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September 2020

CORPORATE REVIEW

Systems-Based Approaches to Regulate Immune Response

Nasdaq: ALDX

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Immunology is a Key Component of Many Diseases

~7%
Of Western Society

Suffer from some form of **immune-mediated disease,** and **incidence is increasing**

- Dry Eye Disease
- Psoriasis
- Asthma
- Lupus
- Allergy
- Respiratory Distress
- Inflammatory Bowel Disease
- Alzheimer's
- *... Etc. ...*

Disease control elusive despite existing therapies, and thus **novel approaches are needed**

Inflammation: A Unifying Theory of Disease?

Harvard Health Letter
April, 2006

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Source: Lerner, Jeremias, and Matthias, International Journal of Celiac Disease, vol. 3, no. 4 (2015): 151-155;
Shurin and Smolkin, Advances in Experimental Medicines and Biology 601:3-12, 2007; Kuek et al, Postgraduate Medical Journal 83(978): 251-260, 2007.

Aldeyra is Developing Technology Designed to Modulate Biological *Systems …* Not Single Targets

Traditional

Most immunological drugs shut down **specific molecules,** obstructing the immune system, and leading to toxicity.

The traditional approach is limited to two outcomes.

In contrast, **modulation** of the immune **system** maintains immune function, but allows for lower levels of inflammation.

A systems-based approach allows for infinite control.

Systems-Based

Aldeyra is Developing Novel Approaches for Immune System Regulation

RASP

Reproxalap

ADX-629

Immune Cell Migration
Cytokine Production
Fibroblast Activation

Dihydrofolate Reductase

ADX-2191

Immune Cell Proliferation
Fibroblast Activation
Macrophage Activation

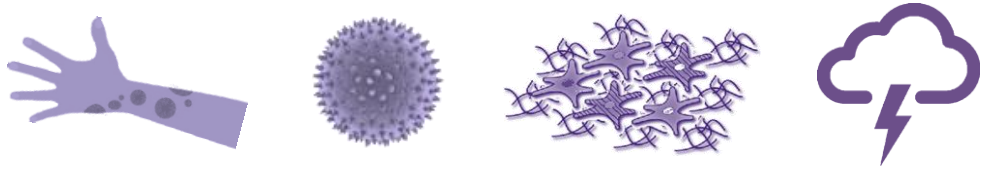
Protein Chaperome

ADX-1612

Immune Cell Proliferation
Antibody Formation
Viral Replication

Immune Mediated Diseases:

Autoimmune Disease, Allergy, Fibrosis, Cytokine Release Syndrome



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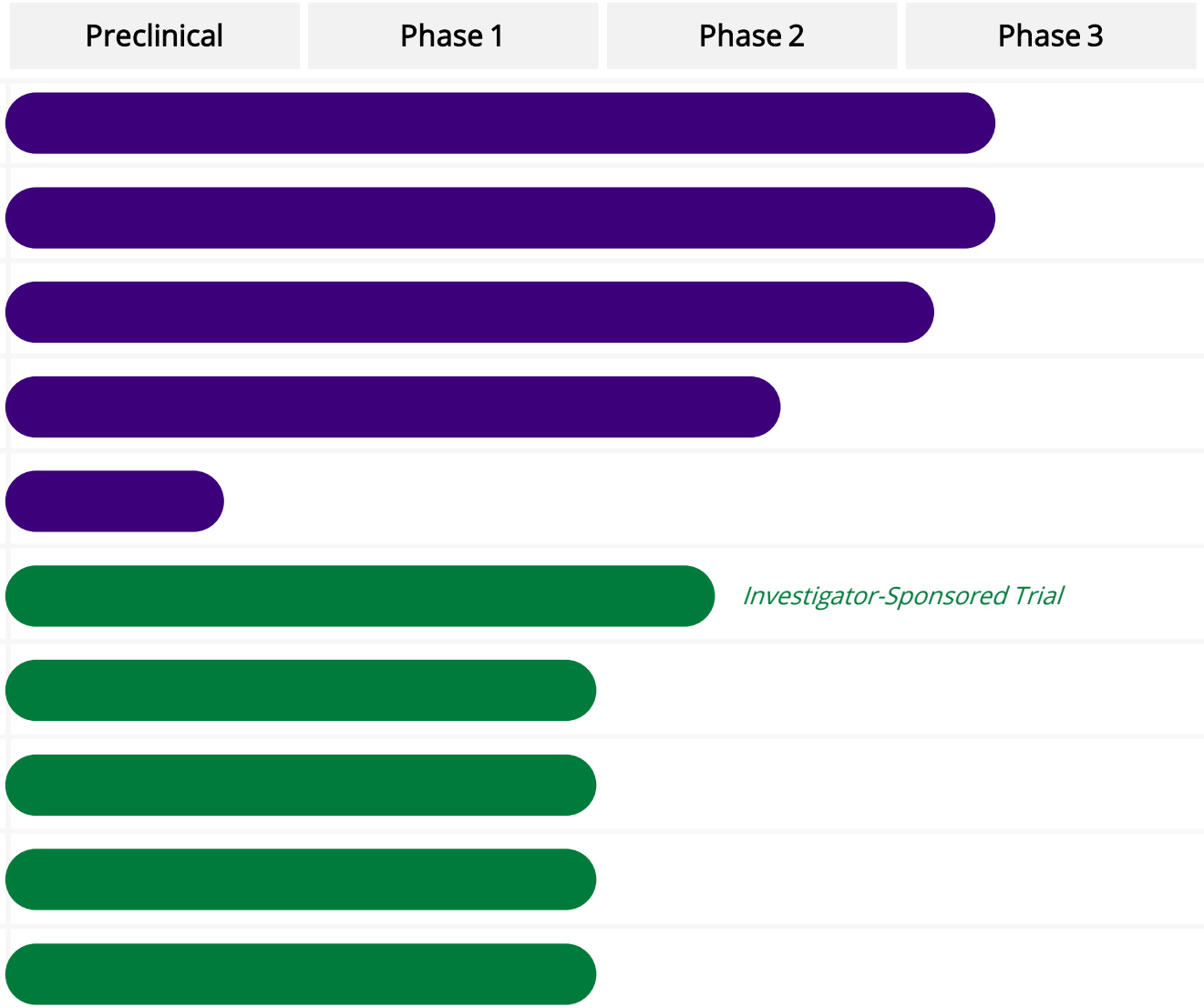
RASP = Reactive Aldehyde Species

Innovative Pipeline Addressing Immunological Disease

Disease Area	Compound	Mechanism	Indication
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-1612	CHP	Ovarian Cancer
			SARS-CoV2 Antiviral (COVID-19)
	ADX-629	RASP	Cytokine Release Syndrome (COVID-19)
			Autoimmune Disease (Psoriasis)
			Allergy (Atopic Asthma)



