



CORPORATE

Innovative Therapeutics for Immune-Mediated and Metabolic Diseases

November 2024

Nasdaq: ALDX

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This presentation contains 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, statements regarding Aldeyra's future expectations, plans and prospects, including, without limitation, statements regarding: FDA agreement with the clinical development and regulatory plan for reproxalap; the outcome and expected timing and results of the clinical development plan; the outcome and timing of the FDA's review, and/or approval of the NDA resubmission for reproxalap and the adequacy of the data included in the NDA resubmission or the supplemental responses to the FDA; the potential for and timing of regulatory approval and commencement of commercialization of reproxalap; Aldeyra's expectations regarding the exercise of the AbbVie option; the potential profile and benefit of reproxalap in dry eye disease and allergic conjunctivitis and its other product candidates in the indications for which they are developed; the goals, opportunity and potential for reproxalap and its other product candidates, anticipated clinical or regulatory milestones for ADX-2191, ADX-248, ADX-743, ADX-631, and ADX-629, including 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; political, economic, legal, social and health risks that may affect Aldeyra's business or the global economy; the structure, timing and success of Aldeyra's planned or pending clinical trials; and 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. 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-248, ADX-743, ADX-631, 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.

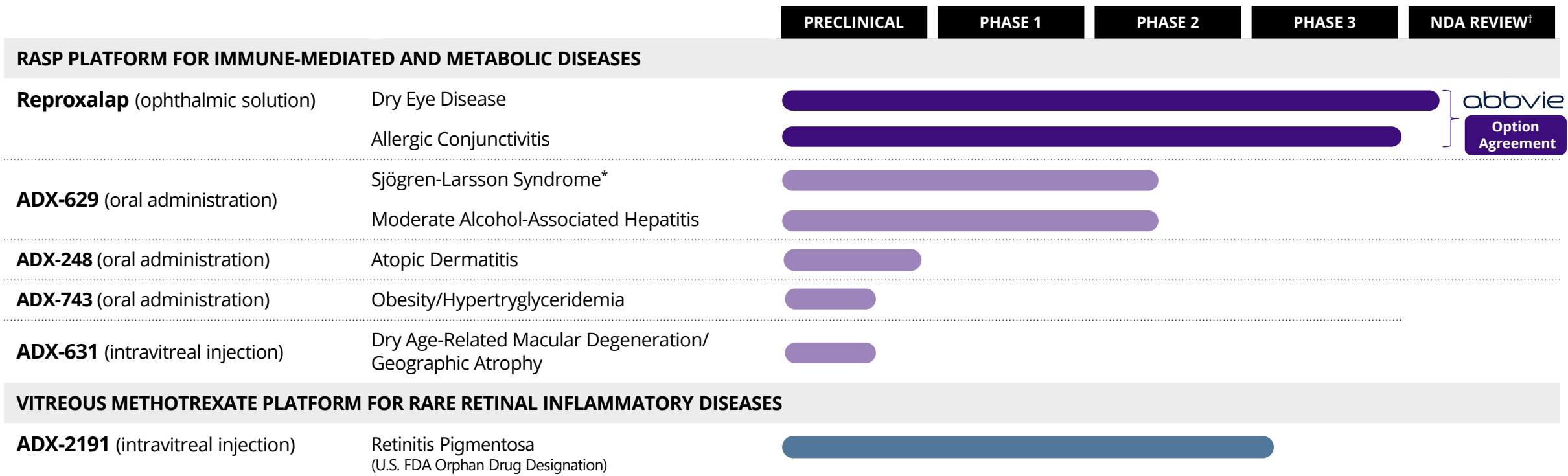
In addition to the risks described above and in Aldeyra's other filings with the SEC, other unknown or unpredictable factors also could affect Aldeyra's results. No forward-looking statements can be guaranteed, and actual results may differ materially from such statements. The information in this presentation is provided only as of November 18, 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.

A close-up photograph of a woman with dark curly hair smiling warmly as she hugs a young girl with her arms around her neck. Both are smiling broadly, and the background is a bright, sunny outdoor setting.

ALDEYRA'S MISSION is to discover innovative therapies that improve the lives of patients who suffer from 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.

Aldeyra Is a Well-Capitalized Biotechnology Company with a Broad Immunology and Metabolic Pipeline



As of 9/30/2024, cash, cash equivalents, and marketable securities were \$112.7M, which Aldeyra believes will be sufficient to fund the Company through 2026.‡



†Regulatory review timelines are flexible and subject to change based on the regulator's workload and other potential review issues. *Company guidance as of November 7, 2024; includes continued early and late-stage development of our product candidates in immune-mediated and metabolic diseases. Guidance does not include any potential licensing or product revenue associated with reproxalap. †Investigator sponsored. NDA = New Drug Application

