



November 2019

---

**JEFFERIES LONDON HEALTHCARE CONFERENCE**

# Innovating Transformative Therapies

Nasdaq: ALDX  
© Aldeyra Therapeutics, Inc. 2019

# 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, trends, 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. 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 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 timelines may be subject to adjustment depending on recruitment rate, regulatory review, preclinical and clinical results, and other factors that could delay the initiation, completion, or reporting of clinical trials.

In addition to the risks described above and in Aldeyra's other filings with the SEC, other unknown or unpredictable factors also could affect Aldeyra's results. No forward-looking statements can be guaranteed and actual results may differ materially from such statements. The information in this presentation is provided only **as of November 21, 2019**, and Aldeyra undertakes no obligation to update any forward-looking statements contained in this presentation on account of new information, future events, or otherwise, except as required by law.

# Our Mission and Value Proposition

**Developing Next-Generation Medicines to Improve the Lives of Patients with Immune-Mediated Diseases**



# Deep and Innovative Pipeline Focused on Immune-Mediated Diseases

Disease Area	Compound	[Mechanism]	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone
Ocular Diseases	Reproxalap	[RASP]	Dry Eye Disease					Phase 3-Part 1 completion Q4 2019
			Allergic Conjunctivitis					Phase 3 initiation H1 2020
	ADX-2191	[DHFR]	Proliferative Vitreoretinopathy					Phase 3-Part 1 initiation Q4 2019
	ADX-103/10X	[RASP]	Retinal Disease					Phase 1/2 initiation 2020
	Undisclosed		Ocular Inflammation	Research Collaboration (undisclosed)				
Systemic Diseases	Reproxalap	[RASP]	Sjögren-Larsson Syndrome					Parallel Regulatory Advice
	ADX-1612	[CHP]	PTLD					Phase 2 initiation H2 2019
			Mesothelioma	Investigator-Sponsored Trial				
			Ovarian Cancer	Investigator-Sponsored Trial				
	ADX-629	[RASP]	Autoimmune / Metabolic Disease					
	ADX-1615	[CHP]	Autoimmune Disease / Cancer					
	Undisclosed	[RASP]	Systemic Inflammatory Disease	Research Collaboration				



# Our Lead Programs Represent Compelling Commercial Opportunities

Late Stage Programs	Estimated U.S. Population <sup>†</sup>	Current Standard of Care	Drug Candidate and Dev. Stage	Potential Competitive Advantages <sup>†</sup>
<i>Ocular Diseases</i>				
Dry Eye Disease	34 million DED Up to 10 million with DED & AC	Xiidra®, Restasis®	Reproxalap: Phase 3	Rapid onset, broad activity, reduction in itch
Allergic Conjunctivitis	30 million AC (addressable market)	Antihistamines	Reproxalap: Phase 3	Non-drying, durable activity; Responder superiority vs. vehicle
Proliferative Vitreoretinopathy	4,000	None (repeat surgeries)	ADX-2191: Phase 3	Clinically demonstrated activity; Currently no FDA- or EMA-approved therapy
<i>Systemic Diseases</i>				
Sjögren-Larsson Syndrome	1,000	None (manage symptoms)	Reproxalap: Phase 3	Clinically demonstrated activity; Currently no FDA- or EMA-approved therapy

<sup>†</sup>Pending clinical data, regulatory discussions, payor negotiations, competition, potential legislative changes, and other factors, which may not be in Aldeyra's control. Preliminary assumptions are subject to change.  
Source: Aldeyra internal estimates based on primary and secondary market research; published literature

DED = Dry eye disease  
AC = Allergic conjunctivitis



November 2019

---

**JEFFERIES LONDON HEALTHCARE CONFERENCE**

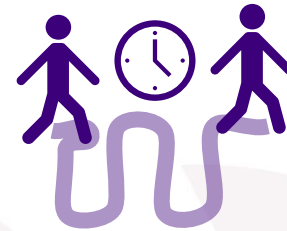
# Ocular Disease Area

- **DRY EYE DISEASE**
- ALLERGIC CONJUNCTIVITIS
- PROLIFERATIVE VITREORETINOPATHY

# Dry Eye Disease is a Persistently Disturbing And Inadequately Treated Condition in Need of New Treatments



34 million or more **adults in the U.S. suffer** from DED.



Current Rx options **may require up to six weeks or longer** to achieve even modest efficacy.



DED **increases with age**, with those over age 50 three times more likely to suffer from DED.

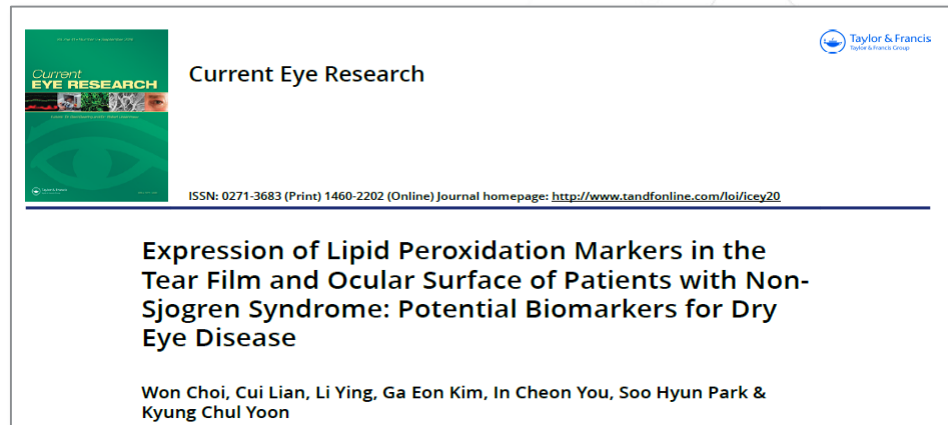


Up to 75% of patients with DED **are not satisfied with current prescription options.**

**The dry eye disease patient population is underserved, and novel therapies are in demand.**

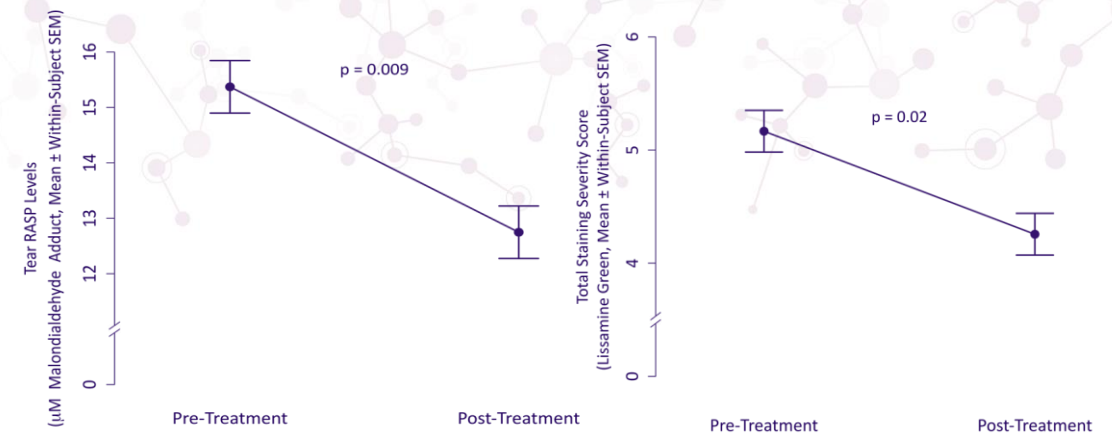
# Reproxalap's Novel Mechanism of Action Has The Potential to Provide Differentiated Activity Versus Existing Treatments

- RASP markers are upregulated in patients with dry eye disease.
- RASP accumulation leads to changes in tear film, triggering an inflammatory response that can lead to chronic inflammation.
- RASP levels correlate with worsening of dry eye disease symptoms and signs (Choi W. et al).



