



September 2019

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**CORPORATE REVIEW**

# Innovating Transformative Therapies

Nasdaq: ALDX  
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# Our Mission

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

~7%

Of Western Society

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

Unmet Needs

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

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.

# 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	[RASPI]	Dry Eye Disease					Phase 3-Part 1 completion Q4 2019
			Allergic Conjunctivitis					
	ADX-2191	[DHFR]	Proliferative Vitreoretinopathy					Phase 3-Part 1 initiation Q4 2019
	ADX-103/10X	[RASPI]	Retinal Disease					Phase 1/2 initiation 2020
	Undisclosed		Ocular Inflammation	Research Collaboration (undisclosed)				
Systemic Diseases	Reproxalap	[RASPI]	Sjögren-Larsson Syndrome					
	ADX-1612	[CHP]	PTLD					Phase 2 initiation H2 2019
			Mesothelioma	Investigator-Sponsored Trial				
			Ovarian Cancer	Investigator-Sponsored Trial				
	ADX-629	[RASPI]	Autoimmune / Metabolic Disease					
	ADX-1615	[CHP]	Autoimmune Disease / Cancer					
	Undisclosed	[RASPI]	Systemic Inflammatory Disease	Research Collaboration janssen				

# Our Lead Programs May Offer Potential Benefits Over Standard of Care

Late Stage Programs <i>Ocular Diseases</i>	Current Standard of Care	Pricing Benchmarks <sup>†</sup>	Drug Candidate and Dev. Stage	Potential Competitive Advantages <sup>†</sup>
Dry Eye Disease	Xiidra®, Restasis®	\$500-550 per month (dry eye disease pricing)	Reproxalap: Phase 3	Rapid onset, broad activity, reduction in itch
Allergic Conjunctivitis	Antihistamines		Reproxalap: Phase 3	Non-drying, durable activity; Responder superiority vs. vehicle
Proliferative Vitreoretinopathy	None (repeat surgeries)	\$30,000 per course (avg. cost of surgeries)	ADX-2191: Phase 3	Clinically demonstrated activity; Currently no FDA- or EMA-approved therapy
<i>Systemic Diseases</i>				
Sjögren-Larsson Syndrome	None (manage symptoms)	\$200,000 - \$400,000 per year	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



# Our Lead Programs Represent Compelling Commercial Opportunities

## Late Stage Programs

### Ocular Diseases

#### Dry Eye Disease

Estimated  
U.S. Population<sup>†</sup>

20 million DED

Up to 10 million with  
DED & AC

30 million AC

U.S. Healthcare  
Providers

~18,000  
ophthalmologists  
and ~40,000  
optometrists

Competitive  
Value Proposition

Potential benefits over  
current therapies, which  
do not work well  
for many patients

Infrastructure  
Requirement<sup>‡</sup>

Medium sized  
sales force for national reach

#### Allergic Conjunctivitis

#### Proliferative Vitreoretinopathy

4,000

Retina specialists  
at targeted centers

Potential first and only  
Rx treatment

Small specialized operation

### Systemic Diseases

#### Sjögren-Larsson Syndrome

1,000

Geneticists and ped.  
neurologists

Potential first and only  
Rx treatment

Small specialized operation

<sup>†</sup>Pending clinical data, regulatory discussions, payor negotiations, competition, potential legislative changes, and other factors, which may not be in Aldeyra's control.

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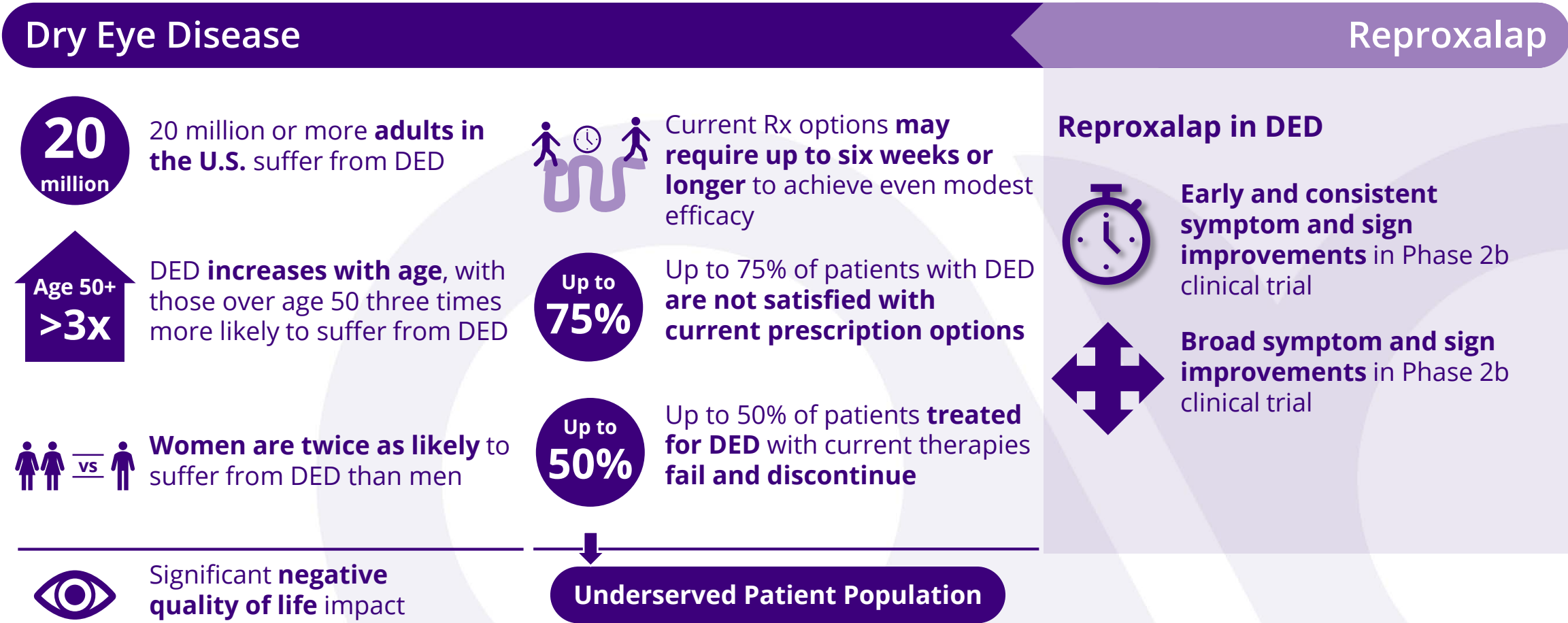
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## **CORPORATE REVIEW**

