



# Corporate Review

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August 2018

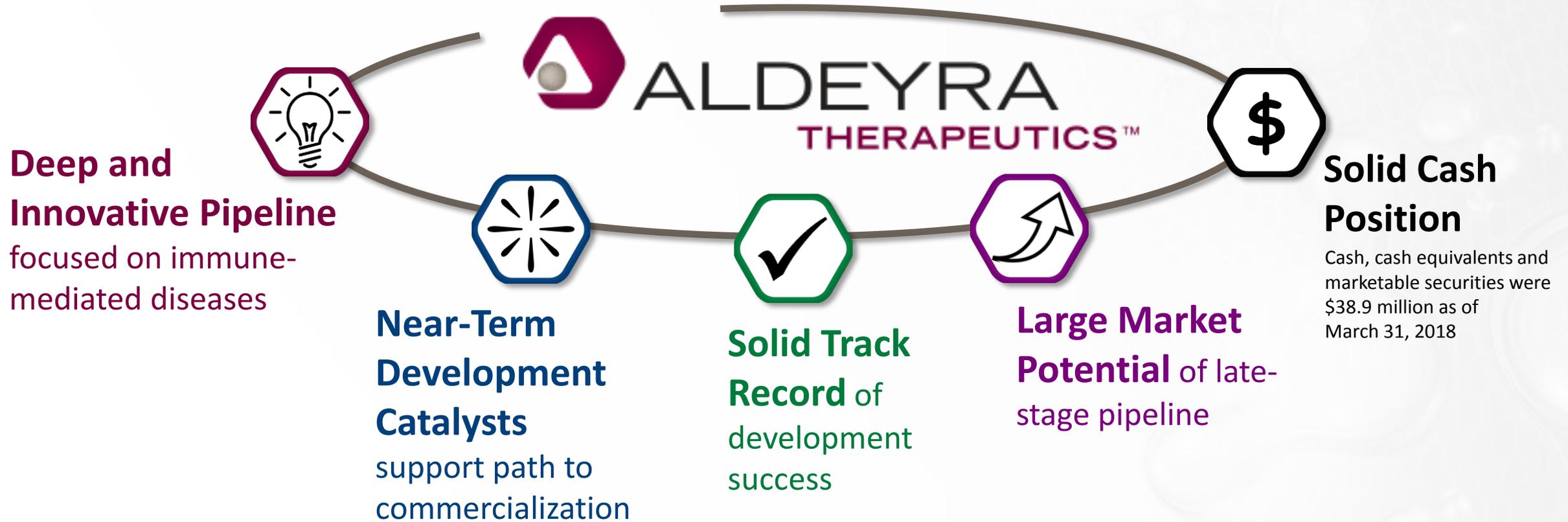
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# Developing Next-Generation Medicines to Improve the Lives of Patients with Immune-Mediated Diseases



## Our Mission

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



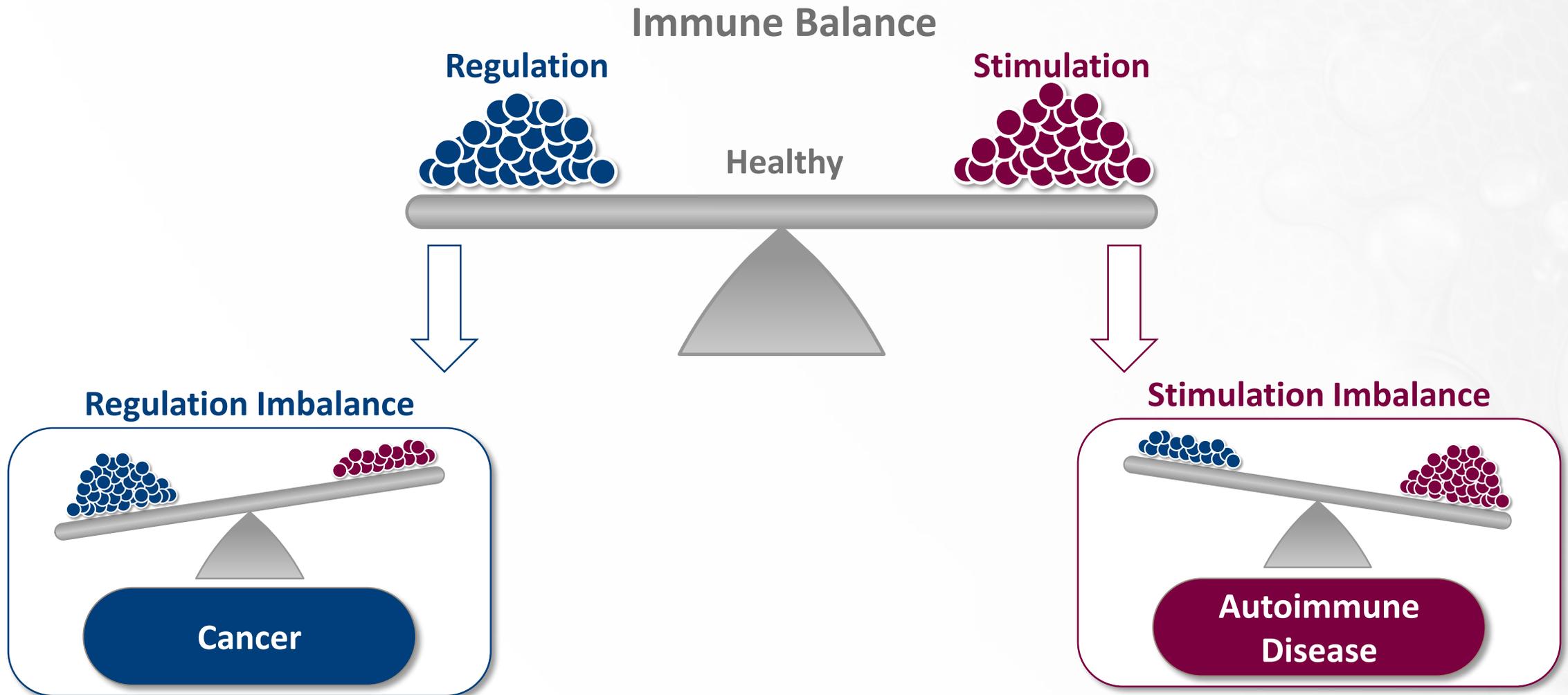
Suffer from some form of **immune-mediated disease**



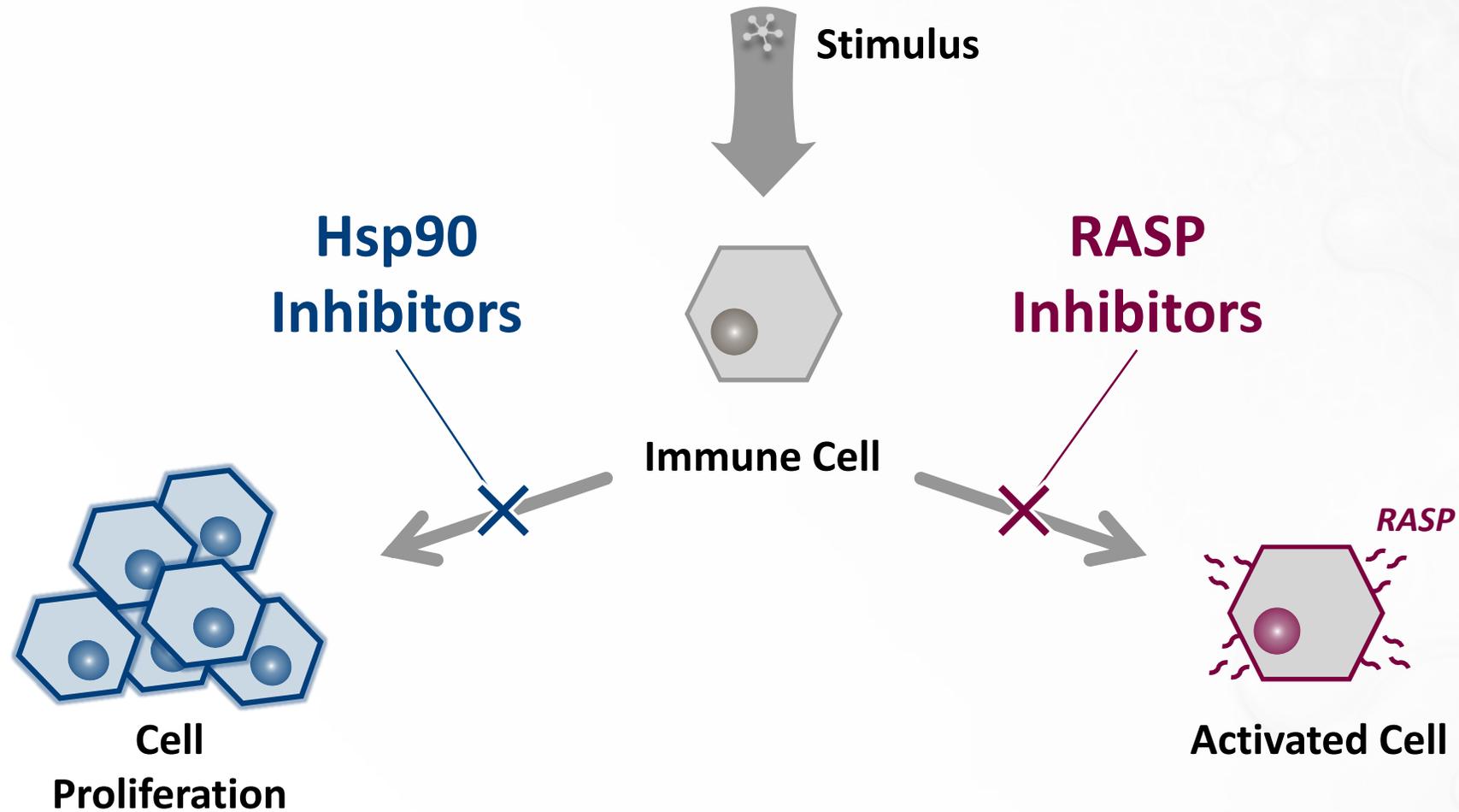
Disease control elusive despite existing therapies, and thus **novel approaches are needed**

