

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): April 25, 2024

ALDEYRA THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-36332
(Commission File No.)

20-1968197
(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.

On April 25, 2024, Aldeyra Therapeutics, Inc. (“Aldeyra”) intends to make a slide presentation at its 2024 Research & Development Day (the “2024 Research and Development Day”) in person in New York City and by webcast on Aldeyra’s website. A copy of Aldeyra’s slide presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

The furnishing of the attached slide presentation is not an admission as to the materiality of any information contained therein. The information contained in the slide presentation is summary information that is intended to be considered in the context of more complete information included in Aldeyra’s filings with the Securities and Exchange Commission (“SEC”) and other public announcements that Aldeyra has made and may make from time to time by press release or otherwise. Aldeyra undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate.

Various statements to be made during the conference call are “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 reproxalap and other product candidates; the outcome and expected timing and the results of Aldeyra’s planned clinical trials; the outcome and timing of the FDA’s review, acceptance and/or approval of a NDA resubmission for reproxalap and the adequacy of the data included in the original NDA and the potential NDA resubmission. 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, 2023, which is on file with the SEC and available on the SEC’s 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 March 31, 2024, expected to be filed with the SEC in the second quarter of 2024, 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 conveyed on the conference call is provided only as of the date of the call, and Aldeyra undertakes no obligation to update any forward-looking statements presented on the conference call on account of new information, future events, or otherwise, except as required by law.

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.

On April 25, 2024, Aldeyra issued a press release regarding its 2024 Research & Development Day (the “Press Release”). 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	Slide Presentation of Aldeyra Therapeutics, Inc. dated April 25, 2024.
99.2	Press Release of Aldeyra Therapeutics, Inc. dated April 25, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, 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: April 25, 2024



CORPORATE

2024 Research & Development Day

April 25, 2024

Nasdaq: ALDX

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Todd C. Brady, M.D., Ph.D., Chief Executive Officer, Aldeyra Therapeutics

Welcome and Opening Remarks

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 future expectations, plans and prospects, including, without limitation, statements regarding: the goals, opportunity, and potential for reproxalap, ADX-2191, ADX-246, ADX-248, and ADX-629; anticipated clinical or regulatory milestones for reproxalap, ADX-2191, ADX-246, ADX-248, and ADX-629; FDA agreement with the clinical development plan for reproxalap; expectations regarding the results of scheduled FDA meetings and discussions, clinical trial initiations and completions, and the timing and nature of NDA or other submissions to the FDA; Aldeyra's business, research, development and regulatory plans or expectations; and the structure, timing and success of Aldeyra's planned or pending clinical trials. The results of earlier preclinical or clinical trials may not be predictive of future results. 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," "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.

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 of, and clinical and regulatory plans or expectations for Aldeyra's investigational new drugs (including reproxalap, ADX-2191, ADX-246, ADX-248, and ADX-629), 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, which regulatory review timeline may be flexible and subject to change based on the regulator's workload and other potential review issues, preclinical and clinical results, regulatory developments in the United States and other countries, and other factors any of which could result in changes to Aldeyra's development plans and programs or delay the initiation, enrolment, 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 April 25, 2024**, 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.



Agenda

9:00 – 9:45 a.m.

TOPIC

**Opening Remarks, RASP Overview, and
ReproXalap Dry Eye Disease Development Plan**

PRESENTER

Todd C. Brady, M.D., Ph.D.
Chief Executive Officer, Aldeyra Therapeutics

9:45 – 10:30 a.m.

Next-Generation RASP Modulators

Adam Brockman, Ph.D.
Senior Director Translational Science, Aldeyra Therapeutics

10:30 – 10:45 a.m.

Break

10:45 – 11:30 a.m.

Retinitis Pigmentosa Overview

Ramiro S. Maldonado MD
Ophthalmologist, Duke Center for Ophthalmic Genetics

11:30 a.m. – 12:00 p.m.

**ADX-2191 for the Treatment of Retinitis
Pigmentosa**

Todd C. Brady, M.D., Ph.D.

12:00 – 12:30 p.m.

Lunch

12:30 – 1:00 p.m.

Pipeline, Milestones, and Concluding Remarks

Todd C. Brady, M.D., Ph.D.



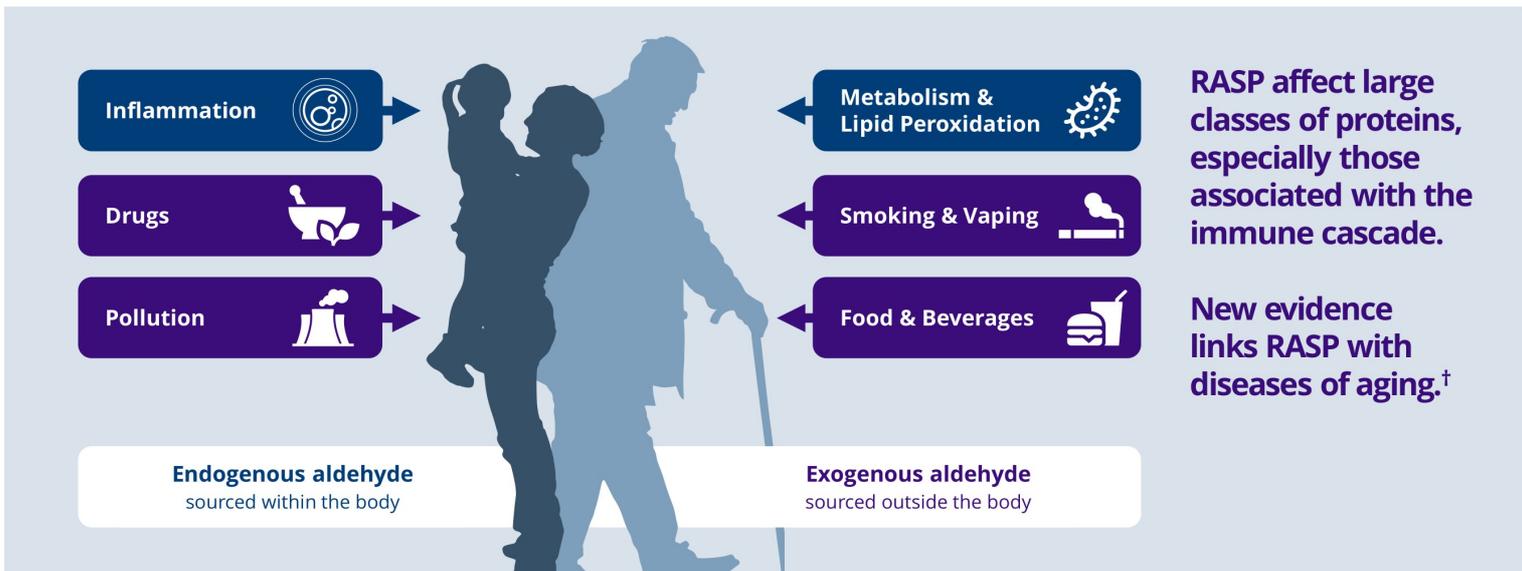
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Todd C. Brady, M.D., Ph.D., Chief Executive Officer, Aldeyra Therapeutics

RASP Overview

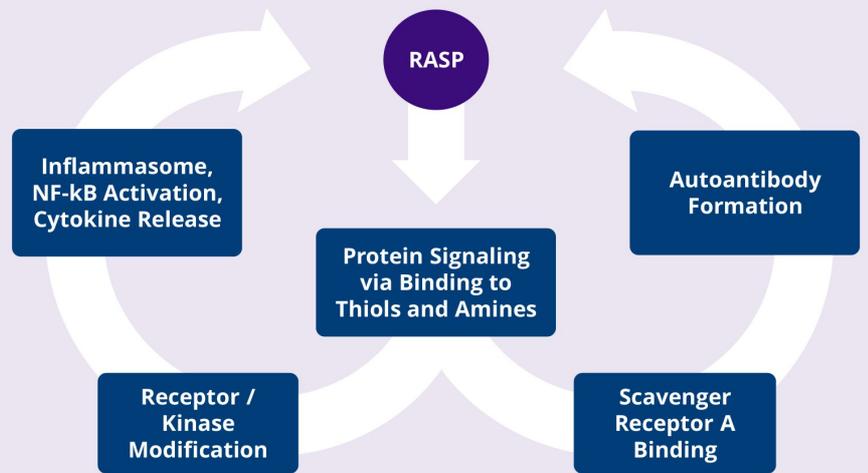
RASP Are Toxic, and Represent a Novel, Potentially Broadly Applicable Pharmaceutical Target



[†]Oka Y, Nakazawa Y, Shimada M, Ogi T. Endogenous aldehyde-induced DNA-protein crosslinks are resolved by transcription-coupled repair. Nat Cell Biol. 2024 Apr 10. RASP = reactive aldehyde species.

RASP Induce Inflammation via Multiple Mechanisms

- Aldehydes **covalently bind** thiol (Michael addition) and amine (Schiff base) residues on proteins.
- Direct protein binding leads to **conformational and functional** changes in proteins, which in turn initiate a pro-inflammatory signaling cascade.
- Aldehyde-protein adducts are ligands for **Scavenger Receptor A**, subsequently leading to autoantibody formation against the adducted protein.



RASP Modulation Represents a Novel Pharmacology

Traditional pharmacology targets specific proteins and is generally limited to two actions: on or off.



Activating or inhibiting specific proteins on a sustained basis, which rarely occurs in nature, may lead to toxicity and could limit activity.



RASP modulation may allow for control of protein *systems*, without turning any single protein on or off.