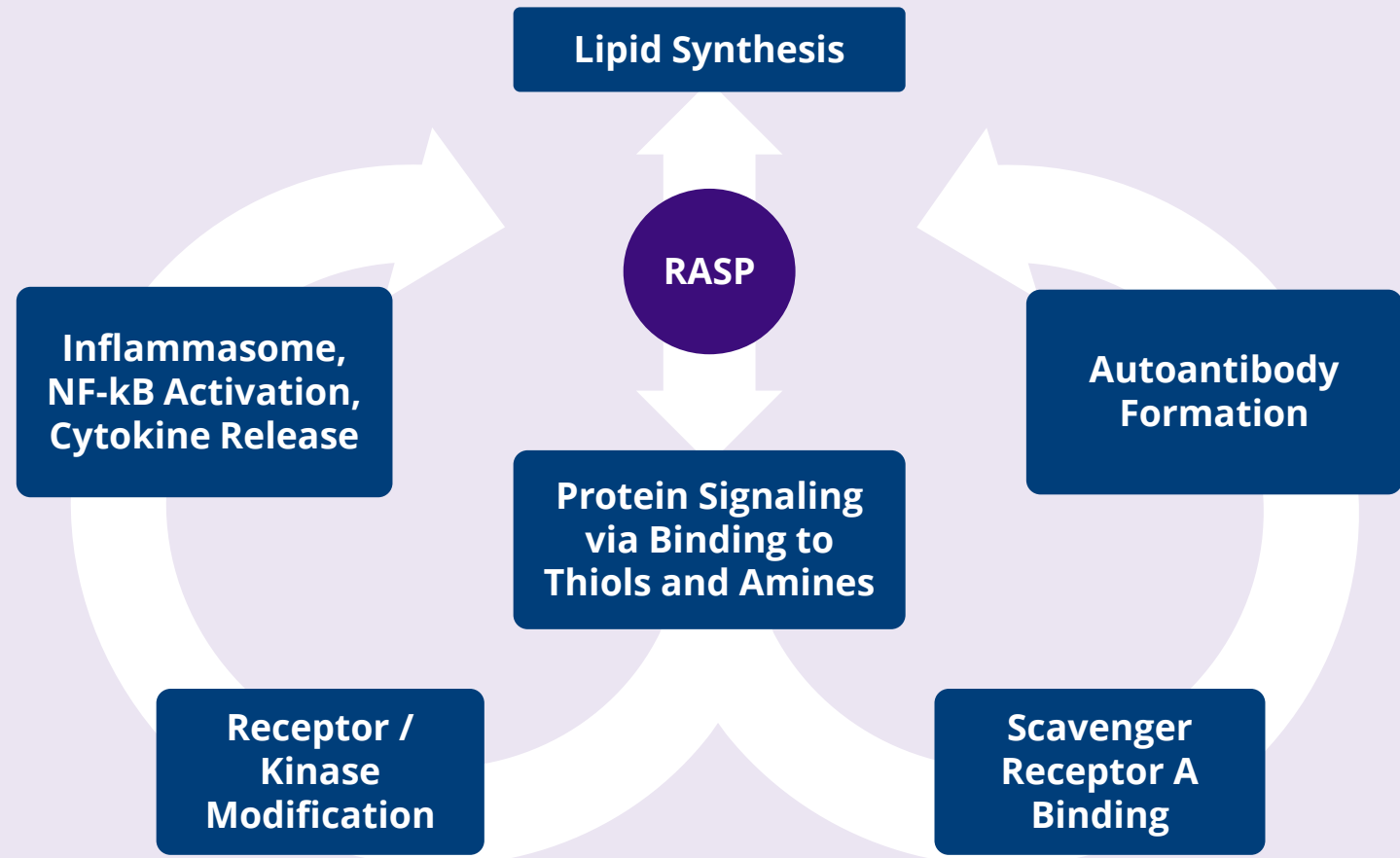




Modulating RASP – A First-in-Class, Systems-Based Therapeutic Approach

RASP Represent a Novel, Potentially Broadly Applicable Pharmaceutical Target that Modulates Many Proteins at Once

- RASP are formed by oxidation of alcohols and other metabolic processes.
- RASP bind thiol (Michael addition) and amine (Schiff base) residues on proteins, leading to conformational and functional changes in certain proteins that **initiate pro-inflammatory signaling cascades**.
- RASP are also precursors of lipids and **may contribute to obesity and dyslipidemia**.



RASP Modulation Represents a Novel Pharmacology

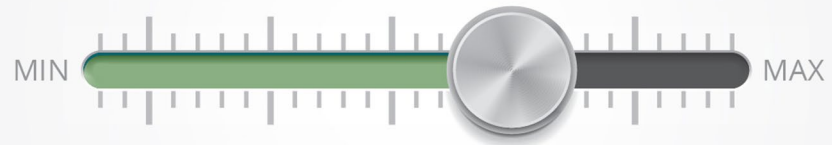
Traditional pharmacology targets specific proteins and is generally limited to two actions: on or off.



