



March 2021

CORPORATE REVIEW

Systems-Based Approaches to Regulate Immune Response

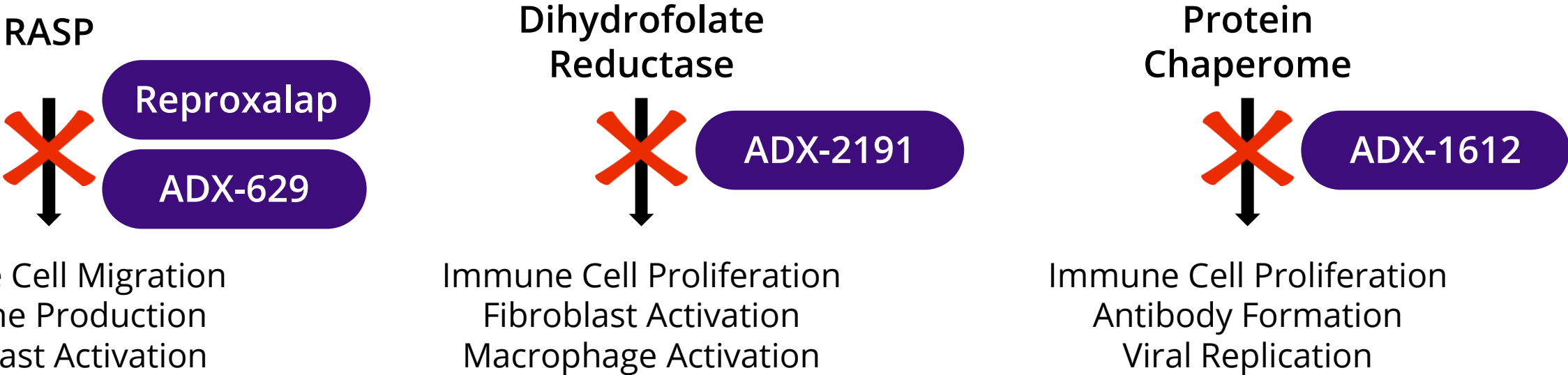
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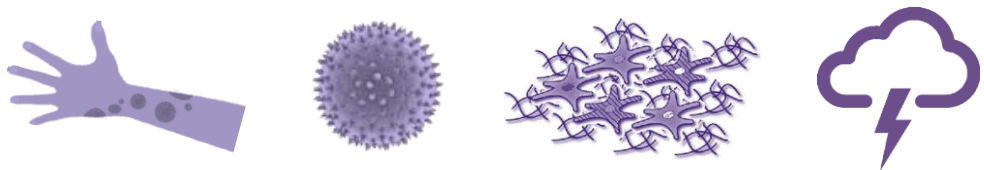
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Aldeyra is Developing Novel Systems-Based Approaches for Immune System Regulation



Immune Mediated Diseases:
Autoimmune Disease, Allergy, Fibrosis, Cytokine Release Syndrome



Innovative Pipeline Addressing Immunological Disease

Disease Area	Compound	Mechanism	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Ocular Diseases	Reproxalap	RASP	Dry Eye Disease				
			Allergic Conjunctivitis				
	ADX-2191	DHFR	Proliferative Vitreoretinopathy				
			Primary Vitreoretinal Lymphoma				
	ADX-103/10X	RASP	Retinal Disease				
Systemic Diseases	ADX-629	RASP	Cytokine Release Syndrome (COVID-19)				
			Allergy (Atopic Asthma)				
			Autoimmune Disease (Psoriasis)				
	ADX-1612	CHP	Ovarian Cancer				
			SARS-CoV2 Antiviral (COVID-19)				

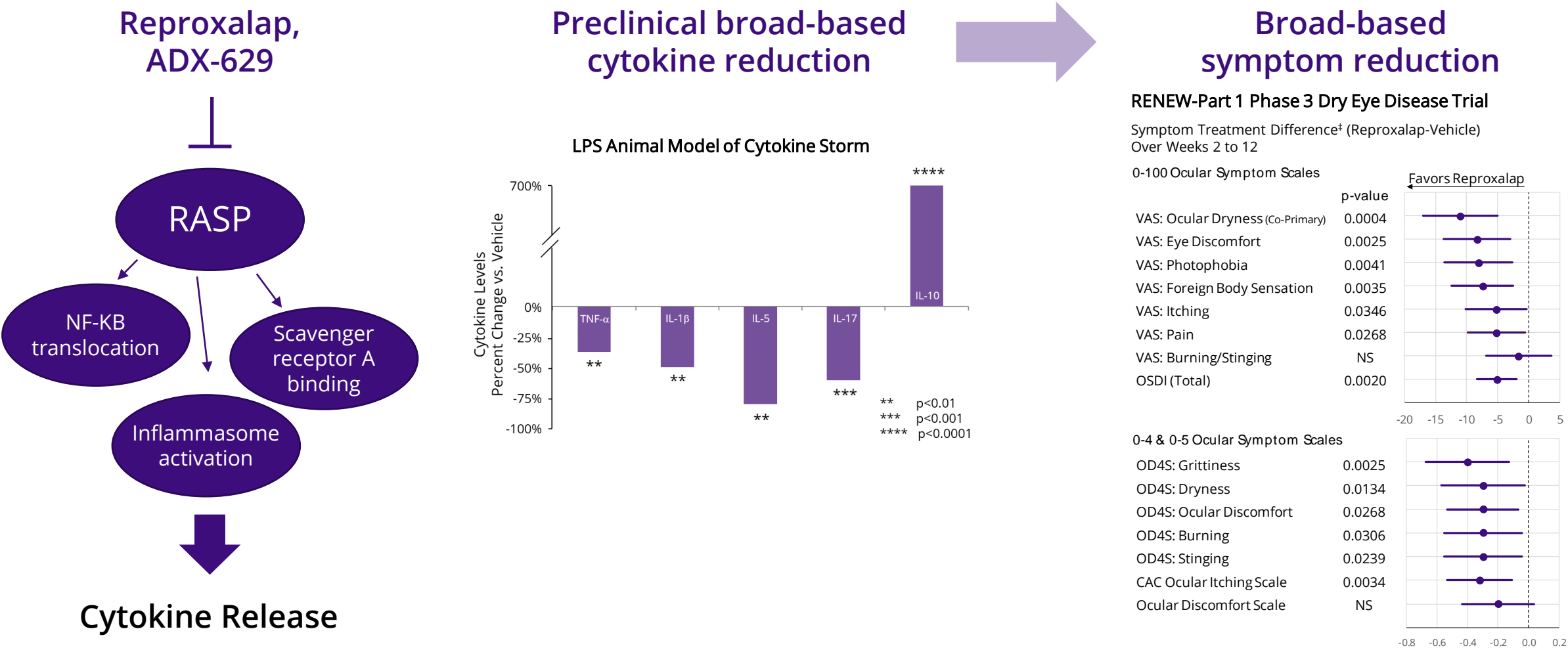


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Reactive Aldehyde Species (RASP) Inhibition

