

November 2021

CORPORATE OVERVIEW

Innovative Approaches to Regulating Immune Response

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Compelling Value Proposition



NOVEL SYSTEMS-BASED APPROACHES FOR IMMUNOLOGY

- Ocular and systemic RASPinhibition represent first-in-class, pre-cytokine therapeutic approaches.
- Rare retinal disease methotrexate platform provides potential nearterm, 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.

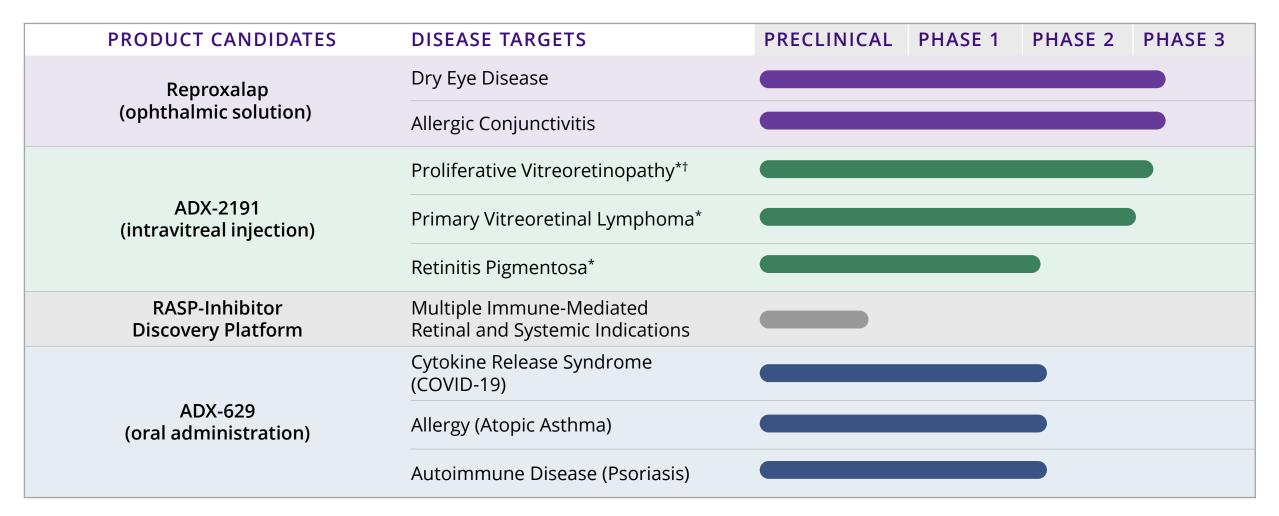


SOLID CASH POSITION

- 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*



Deep and Innovative Pipeline Addressing Immunological Disease





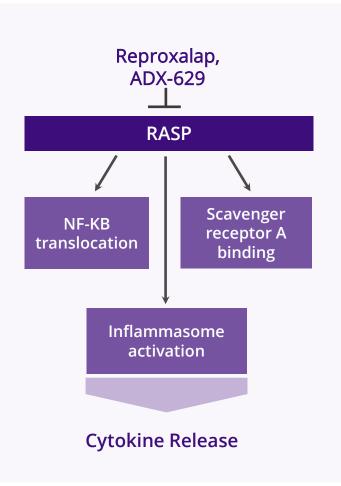


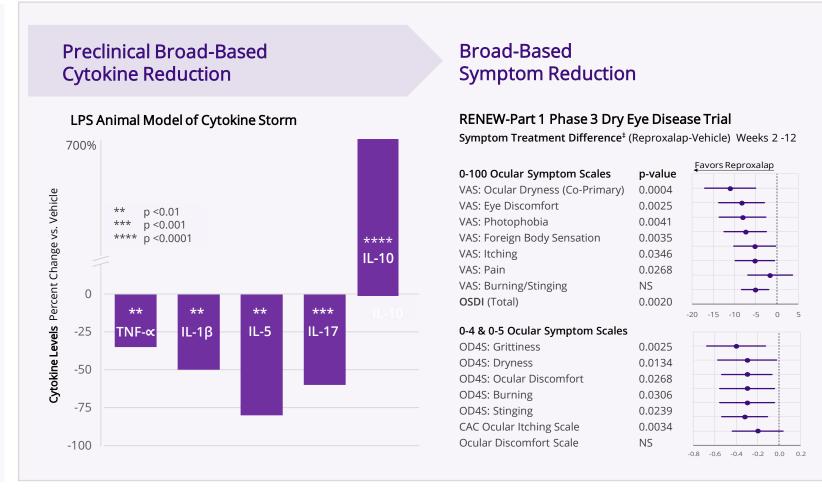
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REPROXALAP AND ADX-629