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

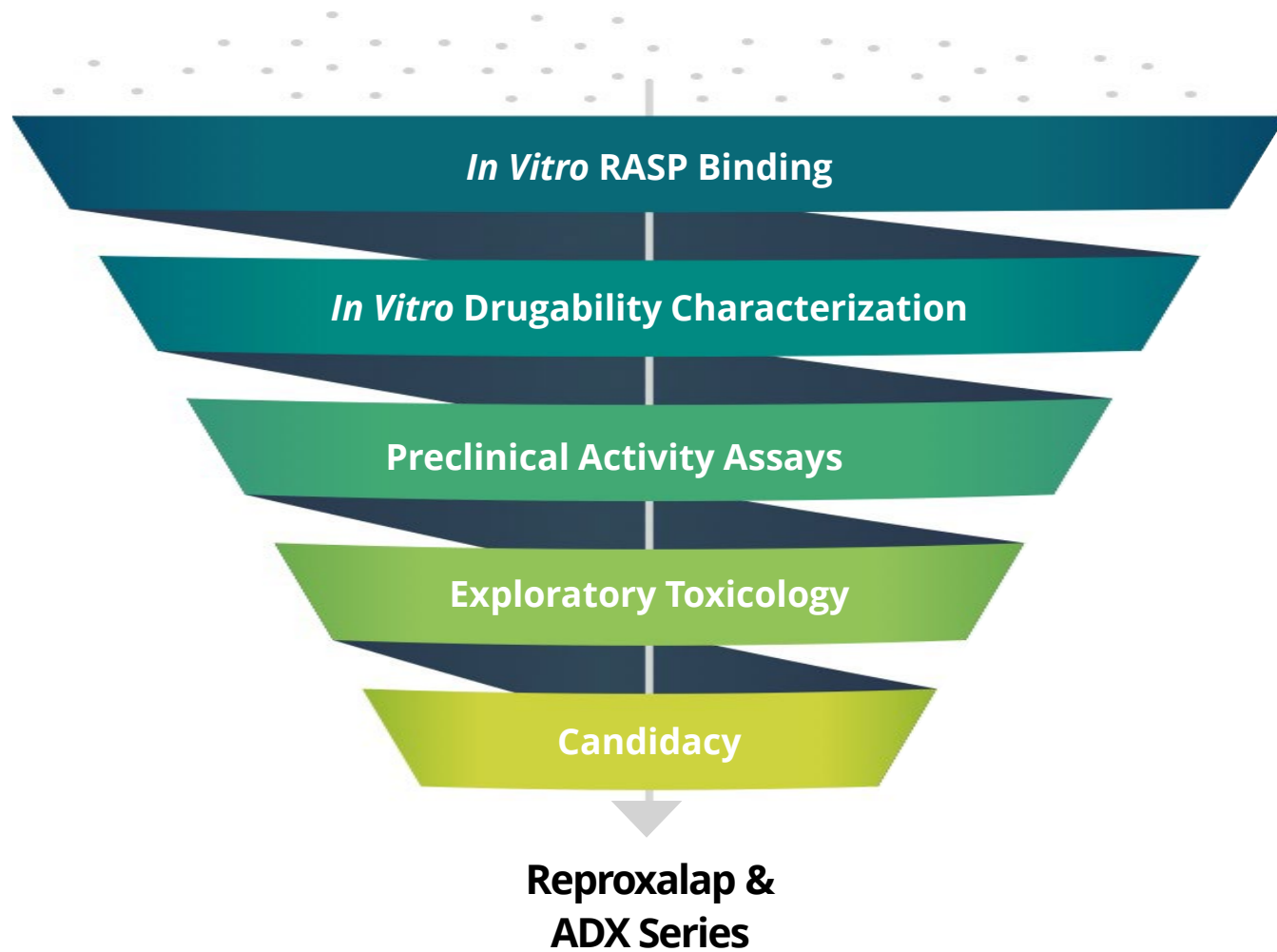


RASP modulation may allow for control of protein *systems*, without turning any single protein on or off.



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

Aldeyra Has Developed the Leading RASP Modulator Platform



The Immune-Modulating Activity of Lead RASP Modulator Reproxalap is Supported by Peer-Reviewed Publications

AMERICAN JOURNAL OF OPHTHALMOLOGY

Early Onset and Broad Activity of Reproxalap in a Randomized, Double-Masked, Vehicle-Controlled Phase 2b Trial in Dry Eye Disease

AMERICAN JOURNAL OF OPHTHALMOLOGY

Clinically Relevant Activity of the Novel RASP Inhibitor Reproxalap in Allergic Conjunctivitis: The Phase 3 ALLEVIATE Trial

JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS

A Randomized Double-Masked Phase 2a Trial to Evaluate Activity and Safety of Topical Ocular Reproxalap, a Novel RASP Inhibitor, in Dry Eye Disease

Clinical Ophthalmology

CLINICAL TRIAL REPORT

The Phase 3 INVIGORATE Trial of Reproxalap in Patients with Seasonal Allergic Conjunctivitis

Christopher E. Starr, Kelly K. Nichols, Jacob R. Lang, Todd C. Brady

Clinical Ophthalmology

ORIGINAL RESEARCH

A Post-Acute Ocular Tolerability Comparison of Topical Reproxalap 0.25% and Lifitegrast 5% in Patients with Dry Eye Disease

Clinical Ophthalmology

ORIGINAL RESEARCH

Reproxalap Improves Signs and Symptoms of Allergic Conjunctivitis in an Allergen Chamber: A Real-World Model of Allergen Exposure

JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS

Randomized Phase 2 Trial of Reproxalap, a Novel Reactive Aldehyde Species Inhibitor, in Patients with Noninfectious Anterior Uveitis: Model for Corticosteroid Replacement

Ophthalmology and Therapy

Reproxalap Activity and Estimation of Clinically Relevant Thresholds for Ocular Itching and Redness in a Randomized Allergic Conjunctivitis Field Trial

Bill Cavanagh . Paul J. Gomes . Christopher E. Starr . Kelly K. Nichols . Todd C. Brady

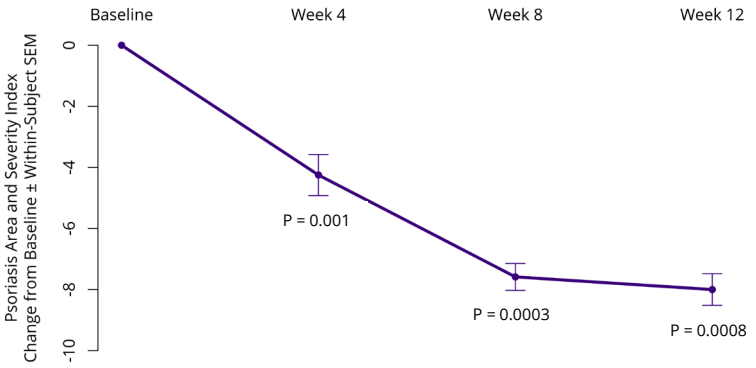


Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 2,400 patients with no observed safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

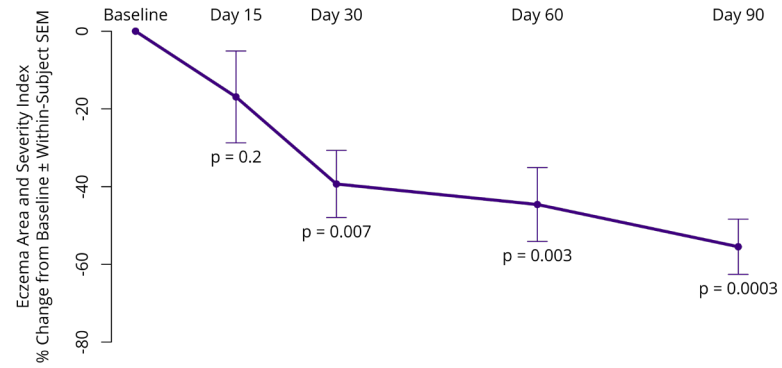
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ADX-629, a First-in-Class Orally Administered RASP Modulator, Has Demonstrated Activity in Phase 2 Clinical Trials