RASP Inhibition is a Pre-Cytokine, Systems-Based Approach that Has Been Clinically Validated in Late-Stage 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.¹

Allergic Conjunctivitis



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

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

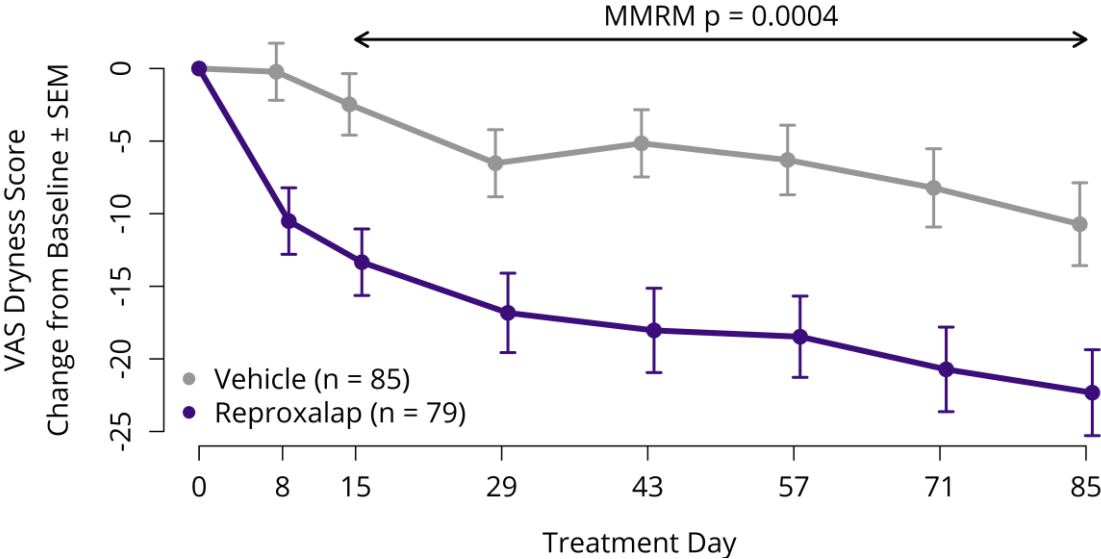
Reproxalap poised to potentially be the next novel entrant in the dry eye disease and allergic conjunctivitis markets.

¹Paulsen 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.

²Singh 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

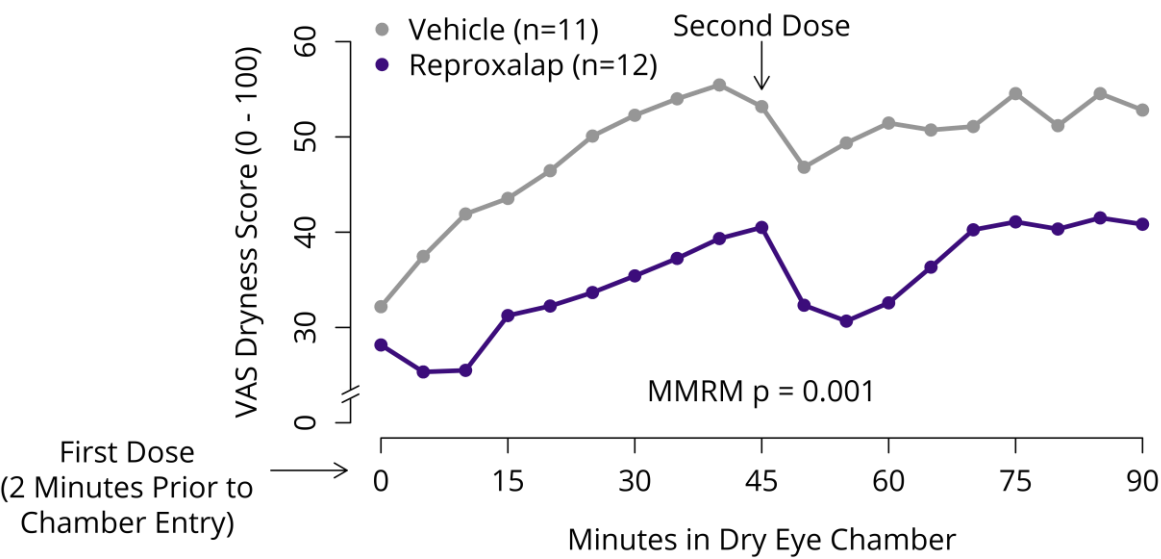
Reproxalap Exhibited First-Line Ocular Symptom Control in Dry Eye Disease Clinical Trials

RENEW-Part 1 Phase 3 Trial
(Induction-Maintenance Dosing)



Rapid and durable symptom improvement over 12 weeks of chronic therapy.

Phase 3 TRANQUILITY Run-In Cohort
(Dry Eye Chamber Results)



Near-immediate (within minutes) and sustained symptom improvement with acute therapy during ocular surface challenge.

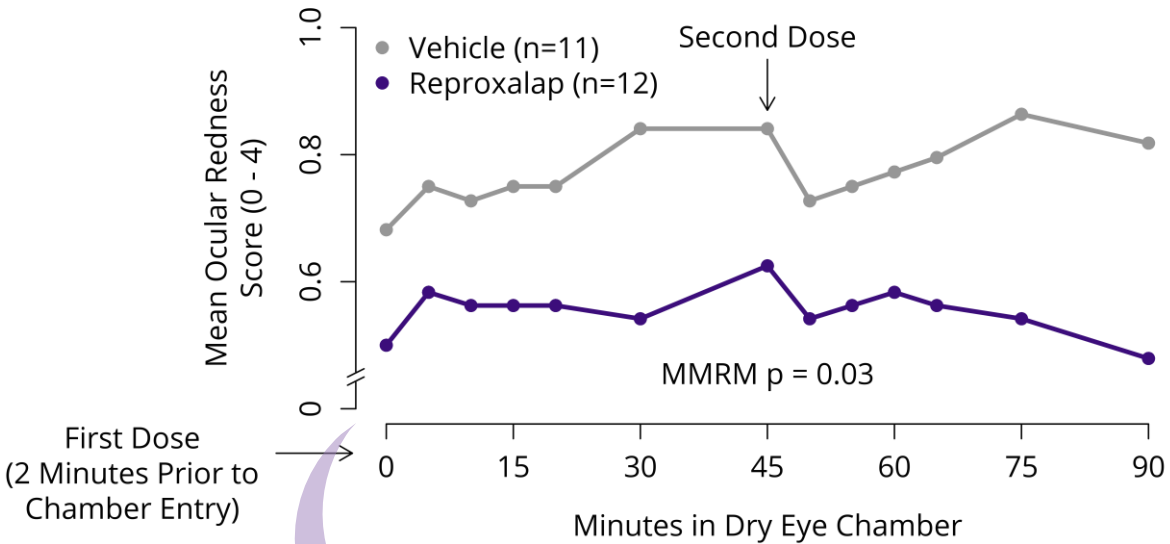


Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.
Source: Reproxalap RENEW-Part 1 clinical trial results and TRANQUILITY Run-In Cohort initial results.