# Ocular Disease Area

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

# Dry Eye Disease: A Persistently Disturbing Condition Inadequately Treated with Currently Available Therapy

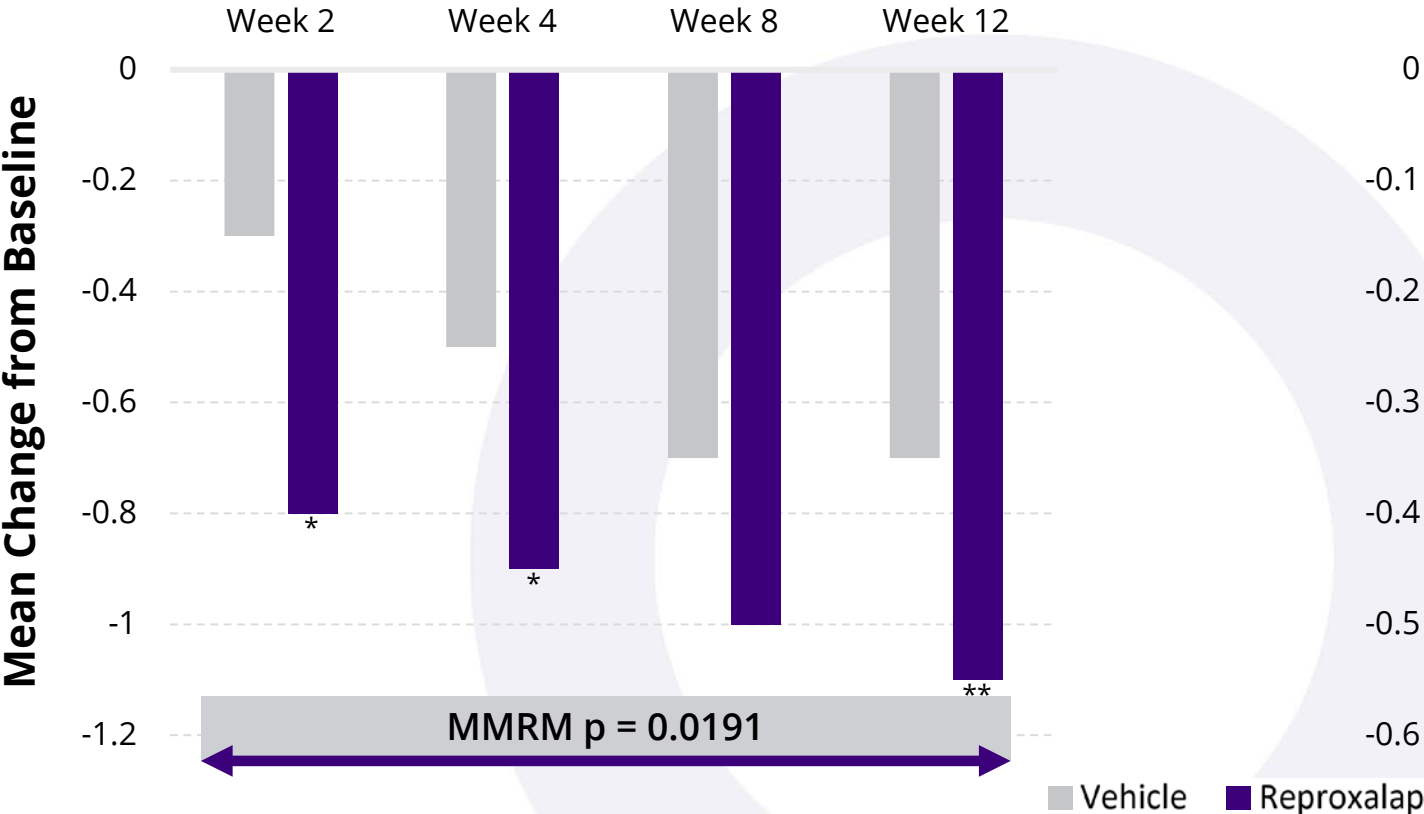




# Phase 3 Dry Eye Disease Symptom and Sign Endpoints Achieved in Phase 2b Clinical Trial

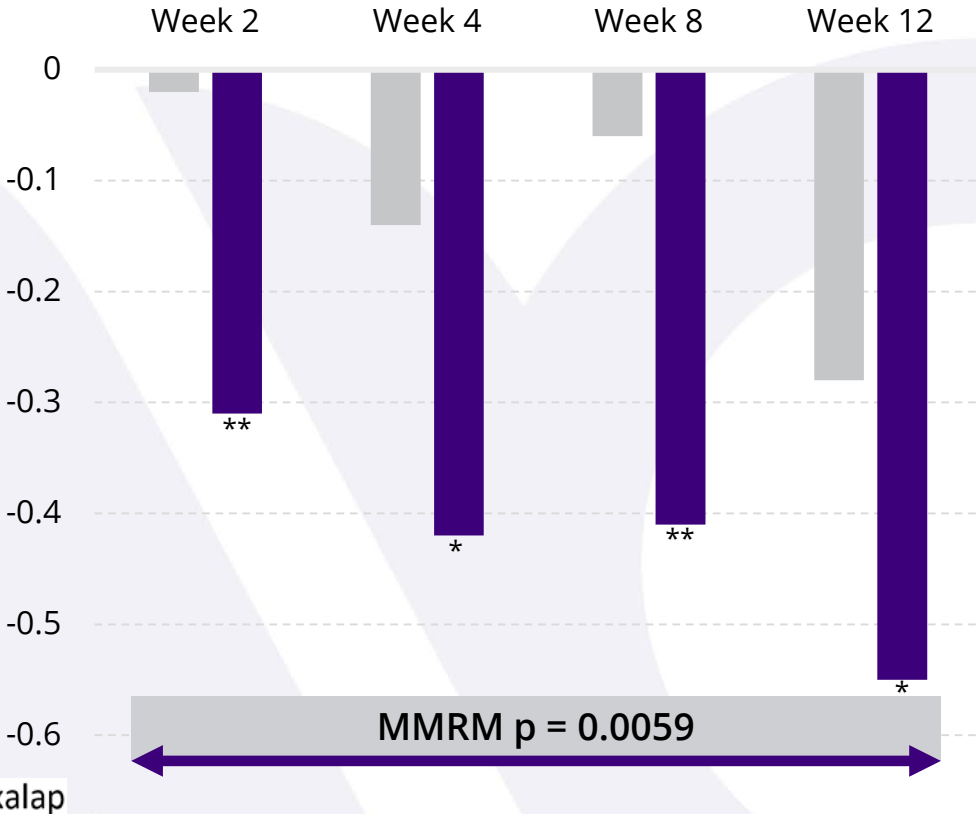
## Primary Symptom Endpoint for Phase 3

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



## Primary Sign Endpoint for Phase 3

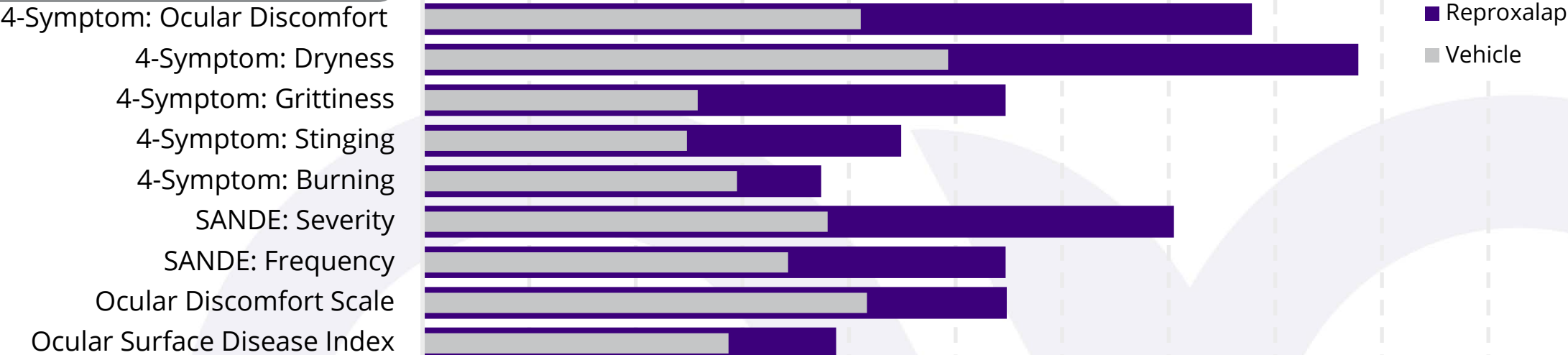
**Fluorescein Staining: Nasal (0-4)**  
Baseline Score  $\geq 2$  (N=62 | 56)