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RASP Mechanism = Reactive Aldehyde Species Inhibitor
DHFR Mechanism = Dihydrofolate Reductase Inhibitor
CHP Mechanism = Chaperome Inhibitor

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Reactive Aldehyde Species (RASP) Inhibition

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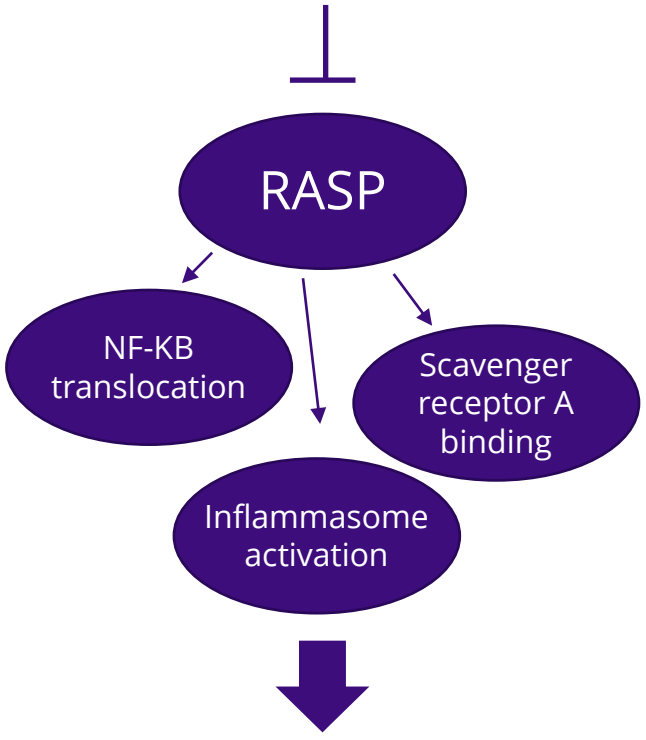
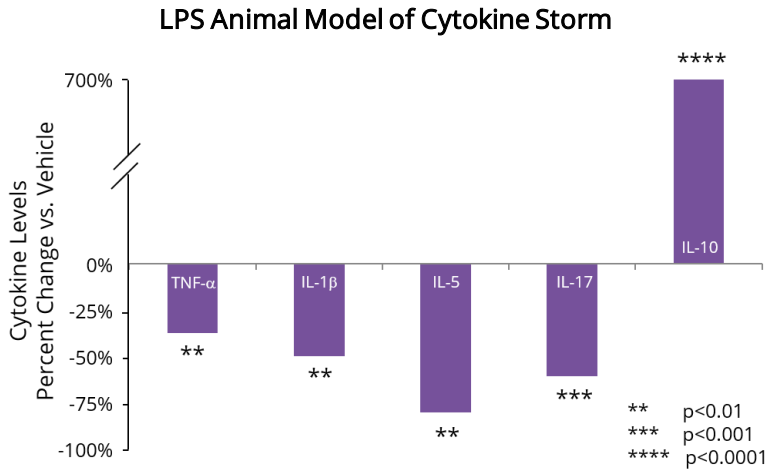
RASP Inhibition is a Pre-Cytokine, Systems-Based Approach that Has Been Clinically Validated in Late-Stage Trials

Reproxalap, ADX-629



Cytokine Release

Preclinical broad-based cytokine reduction

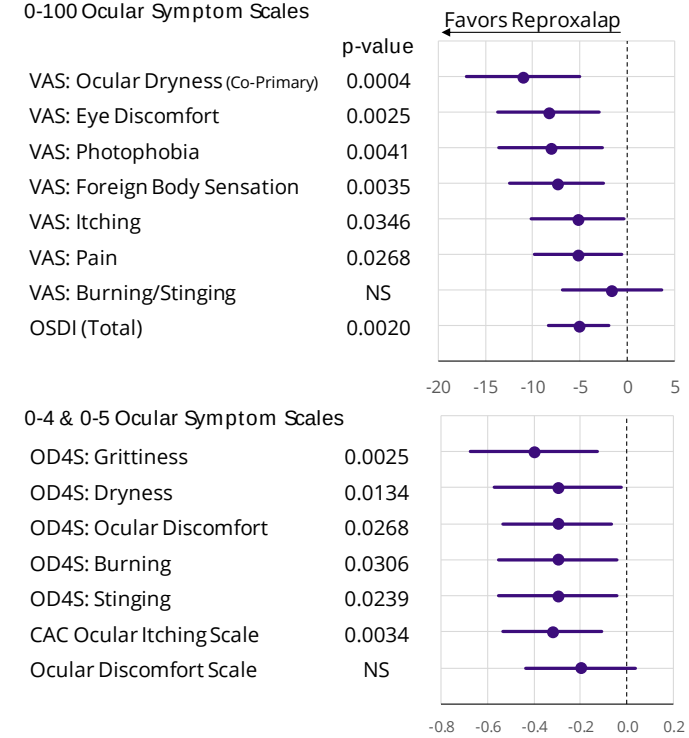


Broad-based symptom reduction

RENEW-Part 1 Phase 3 Dry Eye Disease Trial

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

0-100 Ocular Symptom Scales



‡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).
Source: 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

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.

Allergic Conjunctivitis

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

66 million or more adults in the U.S.