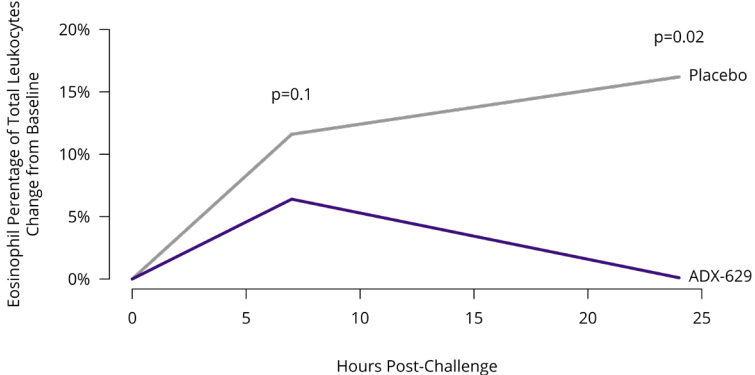
Autoimmune Disease: Psoriasis



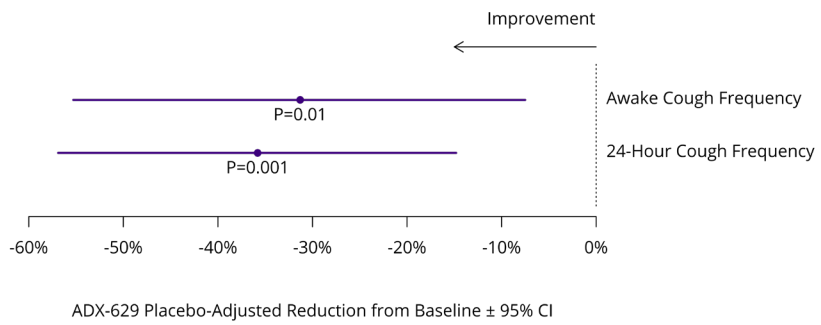
Autoimmune Disease: Atopic Dermatitis



Allergic Inflammation: Asthma

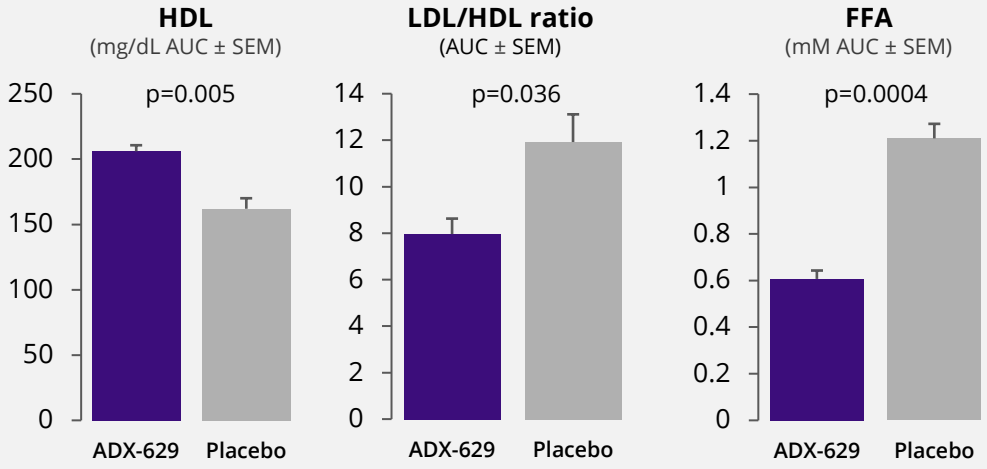


Idiopathic Inflammation: Chronic Cough

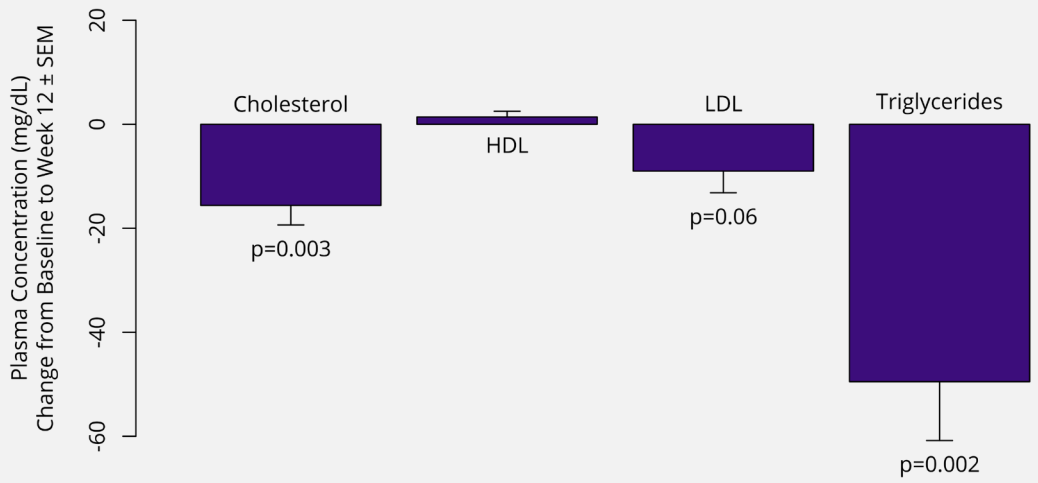


Statistically Significant Changes Observed in Lipid Profiles in Multiple Clinical Trials with RASP Modulator ADX-629

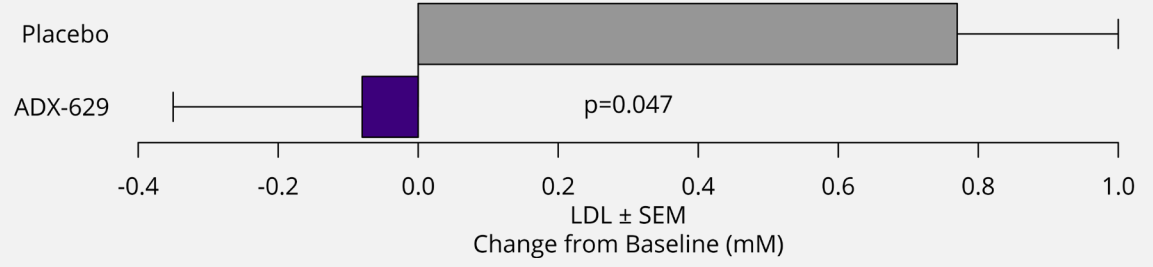
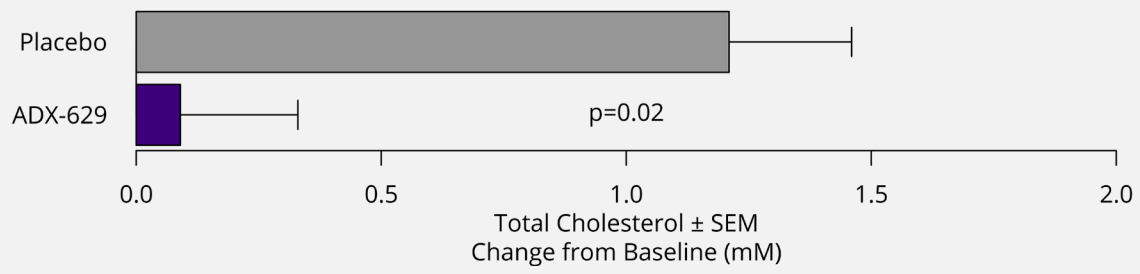
Phase 1 Clinical Trial