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

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

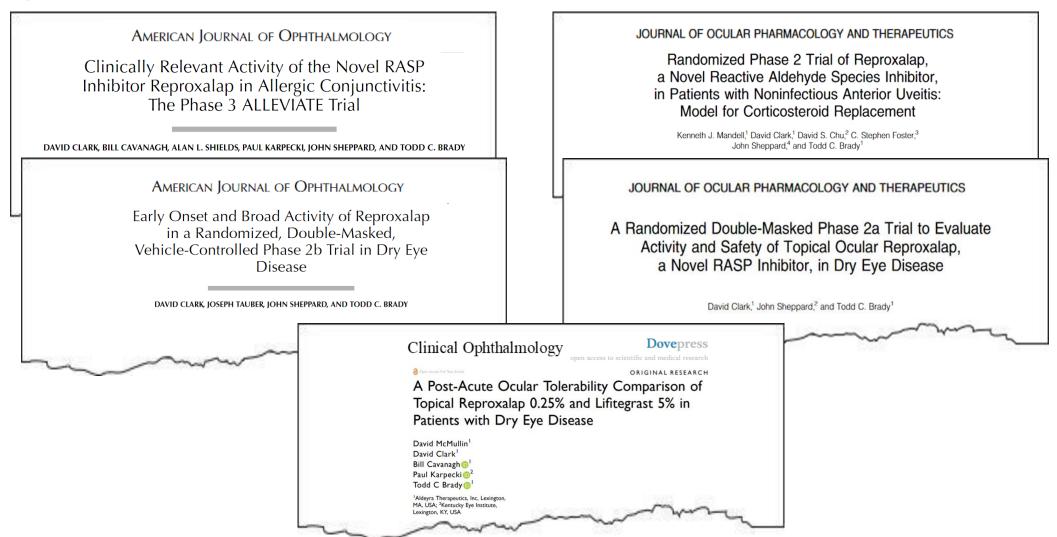






Sources: Cullen, et al. The Small Molecule Aldehyde Trap NS2 Exhibits Potent Anti-Inflammatory Activity in Three Murine Models of Inflammation [abstract]. In: The Journal of Allergy and Clinical Immunology. Volume 135, Issue 2, AB384, Feb 2015; Reproxalap RENEW-Part 1 clinical trial results. ‡Treatment 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



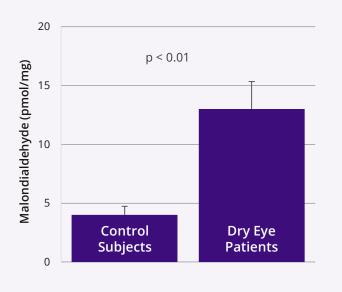


Reproxalap's Mechanism of Action Reduces RASP, a Potential Dry Eye Disease Biomarker

RASP in Dry Eye Disease

RASP markers are upregulated in dry eye disease.

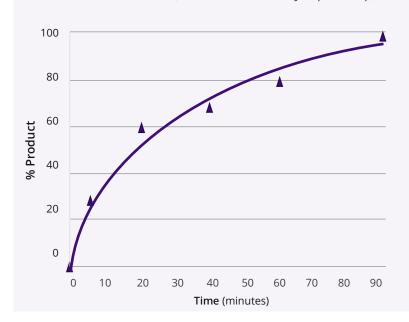
RASP levels have been shown to correlate with worsening symptoms and signs.