Systems-based pharmacology could potentially lead to broader-based activity with less toxicity associated with activation or inhibition of specific proteins.



Todd C. Brady, M.D., Ph.D., Chief Executive Officer, Aldeyra Therapeutics

Reproxalap Dry Eye Disease Development Plan

Phase 3 Clinical Trial of Reproxalap in a Dry Eye Chamber†

Design

- Randomized, double-masked, vehicle-controlled dry eye chamber challenge

Dosing

- Visit 1: Medical screening
- Visit 2: Vehicle dry eye chamber (dosing just before and 50 minutes after entry)
- Visit 3: Four doses of randomized treatment (reproxalap or vehicle)
- Visit 4: Randomized dry eye chamber (dosing just before and 50 minutes after entry)

Size

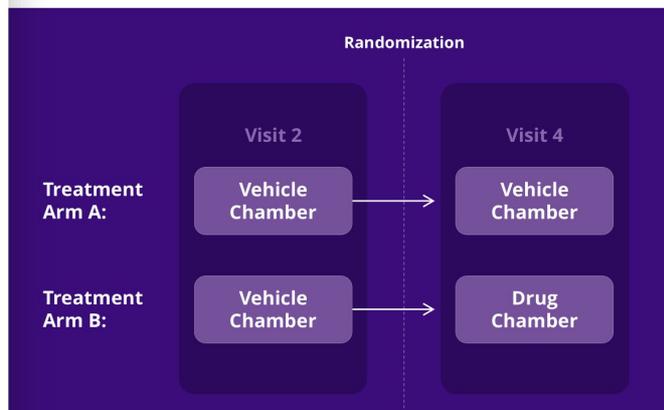
~100 dry eye disease patients

Primary Endpoint

Ocular discomfort score

Other Endpoints

Safety



Pending clinical trial results, feedback from ongoing FDA discussions, and other factors, NDA resubmission expected in H2 2024†‡

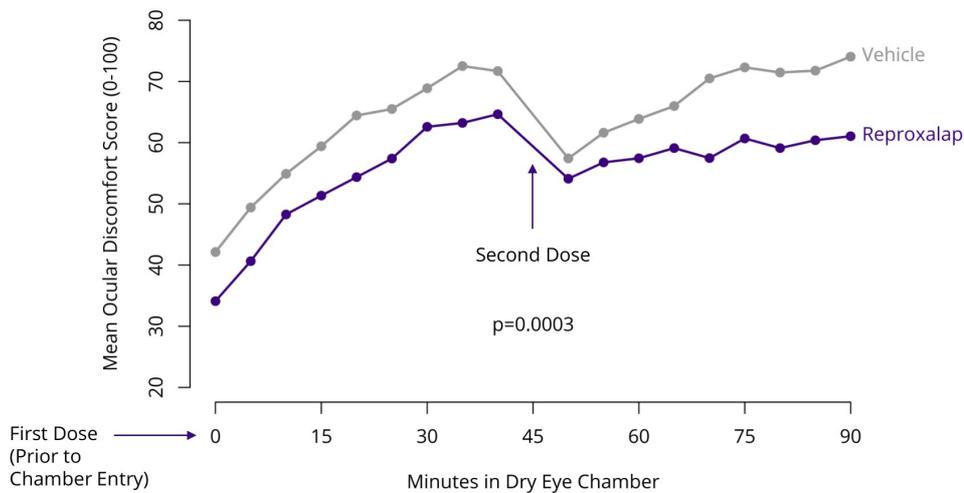


†The timing of clinical trials depends, in part, on the availability of clinical research facilities and staffing, the ability to recruit patients, and the number of patients in the trial.

‡Regulatory review and discussion timelines are flexible and subject to change based on the regulator's workload and other potential review issues.

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Based on Pooled Data from Four Dry Eye Chamber Trials, Ocular Discomfort Score was Lower with Reproxalap than with Vehicle



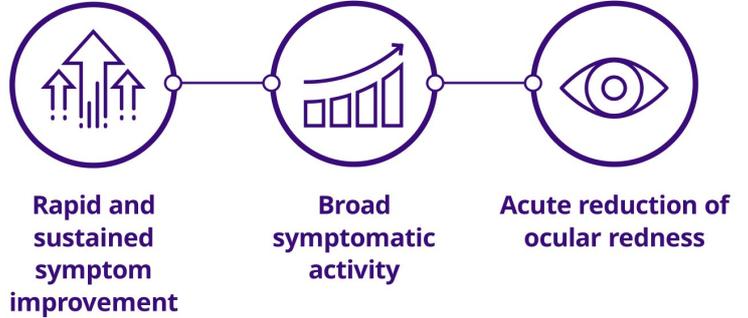
Ocular discomfort data are derived from four previously completed dry eye chamber clinical trials of reproxalap vs. vehicle, encompassing approximately 110 patients and incorporating trial conduct and statistical analysis amendments.

 Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 2,400 patients with no observed safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

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Reproxalap Represents a Novel Potential Therapeutic Approach in Dry Eye Disease with Rapid Activity in Clinical Trials

Potential advantages for patients and healthcare providers could effect a paradigm shift relative to standard of care.



Dry eye disease afflicts 39 million or more adults in the United States.[†]



[†]Company estimates and Am J Ophthalmol. 2014;157(4):799-806. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 2,400 patients with no observed safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

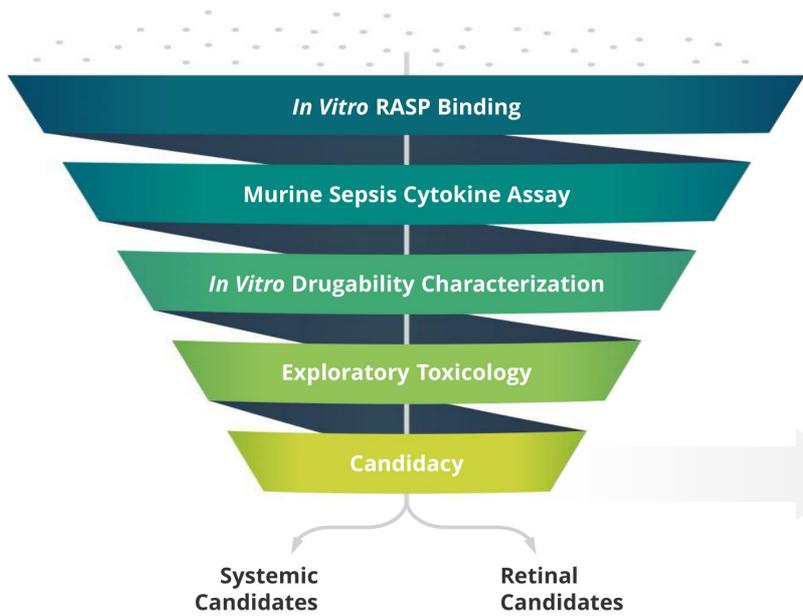
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Adam Brockman, Ph.D., DABT, Senior Director of Translational Science, Aldeyra Therapeutics

Next-Generation RASP Modulators

Aldeyra Has Developed the Leading RASP Modulator Discovery Platform



Aldeyra's RASP modulator discovery and development platform is unparalleled

ADX-629, ADX-246, and ADX-248



ADX-629, ADX-248, and ADX-246 are investigational drug candidates.

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Development Indications for New RASP Modulators Are Supported by Mechanistic Rationale

INDICATION	RASP RATIONALE	MODEL
Atopic Dermatitis	Upregulation of pro-inflammatory cytokines	Oxazolone atopic dermatitis
Alcoholic Hepatitis	Association with hepatotoxicity	Ethanol toxicity
Non-Opiate Analgesia	Activation of TRPV1 and TRPA1 pain receptors	Carrageenan inflammatory pain
Lipogenesis Modulation	Potentialiation of lipid synthesis	Diet-induced obesity



TRPA1 = transient receptor potential ankyrin 1. TRPV1 = transient receptor potential vanilloid 1. RASP = reactive aldehyde species.

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Atopic Dermatitis

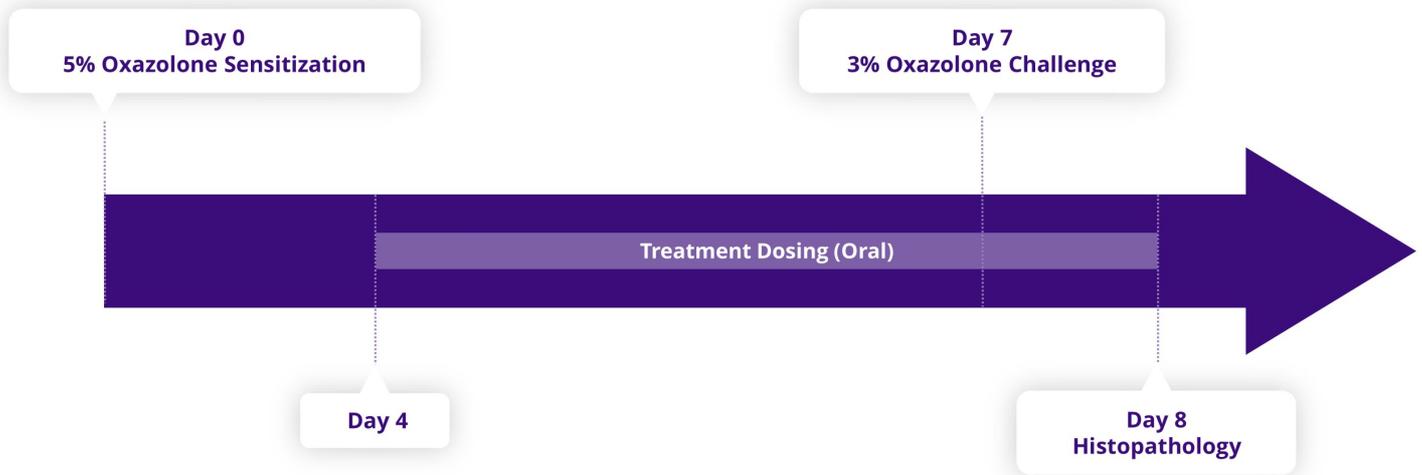
Statistical and Clinically Significant Improvement was Observed in Phase 2 Clinical Trial of RASP Modulator ADX-629 in Atopic Dermatitis



