
# Innovating Transformative Therapies

## Corporate Review

April 2019

Nasdaq: ALDX

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# Our Mission

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

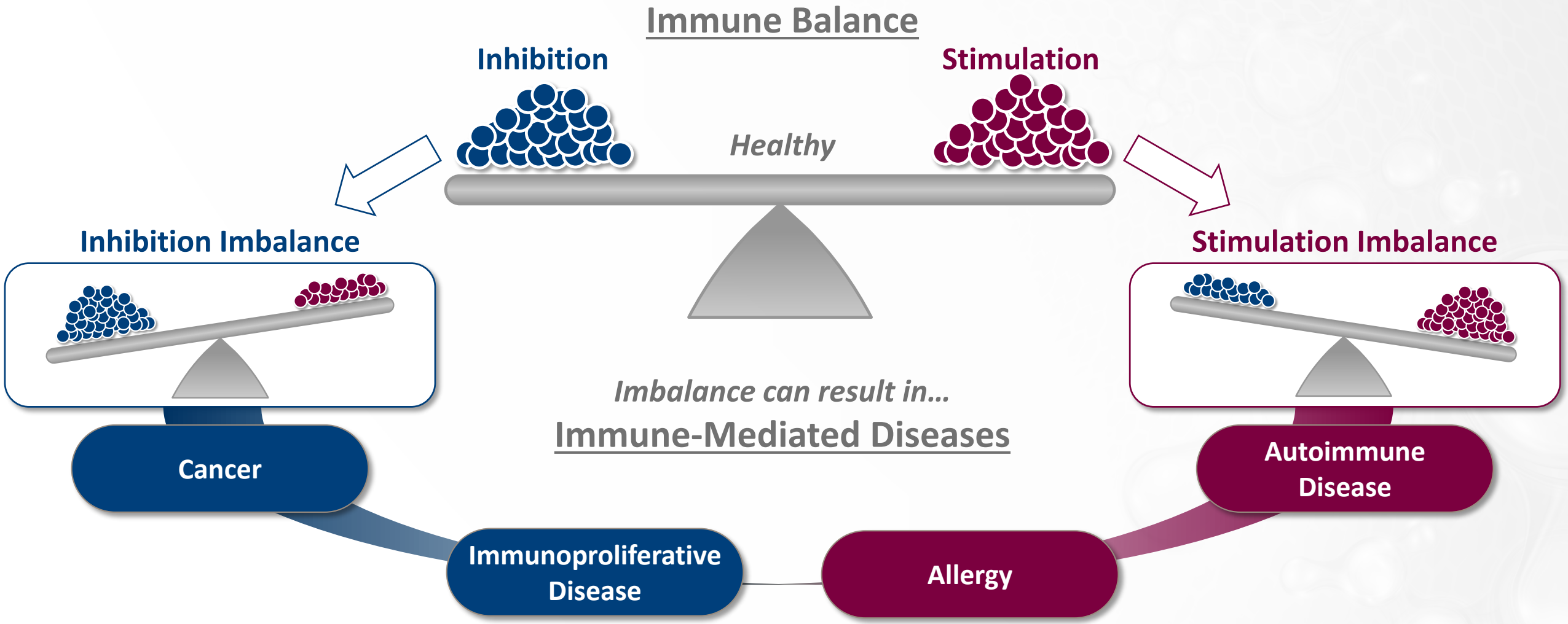
**~7%**
Of Western Society

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


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.

# Immune System Imbalance Leads to Immune-Mediated Disease



# Deliberate Focus on Ocular Diseases and Select Systemic Diseases

ALDEYRA THERAPEUTICS™

| 2004 | … | May 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|---|
| Founded | | IPO; First Phase 2 IND filing | First Phase 2 Initiations | First Phase 2 Completions | First Phase 3 Initiations | Add'l Phase 2; Add'l Phase 3 | Potential First Phase 3 Completions* |

DOMAIN ASSOCIATES

Johnson & Johnson INNOVATION

**Discovery & Preclinical**

**Ocular Diseases**

- RASP Dry Eye Disease
- RASP Allergic Conjunctivitis
- RASP Noninfectious Anterior Uveitis
- DHFR PVR
- RASP Retinal Disease

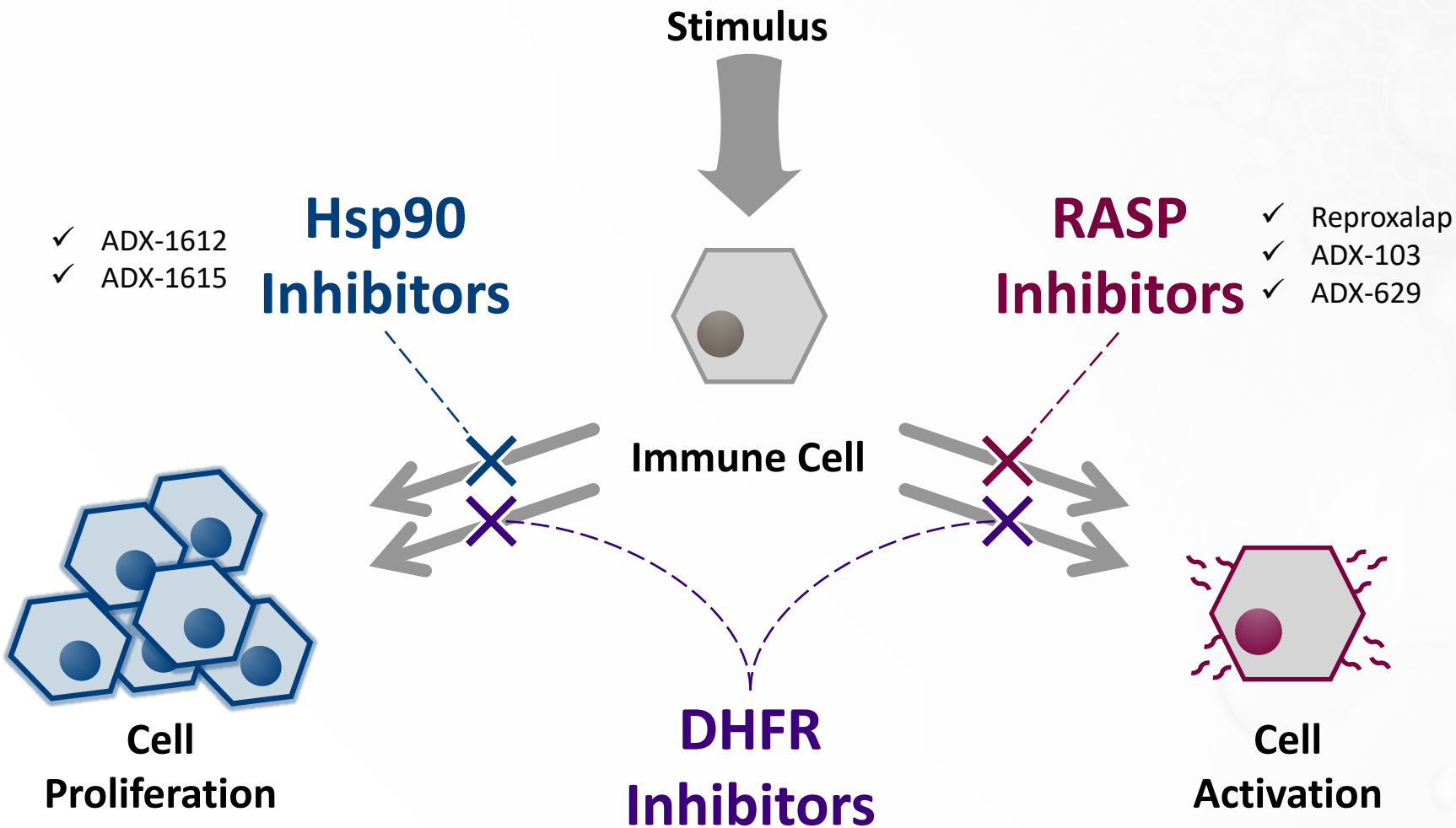
**Systemic Diseases**

- RASP Sjögren-Larsson Syndrome
- Hsp90 PTLD
- Hsp90 Mesothelioma and ovarian cancer**
- RASP Autoimmune

RASP = Reactive Aldehyde Species Inhibitor
DHFR = Dihydrofolate Reductase Inhibitor
Hsp90 = Heat Shock Protein 90 Inhibitor
PTLD = Post-Transplant Lymphoproliferative Disorder
PVR = Proliferative Vitreoretinopathy

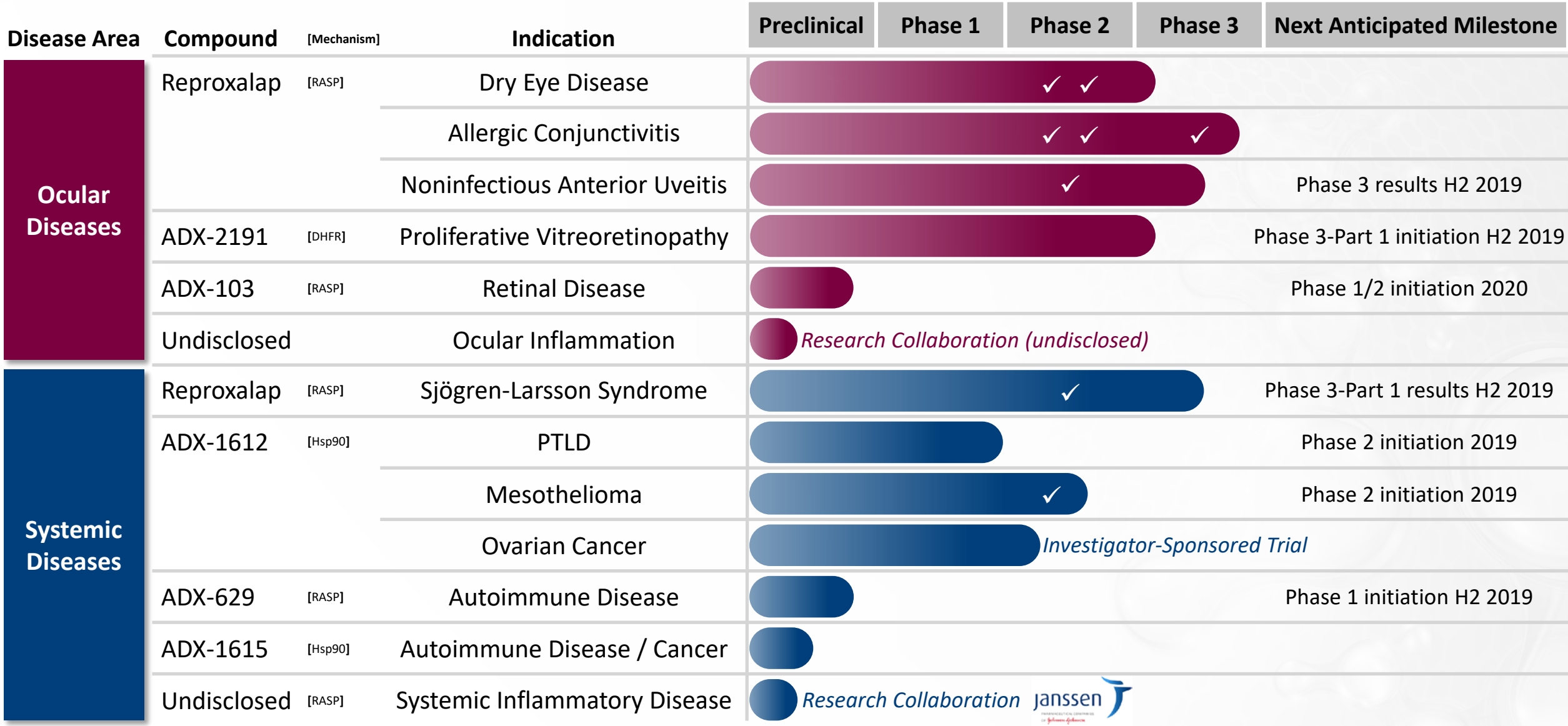
*Contingent on funding, regulatory review, and other factors.
**Initially supporting Investigator Sponsored Trials following ALDX in-licensing.

# Our Novel Approaches to Address Immune-Mediated Disease




RASP = Reactive Aldehyde Species
DHFR = Dihydrofolate Reductase
Hsp90 = Heat Shock Protein 90

# Deep and Innovative Pipeline Focused on Immune-Mediated Diseases




RASP = Reactive Aldehyde Species Inhibitor
DHFR = Dihydrofolate Reductase Inhibitor
Hsp90 = Heat Shock Protein 90 Inhibitor
PTLD = Post-Transplant Lymphoproliferative Disorder

✓ = Positive Phase 2/3 clinical trial data reported in 2016-2019
Trial initiations contingent on funding, regulatory review, and other factors

ALDEYRA THERAPEUTICS™

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

| **Late Stage Programs** | Current Standard of Care | Pricing Benchmarks† | Drug Candidate and Dev. Stage | Potential Competitive Advantages † |
|---|---|---|---|---|
| *Ocular Diseases* | | | | |
| 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** |
| Noninfectious Anterior Uveitis | Corticosteroids | $1,500 per regimen (to treat one flare) | **Reproxalap: Phase 3** | **No expected risk of glaucoma or other corticosteroid toxicities** |
| 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** |
| *Systemic Diseases* | | | | |
| 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** |

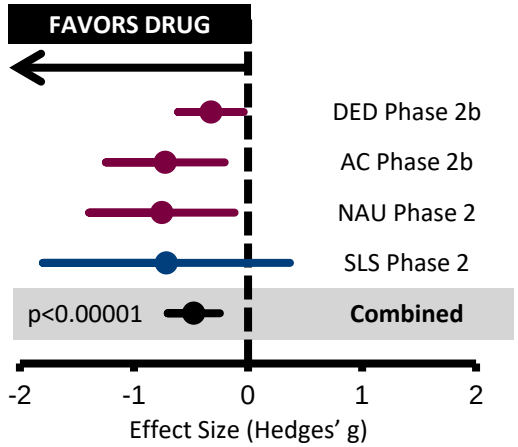
†Pending clinical data, regulatory discussions, payor negotiations, competition, potential legislative changes, and other factors, which may not be in Aldeyra's control. Preliminary assumptions are subject to change.

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

# Our Lead Drug Candidates Are Well Positioned

## Reproxalap

- **Worldwide rights**
- **Composition of matter IP** and extensive additional patent protection
- **FDA Orphan drug designation** for the treatment of congenital ichthyosis (a primary symptom of SLS)
- **Meta analysis strongly supports drug activity**




Bars represent 95% confidence intervals. Between-group comparisons used for vehicle controlled trials (DED, AC, SLS). Change from baseline (within-group comparison) used for active controlled trial (NAU). Results based on dryness (OD & 4 Symptom Score) in DED, area under the curve ocular itch in AC, anterior chamber inflammatory cell grade in NAU, and scaling in SLS.

## 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

Source: Aldeyra analysis of Phase 2 clinical trial data on file.