VAS = Visual Analog Scale
MMRM = Mixed Effect Model Repeated Measures

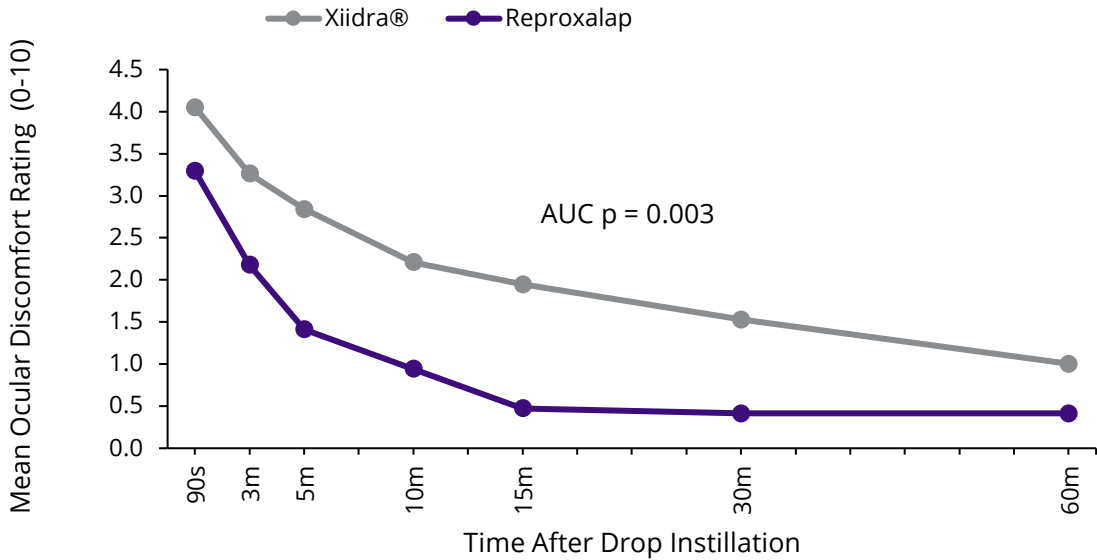
Reproxalap Exhibited Acute and Durable Improvements in Redness and Tolerability in Dry Eye Disease Clinical Trials

Phase 3 TRANQUILITY Run-In Cohort
(Dry Eye Chamber Results)



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

Head-to-Head Tolerability Trial
vs. Xiidra®



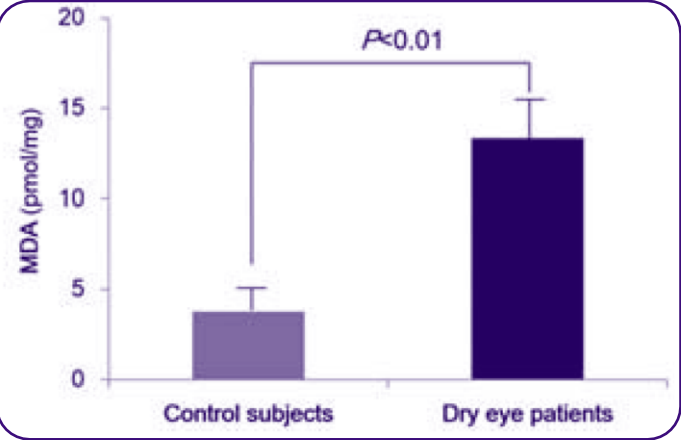
*Currently FDA approved dry eye products have utilized Schirmer's Test, corneal staining, and conjunctival hyperemia (redness) as objective sign measures. Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.
Source: Reproxalap TRANQUILITY Run-In Cohort initial results and Drop Experience clinical trial results.



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.

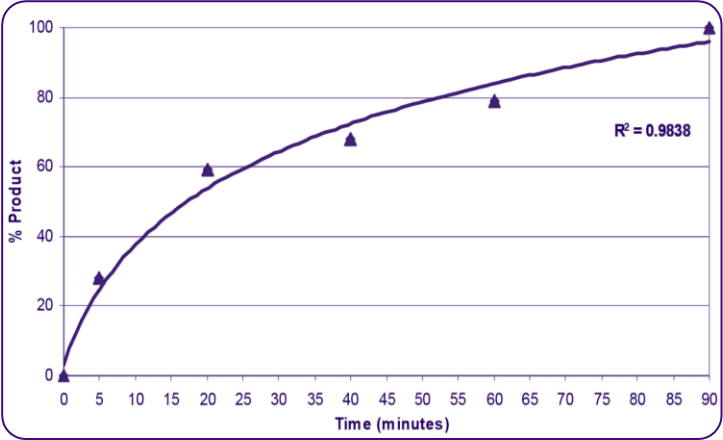


Source: Curr Eye Res. 2016, 41(9):1143-9

Reproxalap

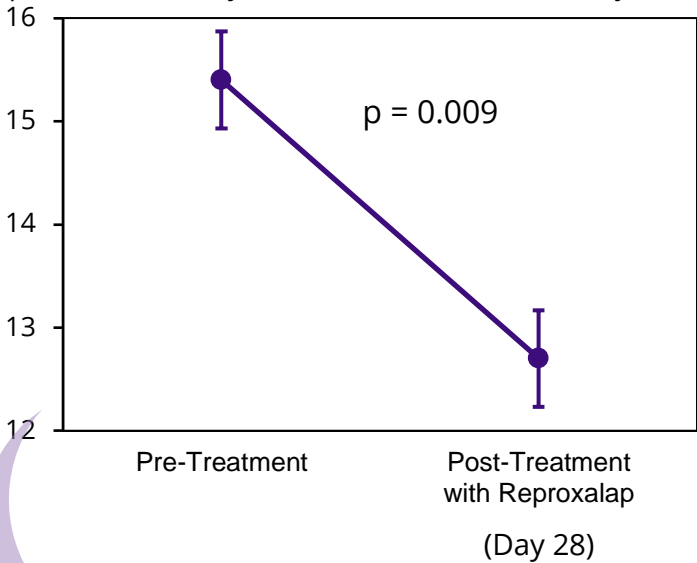
Preclinical rapid and complete RASP binding

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
(μ M Malondialdehyde Adduct; Mean \pm 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.
Source: 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.