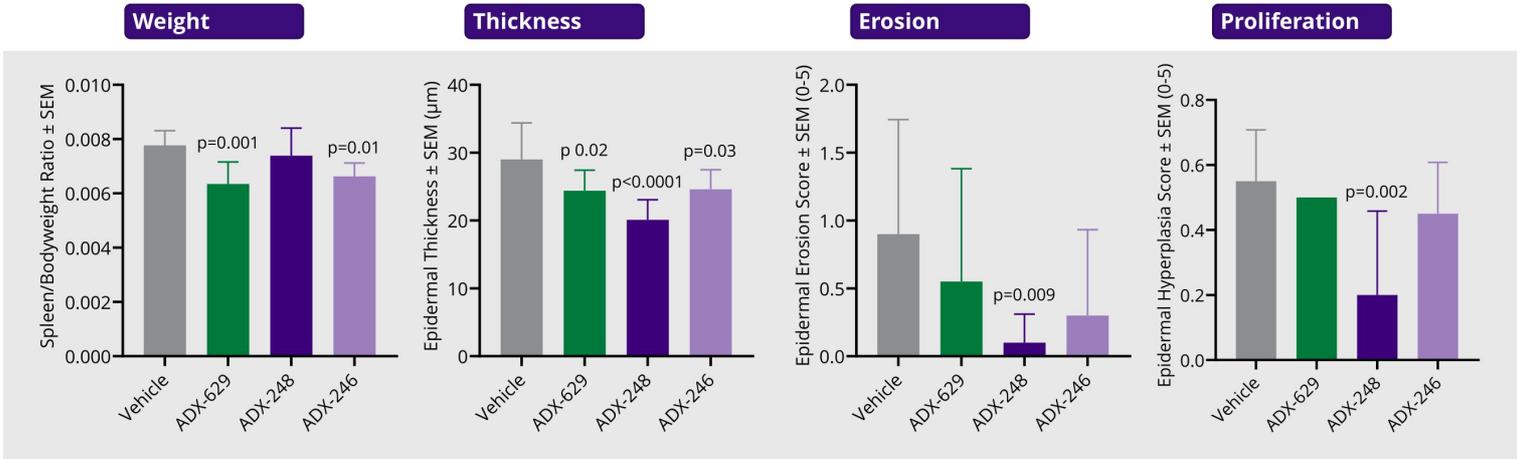
ADX-629 is an investigational drug candidate. SEM = standard error of mean.



Oxazolone Sensitization is a Well-Characterized Preclinical Model of Atopic Dermatitis



RASP Modulators ADX-629, ADX-248, and ADX-246 Reduced Histopathology and Spleen Weight in a Preclinical Model of Atopic Dermatitis



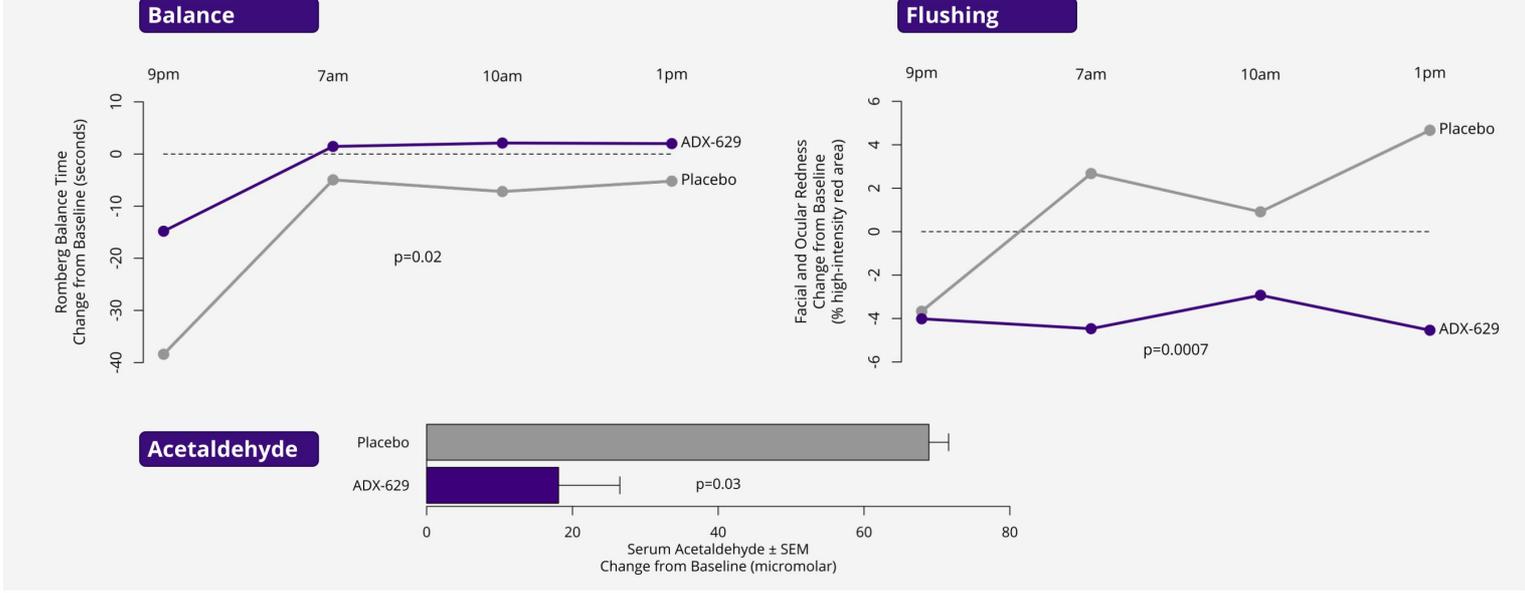
ADX-629, ADX-248, and ADX-246 are investigational drug candidates. SEM = standard error of mean.

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Alcoholic Hepatitis

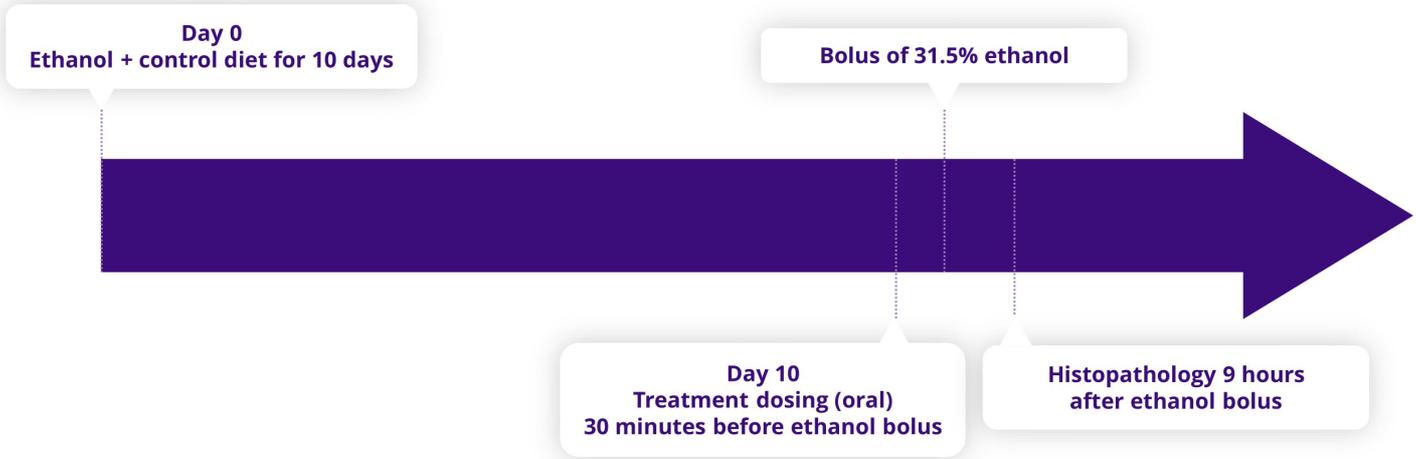
ADX-629 Improved Balance and Reduced Dermal Flushing and Acetaldehyde Levels in Phase 1/2 Ethanol Toxicity Clinical Trial