DED = Dry eye disease
AC = Allergic conjunctivitis
NAU = Noninfectious anterior uveitis
SLS = Sjögren-Larsson Syndrome
PVR = Proliferative vitreoretinopathy
IP = Intellectual property

# We Intend to Commercialize* Directly and Through Partnerships

| Late Stage Programs | Estimated U.S. Population† | U.S. Healthcare Providers | Competitive Value Proposition | Infrastructure Requirement‡ |
|---|---|---|---|---|
| *Ocular Diseases* | | | | |
| Dry Eye Disease | 20 million DED<br>Up to 10 million with DED & AC<br>30 million AC | ~18,000 ophthalmologists and ~40,000 optometrists | Potential benefits over current therapies, which do not work well for many patients | Medium sized sales force for national reach |
| Allergic Conjunctivitis | | | | |
| Noninfectious Anterior Uveitis | 260,000 | ~200 U.S. uveitis sub-specialists | Effective non-steroid alternative | Small targeted sales force |
| 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 |

*Following FDA approval, if any, of an applicable new drug application
†Aldeyra estimates of the addressable market
‡Contingent on the results of current and planned clinical trials and other factors
Source: Aldeyra internal estimates based on primary and secondary market research; published literature

DED = Dry eye disease
AC = Allergic conjunctivitis

ALDEYRA THERAPEUTICS™

# Ocular Disease Area

- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Proliferative Vitreoretinopathy

# Dry Eye Disease and Allergic Conjunctivitis: Persistently Disturbing and Overlapping Disease Burdens

## Dry Eye Disease

**20 million** 20 million or more **adults in the U.S.** suffer from DED

**Age 50+ >3x** DED **increases with age**, with those over age 50 three times more likely to suffer from DED

**vs** **Women are twice as likely** to suffer from DED than men

Significant **negative quality of life** impact

## DED+AC Comorbidity

Studies have shown that **DED and AC can be interrelated** and often overlap

**50-60%** ~50-60% of **DED and AC patients experience** clinically significant **itch and dryness**

**DED** **Allergen exposure** can contribute to **DED seasonality**

Significant **negative quality of life** impact **x2**

## Allergic Conjunctivitis

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


AC patients experience symptoms throughout **all decades of adult life**

AC can result in **acute, intermittent, and chronic** symptoms

Significant **negative quality of life** impact

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

DED = Dry eye disease
AC = Allergic conjunctivitis

# Dry Eye Disease and Allergic Conjunctivitis: Chronic Diseases With Inadequate Therapies

## Dry Eye Disease

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

**Up to 75%**

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

**Up to 50%**

Up to 50% of patients **treated for DED** with current therapies **fail and discontinue**

**Underserved Patient Population**

## DED+AC Comorbidity

**DED, AC or both?**

Differential diagnosis is difficult and treating both conditions together is complex

Current Rx **DED treatments are not effective against AC** and vice versa

**Antihistamine use can cause** and exacerbate **eye dryness**

**Unmet Medical Need**

## Allergic Conjunctivitis

Many AC **patients make significant sacrifices** due to lack of drug activity

**24%**

**Antihistamines are not effective** in an estimated 24% of treated AC patients

**2%**

~2% of AC patients have severe symptoms and **may be corticosteroid-dependent**

**Underserved Patient Population**

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

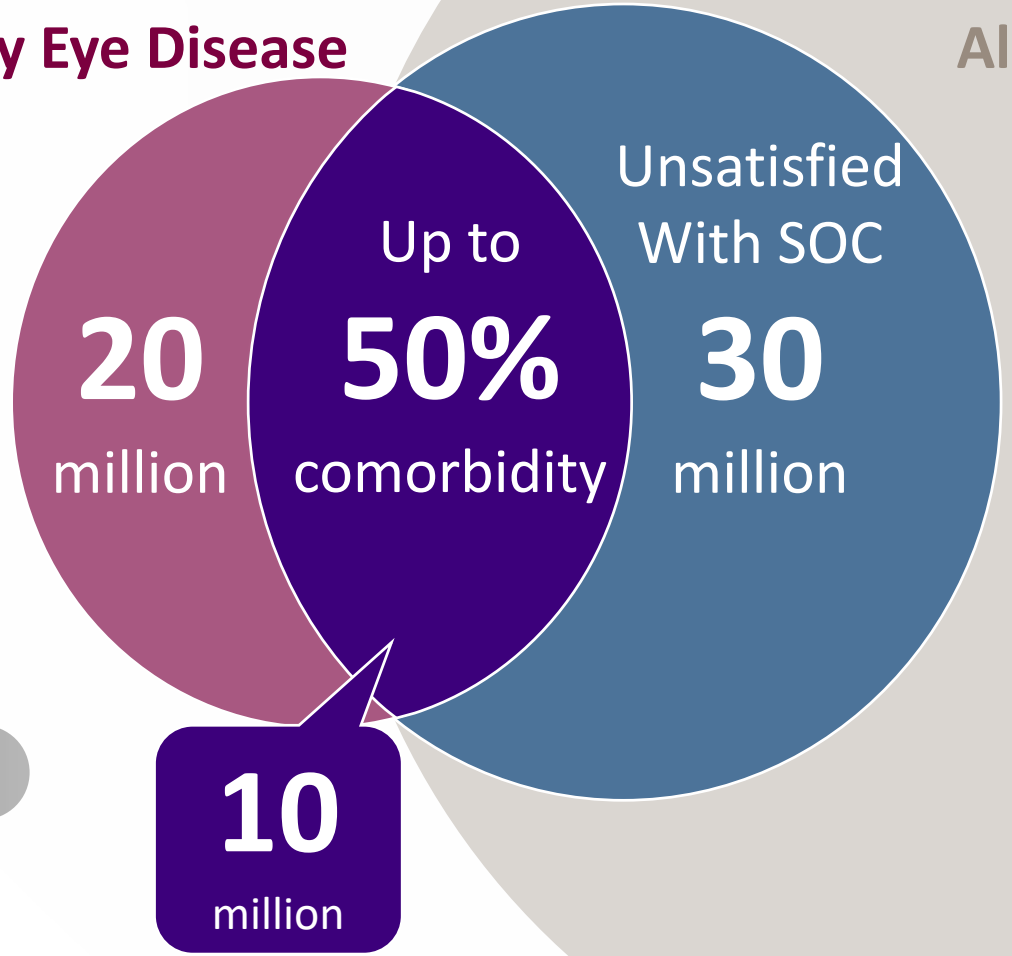
DED = Dry eye disease
AC = Allergic conjunctivitis

# Dry Eye Disease and Allergic Conjunctivitis: Large Market Opportunities With Unmet Medical Needs

U.S. Patient Estimates

- Significant negative quality of life
- Complex, overlapping, and difficult to treat chronic conditions
- Substantial unmet medical need with current treatments

**Novel Approaches Needed**




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

DED = Dry eye disease
AC = Allergic conjunctivitis
SOC = Standard of Care

# Reproxalap: A Unique and Novel Product Candidate for Dry Eye Disease and Allergic Conjunctivitis

## Dry Eye Disease

### Reproxalap in DED

- **Early and consistent symptom and sign improvements** in Phase 2b clinical trial
- **Broad symptom and sign improvements** in Phase 2b clinical trial

## Reproxalap

### Parallel Development in AC and DED

- **Observed improvements in AC** Phase 3 clinical trial **and DED** Phase 2b clinical trial
- Both **patients and physicians** have a **strong desire for better treatments** for DED and AC

## Allergic Conjunctivitis

### Reproxalap in AC

- **Clinically significant and durable symptom response** in Phase 3 clinical trial
- **Active in post-histaminic allergy**, for which no drug is approved

No drug approved has indications for both the treatment of dry eye disease and allergic conjunctivitis

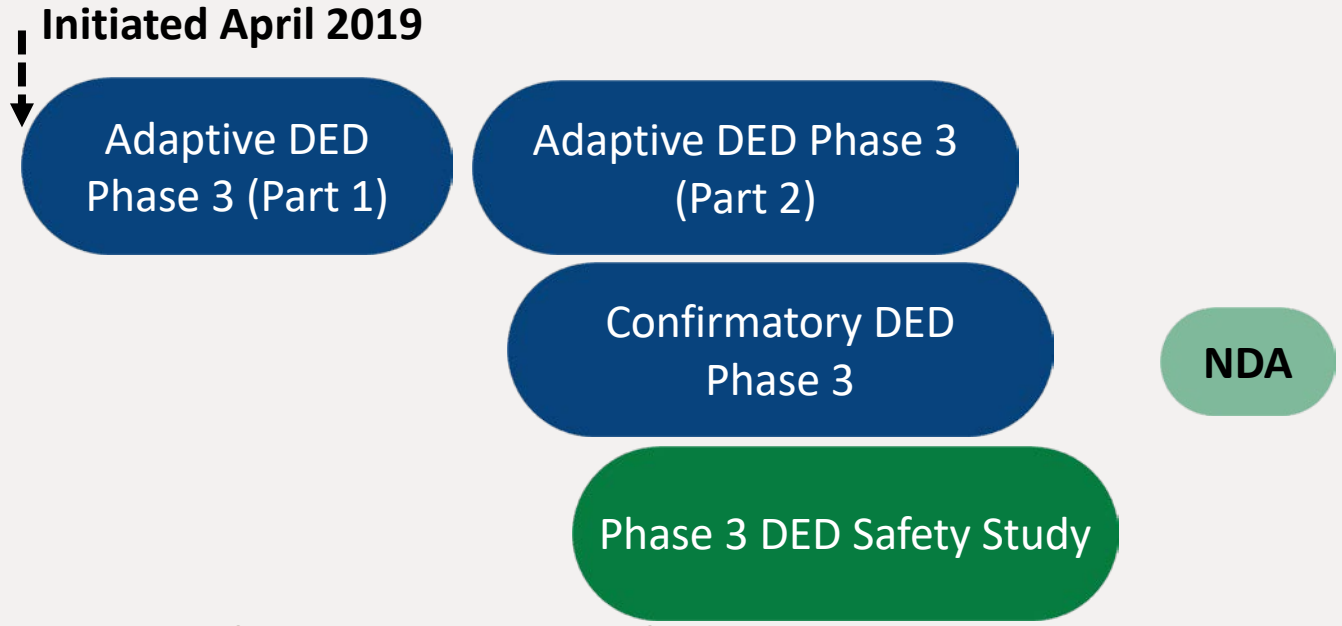
DED = Dry eye disease
AC = Allergic conjunctivitis

# 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

## Phase 3 Program Design Elements




Contingent on funding, regulatory review, and other factors

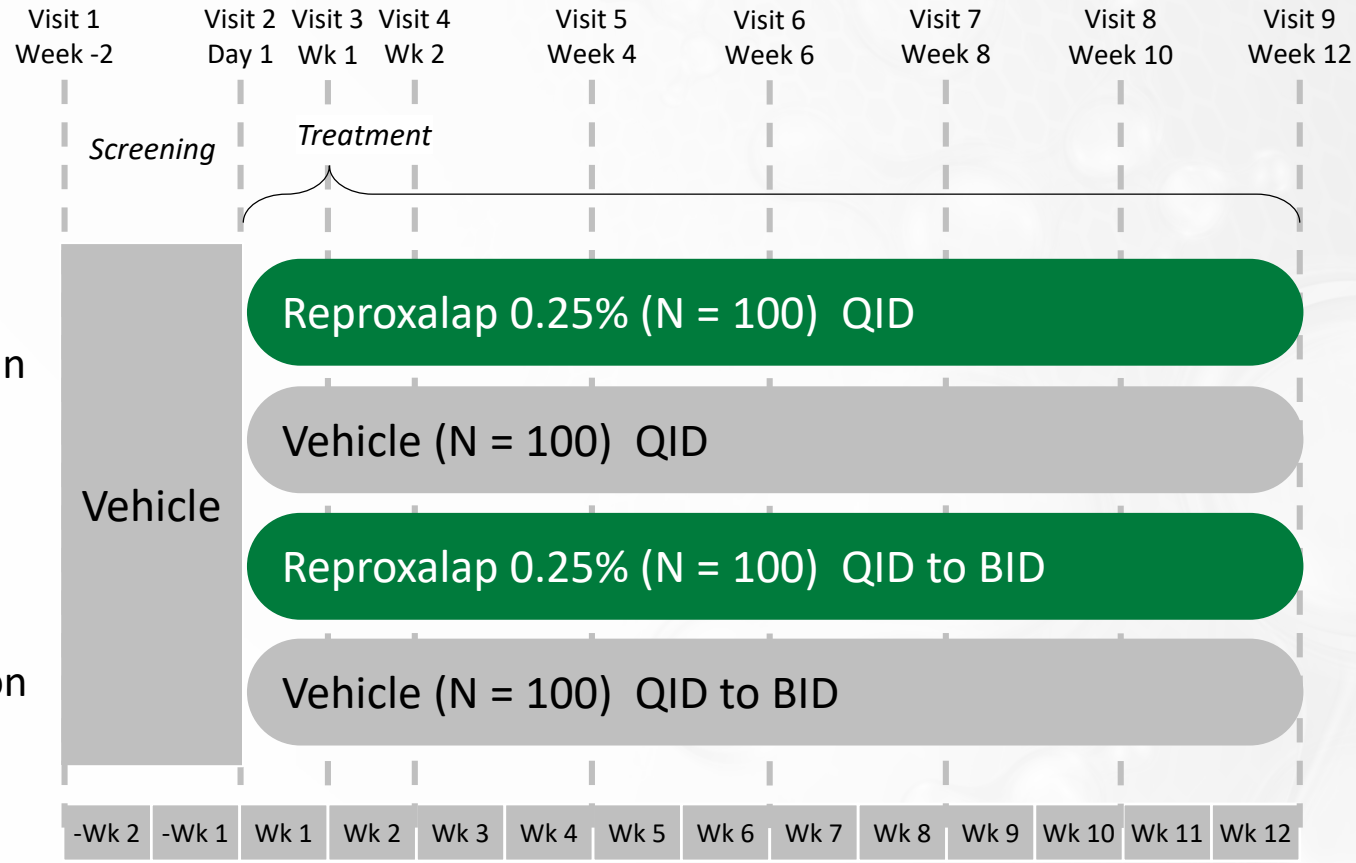
Adaptive design, co-primary endpoints and innovative analysis strategy confirmed with FDA at EOP2 Meeting

DED = Dry eye disease
BID = Two times daily
QID = Four times daily
EOP2 = End of Phase 2

# Adaptive Phase 3 (Part 1) Dry Eye Disease Clinical Trial Design*

- **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 week 12
  - Both co-primary endpoints will be assessed based on 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**