Source: 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 Disease



# Novel Approaches to Address Immune-Mediated Disease



RASP = Reactive Aldehydes Species

# Deep and Innovative Pipeline

Mechanism	Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Expected Milestone
RASP Inhibitors	Reproxalap Ocular	Dry Eye Disease	✓				Phase 2b results H2-2018
		Allergic Conjunctivitis	✓ ✓				Phase 3 results H2-2018 / 2019
		Noninfectious Anterior Uveitis	✓				Phase 3 results 2019
	Reproxalap Dermal	Sjögren-Larsson Syndrome	✓				Phase 3, Part 1 results 2019
	ADX-629 Systemic	Autoimmune Disease					
	ADX-103	Retinal Disease					
	Not Disclosed	Systemic Inflammatory Disease					
Hsp90 Inhibitors	ADX-1612	PTLD					
		Ovarian Cancer					<i>Investigator Sponsored Trial</i>
		Mesothelioma					<i>Investigator Sponsored Trial</i> Phase 2 results H2-2018
	ADX-1615	Autoimmune Disease					
			Cancer				
Anti-Inflammatory	Not Disclosed	Ocular Inflammation					

RASP = Reactive Aldehydes Species  
 PTLD = Post-Transplant Lymphoproliferative Disorder

✓ = Positive Phase 2 clinical data reported in 2016 – 2017

# Reproxalap: Our Lead Product Candidate

## Potential Benefits Over Standard of Care Across Four Indications

	Reproxalap Development Stage	Current Standard of Care	Potential Reproxalap Competitive Advantages†	
 <p><i>Ocular Inflammation</i></p>	Dry Eye Disease	Phase 2b	Xiidra®, Restasis®	Rapid onset, broader activity
	Allergic Conjunctivitis	Phase 3	Antihistamines	Non-drying, durable activity; Responder superiority vs. vehicle
	Noninfectious Anterior Uveitis	Phase 3	Corticosteroids	No expected risk of glaucoma or other corticosteroid toxicities
 <p><i>Inborn Errors of Metabolism</i></p>	Sjögren-Larsson Syndrome	Phase 3	Bathing, Moisturizers	Clinically demonstrated efficacy; 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.

# Reproxalap: Target Therapies with Significant Market Potential

## Market and Commercialization Potential

	Estimated U.S. Population*	Healthcare Providers	Commercial Build-out	Pricing Benchmarks <sup>†</sup>
 <b>Ocular Inflammation</b> <b>Dry Eye Disease</b>	20 million	Ophthalmologists and Optometrists	Internal Sales Force or Partner	↑ \$500 or greater per course ↓
	30 million	Ophthalmologists and Optometrists	Internal Sales Force or Partner	
	150,000	Anterior Segment Ophthalmologists (~30 Centers)	Internal Sales Force or Partner	
 <b>Inborn Errors of Metabolism</b> <b>Sjögren-Larsson Syndrome</b>	1,000 <sup>‡</sup>	Pediatric Geneticists, Tertiary Care Dermatologists	Internal Sales Force or Partner	\$200,000 - \$400,000 per year

\*Aldeyra estimates based on internal market research and publicly available information.

<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.

<sup>‡</sup>Extrapolated from a Swedish estimate and a U.S. genetic mutation analysis, it is generally assumed that there are approximately 1,000 Sjögren-Larsson Syndrome (SLS) patients in the United States and a greater number of SLS patients in Europe.

# Reproxalap: Meta-Analysis Strongly Supports Drug Activity



**Reproxalap Has  
Multiple Successful  
Phase 2 Trials**

Dry Eye Disease

Phase 2a Reproxalap (0.1%)

Allergic Conjunctivitis

Phase 2b Reproxalap (0.5%)

Noninfectious Anterior Uveitis

Phase 2 Reproxalap (0.5%)

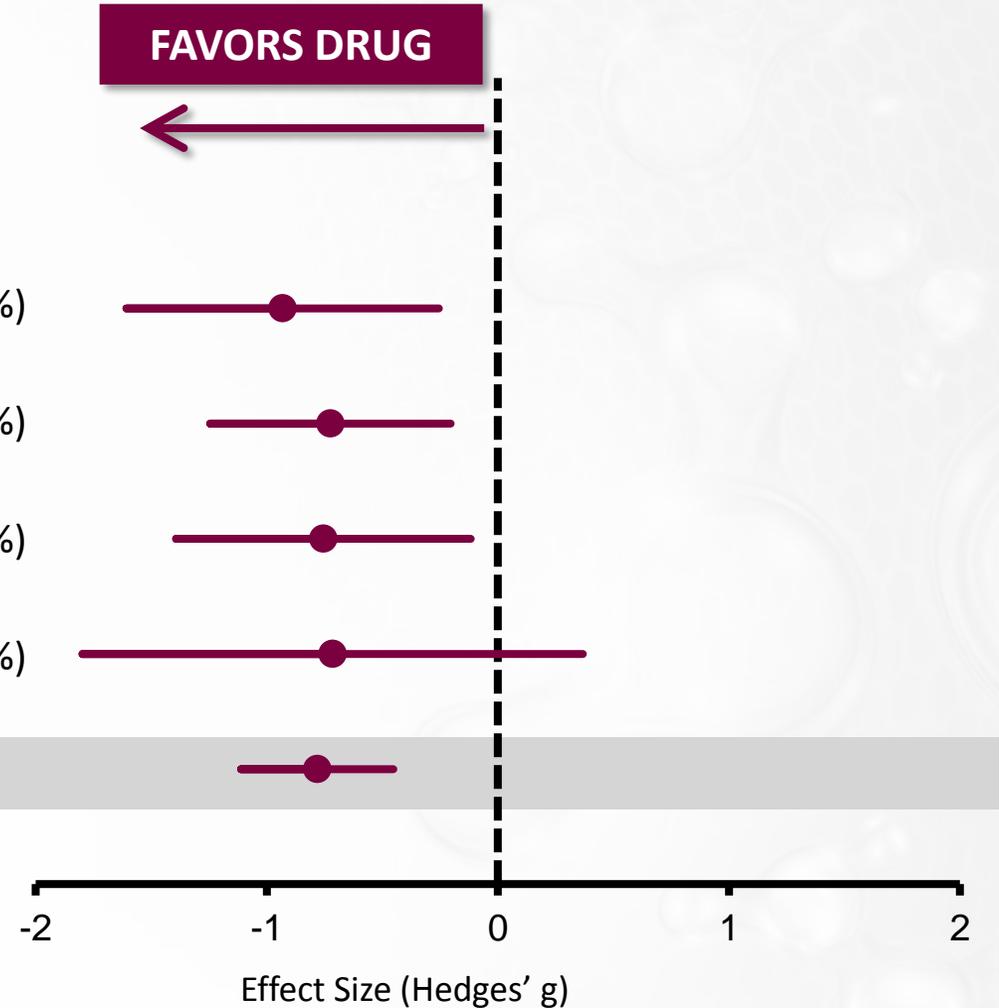
Sjögren-Larsson Syndrome

Phase 2 Reproxalap (1.0%)

**COMBINED**

*p* < 0.0001

**FAVORS DRUG**



Bars represent 95% confidence intervals. Between-group comparisons used where placebo (allergic conjunctivitis) or active control (noninfectious anterior uveitis), otherwise within-group comparisons used (dry eye disease); dry eye disease results based on ocular discomfort symptom score.

