aldeyra

October 2021

CORPORATE OVERVIEW

Innovative Approaches to Regulating Immune Response

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, research and development 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 product candidates 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 or portions of clinical trials 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 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, completion, or reporting of clinical trials.

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Compelling Value Proposition

NOVEL SYSTEMS-BASED APPROACHES FOR IMMUNOLOGY

- Ocular and systemic RASP-inhibition represent first-in-class, pre-cytokine therapeutic approaches.
- Rare retinal disease methotrexate platform provides potential near-term, high-value commercial opportunity.

NEAR-TERM DEVELOPMENT CATALYSTS*

- Phase 3 TRANQUILITY and TRANQUILITY-2 results in dry eye disease expected in Q4 2021.
- ADX-629 Phase 2 clinical testing results in asthma, psoriasis, and COVID-19 expected in Q4 2021 or Q1 2022.

LARGE AND UNDERSERVED MARKET OPPORTUNITY

- Lead product candidate reproxalap targets a U.S. addressable market of >$18B.
- Potential rapid onset and ocular redness control differentiates reproxalap in blockbuster ocular indications of dry eye disease and allergic conjunctivitis.

SOLID CASH POSITION

- Cash, cash equivalents and marketable securities of $241.4M as of 9/30/2021
- Cash runway through the end of 2023, based on projected operating expenses*

*Timing depends, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, the ability to recruit patients, and regulatory feedback.

Deep and Innovative Pipeline Addressing Immunological Disease

PRODUCT CANDIDATES	DISEASE TARGETS	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Reproxalap (ophthalmic solution)	Dry Eye Disease				
	Allergic Conjunctivitis				
ADX-2191 (intravitreal injection)	Proliferative Vitreoretinopathy*†				
	Primary Vitreoretinal Lymphoma*				
	Retinitis Pigmentosa*				
RASP-Inhibitor Discovery Platform	Multiple Immune-Mediated Retinal and Systemic Indications				
ADX-629 (oral administration)	Cytokine Release Syndrome (COVID-19)				
	Allergy (Atopic Asthma)				
	Autoimmune Disease (Psoriasis)				

*U.S. FDA orphan drug designation
†U.S. FDA fast track designation

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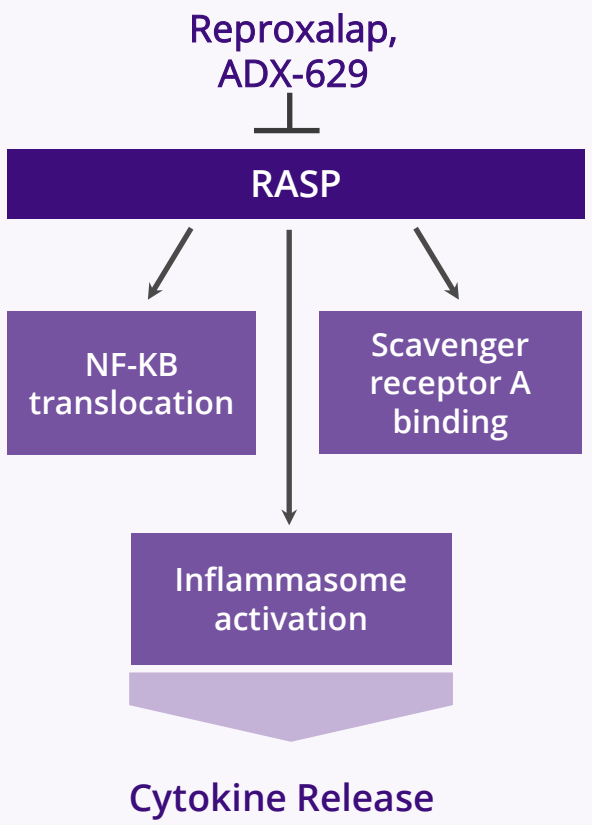
October 2021

REPROXALAP AND ADX-629

RASP Inhibition – A First-in-Class Therapeutic Approach for Immune Modulation

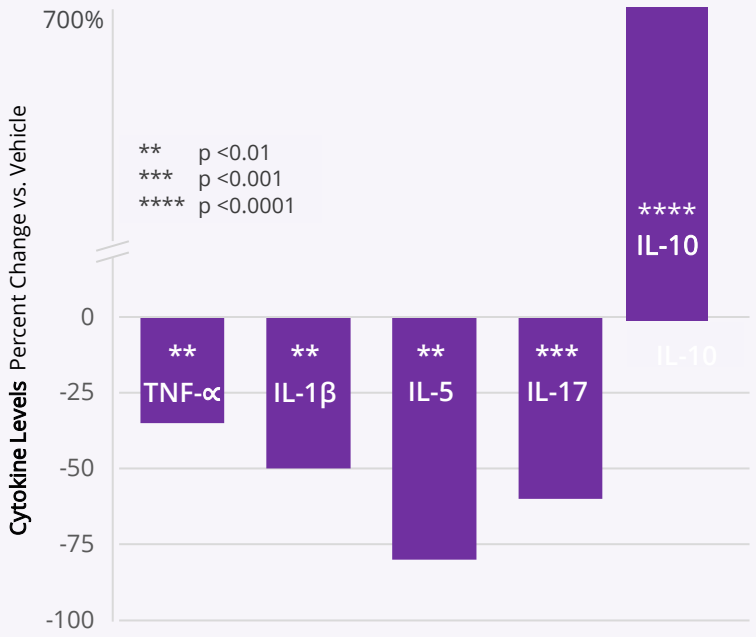
Nasdaq: ALDX

RASP Inhibition is a Pre-Cytokine, Systems-Based Approach that Has Been Clinically Validated in Late-Stage Trials



Preclinical Broad-Based Cytokine Reduction

LPS Animal Model of Cytokine Storm

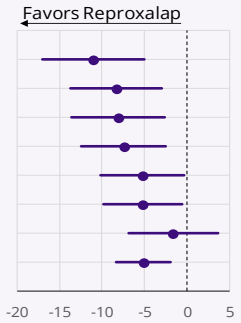


Broad-Based Symptom Reduction

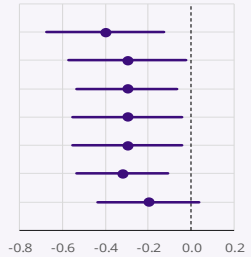
RENEW-Part 1 Phase 3 Dry Eye Disease Trial

Symptom Treatment Difference‡ (Reproxalap-Vehicle) Weeks 2 -12

0-100 Ocular Symptom Scales	p-value
VAS: Ocular Dryness (Co-Primary)	0.0004
VAS: Eye Discomfort	0.0025
VAS: Photophobia	0.0041
VAS: Foreign Body Sensation	0.0035
VAS: Itching	0.0346
VAS: Pain	0.0268
VAS: Burning/Stinging	NS
OSDI (Total)	0.0020



0-4 & 0-5 Ocular Symptom Scales	
OD4S: Grittiness	0.0025
OD4S: Dryness	0.0134
OD4S: Ocular Discomfort	0.0268
OD4S: Burning	0.0306
OD4S: Stinging	0.0239
CAC Ocular Itching Scale	0.0034
Ocular Discomfort Scale	NS



Sources: Cullen, et al. The Small Molecule Aldehyde Trap NS2 Exhibits Potent Anti-Inflammatory Activity in Three Murine Models of Inflammation [abstract]. In: The Journal of Allergy and Clinical Immunology. Volume 135, Issue 2, AB384, Feb 2015; Reproxalap RENEW-Part 1 clinical trial results. ‡Treatment Difference of induction-maintenance dosing, defined as the difference between the changes from baseline for the evaluated drug vs. vehicle (LS Mean Difference ± 95% CI). Ocular Dryness Score co-primary endpoint assessed in pre-specified patient population having an OD4S dryness baseline score of ≥ 3 (N=170). **RASP** = Reactive Aldehyde Species **VAS** = Visual Analog Scale **OSDI** = Ocular Surface Disease Index **NS** = Not Significant **OD4S** = Ocular Discomfort & 4-Symptom **CAC** = Conjunctival Allergen Challenge

Reproxalap Activity in Ocular Inflammatory Diseases is Supported by Marquee Peer-Reviewed Publications

AMERICAN JOURNAL OF OPHTHALMOLOGY

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

DAVID CLARK, BILL CAVANAGH, ALAN L. SHIELDS, PAUL KARPECKI, JOHN SHEPPARD, AND TODD C. BRADY

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

Kenneth J. Mandell,[1] David Clark,[1] David S. Chu,[2] C. Stephen Foster,[3] John Sheppard,[4] and Todd C. Brady[1]

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

DAVID CLARK, JOSEPH TAUBER, JOHN SHEPPARD, AND TODD C. BRADY

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

David Clark,[1] John Sheppard,[2] and Todd C. Brady[1]

Clinical Ophthalmology

Dovepress

open access to scientific and medical research

ORIGINAL RESEARCH

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

David McMullin[1]
David Clark[1]
Bill Cavanagh[1]
Paul Karpecki[2]
Todd C Brady[1]

[1]Aldeyra Therapeutics, Inc, Lexington, MA, USA; [2]Kentucky Eye Institute, Lexington, KY, USA

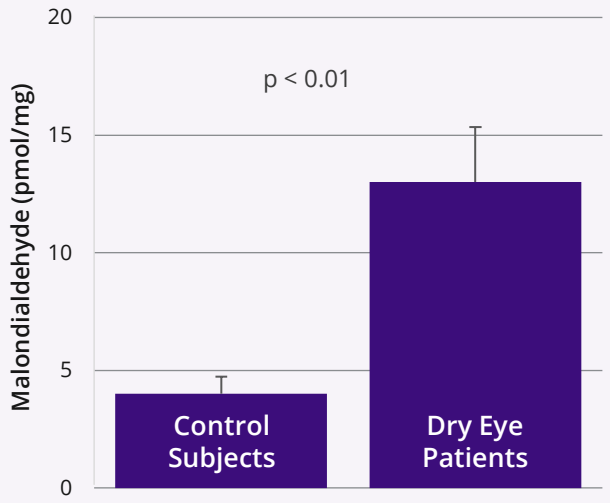
Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Reproxalap's Mechanism of Action Reduces RASP, a Potential Dry Eye Disease Biomarker

RASP in Dry Eye Disease

RASP markers are upregulated in dry eye disease.