Phase 3 TRANQUILITY Dry Eye Disease Trial Design

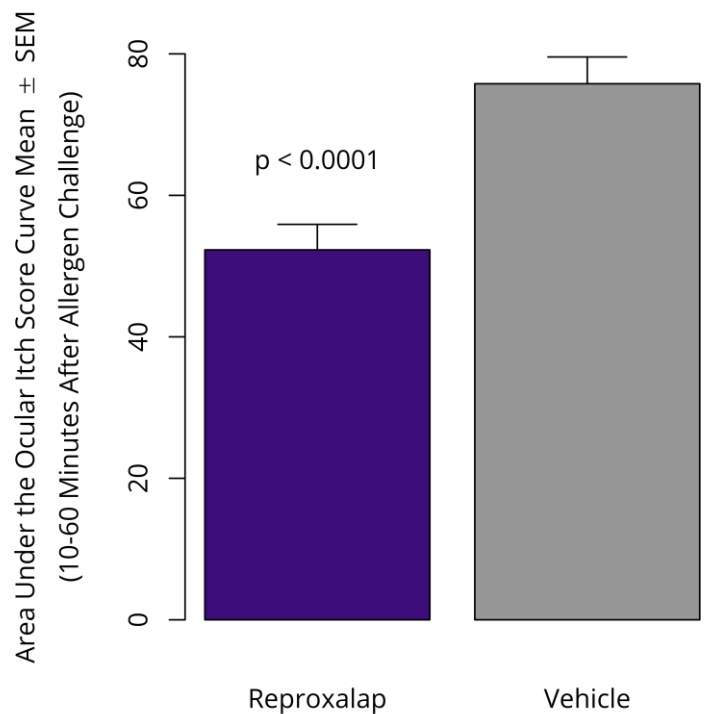
Dry Eye Chamber Challenge Model

Design	Multi-center, randomized, double-masked, parallel group, vehicle-controlled
Dosing	Day 1: QID; Day 2 (chamber): BID
Size	~150 patients per arm
Primary Endpoint	Ocular redness over 90 minutes in a dry eye chamber
Secondary Endpoints	<ul style="list-style-type: none">• Tear RASP levels• Schirmer's Test• Dry eye symptoms

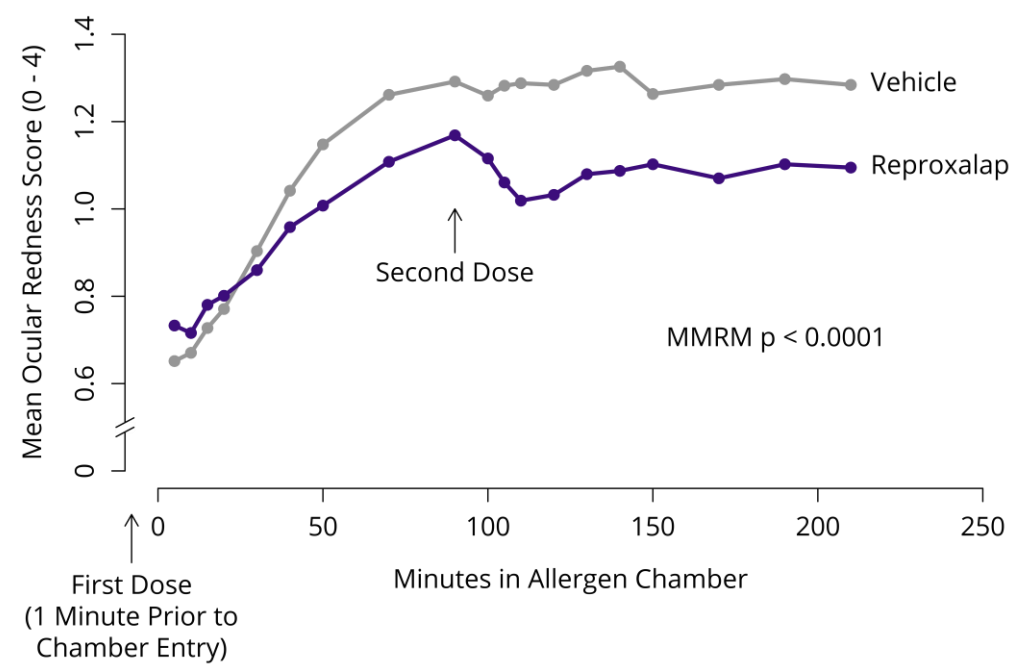
Main cohort expected to begin enrollment in H1 2021.
Results expected H2 2021.

Reproxalap Reduced Itching and Redness in Late-Stage Clinical Trials for Allergic Conjunctivitis

ALLEVIATE Phase 3 Trial



Phase 2 Allergen Chamber Trial



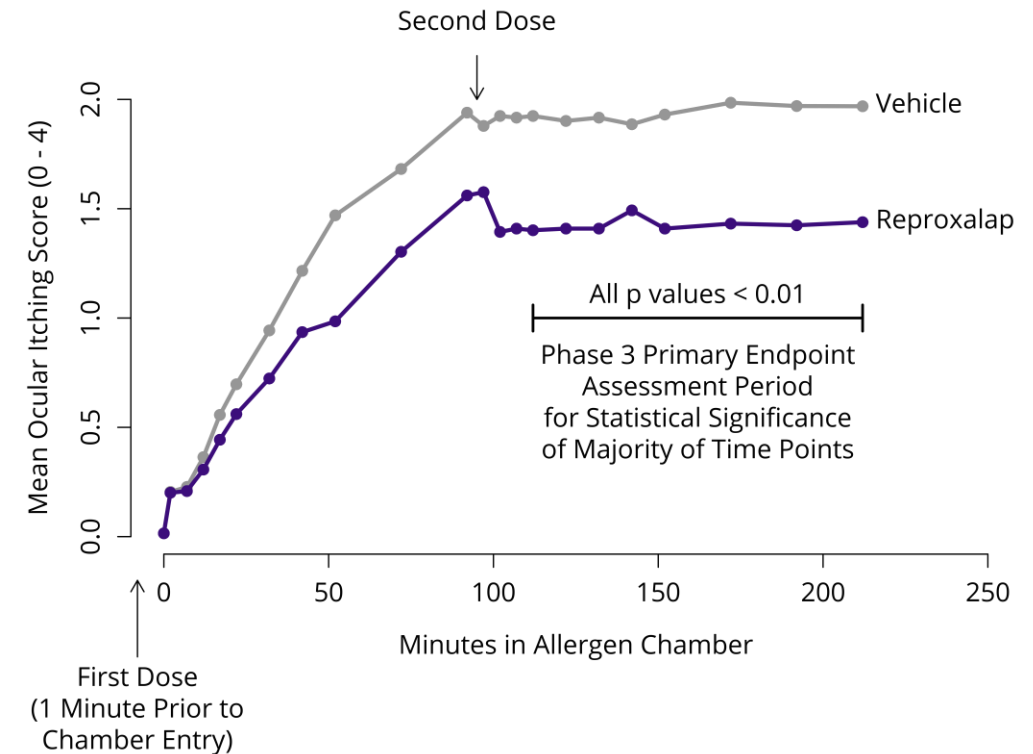
Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns reported; mild instillation site irritation is the most commonly reported adverse event in clinical trials.
Source: Reproxalap ALLEVIATE Phase 3 and allergen chamber Phase 2 clinical trial results; Ocular itch scale (0-4); Ocular redness scale (0-4). MMRM = Mixed Effect Model Repeated Measures