REPROXALAP

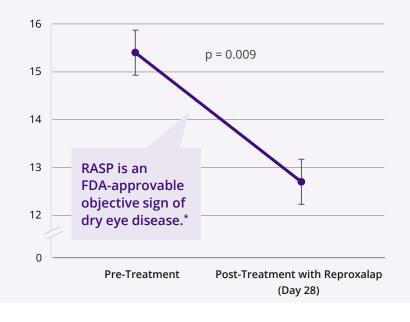
Rapid RASP binding in vitro

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 more than 1,300 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



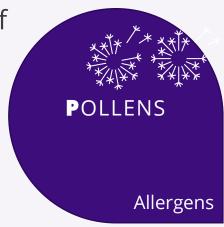
66 million or more adults in the U.S.²

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.



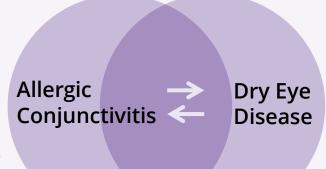
Allergic Conjunctivitis and Dry Eye Disease Are Interrelated Inflammatory Ocular Surface Diseases

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.



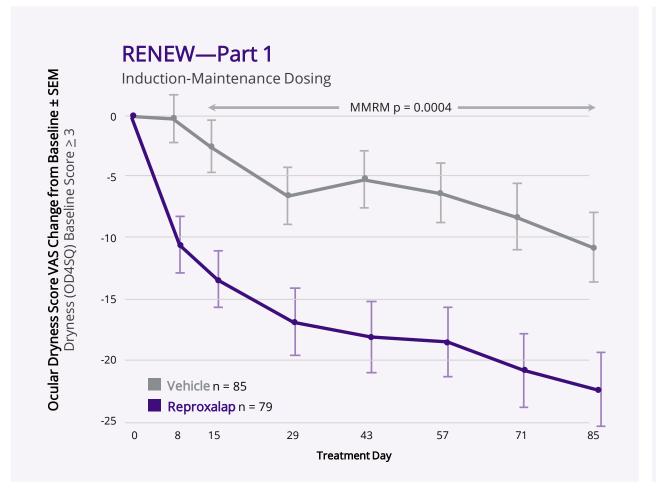


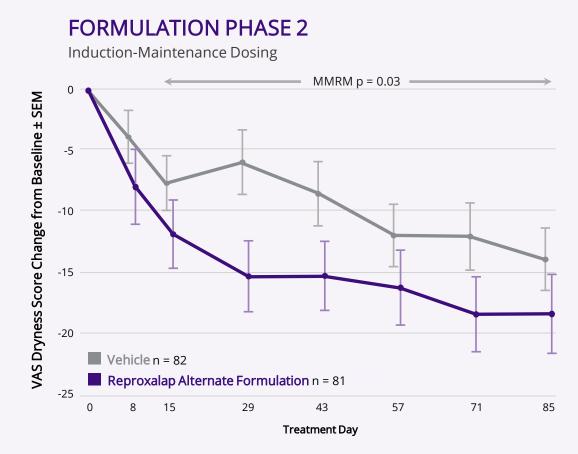


"The clear interaction of allergy, dry eye and environmental irritants makes untangling their etiology in prevalence studies difficult."

-Mark B. Abelson, MD et. al.

