December 3, 2019

**DATA RELEASE**

# The RENEW Trial in Dry Eye Disease: Part 1 Top-Line Results

Nasdaq: ALDX

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# In Part 1 of RENEW, Reproxalap Demonstrated Early Onset and Broad Improvements in Symptoms

- **The RENEW Trial is an ongoing adaptive, two-part, Phase 3 clinical trial.**
  - The primary objective of Part 1 was to confirm dosing regimen, endpoints, and sample size for RENEW-Part 2.
- **The primary objective of RENEW-Part 1 was achieved.**
  - Reproxalap will advance to RENEW-Part 2.
  - Dosing regimen, endpoints, and sample size for RENEW-Part 2 were confirmed.
- **RENEW-Part 1 top-line results demonstrated early onset and broad symptomatic control following induction-maintenance dosing.**
  - Induction-maintenance dosing demonstrated greater activity vs. vehicle than constant dosing.
  - Statistical significance achieved for RENEW co-primary endpoint of ocular dryness score.
  - Rapid (as early as 1 week), broad, and statistically significant activity achieved across majority of assessed symptoms.
  - Improvement in fluorescein staining, although not statistically significant, enables powering of RENEW-Part 2.
- **RENEW-Part 2 to initiate in the first half of 2020.**
  - 0.25% topical ocular reproxalap to be administered via induction-maintenance dosing schedule.
  - Co-primary endpoints expected to be ocular dryness score and fluorescein nasal region ocular staining.
  - Approximately 400 patients per arm expected to be enrolled to achieve 90% statistical power.

# Dry Eye Disease is a Persistently Disturbing Condition that is Inadequately Treated


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

Up to **75%**

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

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

Up to **80%**

**Between 50% and 80% of** Rx-treated **DED patients drop off of therapy** between their second and third refill.

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

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

DED = Dry eye disease

# The RENEW Trial in Dry Eye Disease

**RENEW: An Ongoing Adaptive Two-Part, Multi-Center, Randomized, Vehicle-Controlled, Double-Masked, Parallel-Group Phase 3 Clinical Trial**

April 2019

*Part 1 Top-Line Results*
December 2019

## RENEW-Part 1
Reproxalap 0.25%

- 422 patients
- 10 sites
- 2 dosing regimens
- Pre-specified analyses for protocol optimization

### Primary Objective

- ☑ Confirm dosing regimen
- ☑ Confirm endpoints
- ☑ Confirm sample size

## RENEW-Part 2
Reproxalap 0.25%

### Advancing to Part 2

- ✓ Induction-maintenance dosing
- ✓ Ocular dryness and fluorescein staining co-primary endpoints
- ✓ Approximately 400 patients per arm for 90% statistical power

Further information can be found on www.clinicaltrials.gov: Trial #NCT03879863.

