomfort, grittiness, stinging, burning, and itching).
- Consistent with prior trials, no clinically significant safety signals were observed.
- A pre-NDA (New Drug Application) meeting has been scheduled for third quarter of 2022.
- Clinical data submitted to the NDA[‡] is expected to encompass acute (single-day dosing, dry eye chamber) and chronic (12-week) assessments, as well as parallel-group and crossover clinical designs, offering what is expected to be unparalleled analysis of rapid and sustained activity across a combination of challenge and field-based assessments.

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[†]Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000;118(5):615-21. [‡]NDA submission requirements depend, in part, on clinical safety results and regulatory feedback. The NDA submission is expected to include a combination of prespecified, post-hoc, primary, secondary, multiplicity-controlled, and nominal p-value endpoints. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

Reproxalap May Have the Potential to Address Significant Unmet Needs in Dry Eye Disease

- Over the past ~12 months, Aldeyra has met with 40 MDs and 25 ODs, attended 8 conferences, and published 1 abstract[†] and 6 peer-reviewed manuscripts.[‡]
- In conjunction with ClearView Healthcare Partners, Aldeyra has completed target product profile testing with 40 eyecare professionals and 20 dry eye disease patients.
  - With lifitegrast and cyclosporine, ~60%-70% of patients discontinue treatment with median time to discontinuation of ~1 month and ~3 months, respectively.[*]
  - Among healthcare providers, the target product profile of rapid onset of action and improvement in dryness symptoms was viewed as highly favorable.[§]
  - Among dry eye disease patients, the target product profile of reduction in symptoms and redness was viewed as highly favorable.[§]
- Pending FDA feedback, reproxalap, if approved, has the potential to be the first drug label to include clinical data for multiple objective signs of dry eye disease.

[†]Holland EJ, Cavanagh B, Machatha ST, et al. The Novel RASP Modulator Reproxalap Rapidly Improves Signs and Symptoms of Dry Eye Disease: The TRANQUILITY Run-In Cohort. Paper session presented at: Ocular Surface Disease III. ASCRS;2022 Apr 23; Washington, D.C. [‡]Cavanagh B, Gomes PJ, Starr CE, et al. Ophthalmol Ther. 2022;11(4):1449-61. Clark D, Karpecki P, Salapatek AM, et al. Clin Ophthalmol. 2022;16:15-23. McMullin D, Clark D, Cavanagh B, et al. Clin Ophthalmol. 2021;15:3889-3900. Clark D, Sheppard J, Brady TC. J Ocul Pharmacol Ther. 2021;37(4):193-99. Clark D, Cavanagh B, Shields AL, et al. Am J Ophthalmol. 2021;230:60-7. Clark D, Tauber J, Sheppard J, Brady TC. Early Onset and Broad Activity of Reproxalap in a Randomized, Double-Masked, Vehicle-Controlled Phase 2b Trial in Dry Eye Disease. Am J Ophthalmol. 2021 Jun;226:22-31. [§]ClearView analysis of market research conducted Q4 2021 – Q1 2022. [*]White DE, Zhao Y, Ogundele A, Fulcher N, Acs A, Moore-Schiltz L, Karpecki PM. Real-World Treatment Patterns Of Cyclosporine Ophthalmic Emulsion And Lifitegrast Ophthalmic Solution Among Patients With Dry Eye. Clin Ophthalmol. 2019 Nov 22;13:2285-2292.Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