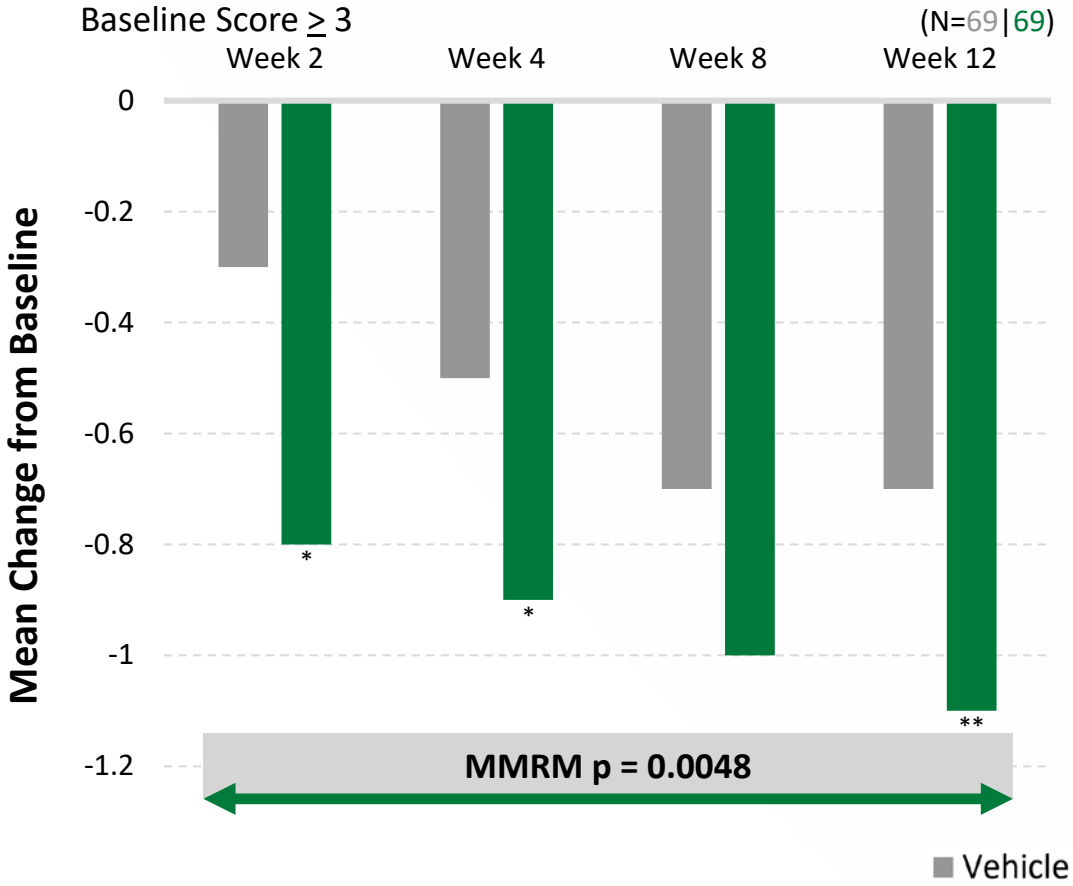

VAS = Visual analog scale
OD4SS = Ocular Discomfort 4-Symptom Score

*Contingent on funding, regulatory review, and other factors

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

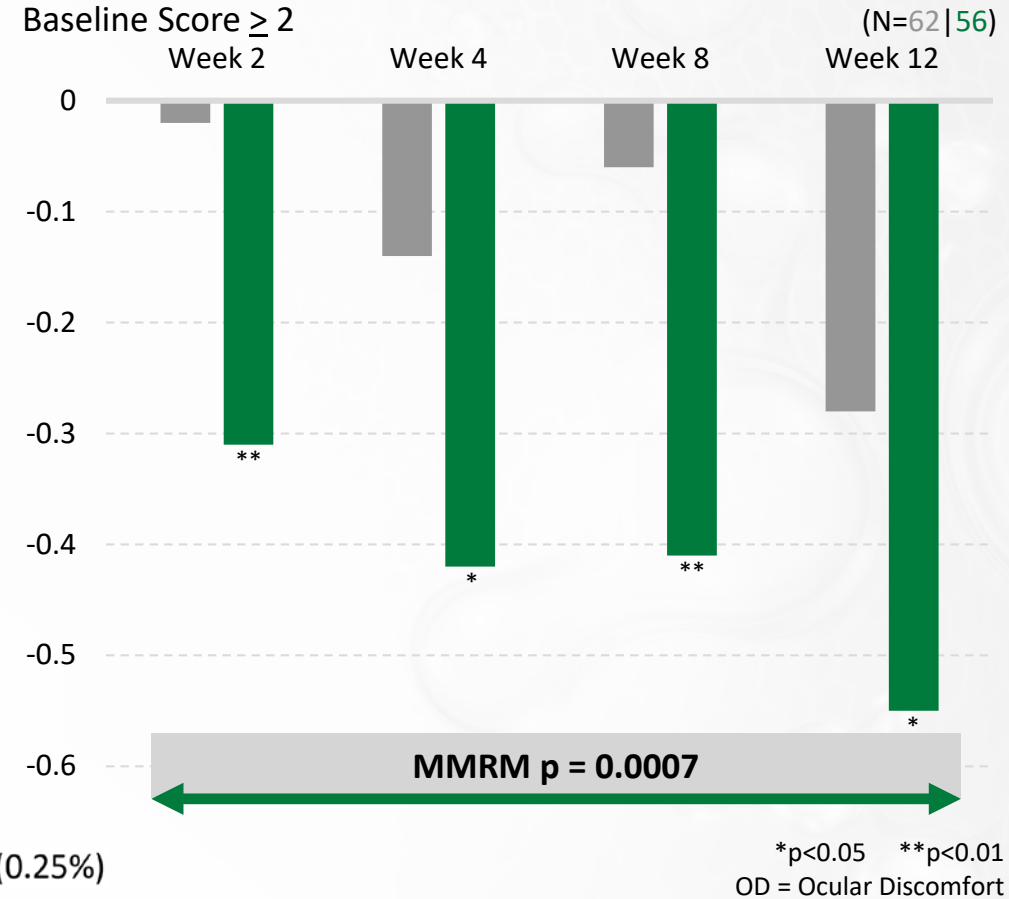
## Primary Symptom Endpoint for Phase 3 DED

**OD & 4-Symptom Questionnaire: Dryness (0-5)**




## Primary Sign Endpoint for Phase 3 DED

**Fluorescein Staining: Nasal (0-4)**



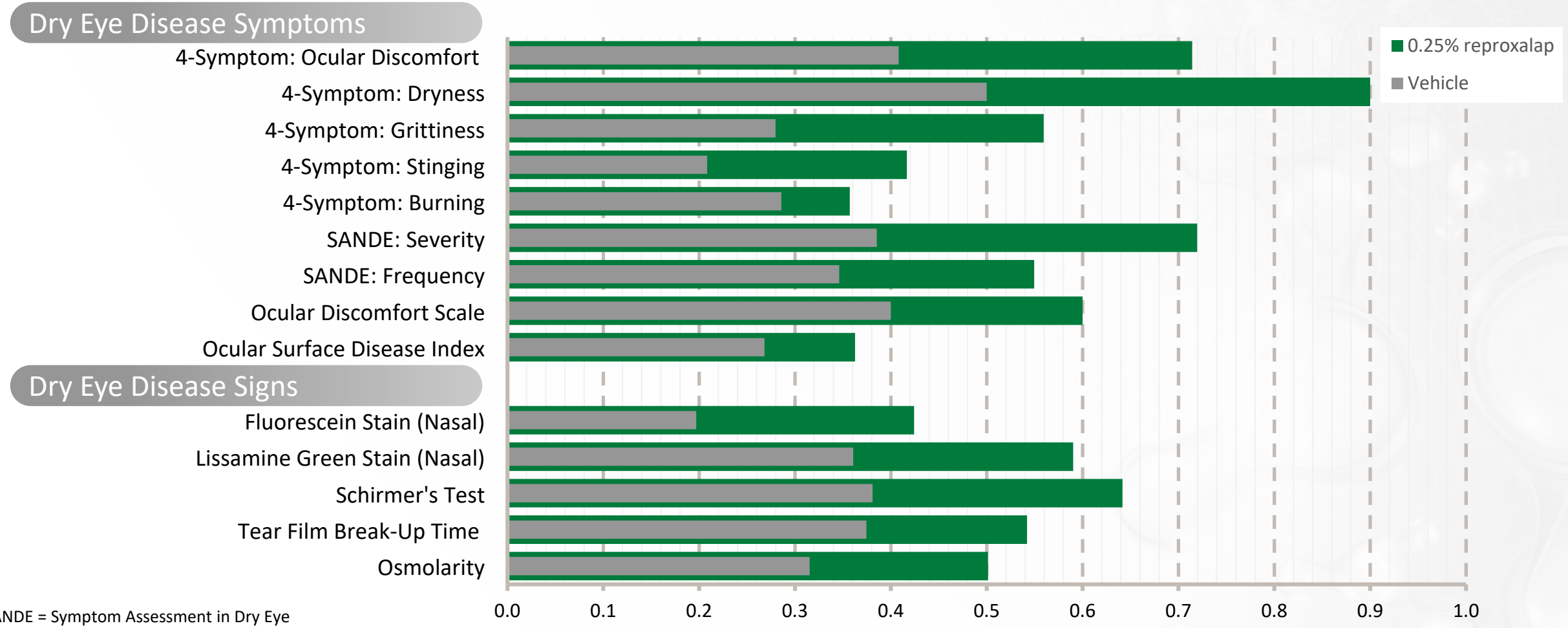

Vehicle  Reproxalap (0.25%)

*p<0.05  **p<0.01
OD = Ocular Discomfort
MMRM = Mixed Effect Model Repeated Measures

Source: Reproxalap DED Phase 2b clinical trial results

# Broad Pattern of Drug Activity Across Dry Eye Disease Symptoms and Signs Supports Differentiated Product Profile

**Improvement Effect Size at Week 12**




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)

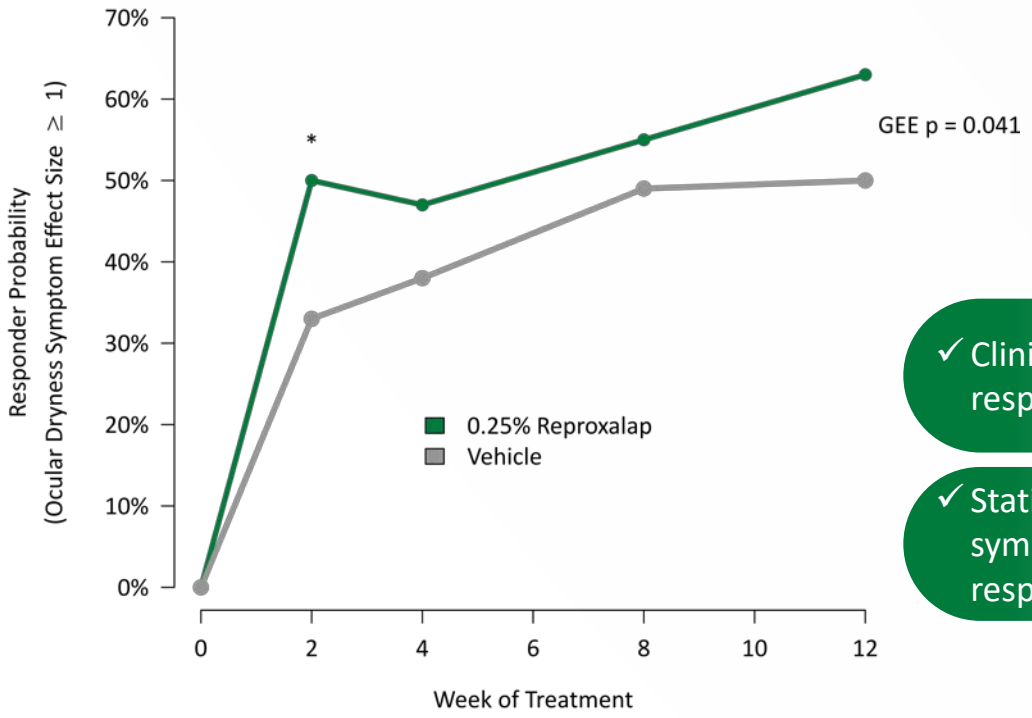
Improvement Effect size = Change from Baseline / Standard Deviation at Baseline

Source: Reproxalap DED Phase 2b clinical trial results

# Differentiated Dry Eye Disease Product Profile Evidenced by Responder Analyses – Rapid and Symptom-Free (Eye Dryness)

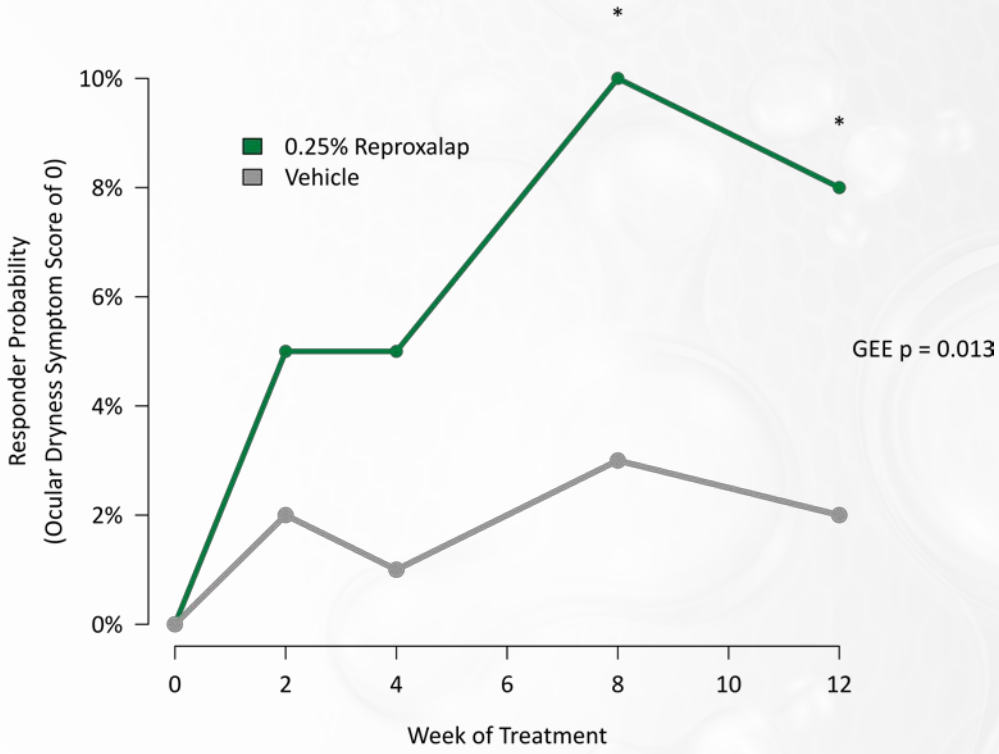
**OD & 4-Symptom Questionnaire: Dryness**

Probability of Response (Improvement Effect Size ≥1)




- ✓ Clinically significant response in 2 weeks
- ✓ Statistically significant symptom-free response vs. vehicle

Probability of Symptom-Free (Eye Dryness Score = 0)

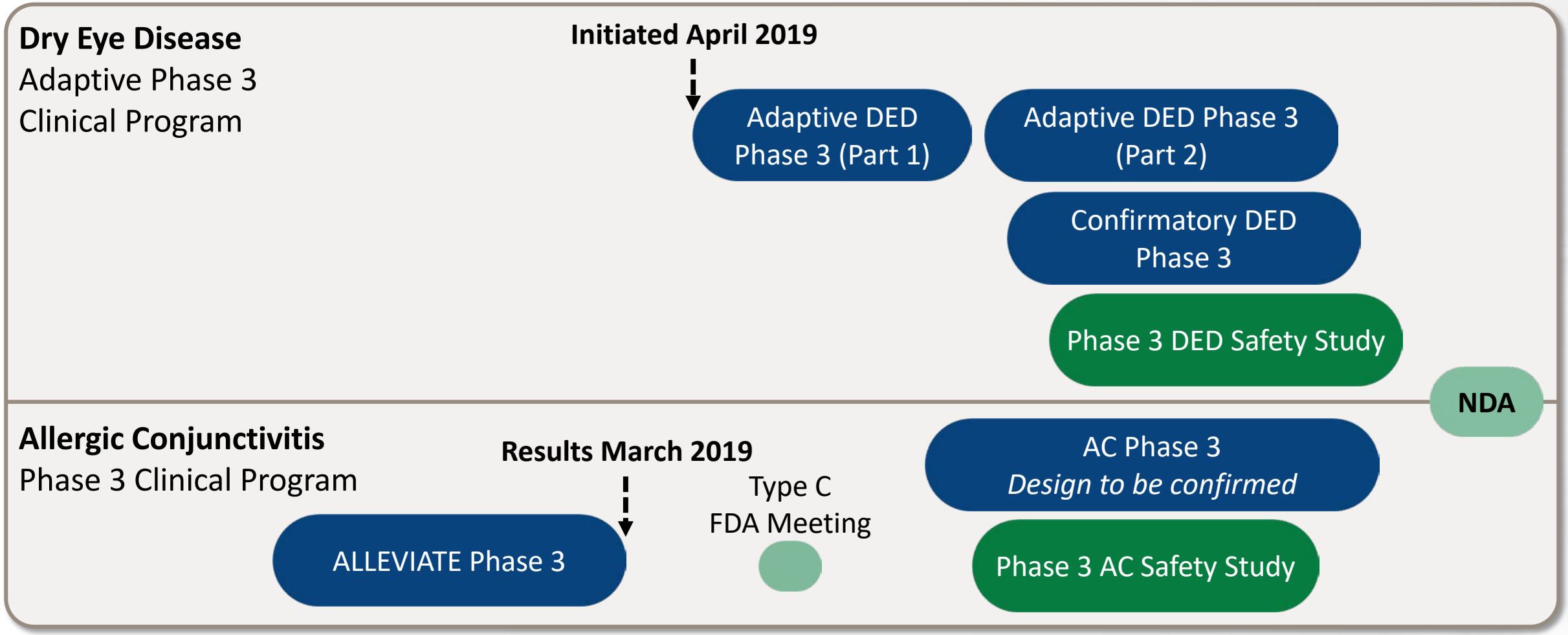



p values subject to change based on quality control analysis
Source: Reproxalap DED Phase 2b clinical trial results