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



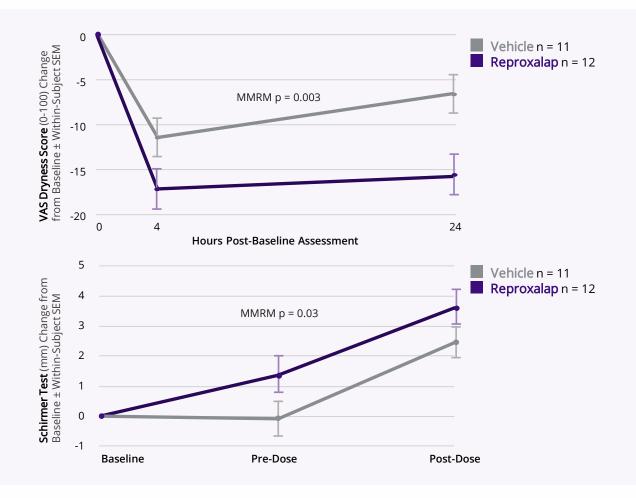




Reproxalap Demonstrated Rapid and Broad Improvements After Only One Day of Treatment in the TRANQUILITY Run-In Cohort

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

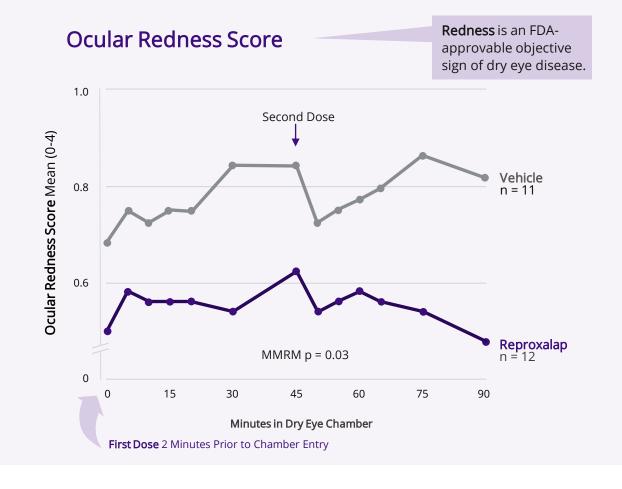
Dry Eye Assessment (Scale) After Environmental Dosing	Change from Baseline		
	Reproxalap n=12	Vehicle n=11	p-Value
VAS Dryness (0-100)	-26	+2	0.003
OD4S: Discomfort (0-5)	-0.7	+0.4	0.003
OD4S: Dryness (0-5)	-1.2	+0.1	0.006
OD4S: Grittiness (0-5)	-1.1	+0.1	0.006
OD4S: Burn (0-5)	-0.1	+0.8	0.07
OD4S: Sting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





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

Visual Analog Dryness Score 60 Second Dose Visual Analog Dryness Score (0-100) n = 11**Reproxalap** n = 12 MMRM p = 0.00115 30 45 75 90 Minutes in Dry Eye Chamber First Dose 2 Minutes Prior to Chamber Entry





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 more than 1,300 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

Primary Endpoint of Ocular Redness Achieved in Phase 2 Dry Eye Disease Chamber Trial

- Randomized, double-masked, vehicle-controlled Phase 2 clinical trial in 158 patients with dry eye disease
- Drug administration and dry eye chamber exposure identical to TRANQUILITY and TRANQUILITY-2
- Based on TRANQUILITY run-in results, more than 90% powered to achieve primary endpoint of ocular redness assessed over all chamber time points in aggregate
- Ocular redness scores in the reproxalap group were observed to be statistically lower than those of vehicle (p = 0.016)