# 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



0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0



SANDE = Symptom Assessment in Dry Eye  
Average improvement effect size across both eyes for tear quality and tear quantity measures  
(Schirmer's Test, Tear Film Break-Up Time, and Osmolarity)

Improvement Effect size = Change from Baseline / Standard Deviation at Baseline  
Source: Reproxalap DED Phase 2b clinical trial results (reproxalap 0.25%)

# 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)

Confirmatory DED  
Phase 3

NDA\*

Initiated April 2019

Formulation Trial

DED Safety Study

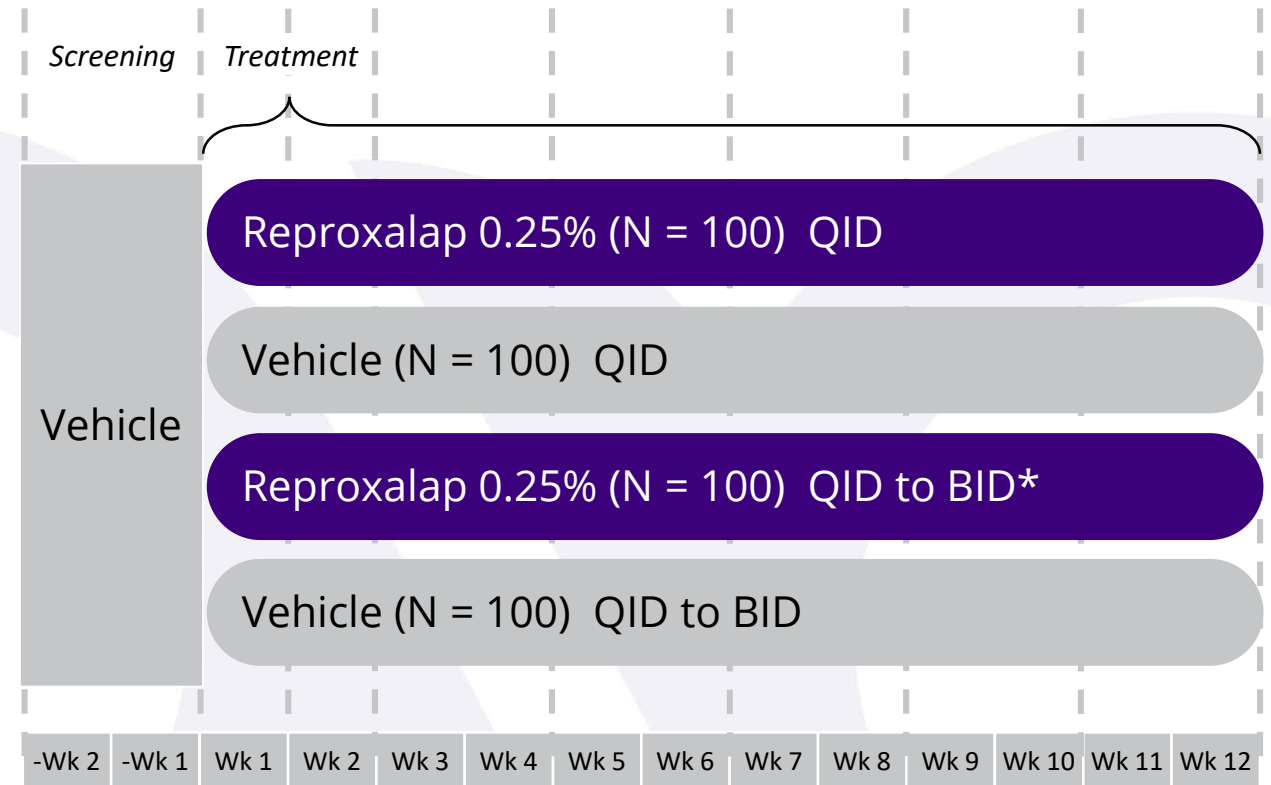
Adaptive design, co-primary endpoints, and innovative analysis strategy confirmed with FDA at EOP2 Meeting

# The RENEW Phase 3 Clinical Trial in Dry Eye Disease

## Part 1 Initiated April 2019

- **Primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle to confirm dosing regimen and sample size for Part 2
- **Inclusion/exclusion criteria:**
  - Same as used for Phase 2b
  - Moderate to severe dry eye disease
- **Co-primary endpoints:**
  - Ocular dryness score (0-100mm VAS) and fluorescein nasal region staining
- **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





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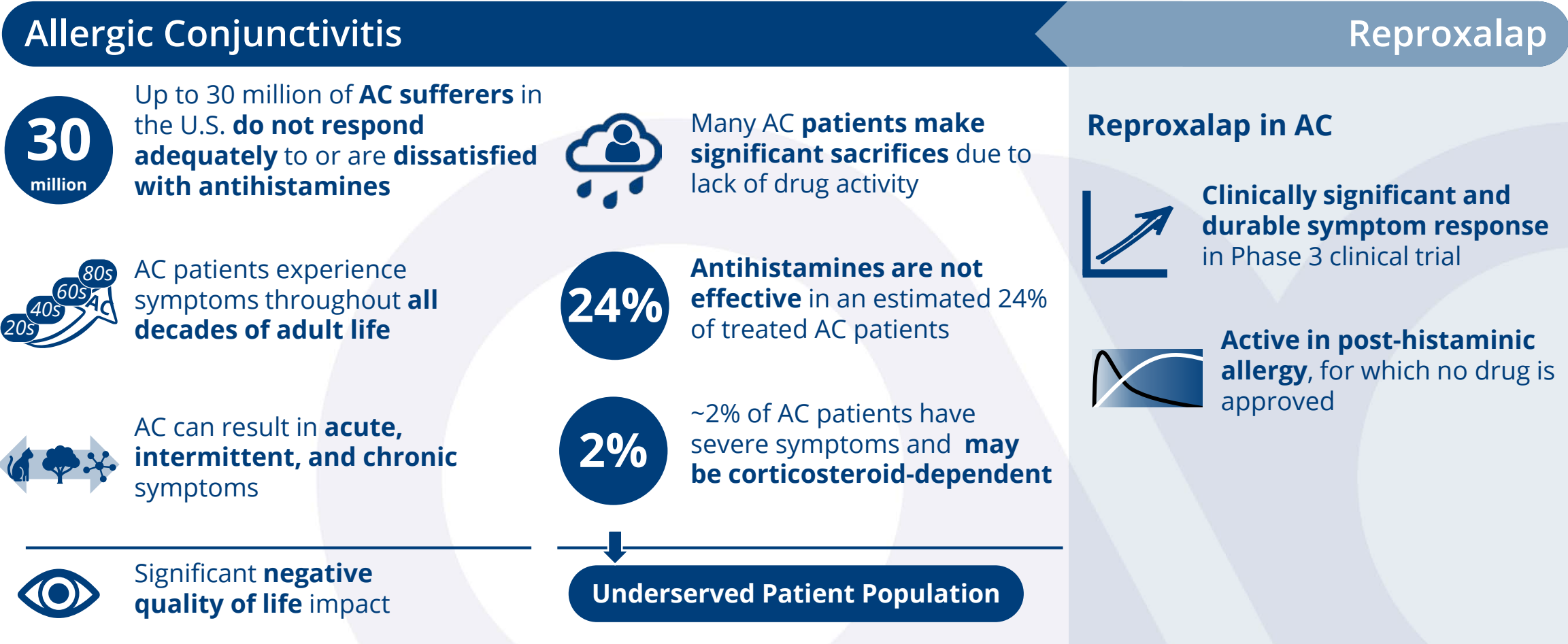
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## **CORPORATE REVIEW**