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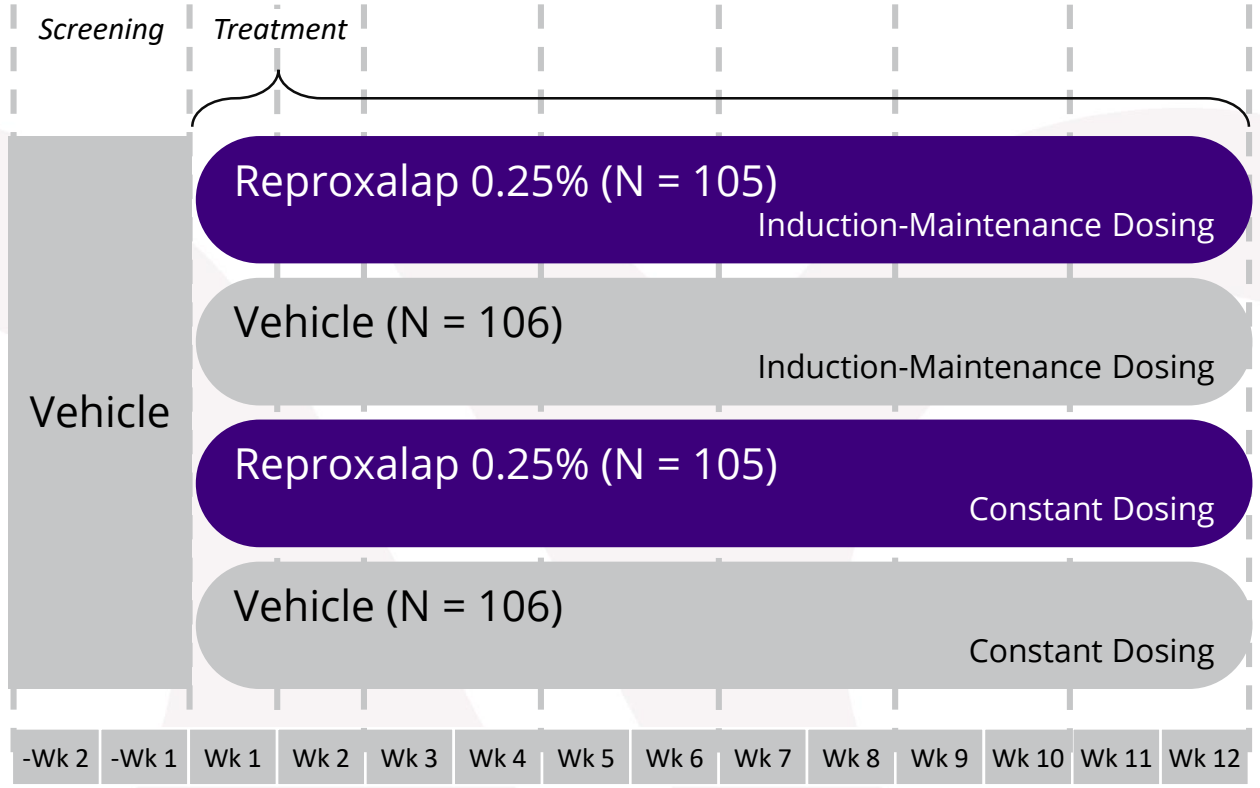
Induction-Maintenance Dosing = QID for Weeks 1-4 and BID for Weeks 5-12

# RENEW-Part 1 Clinical Trial Design

- **RENEW-Part 1 primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle to confirm dosing regimen, endpoints, and sample size of RENEW-Part 2
- **RENEW-Part 1 inclusion/exclusion criteria:**
  - Moderate to severe dry eye disease
- **RENEW co-primary endpoints:**
  - Ocular dryness score (0-100mm VAS)
  - Fluorescein nasal region staining score
- **RENEW analysis strategy:**
  - Co-primary endpoints assessed using Mixed Model Repeated Measures (MMRM) from Week 2 to 12
  - Co-primary endpoints assessed in separate pre-specified patient populations
    - Ocular dryness score (OD4S): baseline score of ≥ 3
    - Fluorescein nasal region staining: baseline score ≥ 2

**RENEW Phase 3 Dry Eye Disease Clinical Trial: Part 1**




Further information can be found on www.clinicaltrials.gov: Trial #NCT03879863.