Results from the INVIGORATE Phase 3 Trial in Allergic Conjunctivitis Expected in H1 2021*

- **Design:**
 - Two-way randomized crossover, ~100 patients total
- **Primary endpoint:**
 - Statistical significance in ocular itch (0-4 scale) at a majority of 11 time points between 110 and 210 minutes
- **Secondary endpoints:**
 - Investigator-assessed ocular redness score
 - Patient-reported ocular tearing score
 - Total ocular symptom score
- **Inclusion/exclusion criteria:**
 - History of moderate to severe allergic conjunctivitis to ragweed pollen
 - Itching score of ≥ 2.5 or redness score ≥ 2.0 in baseline chamber test
- **Chamber exposure and dosing schedule:**
 - 3.5 hours continuous allergen exposure
 - First dose 5 minutes before chamber entry
 - Second dose 90 minutes after chamber entry (when non-treated patients reach peak allergy symptoms)



Phase 2 Results Were Statistically Significant During Phase 3 Primary Endpoint Time Points*

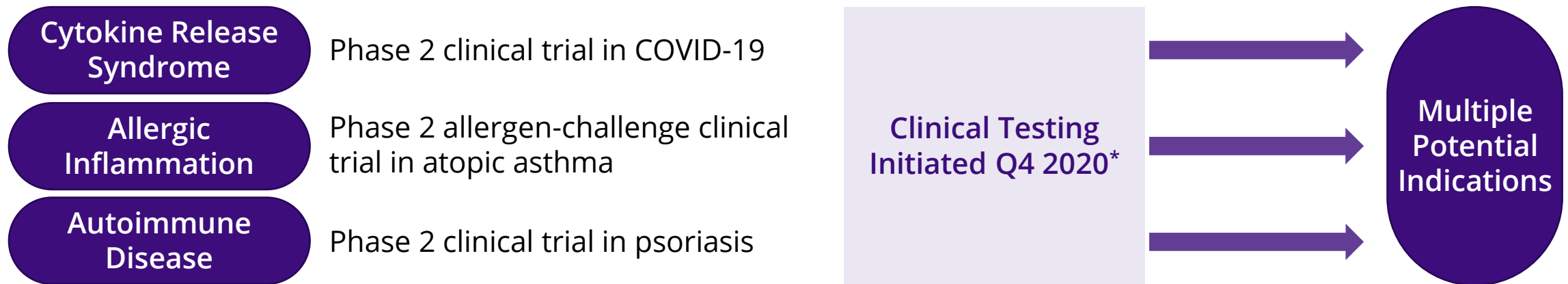


ADX-629 Clinical Initiative in Systemic Inflammatory Disease Complements Late-Stage Programs

- 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.