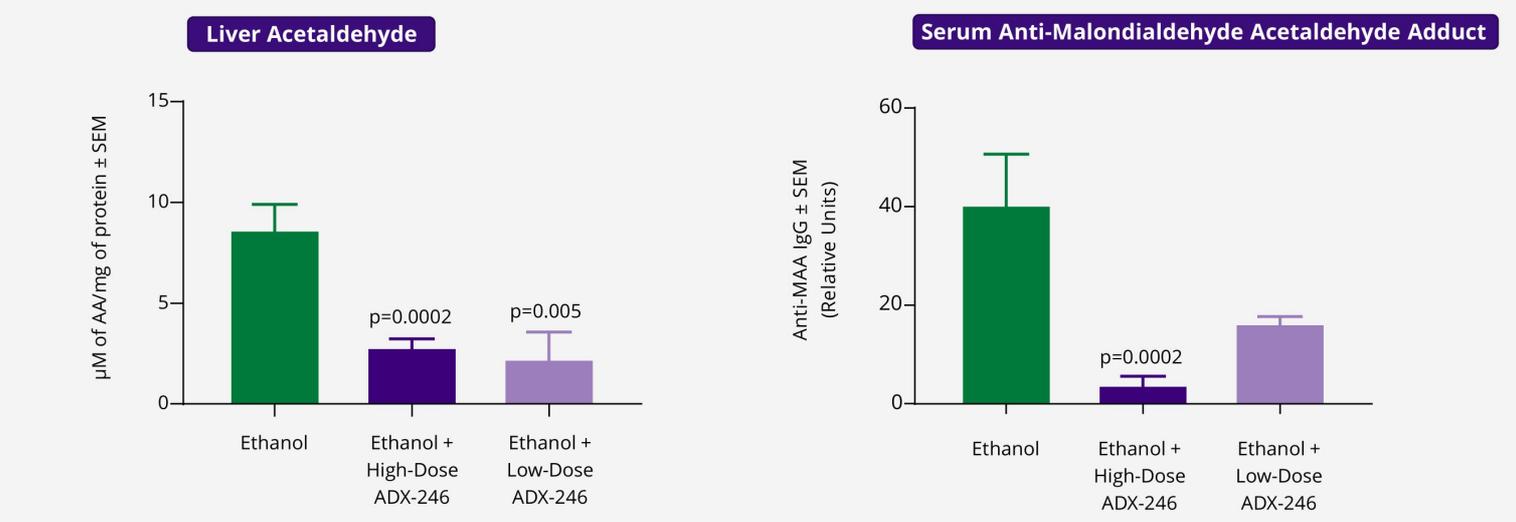
ADX-629 is an investigational drug candidate. SEM = standard error of mean. Data derived from mixed model for repeated measures adjusted for emesis, sequence, visit, and time point.



Preclinical Model of Ethanol-Induced Hepatitis Enables Detailed Assessment of the Pharmacodynamic Activity of RASP Modulation



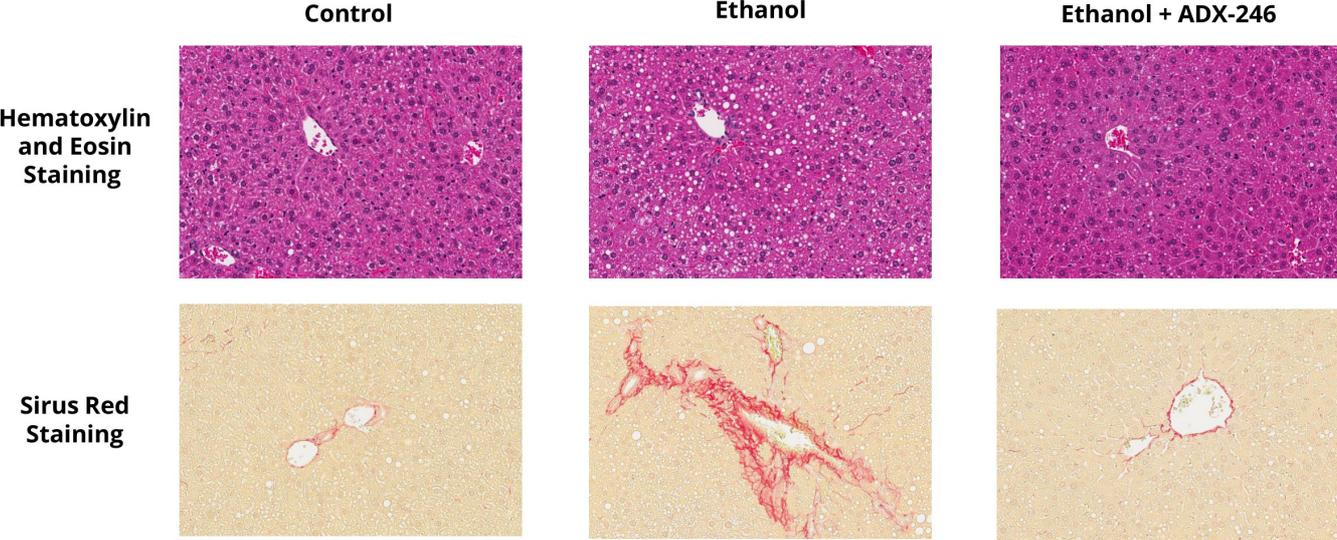
ADX-246 Decreased RASP Levels in Preclinical Model of Ethanol-Induced Hepatitis



ADX-246 is an investigational drug candidate. AA = acetaldehyde. MAA = malondialdehyde acetaldehyde adduct. SEM = standard error of mean.



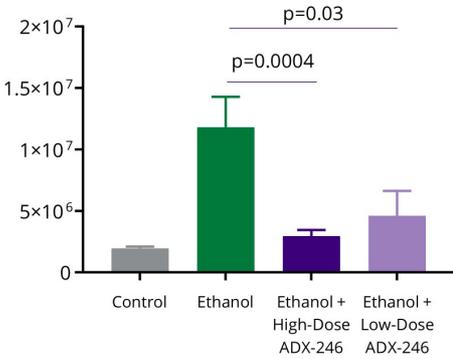
ADX-246 Diminished Histopathological Changes in Preclinical Model of Ethanol-Induced Hepatitis



ADX-246 Reduced Hepatic Levels of Lipids and Collagen in Preclinical Model of Ethanol-Induced Hepatitis

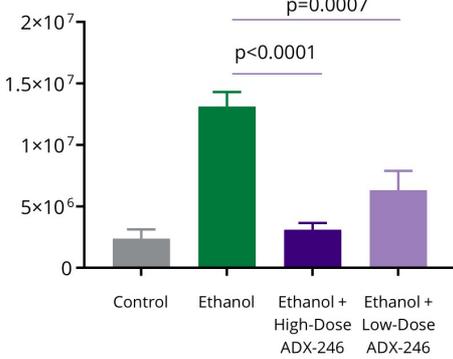
Collagen

Integrated Density \pm SEM (pixels)



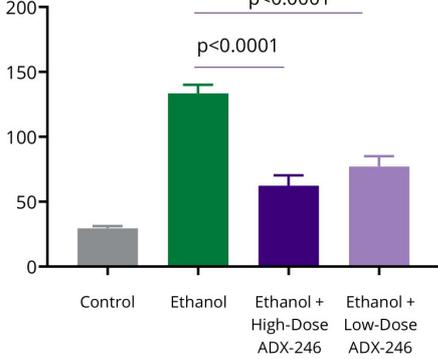
Total Lipids

Integrated Density \pm SEM (pixels)



Triglycerides

mg/dL Triglycerides per mg Protein \pm SEM

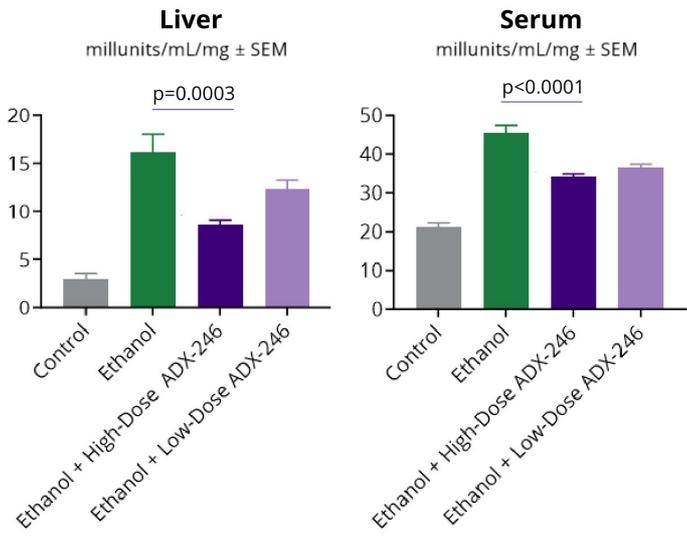


ADX-246 is an investigational drug candidate. SEM = standard error of mean.

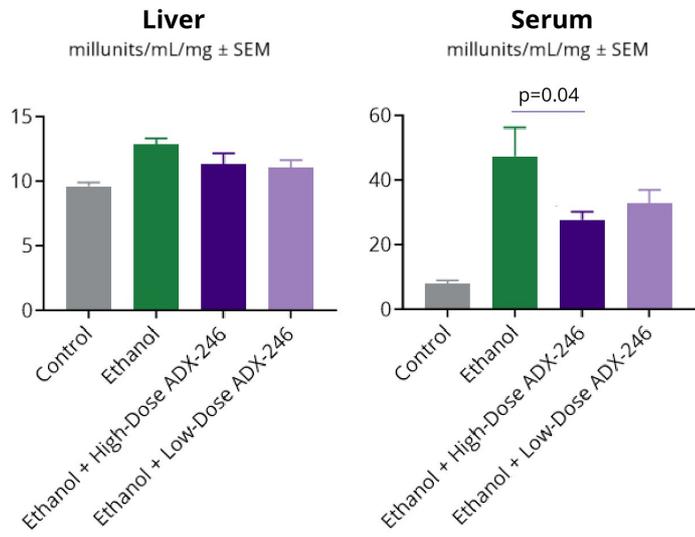
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ADX-246 Improved Liver Function Tests in Preclinical Model of Ethanol-Induced Hepatitis

Aspartate Aminotransferase (AST)