OD = Ocular Discomfort
Effect Size = Change from Baseline / Standard Deviation at Baseline

* $p < 0.05$
GEE = Generalized Estimating Equations

# Parallel Dry Eye Disease and Allergic Conjunctivitis Phase 3 Clinical Programs May Support Concurrent NDA Filings



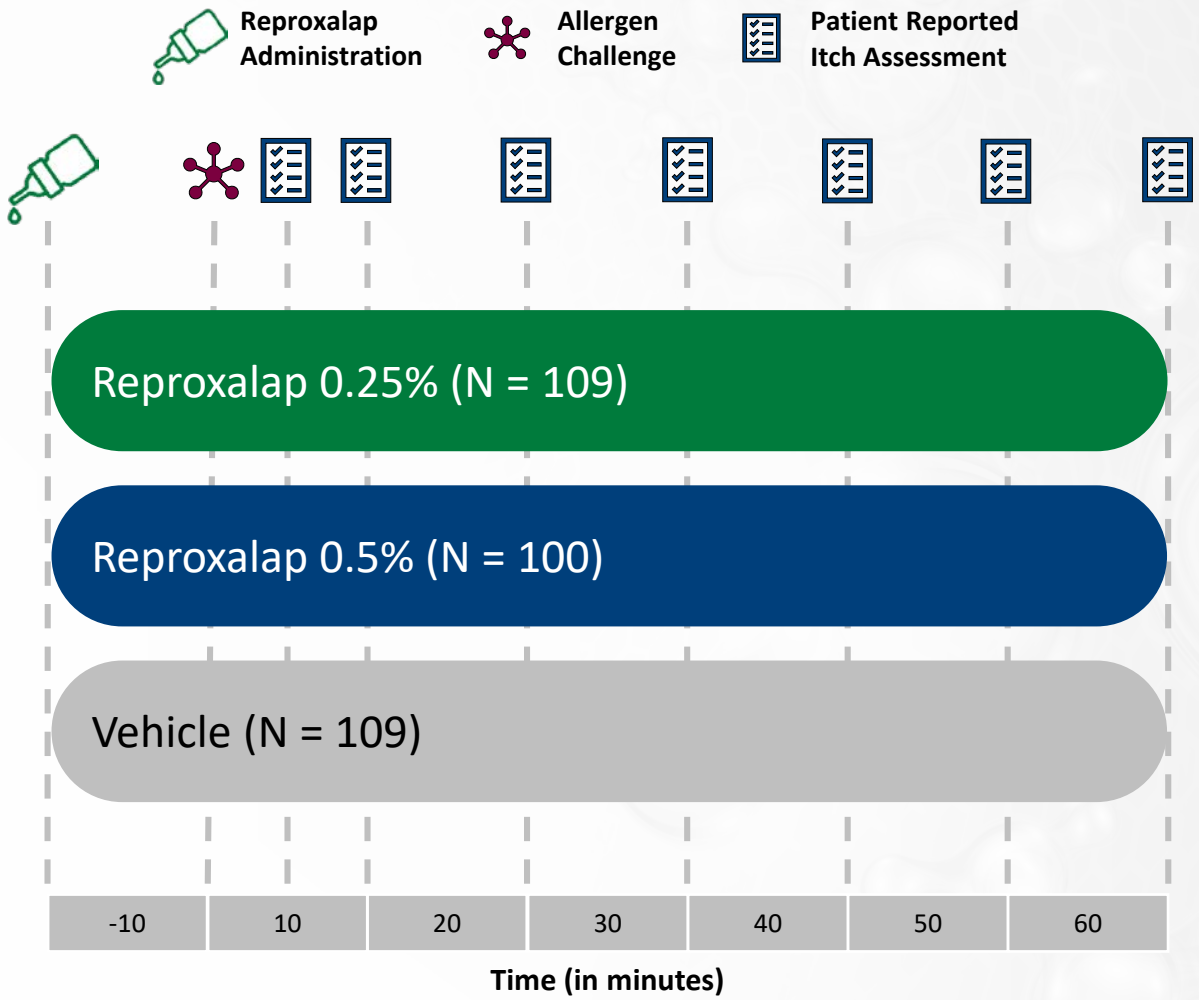

Contingent on funding, clinical results, regulatory review, and other factors.

DED = Dry eye disease
AC = Allergic conjunctivitis

# ALLEVIATE Phase 3 Trial Design in Allergic Conjunctivitis
## *Results Announced March 2019*

- **Primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solutions (0.25% & 0.5%) compared to vehicle for the treatment of ocular itching associated with acute allergic conjunctivitis
- **Inclusion/exclusion highlights:**
  - Positive history of ocular allergies and positive skin test reaction to a seasonal allergen
  - Positive bilateral conjunctival allergen challenge (CAC) ocular itch score (0-4 scale) reaction of ≥2.5 for itching and ≥2 for redness within 10 min of allergen instillation at first baseline visit
  - Positive bilateral CAC reaction for at least two out of first three time points following challenge at second baseline visit
- **Endpoints:**
  - Ocular itch score area under the curve (primary)
  - Two-point responder comparison (key secondary) to assess clinical relevance

**Phase 3 Conjunctival Allergen Challenge Trial**




Further information can be found on www.clinicaltrials.gov: Trial #NCT03494504.

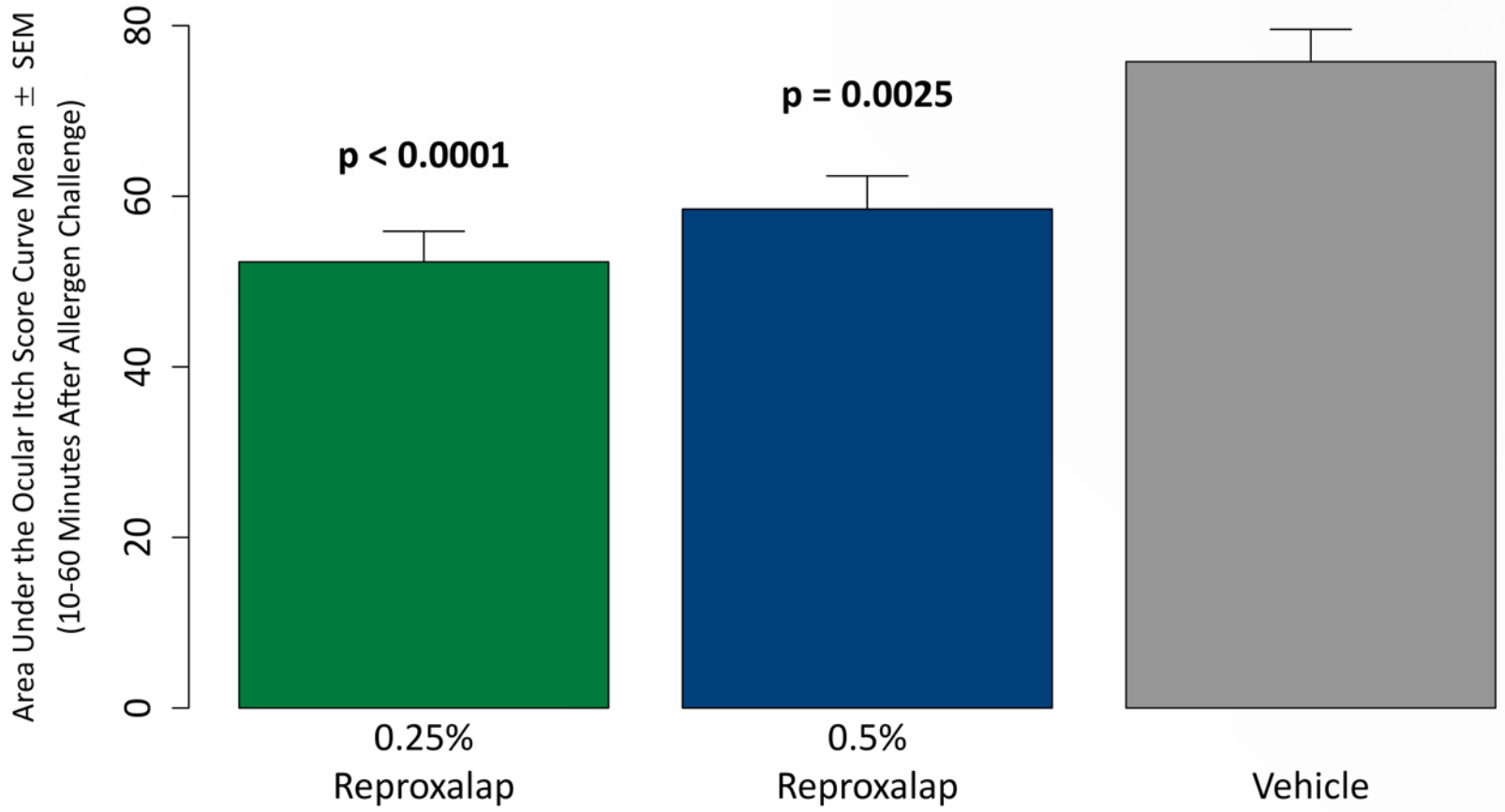
# Reproxalap:
# A Novel Drug Candidate for the Treatment of Ocular Inflammation

## Positive ALLEVIATE Phase 3 Allergic Conjunctivitis Clinical Trial Results

- **Primary and key secondary endpoints achieved for 0.25% and 0.5% concentrations:**
  - Statistically significant improvement vs. vehicle ($p < 0.0001$ and $p = 0.0025$, respectively) on primary endpoint of ocular itch score area under the curve from 10-60 minutes after allergen challenge
  - Statistically significant improvement vs. vehicle ($p = 0.0005$ and $p = 0.0169$, respectively) on key secondary responder analysis of two-point improvement in ocular itch score (0-4 scale)
- **No observed safety or tolerability concerns**
- In second half of 2019, Aldeyra plans to discuss with regulatory authorities the ALLEVIATE results and ongoing method development studies to confirm remaining clinical requirements for a potential New Drug Application submission
  - **Expected to advance 0.25% reproxalap concentration**
  - 0.25% reproxalap is **the same concentration in Phase 3 clinical program for dry eye disease**, an underserved disease that is frequently co-morbid with allergic conjunctivitis

# ALLEVIATE Primary Endpoint Achieved For Both Concentrations of Reproxalap

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



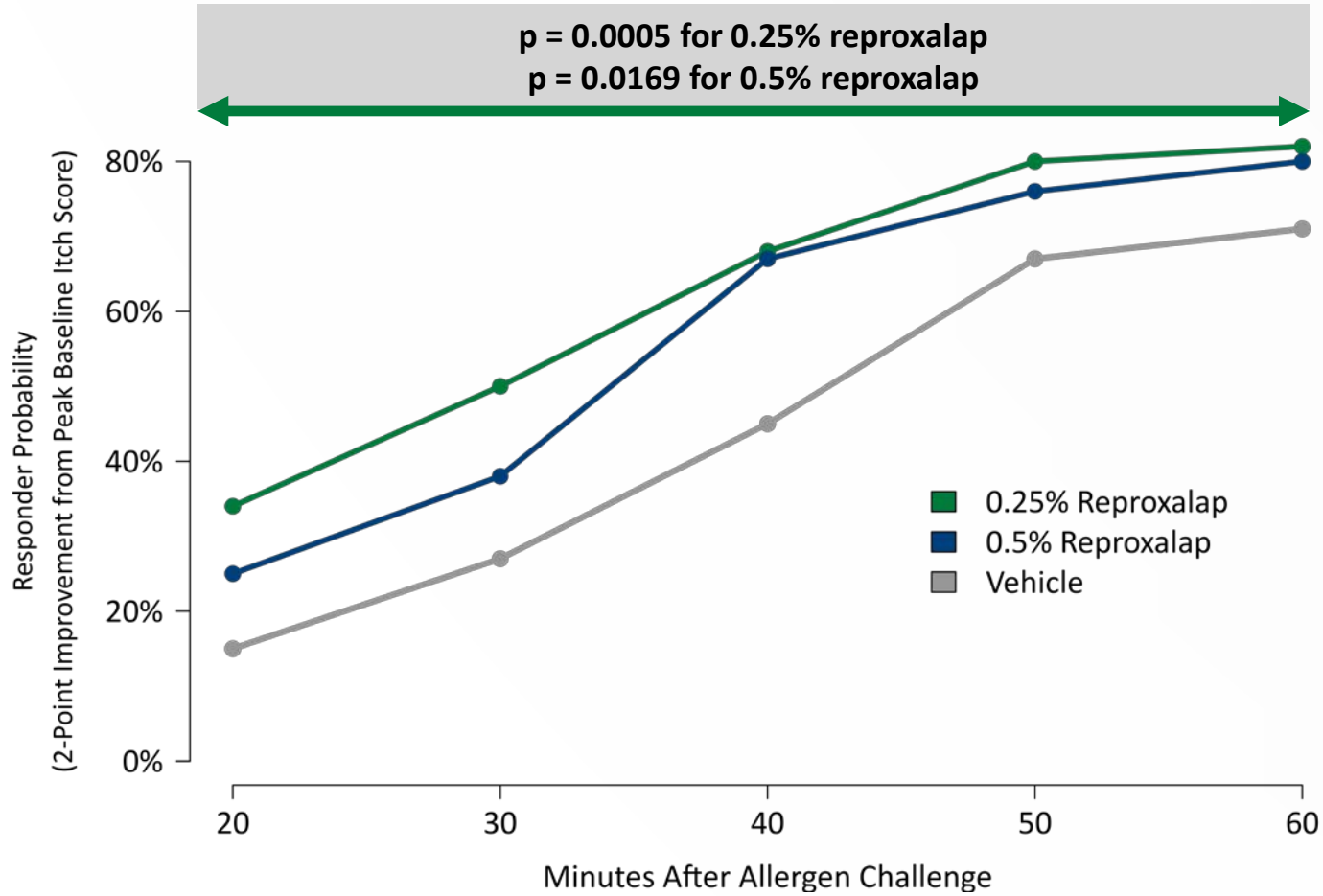

Improvement in itch score over one hour after allergen exposure statistically greater for reproxalap vs. vehicle

Source: ALLEVIATE allergic conjunctivitis Phase 3 clinical trial results; Ocular itch scale 0 (no itch) to 4 (incapacitating itch)