## Reproxalap

In a Phase 2a clinical trial, reproxalap significantly reduced RASP adduct levels.

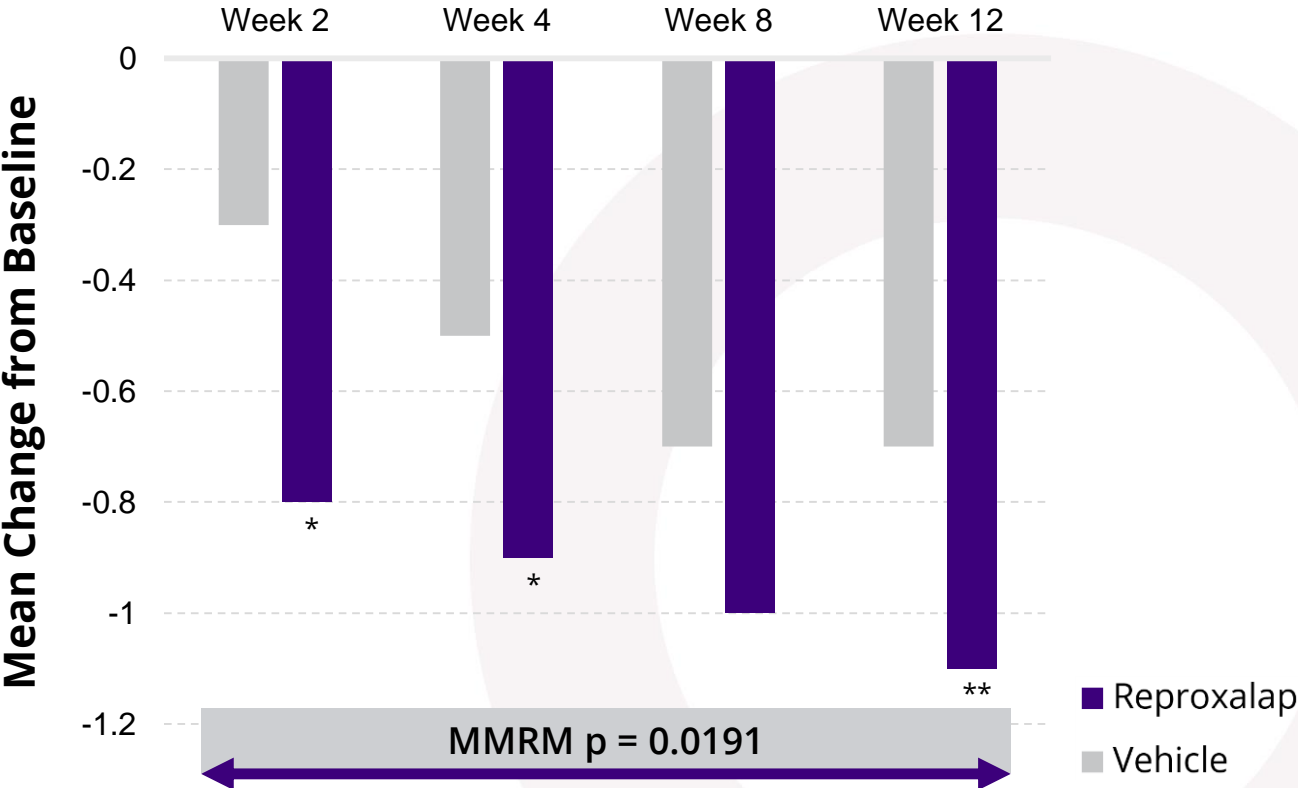


- Statistically significant RASP reduction correlated with statistically significant reductions in ocular staining score and tear osmolarity.
- To our knowledge, reproxalap is the first agent to show biomarker changes correlated with clinical efficacy.

# Phase 3 Dry Eye Disease Symptom and Sign Endpoints Achieved in Phase 2b Clinical Trial†

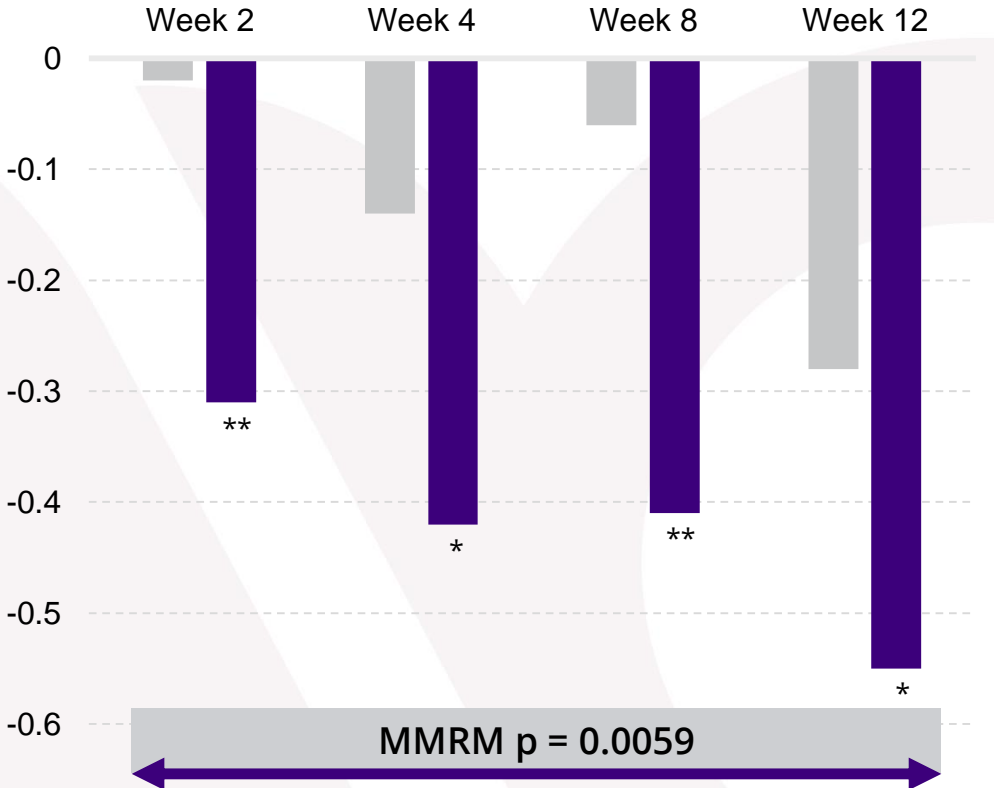
## Primary Symptom Endpoint for Phase 3‡