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



## Reproxalap: Ocular Inflammation

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- Dry Eye Disease
- Allergic Conjunctivitis
- Noninfectious Anterior Uveitis

# Dry Eye Disease: A Chronic Disease with Inadequate Therapy

## Large Disease Burden

**20**  
million

# of **adults in the U.S.** estimated to suffer from Dry Eye Disease (DED)



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

Age 50+  
**>3x**

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



DED can significantly effect vision-related **quality of life**

## Inadequate Current Therapy

**Restasis®**

**2017 Sales: \$1.5 billion**

- Only a subset of patients respond favorably
- May take up to six weeks or longer to have an effect

**Xiidra®** (launched 2016)

**2017 Sales: \$259 million**

- Up to 25% of users experience eye irritation or discomfort and an associated bad taste

## A Unique Opportunity

**Reproxalap**

- A **novel and differentiated approach** to treat DED
- **Rapid Improvement of multiple signs and symptoms** observed in patients with DED in a Phase 2a clinical trial
- Phase 2b **results expected H2 2018**

Sources: "Dry Eyes" by R. M. Shtein, MD; [www.uptodate.com](http://www.uptodate.com), May 2018; Farrand et al; American Journal of Ophthalmology 90:98, 2017; Allergan 10K and Shire 10K; Aldeyra research.

# Reproxalap Improved Numerous Dry Eye Disease Signs and Symptoms in Phase 2a Clinical Trial

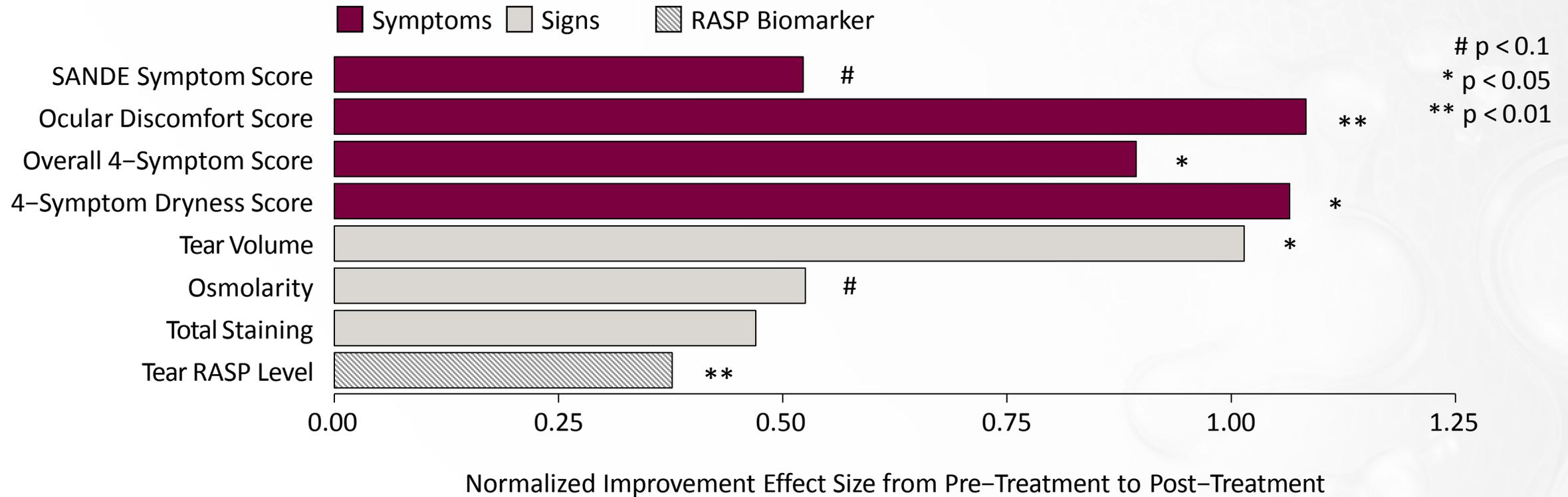
		Endpoint (Pooled Data)	Pre-Treatment*	Post-Treatment*	p value
Symptoms	}	Symptom Assessment in Dry Eye (SANDE) Score (0-100)	61	52	0.003
		Ocular Discomfort Score (0-4)	2.3	1.5	0.00002
		Overall 4-Symptom Score (0-4)	2.6	2.0	0.0004
Signs	}	Tear Volume (Schirmer Test)	5.6 mm	8.3 mm	0.008
		Osmolarity	304 mOsm/L	294 mOsm/L	0.003
		Total Staining (Lissamine Green) (0-20)	5.2	4.3	0.002

After one month of therapy, multiple signs and symptoms of dry eye disease improved, a broad and rapid therapeutic response.

\*Pre-Treatment = Day 0; Post-Treatment = Day 28; units are subject reported scores unless otherwise indicated.

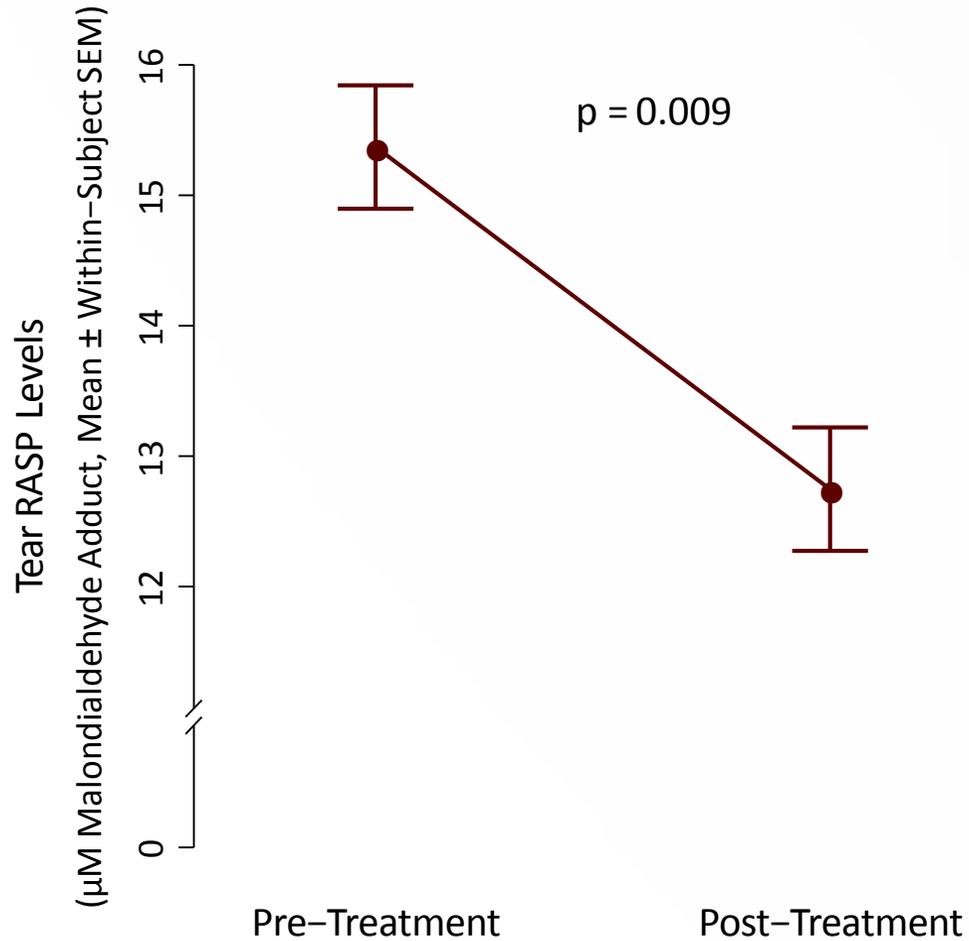
# Improvement Effect Sizes Were Robust and Statistically Significant in Phase 2a Clinical Trial

