



May 2021

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## **CORPORATE OVERVIEW**

# Innovative Approaches to Regulating Immune Response

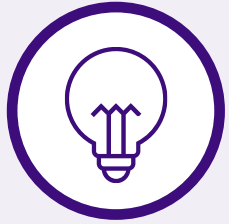
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# Compelling Value Proposition



## NOVEL SYSTEMS-BASED APPROACHES FOR IMMUNOLOGY

- RASP-inhibition represents a first-in-class therapeutic approach.
- Three unique immune-modulating mechanisms of action in development.



## NEAR-TERM DEVELOPMENT CATALYSTS\*

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



## LARGE AND UNDERSERVED MARKET OPPORTUNITY

- Lead product candidate reproxalap targets a U.S. addressable market of >\$20B.
- Significant potential commercial advantages of reproxalap in two blockbuster ocular indications.



## SOLID CASH POSITION

- Cash, cash equivalents and marketable securities of \$138.4M as of 3/31/2021
- Cash runway through the end of 2023, based on projected operating expenses\*\*

# Deep and Innovative Pipeline Addressing Immunological Disease

DISEASE AREA	COMPOUND	MECHANISM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Ocular Diseases	Reproxalap	RASP	Dry Eye Disease	<div></div>			
			Allergic Conjunctivitis	<div></div>			
	ADX-2191	DHFR	Proliferative Vitreoretinopathy	<div></div>			
			Primary Vitreoretinal Lymphoma	<div></div>			
	ADX-103/10X	RASP	Retinal Disease	<div></div>			
Systemic Diseases	ADX-629	RASP	Cytokine Release Syndrome (COVID-19)	<div></div>			
			Allergy (Atopic Asthma)	<div></div>			
			Autoimmune Disease (Psoriasis)	<div></div>			
	ADX-1612	CHP	Ovarian Cancer	<div>Investigator-Sponsored Trial</div>			
			SARS-CoV2 Antiviral (COVID-19)	<div></div>			



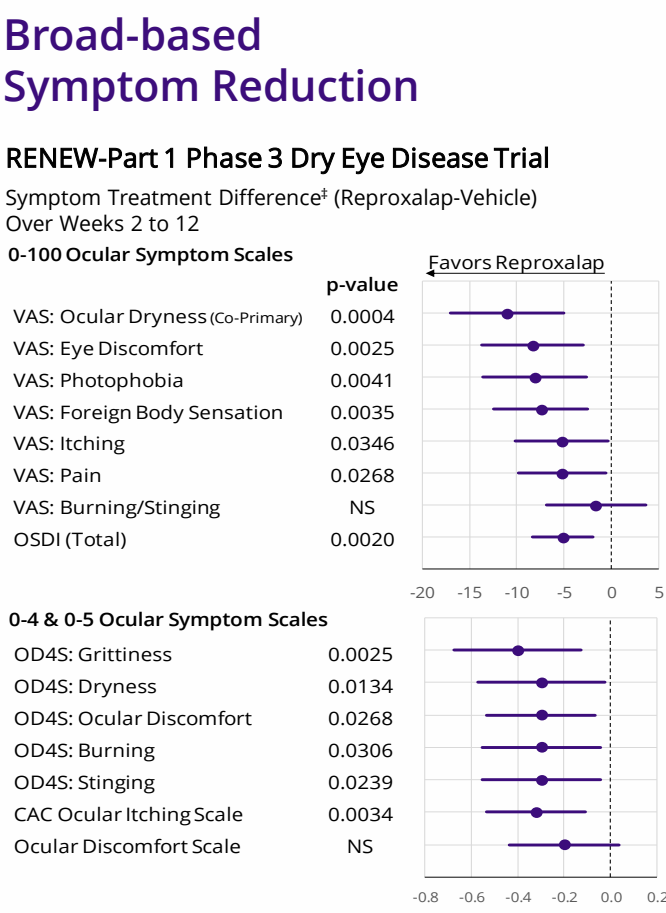
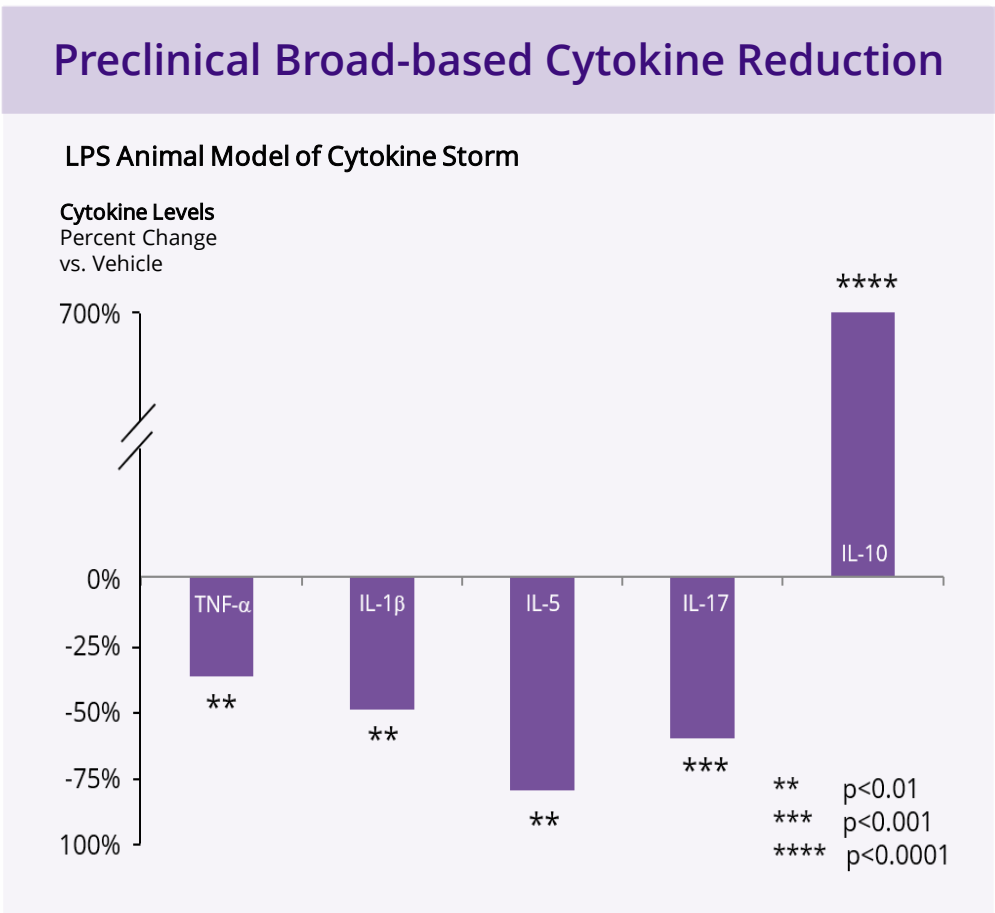
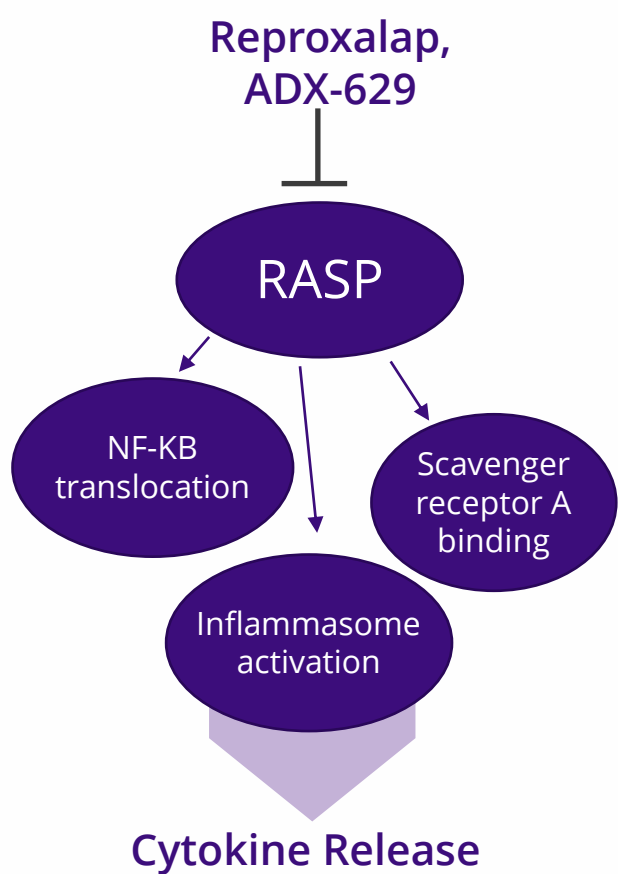
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## **REPROXALAP AND ADX-629**