# Ocular Disease Area

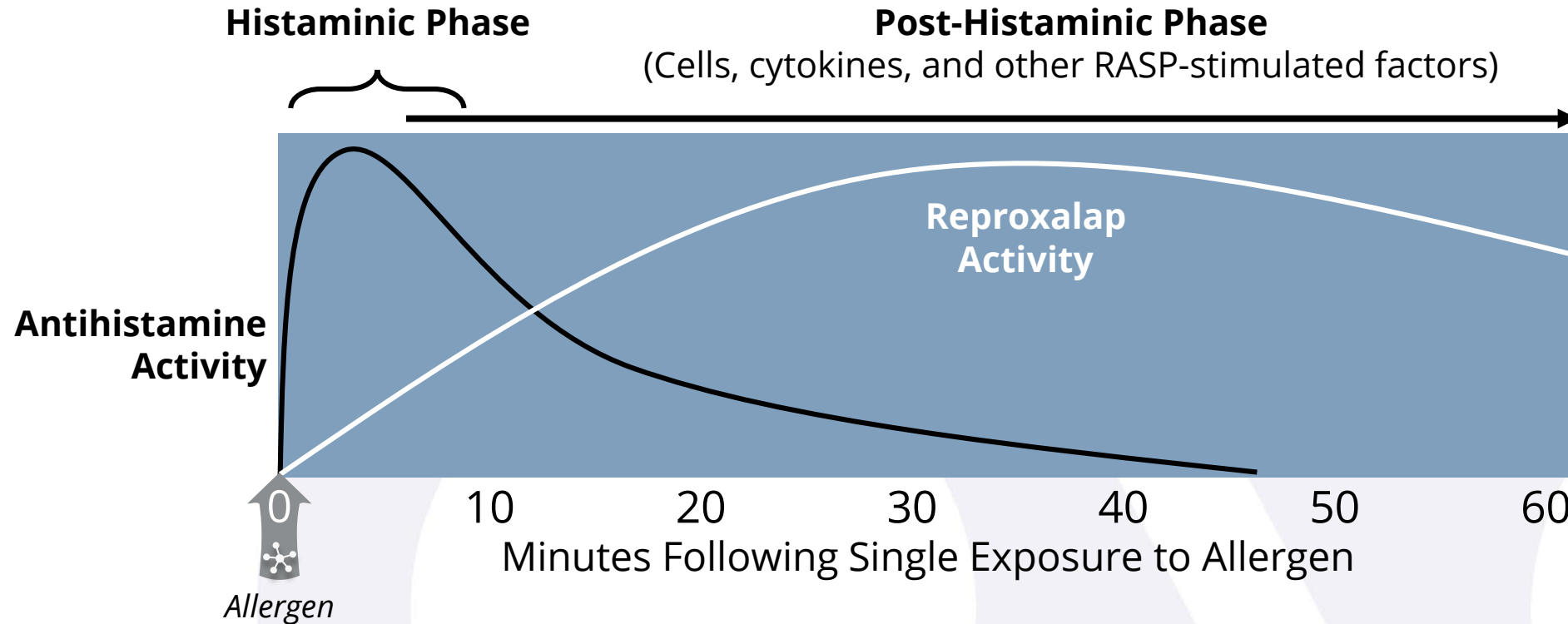
- DRY EYE DISEASE
- **ALLERGIC CONJUNCTIVITIS**
- PROLIFERATIVE VITREORETINOPATHY

# Allergic Conjunctivitis: A Common Disease with Unmet Medical Need





# Reproxalap's Novel Mechanism of Action has the Potential to Provide Differentiated Activity Versus Antihistamines

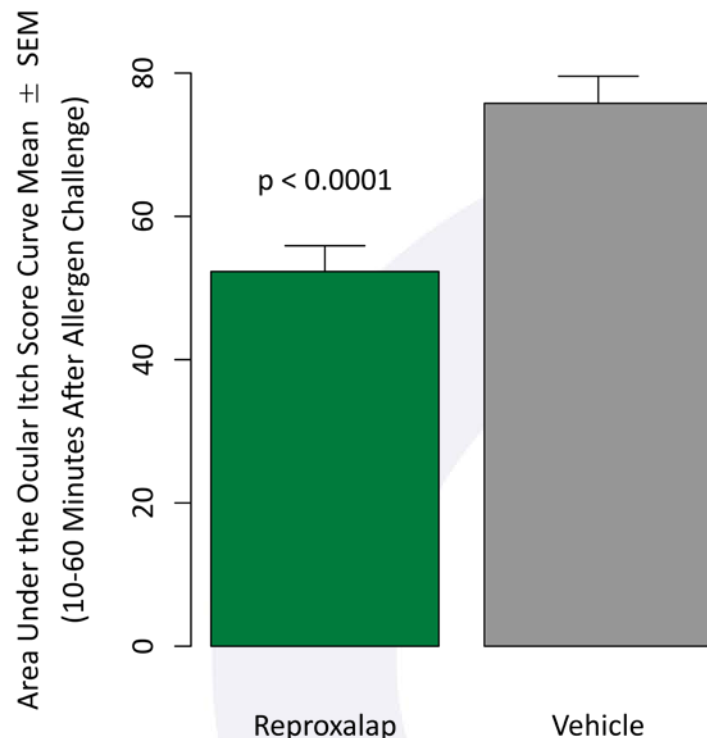


Reproxalap has the potential to be uniquely effective in post-histaminic allergy, which affects all allergic conjunctivitis patients