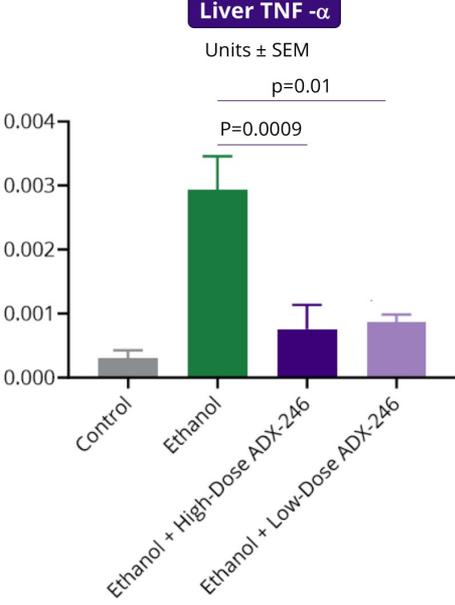
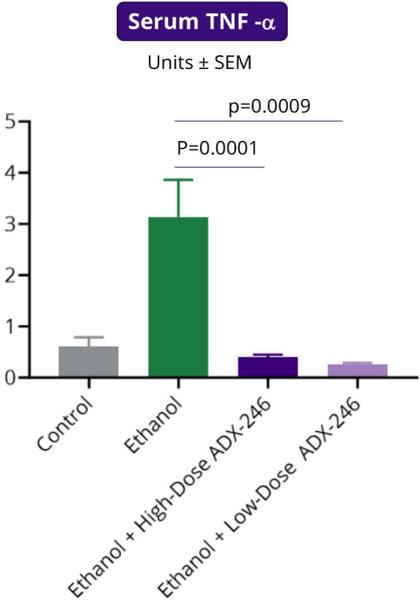
Alanine Aminotransferase (ALT)



ADX-246 is an investigational drug candidate. SEM = standard error of mean.



ADX-246 Decreased Levels of the Inflammatory Cytokine TNF- α in Preclinical Model of Ethanol-Induced Hepatitis



ADX-246 is an investigational drug candidate. SEM = standard error of mean. pg/mL = picogram/milliliter. TNF = tumor necrosis factor.

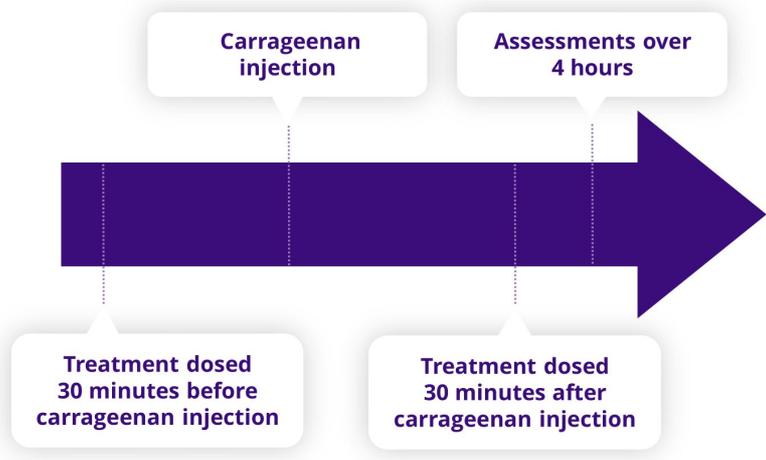


Non-Opiate Analgesia

The Carrageenan Inflammatory Pain Model Allows for Evaluation of Three Different Outcomes Associated with Inflammation

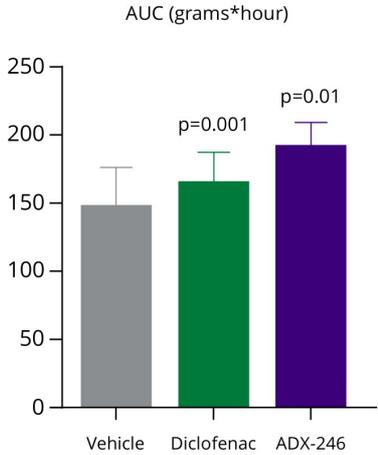
Test	Model	Assessment (units)
Von Frey	Mechanical Pain Tolerance	Force required for paw withdrawal (grams)
Hargreaves	Thermal Pain Tolerance	Time to withdrawal in response to heat (seconds)
Ankle Caliper	Swelling	Diameter of ankle (millimeters)

Orally Administered Diclofenac or ADX-246

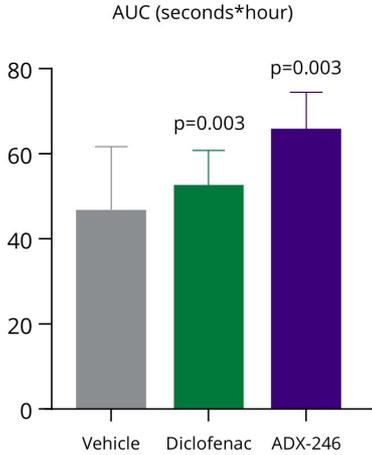


ADX-246 Demonstrated Statistically Significant Activity in the Carrageenan Inflammatory Pain Model

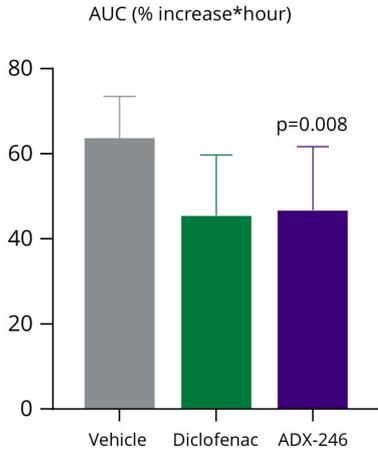
Mechanical Pain Tolerance



Thermal Pain Tolerance



Swelling



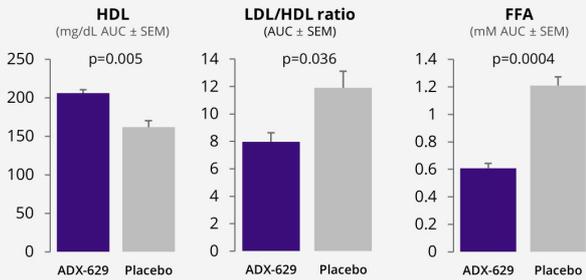
ADX-246 is an investigational drug candidate. SEM = standard error of mean. AUC = area under the curve.



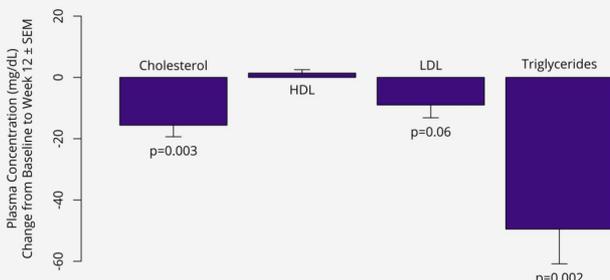
Lipogenesis Modulation

Statistically Significant Changes Observed in Lipid Profiles in Multiple Clinical Trials with RASP-Sequestering Molecule ADX-629

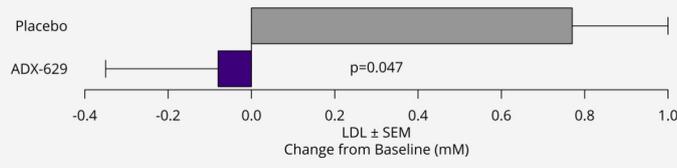
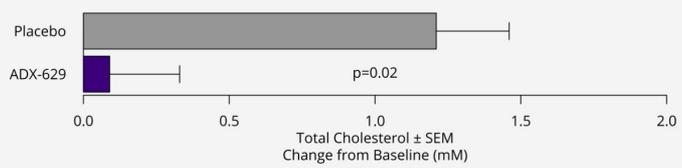
Phase 1 Clinical Trial



Phase 2 Psoriasis Clinical Trial



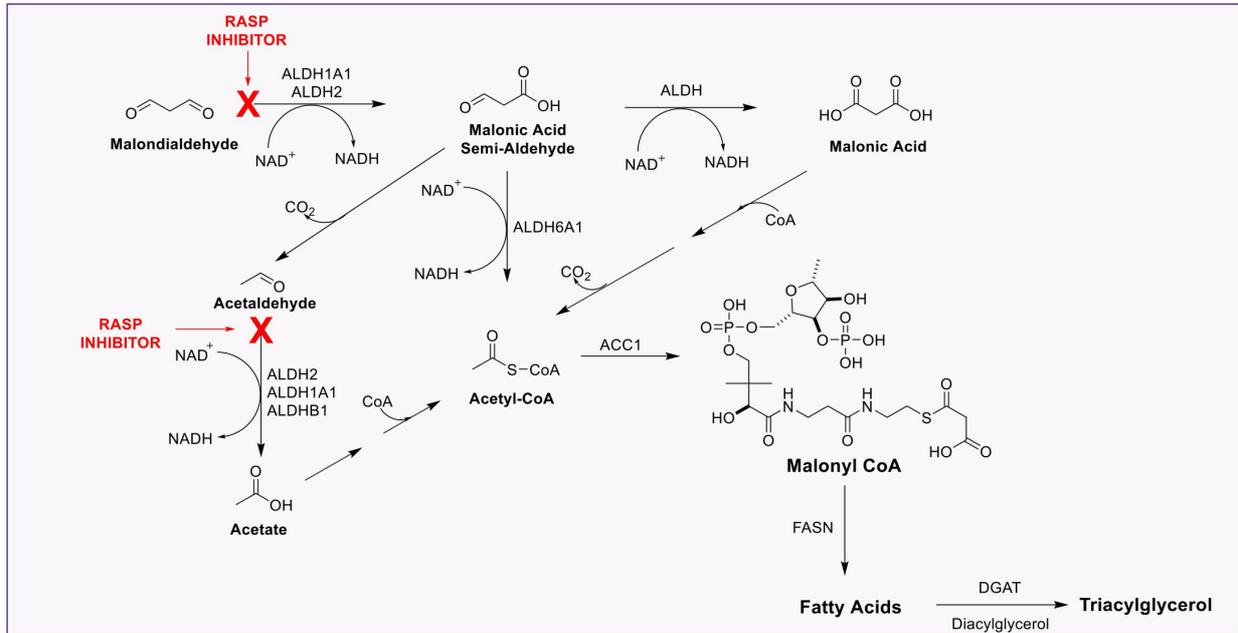
Phase 1/2 Ethanol Toxicity Clinical Trial



ADX-629 is an investigational drug candidate. SEM = standard error of the mean. HDL = high-density lipoprotein. LDL = low-density lipoprotein. FFA = free fatty acids. AUC = area under the curve. mM = millimolar.