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

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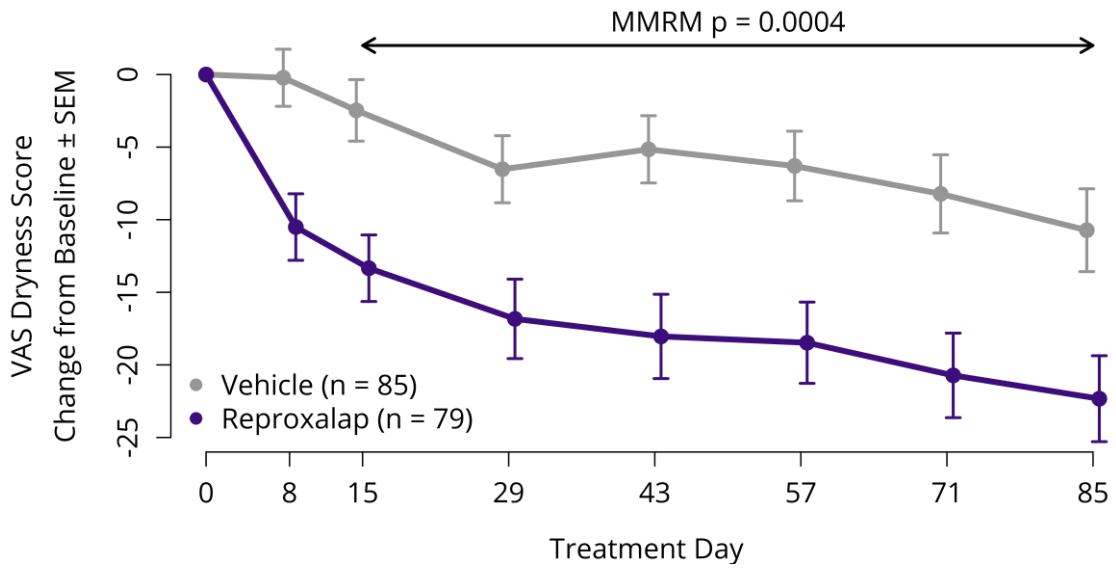
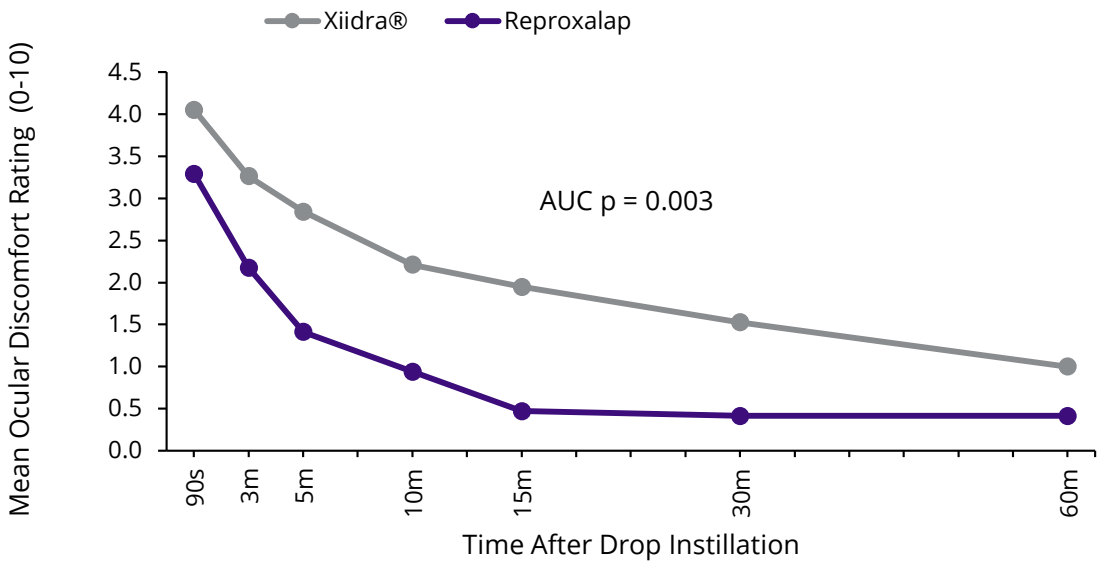
Reproxalap Exhibited First-Line Symptom Control and Tolerability in Dry Eye Disease Clinical Trials

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



Head-to-Head Tolerability Trial vs. Xiidra®



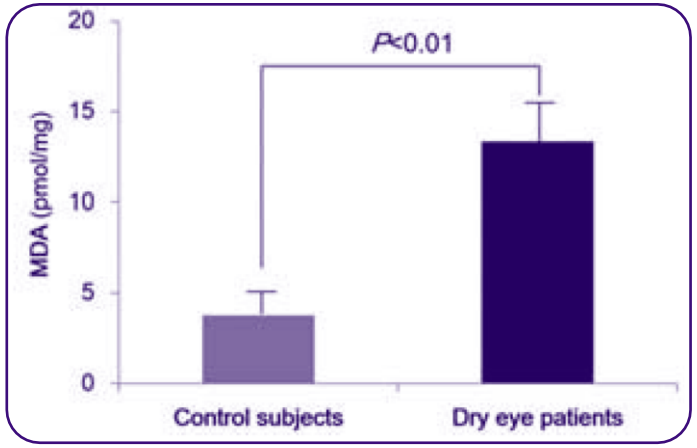
Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.
Source: Reproxalap RENEW-Part 1 and Drop Experience clinical trial results.

VAS = Visual Analog Scale
MMRM = Mixed Effect Model Repeated Measures
AUC = Area Under The Curve

Reproxalap's Mechanism of Action Reduces RASP, a Novel Dry Eye Disease Sign

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.

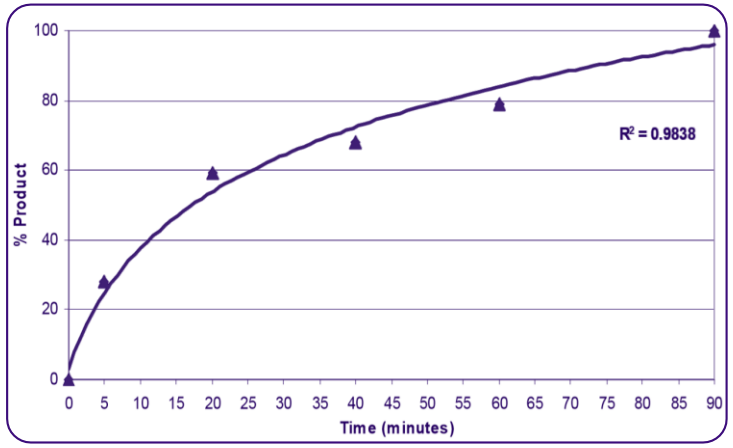


Source: Curr Eye Res. 2016, 41(9):1143-9

Reproxalap

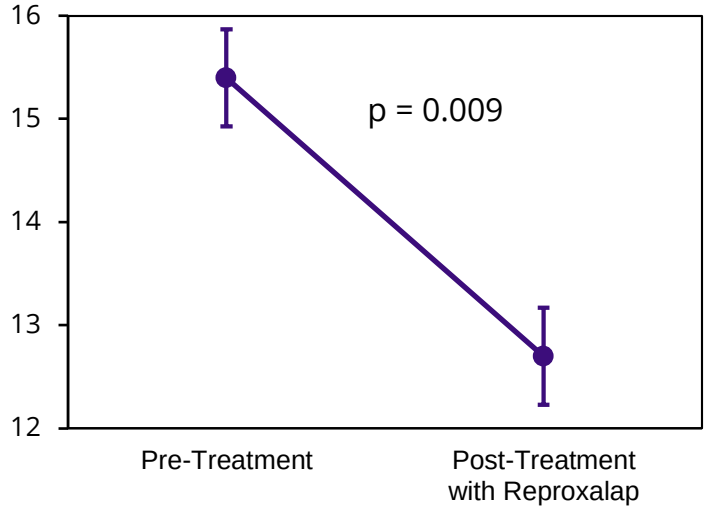
Preclinical rapid and complete RASP binding

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
(µM Malondialdehyde Adduct; Mean ± Within-Subject SEM)