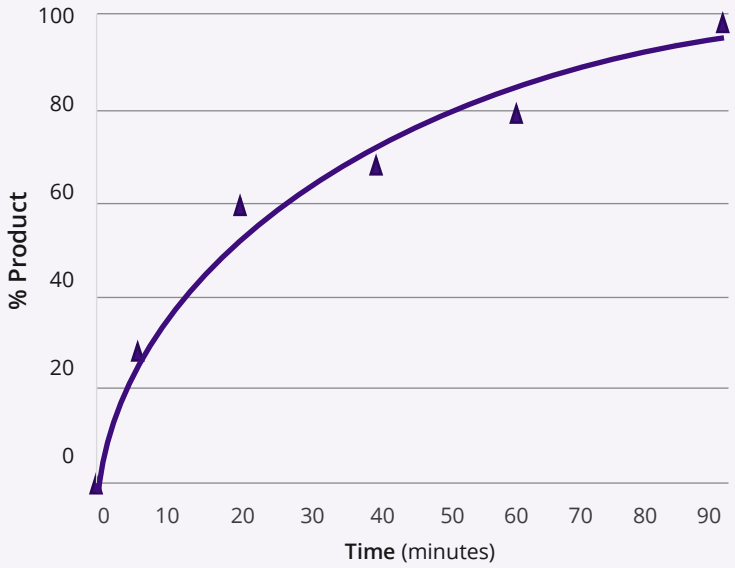
RASP levels have been shown to correlate with worsening symptoms and signs.



REPROXALAP

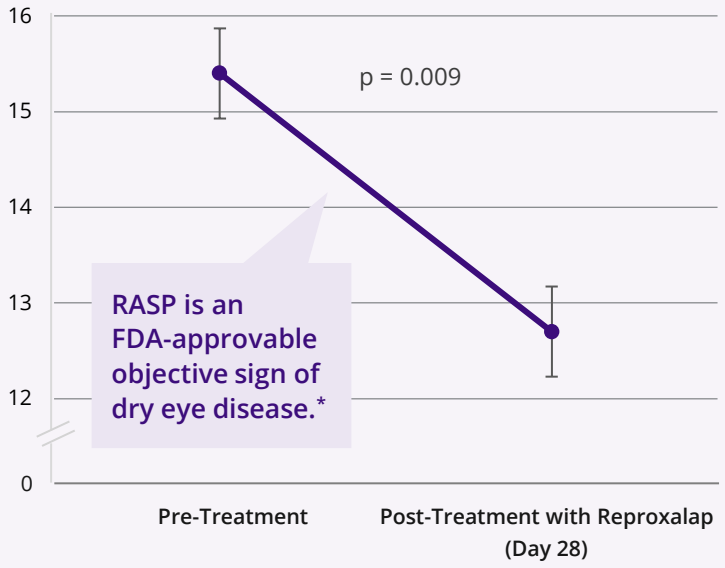
Rapid RASP binding in vitro

In vitro Reproxalap-Malondialdehyde (MDA) adduct formation over time (% of MDA bound by reproxalap)



Clinical reduction in RASP adducts

Phase 2a: Tear RASP Levels in Dry Eye Disease Patients
(μM Malondialdehyde Adduct; Mean ± Within-Subject SEM)



Sources: Choi W., et al. 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, 41(9):1143-9; Clark D, Sheppard J, Brady TC. A Randomized Double-Masked Phase 2a Trial to Evaluate Activity and Safety of Topical Ocular Reproxalap, a Novel RASP Inhibitor, in Dry Eye Disease. J Ocul Pharmacol Ther. 2021 May; 37(4):193-199; reproxalap preclinical results on file. *Aldeyra's written meeting minutes with the FDA confirmed the use of redness or RASP as accepted objective signs for the treatment of dry eye disease. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

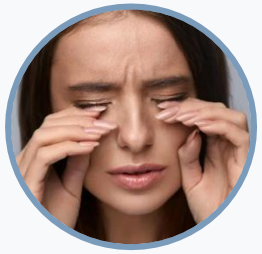
Lead RASP Inhibitor Reproxalap, a Novel Topical Ocular Drug, Now in Two Phase 3 Programs for Ocular Inflammation

DRY EYE DISEASE

34 million or more adults in the U.S.[1]

Often months to demonstrate even modest efficacy with current Rx

ALLERGIC CONJUNCTIVITIS



66 million or more adults in the U.S.[2]

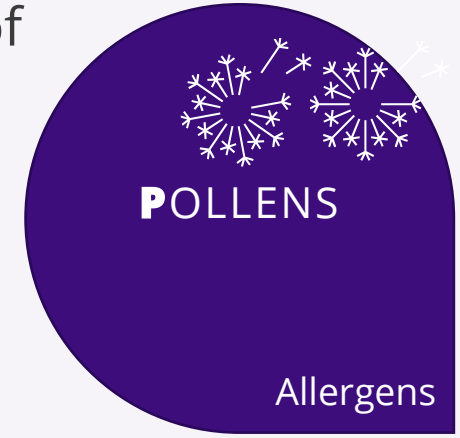
Unchecked growing disease burden and limited options beyond OTC antihistamines

Reproxalap is poised to potentially be the next novel entrant in the dry eye disease and allergic conjunctivitis markets.

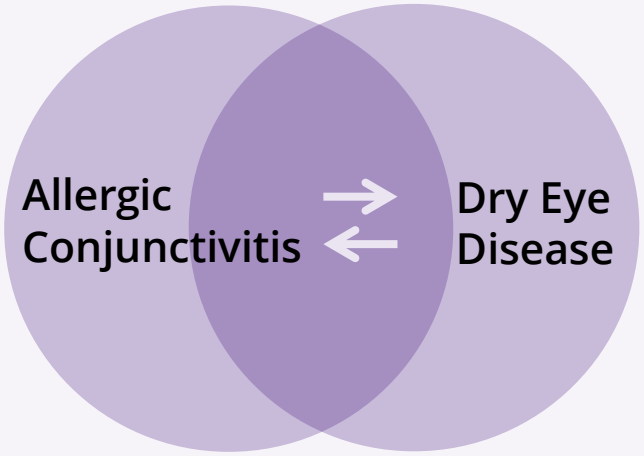
Sources: [1]Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014;157(4):799-806. doi:10.1016/j.ajo.2013.12.023; [2]Singh K, Axelrod S, Bielory L. The epidemiology of ocular and nasal allergy in the United States, 1988-1994. J Allergy Clin Immunol. 2010;126(4):778-783.e6. doi:10.1016/j.jaci.2010.06.050. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Allergic Conjunctivitis and Dry Eye Disease Are Interrelated Inflammatory Ocular Surface Diseases

The Three **P's** of Ocular Surface Inflammation



- Allergic response can compromise tear film.
- Dry eye inflammation can enhance allergic response.
- Dry, polluted environments exacerbate both conditions.