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

## Primary Endpoint

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

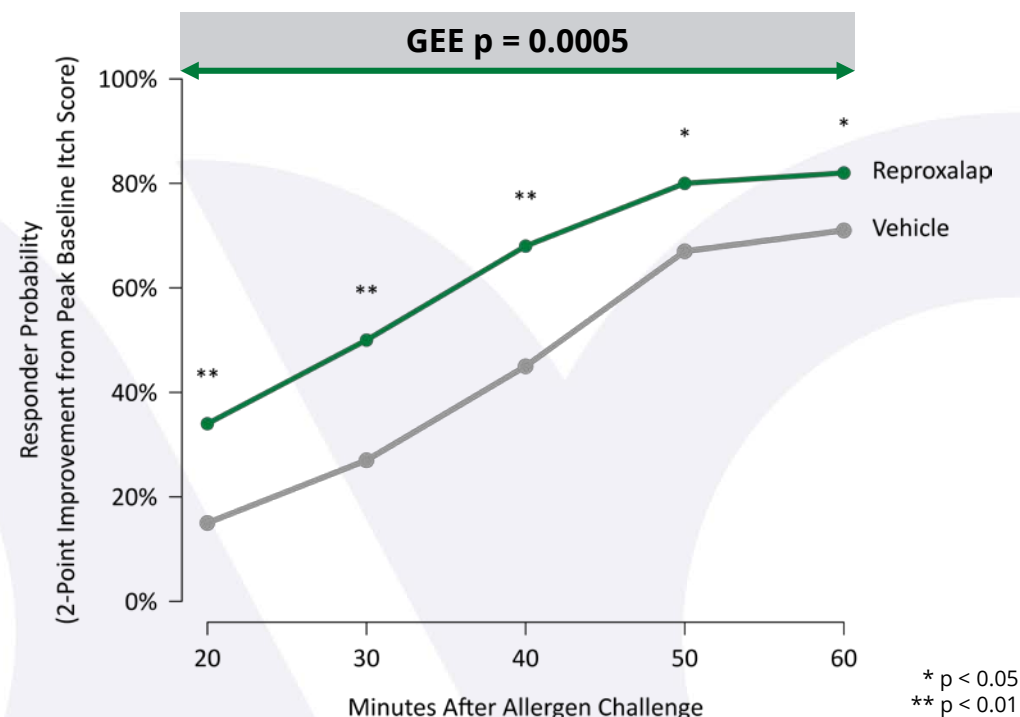


Improvement in itch score over one hour after allergen exposure statistically greater for reproxalap vs. vehicle

SEM = Standard error of the mean

## Key Secondary Endpoint

Probability of Two-Point Response: Ocular Itch Score (0-4)

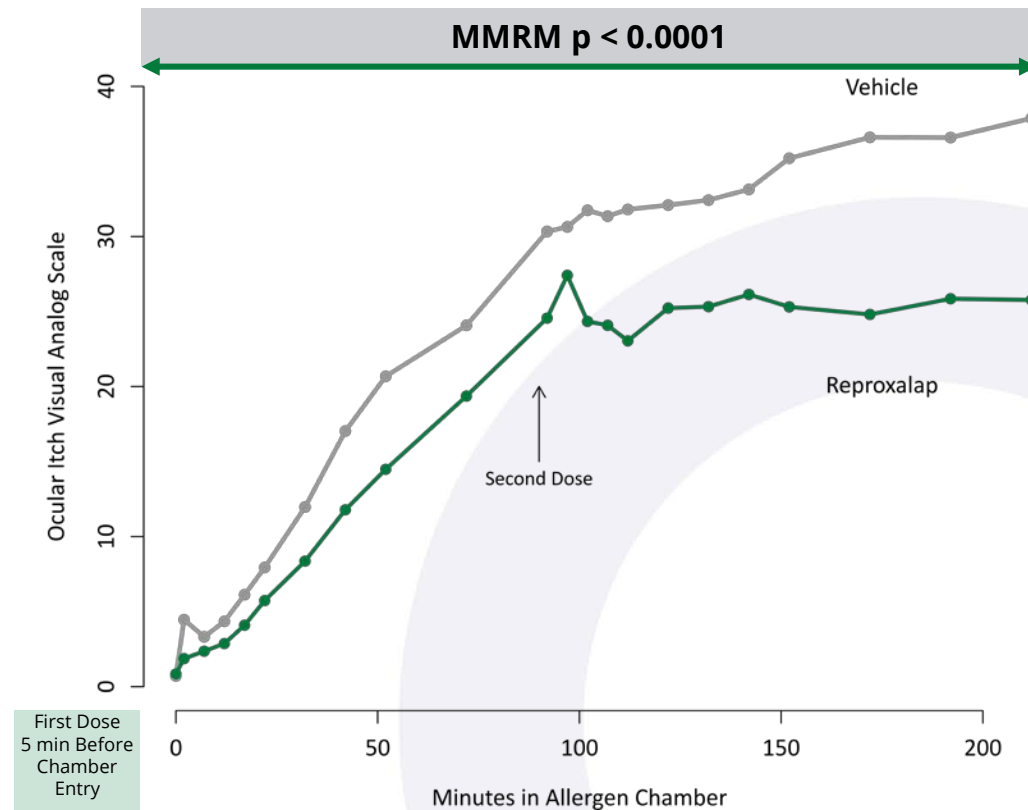


Clinically significant response rate of reproxalap statistically higher than that of vehicle

GEE = Generalized estimating equation analysis

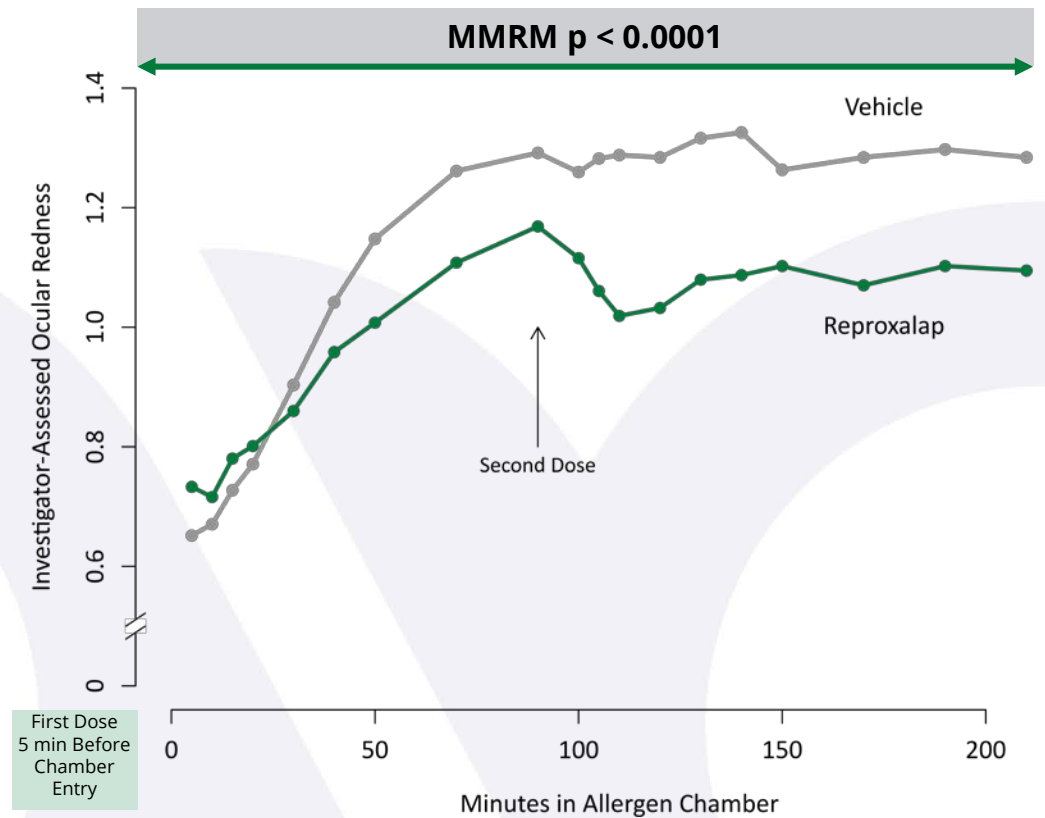
# Reproxalap Treatment Led to Durable Reduction in Ocular Itch and Redness in Allergen Chamber Clinical Trial