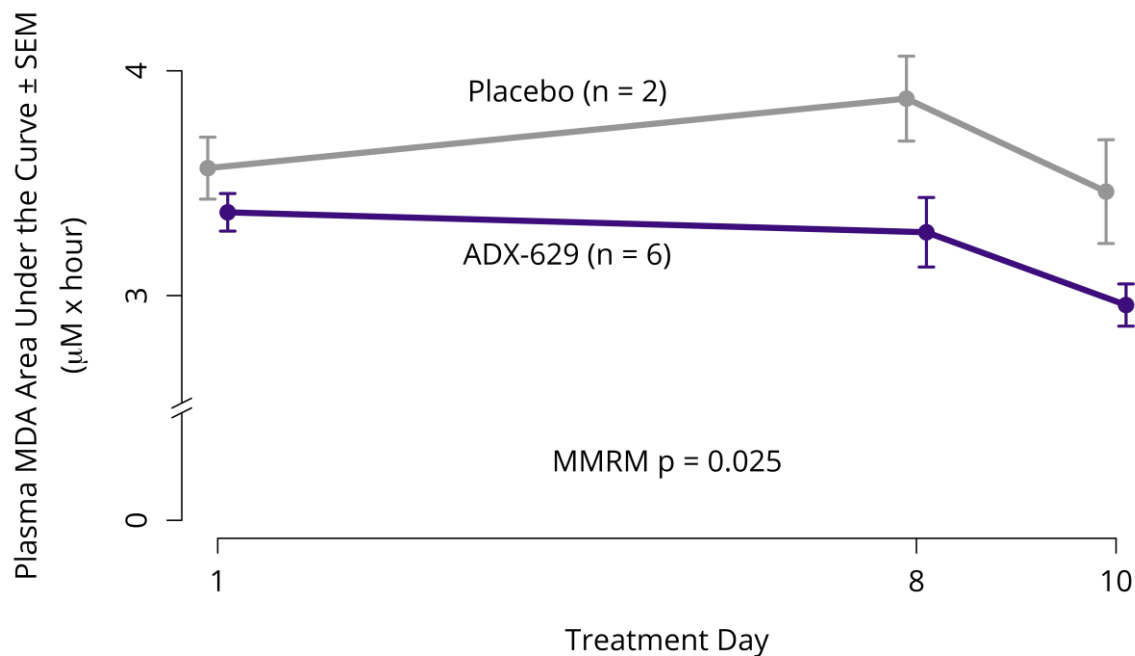
RASP-Inhibition in Systemic Diseases

ADX-629 Proof of Concept in Three Types of Severe Inflammation

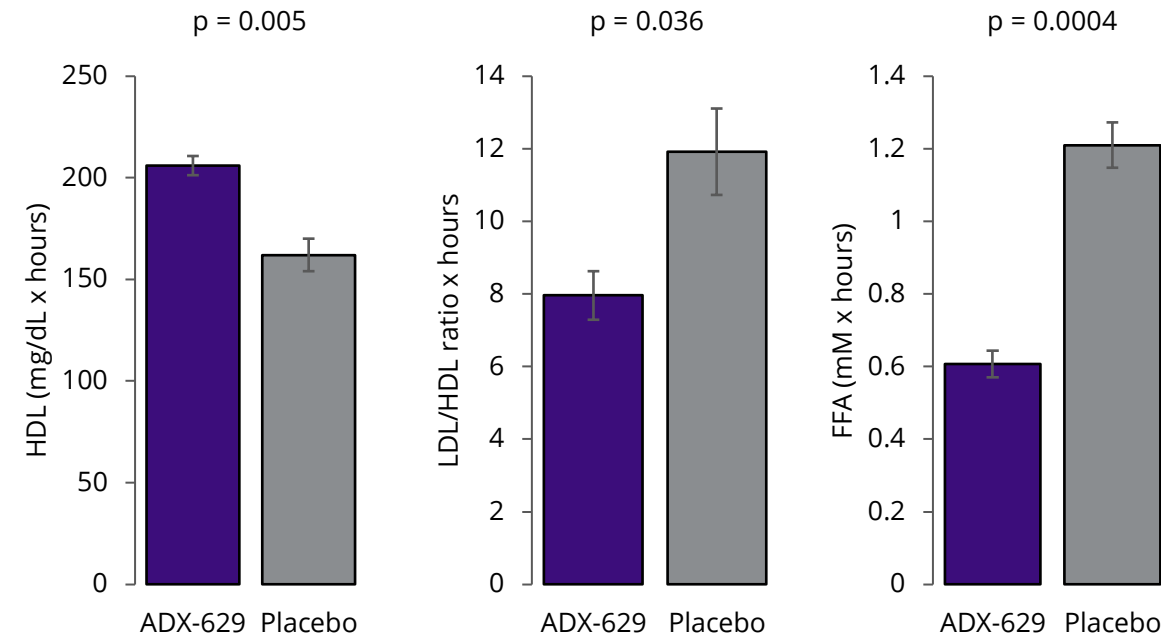


ADX-629 Reduced RASP vs. Placebo in Phase 1 Clinical Trial, Demonstrating Target Engagement, and Also Improved Lipid Profiles

MDA Levels Over 10 Days of Dosing








Plasma Lipid Profile After Fatty Meal



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.

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

Upcoming Expected RASP Inhibition Development Milestones*

-  Reproxalap dry eye disease **Phase 3 TRANQUILITY main cohort initiation H1 2021**
-  Reproxalap dry eye disease **Phase 3 TRANQUILITY-2 initiation H1 2021**
-  Reproxalap allergic conjunctivitis **Phase 3 INVIGORATE top-line results H1 2021**
-  Reproxalap dry eye disease **Phase 3 TRANQUILITY and TRANQUILITY-2 top-line results H2 2021**
-  ADX-629 **Phase 2 clinical testing results in systemic diseases in 2021** to assess activity across different types of severe inflammation: cytokine release syndrome (COVID-19), allergic inflammation (atopic asthma), and autoimmune disease (psoriasis)



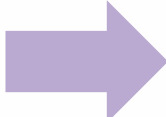
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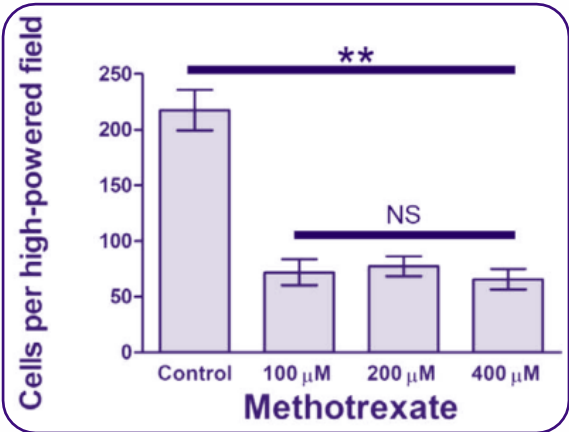
Dihydrofolate Reductase Inhibition

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

Preclinical reduction in cellular proliferation

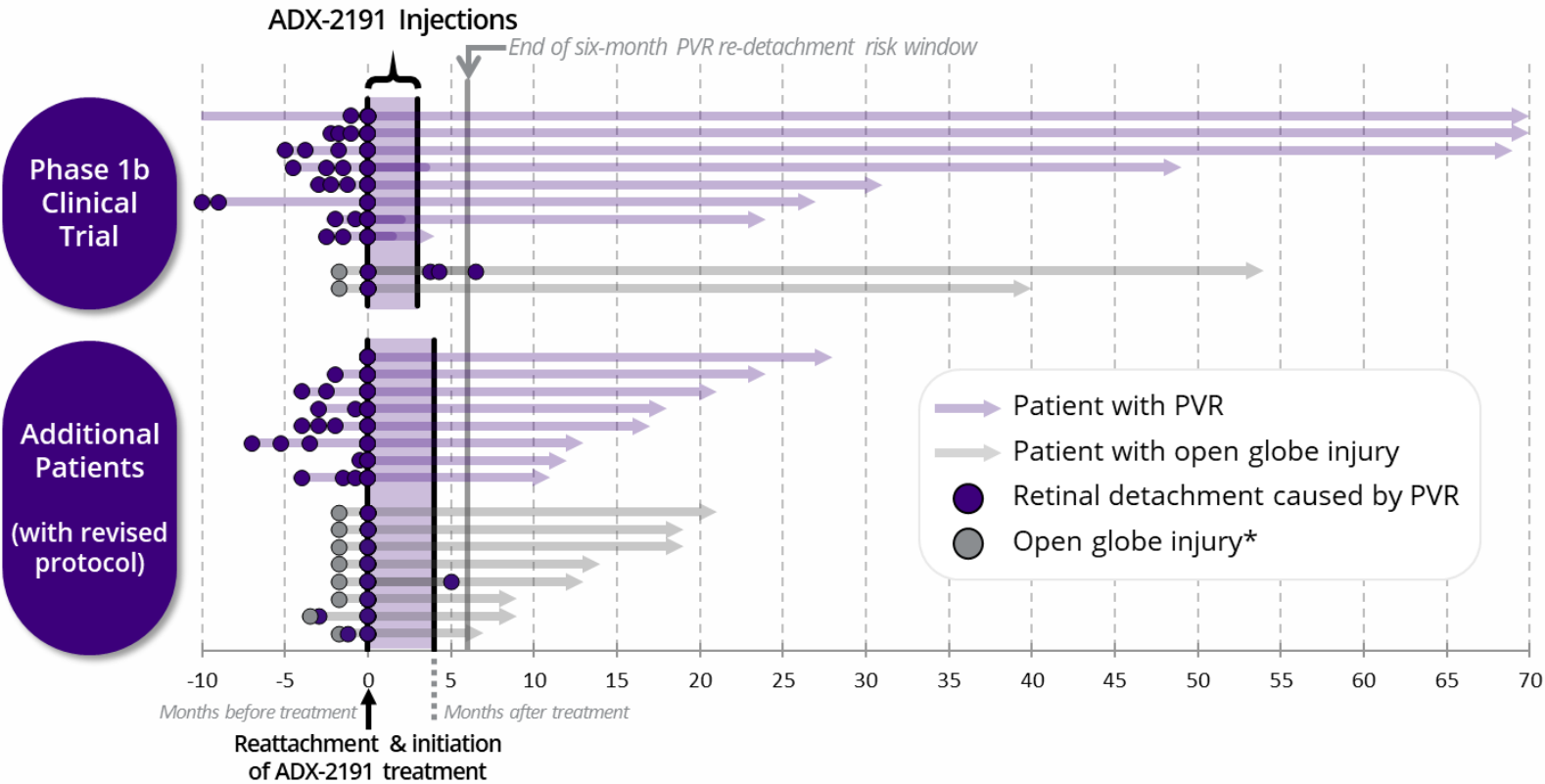


Clinical reduction in retinal detachment



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

Retinal Detachments Over Time by Patient



*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

ADX-2191

4,000
U.S.