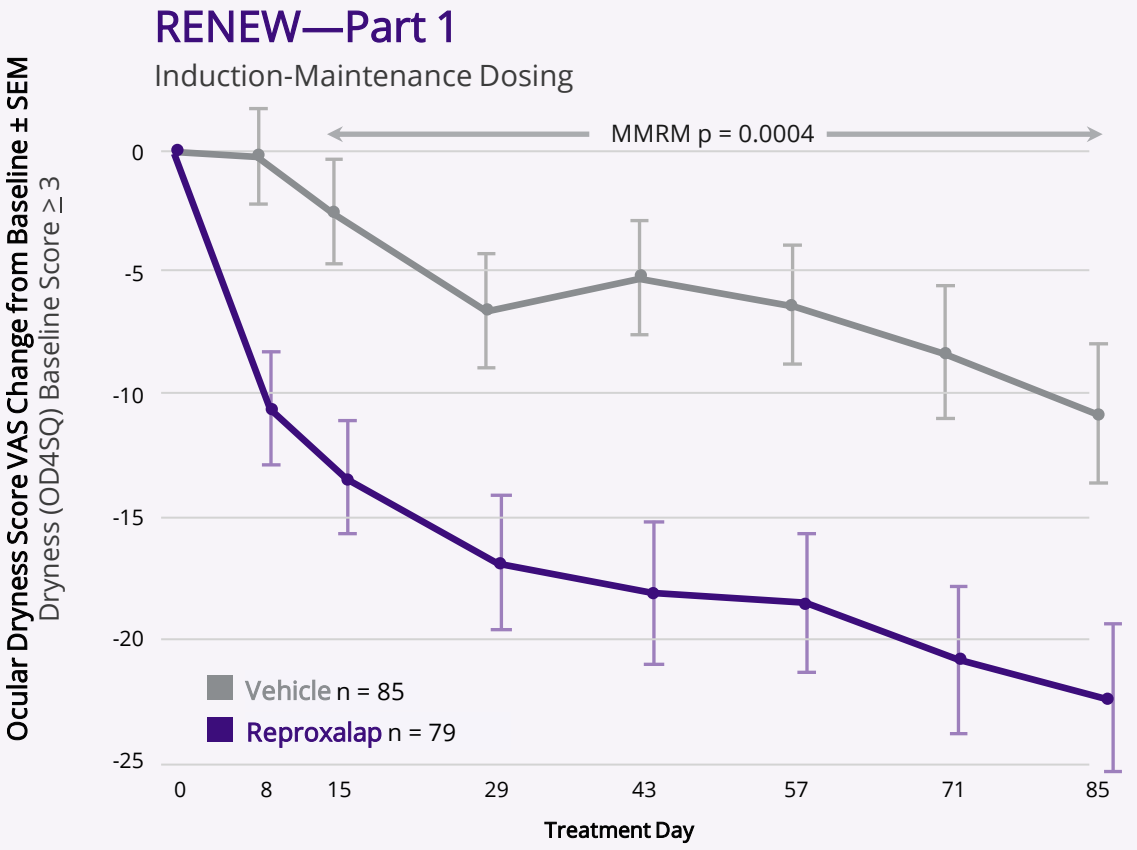


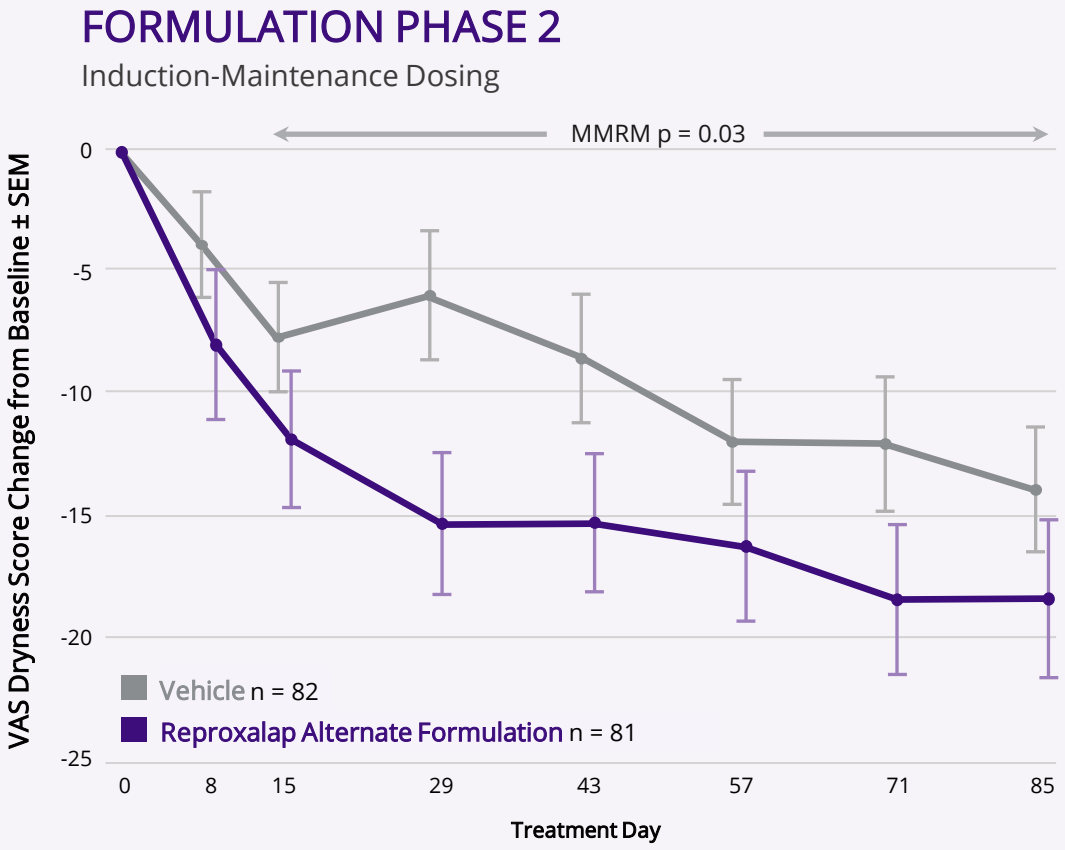
"The clear interaction of allergy, dry eye and environmental irritants makes untangling their etiology in prevalence studies difficult."

-Mark B. Abelson, MD et. al.

Sources: Concepts adapted from "The Whipsaw of Allergic Dry Eye" by Mark B. Abelson, MD and Lauren Lilyestrom in REVIEW of Ophthalmology; October 2008; and Hom MM, Nguyen AL, Bielory L. Allergic conjunctivitis and dry eye syndrome. Ann Allergy Asthma Immunol. 2012 Mar;108(3):163-6.

Reproxalap Met 12-Week (Chronic) Dryness Symptom Primary Endpoint in RENEW-Part 1 and Formulation Phase 2 Clinical Trials



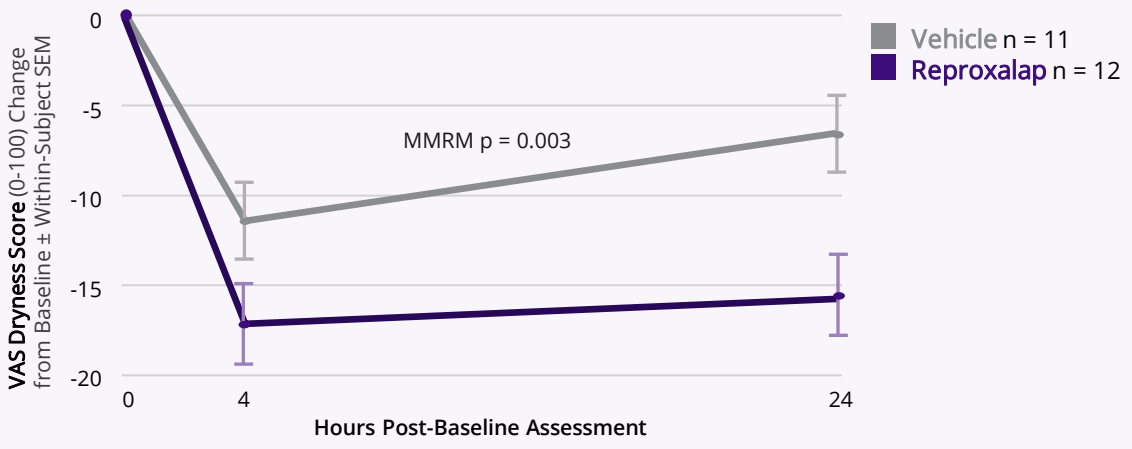


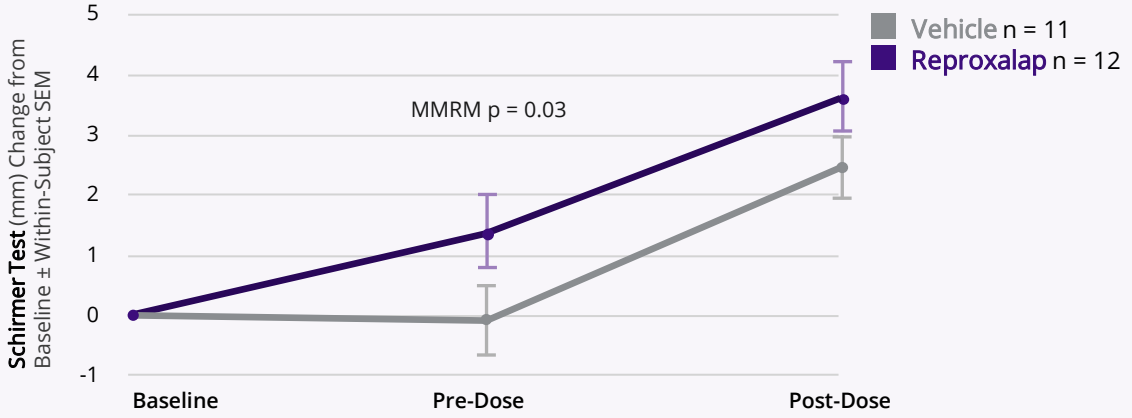
Sources: Reproxalap RENEW-Part 1 and Formulation Phase 2 DED clinical trial results. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials. **Induction-Maintenance Dosing** = QID for Weeks 1-4 and BID for Weeks 5-12
QID = 4 times daily **BID** = 2 times daily **OD4SQ** = Ocular Dryness 4-Symptom Questionnaire **VAS** = Visual Analog Scale **MMRM** = Mixed Effect Model Repeated Measures

Reproxalap Demonstrated Rapid and Broad Improvements After Only One Day of Treatment in the TRANQUILITY Run-In Cohort

A single day of dosing led to statistically significant changes in symptoms and Schirmer Test.

Dry Eye Assessment (Scale) After Environmental Dosing	Change from Baseline		
	Reproxalap n=12	Vehicle n=11	p-Value
VAS Dryness (0-100)	-26	+2	**0.003**
OD4S: Discomfort (0-5)	-0.7	+0.4	**0.003**
OD4S: Dryness (0-5)	-1.2	+0.1	**0.006**
OD4S: Grittiness (0-5)	-1.1	+0.1	**0.006**
OD4S: Burn (0-5)	-0.1	+0.8	0.07
OD4S: Sting (0-5)	-0.1	+0.4	0.23
Ocular Discomfort Scale (0-4)	-0.7	+0.4	0.07
Schirmer's Test (mm)*	+2.9	+0.7	**0.03**

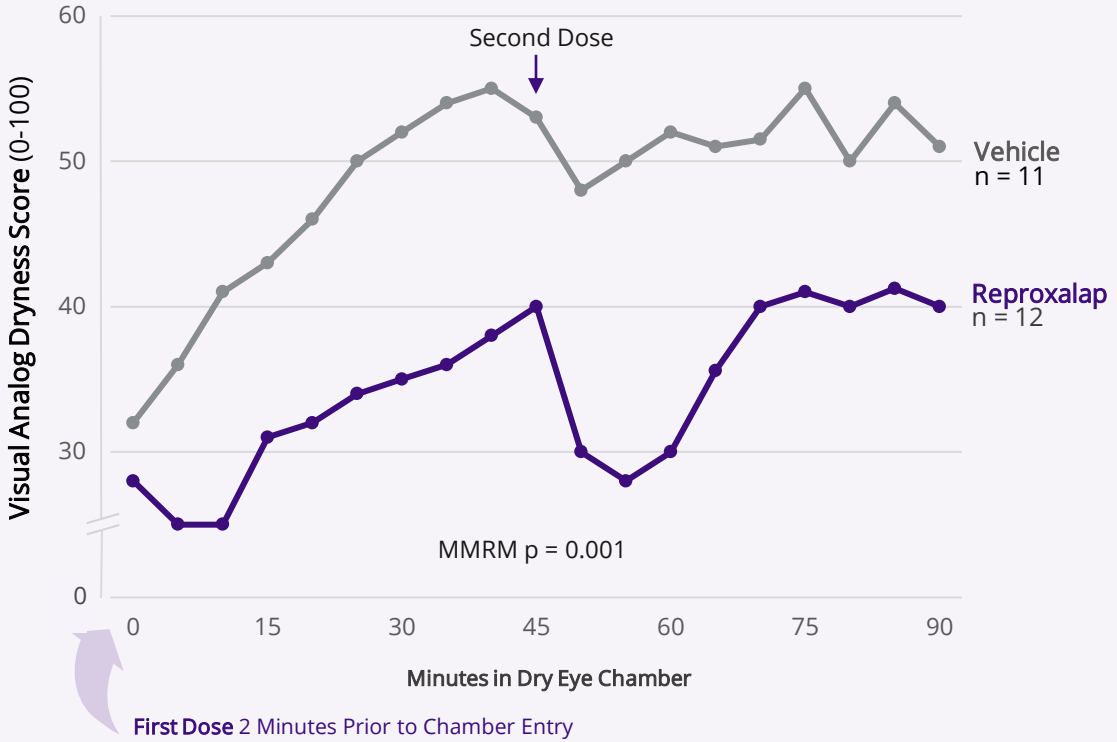




Source: TRANQUILITY Run-In Cohort initial results. *Schirmer's Test results based on improvement after a second dose of Day 1 relative to screening baseline; all other Day 1 assessments performed over 24 hours after QID dosing. Change from baseline estimates and p values derived from MMRM analyses. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials. **VAS** = Visual Analog Scale **OD4S** = Ocular Discomfort & 4-Symptom Questionnaire **QID** = Four times daily **MMRM** = Mixed-effect Model Repeated Measures