Ocular Itch Score (0-100) During 3.5 Hours of Allergen Exposure



Statistically significant reduction in ocular itch vs. vehicle for more than three hours of exposure to allergen

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



Statistically significant reduction in ocular redness vs. vehicle for more than three hours of exposure to allergen

# Allergic Conjunctivitis Phase 3 Clinical Program

## Allergic Conjunctivitis

Clinical Program to NDA Submission

**Results Announced  
March 2019**

ALLEVIATE Phase 3 (CAC)

Type C  
FDA Meeting

Additional Phase 3 Testing

**NDA\***

Methods Development Trials  
(Environment / Chamber)

AC Safety Study

**Results Announced  
June 2019**



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## **CORPORATE REVIEW**

# Ocular Disease Area

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

# Proliferative Vitreoretinopathy: A Rare Sight-Threatening Retinal Disease With No Approved Therapy

## Proliferative vitreoretinopathy

ADX-2191

**4,000**  
U.S.

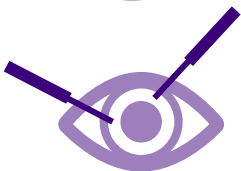
PVR is a **rare disease**, with ~4,000 patients per year in the U.S. and nearly twice as many in Europe and Japan.



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



**No FDA- or EMA-approved therapy**



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

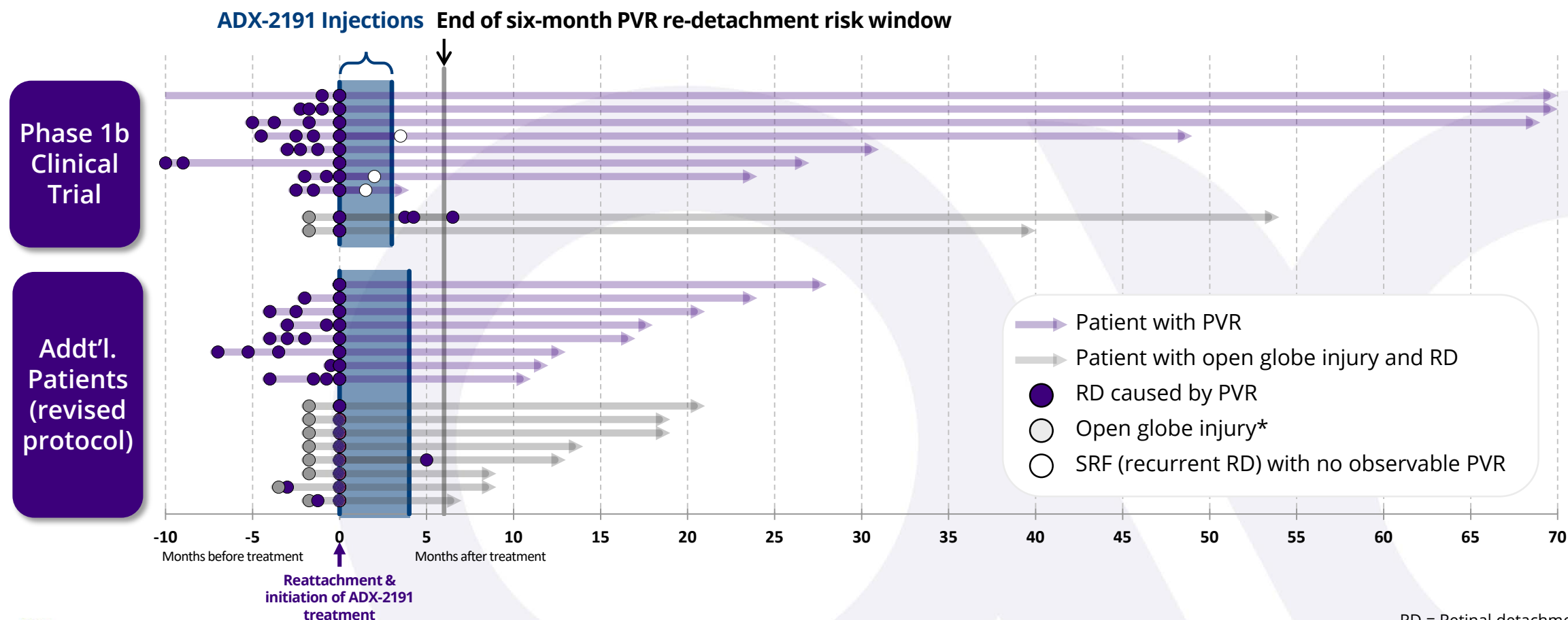
## ADX-2191

- A **novel approach and potential therapeutic breakthrough** in PVR treatment
- **Granted U.S. orphan designation** for the prevention of PVR
- **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