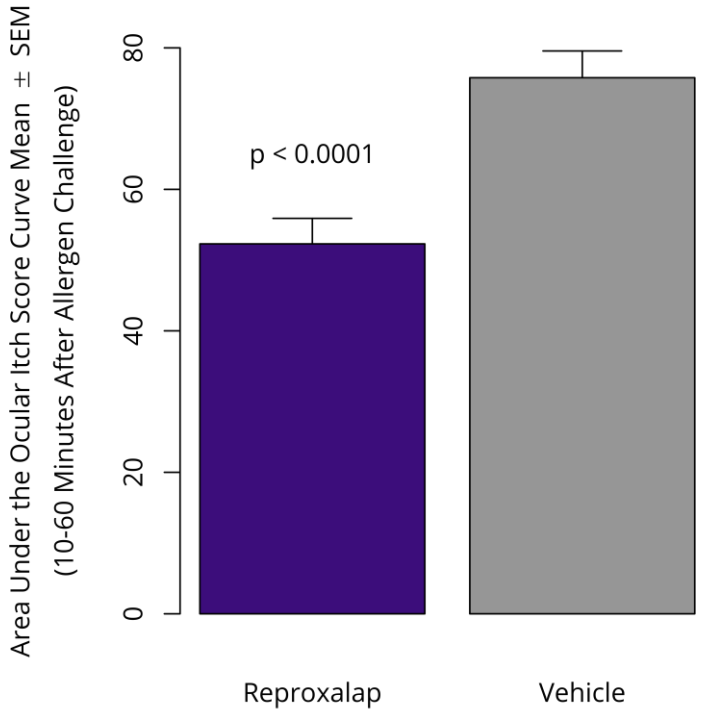


RASP is a novel and FDA-approvable dry eye disease sign.

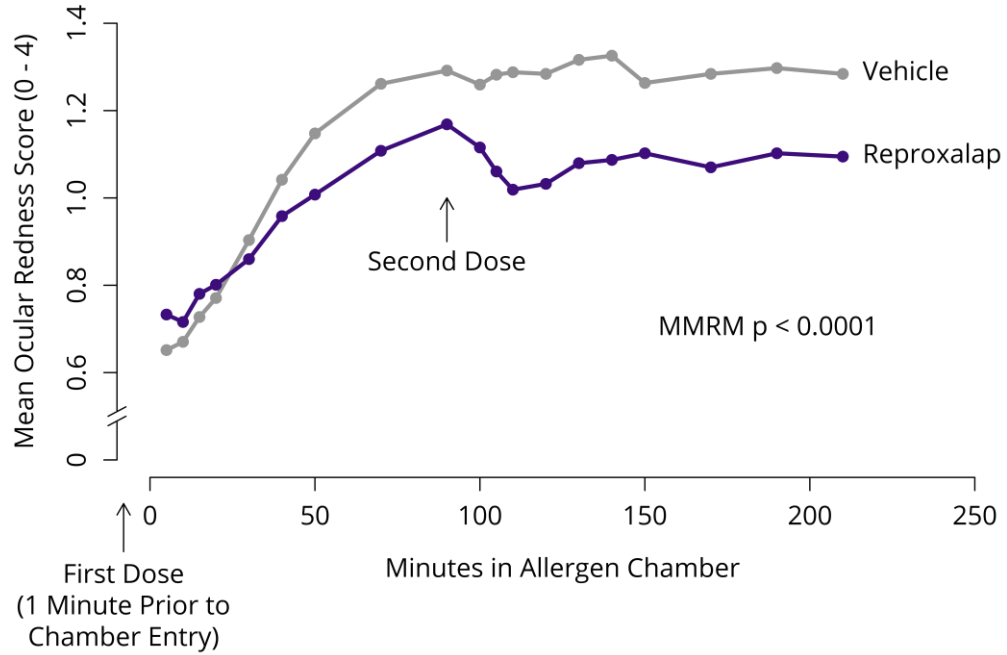
Source: Choi W., et al. Expression of Lipid Peroxidation Markers in the Tear Film and Ocular Surface of Patients with Non-Sjogren Syndrome: Potential Biomarkers for Dry Eye Disease. Curr Eye Res. 2016, 41(9):1143-9; Reproxalap preclinical and Phase 2a in dry eye disease clinical trial results on file.

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

ALLEVIATE Phase 3 Trial



Phase 2 Allergen Chamber Trial



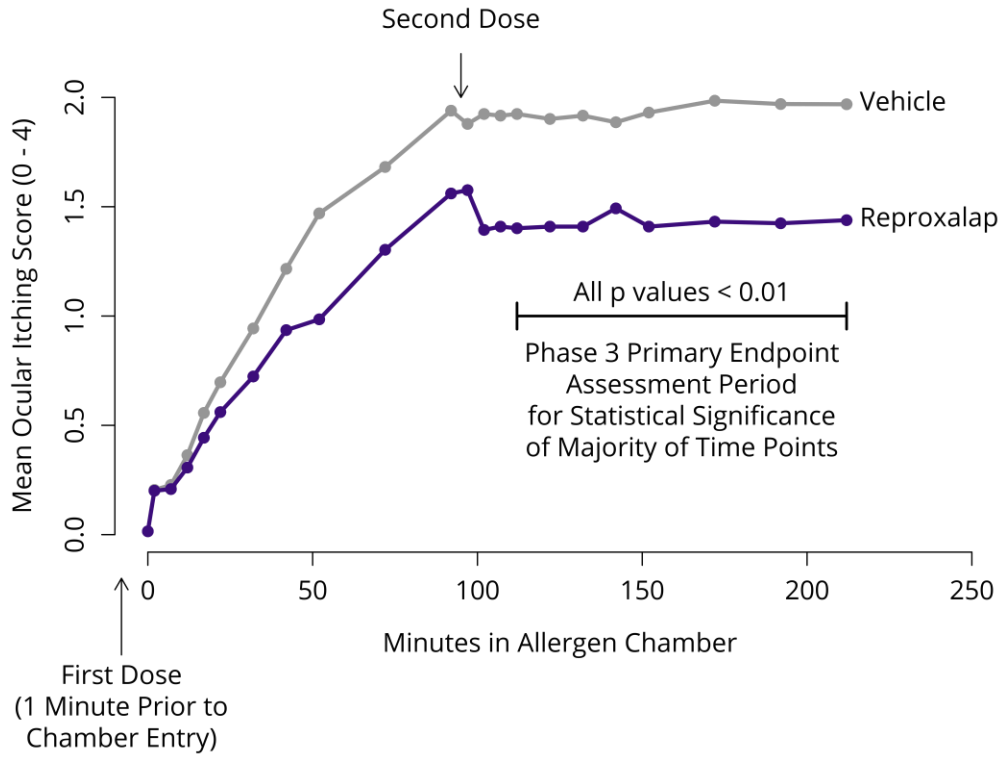
Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns reported; mild instillation site irritation is the most commonly reported adverse event in clinical trials.

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 eleven 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 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 entry (when non-treated patients reach peak allergy symptoms)

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



ClinicalTrials.gov Identifier: NCT04207736

*The safety and efficacy results of later phase or subsequent clinical trials may not confirm the results of earlier trials. 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 allergen chamber Phase 2 clinical trial results; Ocular itch scale (0-4).