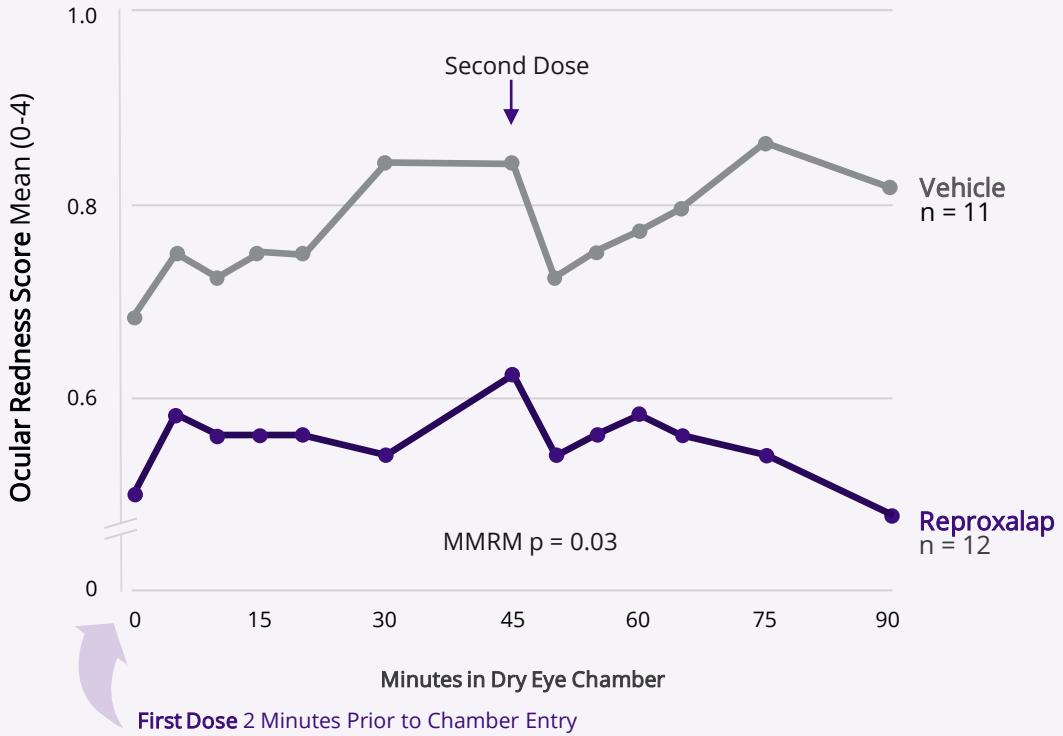
Phase 3 TRANQUILITY Trial Run-In Cohort: Symptom and Sign Activity Demonstrated within Minutes in a Dry Eye Chamber

Visual Analog Dryness Score



Ocular Redness Score

Redness is an FDA-approvable objective sign of dry eye disease.



Source: TRANQUILITY Run-In Cohort initial results. p values derived from MMRM of change from baseline, where baseline defined as Time 0. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials. **MMRM** = Mixed Effect Model Repeated Measures

Phase 3 TRANQUILITY Dry Eye Disease Trial Design

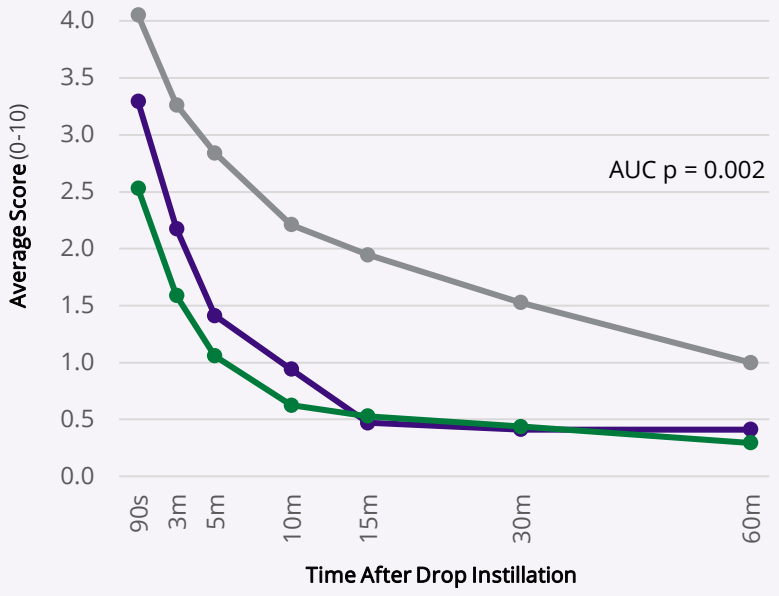
Dry Eye Chamber Challenge Model

Design	Multi-center, randomized, double-masked, parallel group, vehicle-controlled
Dosing	Day 1: QID; Day 2 (chamber): BID
Size	~150 patients per arm; 300 patients total
Primary Endpoint	Ocular redness over 90 minutes in a dry eye chamber
Secondary Endpoints	• Tear RASP levels • Schirmer's Test • Dry eye symptoms

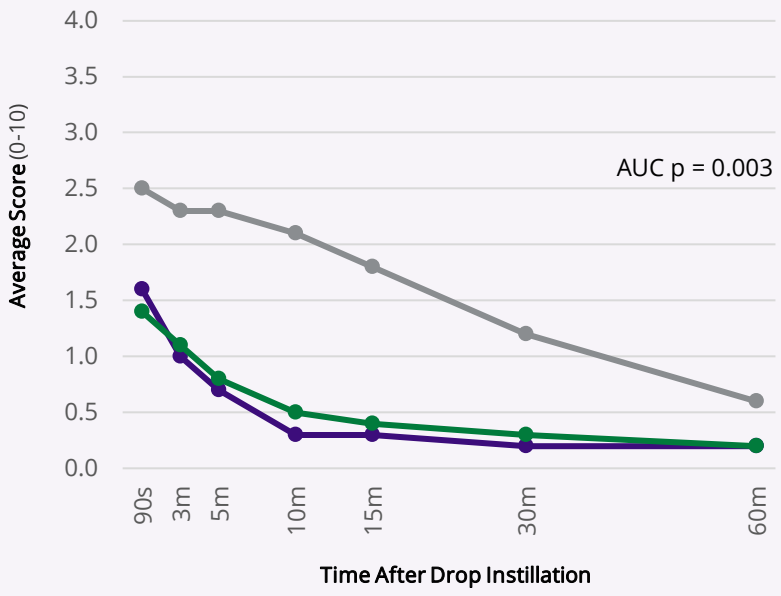
Results from the identical TRANQUILITY and TRANQUILITY-2 Trials are expected in Q4 2021.

Tolerability of Reproxalap Over One Hour Post-Instillation Significantly Improved vs. Xiidra® in Dry Eye Disease Patients

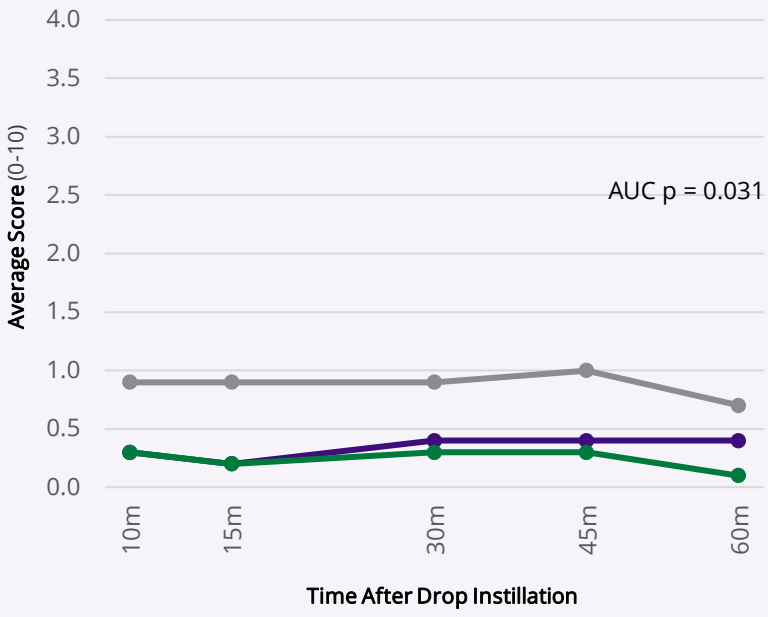
Ocular Discomfort



Blurry Vision



Dysgeusia (Taste Disturbance)



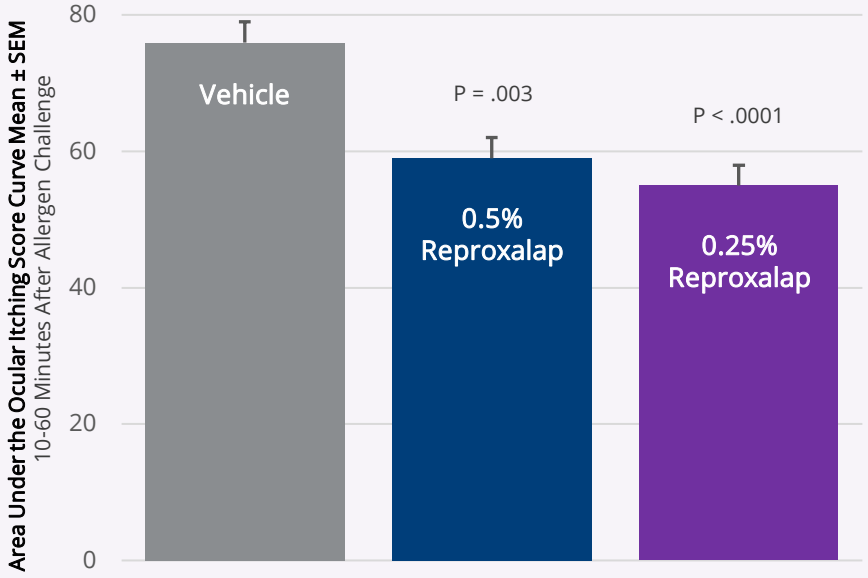
Xiidra® Reproxalap Reproxalap Alternate Formulation

Source: McMullin D, Clark D, Cavanagh B, Karpecki P, Brady TC. A Post-Acute Ocular Tolerability Comparison of Topical Reproxalap 0.25% and Lifitegrast 5% in Patients with Dry Eye Disease. Clin Ophthalmol. 2021 Sep 22;15:3889-3900. doi: 10.2147/OPTH.S327691. PMID: 34588761; PMCID: PMC8473572.. p-values represent MMRM of vehicle area under the curve vs. pooled reproxalap AUC. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials. **AUC** = area under the curve