# Reactive Aldehyde Species (RASPs) Inhibition

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



 <sup>‡</sup>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). **Slide sources:** Cullen et. al., J. of Allergy and Clinical Immunology, Volume 135, Issue 2, AB384, Feb 2015; Reproxalap RENEW-Part 1 clinical trial results. **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

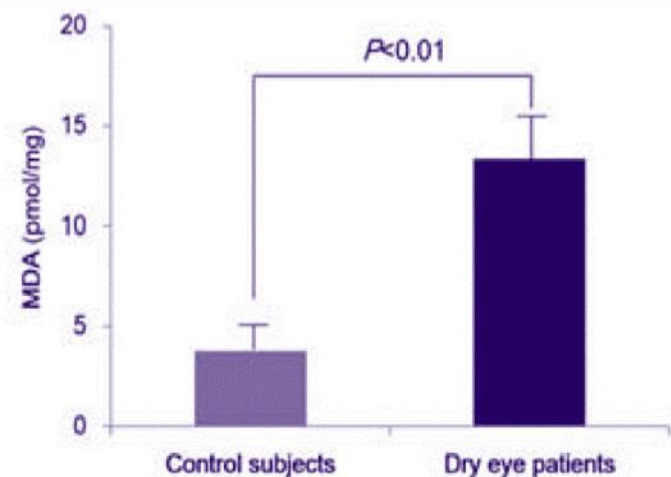
Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

# 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.



Source: Curr Eye Res. 2016, 41(9):1143-9

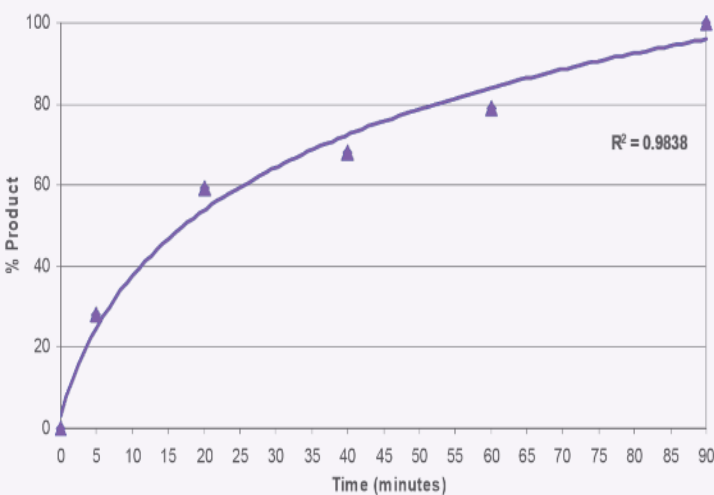
## REPROXALAP

Preclinical rapid and complete RASP binding

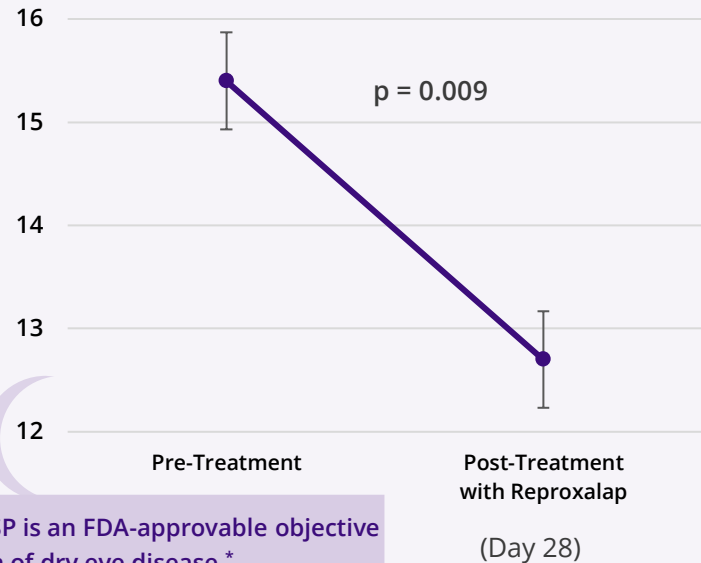


Clinical reduction in RASP adducts

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



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



RASP is an FDA-approvable objective sign of dry eye disease.\*



\*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. Slide 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; Reproxalap preclinical and Phase 2a in dry eye disease clinical trial results on file.