**OD & 4-Symptom Questionnaire: Dryness (0-5)**  
Baseline Score  $\geq 3$  (N=69 | 69)



## Primary Sign Endpoint for Phase 3‡

**Fluorescein Staining: Nasal (0-4)**  
Baseline Score  $\geq 2$  (N=62 | 56)



Topical ocular reproxalap has been studied in over 1,000 patients thus far with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.  
† The safety and efficacy results of later phase or subsequent clinical trials may not confirm the results of earlier trials.  
‡ RENEW Phase 3 symptom co-endpoints are ocular dryness score VAS (0-100mm) and fluorescein nasal region staining.  
Source: Reproxalap 0.25% DED Phase 2b clinical trial results; p values shown represent reproxalap effect vs vehicle.

\*p<0.05 \*\*p<0.01  
OD = Ocular Discomfort  
MMRM = Mixed Effect Model Repeated Measures (across 12 weeks)

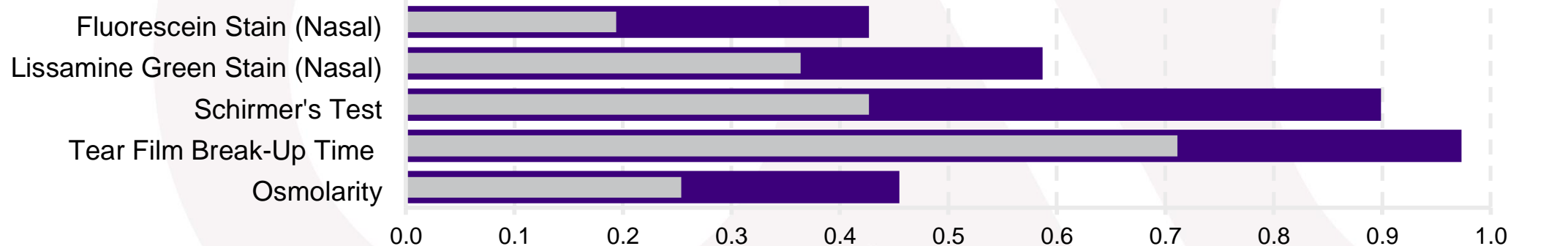
# Broad Drug Activity Across All Measured Dry Eye Disease Symptoms and Signs in Phase 2b Clinical Trial Supports Differentiated Product Profile

## Improvement Effect Size at Week 12

### Dry Eye Disease Symptoms



### Dry Eye Disease Signs



Average improvement effect size across both eyes for Schirmer's Test, Tear Film Break-Up Time, and Osmolarity  
Topical ocular reproxalap has been studied in over 1,000 patients thus far with no observed safety concerns;  
mild instillation site irritation is the most commonly reported adverse event in clinical trials.

SANDE = Symptom Assessment in Dry Eye  
Improvement Effect size = Change from Baseline / Standard Deviation at Baseline  
Source: Reproxalap 0.25% DED Phase 2b clinical trial results

# Adaptive Phase 3 Dry Eye Disease Clinical Program

## Adaptive Phase 3 Program

- ✓ Confirm symptom and sign endpoints from Phase 2b trial
- ✓ Confirm dosing regimen (QID vs. QID to BID taper)
- ✓ Confirm sample size for subsequent trial

## Dry Eye Disease

Clinical Program to NDA Submission

Initiated April 2019



RENEW  
Phase 3 (Part 1)

RENEW  
Phase 3 (Part 2)

Initiated April 2019



Formulation Trial

Confirmatory DED  
Phase 3

DED Safety Study

NDA\*

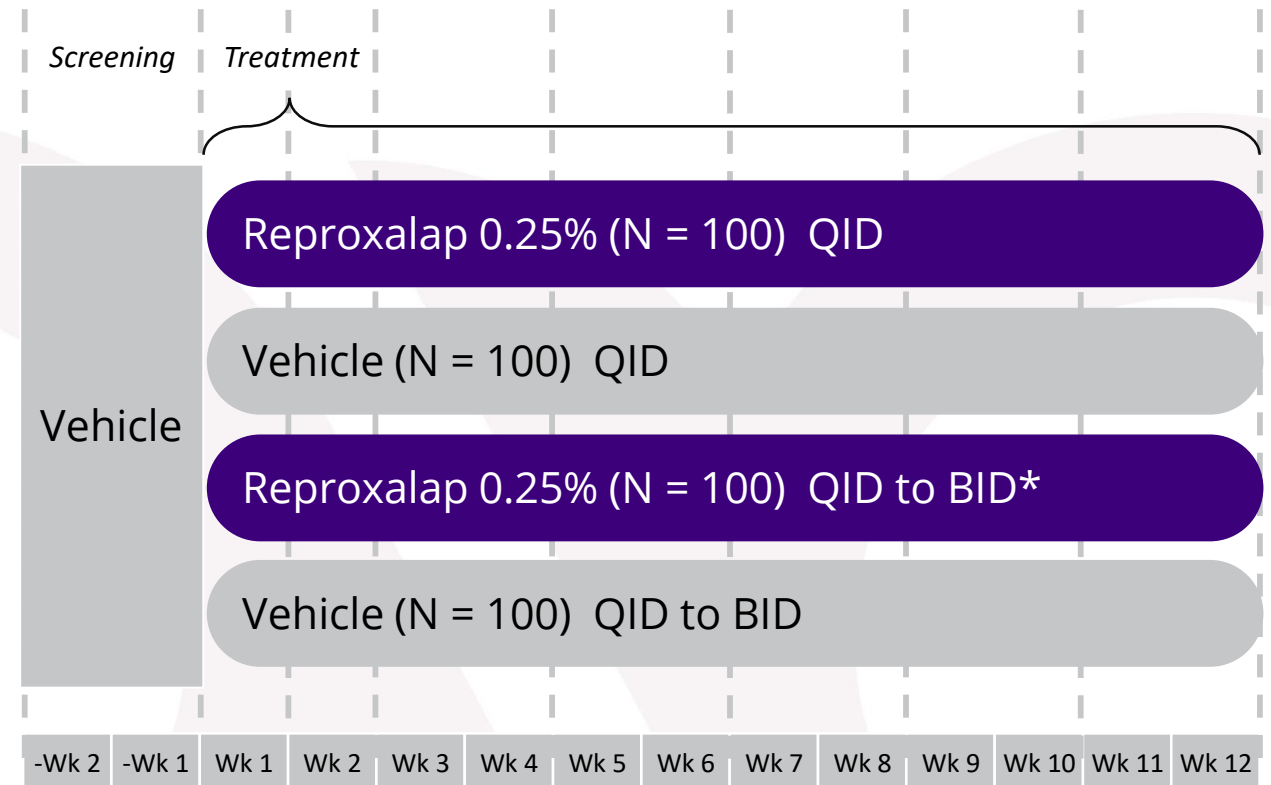
Adaptive design, co-primary endpoints, and innovative analysis strategy confirmed with FDA at EOP2 Meeting