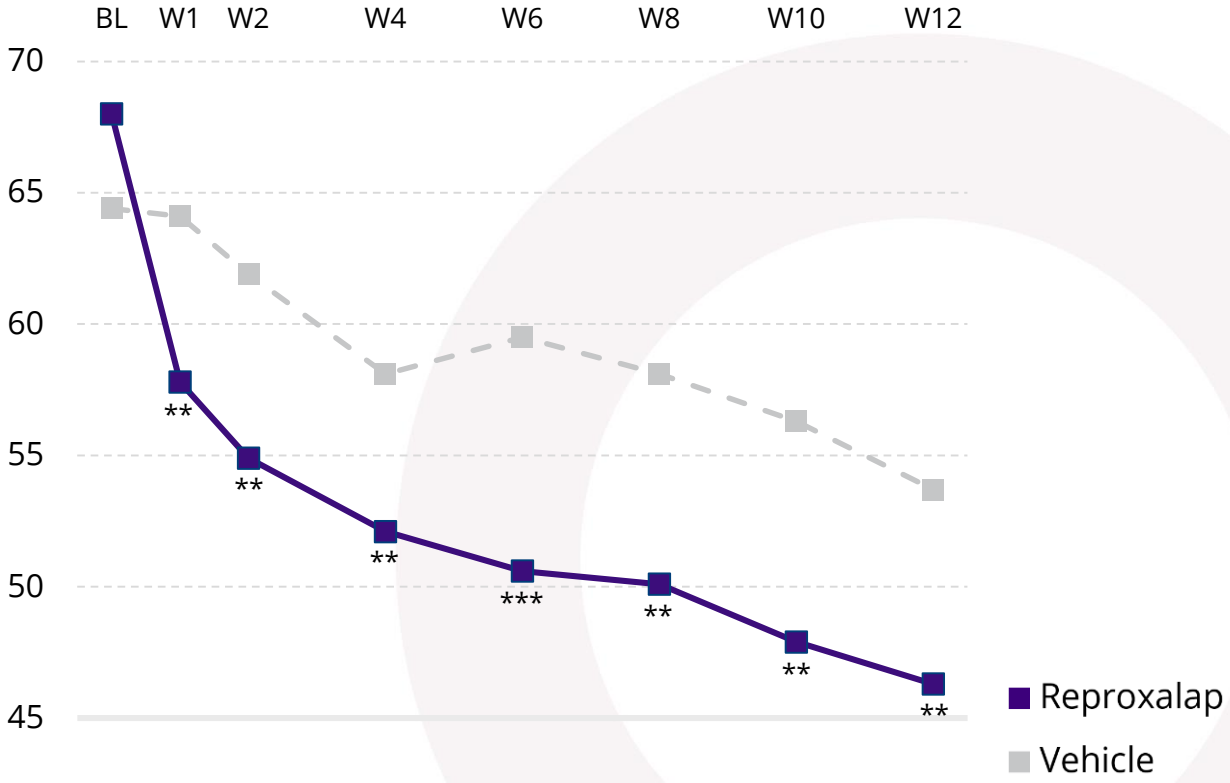
VAS = Visual Analog Scale
OD4S = Ocular Discomfort & 4-Symptom Questionnaire

Constant Dosing = QID for Weeks 1-12
Induction-Maintenance Dosing = QID for Weeks 1-4 and BID for Weeks 5-12

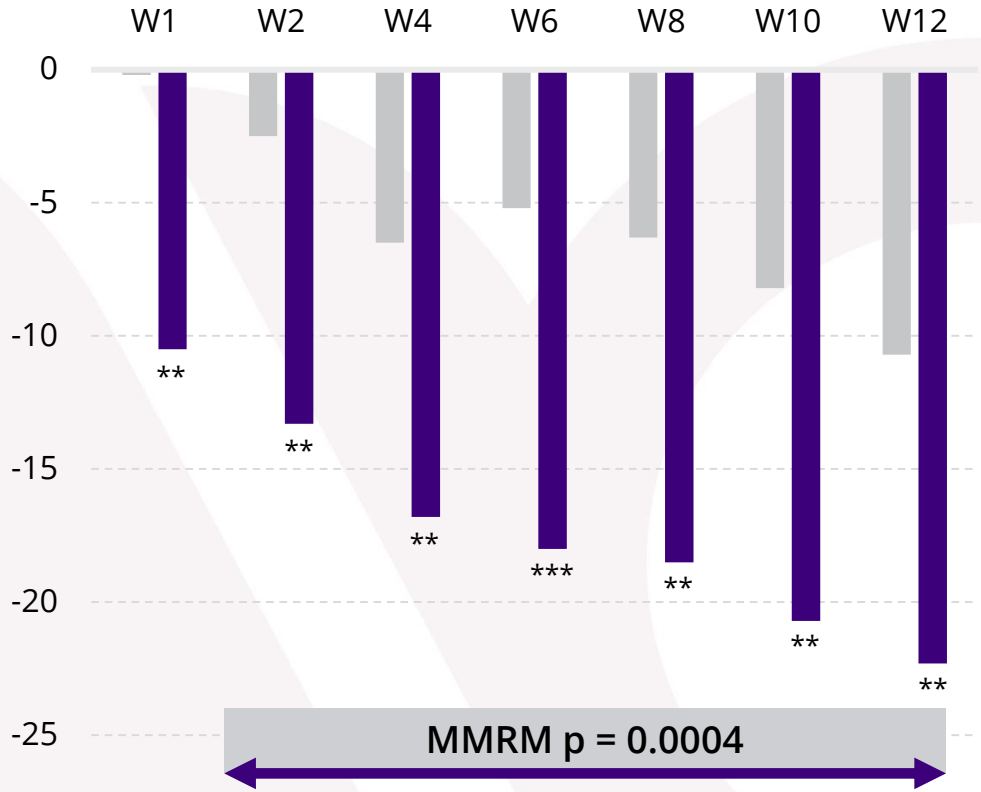
# Reproxalap Demonstrated Rapid and Durable Improvement in Co-Primary Endpoint of Ocular Dryness Score in RENEW-Part 1