SEM = Standard error of the mean

# ALLEVIATE Key Secondary Endpoint Achieved For Both Concentrations of Reproxalap

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

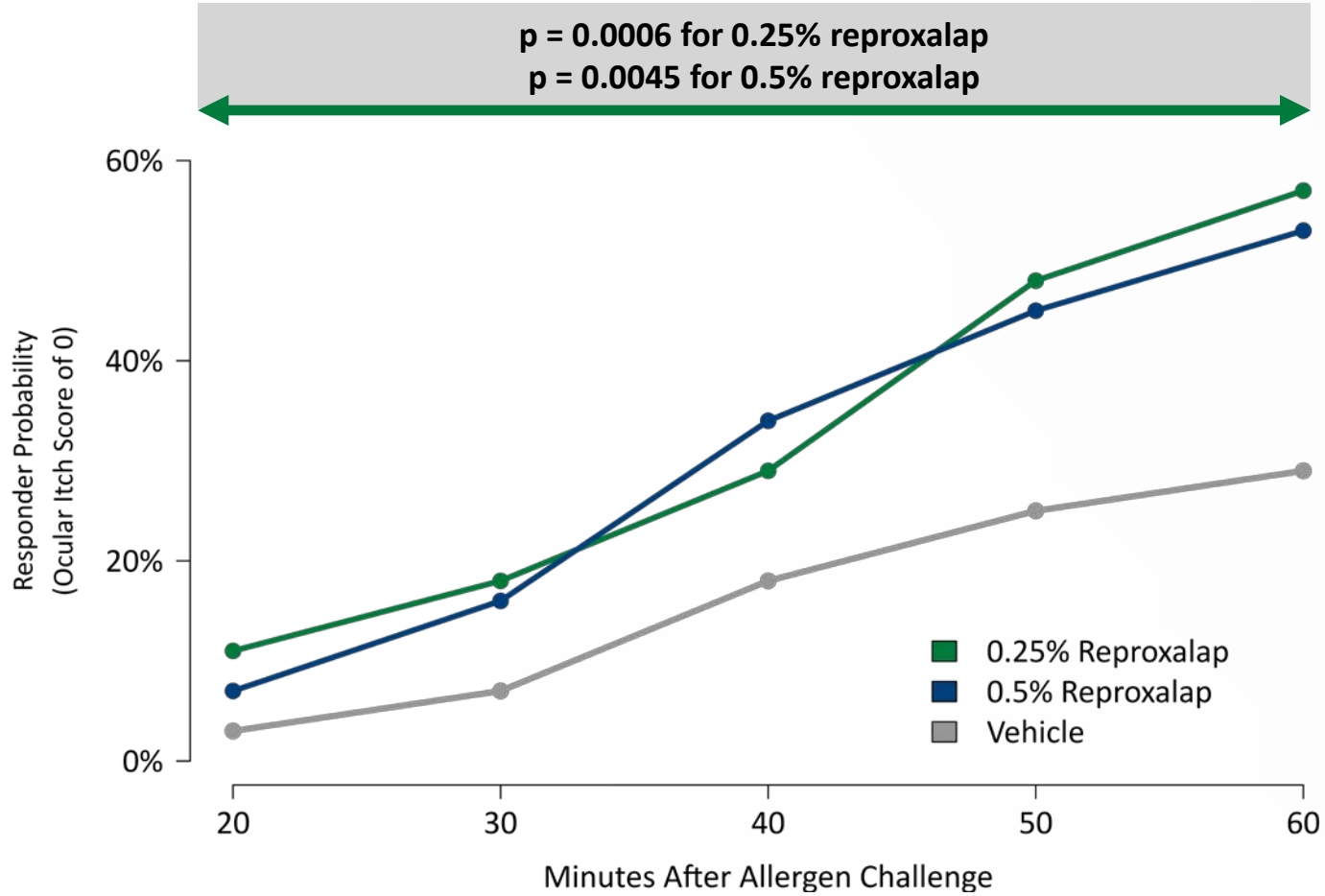



Clinically significant two-point improvement of ocular itch response rate with reproxalap statistically superior to vehicle, supporting the clinical relevance of the primary endpoint improvement

Generalized estimating equation analysis
Source: ALLEVIATE allergic conjunctivitis Phase 3 clinical trial results

# In ALLEVIATE, Reproxalap Was Statistically Superior to Vehicle in Achieving Complete Resolution of Ocular Itch

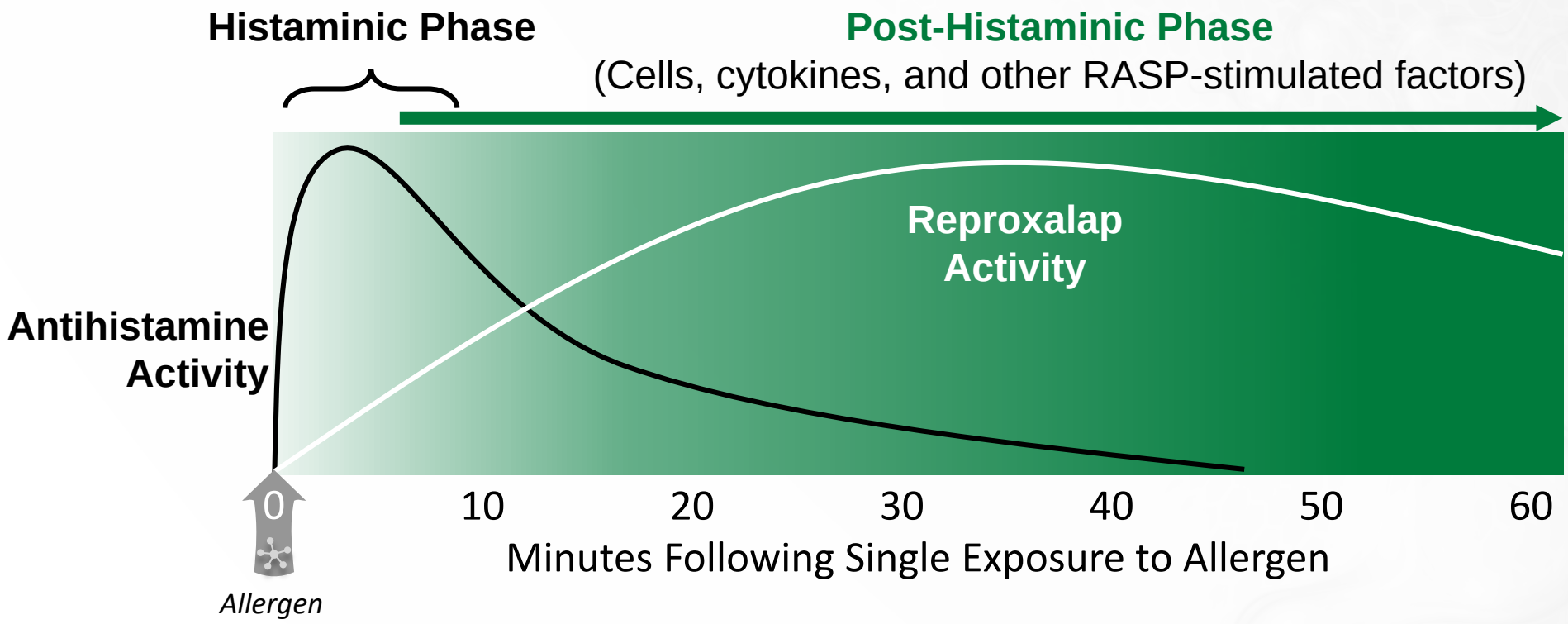
**Probability of Therapeutic Cure (Zero Itch) Post-Allergen Challenge:**




Complete resolution of ocular itch (zero itch score) response rate with reproxalap statistically superior to vehicle, confirming clinical relevance of drug-mediated improvement

Generalized estimating equation analysis
Source: ALLEVIATE allergic conjunctivitis Phase 3 clinical trial results

# 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

RASP = Reactive Aldehyde Species
Illustrative only, based on published literature and internal estimates

# Planned Phase 3 Allergic Conjunctivitis Program

- Remaining clinical requirements for potential New Drug Application submission expected to be confirmed H2 2019, following discussion with regulatory authorities
- Aldeyra is conducting clinical method development studies to assess the feasibility of measuring ocular itching following environmental exposure to allergen
  - Environmental (outdoor) exposure
  - Chamber (controlled environment) exposure
- Expected to advance 0.25% reproxalap
- 0.25% reproxalap is the same concentration in Phase 3 clinical program for dry eye disease, an underserved condition that is frequently co-morbid with allergic conjunctivitis

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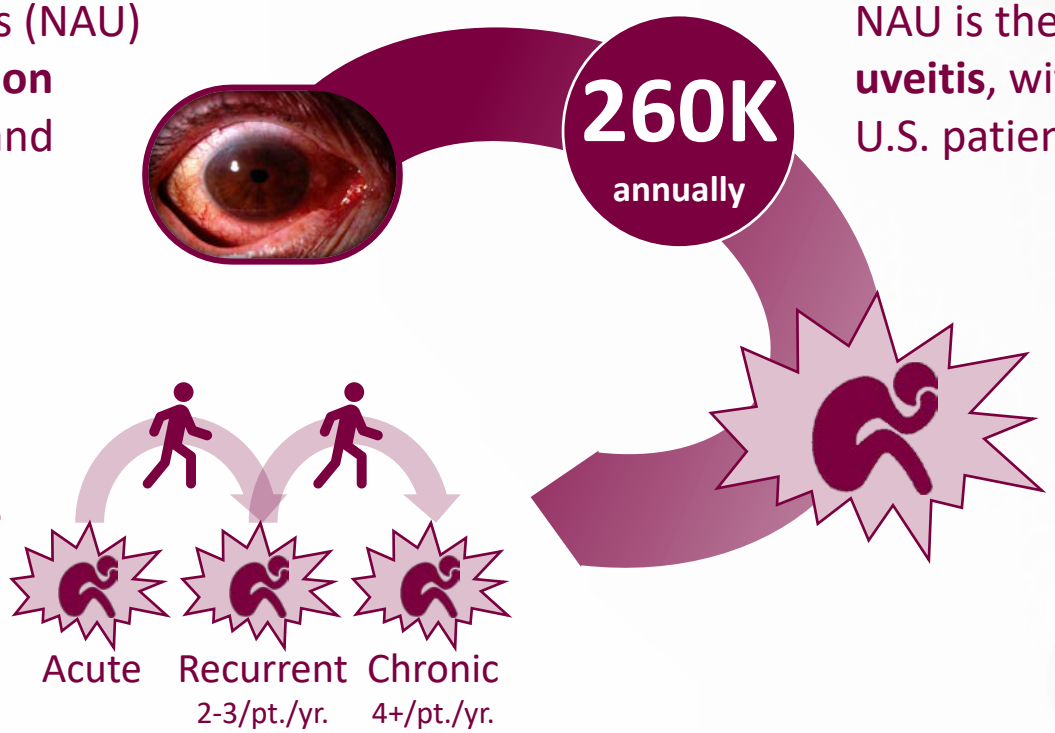
# Ocular Disease Area

- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Proliferative Vitreoretinopathy

# NAU: A Severe Ocular Inflammatory Disease

Disease Burden Overview

Noninfectious anterior uveitis (NAU) is a **severe ocular inflammation** causing **pain**, **photophobia**, and **vision loss**




NAU is the **most common form of uveitis**, with an estimated 260,000 U.S. patients per year

~50% of NAU patients have **recurrent or chronic conditions** requiring multiple interventions per year

NAU **dramatically impacts quality of life**, leading to loss of work and significant economic burden

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

# NAU: Significant Repeat Episodes and Steroid Toxicity Creates the Need for Novel Approaches

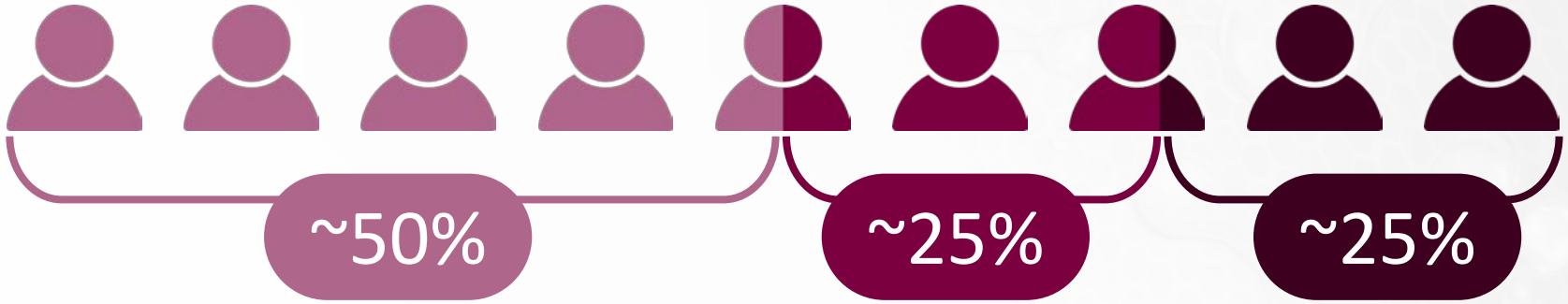
U.S. Estimates

**Prevalence:**
Approximately 260,000 noninfectious anterior uveitis (NAU) patients in the U.S.

**Corticosteroid treatment:**
8-12 times/day tapered over 4-6 weeks

**Prolonged corticosteroid usage increases risks of serious side effects**

**NAU episode frequency:**

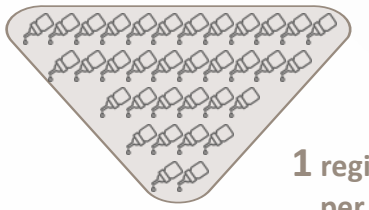



**Acute**
*Single flare within a year*

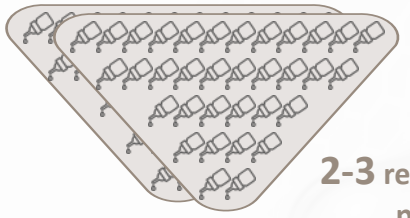
**Recurrent**
*Relapse 3-12 months after initial episode*

**Chronic**
*Relapse <3 months after initial episode*

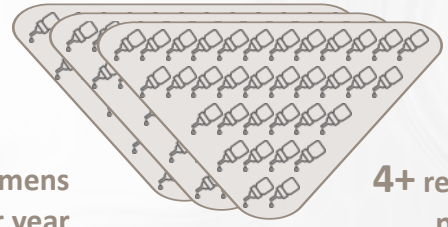
**Steroid use:**



**1** regimen per year



**2-3** regimens per year



**4+** regimens per year

**Safety risk:**

***4-6** weeks of treatment*

***8-12+** weeks of treatment*

***12-18+** wks. of treatment*

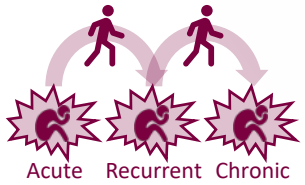
*Potential corticosteroid side-effects include glaucoma, cataracts, corneal ulceration, ptosis, delayed wound healing, and ocular infection*

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

NAU = Noninfectious anterior uveitis

# Reproxalap: A Unique and Novel Product Candidate for NAU

## NAU: A Serious Inflammatory Disease With Inadequate Current Therapy




~50% of noninfectious anterior uveitis (NAU) patients have **recurrent or chronic conditions** requiring multiple interventions per year


**Corticosteroids** are currently SOC and **require monitoring due to serious toxicities**

Prolonged usage may lead to **glaucoma**, **cataracts**, **corneal ulceration**, and other serious side effects

## A Unique Opportunity

### Reproxalap

- A **novel and differentiated** approach to treat NAU
- **Reduced anterior chamber cell count** in a Phase 2 clinical trial, and was **statistically non-inferior to corticosteroid treatment**
- **Safety and tolerability without intraocular pressure increase** in a Phase 2 clinical trial
- SOLACE Phase 3 clinical trial **results expected H2 2019**

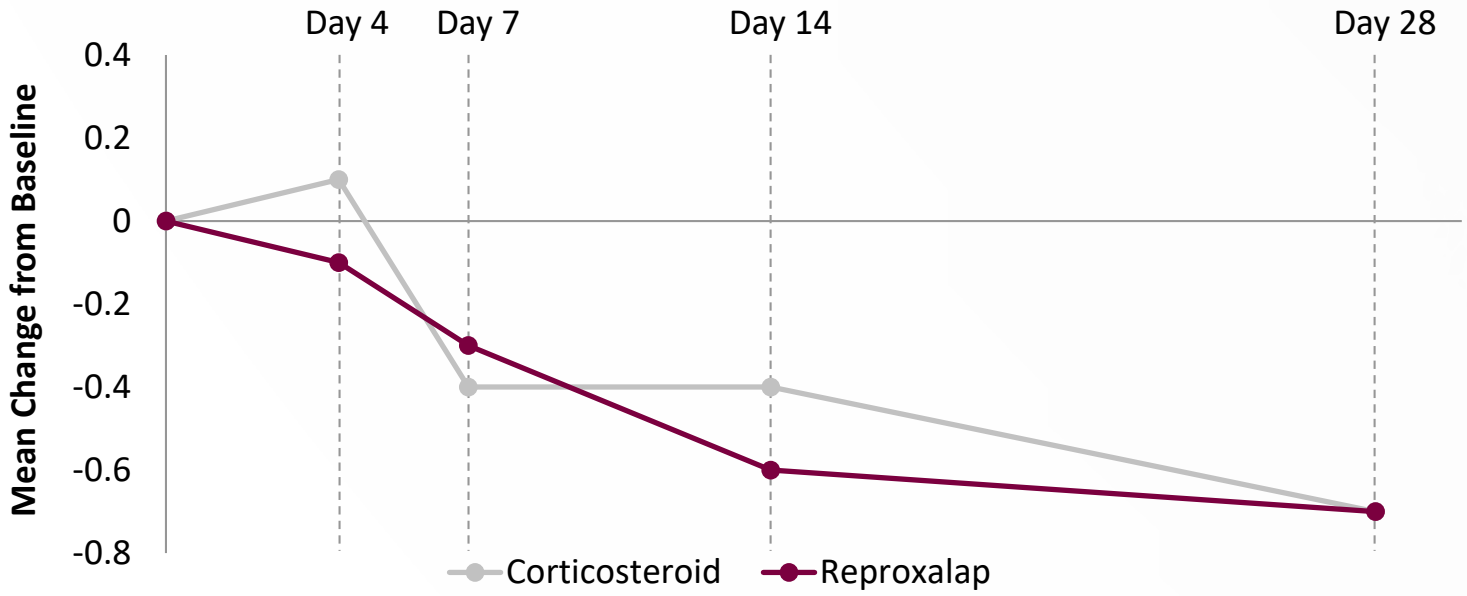
Source: Aldeyra internal estimates based on primary and secondary market research; published literature