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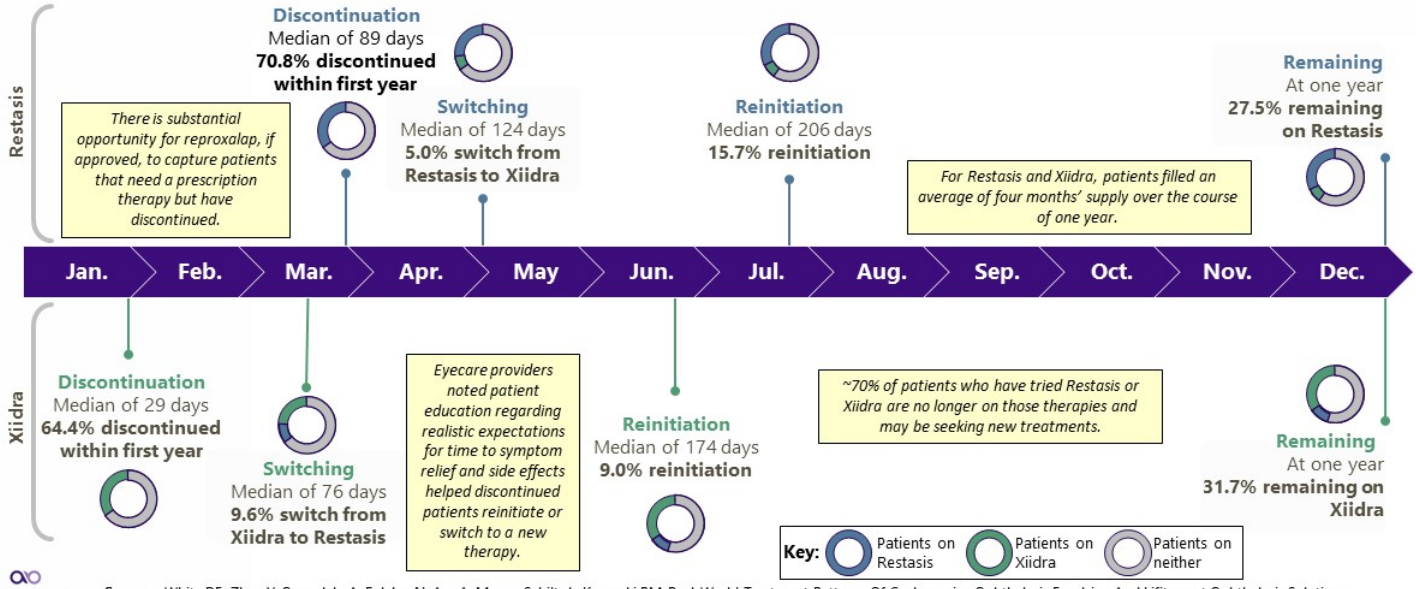
With Currently Available Dry Eye Disease Therapies, Discontinuation and Switching Rates are Early and Prevalent for Most Patients

Illustrative Patient Experience with Restasis® and Xiidra® in Year One



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Sources: White DE, Zhao Y, Ogundele A, Fulcher N, Acs A, Moore-Schiltz L, Karpecki PM. Real-World Treatment Patterns Of Cyclosporine Ophthalmic Emulsion And Lifitegrast Ophthalmic Solution Among Patients With Dry Eye. Clin Ophthalmol. 2019 Nov 22;13:2285-2292. Eyecare provider Interviews; ClearView analysis of market research conducted Q4 2021 – Q1 2022.

Surveyed Eyecare Providers Viewed Reproxalap's Potential Benefits Highly Favorably

Key Healthcare Provider Feedback

- Rapid onset of action is differentiated from existing options and likely to improve compliance.
- Ocular dryness and related symptoms are the key metrics for activity in dry eye disease.
- Redness improvement may allow for reduction in number of therapies used (e.g., not needing vasoconstrictors).

Key Drivers of Eyecare Provider Enthusiasm

Strength of Value Proposition

Onset of Action

Enthusiasm: Low — High

- Rapid impact on dryness may improve patient compliance
- 90-minute redness reduction is valuable for a subset of patients

"Significant dryness improvement in 8 days is impressive and highly valuable." – MO Ophtho.

Dryness

Enthusiasm: Low — High

- Considered an important measure of efficacy as dryness is a common driver of patient discomfort

"Getting the patient comfortable by reducing dryness is what's most important." – SO Ophtho.

Redness

Enthusiasm: Low — High

- 15 – 30% of DED patients report redness as a driving concern

"I have some patients who complain about redness, and this could help with compliance for them." – HP Optom.

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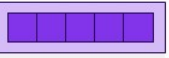
Source: Eyecare provider Interviews (n=40); ClearView analysis of market research conducted Q4 2021 – Q1 2022. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials.