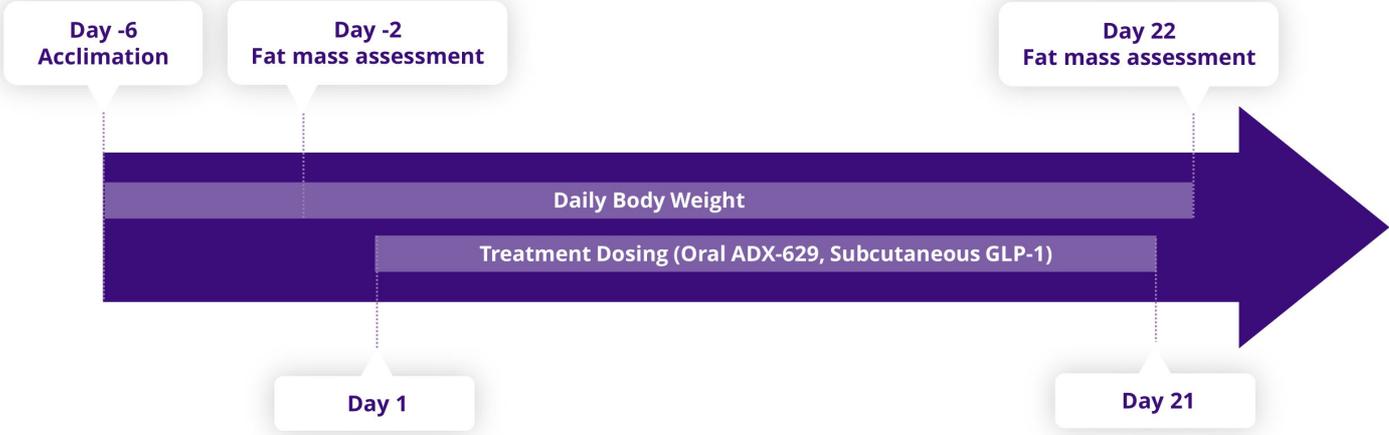


RASP May Potentiate Triglyceride Synthesis



ALDH = aldehyde dehydrogenase. DGAT = diglyceride acyl transferase. ACC1 = acetyl coenzyme A carboxylase. FASN = fatty acid synthase. CoA = coenzyme A. NAD = nicotinamide adenine dinucleotide.

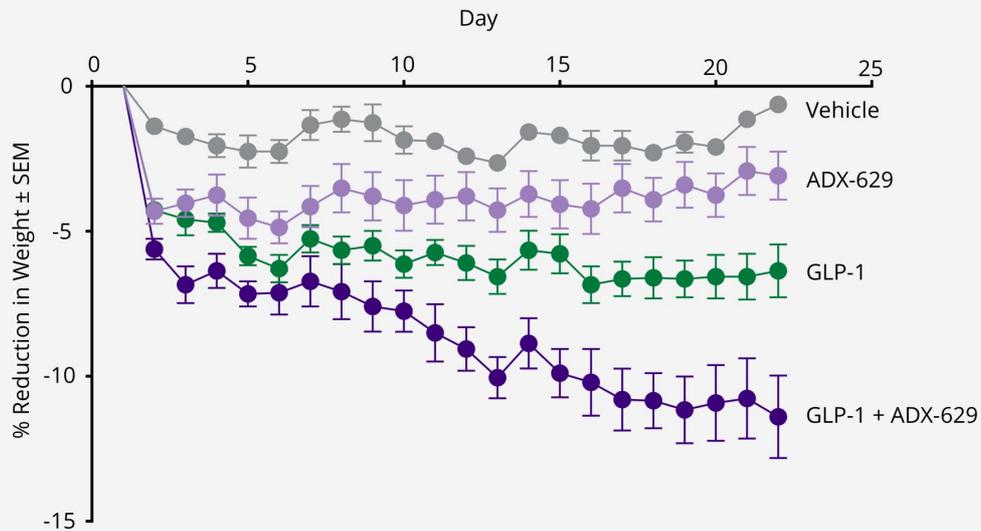
High-Fat Diet-Induced Obesity Model Allows for Assessment of Weight Loss and Body Composition



ADX-629 is an investigational drug candidate. GLP-1 = glucagon-like peptide 1.

Treatment with Oral ADX-629 Enhanced GLP-1 Weight Loss in Preclinical Model of Obesity

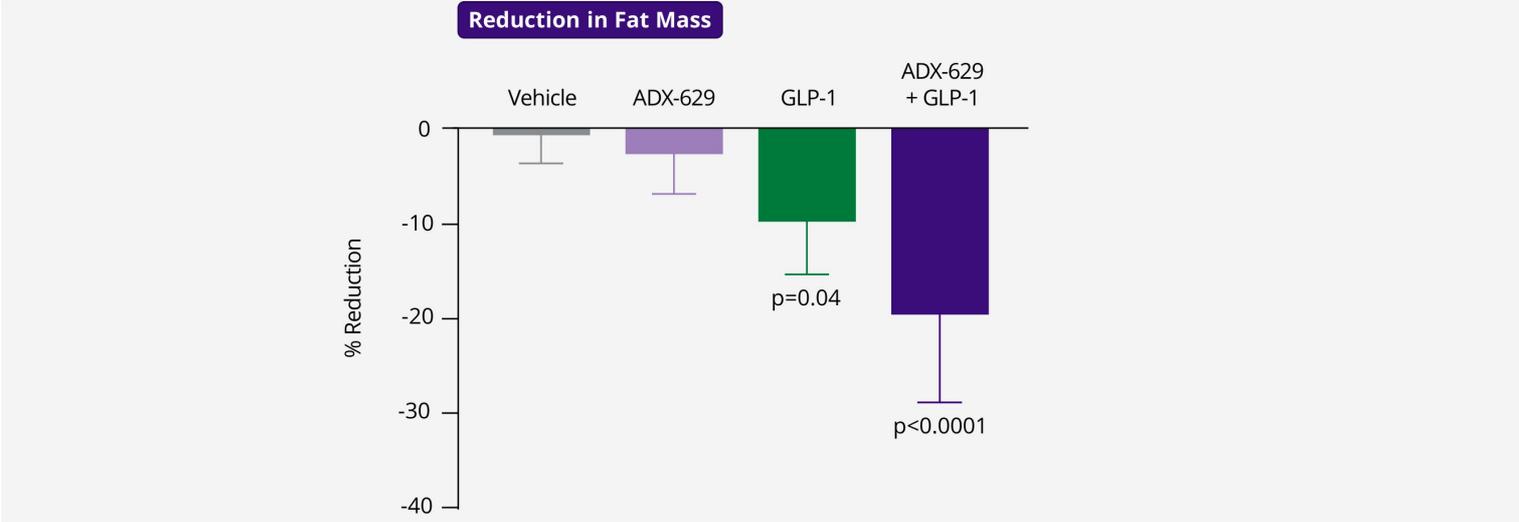
Weight Loss



ADX-629 is an investigational drug candidate. SEM = standard error of the mean. GLP-1 = glucagon-like peptide 1.



Treatment with Oral ADX-629 Enhanced GLP-1 Fat Mass Loss in Preclinical Model of Obesity



ADX-629 is an investigational drug candidate. SEM = standard error of the mean. GLP-1 = glucagon-like peptide 1.



Ramiro S. Maldonado, M.D., Assistant Professor of Ophthalmology, Duke University

Retinitis Pigmentosa: An Overview





Todd C. Brady, M.D., Ph.D. Chief Executive Officer

Phase 2 Clinical Trial of ADX-2191 in Retinitis Pigmentosa

ADX-2191 has the potential to be the first approved drug for retinitis pigmentosa, a clinical group of rare genetic eye diseases.

Retinitis pigmentosa refers to a group of inherited retinal diseases characterized by cell death and loss of vision.



- Retinitis pigmentosa **affects more than 1 million people** worldwide. Mutations leading to rhodopsin misfolding account for approximately one-third of cases.
- There is **no approved therapy** for retinitis pigmentosa.
- **U.S. FDA Orphan Drug Designation** for ADX-2191 for the treatment of retinitis pigmentosa was granted in August 2021.



Preclinical electroretinographic evidence in a P23H rhodopsin mutation mouse model of retinitis pigmentosa **suggests that methotrexate improves retinal function.**

ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. Sources: Aldeyra internal estimates; FASEB J. 34(8): 10146-10167, 2020. PBS = phosphate-buffered saline. MTX = methotrexate.