## 0.1% Reproxalap Improvement Effect Size Across Dry Eye Disease Signs and Symptoms

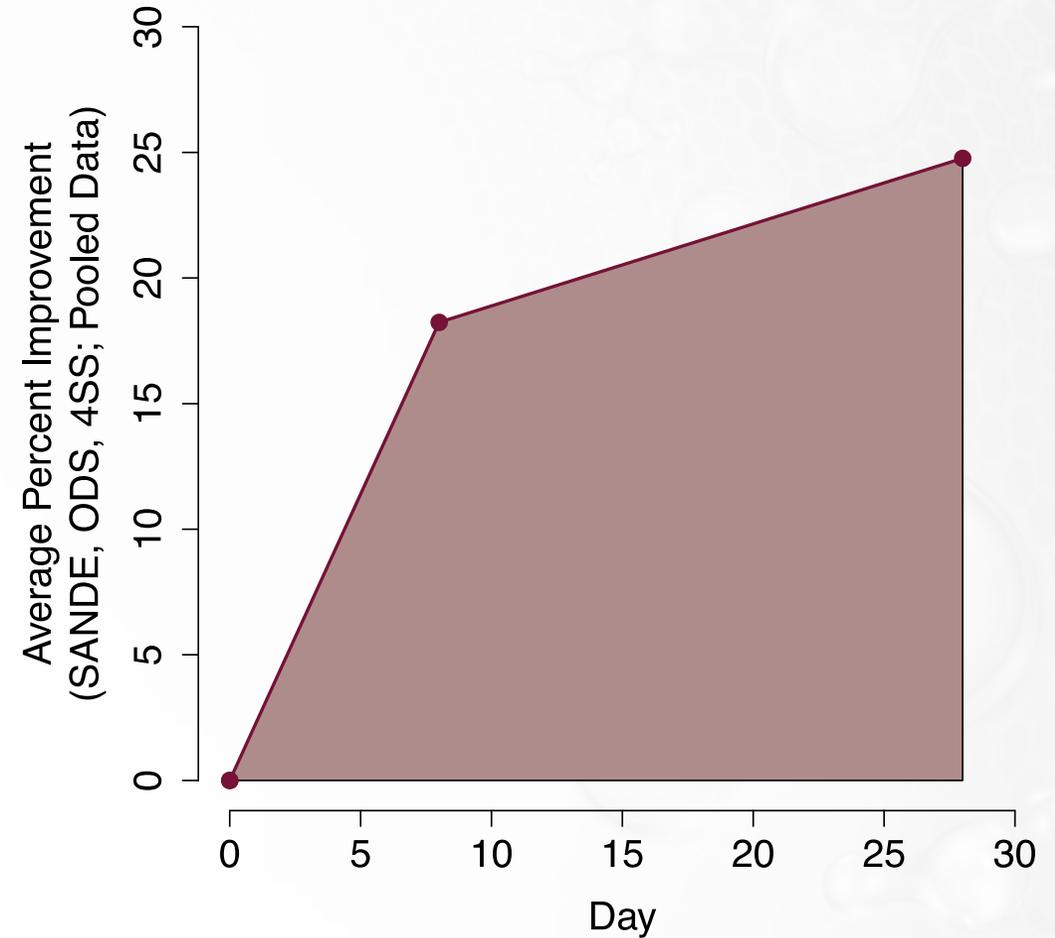


RASP = Reactive Aldehydes Species  
 Effect size = Mean difference from Day 0 to Day 28 / Standard Deviation of Day 0.

# Drug Activity in Phase 2a Clinical Trial Supported by Biomarker Reduction and Increased Efficacy Over Time



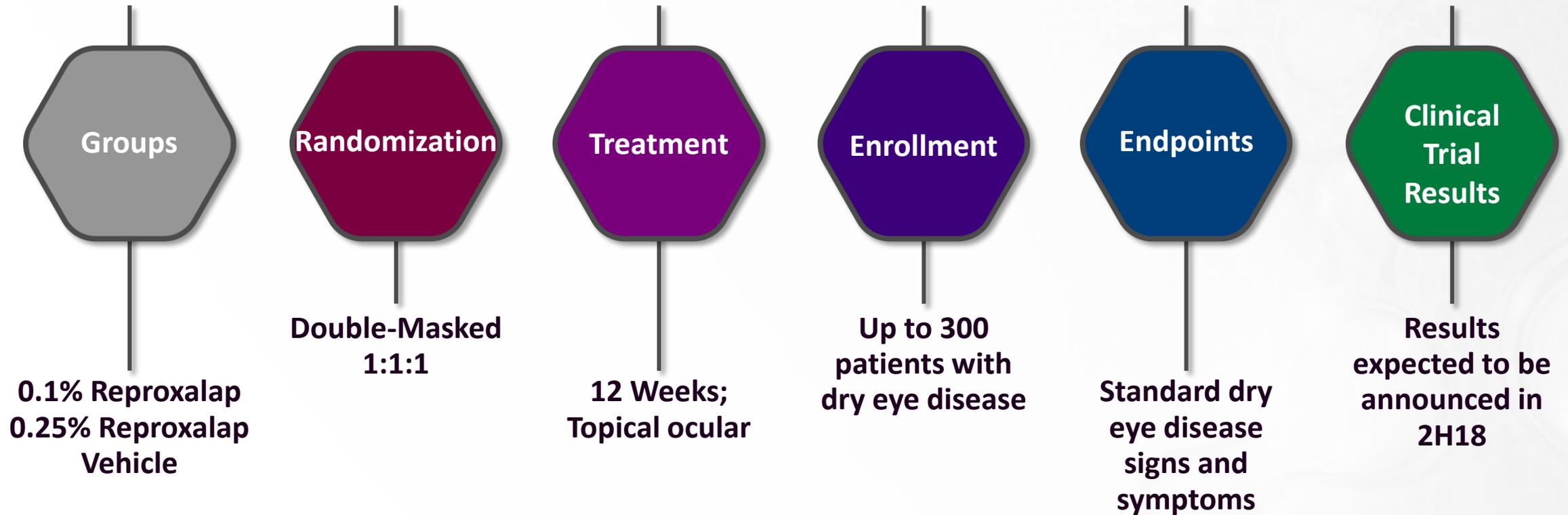
RASP = Reactive Aldehydes Species  
Pre-Treatment = Day 0, Post-Treatment = Day 28.



SANDE=Symptom Assessment in Dry Eye Score, ODS=Ocular Discomfort Score,  
4SS=Overall 4-Symptom Score

# Dry Eye Disease Phase 2b Clinical Trial Design

*Initiated January 2018*



Further information can be found on [www.clinicaltrials.gov](http://www.clinicaltrials.gov): Trial #NCT03404115.

# Allergic Conjunctivitis: A Common Disease with Unmet Medical Need

## Large Disease Burden

**20%**  
globally

20% or more of people globally suffer from allergic conjunctivitis (AC) annually, and prevalence is increasing



AC can cause persistently disturbing symptoms **acutely, seasonally, and perennially**



**Comorbidities with AC are common**, including ocular conditions such as dry eye disease



AC may limit patient **quality of life**, affecting daily activities and psychosocial relations

## Unmet Medical Need

**24%**

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

**2%**

• Approximately 2% of AC patients have **severe conditions** and may be **steroid-dependent**

## A Unique Opportunity

### Reproxalap

- A **novel and differentiated approach** to treat AC
- **Mitigated post-histaminic allergy** at levels statistically superior to control in two Phase 2 clinical trials
- Phase 3 **results expected H2 2018 or early 2019**

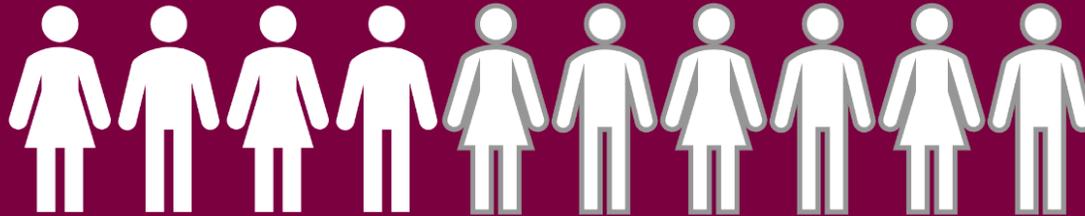
Sources: "Allergic Conjunctivitis" by Hemran et al; [www.uptodate.com](http://www.uptodate.com), Dec. 2017; Sanchez et al; J Investig Allergol Clin Immunol Suppl. 2: 1-19, 2011; Leonardi et al, Clinical & Experimental Allergy, 45, 1118, 2015; Abelson et al, Allergy Clin Immunol 115:118, 2005; Aldeyra 2017 US physician market research.

# Allergic Conjunctivitis and Dry Eye Disease are Related, and Comorbidity is Common

## 2011 Study of Allergic Conjunctivitis and Dry Eye Syndrome

Clinically significant  
“itch” AND “dryness”

*“DES and AC are usually regarded as 2 separate entities. Differential diagnosis is difficult because the signs and symptoms as demonstrated in this study are very similar.”*