ADX-629 Clinical Initiative in Systemic Inflammatory Disease Compliments 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, autoimmune disease, and allergy.

RASP-Inhibition in Systemic Diseases

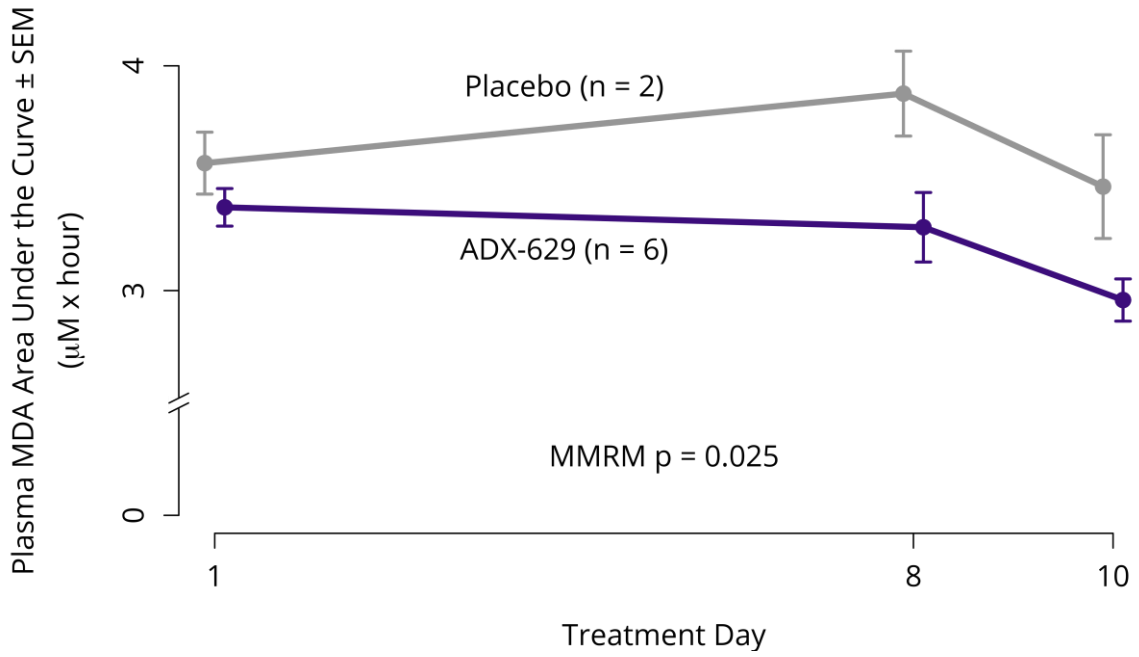
ADX-629 Proof of Concept in Three Types of Severe Inflammation

		Expected Initiation*	
Cytokine Release Syndrome	Phase 2 clinical trial in adult patients hospitalized for COVID-19	H2 2020	→ Multiple Potential Indications
Autoimmune Disease	Phase 2a clinical trial in psoriasis	Q4 2020	→ Multiple Potential Indications
Allergy	Phase 2a allergen-challenge clinical trial in atopic asthma	Q4 2020	→ Multiple Potential Indications

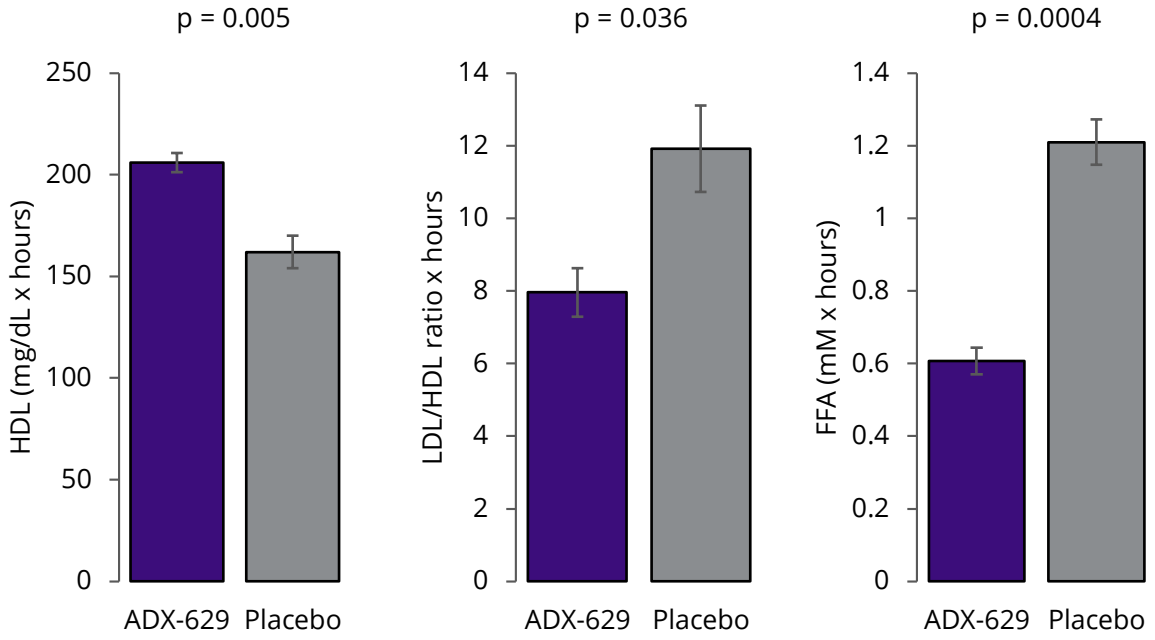
*The timing of clinical trial initiation depends, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, and the ability to recruit patients.

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

MDA Levels Over Ten 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 **subsequent development plans update following June Type C FDA meeting final minutes July 2020**
- ○ Reproxalap dry eye disease **tear level RASP reduction clinical trial initiation H2 2020**
- ○ Reproxalap allergic conjunctivitis **INVIGORATE Phase 3 study results H1 2021**
- ○ ADX-629 **cytokine release syndrome Phase 2 clinical trial initiation** in COVID-19 associated respiratory compromise H2 2020*
- ○ ADX-629 **autoimmune disease Phase 2a clinical trial initiation** in psoriasis Q4 2020*
- ○ ADX-629 **allergy Phase 2a allergen-challenge clinical trial initiation** in atopic asthma Q4 2020*

*The timing of clinical trial initiation 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.