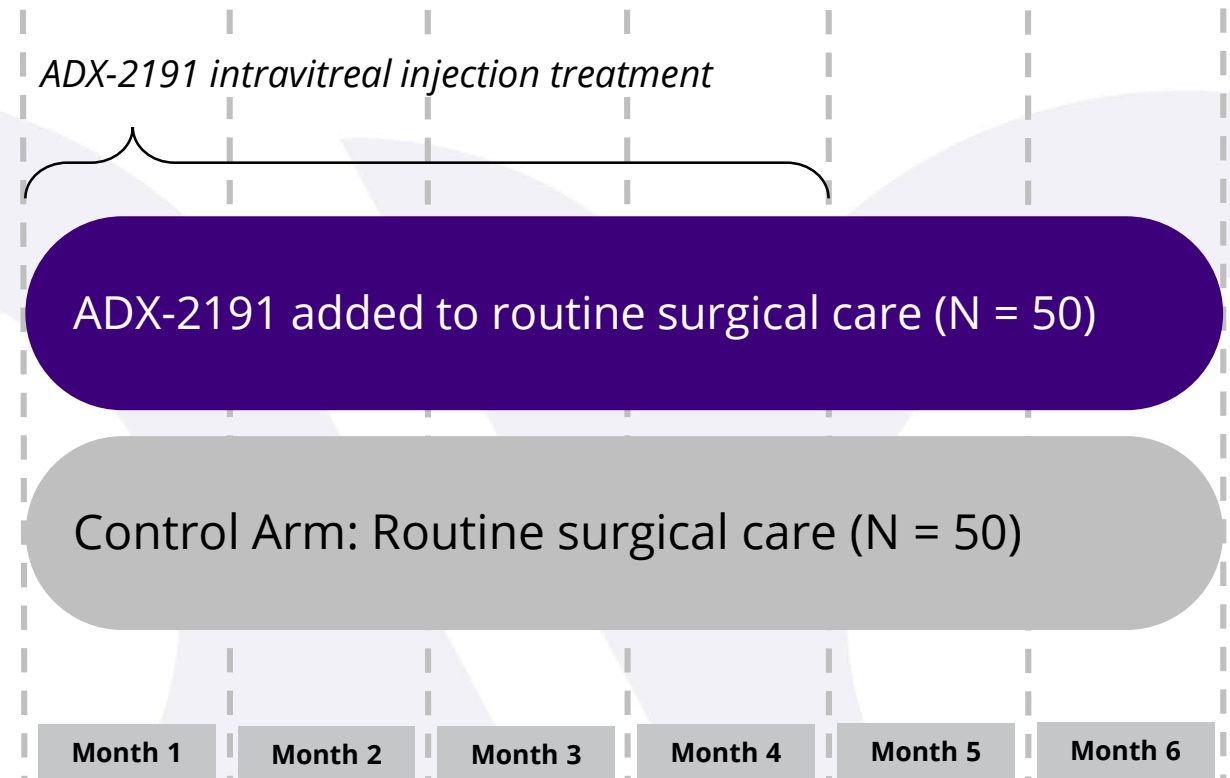


# ADX-2191: GUARD Trial Design in Proliferative Vitreoretinopathy

## 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

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





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## **CORPORATE REVIEW**

# Systemic Disease Area

- **SJÖGREN-LARSSON SYNDROME**

# Sjögren-Larsson Syndrome: A Rare RASP-Mediated Disease with No Approved Therapy

## Sjögren-Larsson Syndrome

**1,000**  
U.S.

SLS is a **rare inborn error of metabolism** caused by a mutation in the gene encoding fatty aldehyde dehydrogenase; there are ~1,000 SLS patients in the U.S. and a greater number in Europe.



Severe symptoms significantly impact **SLS patient and caregiver quality of life.**



**No FDA- or EMA-approved therapy**



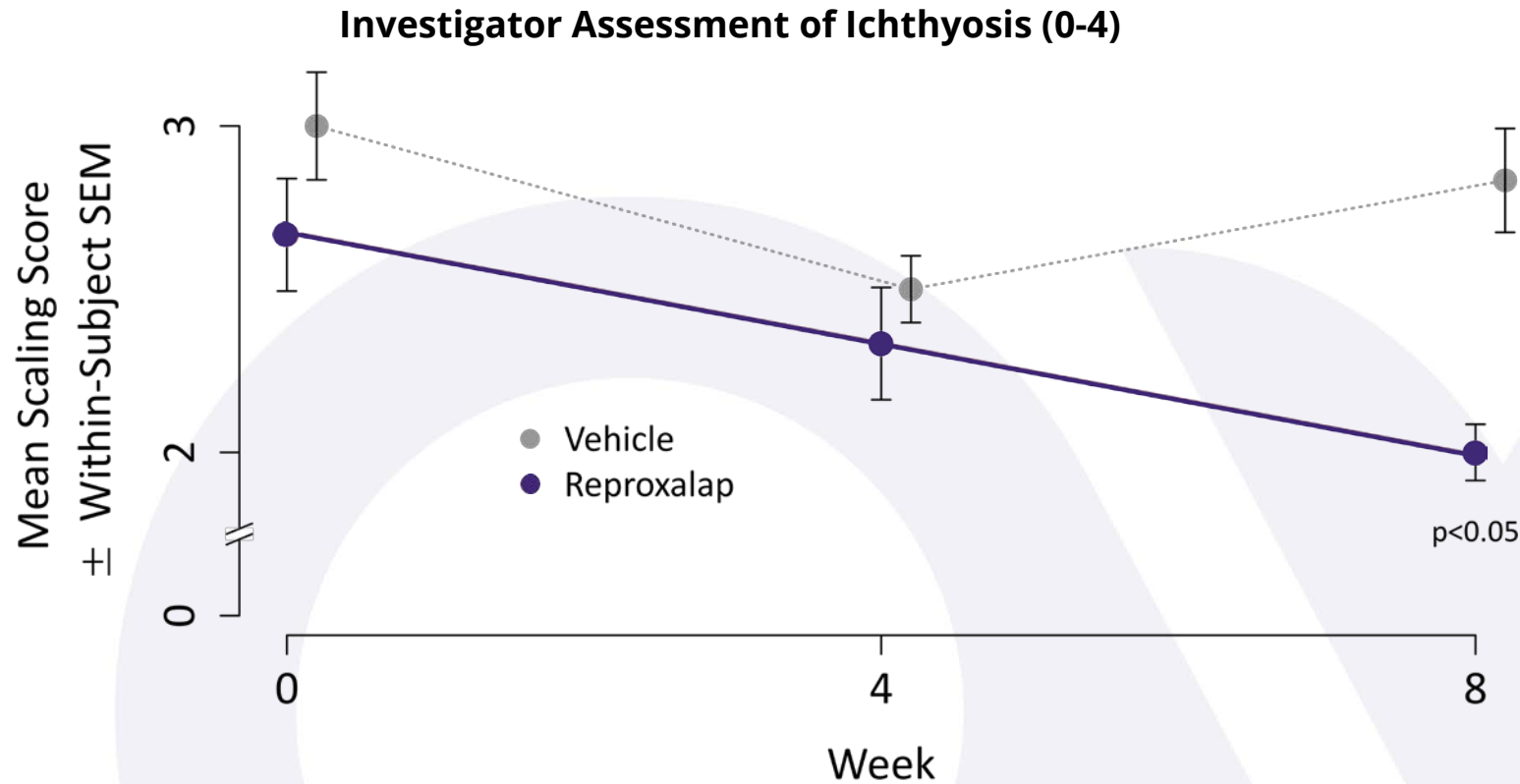
**Nonstop disease burden diminishes quality of patient/caregiver life**, with hours devoted to managing painful scaling, monitoring, & care.