Patients with clinically significant itch

58%  
Have dryness

45%  
Have itch

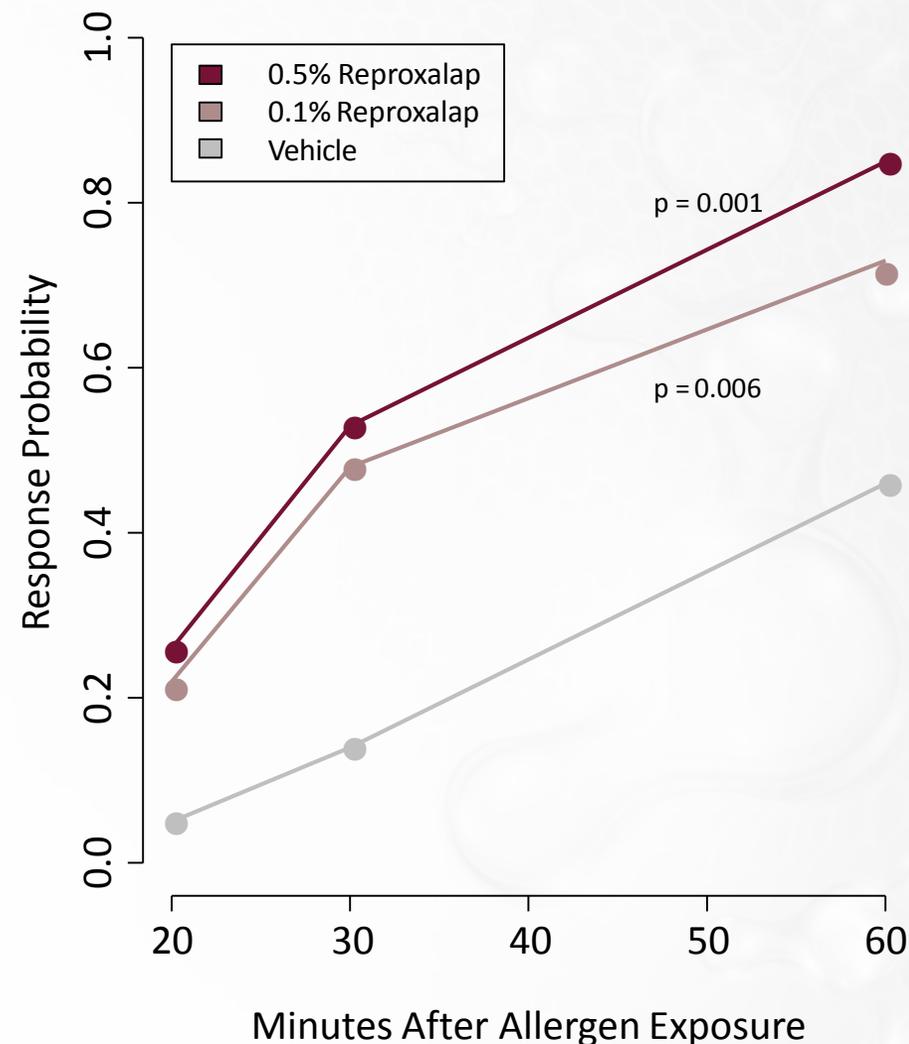
Patients with clinically significant dryness



Source: M.M. Hom et al. / Ann Allergy Asthma Immunol 108 (2012) 163–166.

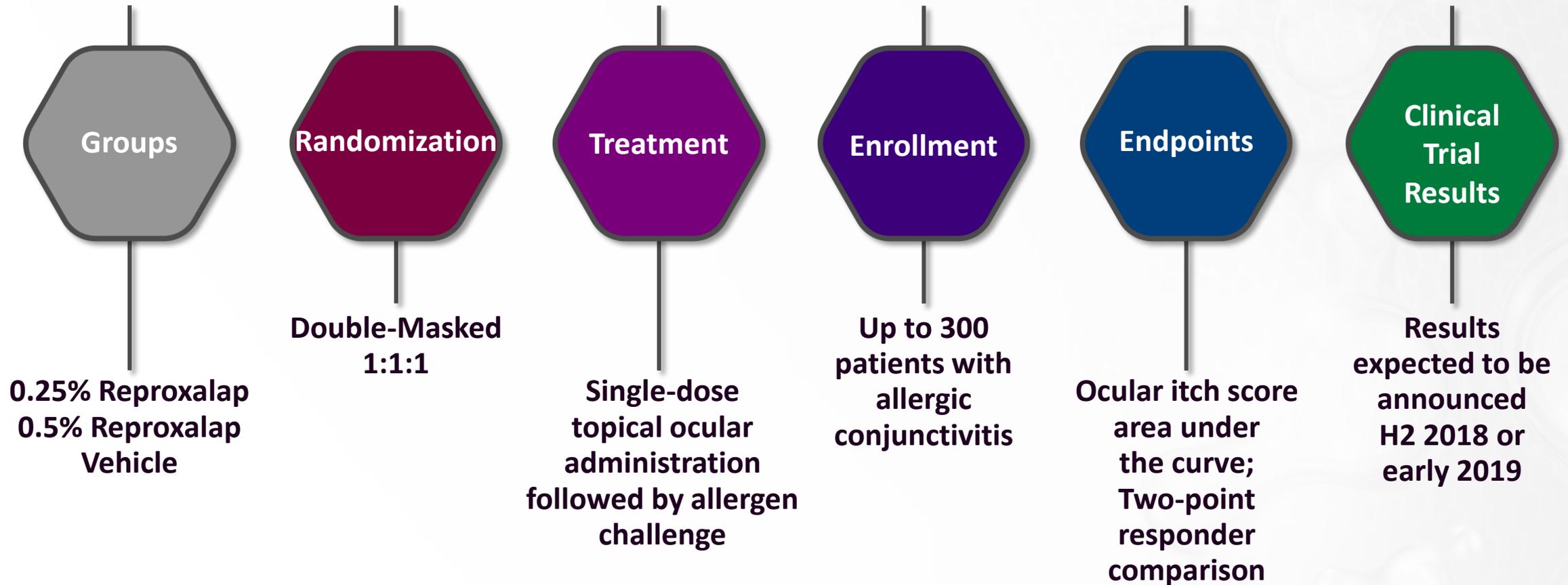
## Reproxalap Groups Showed Higher and More Durable Clinical Responses vs. Vehicle Group in Phase 2b Clinical Trial

- On the ocular itch scale (range 0 – 4), clinical response was defined as improvement of two points from peak itch score.
- Probability of response statistically higher in 0.1% and 0.5% reproxalap groups vs. vehicle ( $p=0.006$  and  $p=0.001$ , respectively).



# ALLEVIATE Trial Design in Allergic Conjunctivitis

## Phase 3 Clinical Trial Initiated April 2018



Further information can be found on [www.clinicaltrials.gov](http://www.clinicaltrials.gov): Trial #NCT03494504.

# Noninfectious Anterior Uveitis: A Serious Disease That Can Cause Loss of Vision

## Serious Inflammatory Disease



Noninfectious Anterior Uveitis (NAU) is a severe **autoimmune acute ocular inflammation**



Inflammatory cells in front of eye cause **pain, photophobia, and loss of vision**

**150K**  
annually

NAU is a **rare disease** with an estimated 150,000 U.S. patients per year



NAU has a big impact on **quality of life**, leading to loss of work and significant economic burden

## Inadequate Current Therapy

### Steroids

- Currently treated with **corticosteroids**, which may lead to **cataracts and glaucoma**