○ = Ocular Diseases
○ = Systemic Diseases

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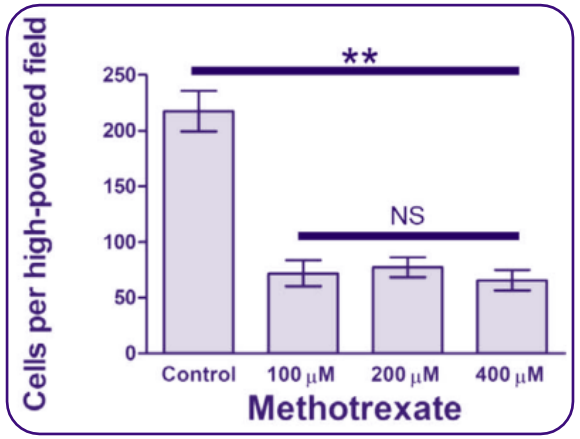
Dihydrofolate Reductase Inhibition

Nasdaq: ALDX

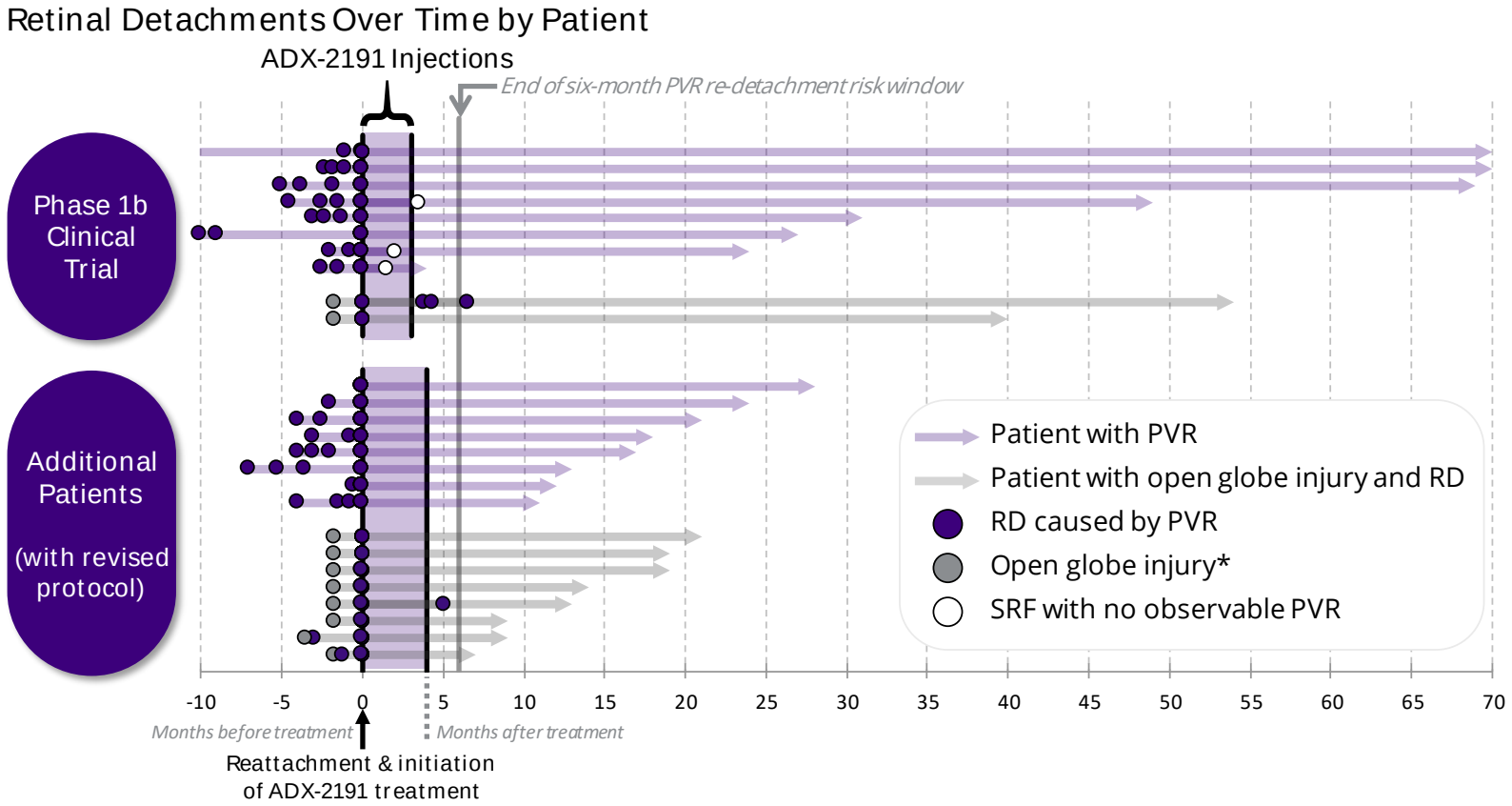
ADX-2191, a Novel Intravitreal Formulation of Methotrexate, Represents a Clinically Proven Systems Modulating Approach

Preclinical reduction in cellular proliferation



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)

RD = Retinal detachment
PVR = Proliferative vitreoretinopathy
SRF = Subretinal fluid

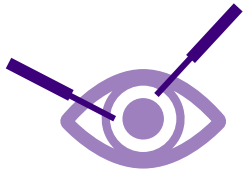
ADX-2191 Represents a Novel Approach and Potential Therapeutic Breakthrough in Proliferative Vitreoretinopathy Treatment

Proliferative vitreoretinopathy

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

ADX-2191

- A **potential therapeutic breakthrough** in PVR treatment
- **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