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



Often months to demonstrate even modest efficacy with current Rx

**34 million** or more adults in the U.S.<sup>1</sup>

## ALLERGIC CONJUNCTIVITIS



Unchecked growing disease burden and limited options beyond OTC/Rx antihistamines

**66 million** or more adults in the U.S.<sup>2</sup>

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

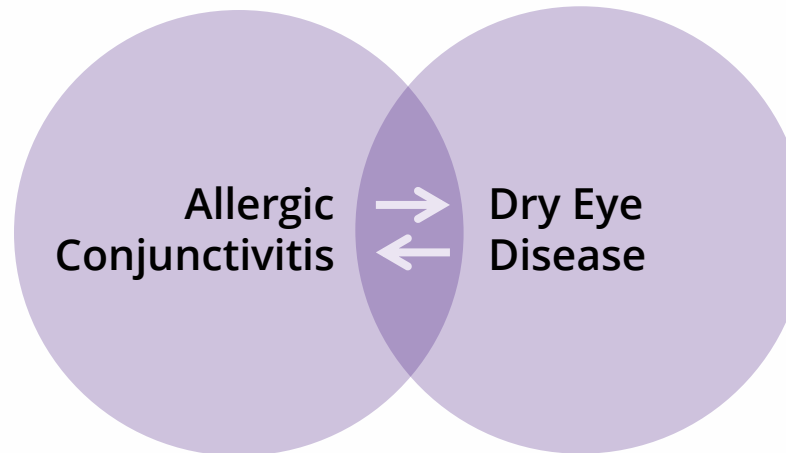


# Allergic Conjunctivitis and Dry Eye Disease Are Interrelated Inflammatory Ocular Surface Diseases

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



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

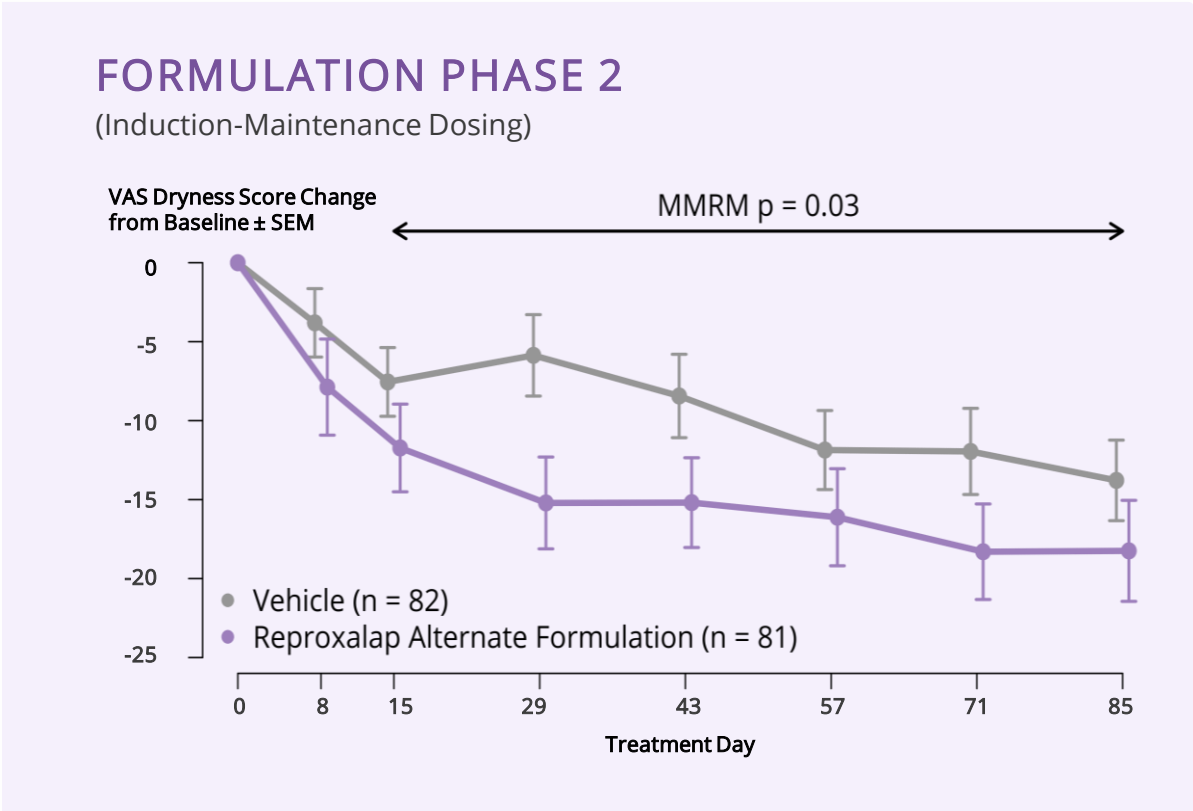
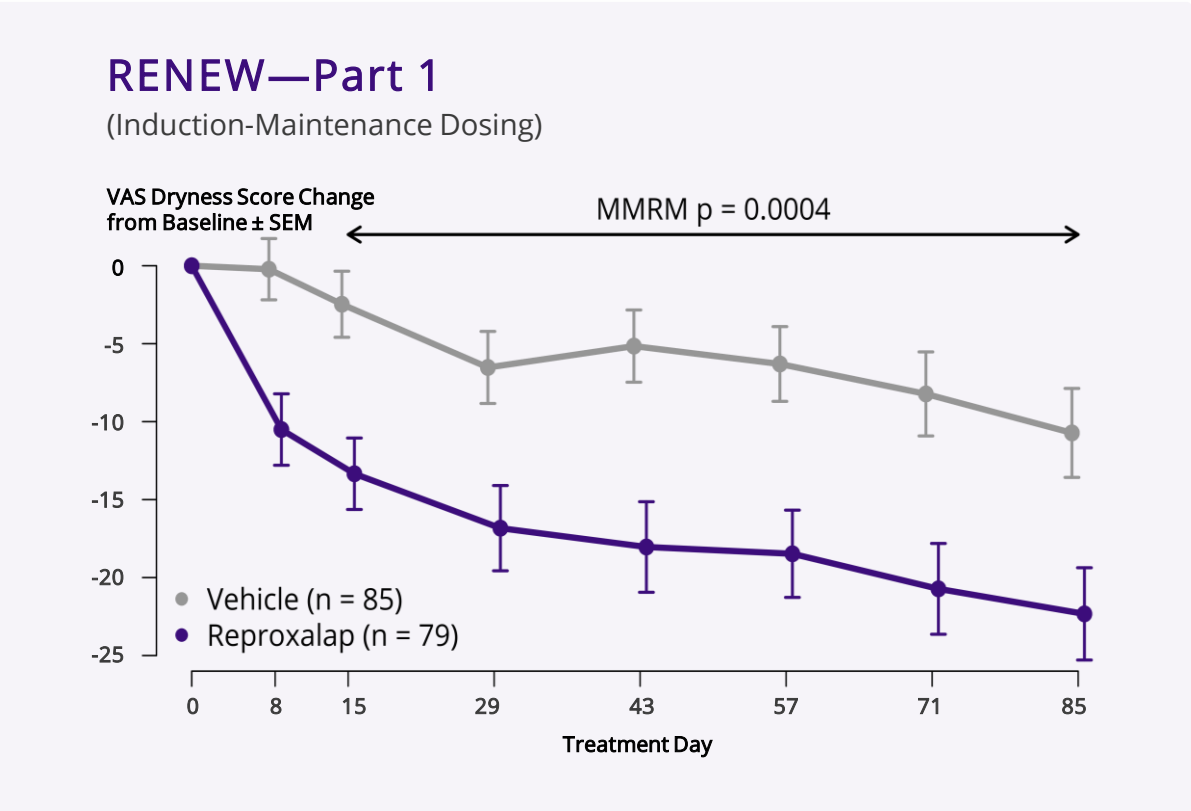


“The clear interaction of allergy, dry eye and environmental irritants makes untangling their etiology in prevalence studies difficult.”