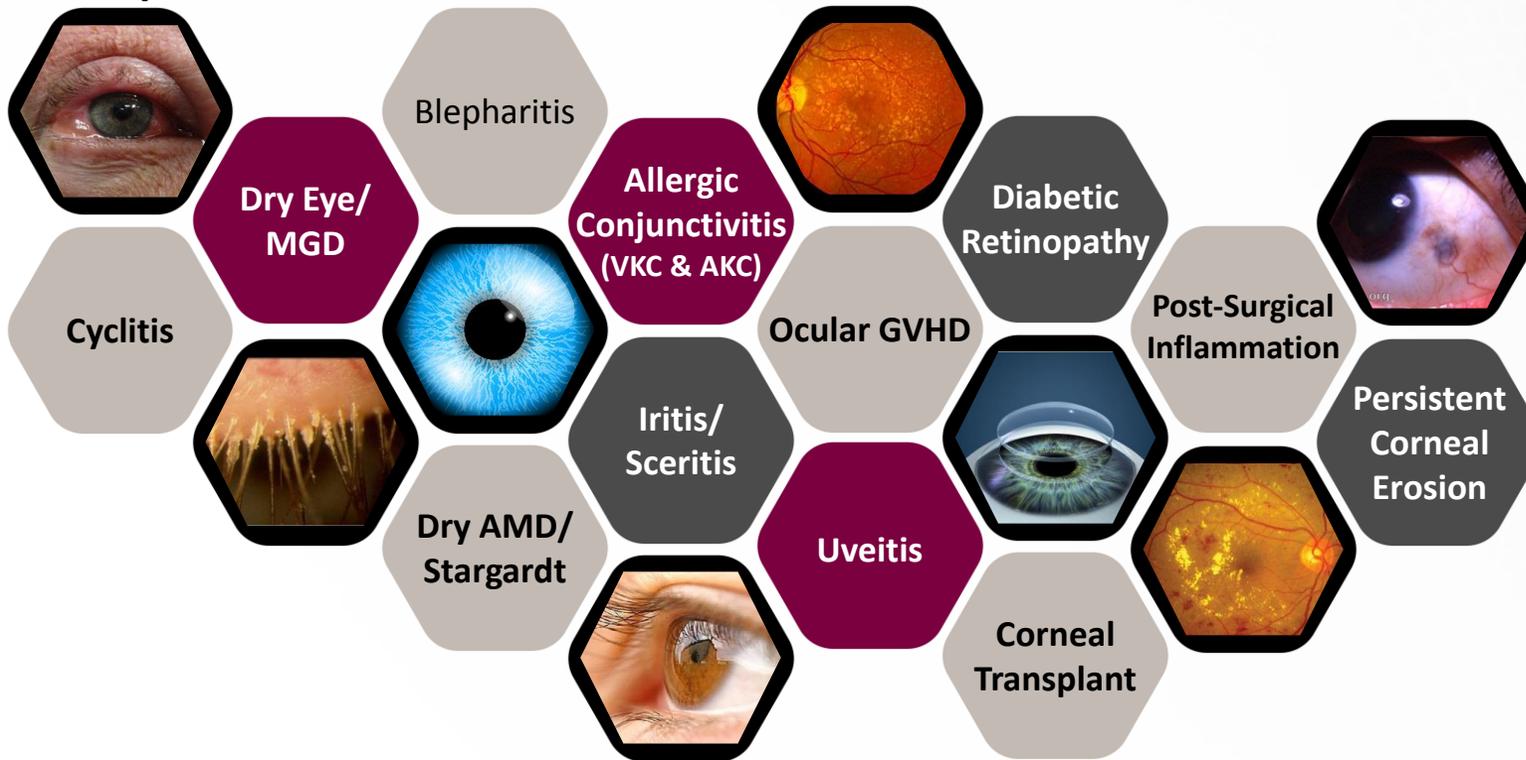
## A Unique Opportunity

### Reproxalap

- A **novel and differentiated approach** to treat NAU
- **Reduced anterior chamber cell count** in a randomized, vehicle controlled Phase 2 clinical trial, but **did not cause corticosteroid-related side effects**
- Phase 3 **results expected 2019**

# Steroid Toxicity Creates Significant Demand for Novel Approaches

Widespread corticosteroid use:



Potential corticosteroid side-effects:

- Blurred vision
- Cataracts
- Corneal ulceration
- Delayed wound healing
- Glaucoma
- Ocular infection
- Ptosis
- Redness
- Swelling
- Tear film instability

Despite toxicity, current topical ocular corticosteroid usage generates annual sales around \$800M\*

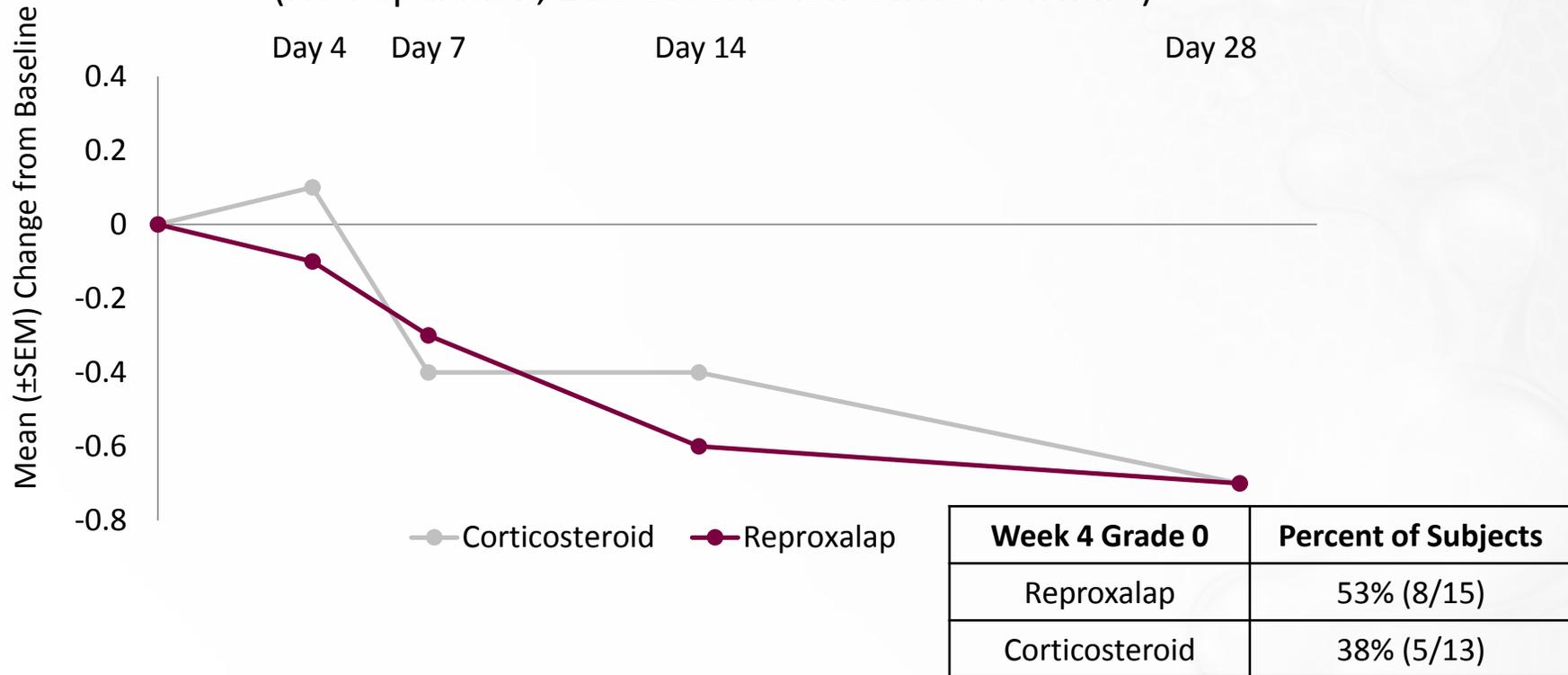
MGD: meibomian gland dysfunction, VKC: vernal keratoconjunctivitis, AKC: atopic keratoconjunctivitis, AMD: age-related macular degeneration.

Post-Surgical Inflammation includes inflammation resulting from corneal trauma, including cataract and refractive surgery.

\*Based on 2016 IMS data; Neither reproxalap nor any of Aldeyra's other product candidates are currently in clinical development for any of the above diseases, other than dry eye disease, allergic conjunctivitis, and noninfectious anterior uveitis.

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

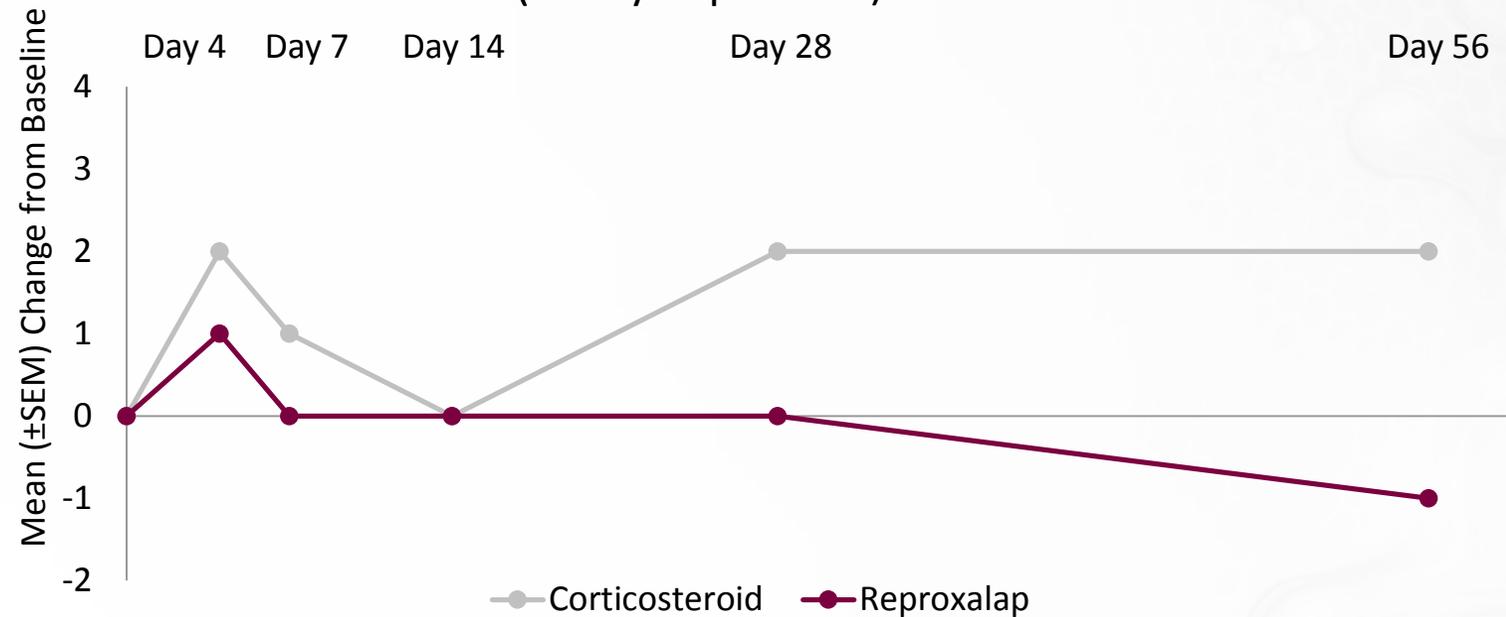
Change from Baseline in Anterior Chamber Inflammatory Cell Grade over Time (ITT Population, Last Observation Carried Forward)