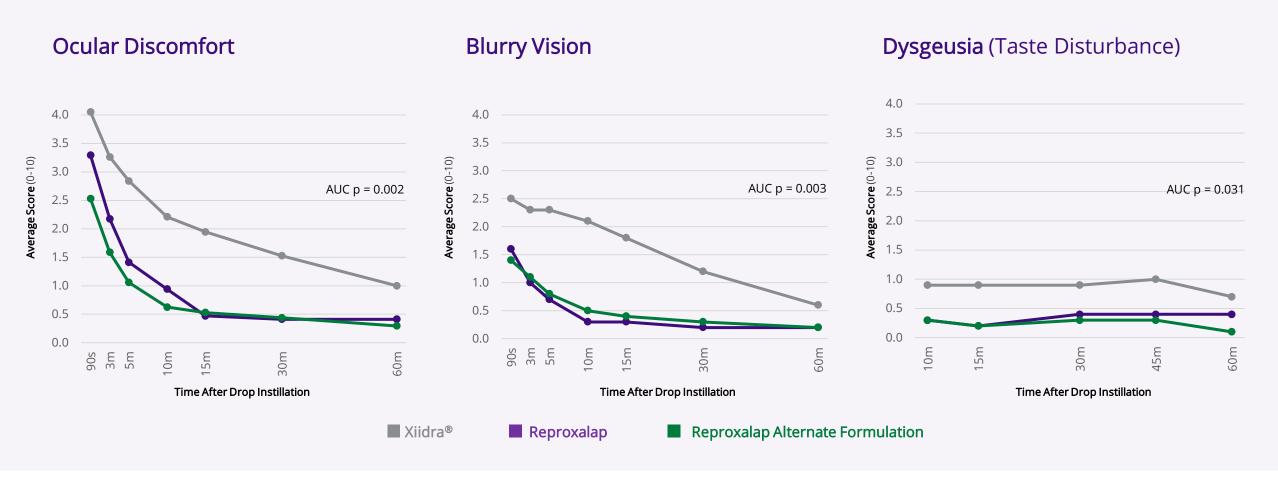
Phase 3 TRANQUILITY Dry Eye Disease Trial Design

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 levelsSchirmer's TestDry 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



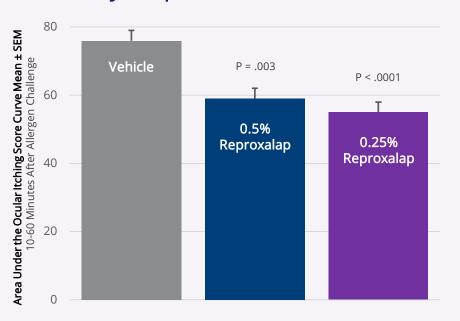


Reproxalap Achieved Primary and Key Secondary Endpoints in ALLEVIATE Phase 3 Trial in Allergic Conjunctivitis

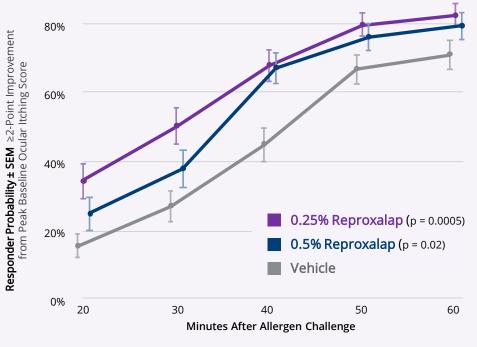
CONJUNCTIVAL ALLERGEN CHALLENGE



Primary Endpoint



Key Secondary Endpoint



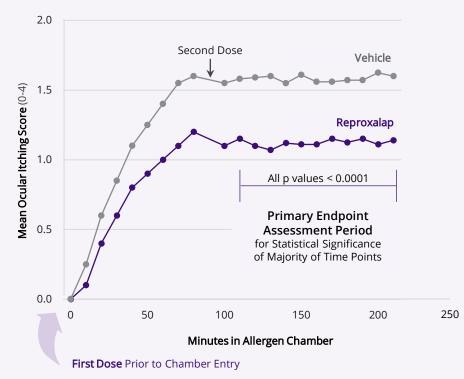


Primary and Key Secondary Endpoints Achieved in Phase 3 INVIGORATE Allergen Chamber Trial

Primary Endpoint

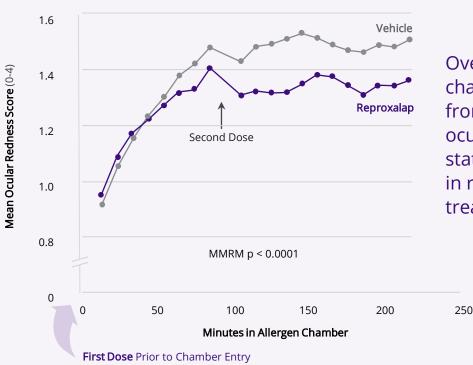
Reduction in Ocular Itching Over Pre-Specified Time Frame