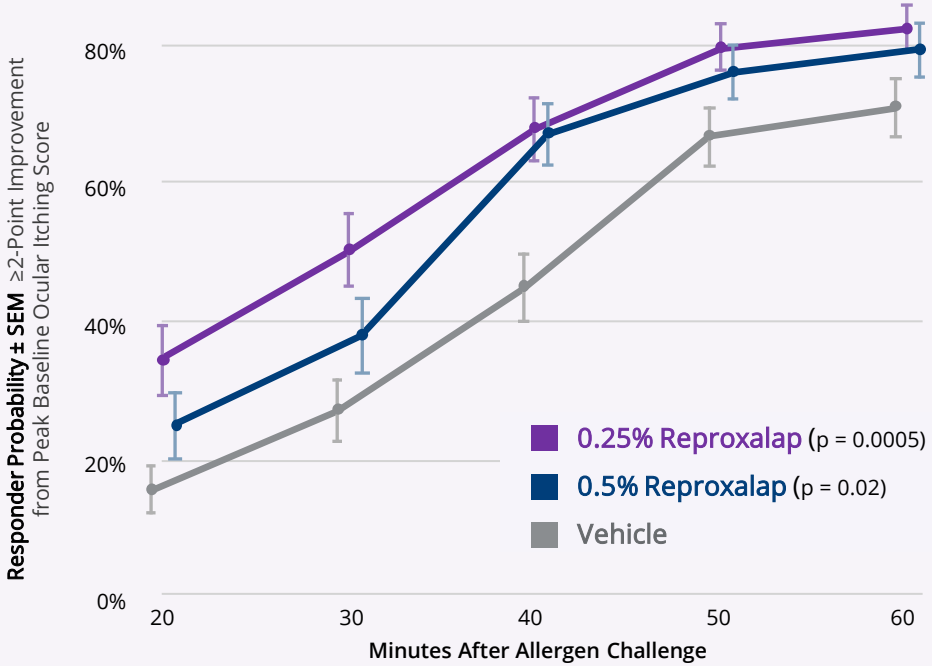
Reproxalap Achieved Primary and Key Secondary Endpoints in ALLEVIATE Phase 3 Trial in Allergic Conjunctivitis

CONJUNCTIVAL ALLERGEN CHALLENGE

Primary Endpoint



Key Secondary Endpoint



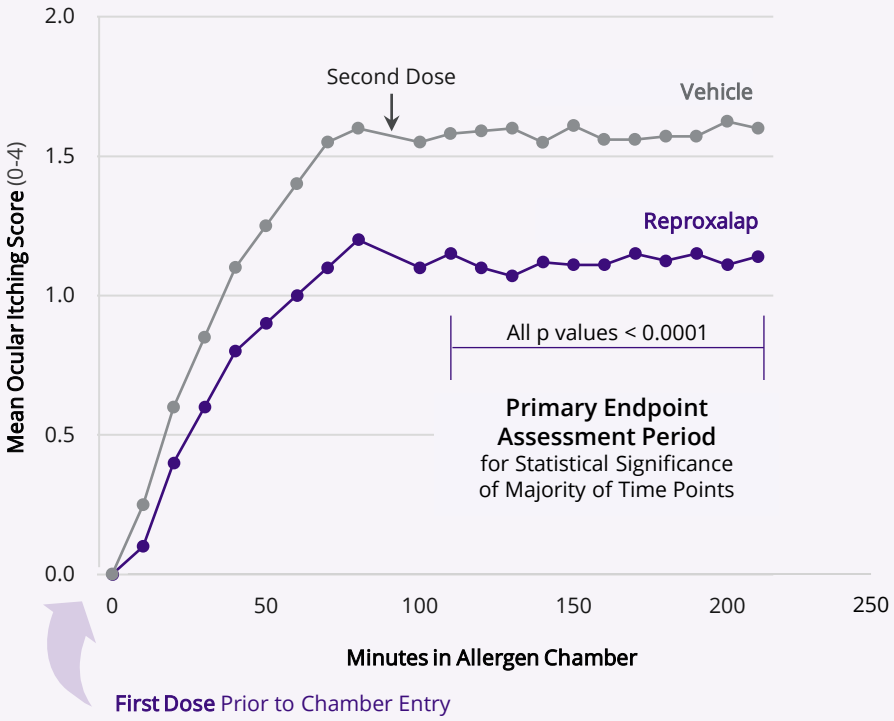
Source: Clark D, Cavanagh B, Shields AL, Karpecki P, Sheppard J, Brady TC. Clinically Relevant Activity of the Novel RASP Inhibitor Reproxalap in Allergic Conjunctivitis: The Phase 3 ALLEVIATE Trial. Am J Ophthalmol. 2021 May 1:S0002-9394(21)00222-1. doi: 10.1016/j.ajo.2021.04.023. Epub ahead of print. PMID: 33945820. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Primary and Key Secondary Endpoints Achieved in Phase 3 INVIGORATE Allergen Chamber Trial

Prophylactic and treatment effects of reproxalap demonstrated

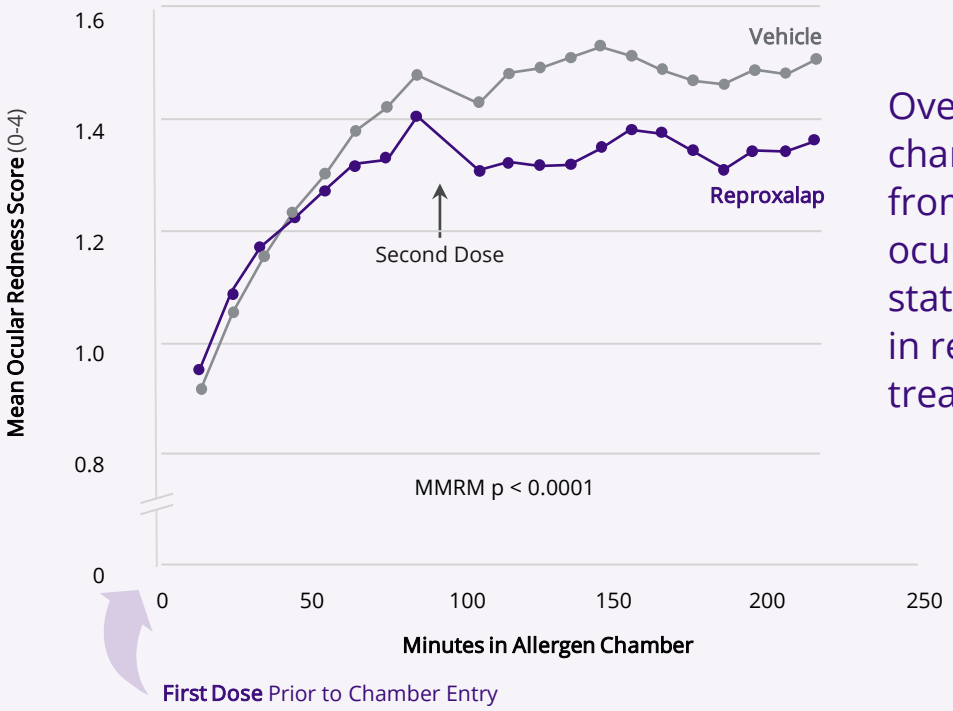
Primary Endpoint

Reduction in Ocular Itching Over Pre-Specified Time Frame



Key Secondary Endpoint

Reduction in Ocular Redness Over the Entire Chamber



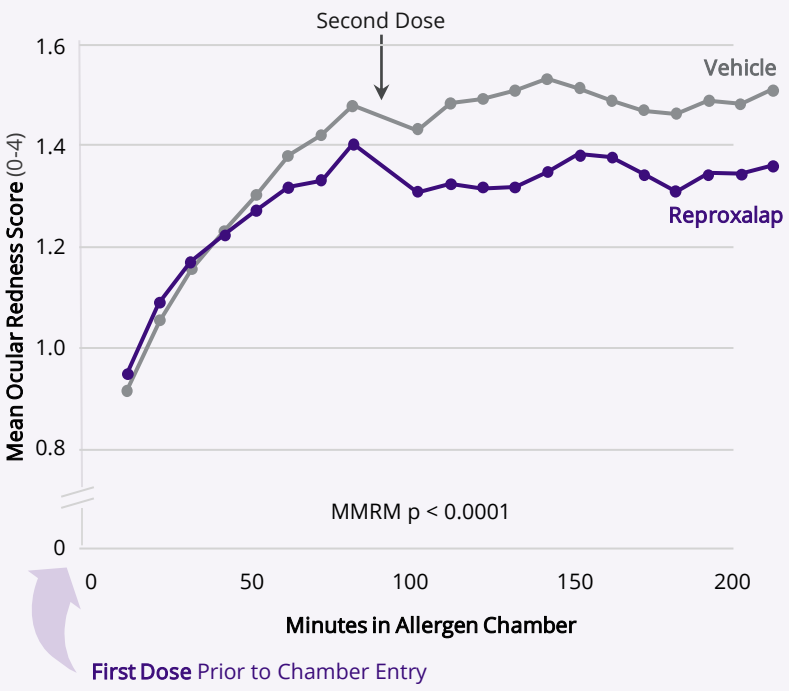
Over entire chamber, change from baseline in ocular redness statistically lower in reproxalap-treated subjects

Source: INVIGORATE clinical trial results. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials. **MMRM** = Mixed Effect Model Repeated Measures

Reproxalap Has Demonstrated Consistent Effect on Redness Across Two Distinct Chamber Challenge Models in Ocular Surface Disease