## Co-Primary Symptom Endpoint for RENEW

**Ocular Dryness Score (VAS)†**
Baseline and Weeks 1 to 12




**Ocular Dryness Score (VAS)† Change From Baseline**
Weeks 1 to 12




†Ocular Dryness Score co-primary endpoint assessed in pre-specified patient population having an ocular dryness (Ocular Dryness 4-Symptom) baseline score of ≥ 3 (N=170).
Source: RENEW-Part 1 induction-maintenance top-line results

**p<0.01 ***p<0.001
VAS = Visual Analog Scale
BL = Baseline; W = Week
MMRM = Mixed Effect Model Repeated Measures

# Reproxalap Demonstrated Highly Statistically Significant Reductions in Ocular Dryness in RENEW-Part 1

**Ocular Dryness Score (VAS) Treatment Difference (Reproxalap-Vehicle)***

| | p-value |
|---|---|
| Week 1 | 0.0012 |
| Week 2 | 0.0015 |
| Week 4 | 0.0062 |
| Week 6 | 0.0009 |
| Week 8 | 0.0015 |
| Week 10 | 0.0025 |
| Week 12 | 0.0066 |
| **Week 2 to 12 (Co-Primary)** | **0.0004** |


## Potential Competitive Advantages†

- Rapid symptom improvement supports differentiated product profile.
- Reproxalap demonstrated large and statistically significant improvements in ocular dryness at every time point.

†Pending clinical data, regulatory discussions, payor negotiations, competition, potential legislative changes, and other factors, which may not be in Aldeyra's control.
*Treatment Difference defined as the difference between the changes from baseline for the evaluated drug vs. vehicle (LS Mean Difference ± 95% CI). Ocular Dryness Score co-primary endpoint assessed in pre-specified patient population having an OD4S dryness baseline score of ≥ 3 (N=170).
Source: RENEW-Part 1 induction-maintenance top-line results