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

## Ocular Dryness Score (VAS) Change From Baseline

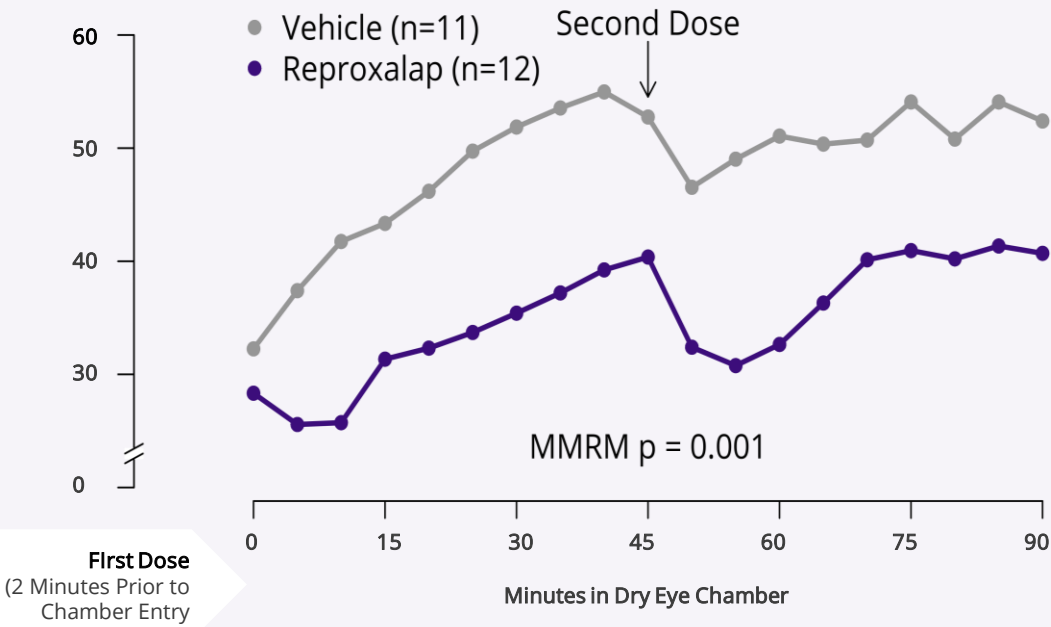
Dryness (OD4SQ) Baseline Score  $\geq 3$



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

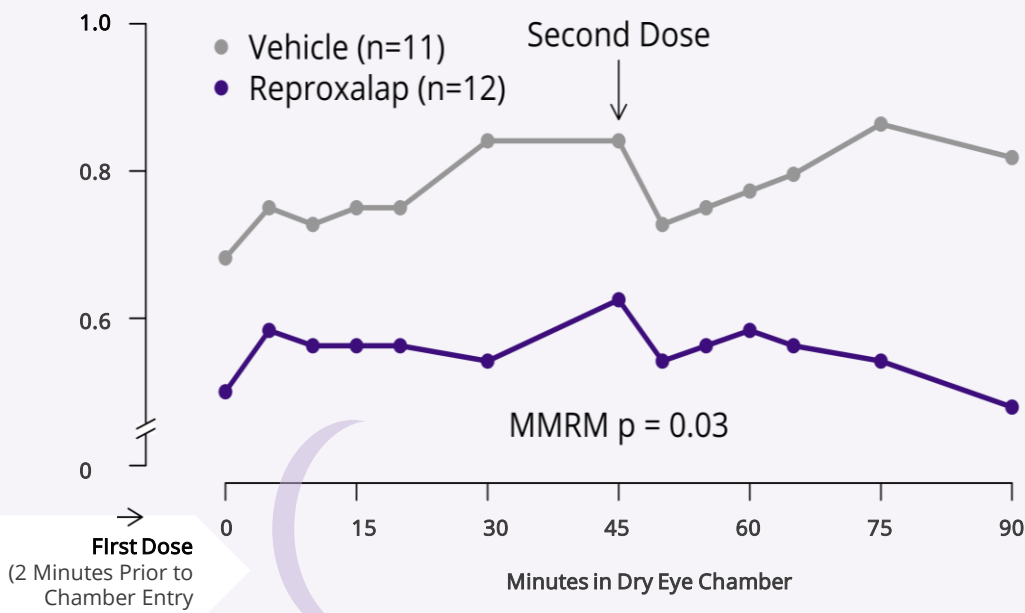
## VISUAL ANALOG DRYNESS SCORE (0-100)

VAS Dryness Score  
(0-100)



## OCULAR REDNESS SCORE (0-4)

Mean Ocular Redness Score  
(0-4)