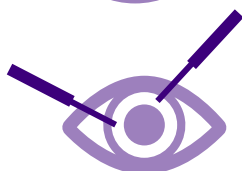
PVR is a **rare disease**, with ~4,000 patients per year in the U.S. and nearly twice as many in Europe and Japan combined.



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

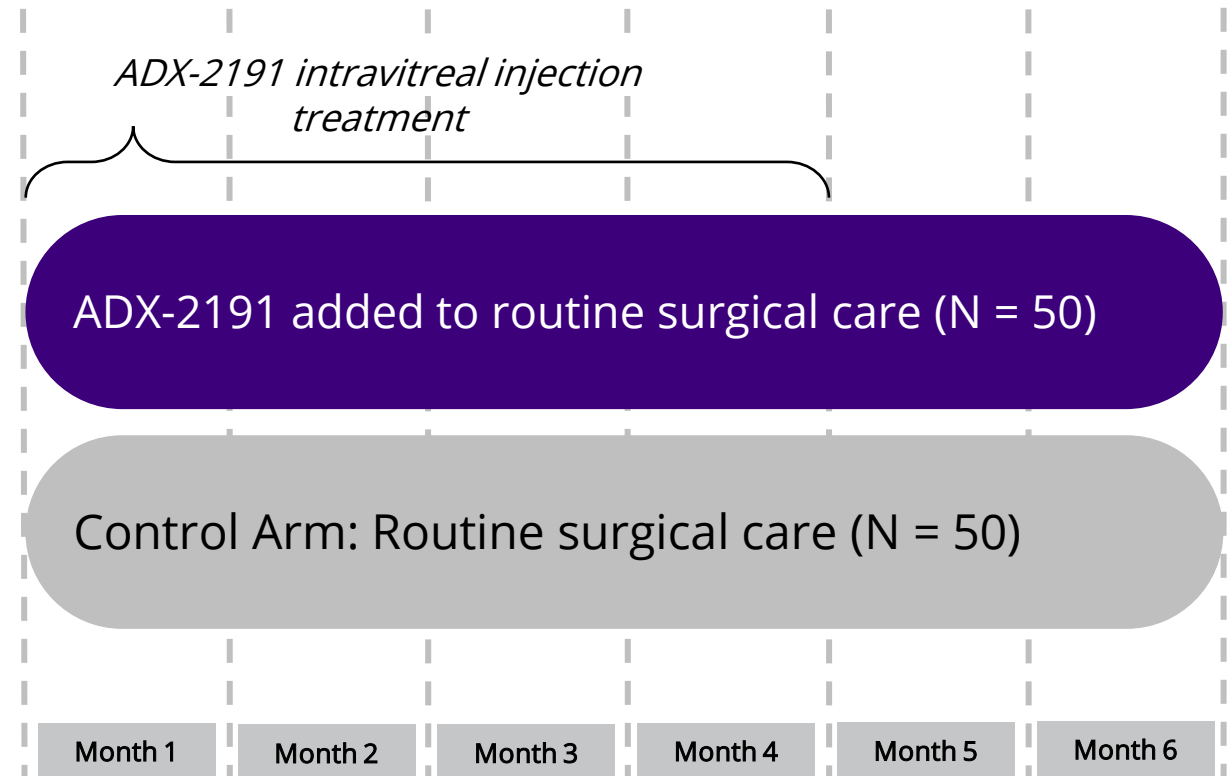
- A **potential therapeutic option** for the treatment of PVR
- **Granted U.S. orphan designation and FDA fast track designation** for the prevention of PVR
- **Tolerability and reattachment success** during study period **demonstrated in Phase 1b** open-label investigator sponsored clinical trial
- **GUARD adaptive Phase 3 clinical trial** for the prevention of recurrent retinal detachment due to PVR ongoing
- **Exploring additional indications**, including primary intraocular lymphoma

ADX-2191: GUARD Trial Design in Proliferative Vitreoretinopathy

Adaptive Phase 3 (Part 1) Clinical Trial Design

- **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



Completion of Enrollment Expected in 2021

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



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

- Primary vitreoretinal lymphoma (PVRL) is a rare, aggressive, high-grade cancer that 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.
- The median survival for newly diagnosed patients is 4.83 years.
- 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.

Upcoming Expected ADX-2191 Regulatory and Development Milestones

- Primary Vitreoretinal Lymphoma orphan drug designation in H1 2021
- GUARD Phase 3 Trial completion of enrollment in 2021*



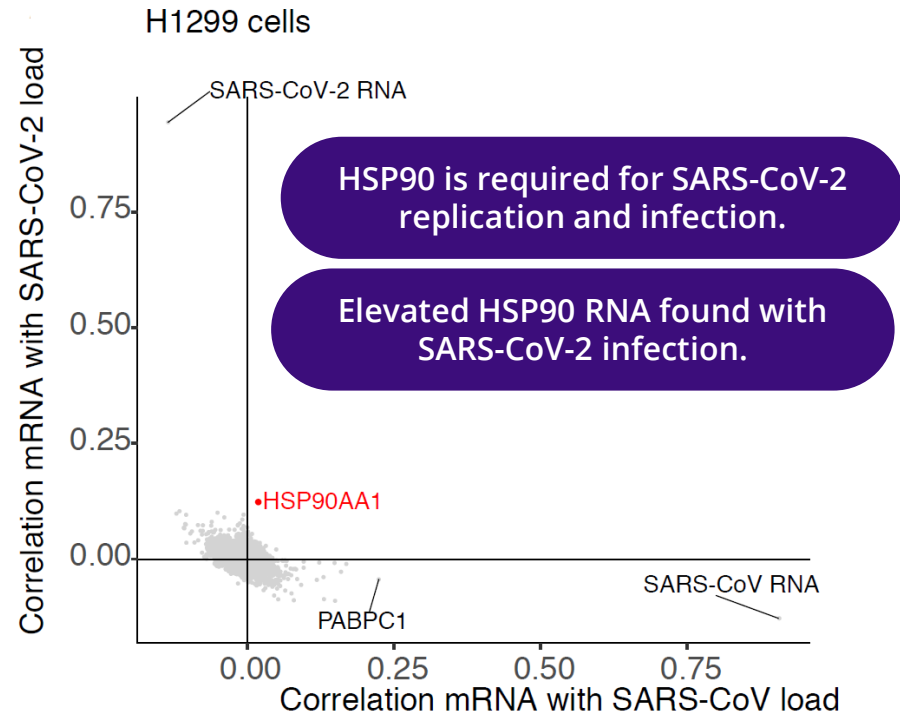
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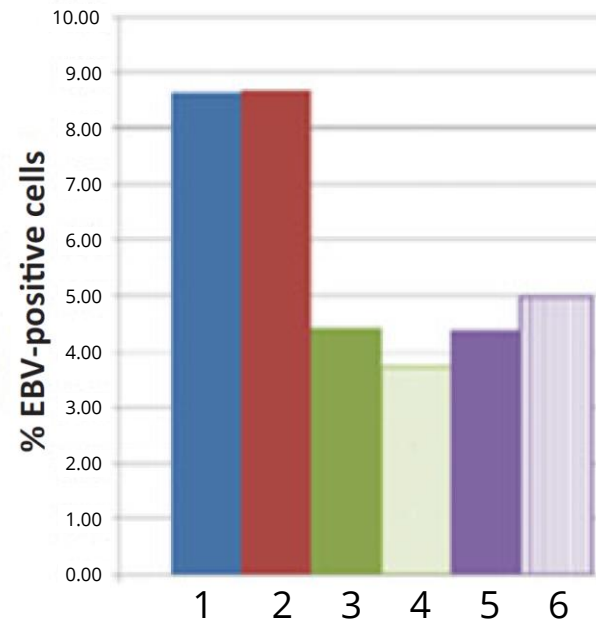
Protein Chaperome Inhibition