NAU = Noninfectious anterior uveitis
SOC = Standard of Care

# Reproxalap Reduced Inflammation in Noninfectious Anterior Uveitis Phase 2 Clinical Trial

**Change from Baseline in Anterior Chamber Inflammatory Cell Grade over Time**

ITT Population with Last Observation Carried Forward




| Proportion Cured (Grade 0 = no inflammatory cells observed) | |
|---|---|
| Week 4 Grade 0 | Percent of Subjects |
| Reproxalap | 53% (8/15) |
| Corticosteroid | 38% (5/13) |

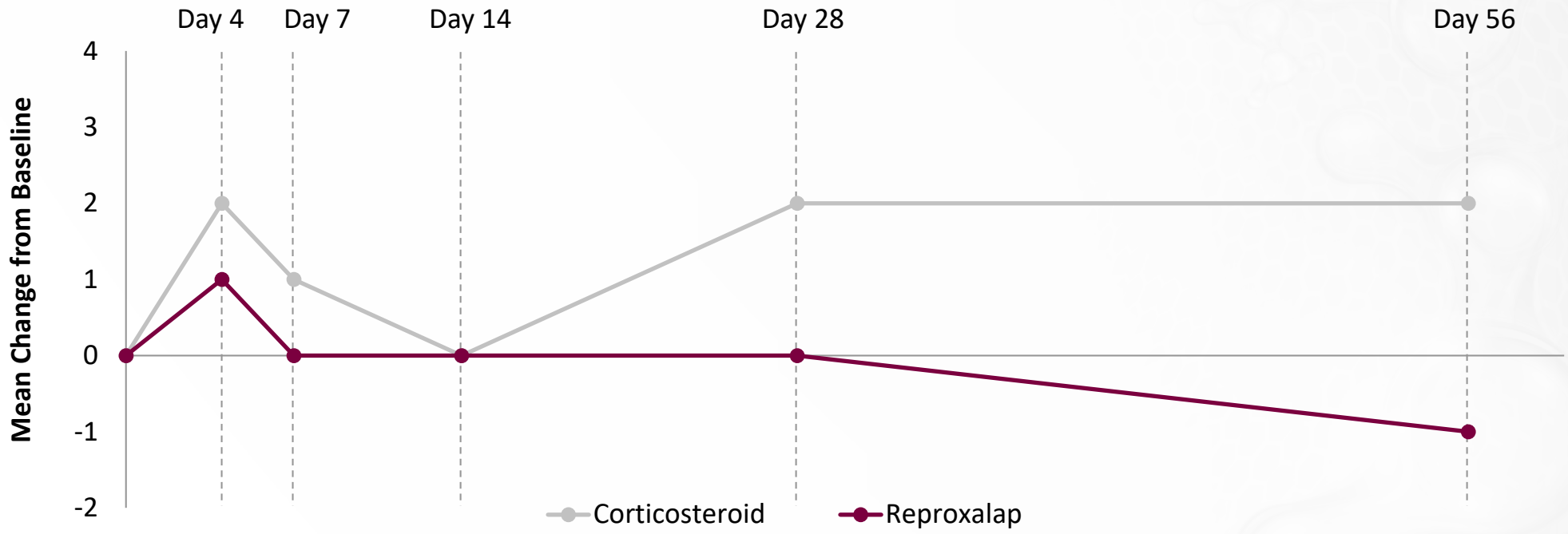
Reproxalap was statistically non-inferior to corticosteroid in a noninfectious anterior uveitis Phase 2 clinical trial.

Source: Reproxalap NAU Phase 2b clinical trial results

# Reproxalap Did Not Increase Intraocular Pressure in Noninfectious Anterior Uveitis Phase 2 Clinical Trial

**Change from Baseline in Intraocular Pressure (mmHg) over Time**

Safety Population



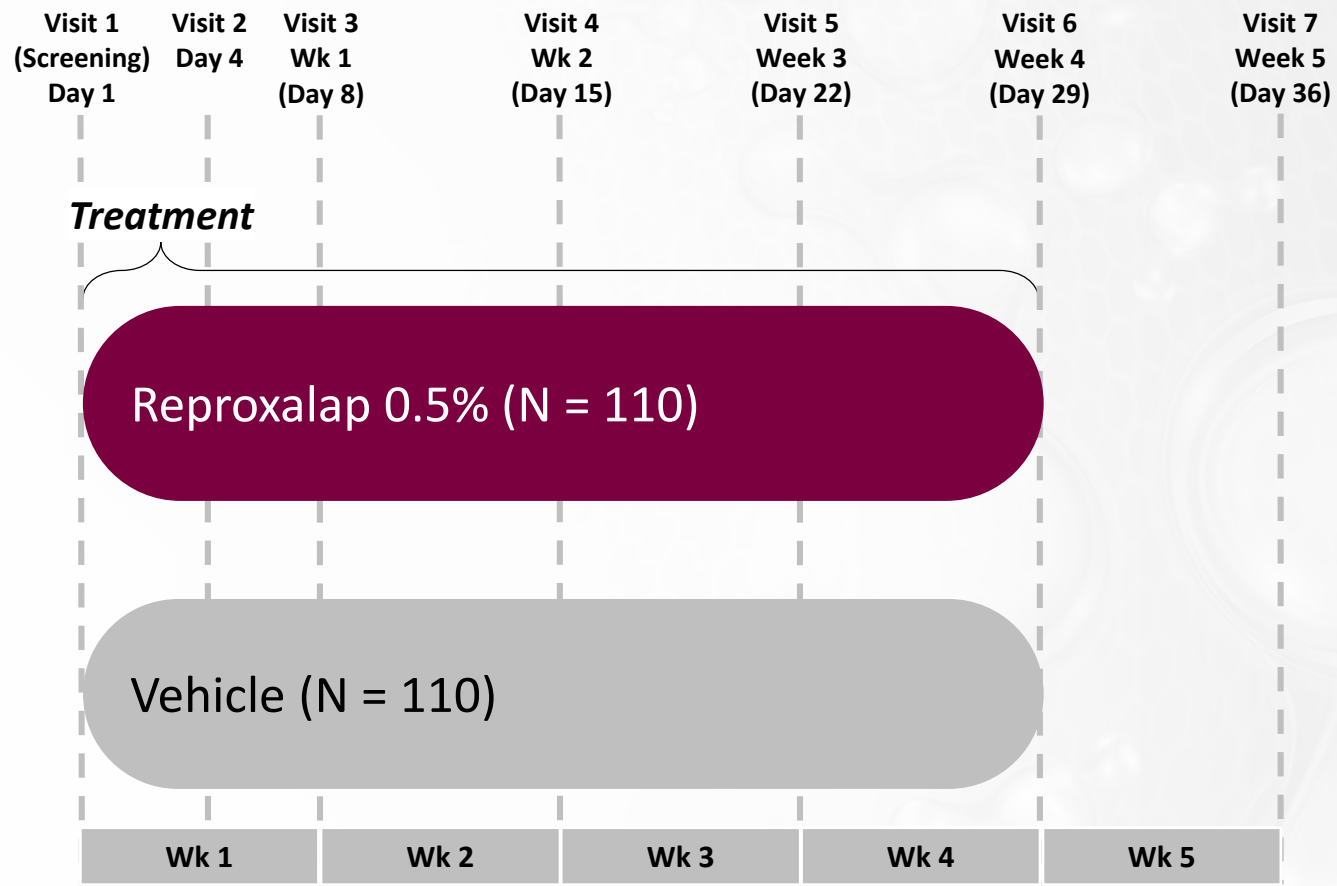

Increase in intraocular pressure, which may lead to glaucoma, is a major corticosteroid toxicity that is not apparent with reproxalap.

Source: Reproxalap NAU Phase 2b clinical trial results

# SOLACE Trial Design in Noninfectious Anterior Uveitis
## *Phase 3 Clinical Trial Initiated April 2017*

- **Primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solution (0.5%) on anterior chamber cell count (ACC) vs. vehicle
- **Inclusion highlights:**
  - Acute endogenous NAU with onset of symptoms within the previous 2 weeks
  - 6-50 ACC in the study eye
  - Intraocular pressure <21
- **Dosing regimen:**
  - Week 1 8x/day
  - Week 2 6x/day
  - Weeks 3-4 4x/day
  - Week 5 None
- **Endpoints:**
  - Time-to-cure (zero inflammatory cells in anterior chamber) without rescue
- **Results expected to be announced H2 2019**

**Phase 3 Noninfectious Anterior Uveitis Trial 1**




Further information can be found on www.clinicaltrials.gov: Trial #NCT03131154.

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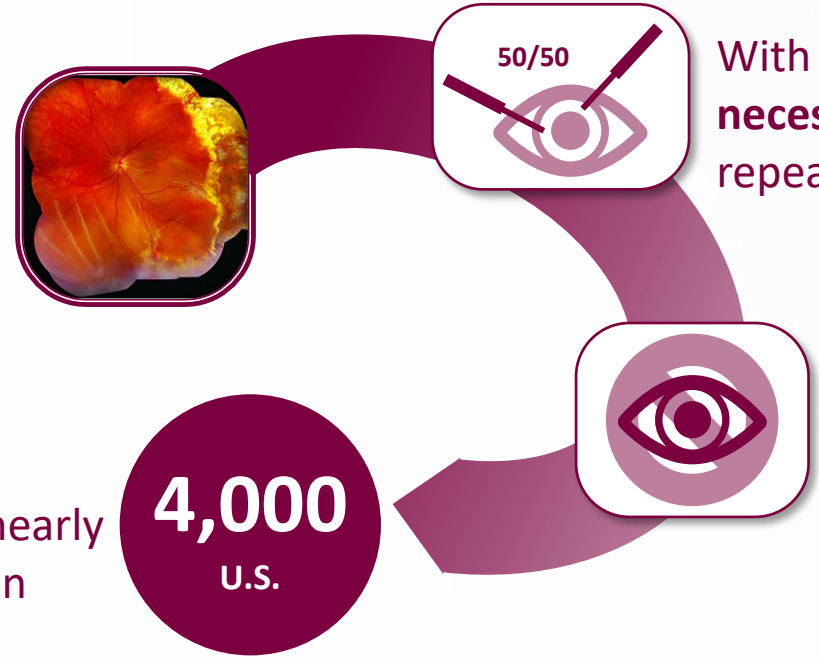
# Ocular Disease Area

- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Proliferative Vitreoretinopathy

# PVR: A Rare Sight-Threatening Retinal Disease

PVR is the **leading complication** of retinal detachment surgery and **prevents successful reattachment**




With no therapies available, PVR **necessitates repeat surgery** with a repeat surgery **failure rate of ~50%**

PVR is a **serious condition leading to permanent vision loss** in up to 75% of cases

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

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

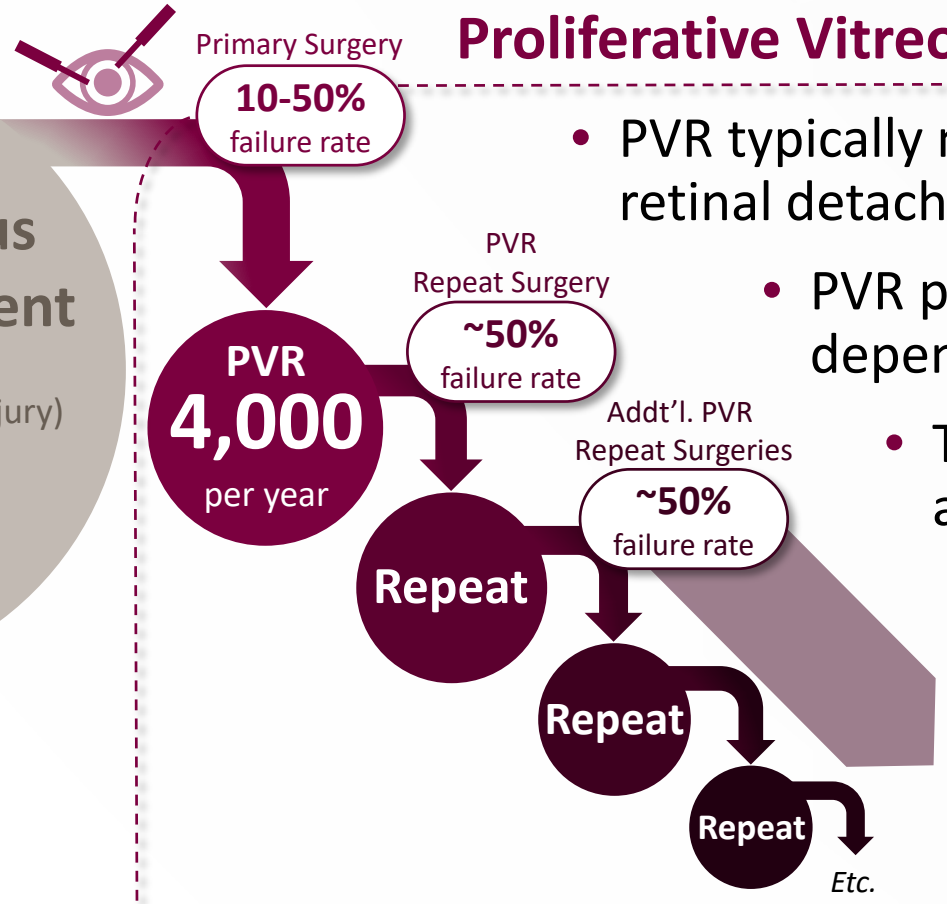
PVR = Proliferative vitreoretinopathy

# PVR: High Unmet Medical Need With No Approved Therapies

U.S. Estimates

**Rhegmatogenous Retinal Detachment**
- Non-traumatic
- Traumatic (open-globe injury)

**>28,000**
per year




## Proliferative Vitreoretinopathy

- PVR typically manifests 1-2 months after primary retinal detachment surgery
- PVR primary surgery failure rates vary depending on detachment etiology
- Today, PVR patients undergo 3-to-4 additional surgeries on average
- Vision and quality of life decreases with each procedure
- No FDA-approved therapy

**Novel Approaches Needed**

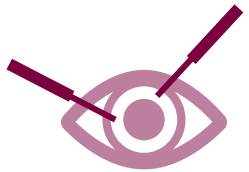
Source: Aldeyra internal estimates based on primary and secondary market research; published literature