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

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

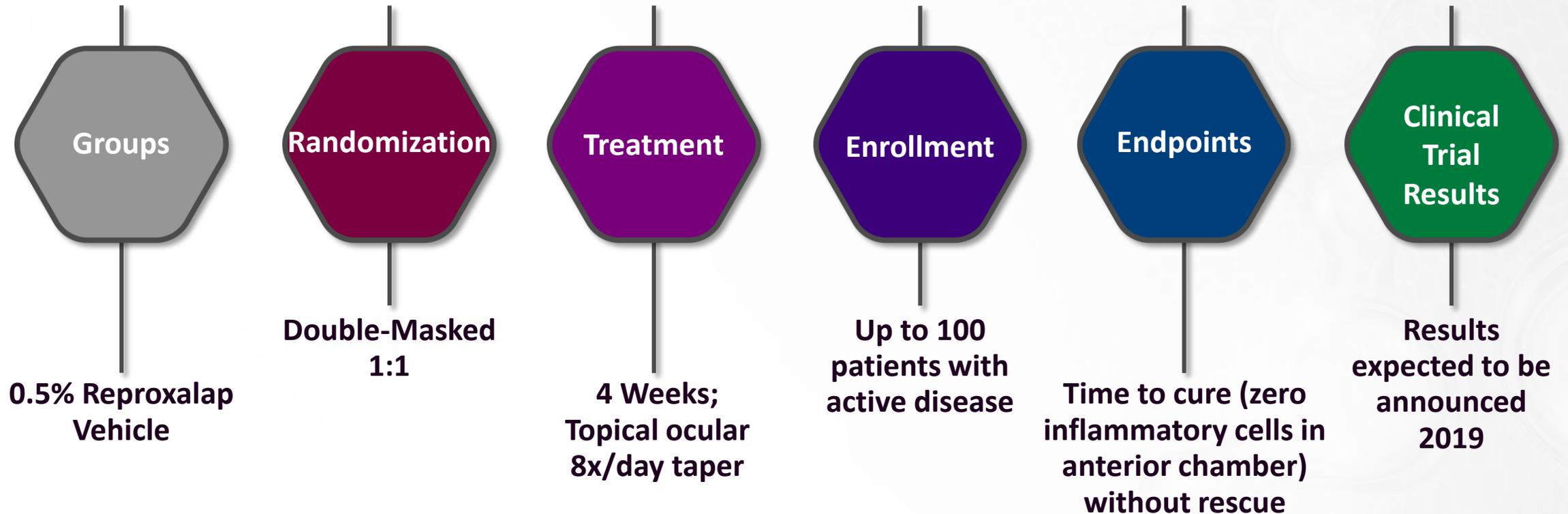
Change from Baseline in Intraocular Pressure (mmHg) over Time  
(Safety Population)



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

# SOLACE Trial Design in Noninfectious Anterior Uveitis

## Phase 3 Clinical Trial Initiated April 2017



Further information can be found on [www.clinicaltrials.gov](http://www.clinicaltrials.gov): Trial #NCT03131154.



## **Reproxalap: Sjögren-Larsson Syndrome**

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

## An Inborn Error of Metabolism



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

birth

50s

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

1,000  
U.S.

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



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

RASP = Reactive Aldehydes Species

<sup>1</sup>Extrapolating from a Swedish estimate in addition to a U.S. genetic mutation analysis. It is generally assumed that there are approximately 1,000 SLS patients in the United States and a greater number of SLS patients in Europe.

## Inadequate Current Therapy



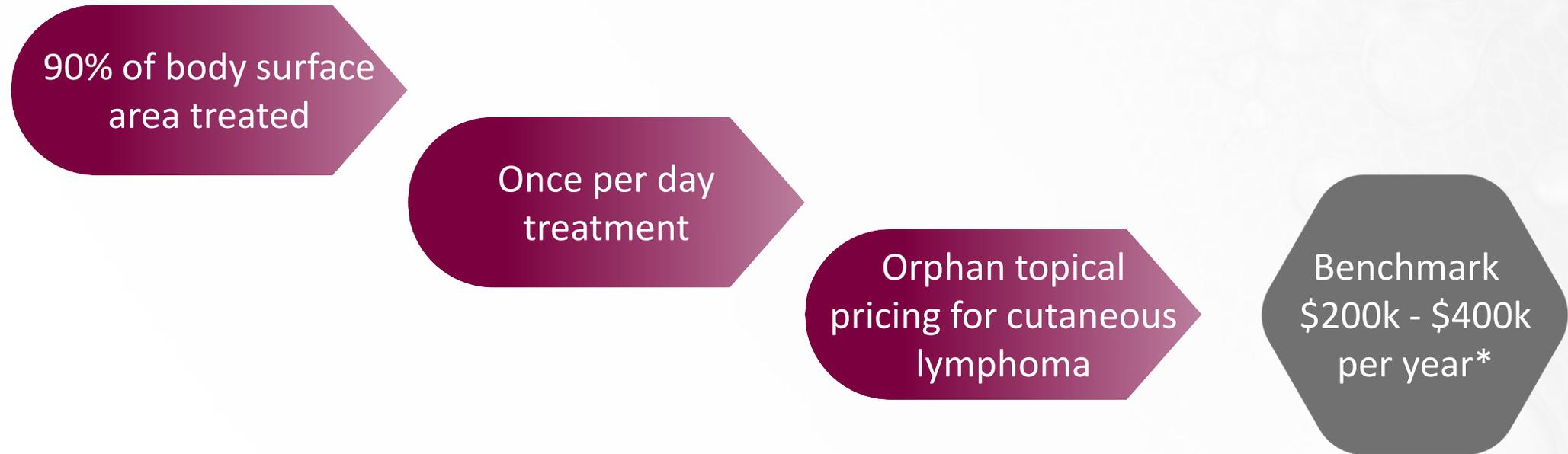
- No FDA or EMA approved therapy that addresses the disease

## A Unique Opportunity

### Reproxalap (topical dermatologic)

- 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
- Phase 3, Part 1 **results expected 2019**

# Potential Lifelong Therapy for Sjögren-Larsson Syndrome



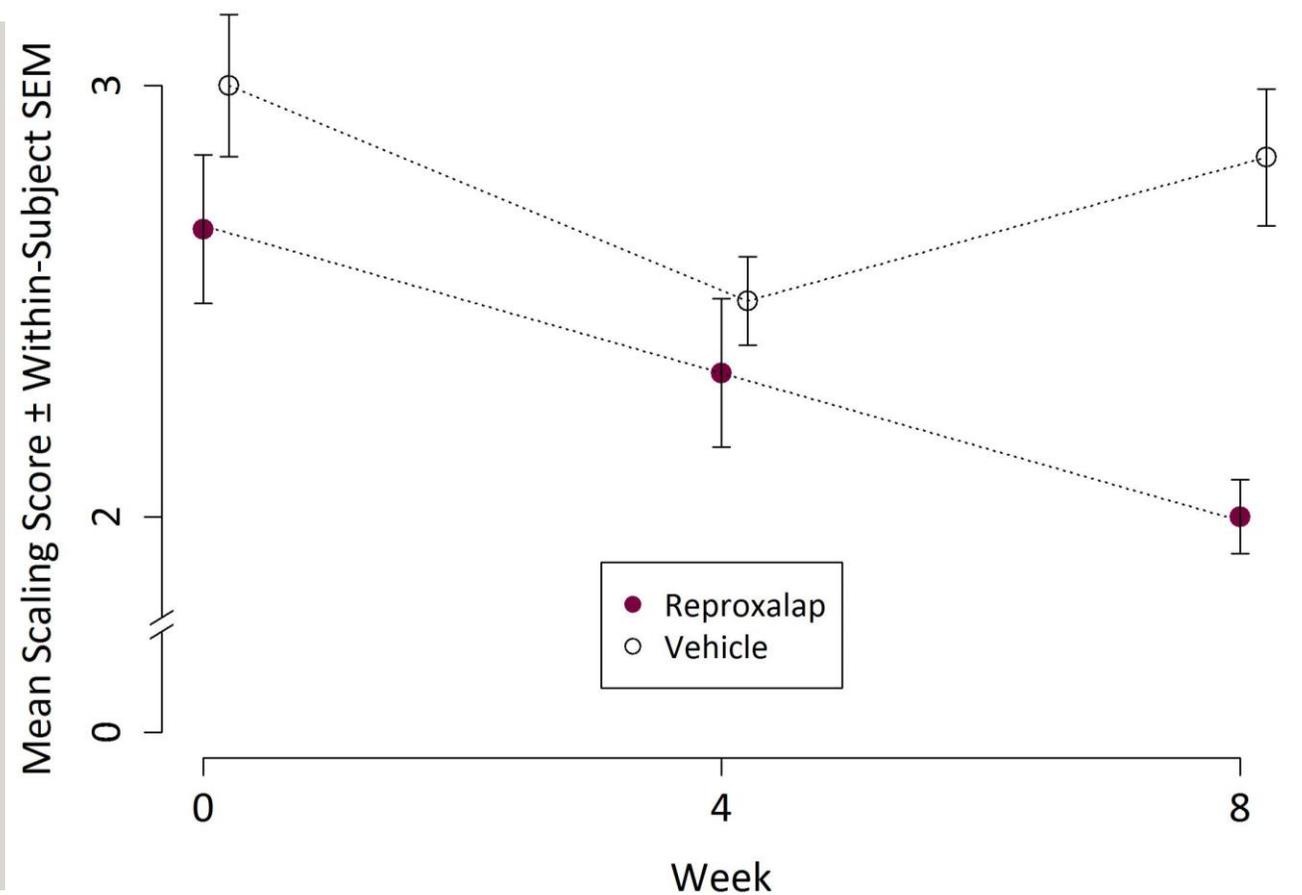
Estimated 0.4 births/100,000 (about 1,000 patients in U.S.)†  
Total Estimated U.S. SLS market: ~\$200M