Phase 2 Psoriasis Clinical Trial

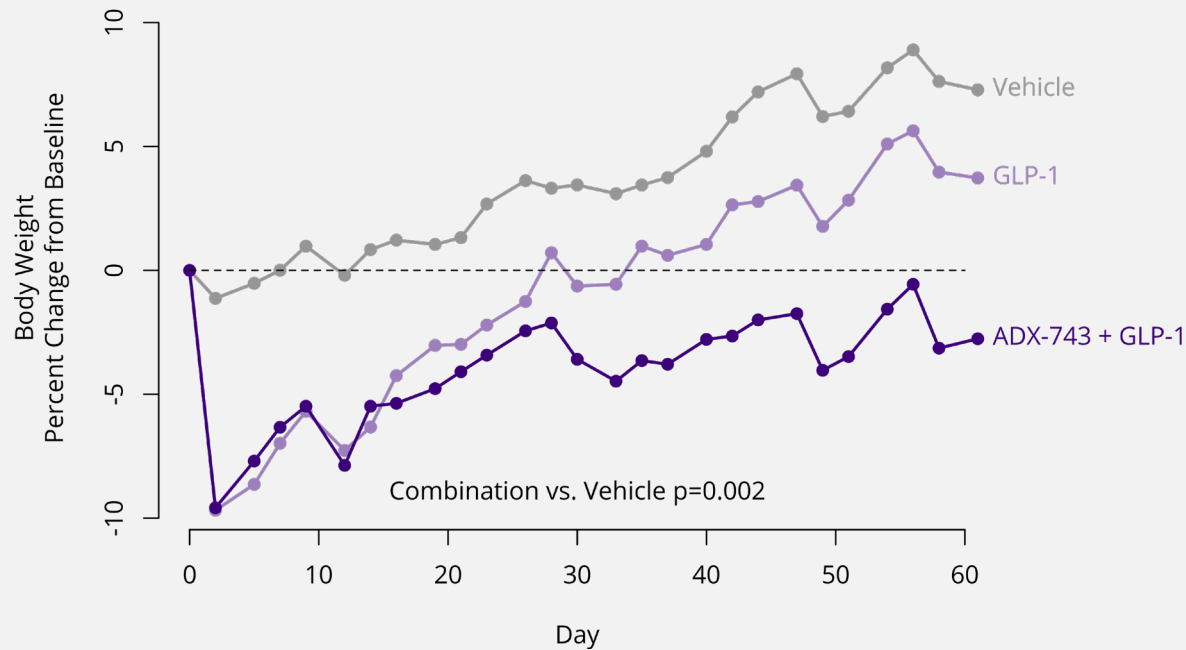


Phase 1/2 Ethanol Toxicity Clinical Trial

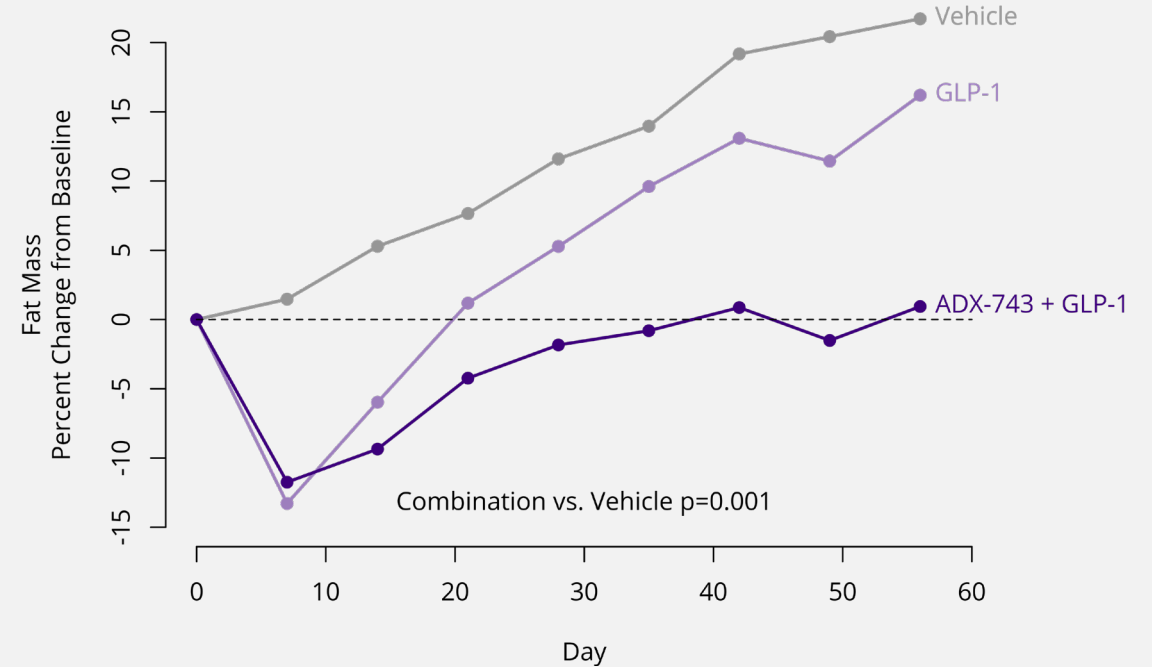


ADX-743, an Analog of ADX-629, Demonstrated Preclinical Weight Loss and Reduction of Fat Mass in Combination with GLP-1 Agonist

Body Weight



Fat Mass





Reproxalap: A Novel RASP Modulator for the Treatment of Dry Eye Disease

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

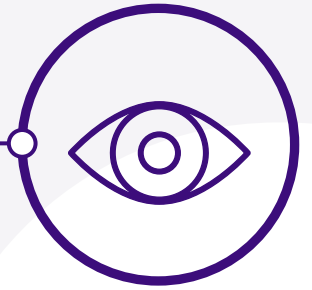
Potential advantages for patients and healthcare providers could effect a paradigm shift relative to standard of care.