Patient Research Indicates Value for a Dry Eye Disease Therapy that May Reduce Symptomatic Burden and Ocular Redness

Efficacy Feedback (Patients)

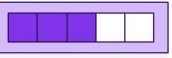
Dryness *Importance* 

- Patients noted ocular dryness as one of their top complaints amongst symptoms of dry eye disease.
  - Reproxalap's targeting of dryness was **viewed highly favorably** as this symptom impacts daily activities and leads to a lower quality of life.
- Overall, **patients placed a greater value on dryness** than redness.

"The eye dryness is so terrible it really does affect my daily life. I love that this drug is going after dryness." – Severe Patient

"I definitely care about my dryness being resolved first before anything else." – Mild Patient

"I don't think I would take a drug if it didn't help my dryness because that's my biggest problem." – Moderate Patient

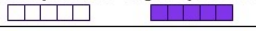
Redness *Importance* 

- Redness was mainly viewed as **"a nice-to-have not a need-to-have."**
- Some patients expressed redness as a top complaint and **viewed the redness endpoint as highly valuable.**

"I hate when my eyes are red. This sounds amazing because it can help my dry eye and resolve my redness!" – Moderate Patient

"My eyes never really get red, so I don't care very much about the redness endpoint." – Moderate Patient

"My eyes get red sometimes. Its annoying so I guess the fact that this targets redness too is a bonus." – Severe Patient

Key: ***Low Importance*** ***High Importance*** 

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Source: Patient Interviews (n=40); ClearView analysis of market research conducted Q4 2021 – Q1 2022. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials

Pending FDA Feedback, Reproxalap Has the Potential to Be the First Dry Eye Disease Drug Approved Based on Multiple Objective Signs

Drug	Indication Excerpt from Label	Clinical Data in Label
Restasis®	Increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca	Schirmer test ≥10 mm responder analysis
Tyrvaya®	Treatment of the signs and symptoms of dry eye disease	Schirmer test ≥10 mm responder analysis, mean change in Schirmer test score
Cequa®	Increase tear production in patients with keratoconjunctivitis sicca (dry eye)	Schirmer test ≥10 mm responder analysis
Eysuvis®	Short-term (up to two weeks) treatment of the signs and symptoms of dry eye disease	Ocular discomfort severity score, conjunctival hyperemia score
Xiidra®	Treatment of the signs and symptoms of dry eye disease	Eye dryness score, inferior fluorescein staining score

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Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 1,800 patients with no observed safety concerns; mild and transient instillation site discomfort is the most commonly reported adverse event in clinical trials. All trademarks are the property of their respective owners.

Exhibit 99.2

Aldeyra Therapeutics Achieves Primary Endpoints in Dry Eye Disease Chamber Crossover Clinical Trial

- ***Reproxalap Statistically Superior to Vehicle for Both Primary Endpoints of Ocular Redness (P=0.0004) and Schirmer Test (P=0.0005)***
- ***Schirmer Test ≥10mm Responder Analysis Multiplicity-Controlled Secondary Endpoint Achieved (P=0.0361)***
- ***Secondary Endpoints Achieved for All Symptoms Assessed: Dryness (P=0.0068), Discomfort (P<0.0001), Grittiness (P=0.0001), Stinging (P=0.0001), Burning (P<0.0001), and Itching (P=0.0003)***
- ***Company to Host Conference Call at 8:00 a.m. ET Today***

LEXINGTON, Mass.--(BUSINESS WIRE)--July 12, 2022--Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra) today announced the achievement of the primary endpoints in a sequence-randomized, double-masked, vehicle-controlled crossover clinical trial of 0.25% reproxalap ophthalmic solution, an investigational new drug candidate, for the treatment of dry eye disease. Reproxalap was statistically superior to vehicle for each of the two prespecified primary endpoints, ocular redness in a dry eye chamber (P=0.0004) and Schirmer test (P=0.0005), a measure of tear production, after a single day of dosing. The secondary endpoint of Schirmer test ≥10 mm responder analysis, which was multiplicity-controlled, was also achieved (P=0.0361).