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

# Phase 3 TRANQUILITY Dry Eye Disease Trial Design

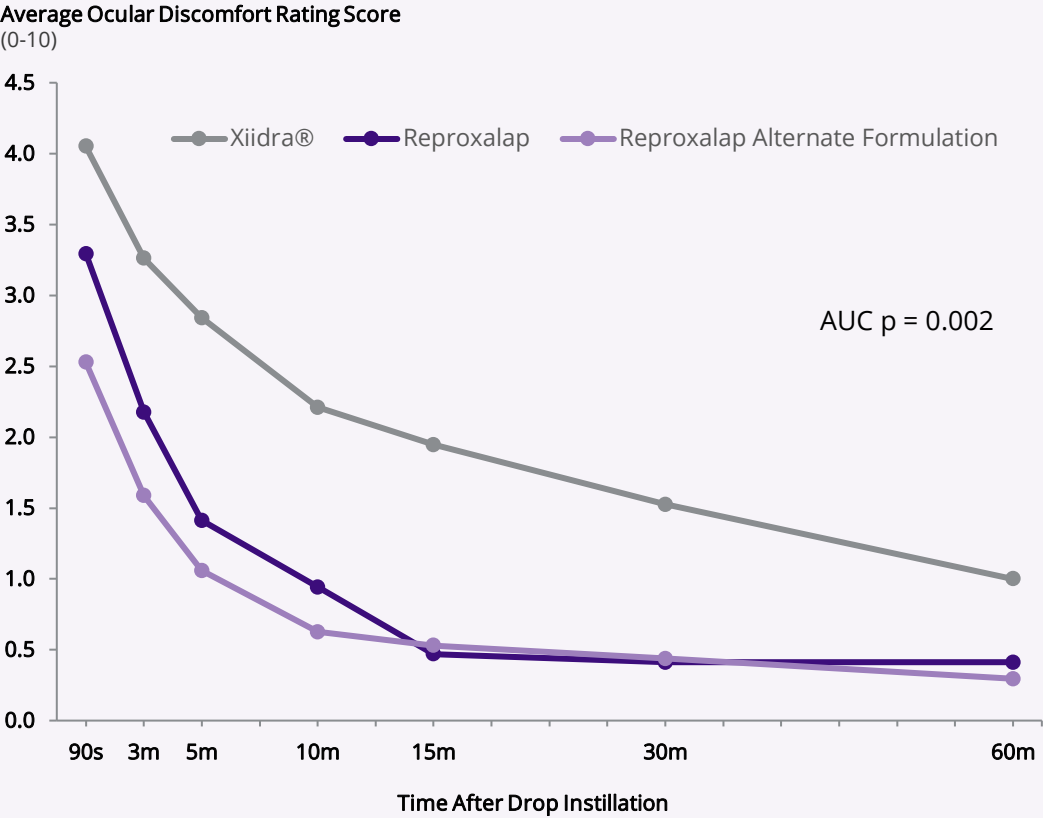
## DRY EYE CHAMBER CHALLENGE MODEL

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	<ul style="list-style-type: none"><li>• Tear RASP levels</li><li>• Schirmer's Test</li><li>• Dry eye symptoms</li></ul>

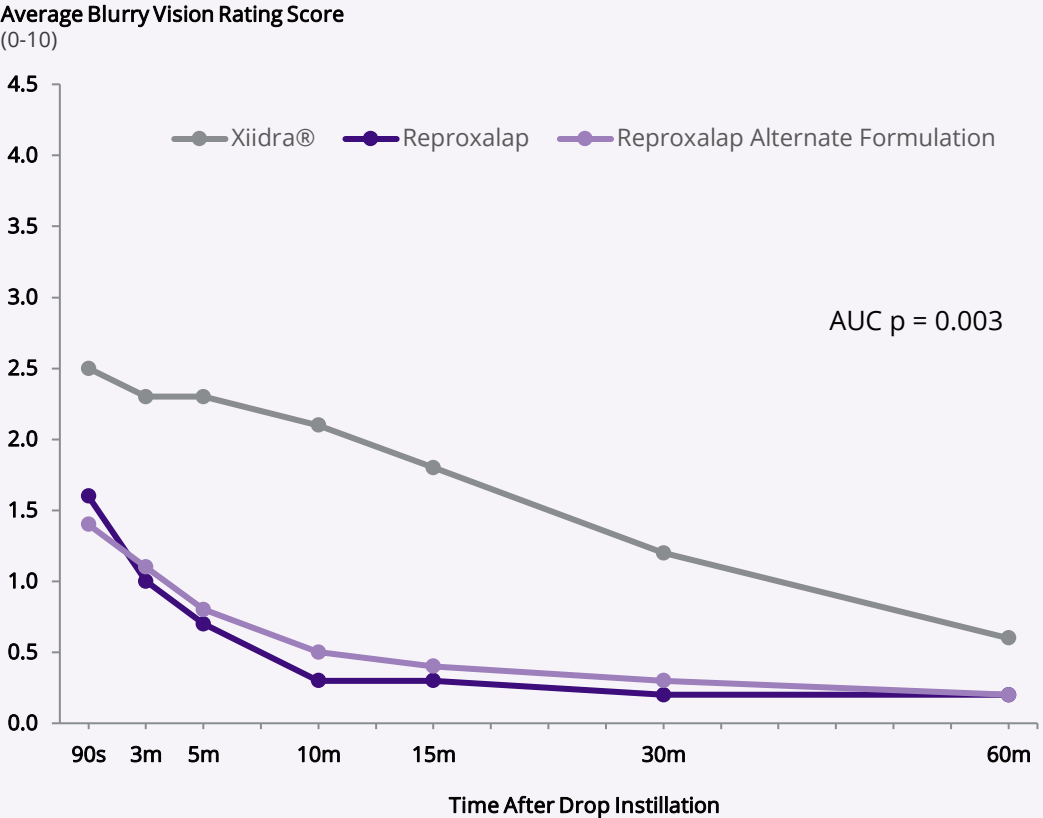
Results from the identical TRANQUILITY and TRANQUILITY-2 Trials are expected in H2 2021.

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

## OCULAR DISCOMFORT RATING



## BLURRY VISION RATING



P-values represent MMRM of vehicle AUC vs. pooled Reproxalap AUC.

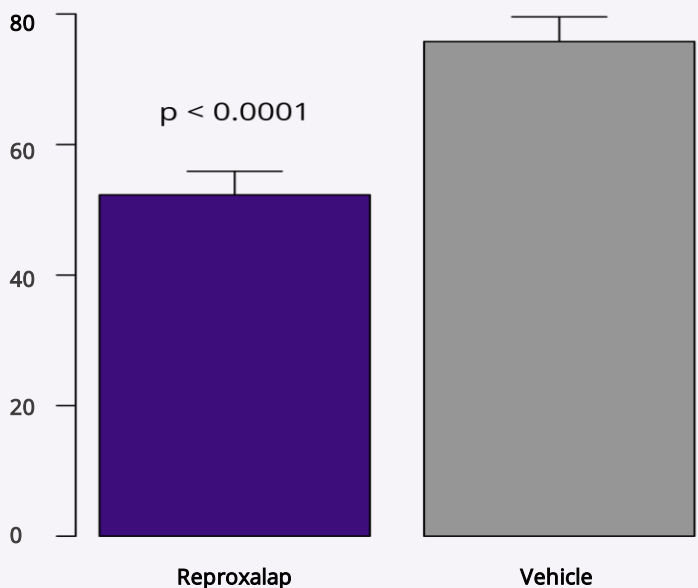
Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

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



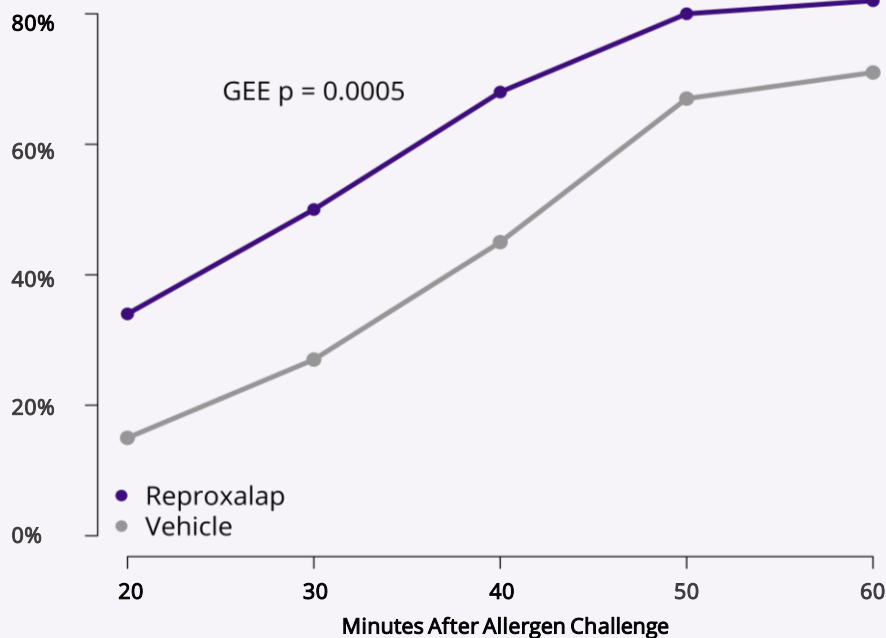
## CONJUNCTIVAL ALLERGEN CHALLENGE

Area Under the Ocular Itch Score Curve Mean  $\pm$  SEM (10-60 minutes after allergen challenge)