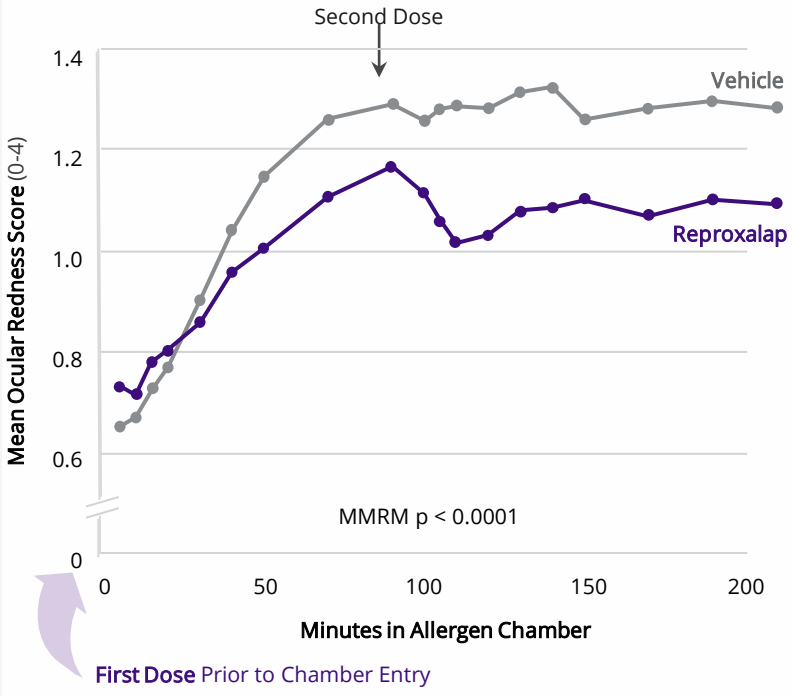
Allergen Chamber

INVIGORATE Phase 3 Trial



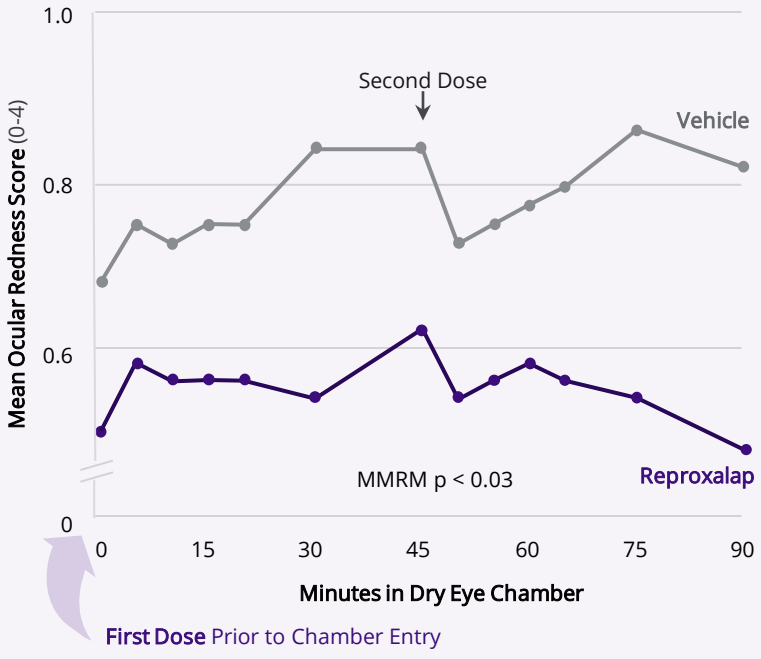
Allergen Chamber

Phase 2 Trial



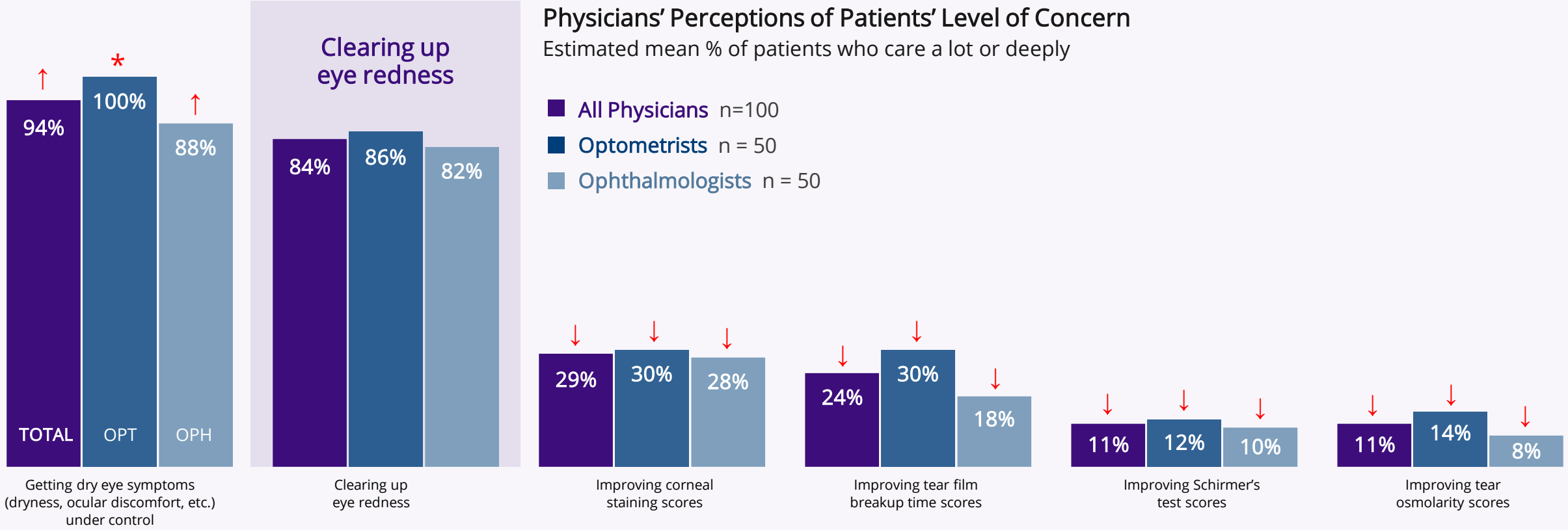
Dry Eye Chamber

TRANQUILITY Run-In Cohort



Sources: TRANQUILITY run-in cohort results; Phase 2 Allergen Chamber clinical trial for 0.25% reproxalap (ClinicalTrials.gov #NCT03709121), INVIGORATE Phase 3 results. Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials. **MMRM** = mixed effect model of repeated measures

Physicians Believe Most of Their Patients Care More About Clearing Up Eye Redness Than Other Signs of Dry Eye Disease



* Significantly higher than comparison group (90% confidence level) ↑↓ Significantly higher/lower than redness (90% confidence level)
A5. In your experience, how much do patients with dry eye disease care about each of the following?

Reproxalap Represents a Novel, Rapid-Onset Potential Therapeutic Approach in Dry Eye Disease

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

Rapid symptom improvement within minutes

Broad symptomatic activity

Acute conjunctival redness control

Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

ADX-629, A RASP Inhibitor for Oral Administration, Expands Pipeline Beyond Ocular Disease

ADX-629 is a first-in-class, orally available and irreversible covalent inhibitor of pro-inflammatory RASP, and potentially represents a new paradigm in the understanding and treatment of systemic immune-mediated disease.

A comprehensive systemic disease initiative is in process to assess the activity of ADX-629 in three types of severe inflammation: cytokine release syndrome, allergic inflammation, and autoimmune disease.

RASP-INHIBITION IN SYSTEMIC DISEASES

Phase 2 Proof-of-Concept Clinical Trials in Three Types of Severe Inflammation

1. Phase 2 clinical trial in COVID-19
2. Phase 2 allergen-challenge clinical trial in atopic asthma
3. Phase 2 clinical trial in psoriasis

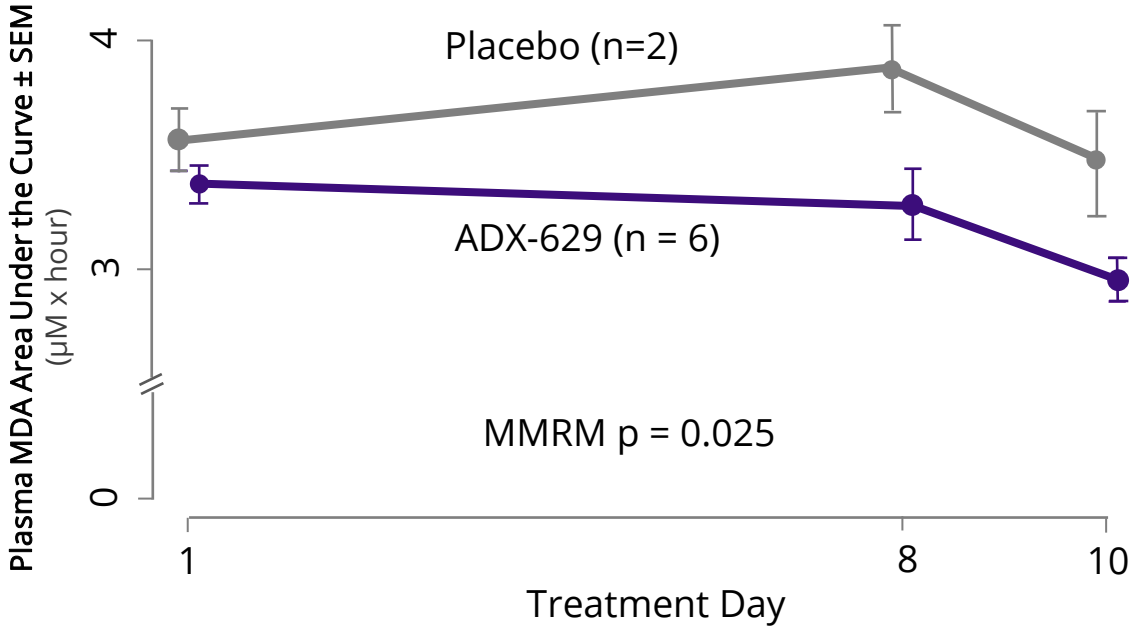
Results Expected in Q4 2021 or Q1 2022

- Cytokine Release Syndrome
- Allergic Inflammation
- Autoimmune Disease

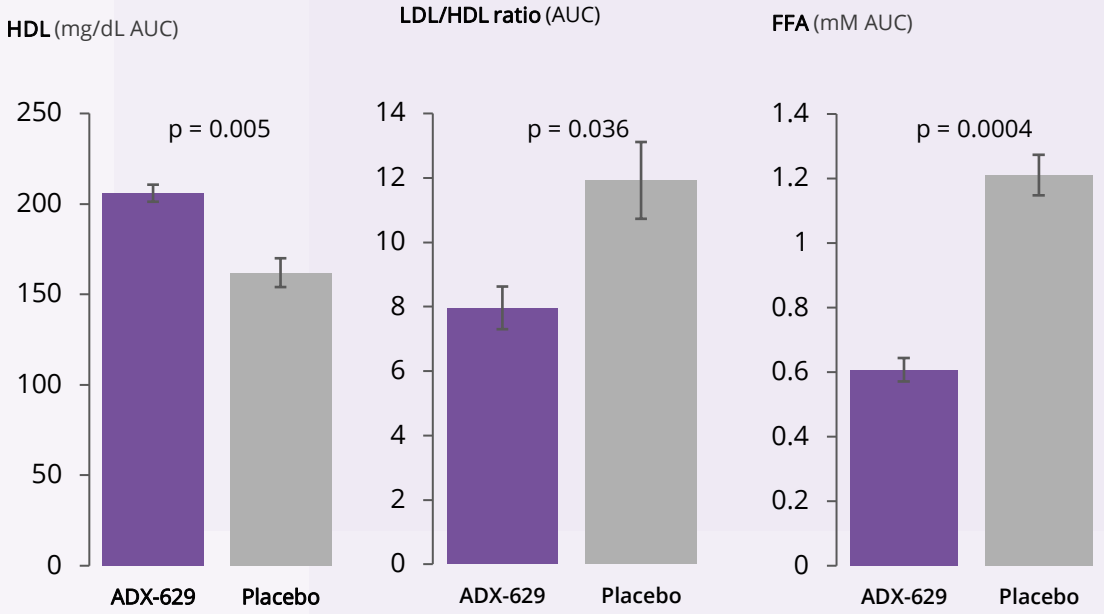
The timing of clinical trial initiation and completion depends, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, and the ability to recruit patients.