“Statistical significance in favor of reproxalap over vehicle for all three dry eye disease signs that we intend to submit to a New Drug Application, in addition to observed rapid symptomatic improvement, favorably positions reproxalap, if approved for sale, as a potentially differentiated therapeutic option for the treatment of dry eye disease,” stated Todd C. Brady, M.D., Ph.D., President and Chief Executive Officer of Aldeyra.

Relative to vehicle, statistically significant reduction in ocular redness was observed following treatment with reproxalap as soon as 10 minutes after dry eye chamber entry, which was the first time point assessed, and over the majority of chamber assessment time points, including the final time point 90 minutes after chamber entry. Schirmer test, which was assessed approximately 10 minutes before and after the fourth dose of reproxalap or vehicle, was statistically significant in favor of reproxalap at both time points, indicating the potential activity of prior dosing as well as additional activity of the fourth dose over a single day of drug administration. The Schirmer test ≥10 mm responder analysis has been reported to correlate with symptomatic improvement in dry eye disease,[1] and achievement of the responder endpoint is consistent with the symptomatic improvement observed in the crossover clinical trial: reproxalap was statistically lower than vehicle for the secondary endpoints of ocular dryness (P=0.0068), discomfort (P<0.0001), grittiness (P=0.0001), stinging (P=0.0001), burning (P<0.0001), and itching (P=0.0003) symptoms.

No safety signals were observed in the trial, and reproxalap was well tolerated; there were no treatment-emergent moderate or serious adverse events. Three patients discontinued due to adverse events, two during vehicle administration and one during reproxalap administration. Reproxalap has now been studied in over 1,800 patients. The most common reported adverse event in clinical trials is mild and transient instillation site discomfort.

Pending discussion with the U.S. Food and Drug Administration (FDA), Aldeyra intends to submit the crossover clinical trial, which was designed to be adequate and well-controlled, as part of a dry eye disease New Drug Application (NDA) for reproxalap, including data on ocular redness, Schirmer test, and the Schirmer test ≥10 mm responder analysis. A pre-NDA meeting with the FDA has been scheduled for the third quarter of 2022. The NDA submission is expected to include a comprehensive set of data from acute and chronic clinical trials, as well as a combination of challenge and field-based assessments and parallel-group and crossover clinical trial designs.

“With another set of positive clinical results showing improvement in both the signs and symptoms of dry eye disease, I believe that reproxalap is an eagerly anticipated advancement for our patients suffering from dry eye disease because available therapies are often inadequate,” stated John P. Berdahl, M.D., a specialist in diseases of the anterior segment at Vance Thompson Vision and Professor of Ophthalmology at the Sanford School of Medicine.

Conference Call Information

Aldeyra will host a conference call to discuss this announcement at 8:00 a.m. ET today, July 12, 2022. The dial-in numbers are (844) 200-6205 for domestic callers and (646) 904-5544 for international callers. The access code is 853619. 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 Reproxalap

Reproxalap is an investigational first-in-class small-molecule modulator of RASP (reactive aldehyde species), which are elevated in ocular and systemic inflammatory disease. Reproxalap's unique mechanism of action has been supported by the demonstration of statistically significant and clinically relevant activity in multiple physiologically distinct late-phase clinical indications.

About Dry Eye Disease

Dry eye disease is a common inflammatory disease estimated to affect 39 million or more adults in the United States.[2] 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, RASP may contribute to ocular inflammation, diminished tear production, ocular redness, and changes in tear lipid composition.[3] By diminishing RASP levels, Aldeyra's lead RASP modulator reproxalap represents a novel and differentiated approach for the treatment of the symptoms and signs of dry eye disease.

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 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 (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 the timing and submission of a potential NDA; the anticipated timing of enrollment and results from Aldeyra's clinical trials; expectations regarding the results of the upcoming Type B Pre-NDA meeting, including the FDA's acceptance of Aldeyra's post-hoc review of data, the FDA's agreement with Aldeyra's methods of analyzing data and Aldeyra's intention to submit the crossover clinical trial as part of its NDA; 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, 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 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/. Additional factors may be set forth in those sections of Aldeyra's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, expected to be filed with the SEC in the third 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.

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[1] Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol. 2000;118(5):615-21.
[2] Company estimates and Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014;157(4):799-806.
[3] 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.

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