## ALLEVIATE PHASE 3 TRIAL

Responder Probability  
(2-Point Improvement from Peak Baseline Itch Score)

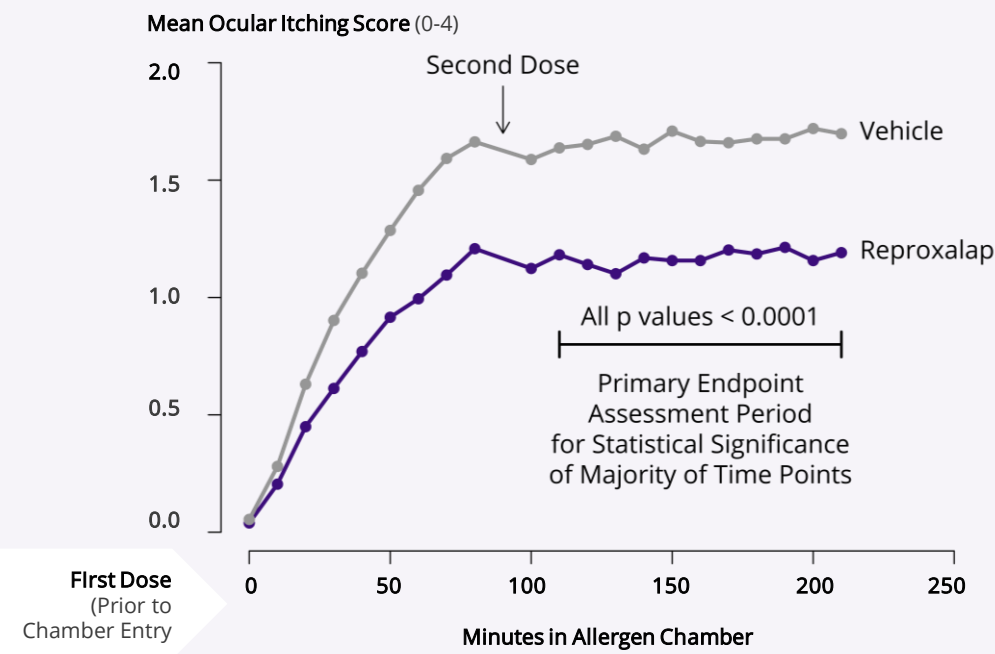




# Primary and Key Secondary Endpoints Achieved in Phase 3 INVIGORATE Allergen Chamber Trial

## PRIMARY ENDPOINT

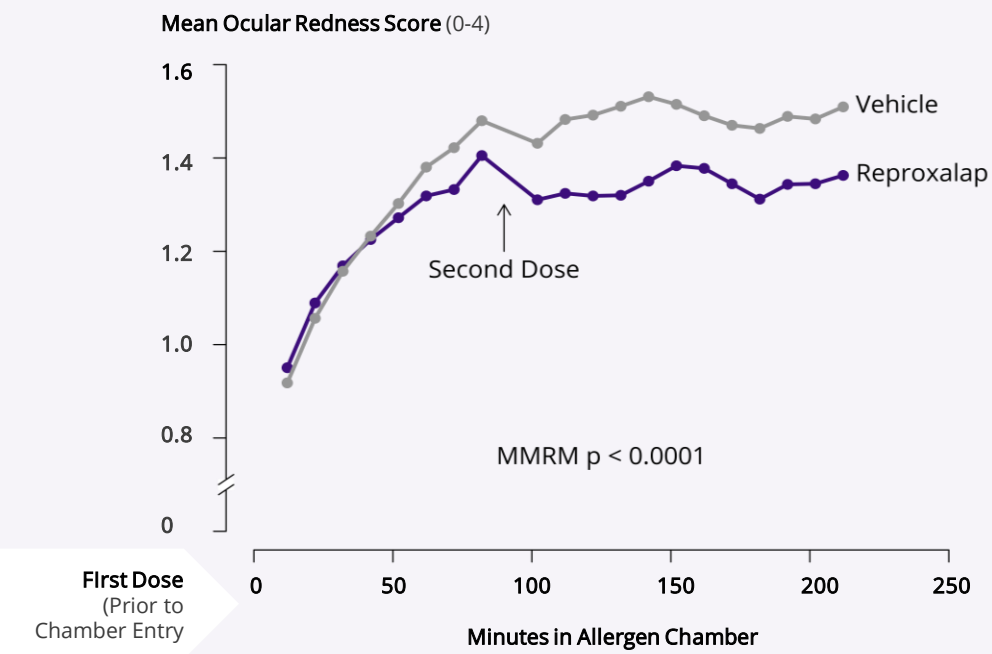
(Reduction in Ocular Itching Over Pre-Specified Time Frame)



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 reproxalap-treated subjects