Prophylactic and treatment effects of reproxalap demonstrated



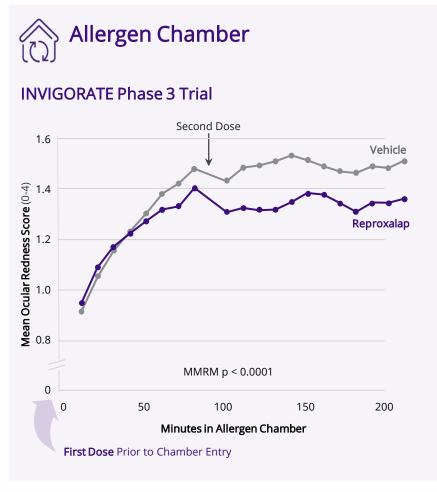
Key Secondary Endpoint

Reduction in Ocular Redness Over the Entire Chamber

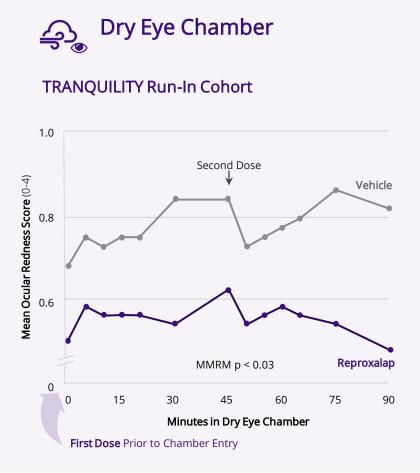


Over entire chamber, change from baseline in ocular redness statistically lower in reproxalaptreated subjects

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

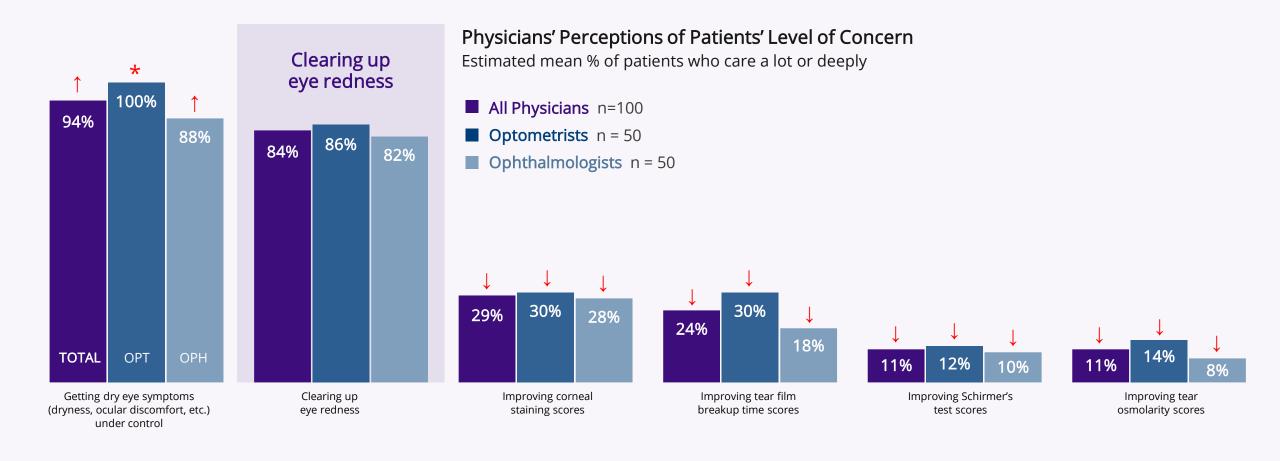








Physicians Believe Most of Their Patients Care More About Clearing Up Eye Redness Than Other Signs of Dry Eye Disease