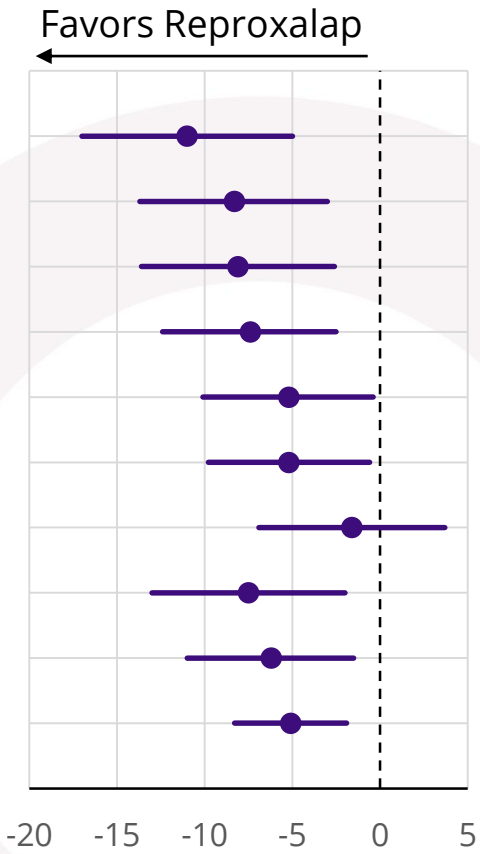
VAS = Visual Analog Scale

# Reproxalap Demonstrated Broad Statistically Significant Symptom Improvement in RENEW-Part 1

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

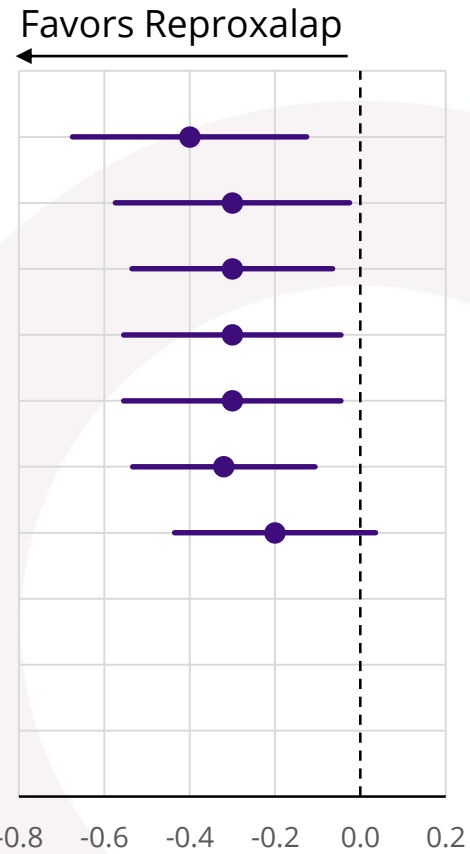
### 0-100 Ocular Symptom Scales

| | p-value |
|---|---|
| VAS: Ocular Dryness (Co-Primary) | 0.0004 |
| VAS: Eye Discomfort | 0.0025 |
| VAS: Photophobia | 0.0041 |
| VAS: Foreign Body Sensation | 0.0035 |
| VAS: Itching | 0.0346 |
| VAS: Pain | 0.0268 |
| VAS: Burning/Stinging | NS |
| SANDE: Frequency | 0.0080 |
| SANDE: Severity | 0.0102 |
| OSDI (Total) | 0.0020 |




### 0-4 & 0-5 Ocular Symptom Scales

| | p-value |
|---|---|
| OD4S: Grittiness | 0.0025 |
| OD4S: Dryness | 0.0134 |
| OD4S: Ocular Discomfort | 0.0268 |
| OD4S: Burning | 0.0306 |
| OD4S: Stinging | 0.0239 |
| CAC Ocular Itching Scale | 0.0034 |
| Ocular Discomfort Scale | NS |

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Source: RENEW-Part 1 induction-maintenance top-line results

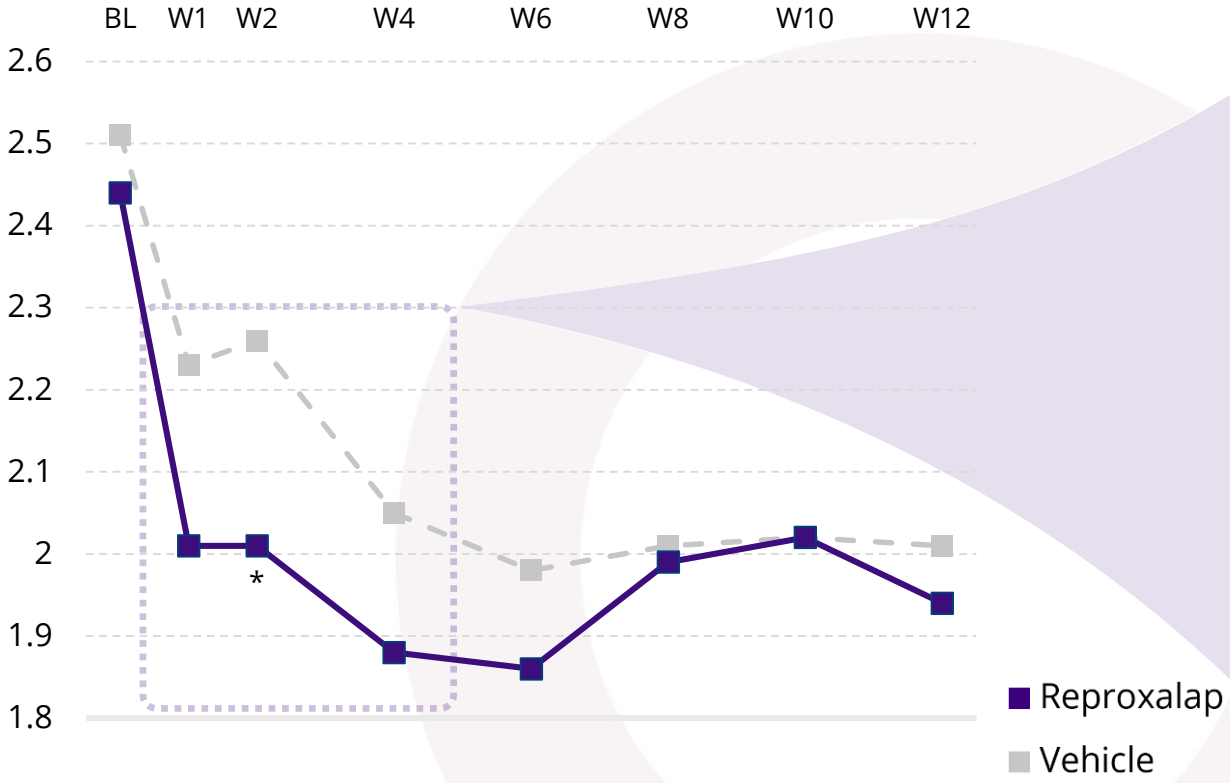
VAS = Visual Analog Scale
SANDE = Symptom Assessment in Dry Eye
OSDI = Ocular Surface Disease Index