\*Managed Care Qualitative Market Research of Reproxalap as a Potential Topically Applied Treatment for the Dermatologic Aspects of Sjögren-Larsson Syndrome, CPD Research & Consulting; pricing pending clinical data, regulatory approval, regulatory discussions, payor negotiations, competition, potential legislative changes, and other factors.

†Extrapolating from a Swedish estimate in addition to a U.S. genetic mutation analysis. It is generally assumed that there are approximately 1,000 SLS patients in the United States and a greater number of SLS patients in Europe.

# Every Drug-Treated Subject Showed Signs of Improvement in a Phase 2 Clinical Trial

## Investigator Assessment of Ichthyosis



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

## Representative Improvement in Reproxalap-Treated Patients in Phase 2 Clinical Trial



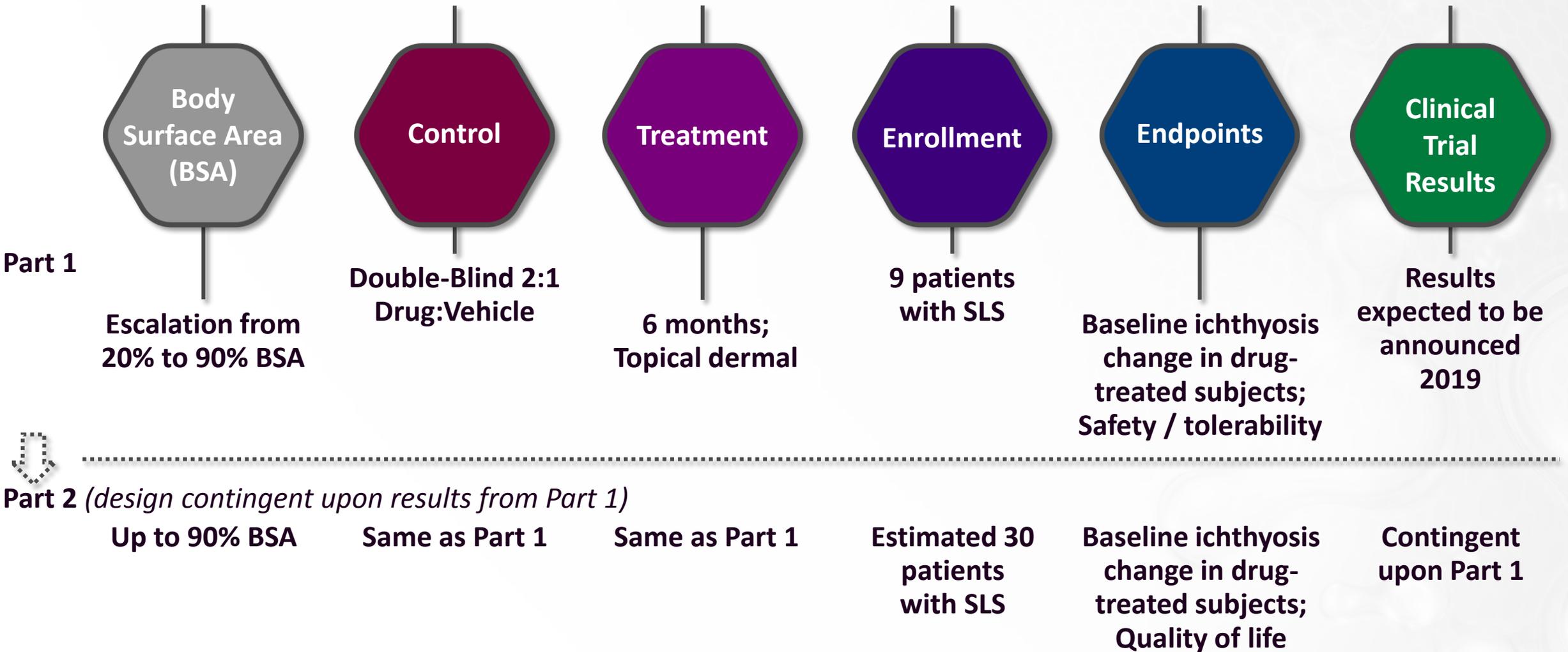
**Before Treatment (Week 0)**



**After Treatment (Week 8)**

# RESET Trial Design in Sjögren-Larsson Syndrome

## Phase 3 Part 1 Clinical Trial Initiated June 2018





**Building The Future**

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# Experienced Management Team and Board of Directors

## Management Team

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

**DOMAIN**  
ASSOCIATES

**ADERIS**  
PHARMACEUTICALS<sup>1</sup>

**Joshua Reed**  
Chief Financial Officer

 **Bristol-Myers Squibb**  
J.P.Morgan

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

   
**WILSON**  
THERAPEUTICS

**David McMullin**  
SVP Corporate Development

   
**NOVARTIS**

## Board of Directors

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

**Gary Phillips**, M.D. CEO OrphoMed

**Neal Walker**, D.O. CEO Aclaris Therapeutics

**Ben Bronstein**, M.D. Former CEO Peptimmune<sup>3</sup>

**Marty Joyce** Former CFO of Serono USA

**Jesse Treu**, Ph.D. Domain Associates

**Todd Brady**, M.D., Ph.D. CEO Aldeyra Therapeutics

1. Acquired by Schwarz/UCB

3. Acquired by Genzyme

# Deep and Innovative Pipeline

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	ADX-1615	Autoimmune Disease					
			Cancer				
Anti-Inflammatory	Not Disclosed	Ocular Inflammation					

RASP = Reactive Aldehydes Species  
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✓ = Positive Phase 2 clinical data reported in 2016 – 2017

# 2018 Progress and Near-Term Development Catalysts Support Path to Commercialization

## H1 2018

-  Initiated reproxalap **Phase 2b clinical trial in dry eye disease**
-  Initiated reproxalap **ALLEVIATE trial in allergic conjunctivitis**
-  Entered into **research collaboration with Johnson & Johnson Innovation** in systemic inflammatory diseases
-  Disclosed **in-license of a Hsp90 inhibitor**
-  Clinical sites initiated for reproxalap **RESET Part 1 trial in Sjögren-Larsson Syndrome**

## H2 2018

-  First patient enrolled in reproxalap **RESET Part 1 trial in Sjögren-Larsson Syndrome**
- ### Anticipated Milestones\*
-  Reproxalap dry eye disease Phase 2b clinical trial results **H2-2018**
-  ADX-1612 mesothelioma clinical trial results (investigator sponsored trial) **H2-2018**
-  ADX-1612 ovarian cancer clinical trial initiation (investigator sponsored trial) **H2-2018**
-  Reproxalap allergic conjunctivitis ALLEVIATE trial results **H2-2018/early 2019**

\*Contingent on funding, regulatory review, and other factors.

# 2019 Expected Development Milestones: Novel Approaches to Address Immune-Mediated Disease

2019

## Anticipated Milestones\*

-  Reproxalap noninfectious anterior uveitis  
SOLACE trial results **2019**
-  Reproxalap Sjögren-Larsson Syndrome  
RESET Part 1 trial results **2019**
-  ADX-629 Phase 1 clinical trial initiation **2019**
-  ADX-629 NASH and/or IBD Phase 2a clinical trials initiation  
following Phase 1 clinical trial
-  ADX-103 retinal disease Phase 1/2 clinical trial initiation **2019**
-  ADX-1612 post-transplant lymphoproliferative disorder  
Phase 2 clinical trial initiation **2019**

\*Contingent on funding, regulatory review, and other factors.