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

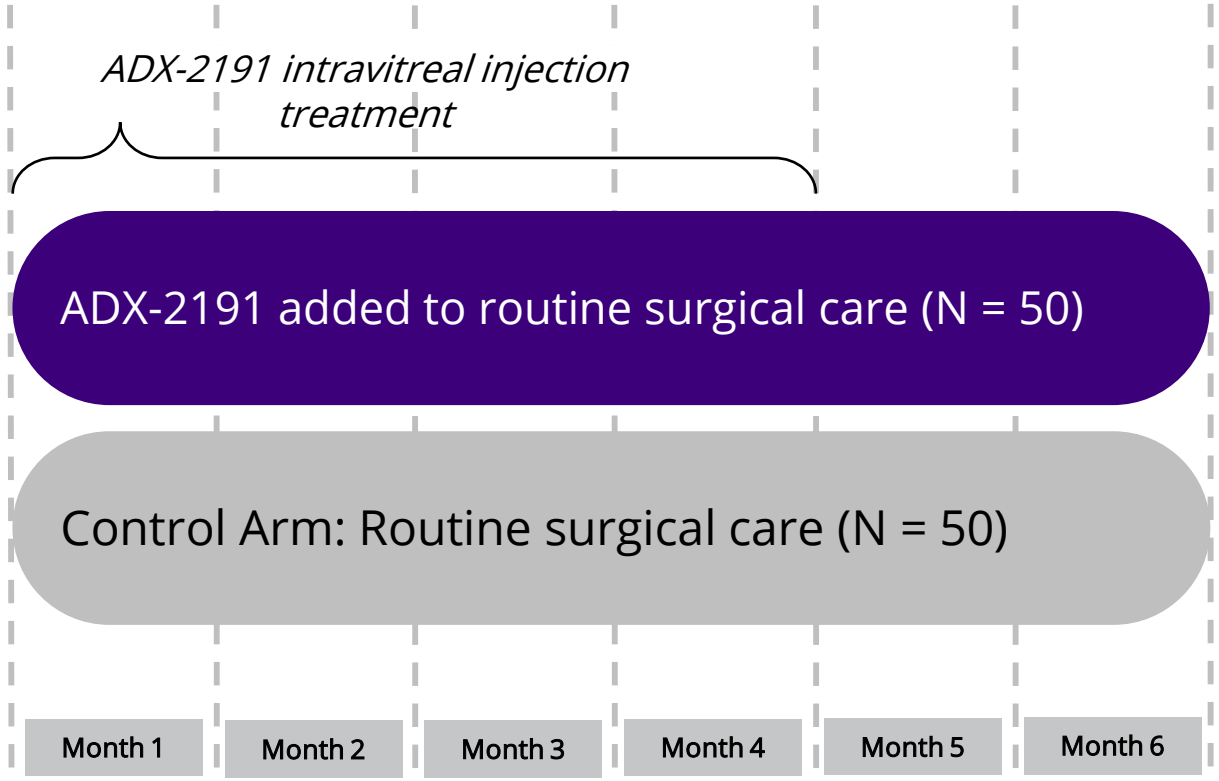
PVR = Proliferative vitreoretinopathy

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

- **Primary objective:**
  - Evaluate efficacy of intravitreal ADX-2191 injections for prevention of recurrent retinal detachment due to proliferative vitreoretinopathy (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

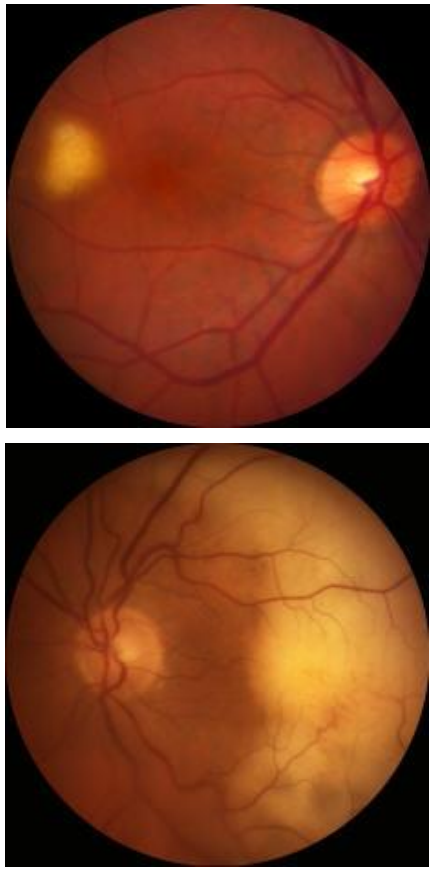
Progress Update Expected H2 2020*

Adaptive Phase 3 PVR Clinical Trial Design: Part 1



OCT = Optical Coherence Tomography
*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.

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.

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

Upcoming Expected ADX-2191 Development Milestones

- Intraocular lymphoma **orphan designation H2 2020**
- GUARD Phase 3 Trial enrollment **update H2 2020***

*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.

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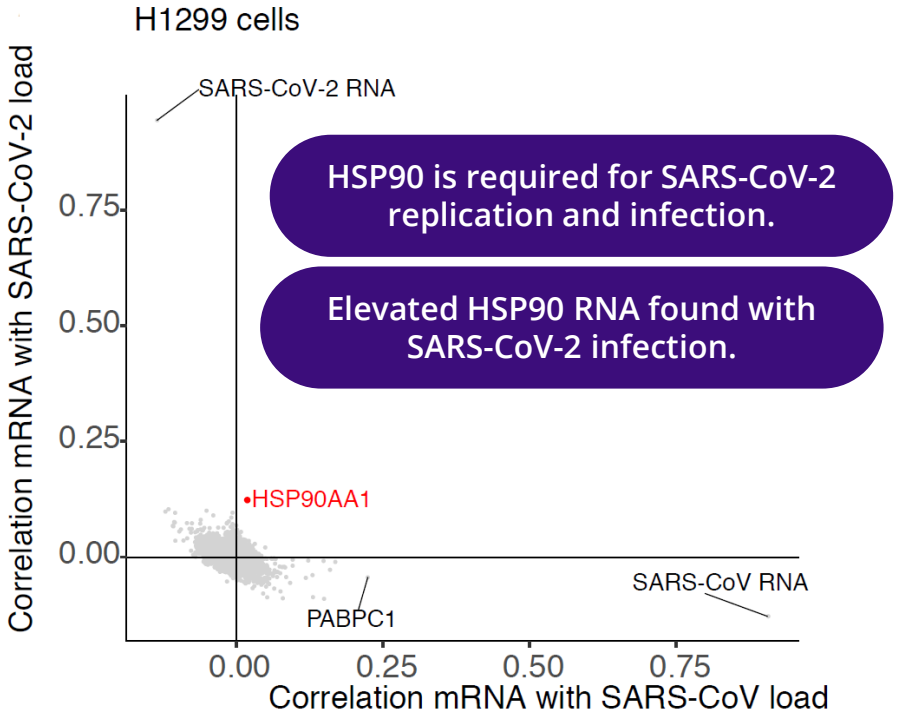
Protein Chaperome Inhibition

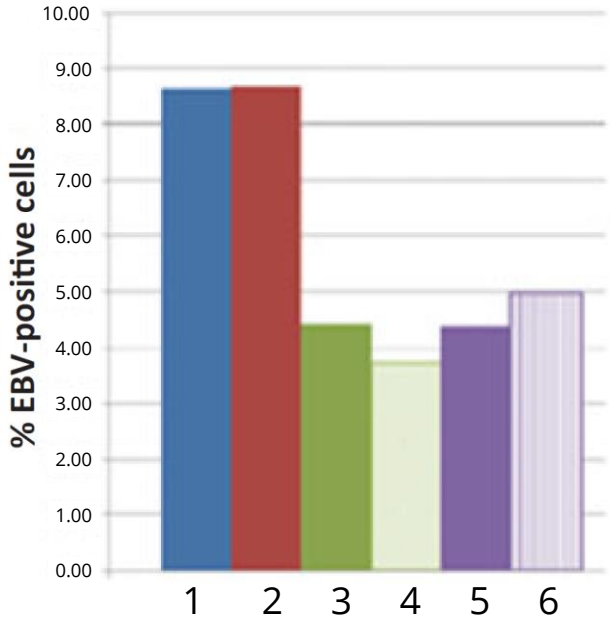
Nasdaq: ALDX

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.