Rapid and sustained symptom improvement



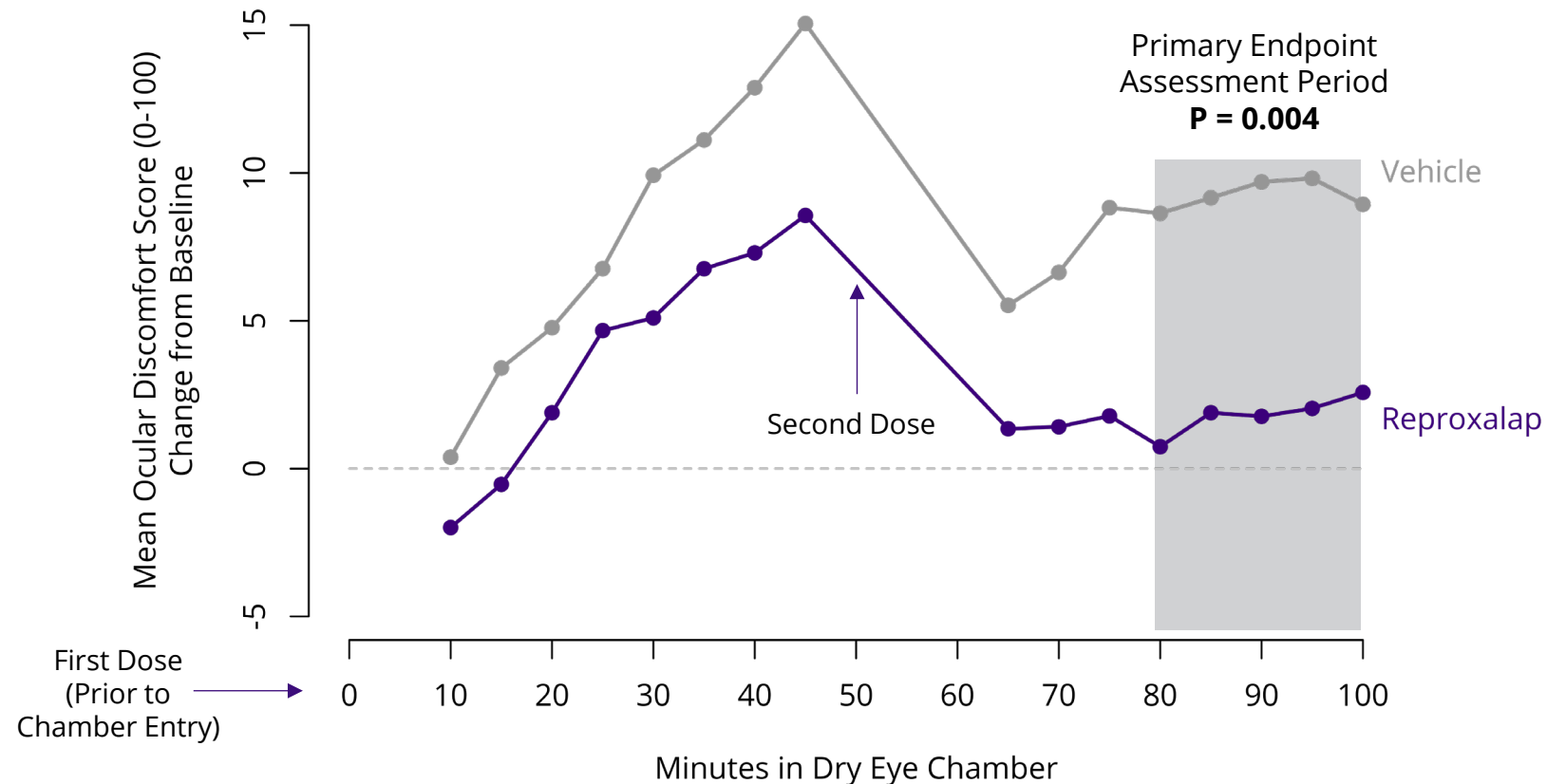
Broad symptomatic activity



Acute reduction of ocular redness

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

Positive Results from a Phase 3 Clinical Trial Included in NDA Resubmission[†] of Reproxalap for Treatment of Dry Eye Disease



To our knowledge, the results represent the first positive Phase 3 clinical trial in a dry eye chamber with a symptom as a primary endpoint, and we believe that the results are supportive of the potential rapid clinical effect of reproxalap on reducing ocular discomfort.

[†]Regulatory review and discussion timelines are flexible and subject to change based on the regulator's workload and other potential review issues. P value derived from primary endpoint mixed model repeated measures analysis. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 2,500 patients with no observed safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

Aldeyra has Entered into an Exclusive Option Agreement with AbbVie Inc. for License to Develop and Commercialize Reproxalap

Key Terms of Reproxalap Option Agreement

Option for AbbVie to obtain:

- Co-exclusive license to develop, manufacture, and commercialize reproxalap in the U.S.
- Exclusive license to develop, manufacture, and commercialize outside the U.S.

Financial terms of license if option exercised:

- Upfront payment of \$100 million less option fees
- \$100 million milestone payment upon U.S. FDA approval in dry eye disease
- \$200 million in additional regulatory and commercial milestones
- Profit and loss share (60% for AbbVie/40% for Aldeyra) from commercialization in U.S.
- Tiered royalties on net sales outside of U.S.