# ADX-2191: A Unique Approach and Novel Product Candidate for PVR

## PVR: A Sight-Threatening Disease

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

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



**Repeat surgery and** subsequent **vision loss** currently the only possible course of action

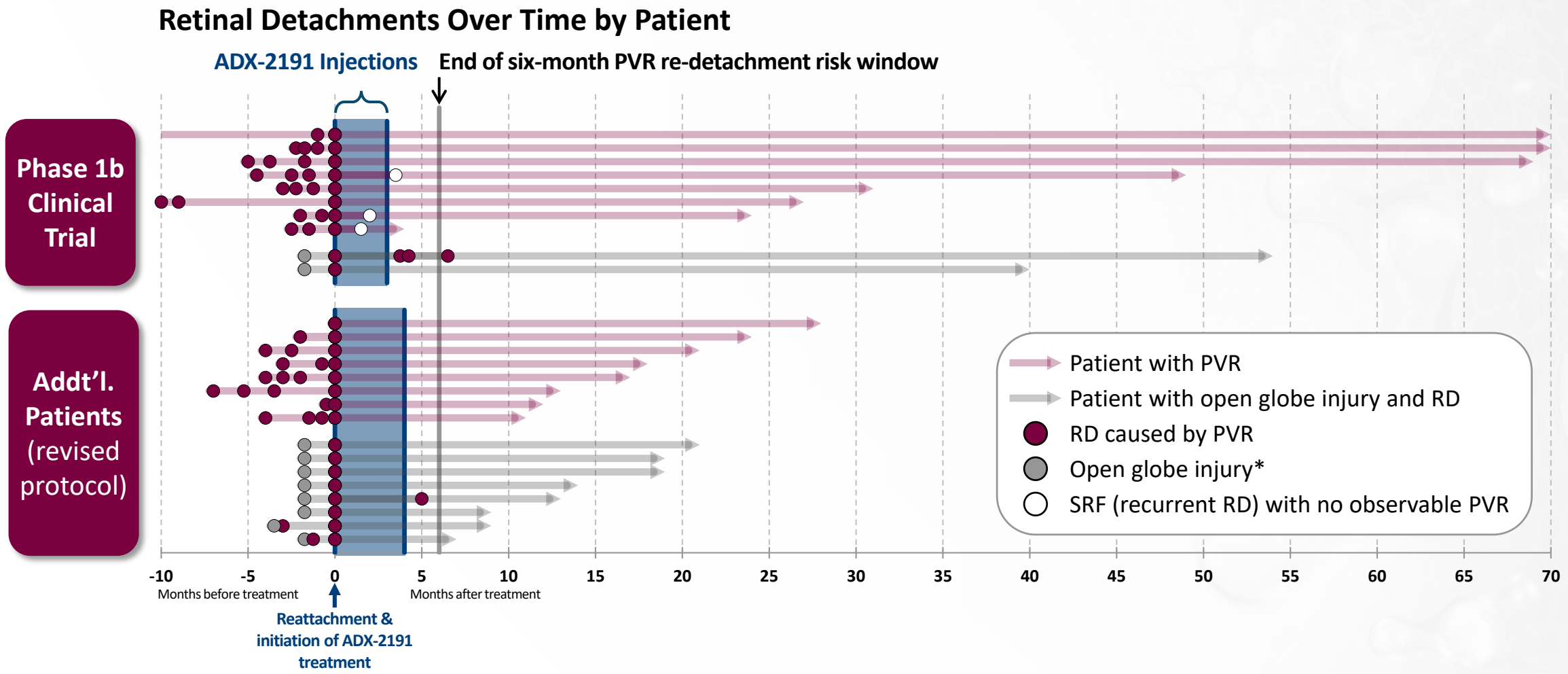
## A Unique Opportunity

### ADX-2191

- A **novel approach and potential therapeutic breakthrough** in PVR treatment
- **Granted U.S. orphan designation**
- **Tolerability and reattachment success** during study period **demonstrated in Phase 1b** open-label investigator sponsored clinical trial
- Adaptive Phase 3 clinical trial **expected to initiate H2 2019**

PVR = Proliferative vitreoretinopathy

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




*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 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

# Favorable ADX-2191 Recurrent Retinal Detachment Reduction vs. Standard of Care Observed in Phase 1b Investigator Sponsored Clinical Trial and in Additional In-Practice Use

Revised protocol expected to be used in Phase 3 clinical trial program

**Patients with at least one retinal detachment due to any cause by protocol and vs. standard of care**
(% and #)

| | PVR Patients | | Open Globe Injury Patients | | All Patients | |
|---|---|---|---|---|---|---|
| **ADX-2191** | | | | | | |
| Phase 1b protocol | 38% | (3/8) | 50% | (1/2) | 40% | (4/10) |
| Revised protocol | 0% | (0/8) | 13% | (1/8) | 6% | (1/16) |
| **Combined** | **19%** | **(3/16)** | **20%** | **(2/10)** | **19%** | **(5/26)** |
| Standard of Care* | 54% | | 47% | | 51% | |

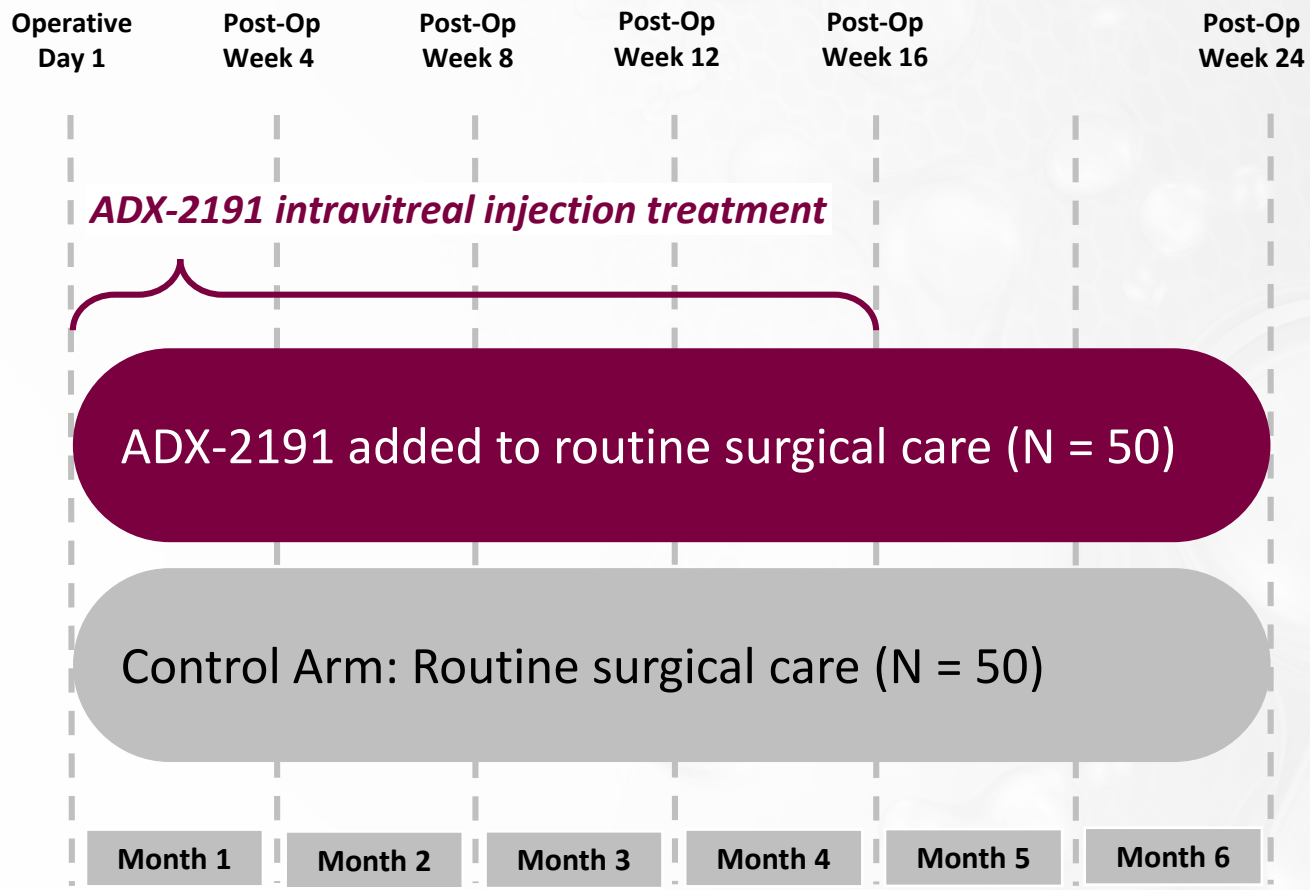
*Banerjee, PJ. (2017). Slow-Release Dexamethasone in Proliferative Vitreoretinopathy: A Prospective, Randomized Controlled Clinical Trial. Ophthalmology, 757–767. Eliott, D. (2016). Smoking is a risk factor for proliferative vitreoretinopathy after traumatic retinal detachment. Retina (Philadelphia), 1229-1235.
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 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

# ADX-2191: Adaptive Phase 3 (Part 1) Proliferative Vitreoretinopathy 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, non-masked, randomized, controlled, two-part, adaptive Phase 3 clinical trial
- **Inclusion highlights:**
  - Recurrent retinal detachment due to PVR, or
  - Retinal detachment associated with open-globe trauma
- **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**




OCT = Optical Coherence Tomography
*Contingent on funding, regulatory review, and other factors

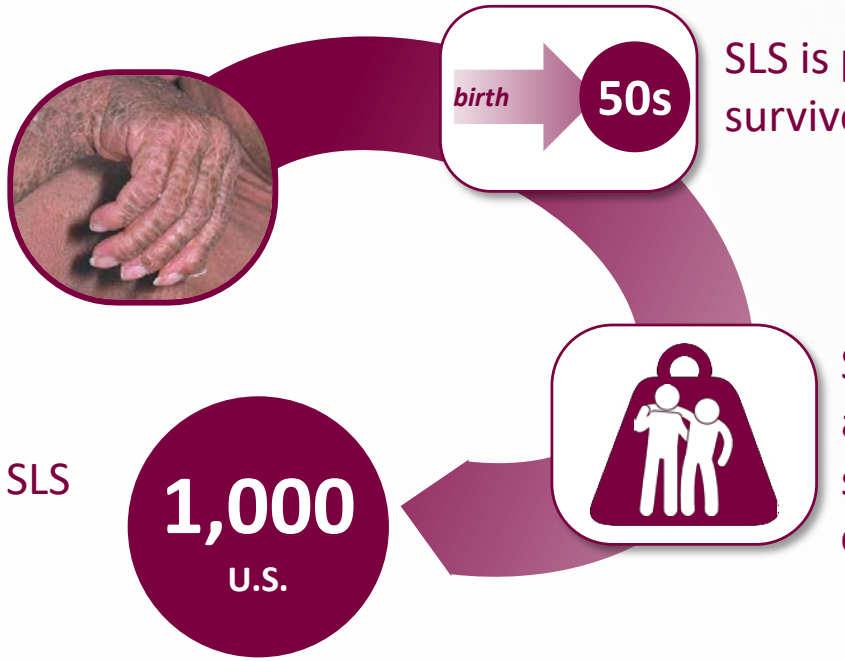
ALDEYRA THERAPEUTICS™

# Systemic Disease Area

- Sjögren-Larsson Syndrome

# SLS: A Rare Disease With no Approved Therapy

SLS is **caused by an enzyme mutation** (Fatty Aldehyde Dehydrogenase), leading to high levels of RASP




SLS is **present at birth** and patients survive into their 50s

Severe skin scaling, retinal disease, and neurological disorders significantly impact **SLS patient and caregiver quality of life**

SLS is a **rare disease**, with ~1,000 SLS patients in the U.S. and a greater number in Europe

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

RASP = Reactive Aldehyde Species
SLS = Sjögren-Larsson Syndrome

# Severe Skin Scaling Diminishes Quality of Life for SLS Patients and Caregivers

## Severe Skin Scaling

Ichthyosis is the **primary dermatologic symptom** and is present in **all SLS patients** with rare exception

SLS ichthyosis is usually present at birth, is **moderate-to-severe**, and **stabilizes within the first 1-2 years of life**

SLS ichthyosis **confirmed by enzymatic and genetic testing**

## Impact on SLS Patients

- Experience **extreme and relentless itching**
- Hours devoted to skin-care to manage **painful scaling**
- Often **unable to care for themselves**
- Dead **skin can putrefy** and emit a foul odor

*"The bathing process requires **multiple cycles of soap and water**– once to remove the previous day's lotion, and further scrubbing to remove the excess skin."*

## Impact on SLS Caregivers

- Provide **24/7 monitoring** and manage frequent doctor visits
- Provide **extended bathing** routines over multiple hours daily
- **Often cannot work** due to the amount of time needed to care for the SLS patient

*"Cutaneous symptoms of SLS require **constant attention**. For this reason, parents and caregivers often perceive the **ichthyosis as the most obvious and time-consuming symptom of SLS**."*

Source: Aldeyra primary market research and published literature

SLS = Sjögren-Larsson Syndrome

# Reproxalap: A Unique Approach and Novel Product Candidate for SLS

## SLS: An Inborn Error of Metabolism

Severe symptoms significantly impacts **SLS patient and caregiver quality of life**


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


**Nonstop disease burden prevents normal patient/caregiver life**, with hours devoted to managing painful scaling, monitoring, & care

## A Unique Opportunity

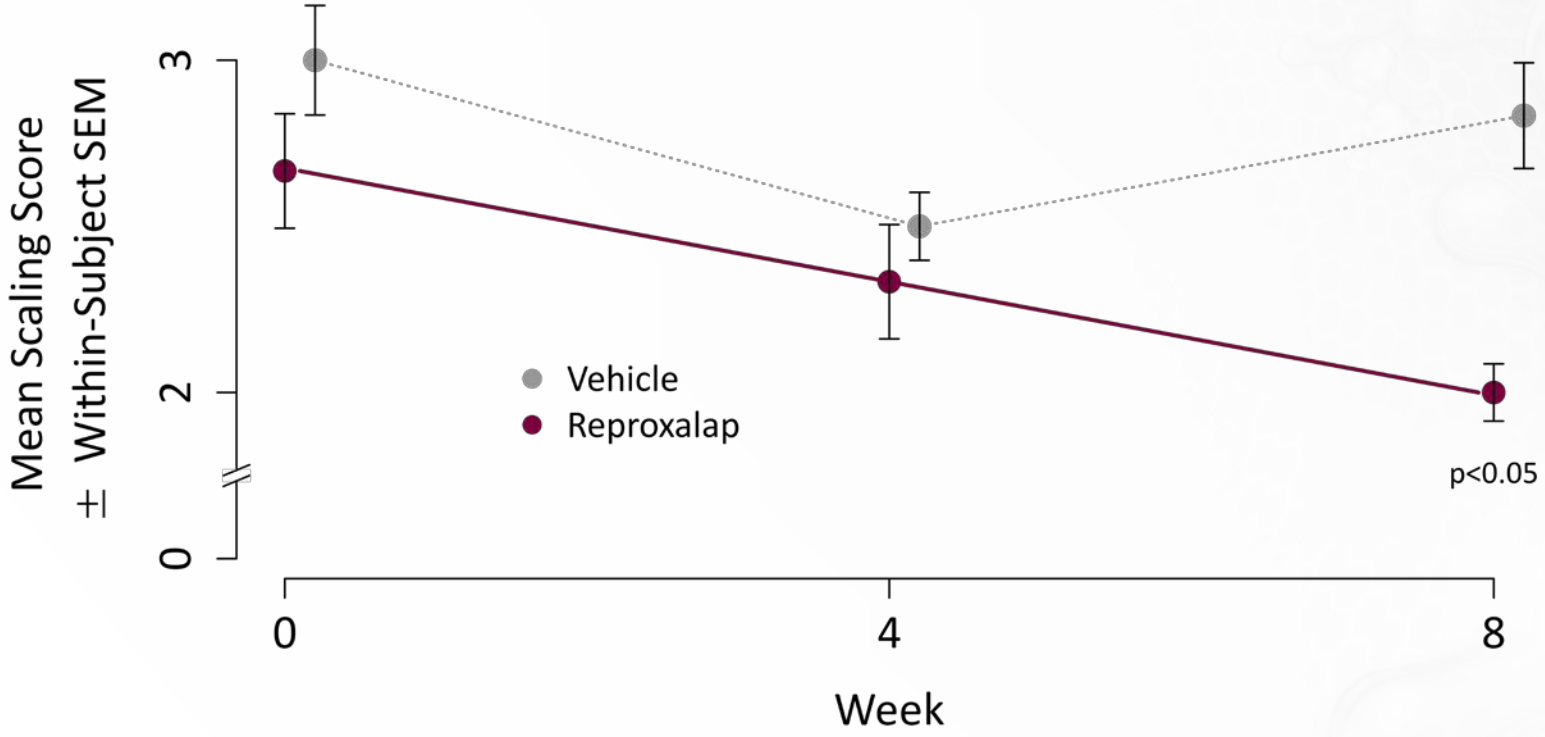
### Reproxalap

- A **novel approach and potential lifelong therapy** to replace missing enzymatic activity in SLS
- **Granted U.S. orphan designation**
- **Significantly reduced SLS ichthyosis** in a randomized, vehicle-controlled Phase 2 clinical trial
- RESET Part 1 Phase 3 clinical trial **results expected 2019**