^{*} Significantly higher than comparison group (90% confidence level) 1 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

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

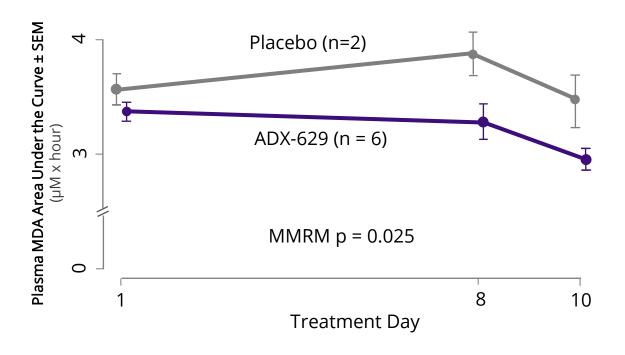
Allergic Inflammation

Autoimmune Disease

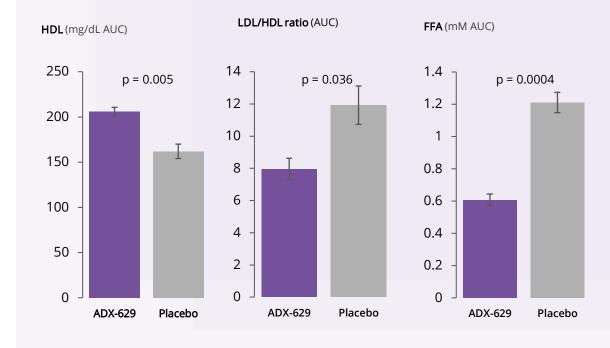


ADX-629 Reduced RASP vs. Placebo in Phase 1 Clinical Trial, Demonstrating Target Engagement and Improved Lipid Profiles

RASP LEVELS OVER 10 DAYS OF DOSING



PLASMA LIPID PROFILE AFTER FATTY MEAL





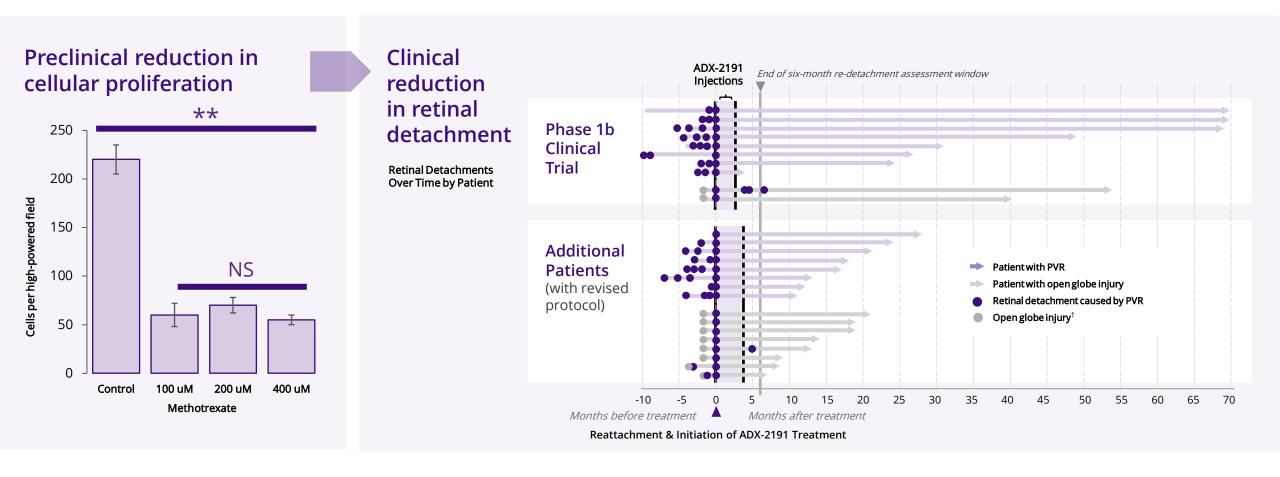


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ADX-2191 (METHOTREXATE FOR INTRAVITREAL INJECTION)

A Platform Approach to Treat Rare Immune-Mediated Retinal Diseases

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





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

PROLIFERATIVE VITREORETINOPATHY (PVR)



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 one of the main courses of action.