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ADX-2191: Phase 2 Clinical Trial Design in Retinitis Pigmentosa

Design

Single-center, dose-ranging, open-label clinical trial of ADX-2191 (400µg methotrexate in 0.05mL) in patients with retinitis pigmentosa

Inclusion Highlights

Diagnosis of retinitis pigmentosa due to rhodopsin gene mutations, including P23H

Dosing Regimen

Cohort A (n = 4):

Monthly injections of ADX-2191 for three months

Cohort B (n = 4):

Twice-monthly injections of ADX-2191 for three months

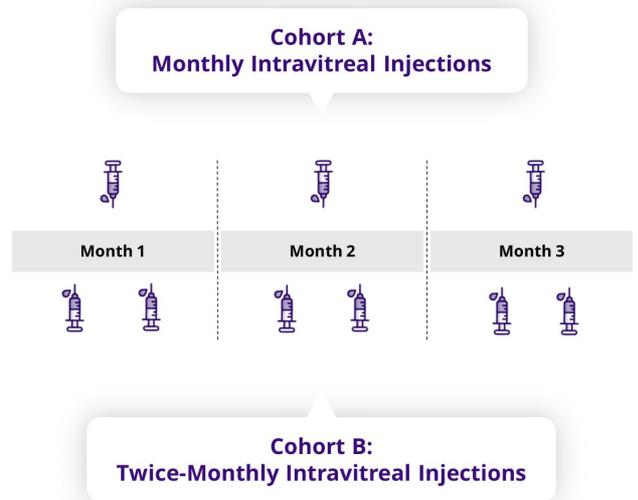
Primary Endpoint

Safety and tolerability

Secondary Endpoints

1. Best corrected and low-light visual acuity
2. Macular retinal sensitivity as assessed by MAIA perimetry
3. Dark-adapted flash analyzed by ERG
4. Peripheral retinal sensitivity as assessed by DAC perimetry
5. Retinal morphology as assessed by OCT

Acuity, perimetry, and OCT assessments were performed monthly for four months from initiation of therapy. ERG was performed at baseline and at 90 days from initiation of therapy.

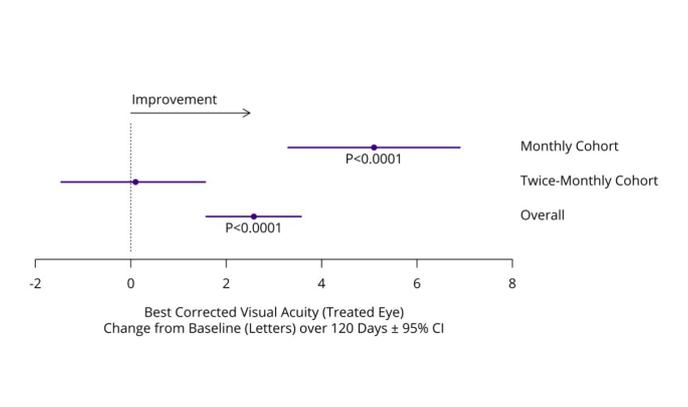


ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. MAIA = Macular Integrity Assessment. ERG = full field electroretinography. DAC = dark-adapted chromatic. OCT = optical coherence tomography.

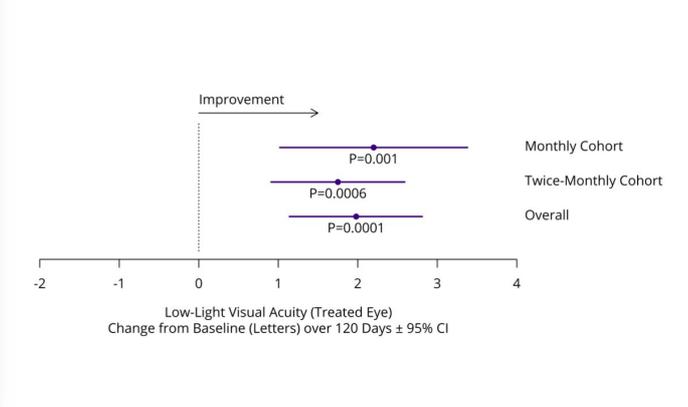
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Statistically Significant Improvement in Visual Acuity Observed in the Retinitis Pigmentosa Phase 2 Clinical Trial

Normal Lighting



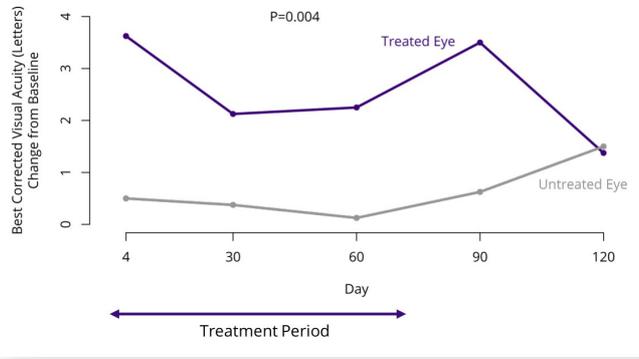
Dim Lighting



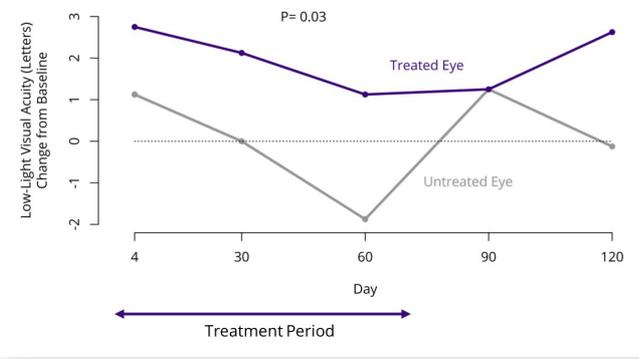
ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. Baseline best corrected visual acuity for the twice-monthly dosing cohort was on average approximately 20/20. Data derived from mixed model for repeated measures with baseline, day, and dose (if applicable) as factors. CI = confidence interval.

In the Retinitis Pigmentosa Phase 2 Clinical Trial, Visual Acuity in ADX-2191-Treated Eyes Was Superior to that of Untreated Eyes

Normal Lighting

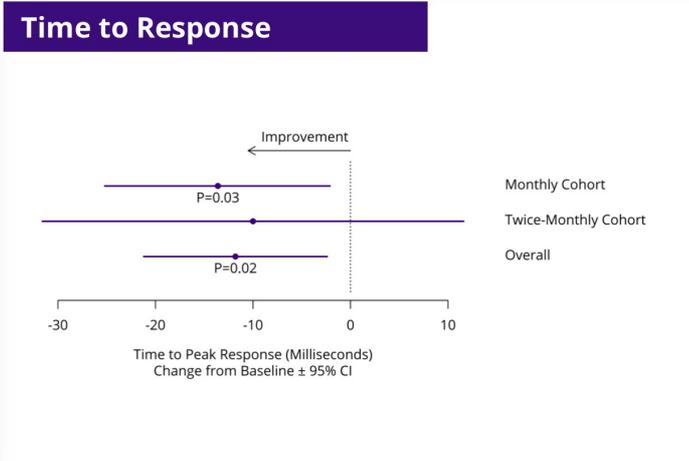
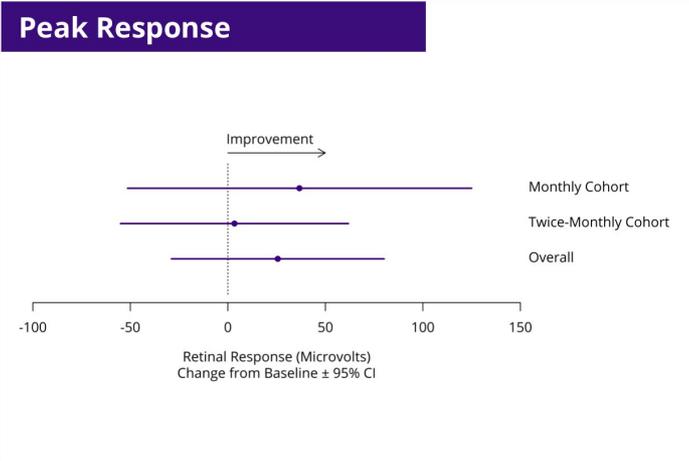


Dim Lighting



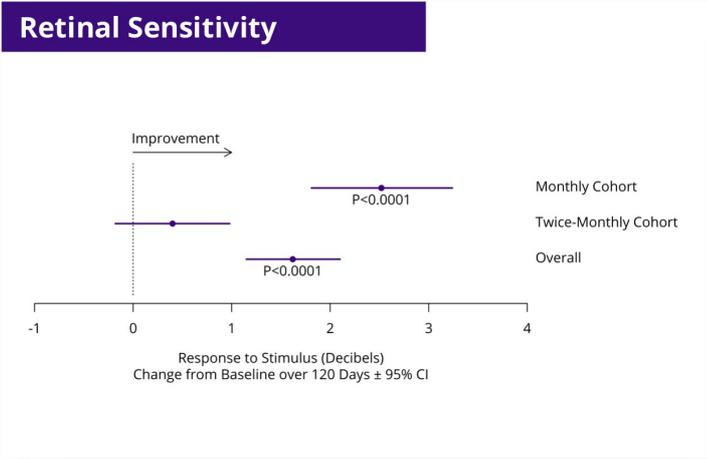
 ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. Data derived from mixed model for repeated measures of both dosing cohorts with baseline, day, dose, and treatment eye as factors.