ADX-629 Reduced RASP vs. Placebo in Phase 1 Clinical Trial, Demonstrating Target Engagement and Improved Lipid Profiles

RASP LEVELS OVER 10 DAYS OF DOSING



PLASMA LIPID PROFILE AFTER FATTY MEAL



Source: ADX-629 Phase 1 clinical trial results. **MDA** = Malondialdehyde **MMRM** = Mixed Model Repeated Measures **HDL** = High-density lipoprotein **LDL** = Low-density lipoprotein **FFA** = Free fatty acids

aldeyra

October 2021

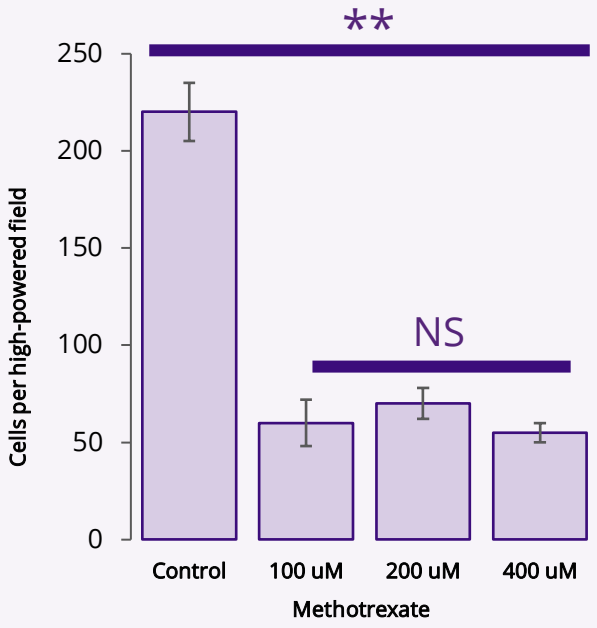
ADX-2191 (METHOTREXATE FOR INTRAVITREAL INJECTION)

A Platform Approach to Treat Rare Immune-Mediated Retinal Diseases

Nasdaq: ALDX

ADX-2191, a Novel Intravitreal Formulation of Methotrexate, Represents a Clinically Proven Systems Modulating Approach

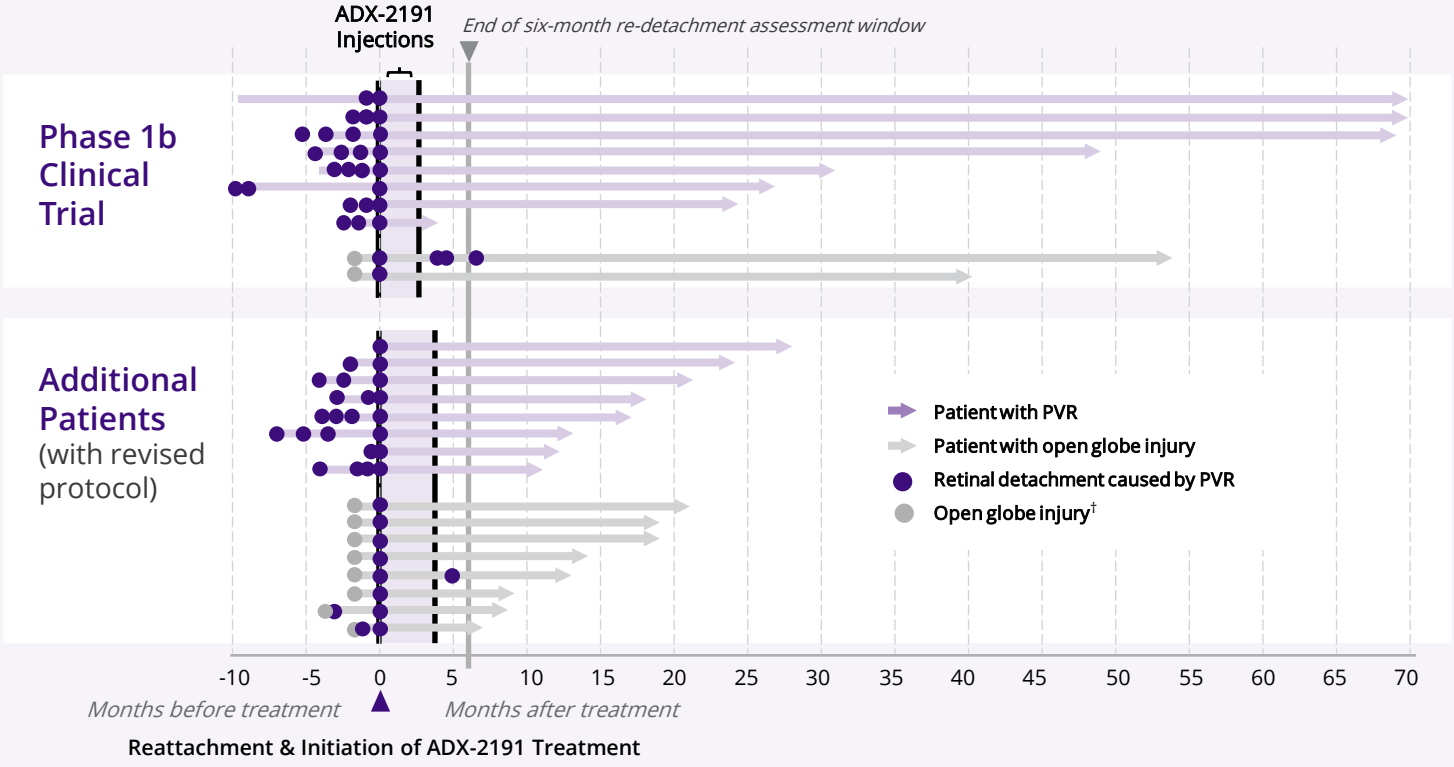
Preclinical reduction in cellular proliferation



Source

Clinical reduction in retinal detachment

Retinal Detachments Over Time by Patient



Sources: ADX-2191 PVR Phase 1b investigator sponsored clinical trial (n=10) results and additional in-practice use (n=16); Invest Ophthalmol Vis. Sci. 2017; 58:3940–3949. †Timing of open globe injury as shown is estimated. There is no assurance that prior results, such as signals of safety, activity or durability of effect, observed from this open label investigator sponsored trial will be replicated in more rigorous clinical trials involving ADX-2191. ** = p value ≤ 0.01 **NS** = Not Significant **PVR** = Proliferative vitreoretinopathy

ADX-2191 Represents a Novel Potential Therapeutic Option For the Prevention of Proliferative Vitreoretinopathy

PROLIFERATIVE VITREORETINOPATHY (PVR)

4,000 U.S.

PVR is a **rare disease**, with ~4,000 patients per year in the U.S. and nearly twice as many in Europe and Japan combined.

Left untreated, retinal detachment due to PVR can progress to **permanent blindness.**

There is currently **no FDA- or EMA-approved therapy**.

Repeat surgery, which can lead to **vision loss**, is currently the only possible course of action.

ADX-2191

Granted U.S. orphan designation and FDA fast track designation for the prevention of PVR

Tolerability and reattachment success demonstrated in Phase 1b open-label investigator sponsored clinical trial

GUARD adaptive Phase 3 clinical trial for the prevention of recurrent retinal detachment due to PVR ongoing

Source: Aldeyra internal estimates based on primary and secondary market research; published literature. **PVR** = Proliferative vitreoretinopathy

ADX-2191: GUARD Trial Design in Proliferative Vitreoretinopathy Adaptive Phase 3 (Part 1) Clinical Trial Design

COMPLETION OF ENROLLMENT EXPECTED IN 2021

Primary Objective
Evaluate efficacy of intravitreal ADX-2191 injections for prevention of recurrent retinal detachment due to PVR

Design
Multi-center, randomized, controlled, two- part, adaptive Phase 3 clinical trial (N≅100)

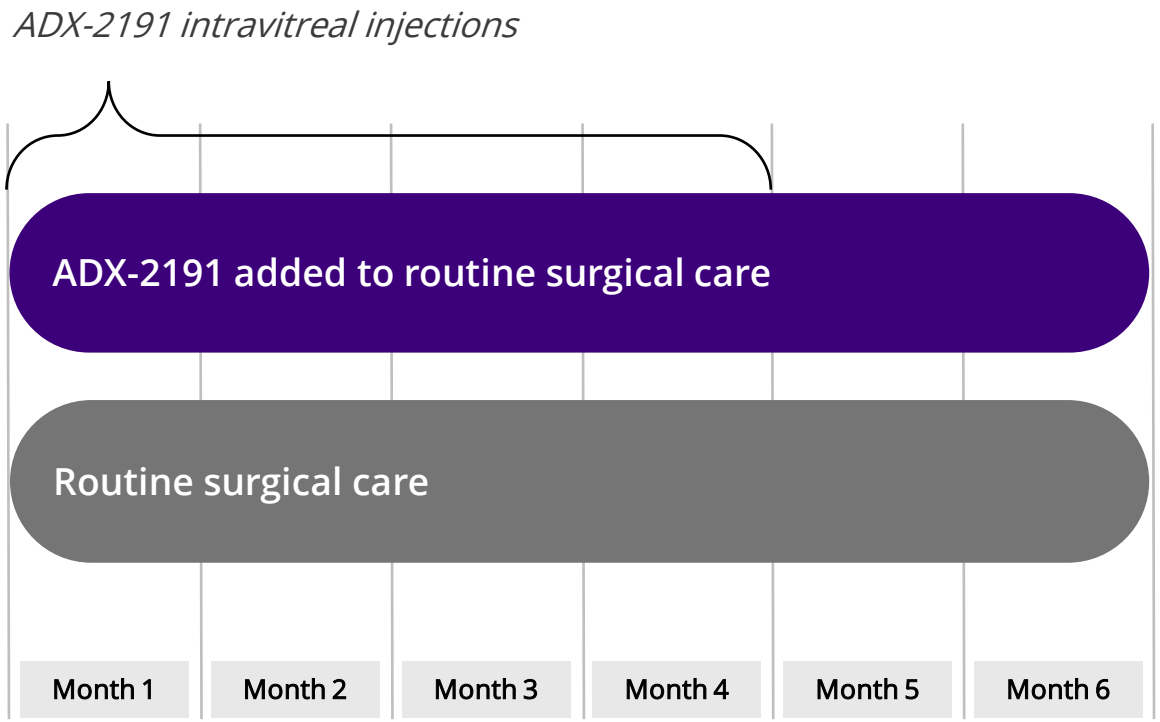
Inclusion Highlights
- Recurrent retinal detachment due to PVR, or
- Retinal detachment associated with open-globe injury

Dosing Regimen
At surgery, weekly (x8), and then every other week (x4) intravitreal ADX-2191 injections

Endpoint
Retinal re-detachments due to PVR requiring re-operation within 6 months:

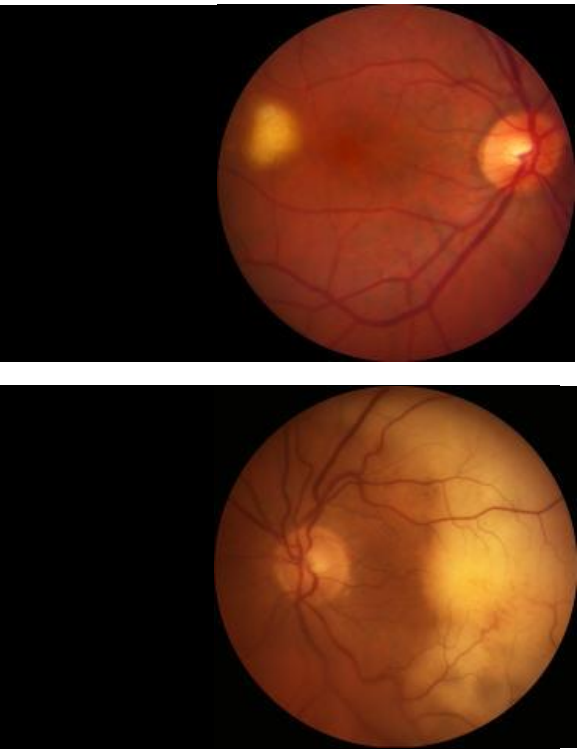
1. OCT demonstrating fovea-off retinal detachment
2. Photographic documentation retinal detachment

ADAPTIVE PHASE 3 PVR CLINICAL TRIAL DESIGN: PART 1



*The timing of ongoing clinical trials depend, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, and the ability to recruit patients. **PVR** = Proliferative Vitreoretinopathy **OCT** = Optical Coherence Tomography

ADX-2191 Has the Potential to be the Only Approved Drug for Primary Vitreoretinal Lymphoma (PVRL), a Rare but Serious Retinal Cancer



***Small** (top) and **large** (bottom) subretinal infiltrates in patients with primary vitreoretinal lymphoma*

A rare, aggressive, high-grade cancer, PVRL arises in the vitreous and retina.