SLS = Sjögren-Larsson Syndrome

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

**Investigator Assessment of Ichthyosis (0-4)**

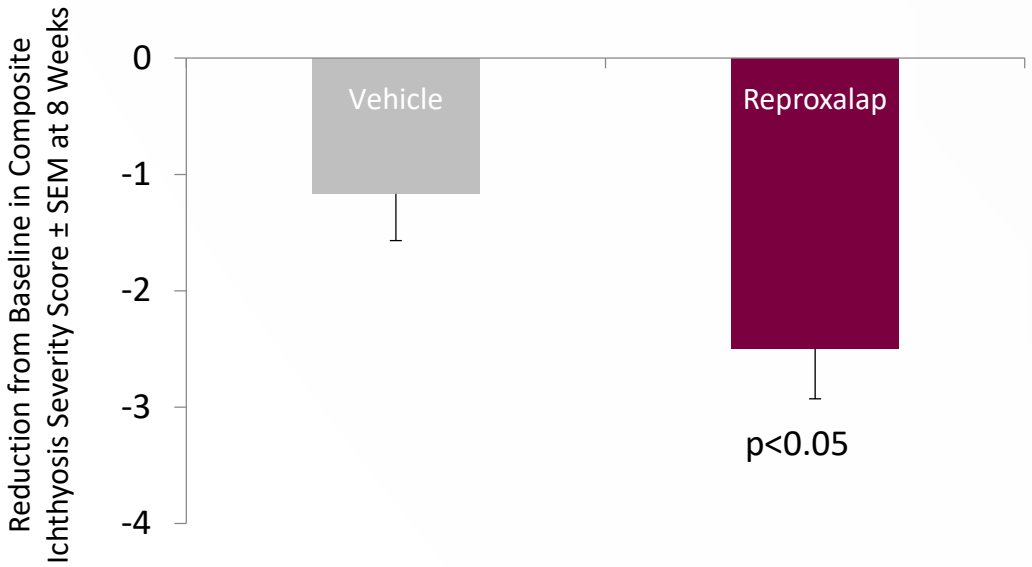


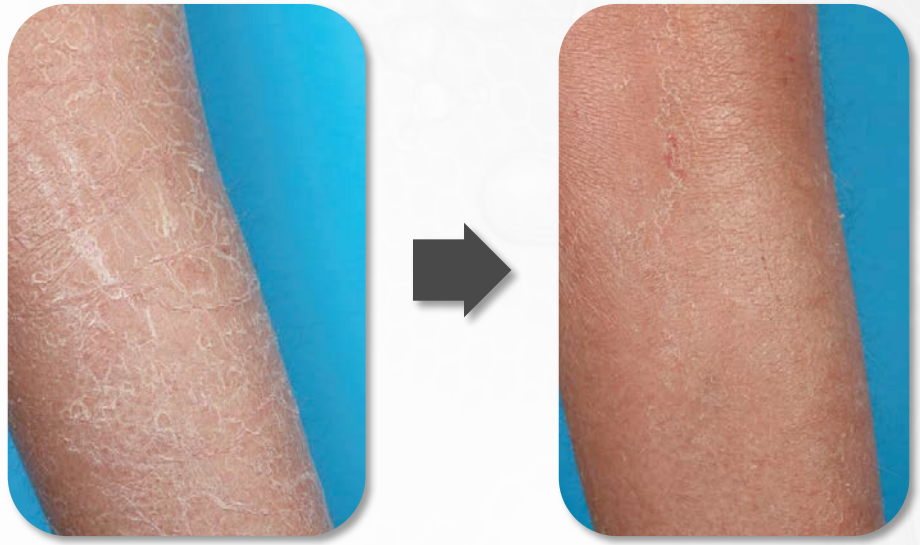

Over two months of treatment, ichthyosis improved consistently from moderate to mild disease.

Source: Reproxalap SLS Phase 2 clinical trial results (6 patients per arm)

# Ichthyosis Improved In Reproxalap-Treated Patients in Phase 2 Clinical Trial

**Central Reader Digital Photography Assessment**



***Before Treatment (Week 0)***

***After Treatment (Week 8)***

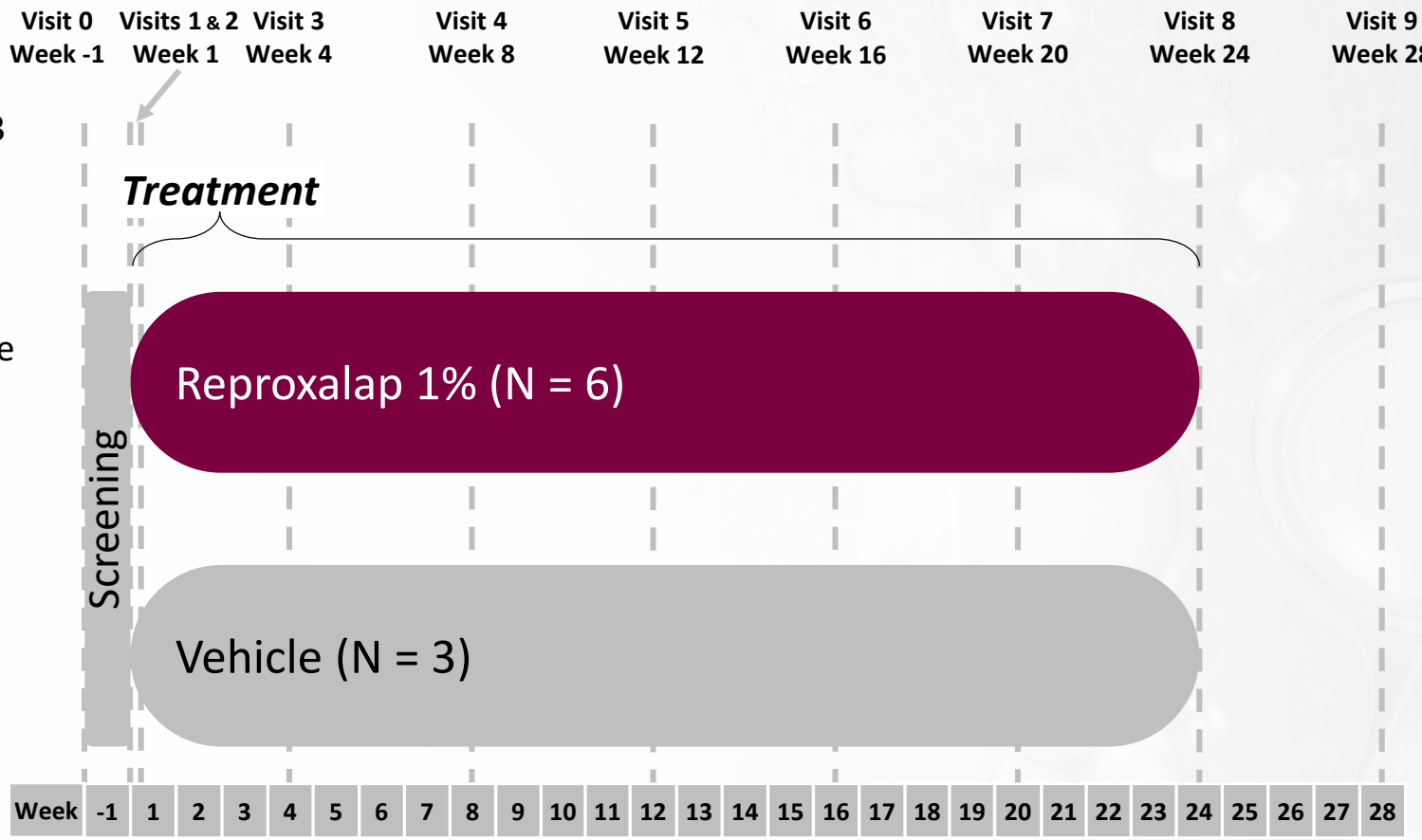
Reproxalap improved Ichthyosis Severity Score to a greater degree than vehicle.

Improvement in reproxalap treated patients was clinically meaningful.

# RESET Trial Design in Sjögren-Larsson Syndrome
## *Phase 3 Part 1 Clinical Trial Initiated July 2018*

- **Primary objective:**
  - Evaluate efficacy of reproxalap topical dermal cream (1%) for the treatment of SLS associated ichthyosis
- **Inclusion/exclusion highlights:**
  - Genetically confirmed diagnosis of SLS and at least 3 years of age or older
  - Active ichthyosis grade of 2 or higher on the VIIS scaling score
  - No systemic or topical retinoids or other topical medications with in the past 30 days prior to baseline visit 1
- **Dosing regimen:**
  - Weeks 1-12: 20% of Body Surface Area (BSA)
  - Weeks 13-20: 40-45% of BSA
  - Weeks 21-24: 90% of BSA
- **Endpoints:**
  - Baseline ichthyosis change in drug-treated subjects
  - Safety / tolerability
- **Results expected to be announced H2 2019**

**Phase 3 SLS-Ichthyosis Study: Part 1**




Further information can be found on www.clinicaltrials.gov: Trial #NCT03445650.

ALDEYRA THERAPEUTICS™

# Building The Future

# Our Investment Case


**Deep and Innovative Pipeline** focused on immune-mediated diseases

**Near-Term Development Catalysts** support path to commercialization

**Solid Track Record** of development success

**Large Market Potential** of late-stage pipeline

**Solid Cash Position**

Cash, cash equivalents and marketable securities were $93.6 million as of December 31, 2018

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

Pfizer gsk
WILSON THERAPEUTICS[3]

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

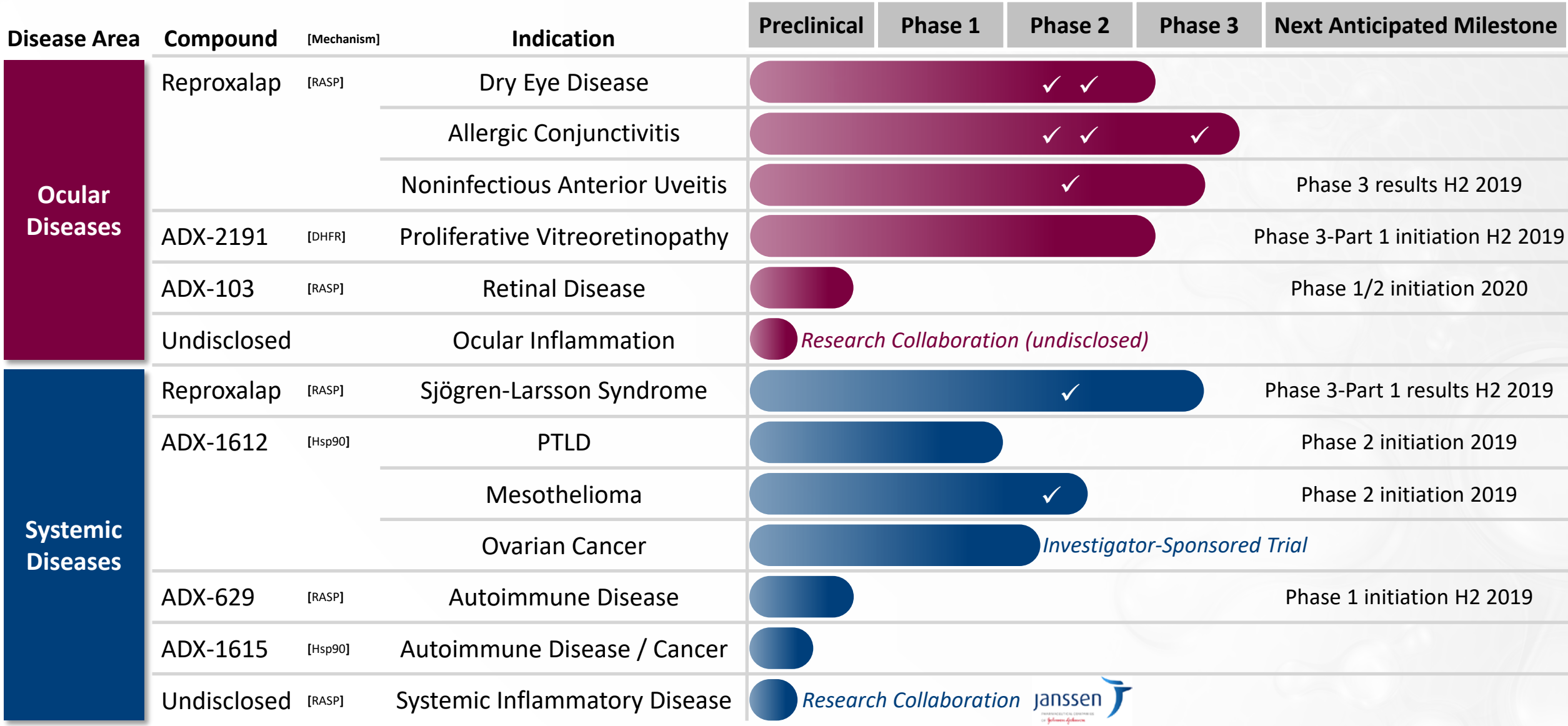
Shire gsk
NOVARTIS

## Board of Directors

| | |
|---|---|
| **Richard Douglas**, Ph.D. CHAIRMAN | Former SVP Corporate Development at Genzyme |
| **Ben Bronstein**, M.D. | Former CEO Peptimmune[4] |
| **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 Genzyme

# Deep and Innovative Pipeline Focused on Immune-Mediated Diseases




RASP = Reactive Aldehyde Species Inhibitor
DHFR = Dihydrofolate Reductase Inhibitor
Hsp90 = Heat Shock Protein 90 Inhibitor
PTLD = Post-Transplant Lymphoproliferative Disorder

✓ = Positive Phase 2/3 clinical trial data reported in 2016-2019
Trial initiations contingent on funding, regulatory review, and other factors

ALDEYRA THERAPEUTICS™

# Expected Development Milestones:* Novel Approaches to Address Immune-Mediated Disease

## Ocular Diseases: Anticipated Milestones

- ✓ **Positive** reproxalap **ALLEVIATE Phase 3 clinical trial results March 2019**
- ✓ Reproxalap dry eye disease **Phase 3 clinical trial program initiation April 2019**
- ○ Reproxalap noninfectious anterior uveitis SOLACE Phase 3 clinical trial **results H2 2019**
- ○ ADX-2191 Proliferative Vitreoretinopathy **Phase 3 clinical program initiation H2 2019**
- New **Remaining clinical requirements** for potential New Drug Application to be **confirmed H2 2019**

## Systemic Diseases: Anticipated Milestones

- ○ Reproxalap Sjögren-Larsson Syndrome RESET Phase 3 - Part 1 clinical trial **results H2 2019**
- ○ ADX-629 **Phase 1 clinical trial initiation H2 2019** followed by NASH and/or IBD Phase 2a
- ○ ADX-1612 post-transplant lymphoproliferative disorder **Phase 2 clinical trial initiation 2019**
- ○ ADX-1612 mesothelioma **Phase 2 clinical trial initiation 2019**

*Contingent on funding, regulatory review, clinical results and other factors

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**Three**

Mechanisms of action in development

**Eight**

Successful Phase 2/3 Clinical Trials 2016-2019

**Five**

Phase 3 Clinical Programs Ongoing or Expected to Initiate

Phase 2/3 count includes mesothelioma investigator-sponsored trial; Phase 3 trials contingent on funding, regulatory review, and other factors.