# The RENEW Phase 3 Clinical Trial in Dry Eye Disease

## Part 1 Initiated April 2019

- **RENEW-Part 1 primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle to confirm dosing regimen and sample size for RENEW-Part 2
- **RENEW-Part 1 inclusion/exclusion criteria:**
  - Same as used for Phase 2b
  - Moderate to severe dry eye disease
- **RENEW co-primary endpoints:**
  - Ocular dryness score (0-100mm VAS) and fluorescein nasal region staining
- **RENEW analysis strategy:**
  - Both co-primary endpoints will be assessed using Mixed Model Repeated Measures (MMRM) from week 2 to 12
  - Both co-primary endpoints will be assessed in separate pre-specified patient populations
    - Ocular dryness score (OD4SS): baseline score of  $\geq 3$
    - Fluorescein nasal staining: baseline score  $\geq 2$

### Phase 3 Dry Eye Disease Clinical Trial: Part 1





November 2019

---

**JEFFERIES LONDON HEALTHCARE CONFERENCE**

# Ocular Disease Area

- DRY EYE DISEASE
- **ALLERGIC CONJUNCTIVITIS**
- PROLIFERATIVE VITREORETINOPATHY

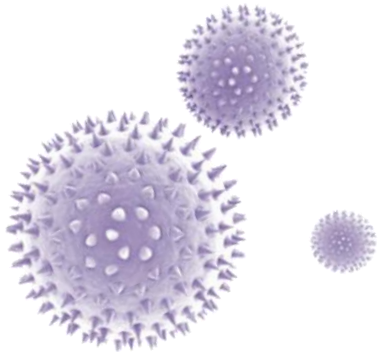
# The Burden of Allergic Conjunctivitis is Rising and Patients Say That Currently Available Treatments Are Inadequate



Allergy seasons are getting **longer and more severe**.



Up to 30 million of allergic conjunctivitis sufferers in the U.S. **do not respond adequately** to or are **dissatisfied with antihistamines**.



Pollen is spreading to **new areas**.

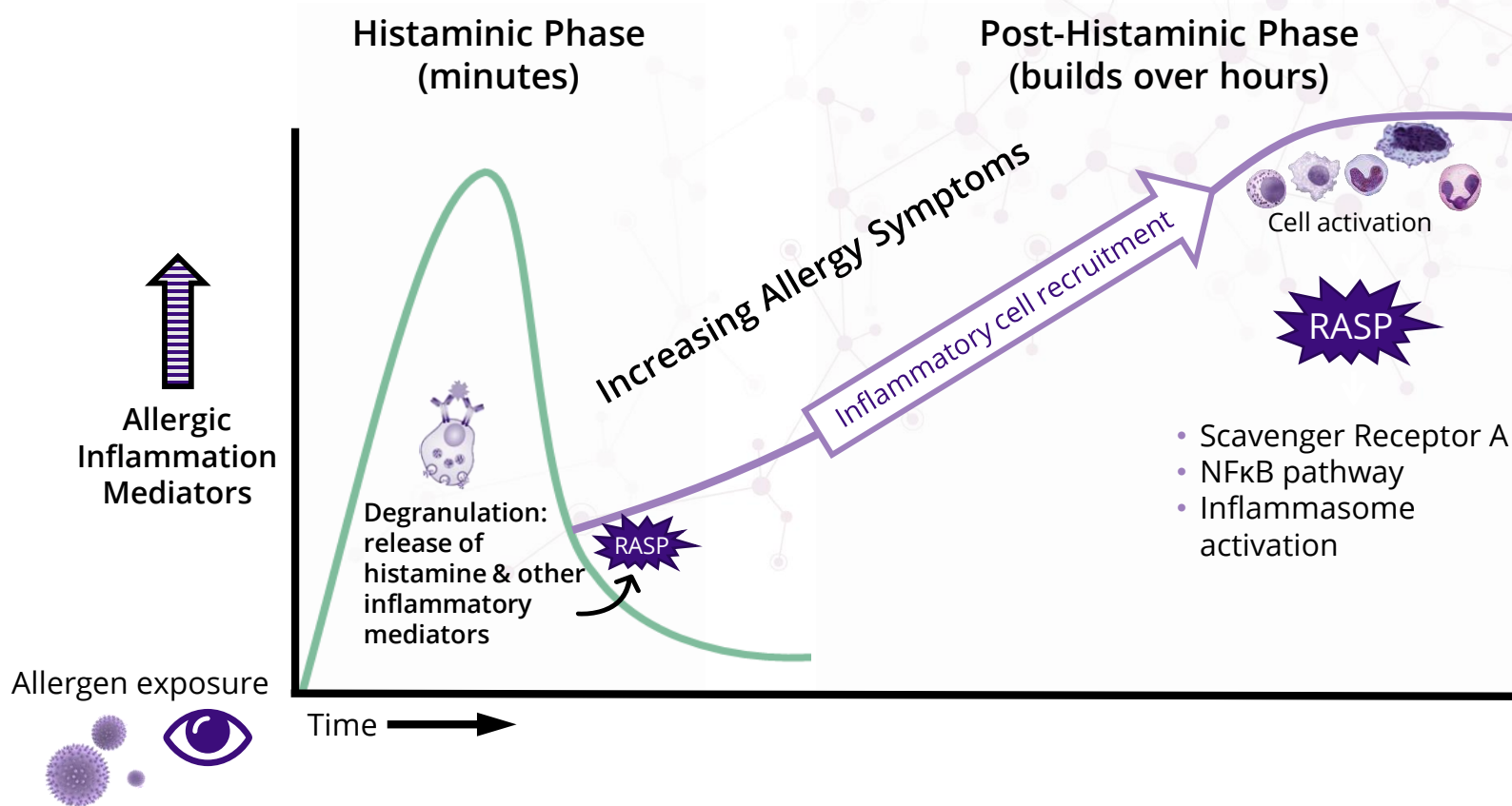


**1 in 5**

Nearly **1 in 5** of allergic conjunctivitis patients are using corticosteroid and/or NSAID eye drops\*.

**The allergic conjunctivitis patient population is underserved, and novel therapies are in demand.**

# Reproxalap's Novel Mechanism of Action Has The Potential to Provide Differentiated Activity Versus Antihistamines

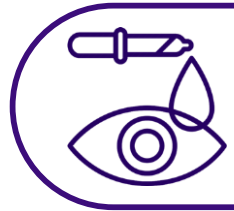


## Reproxalap

- Reproxalap irreversibly inhibits RASP, limiting allergic inflammation.
- Reproxalap has the potential to be uniquely effective in post-histaminic allergy, which affects all allergic conjunctivitis patients.