Wyler 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/m^2)

4 = 1 day post dose 2 (120 mg/m^2)

5 = 2 weeks post dose 2 (120 mg/m^2)

6 = 2 days post dose 1 (150 mg/m^2)

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

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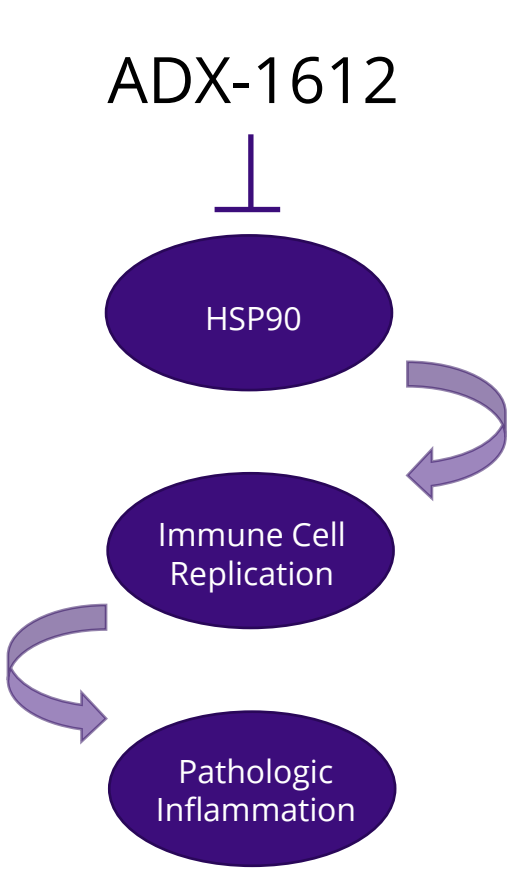
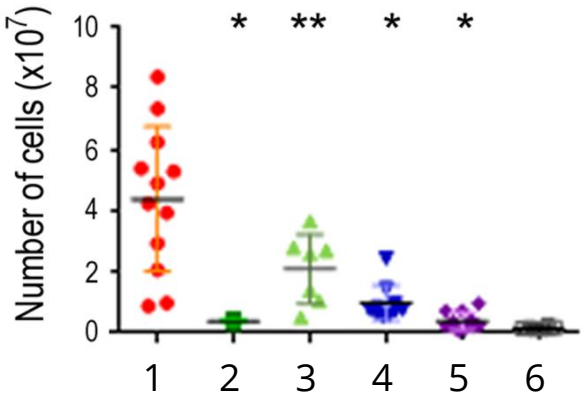
In Addition to Antiviral Activity, ADX-1612 Has Demonstrated Potential Suppression of Pathologic Inflammation

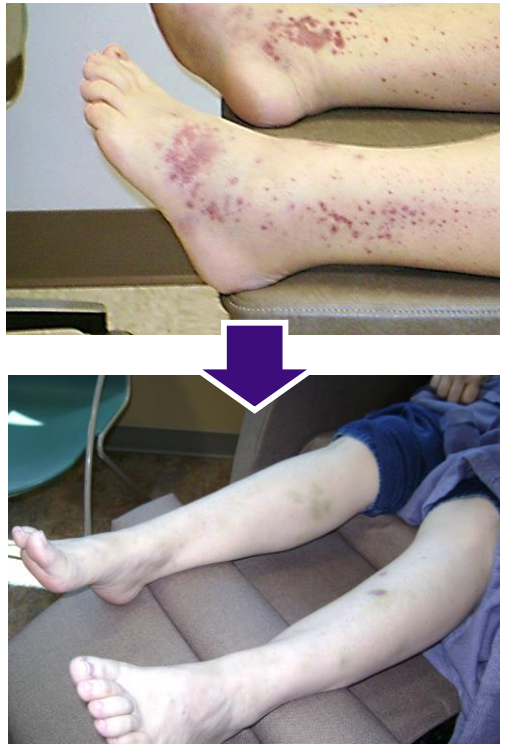


Immune cell count reduction in animal model of lupus[1]



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



[1]Liu et al. *The HSP90 Inhibitor Ganetespib Alleviates Disease Progression and Augments Intermittent Cyclophosphamide Therapy in the MRL/lpr Mouse Model of Systemic Lupus Erythematosus*, PLoS One, May 14, 2015. DOI:10.1371/journal.pone.0127361

Expected ADX-1612 Development Milestones and Clinical Plans*

- ✓ Coronavirus Treatment Acceleration Program (CTAP) **application June 2020**
- ✓ BARDA CoronaWatch **application June 2020**
- ✓ Phase 2 EUDARIO Ovarian Cancer clinical trial **enrollment completion July 2020**
- ○ COVID-19 clinical development **update H2 2020**

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*The timing of clinical trial initiation depends, in part, on restrictions related to COVID-19, the availability of clinical research facilities and staffing, and the ability to recruit patients. Contingent on funding, regulatory review, and other factors.

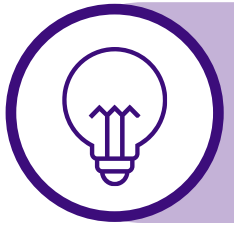
September 2020

CORPORATE REVIEW

The Aldeyra Value Proposition

Nasdaq: ALDX

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

- ADX-629 proof of concept Phase 2 clinical trials planned by year end.*
- INVIGORATE and GUARD Phase 3 clinical trials are ongoing.

SIGNIFICANT MARKET OPPORTUNITY

- Reproxalap targets a U.S. addressable market of >$20B.
- ADX-2191 represents a potential therapeutic breakthrough.

SOLID CASH POSITION

- Cash, cash equivalents and marketable securities were $66.2 million as of June 30, 2020 (not including $25.2 million in cash received subsequent to June 30, 2020 through the ATM program).
- Based on current operating plans and expectations, cash runway through the end of 2022.

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*The timing of clinical trial initiation 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.

RASP = Reactive Aldehyde Species
PVR = Proliferative vitreoretinopathy
ATM = At-The-Market

Experienced Management Team and Board of Directors

Management Team

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

DOMAIN ASSOCIATES
PHENOME SCIENCES INC[1]
ADERIS PHARMACEUTICALS[2]

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

Bristol-Myers Squibb
J.P.Morgan

David McMullin, M.B.A.
Chief Commercial Officer

Shire[3]
gsk
NOVARTIS

James Gow, M.D.
SVP Clinical Development

Shire[3]
NOVARTIS
Alcon
B+L

Stephen Machatha, Ph.D.
SVP Technical Operations

CYDEX PHARMACEUTICALS, INC.[4]
CUBIST PHARMACEUTICALS[5]
Synageva BioPharma[6]

Board of Directors

Richard Douglas, Ph.D. CHAIRMAN	Former SVP Corporate Development at Genzyme
Ben Bronstein, M.D.	Former CEO Peptimmune[7]
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
Jesse Treu, Ph.D.	Domain Associates
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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Systems-Based Approaches to Regulate Immune Response

Nasdaq: ALDX