# ADX-629 Clinical Initiative in Systemic Inflammatory Disease Complements Late-Stage Programs

**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 immune-mediated disease.

**Comprehensive systemic disease** initiative designed 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

Data  
Readouts  
Expected  
in 2021

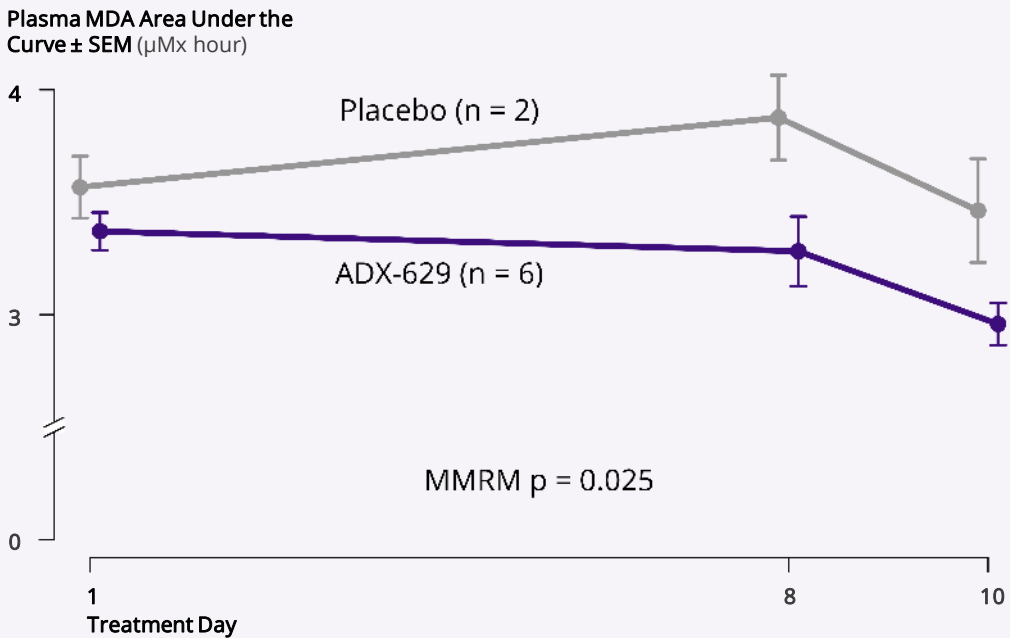
Cytokine Release Syndrome

Allergic Inflammation

Autoimmune Disease

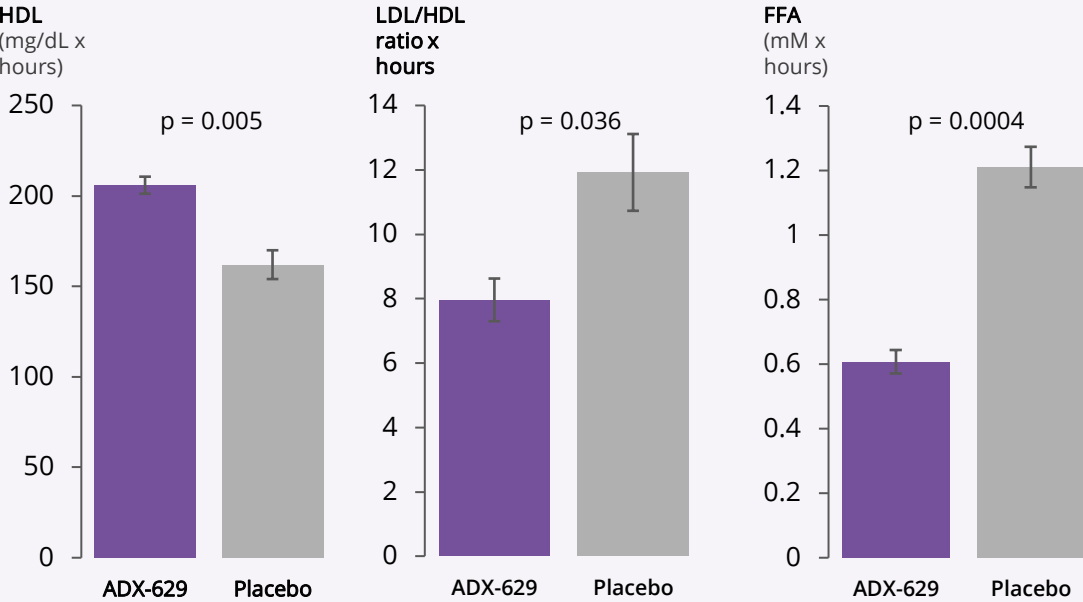
# ADX-629 Reduced RASP vs. Placebo in Phase 1 Clinical Trial, Demonstrating Target Engagement, and Also Improved Lipid Profiles

## MDA LEVELS OVER 10 DAYS OF DOSING



Area under the curve is over four hours post-dose; p-values subject to quality control analysis.  
Source: ADX-629 Phase 1 clinical trial results.

## PLASMA LIPID PROFILE AFTER FATTY MEAL



MDA = Malondialdehyde      Day 10 = Food effect assessment      LDL = Low-density lipoprotein  
MMRM = Mixed Model Repeated Measures      HDL = High-density lipoprotein      FFA = Free fatty acids



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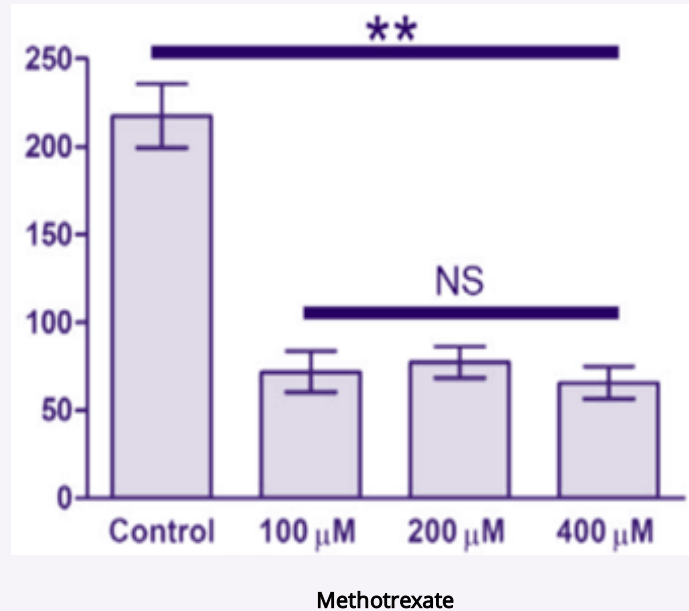
**ADX-2191**