# Reproxalap Has The Potential to be the First Novel Allergic Conjunctivitis New Drug Application in Decades

## Reproxalap's Phase 3 Program Utilizes Two Allergic Conjunctivitis Clinical Models



### Conjunctival Allergen Challenge

*Investigator administers one drop of allergen mixture on to the eye and records results.*

60 minutes post allergen exposure evaluated

### ALLEVIATE

**Positive Results Announced March 2019**



### Allergen Chamber

*Investigator monitors and assists patients in a controlled allergen chamber.*

3.5 hours of continuous allergen exposure evaluated

### INVIGORATE

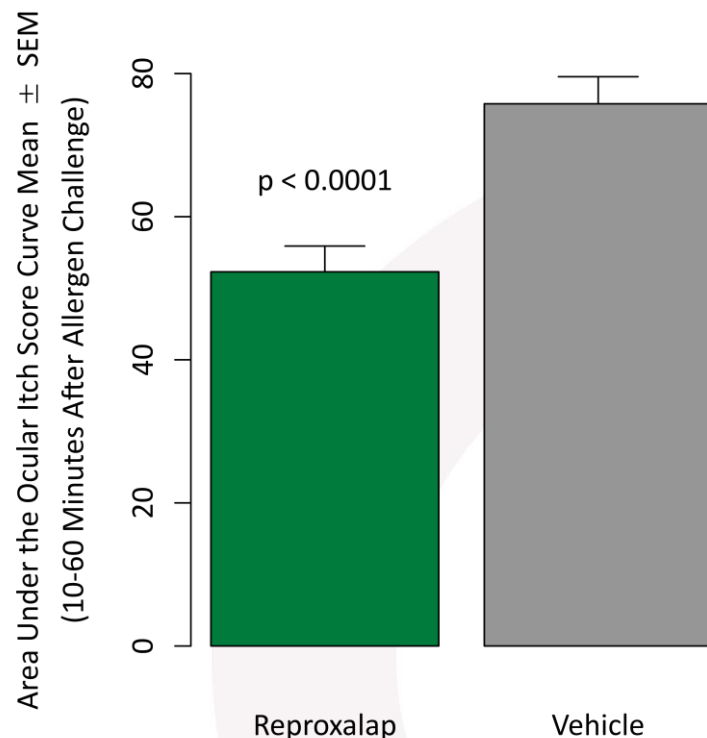
**Expected to initiate H1 2020**

- ✓ Supported by positive allergen chamber trial results

# Reproxalap Demonstrated Greater and More Durable Clinical Responses than Vehicle Group in ALLEVIATE Phase 3 Clinical Trial

## Primary Endpoint

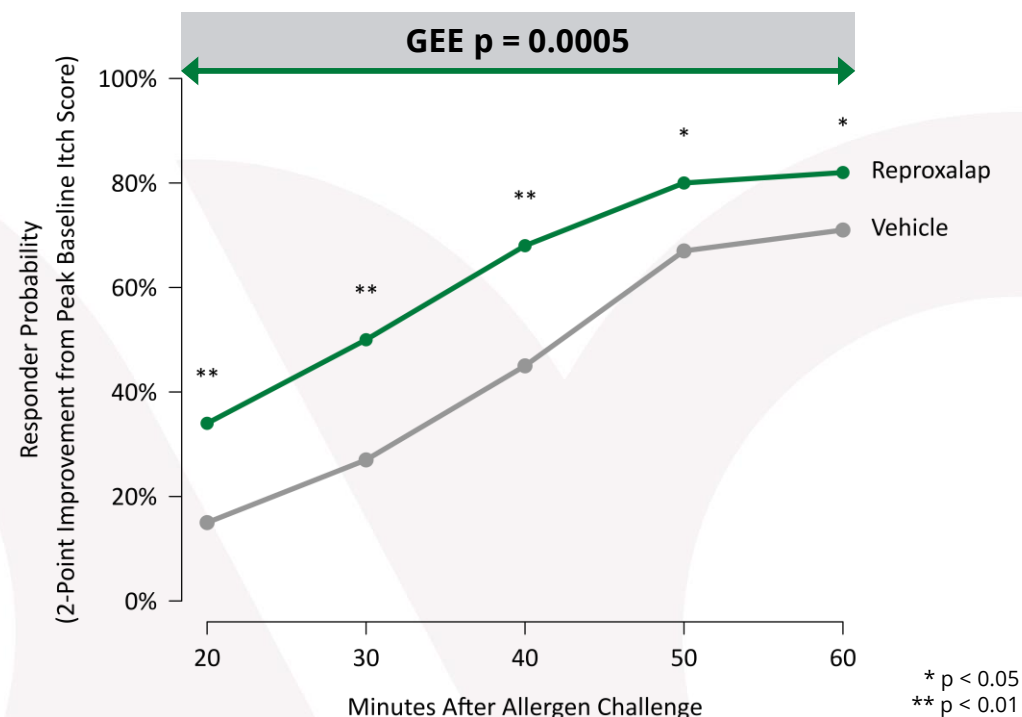
**Area Under the Curve: Ocular Itch Score (0-4) 10 to 60 Minutes After Conjunctival Allergen Challenge**



Improvement in itch score over one hour after allergen exposure statistically greater for reproxalap vs. vehicle

## Key Secondary Endpoint

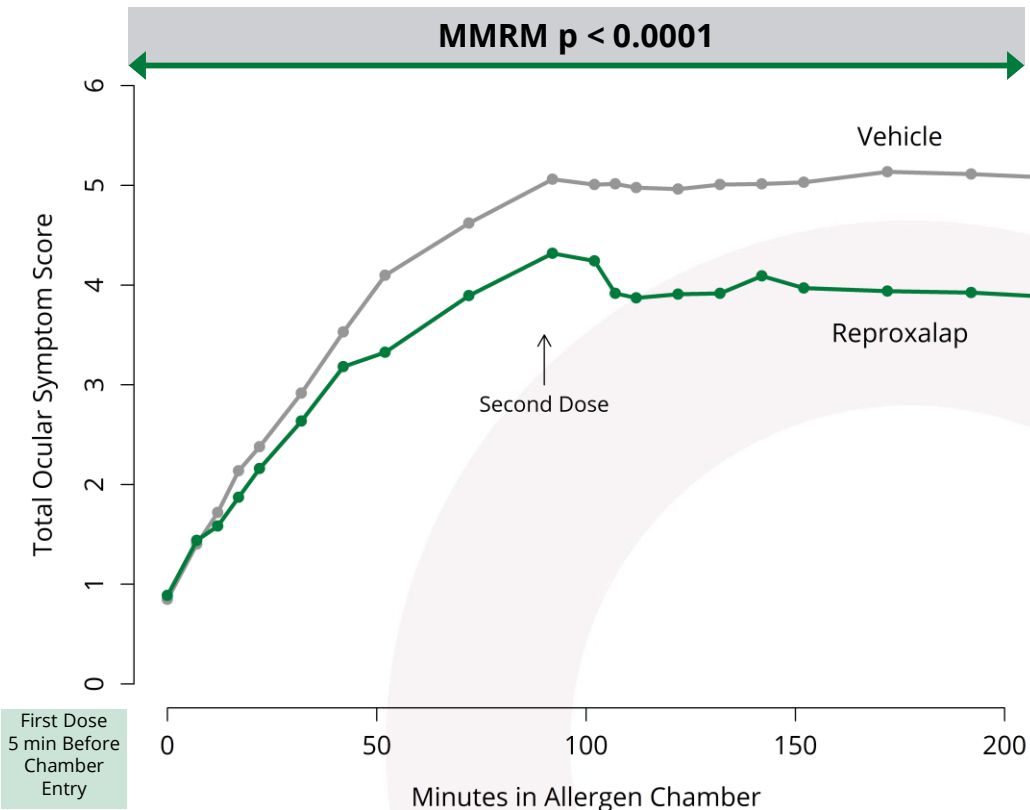
**Probability of Two-Point Response: Ocular Itch Score (0-4) 20 to 60 Minutes After Conjunctival Allergen Challenge**