## Reproxalap

### Reproxalap

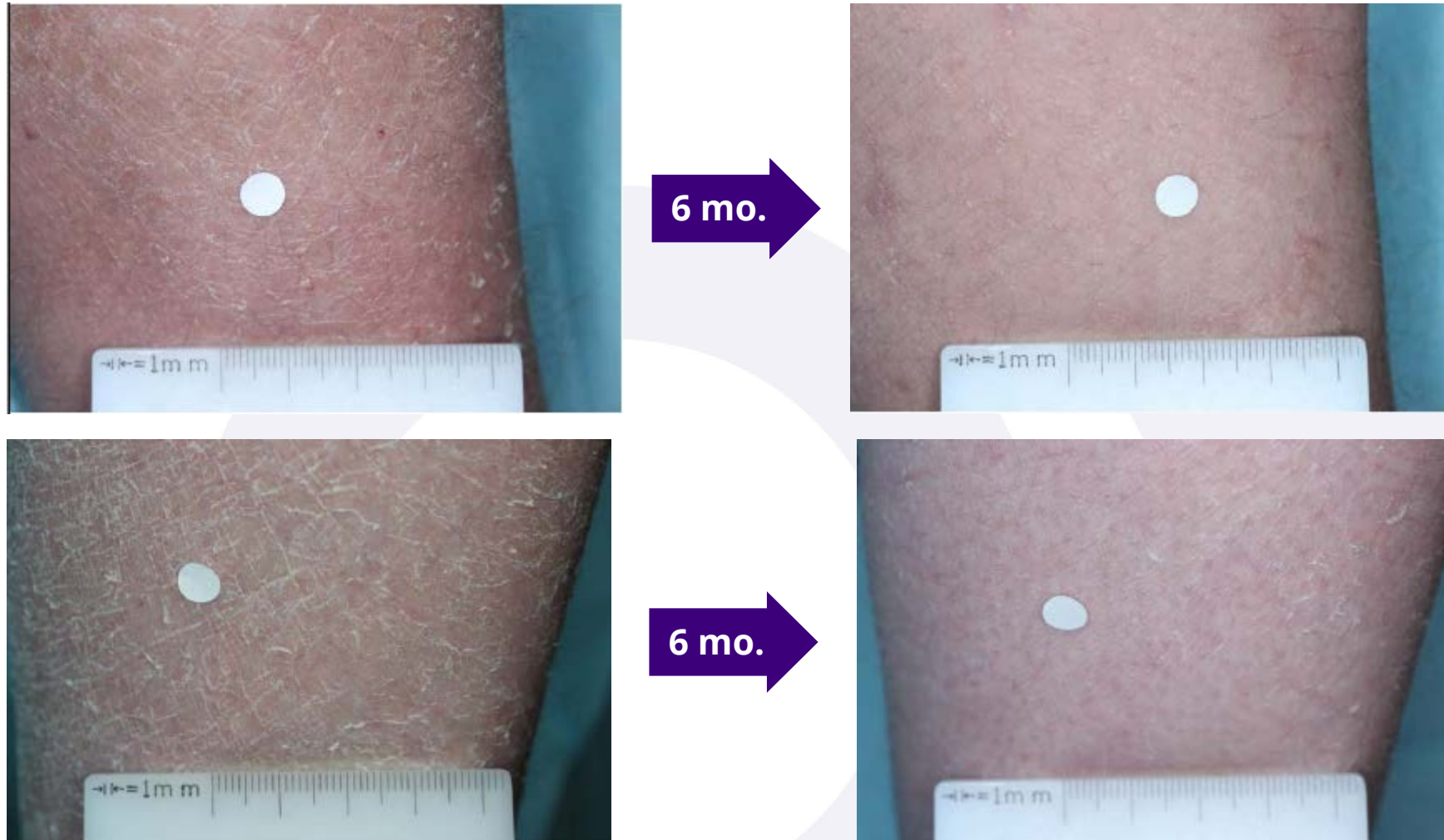
- A **novel approach and potential lifelong therapy** to replace missing enzymatic activity in SLS
- **Granted U.S. orphan designation** for the treatment of congenital ichthyosis (primary symptom of SLS)
- **Significantly reduced SLS ichthyosis** in a randomized, vehicle-controlled Phase 2 clinical trial
- RESET Phase 3-Part 1 **completed Q2 2019**; results to be discussed with regulatory authorities prior to initiating subsequent clinical testing

# Reproxalap Demonstrated Clinically Relevant and Consistent Activity in Phase 2 Clinical Trial



**Over two months of treatment, ichthyosis improved consistently from moderate to mild disease**

# Scaling Scores Statistically Lower Than Baseline Observed in Reproxalap-Treated Patients in RESET Part 1







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**CORPORATE REVIEW**

# Building The Future

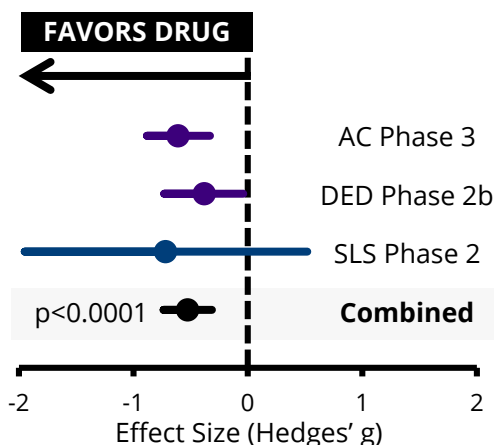
# Our Value Proposition



# Our Phase 3 Drug Candidates Are Protected and Well Positioned

## Reproxalap

- **Worldwide rights**, royalty free
- **Composition of matter IP through 2033** (with Hatch-Waxman extension) and extensive additional patent protection
- **FDA Orphan Drug Designation** for the treatment of congenital ichthyosis (primary symptom of SLS)
- **Meta analysis strongly supports drug activity**



## ADX-2191

- **Worldwide rights**
- **FDA 505(b)(2) approval pathway**
- **Methods of use (therapeutic and delivery) IP** and additional patent work ongoing
- **FDA Orphan Drug Designation** for the prevention of PVR
- If approved, ADX-2191 has the potential to be the only approved form of the drug for use in the eye
- **U.S. Drug Quality and Security Act** prohibits the compounding of approved drugs

# Experienced Management Team and Board of Directors

## Management Team

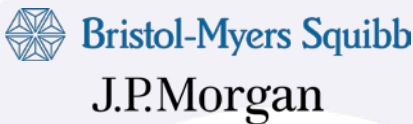
**Todd Brady, M.D., Ph.D.**  
President, CEO, & Director

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

**David Clark, M.D.**  
Chief Medical Officer

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

**Stephen Machatha, Ph.D.**  
SVP Technical Operations



## Board of Directors

**Richard Douglas, Ph.D.**  
CHAIRMAN  
Former SVP Corporate Development at Genzyme

**Ben Bronstein, M.D.**  
Former CEO Peptimmune<sup>8</sup>

**Marty Joyce, M.B.A.**  
Former CFO of Serono USA

**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 Alexion  
4. Acquired by Takeda

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

# Upcoming and Recently Achieved Development Milestones:<sup>\*</sup> Novel Approaches to Address Immune-Mediated Disease

○ = Ocular Diseases  
○ = Systemic Diseases

- |   |   |
|---|---|
|  ADX-2191 proliferative vitreoretinopathy <b>GUARD Phase 3 - Part 1 clinical trial initiation Q4 2019</b> |  ADX-629 systemic <b>Phase 1 clinical trial initiation H2 2019</b>                                       |
|  Reproxalap allergic conjunctivitis design for potential <b>second Phase 3 to be confirmed Q4 2019</b>    |  Reproxalap Sjögren-Larsson Syndrome <b>RESET Phase 3 - Part 1 completion Q2 2019</b>                    |
|  ADX-1612 post-transplant lymphoproliferative disorder <b>Phase 2 clinical trial initiation H2 2019</b>   |  <b>Positive</b> reproxalap allergic conjunctivitis <b>environmental chamber trial results June 2019</b> |
|  Reproxalap dry eye disease <b>RENEW Phase 3 - Part 1 completion Q4 2019</b>                             |  Reproxalap dry eye disease <b>RENEW Phase 3 - Part 1 clinical trial initiation April 2019</b>          |
|   |  <b>Positive</b> reproxalap allergic conjunctivitis <b>ALLEVIATE Phase 3 trial results March 2019</b>  |





# Innovating Transformative Therapies