Approximately **2,900 people** in the United States suffer from PVRL.

Approximately **600 new cases** of PVRL are diagnosed in the United States per year.

4.83 years is the median survival for newly diagnosed patients.

The most common ocular complaints reported by patients include **blurred vision, painless loss of vision, floaters, red eye, and photophobia**.

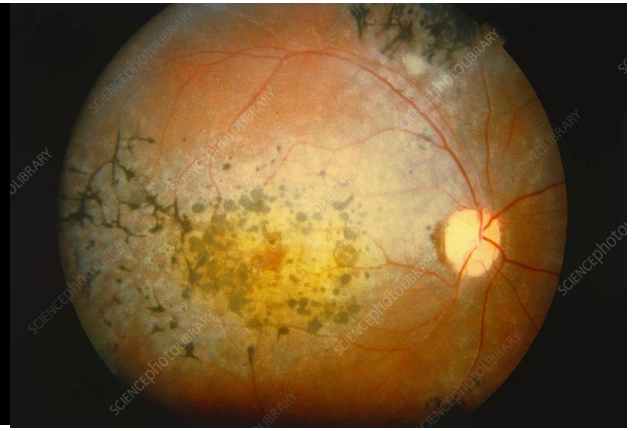
No approved treatments are currently available, though methotrexate represents current standard of care.

U.S. FDA Orphan Drug Designation Received in July 2021

Source: Primary Vitreoretinal Lymphoma by D. J. Wilson on AAO EyeWiki; M. Sagoo, Survey of Ophthalmology (2014); Grimm et. al., Annals of Oncology (2007).

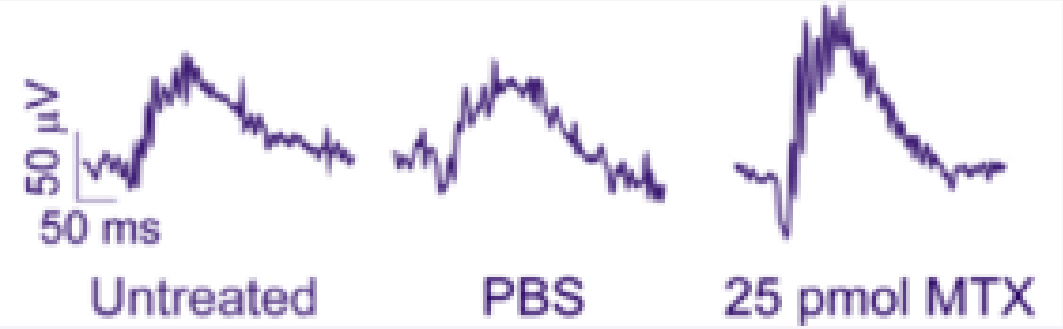
ADX-2191 Has the Potential to be the Only Approved Drug for Retinitis Pigmentosa (RP), a Clinical Group of Rare Genetic Eye Diseases

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



Affects an estimated 82,000-110,000 individuals in the United States, and approximately 1 in 4,000 people worldwide.

Forms of RP and related diseases include usher syndrome, Leber's congenital amaurosis, and Bardet-Biedl syndrome, among others.



Preclinical evidence suggests that methotrexate improves retinal function in a mouse model of RP.

U.S. FDA Orphan Drug Designation Received in August 2021

Source: Liu et al. Pharmacological clearance of misfolded rhodopsin for the treatment of RHO-associated retinitis pigmentosa. FASEB J. 2020 Aug;34(8):10146-10167.
PBS=phosphate-buffered saline, **MTX**=methotrexate.

ADX-2191: Phase 2 Clinical Trial Design in RP

INITIATION EXPECTED IN Q4 2021*

Primary Objective
To evaluate the safety and efficacy of ADX-2191 in patients with RP

Design
Single-center, open label study (N=8)

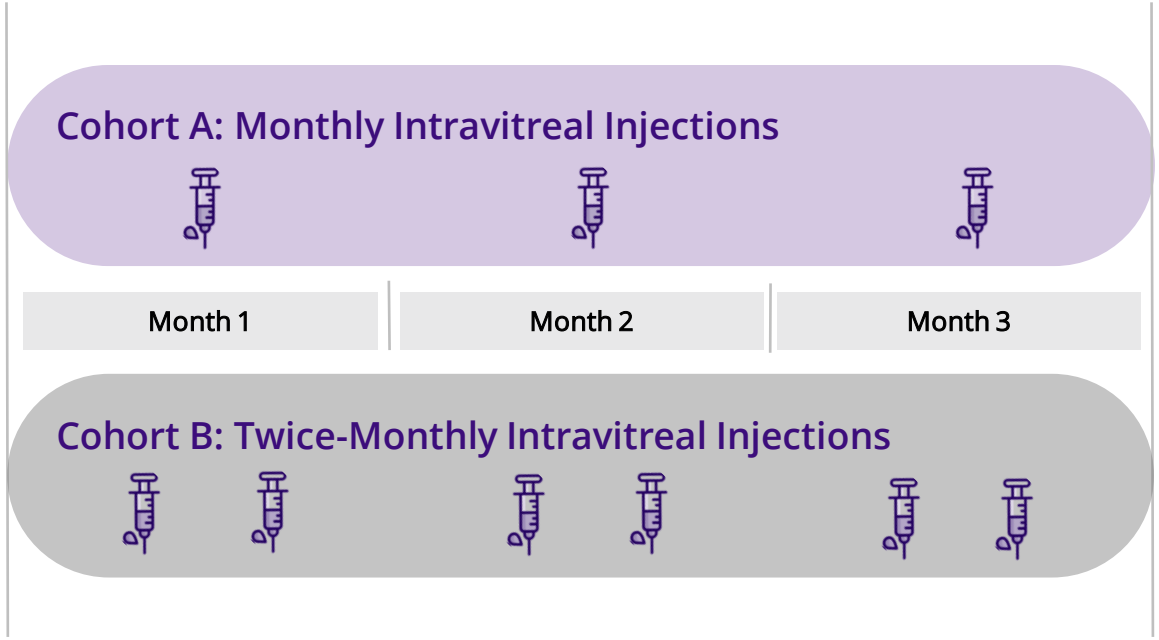
Inclusion Highlights
Diagnosis of RP due to rhodopsin gene mutations, including P23H

Dosing Regimen
Cohort A (N=4): Monthly injections
Cohort B (N=4): Twice-monthly injections

Primary Endpoint
Safety and tolerability of ADX-2191 in RP subjects

Secondary Endpoints
1. Change in visual acuity assessed by ETDRS
2. Central retinal sensitivity assessed by MAIA microperimetry
3. Change in dark-adapted flash analyzed by ffERG
4. Change in dark-adapted retinal sensitivity
5. OCT assessment for change in central subfield foveal thickness and ellipsoid zone area/width

RETINITIS PIGMENTOSA CLINICAL TRIAL DESIGN



*The timing of ongoing clinical trials depends, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, and the ability to recruit patients.
RP = Retinitis Pigmentosa **OCT** = Optical Coherence Tomography **ETDRS** = Early Treatment Diabetic Retinopathy Study **MAIA** = Macular Integrity Assessment **ffERG** = full field Electroretinography

Experienced Management Team and Board of Directors

MANAGEMENT TEAM

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

Joshua Reed, M.B.A.
Chief Financial Officer

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 Peptimmune[6]
Marty Joyce, M.B.A.	Former CFO of Serono USA
Nancy Miller-Rich	Former SVP BD&L and Commercial Strategy at Merck
Gary Phillips, M.D.	CEO OrphoMed
Neal Walker, D.O.	CEO 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

Upcoming Planned Clinical Milestones*

Phase 3 TRANQUILITY and TRANQUILITY-2 Trials of reproxalap in dry eye disease

Top-line results expected in Q4 2021

Part 1 of Phase 3 GUARD Trial of ADX-2191 in proliferative vitreoretinopathy

Completion of enrollment in 2021

Results in 2022

Phase 2 clinical trial of ADX-2191 in retinitis pigmentosa

Initiation in Q4 2021

Phase 2 clinical trials of ADX-629 in multiple systemic indications

Top-line results expected in Q4 2021 or Q1 2022

*The timing of ongoing clinical trials depend, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, and the ability to recruit patients.

Compelling Value Proposition

NOVEL SYSTEMS-BASED APPROACHES FOR IMMUNOLOGY

- Ocular and systemic RASP-inhibition represent first-in-class, pre-cytokine therapeutic approaches.
- Rare retinal disease methotrexate platform provides potential near-term, high-value commercial opportunity.

NEAR-TERM DEVELOPMENT CATALYSTS*

- Phase 3 TRANQUILITY and TRANQUILITY-2 results in dry eye disease expected in Q4 2021.
- ADX-629 Phase 2 clinical testing results in asthma, psoriasis, and COVID-19 expected in Q4 2021 or Q1 2022.

LARGE AND UNDERSERVED MARKET OPPORTUNITY

- Lead product candidate reproxalap targets a U.S. addressable market of >$18B.
- Potential rapid onset and ocular redness control differentiates reproxalap in blockbuster ocular indications of dry eye disease and allergic conjunctivitis.

SOLID CASH POSITION

- Cash, cash equivalents and marketable securities of $241.4M as of 9/30/2021
- Cash runway through the end of 2023, based on projected operating expenses*

*Timing depends, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, the ability to recruit patients, and regulatory feedback.

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October 2021

CORPORATE OVERVIEW

Innovative Approaches to Regulating Immune Response

Nasdaq: ALDX