Clinically significant response rate of reproxalap statistically higher than that of vehicle

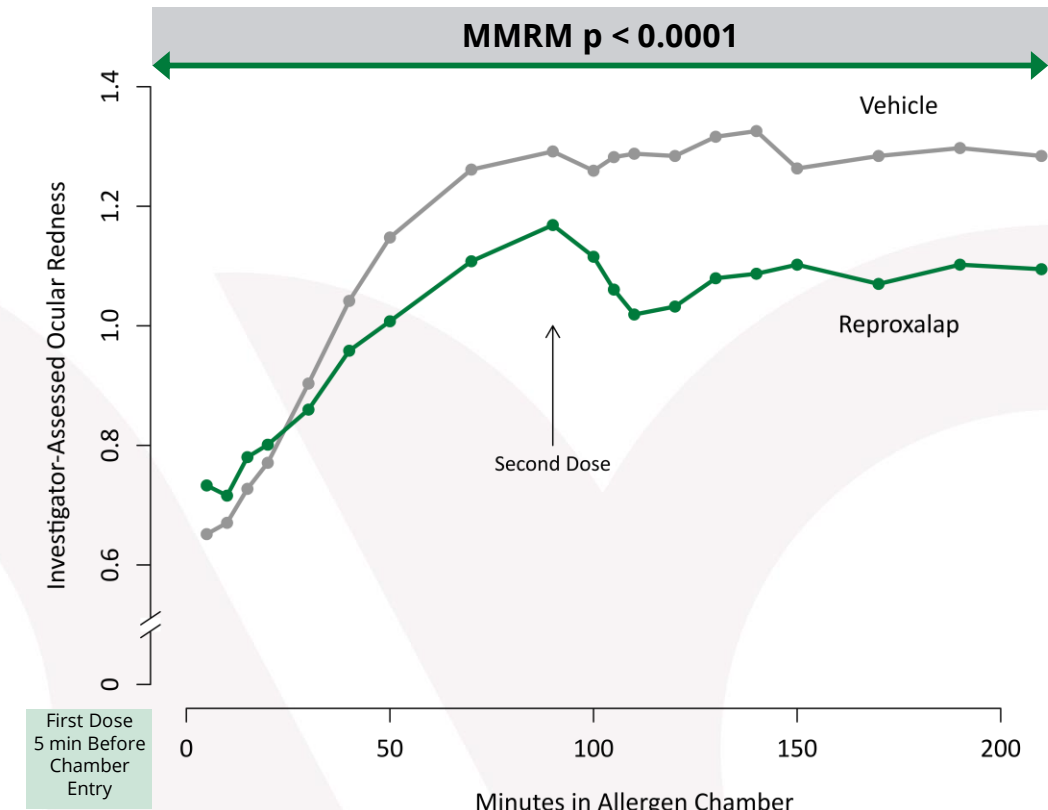
# Reproxalap Demonstrated Greater and More Durable Clinical Responses than Vehicle in Allergen Chamber Clinical Trial

Total Ocular Symptom Score (0-11 scale) During 3.5 Hours of Exposure



Statistically significant reduction in all assessed ocular symptoms and signs (itch, redness, and tearing) for 3.5 hours of continuous exposure to allergen

Ocular Redness Score (0-4) During 3.5 Hours of Exposure

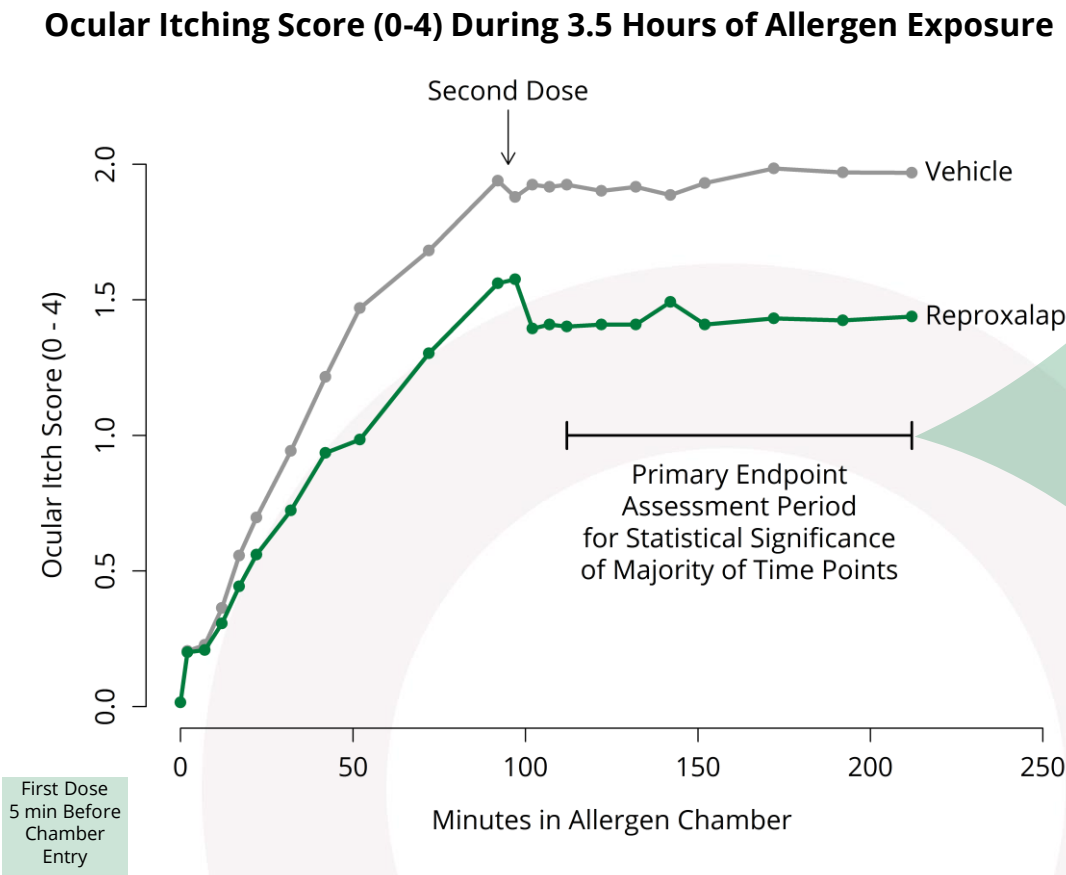


Statistically significant reduction in ocular redness vs. vehicle for 3.5 hours of continuous exposure to allergen