As Assessed by ERG, Retinal Function Improved in the Retinitis Pigmentosa Phase 2 Clinical Trial

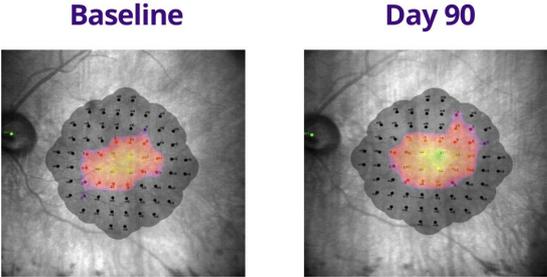


ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. B-wave response and implicit time following dim flash under scotopic conditions were assessed. Data derived from mixed model for repeated measures with baseline and dose (if applicable) as factors. CI = confidence interval. ERG = full field electroretinography.

As Assessed by MAIA Microperimetry, Statistically Significant Improvement in Retinal Sensitivity Observed in the Retinitis Pigmentosa Phase 2 Clinical Trial



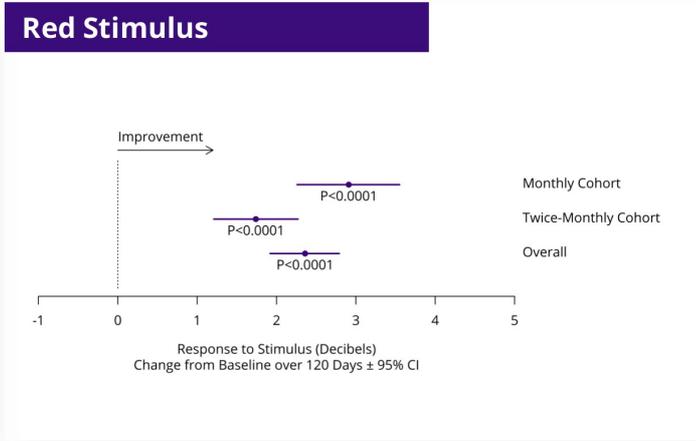
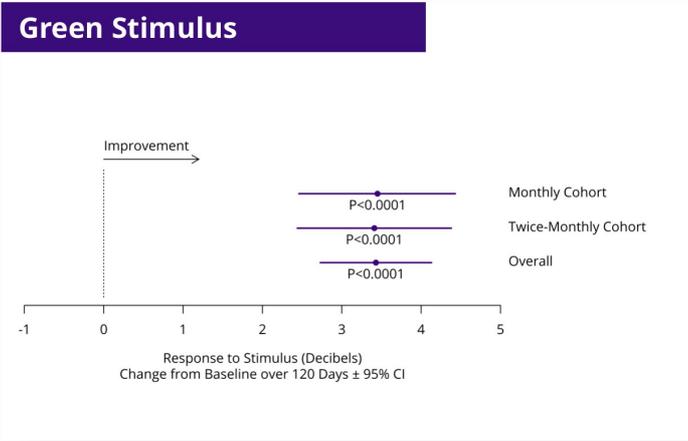
Illustrative results from an enrolled patient indicate central and peripheral improvement in macular retinal sensitivity



ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. Baseline retinal sensitivity was approximately 50% higher in the twice-monthly dosing cohort than in the monthly dosing cohort. Data derived from mixed model for repeated measures with baseline, day, and dose (if applicable) as factors. Retinal sensitivity assessed where non-zero sensitivity losses were ≥ 7 decibels from nearest concentric assessment. MAIA = Macular Integrity Assessment. CI = confidence interval.



As Assessed by DAC Perimetry, Statistically Significant Improvement in Retinal Sensitivity Observed in the Retinitis Pigmentosa Phase 2 Clinical Trial



 ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. Data derived from mixed model for repeated measures with baseline, day, and dose (if applicable) as factors. Retinal sensitivity assessed where non-zero sensitivity losses were ≥ 7 decibels from nearest concentric assessment. DAC = dark-adapted chromatic. CI = confidence interval.

Planned Phase 2/3 Clinical Trial of ADX-2191 in Retinitis Pigmentosa

Design	Randomized, double-masked, clinical trial
Dosing	40 µg vs. 400 µg administered monthly for 12 months
Size	30 retinitis pigmentosa patients with rhodopsin mutations, randomized 1:1
Primary Endpoint	Peripheral vision sensitivity to green (rod-mediated) light under dimly lit (scotopic), dark-adapted conditions
Other Endpoints	Best-corrected and low-light visual acuity, safety

Clinical trial initiation expected in H2 2024[†]

 [†]The timing of clinical trials depends, in part, on the availability of clinical research facilities and staffing, the ability to recruit patients, and the number of patients in the trial.

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Todd C. Brady, M.D., Ph.D., Chief Executive Officer, Aldeyra Therapeutics

Pipeline and Milestone Review

Clinical and Regulatory Milestones



Reproxalap



ADX-629



ADX-246



ADX-248



ADX-2191

[†]Regulatory review and discussion timelines are flexible and subject to change based on the regulator's workload and other potential review issues. [‡]The timing of clinical trials depends, in part, on the availability of clinical research facilities and staffing, the ability to recruit patients, and the number of patients in the trial. [§]Investigator sponsored.



Allergic Conjunctivitis

Positive Phase 3 INVIGORATE 2 trial top-line results announced



Dry Eye Disease

Proposed clinical trial top-line results and potential NDA resubmission expected in second half of 2024, pending clinical trial results, feedback from ongoing FDA discussions, and other factors[†]



Sjögren-Larsson Syndrome

Phase 2 clinical trial top-line results announced*



Moderate Alcohol-Associated Hepatitis

Open-label Phase 2 clinical trial results expected H2 2024[‡]



Atopic Dermatitis

Phase 1 clinical trial initiation expected in H1 2024[‡]



Metabolic Disease

Pre-clinical program initiated



Dry Age-Related Macular Degeneration/Geographic Atrophy

IND expected to be submitted in 2024



Retinitis Pigmentosa

Phase 3 clinical trial initiation expected in H2 2024[‡]





Todd C. Brady, M.D., Ph.D., Chief Executive Officer, Aldeyra Therapeutics

Concluding Remarks

Aldeyra Therapeutics Highlights Recent Preclinical Data in Obesity, Atopic Dermatitis, Pain, and Alcoholic Hepatitis, and Announces Planned Pivotal Clinical Trial in Retinitis Pigmentosa, at 2024 Research & Development Day

Live Webcast Scheduled to Begin at 9 AM EDT Today

LEXINGTON, Mass.--(BUSINESS WIRE)--Apr. 25, 2024-- Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra) will host the Aldeyra 2024 Research & Development Day with investors and financial analysts in New York City to present recent pipeline developments relating to the RASP modulation platform and ADX-2191 for the treatment of retinitis pigmentosa.

Aldeyra will present new preclinical data from investigational RASP modulators in animal models for obesity, atopic dermatitis, inflammatory pain, and alcoholic hepatitis. In the diet-induced model of obesity, ADX-629 decreased weight and fat mass alone and in combination with a GLP-1 agonist. In the oxazolone model of atopic dermatitis, RASP modulators ADX-629, ADX-246, and ADX-248 demonstrated activity in reducing skin thickness and erosion, and in reducing spleen to body weight ratio. In the carrageenan model of inflammatory pain, ADX-246 increased tolerance to mechanical and thermal pain, and decreased joint swelling. Consistent with previously released data from ADX-629 in a model of alcoholic hepatitis, ADX-246 reduced levels of fibrosis and fat in liver.

“The new data released today support the expansion of our novel RASP platform into clinical indications that may include fat-mass-targeted weight loss and inflammatory pain, highlighting the breadth of potential product candidate opportunities afforded by modulating RASP levels,” stated Todd C. Brady, M.D., Ph.D., President and CEO of Aldeyra.

Based on recent discussions with the U.S. Food and Drug Administration (the FDA), Aldeyra intends to initiate a potentially pivotal Phase 2/3 clinical trial of investigational product candidate ADX-2191 (methotrexate injection, USP) in patients with retinitis pigmentosa due to rhodopsin misfolding mutations. The potential activity of ADX-2191 in retinitis pigmentosa is supported by results from a Phase 2 clinical trial, announced in 2023, which demonstrated improvements from baseline in retinal sensitivity following treatment. An overview of the unmet medical need in retinitis pigmentosa will be provided by Ramiro Maldonado, M.D., Principal Investigator of the Phase 2 clinical trial and Assistant Professor of Ophthalmology, Vitreoretinal Diseases, and Surgery at Duke University.

“Due to loss of vision and dramatic impact on quality of life, retinitis pigmentosa remains a highly significant unmet medical need in retinal disease,” stated Dr. Maldonado. “Even with the advent of gene therapy, cell therapy, and other new approaches not yet approved by the FDA for treatment, a safe and effective drug that could slow the progression of retinitis pigmentosa is in critical demand.”

Research & Development Day Webcast Information

Aldeyra’s Research & Development Day will take place from 9:00 AM to 1:00 PM EDT today, Thursday, April 25, 2024, in New York City. A live audio webcast and slide presentation will be accessible from the “Investors & Media” section of the Aldeyra website at <https://ir.aldeyra.com/> for 90 days following the event.

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-246, ADX-248, and chemically related molecules for the potential treatment of 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 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 reproxalap, ADX-2191, and other product candidates; the outcome and expected timing and the results of Aldeyra's planned clinical trials, including planned and ongoing clinical trials for reproxalap and ADX-2191; the outcome and timing of the FDA's review, acceptance and/or approval of a NDA resubmission for reproxalap and the adequacy of the data included in the original NDA; and the potential NDA resubmission. 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, 2023, which is 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, expected to be filed with the SEC in the second quarter of 2024, 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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