abbvie

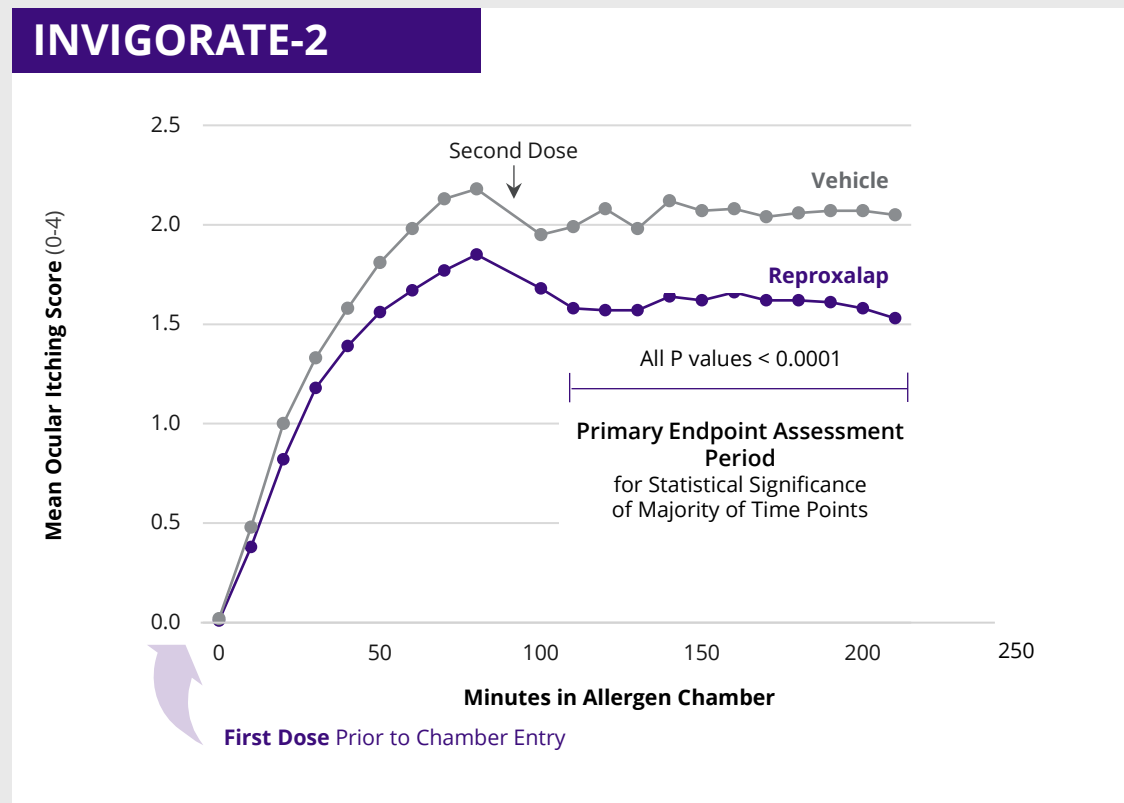
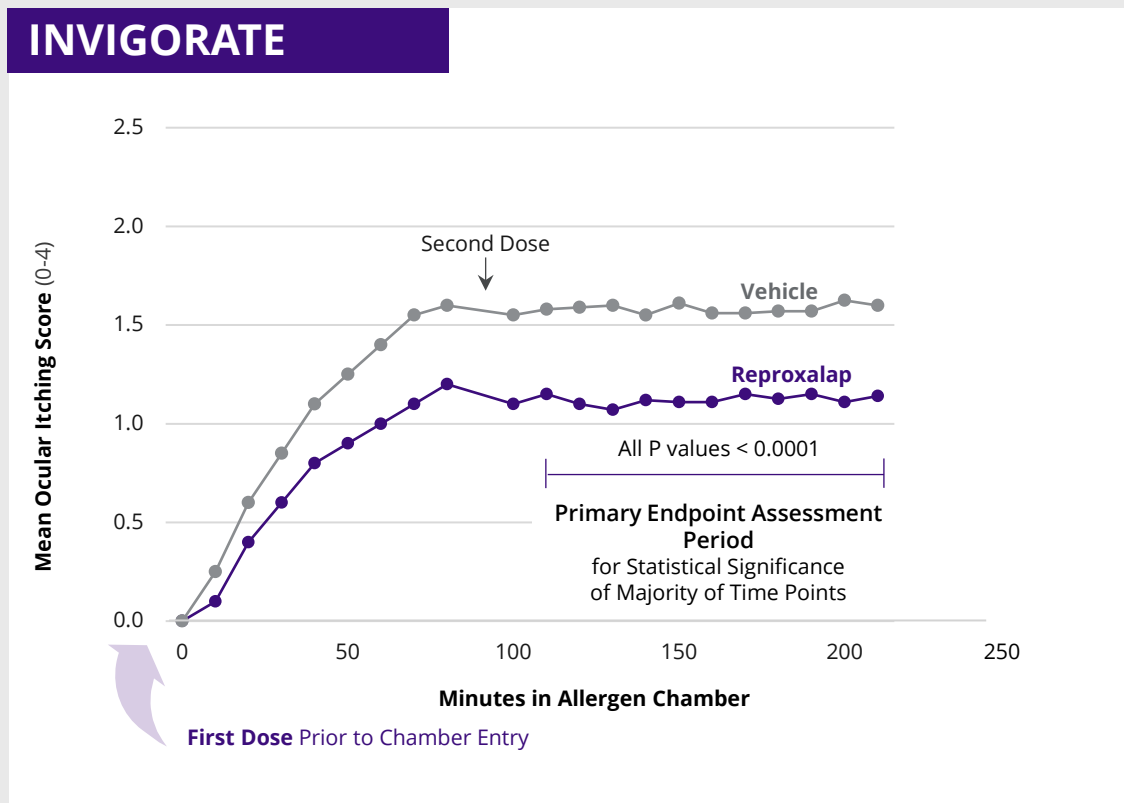


The option terminates on the 10th business day after Aldeyra receives approval from the U.S. FDA of the NDA for reproxalap in dry eye. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 2,500 patients with no observed safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.

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Aldeyra Believes Efficacy Requirements Have Been Met for Potential NDA Resubmission of Reproxalap for Allergic Conjunctivitis†

Phase 3 INVIGORATE Allergen Chamber Trials Primary Endpoint of Patient-Reported Ocular Itching



†NDA submission requirements depend, in part, on clinical results, enrollment, and regulatory feedback. Source: INVIGORATE and INVIGORATE-2 clinical trial results. Topical ocular reproxalap is an investigational new drug candidate that has been studied in more than 2,500 patients with no observed safety concerns; mild and transient instillation site irritation is the most commonly reported adverse event in clinical trials.