Topical ocular reproxalap has been studied in over 1,000 patients thus far with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.  
Source: Aldeyra Therapeutics methodology development clinical trial (reproxalap 0.25%; ClinicalTrials.gov #NCT03709121); n=66

# Confirmed INVIGORATE Phase 3 Primary Endpoint Achieved in Allergen Chamber Clinical Trial\*



Allergen chamber time point	p value
112	0.0002
122	0.0004
132	0.0002
142	0.0044
152	0.0001
172	<0.0001
192	<0.0001
212	0.0002

All time points from 110 to 210 minutes were statistically significant in Allergen Chamber trial



\*The safety and efficacy results of later phase or subsequent clinical trials may not confirm the results of earlier trials; p-value derived from Mixed effect Model Repeat Measurement (MMRM) time point analyses.  
Source: Aldeyra Therapeutics allergen chamber clinical trial – reproxalap 0.25% (ClinicalTrials.gov #NCT03709121); n=66

# Allergic Conjunctivitis Phase 3 Clinical Program

## Allergic Conjunctivitis

Clinical Program to NDA Submission

Results Announced  
March 2019

ALLEVIATE Phase 3 (CAC)

Agreement on INVIGORATE  
Phase 3 Design Reached  
October 2019

Type C  
FDA Meeting

Additional Phase 3 Testing

AC Safety Study

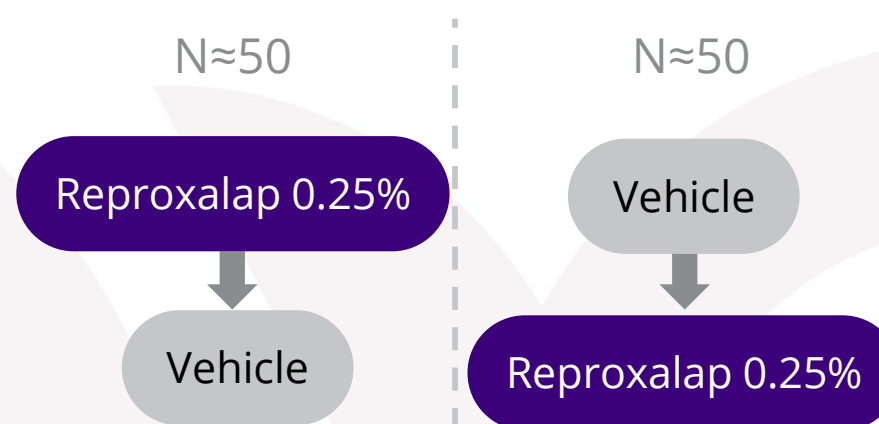
NDA\*

# The INVIGORATE Phase 3 Clinical Trial Design

- **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:**
  - Same as prior allergen chamber trial
- **Dosing schedule and chamber exposure:**
  - Same as prior allergen chamber trial

Expected to initiate H1 2020

## Two-Way Randomized Crossover





November 2019

---

**JEFFERIES LONDON HEALTHCARE CONFERENCE**

# Ocular Disease Area

- DRY EYE DISEASE
- ALLERGIC CONJUNCTIVITIS
- **PROLIFERATIVE VITREORETINOPATHY**

# ADX-2191 Represents a New Approach For PVR

## – A Rare Sight-Threatening Retinal Disease With No Approved Therapy

### 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.



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



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



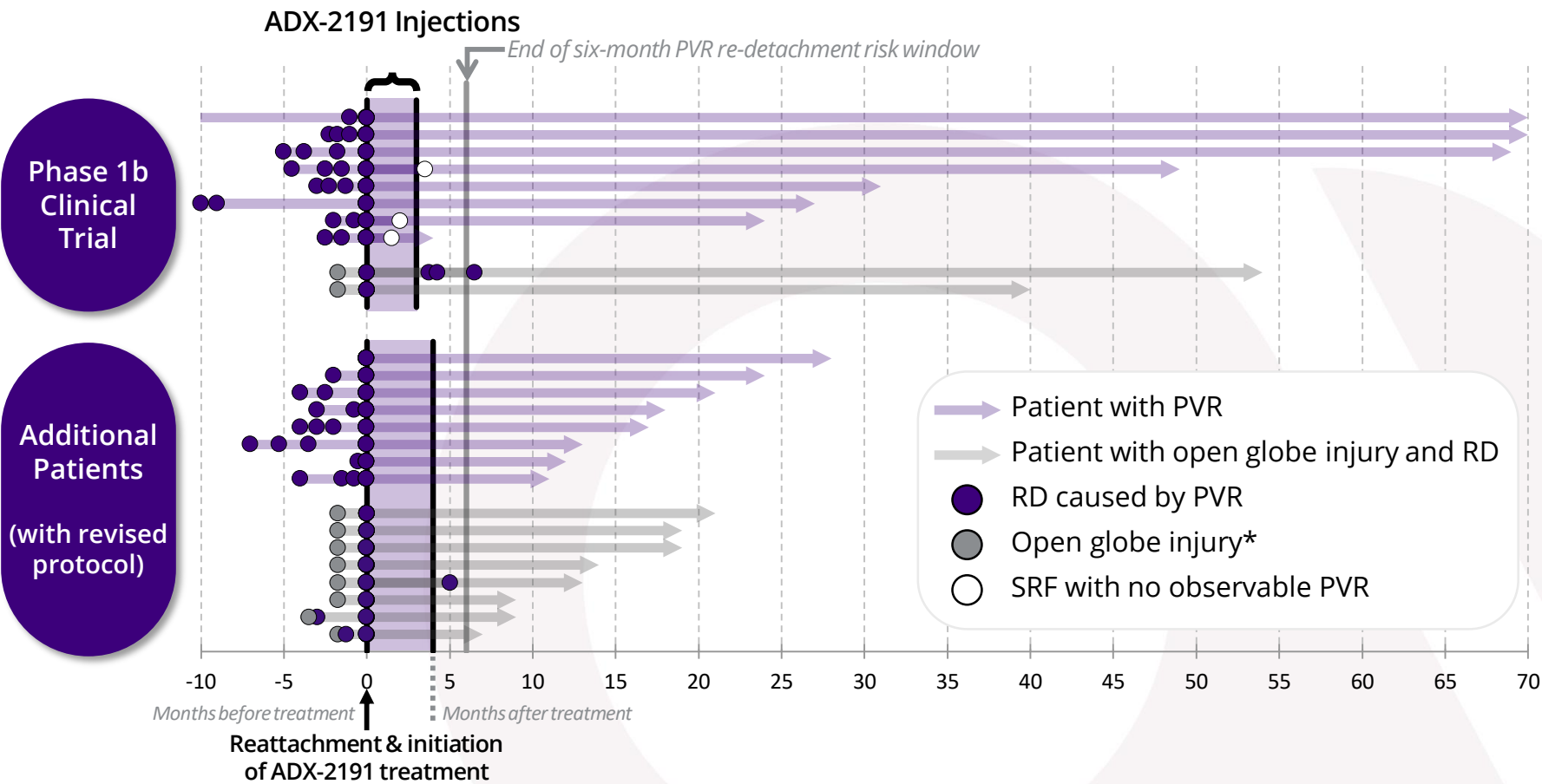
**Repeat surgery**, which can lead to **vision loss**, is currently the only possible course of action.