ADX-2191

Granted U.S. orphan designation, U.S. fast track designation, and EU orphan 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

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

COMPLETION OF ENROLLMENT EXPECTED IN Q4 2021**

Primary Objective

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

Design

Multi-center, 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

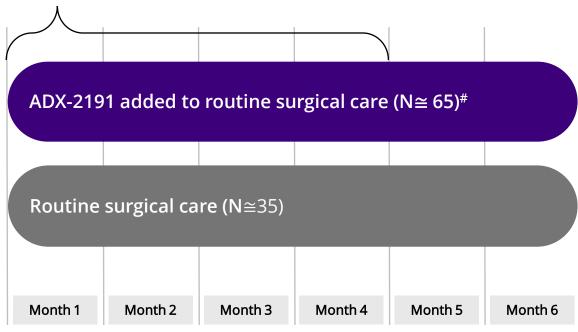
Endpoint

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

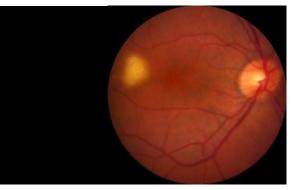
ADX-2191 intravitreal injections

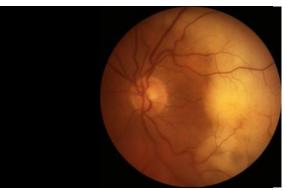


Subjects include N≅30 subjects recruited under open label portion of protocol.



ADX-2191 Has the Potential to be the First 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 patients** 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.

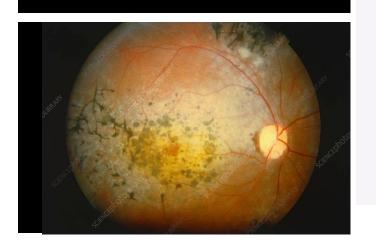
No approved treatments are currently available, though methotrexate represents current standard of care.

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



ADX-2191 Has the Potential to be the First 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 in a P23H rhodopsin mutation mouse model of RP suggests that methotrexate improves retinal function.

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

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

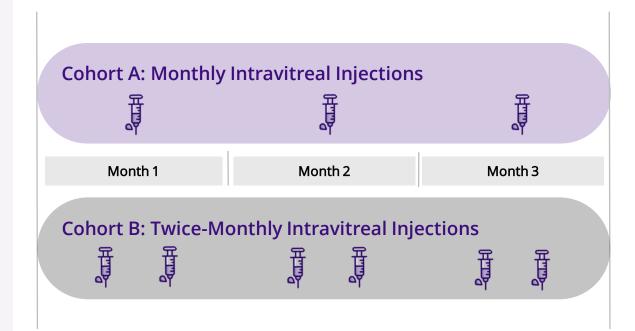
Primary Endpoint

Safety and tolerability of ADX-2191 in RP subjects

Secondary Endpoints

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

RETINITIS PIGMENTOSA CLINICAL TRIAL DESIGN





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 Peptimmune⁶

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Gary Phillips, M.D.

CEO OrphoMed

Neal Walker, D.O.

CEO Aclaris Therapeutics

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



Upcoming Planned Clinical Milestones*



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

Top-line results

expected in Q4 2021

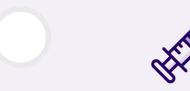


Trial of ADX-2191 in proliferative vitreoretinopathy

Completion of enrollment expected in Q4 2021

Part 1 of Phase 3 GUARD

Results expected in 2022



Phase 2 clinical trial of ADX-2191 in retinitis pigmentosa
Initiation expected in Q4 2021



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

Top-line results expected in Q4 2021 or Q1 2022



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