ADX-2191: A Novel Therapy for the Treatment of 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.
- Preclinical evidence suggests that methotrexate may be active in rhodopsin misfolding mutations by facilitating degradation of mutated rhodopsin.
- **U.S. FDA Orphan Drug Designation** received August 2021

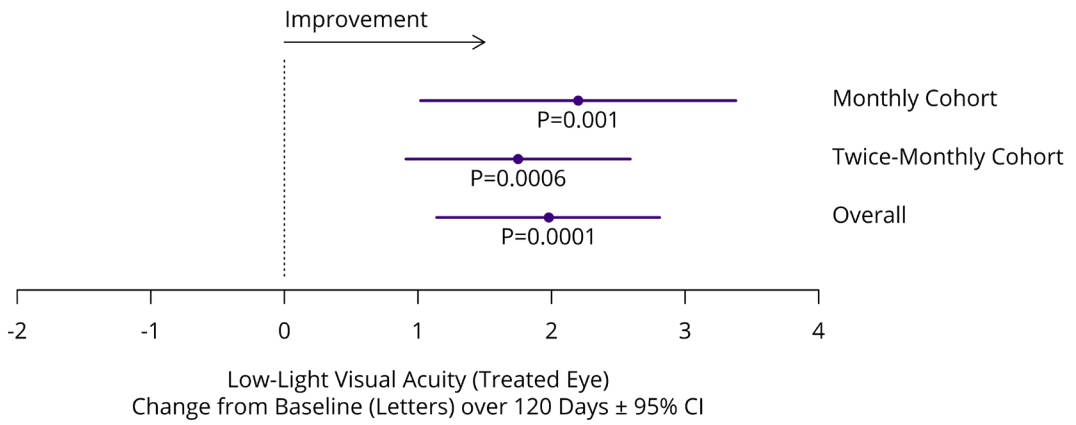


Preclinical electroretinographic evidence in a P23H rhodopsin mutation mouse model of retinitis pigmentosa **suggests that methotrexate improves retinal function.**

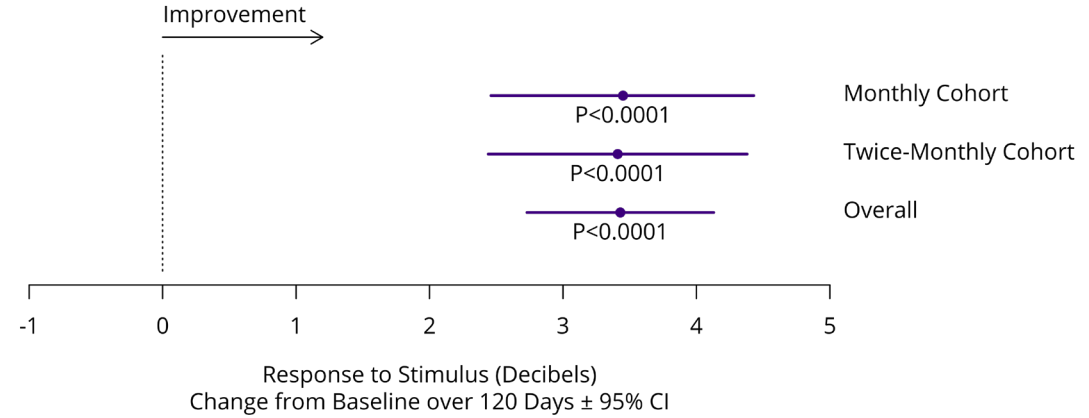
ADX-2191 (methotrexate injection, USP) for intravitreal administration is an investigational drug candidate. Sources: Aldeyra internal estimates; FASEB J. 2020 Aug;34(8):10146-10167. PBS = phosphate-buffered saline; MTX = methotrexate.

In the Phase 2 Retinitis Pigmentosa Clinical Trial of ADX-2191, Retinal Sensitivity Improved from Baseline

Visual Acuity in Dim Light



Dark Adapted Sensitivity to Green Light



Phase 2 clinical trial was performed in eight retinitis pigmentosa patients with rhodopsin misfolding mutations: four patients received monthly injections for three months; four patients received twice-monthly injections for three months. Dark adapted chromatic perimetry used to assess sensitivity to green light stimuli.



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

Design	Randomized, double-masked, clinical trial
Dosing	10 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 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.



Corporate Information

Experienced Management Team and Board of Directors

MANAGEMENT TEAM

Todd Brady, M.D., Ph.D.
President, CEO & Director

Stephen Machatha, Ph.D.
Chief Development Officer

BOARD OF DIRECTORS

- Richard Douglas, Ph.D.** Chairman
Former SVP Corporate Development at Genzyme

- Ben Bronstein, M.D.**
Former CEO Peptimmune⁶


- Marty Joyce**
Former CFO of Serono USA

- Nancy Miller-Rich**
Former SVP BD&L and Commercial Strategy at Merck

- Gary Phillips, M.D.**
CBO Anaveon AG

- Neal Walker, D.O.**
Chairman Aclaris Therapeutics

- Todd Brady, M.D., Ph.D.**
CEO Aldeyra Therapeutics

 1. Acquired by Xanthus/Antisoma. 2. Acquired by Schwarz/UCB. 3. Acquired by Ligand. 4. Acquired by Merck. 5. Acquired by Alexion. 6. Acquired by Genzyme.

Clinical and Regulatory Milestones

2024

- Allergic Conjunctivitis (Reproxalap)**
Positive Phase 3 INVIGORATE 2 trial top-line results announced
- Dry Eye Disease (Reproxalap)**
Positive Phase 3 dry eye chamber clinical trial top-line results announced
- Dry Eye Disease (Reproxalap)**
NDA resubmitted and accepted for review[†]
- Moderate Alcohol-Associated Hepatitis (ADX-629)**
Open-label Phase 2 clinical trial top-line results expected H2 2024[‡]
- Atopic Dermatitis (ADX-248)**
Phase 1 clinical trial initiation expected in H2 2024[‡]
- Retinitis Pigmentosa (ADX-2191)**
Phase 2/3 clinical trial initiation expected in H2 2024[‡]

2025

- Dry Age-Related Macular Degeneration/Geographic Atrophy (ADX-631)**
Investigational New Drug application expected to be submitted in H1 2025
- Sjögren-Larsson Syndrome (ADX-629)**
Phase 2 clinical trial pediatric cohort top-line results expected 2025
- Obesity/Hypertryglyceridemia (ADX-743)**
Investigational New Drug application expected to be submitted in 2025

[†]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.