### ADX-2191

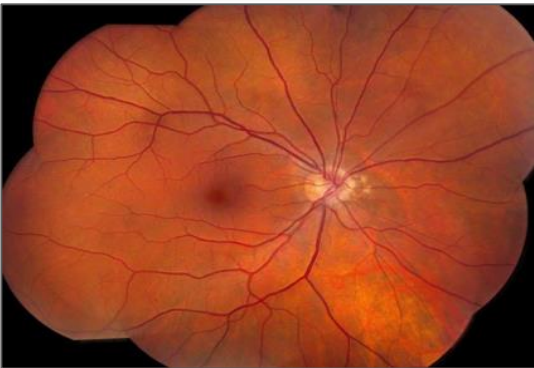
- A **novel approach and potential therapeutic breakthrough** in PVR treatment
- **Granted U.S. orphan designation** for the prevention of PVR
- **Granted FDA fast track designation** for the prevention of PVR
- **Tolerability and reattachment success** during study period **demonstrated in Phase 1b** open-label investigator sponsored clinical trial
- GUARD adaptive Phase 3 clinical trial **expected to initiate Q4 2019**

# ADX-2191 Reduced Recurrent Retinal Detachment in Investigator Sponsored Phase 1b Clinical Trial and in Additional In-Practice Use

## Retinal Detachments Over Time by Patient



### Normal Retina



### Retinal Detachment Due to PVR



\*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)

# 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:**

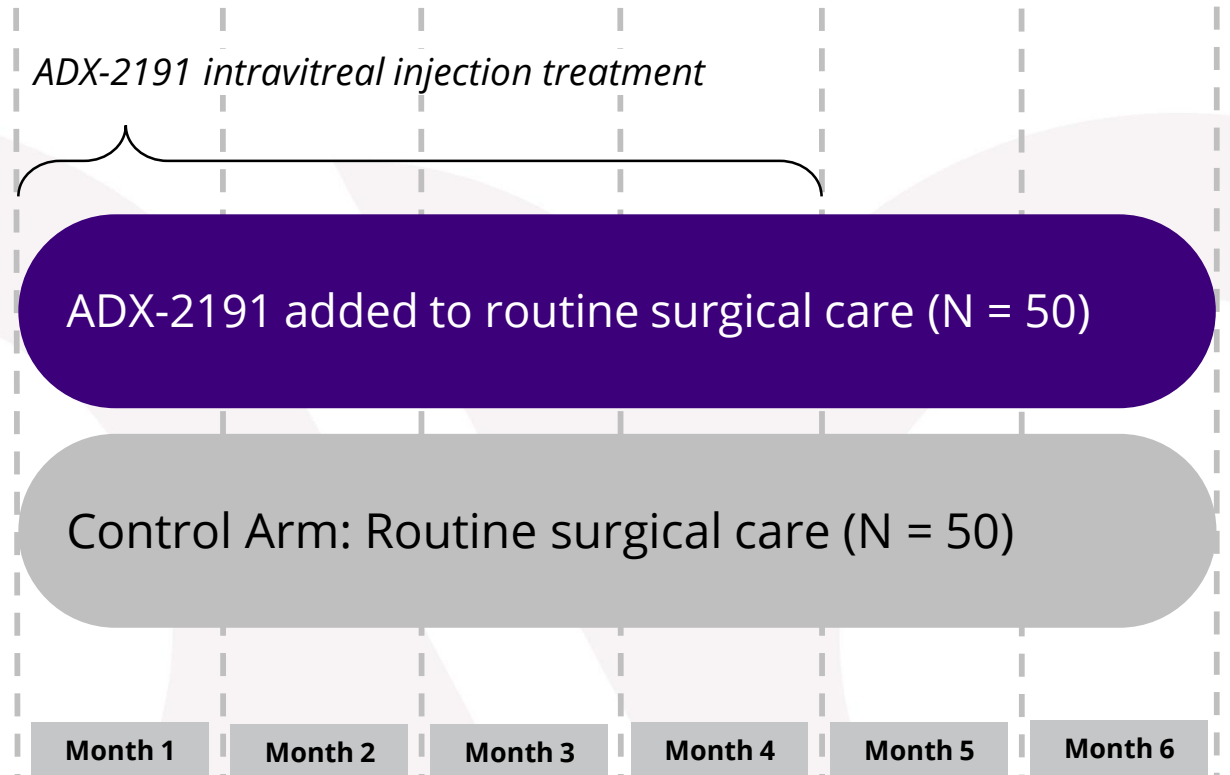
- At surgery, weekly (x8), and then every other week (x4) intravitreal ADX-2191 injections

- **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

Expected to initiate Q4 2019

### Adaptive Phase 3 PVR Clinical Trial Design: Part 1





November 2019

---

**JEFFERIES LONDON HEALTHCARE CONFERENCE**

# Upcoming and Recently Achieved Development Milestones

# Upcoming and Recently Achieved Development Milestones:<sup>\*</sup>

## Novel Approaches to Address Immune-Mediated Disease

○ = Ocular Diseases  
○ = Systemic Diseases

- ✓ Reproxalap allergic conjunctivitis design for **INVIGORATE Phase 3 confirmed October 2019**
- ADX-2191 proliferative vitreoretinopathy **GUARD Phase 3 - Part 1 clinical trial initiation Q4 2019**
- ADX-1612 post-transplant lymphoproliferative disorder **Phase 2 clinical trial initiation H2 2019**
- Reproxalap dry eye disease **RENEW Phase 3 - Part 1 completion Q4 2019**
- NEW ○ Reproxalap allergic conjunctivitis **INVIGORATE Phase 3 initiation H1 2020**

- ✓ ADX-629 systemic **Phase 1 clinical trial initiation H2 2019**
- ✓ Reproxalap Sjögren-Larsson Syndrome **RESET Phase 3 - Part 1 completion Q2 2019**
- ✓ **Positive** reproxalap allergic conjunctivitis **allergen chamber trial top-line results**
- ✓ Reproxalap dry eye disease **RENEW Phase 3 - Part 1 clinical trial initiation April 2019**
- ✓ **Positive** reproxalap allergic conjunctivitis **ALLEVIATE Phase 3 trial results March 2019**



# Innovating Transformative Therapies