HSP90 Recently Identified as a Potential Therapeutic Target of SARS-CoV-2 and Demonstrated Clinical Activity Against EBV

HSP90 is a chaperone protein that controls the function of hundreds of client proteins, a system known collectively as the protein chaperome.



Wyller et al. *Bulk and single-cell gene expression profiling of SARS-CoV-2 infected human cell lines identifies molecular targets for therapeutic intervention*, bioRxiv preprint, May 5, 2020.
DOI:10.1101/2020.05.05.079194. Not certified by peer review.



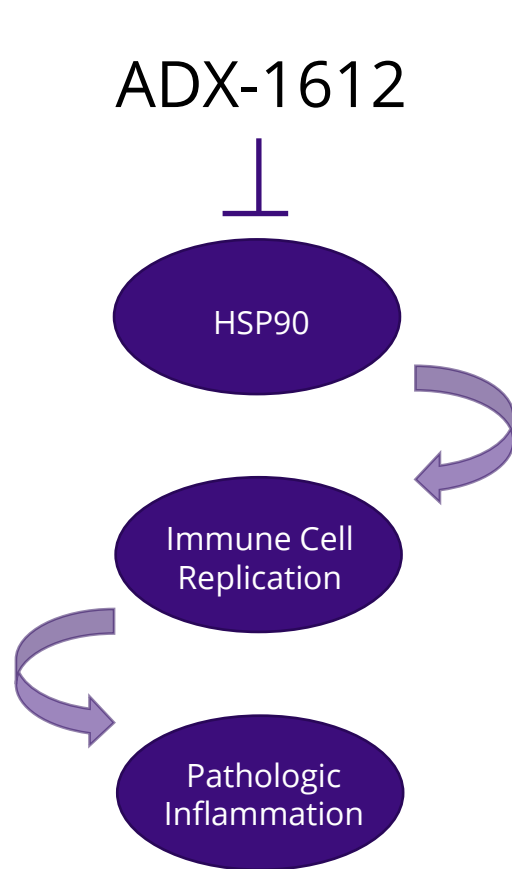
In an EBV-infected patient, ADX-1612 reduced the percentage of circulating EBV-positive cells.

- 1 = Pre-treatment
- 2 = Pre-treatment
- 3 = 1 week post dose 1 (120 mg/m²)
- 4 = 1 day post dose 2 (120 mg/m²)
- 5 = 2 weeks post dose 2 (120 mg/m²)
- 6 = 2 days post dose 1 (150 mg/m²)

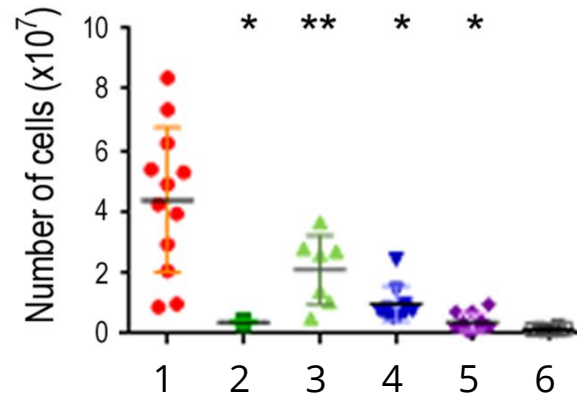
Shatzer et al. *Ganetespib, an HSP90 inhibitor, kills Epstein-Barr virus (EBV)-infected B and T cells and reduces the percentage of EBV-infected cells in the blood*, Leukemia & Lymphoma, 2016, DOI: 10.1080/10428194.2016.1213823

EBV = Epstein Barr Virus

In Addition to Antiviral Activity, ADX-1612 Has Demonstrated Potential Suppression of Pathologic Inflammation



Immune cell count reduction in animal model of lupus¹



- 1 = Vehicle
- 2 = Cyclophosphamide
- 3 = Cyclophosphamide/2
- 4 = ADX-1612
- 5 = ADX-1612 + cyclophosphamide
- 6 = Normal animal

Clinical response in patient with chronic vasculitis after a single dose





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The Aldeyra Value Proposition

The Aldeyra 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*

- Initiation of TRANQUILITY and TRANQUILITY-2 trials in dry eye disease expected H1 2021.
- Top-line results from Phase 3 INVIGORATE Trial in allergic conjunctivitis expected H1 2021.
- Top-line results from TRANQUILITY and TRANQUILITY-2 expected 2H 2021.
- ADX-629 Phase 2 clinical testing results in systemic diseases expected 2021.



SIGNIFICANT MARKET OPPORTUNITY

- Reproxalap targets a U.S. addressable market of >\$20B.
- ADX-2191 represents a potential therapeutic option for PVR and PVRL.



SOLID CASH POSITION

- Cash, cash equivalents and marketable securities were \$86.2 million as of September 30, 2020 (additionally, gross proceeds of \$74.7 million** were raised in a January 2021 public offering).
- Based on current operating plans and expectations, cash runway through the end of 2023.***

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 Peptimmune⁷

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 Takeda
4. Acquired by Ligand

5. Acquired by Merck
6. Acquired by Alexion
7. Acquired by Genzyme



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