# Dihydrofolate Reductase Inhibition

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

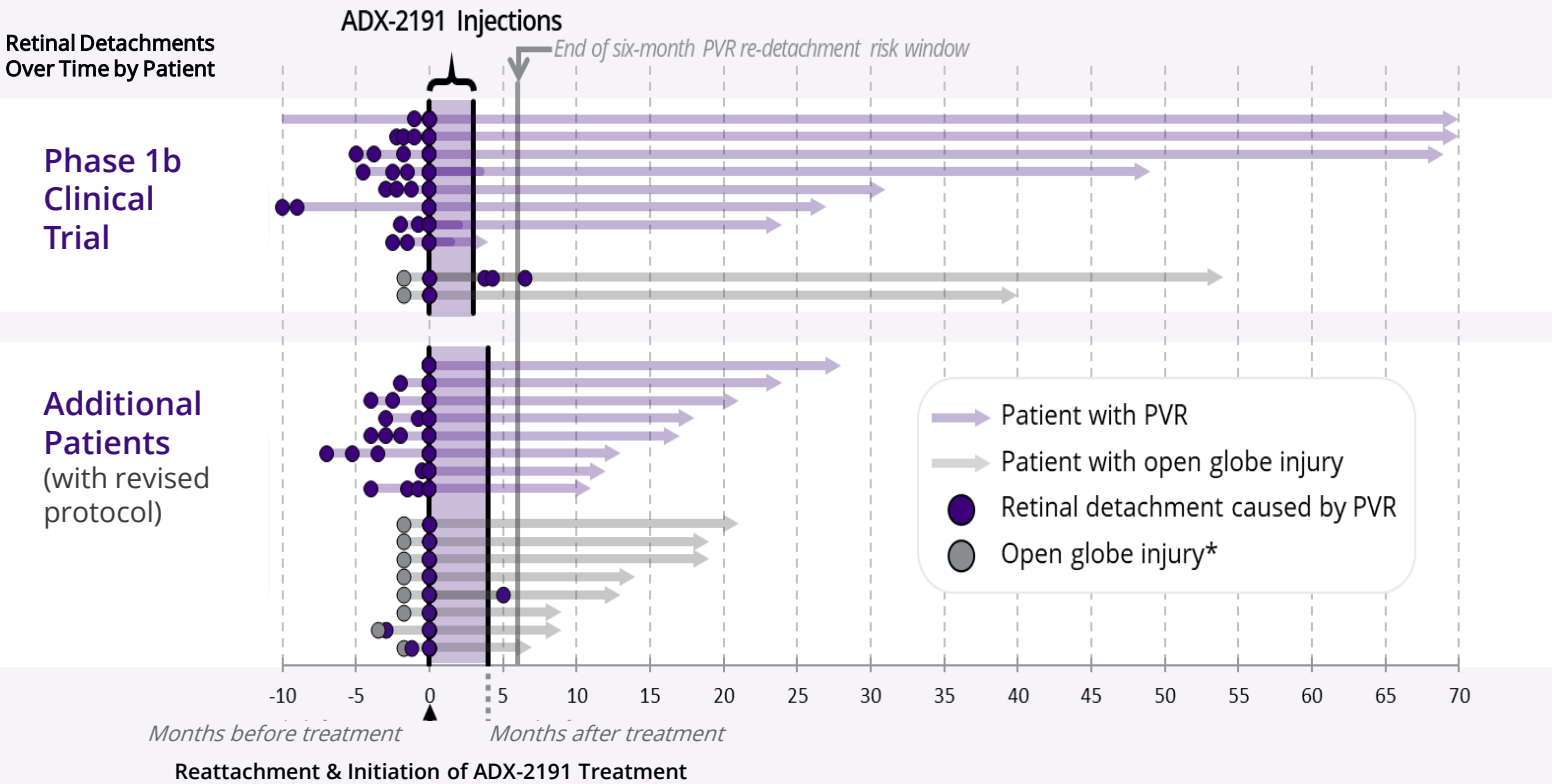
## Preclinical reduction in cellular proliferation

Cells per high-powered field



Source: Invest Ophthalmol Vis. Sci. 2017; 58:3940-3949

## Clinical reduction in retinal detachment



\*Timing of open globe injury as shown is estimated. Typically 6-8 weeks prior to reattachment & initiation of ADX-2191. 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. Source: ADX-2191 PVR Phase 1b investigator sponsored clinical trial (n=10) results and additional in-practice use (n=16). \*\* = p value ≤ 0.01 NS = Not Significant PVR = Proliferative vitreoretinopathy

# ADX-2191 Represents a Novel Approach and Potential Therapeutic Option For Proliferative Vitreoretinopathy Treatment

## 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 the only possible course of action.

## ADX-2191

A **potential therapeutic option** for the treatment of PVR

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

**Tolerability and reattachment success** during study period **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 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

#### 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

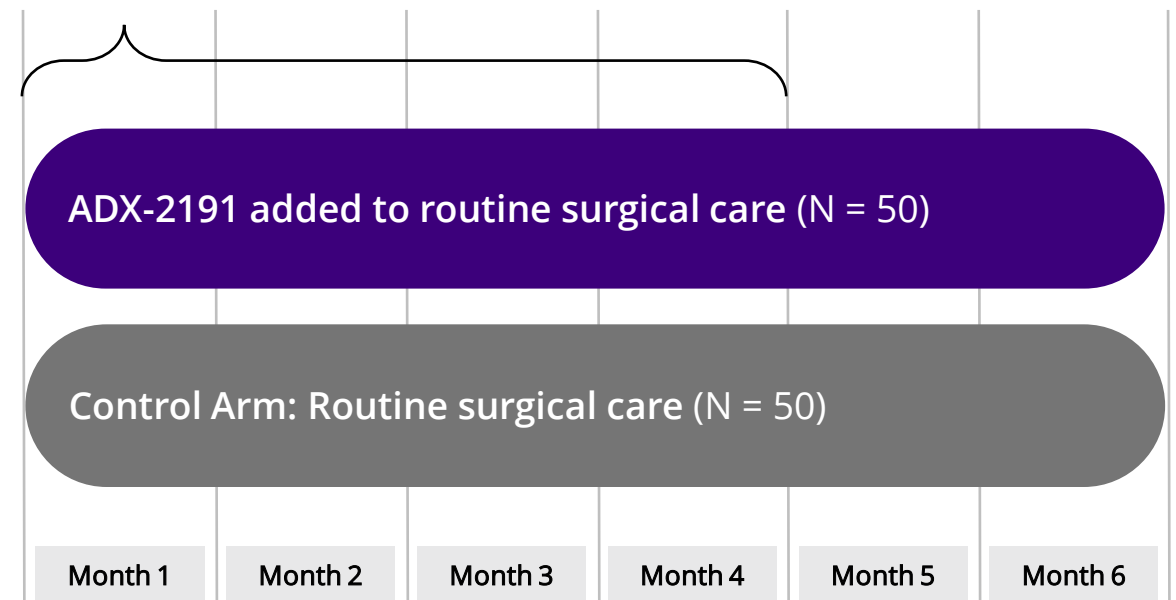
#### Endpoint

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 injection treatment*



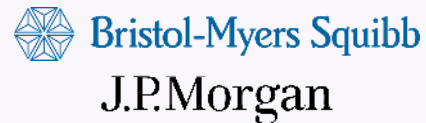
# Experienced Management Team and Board of Directors

## 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<sup>7</sup>

**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

# Upcoming Planned Clinical Milestones\*



Phase 3  
TRANQUILITY and  
TRANQUILITY-2  
top-line results  
H2 2021



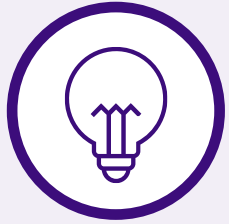
Phase 3 GUARD  
Trial **completion  
of enrollment in  
2021**



Phase 2 clinical trials of  
ADX-629 **top-line  
results in cytokine  
release syndrome,  
allergic inflammation  
and autoimmune  
disease in 2021**

Aldeyra plans to meet  
with the U.S. FDA in the  
second half of 2021 to  
discuss the INVIGORATE  
results and the potential  
submission of a  
New Drug Application.

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