NS = Not Significant
OD4S = Ocular Discomfort & 4-Symptom
CAC = Conjunctival Allergen Challenge

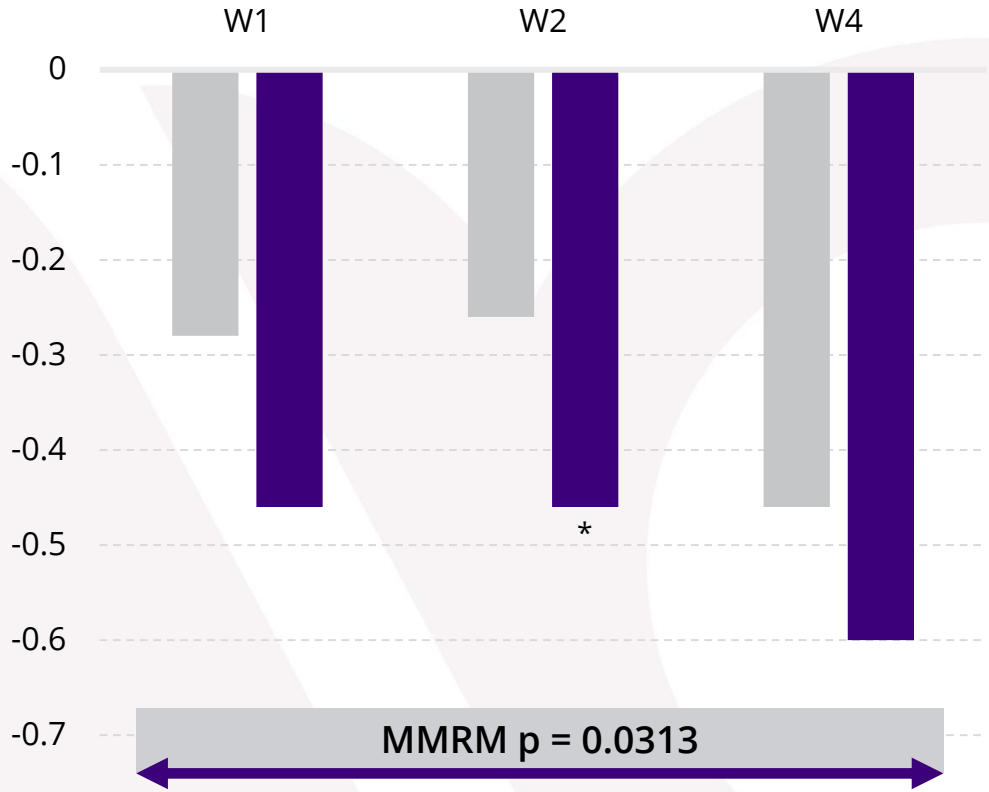
# Reproxalap Demonstrated Rapid Improvement in Co-Primary Endpoint of Fluorescein Staining Score in RENEW-Part 1

## Co-Primary Sign Endpoint for RENEW

**Fluorescein Staining: Nasal Region† (0-4)**
Baseline and Weeks 1 to 12




**Fluorescein Staining: Nasal Region† Change From Baseline**
Weeks 1 to 4




†Fluorescein Staining co-primary endpoint assessed in pre-specified patient population having a nasal region baseline score of ≥ 2 (N=179).
Source: RENEW-Part 1 induction-maintenance top-line results

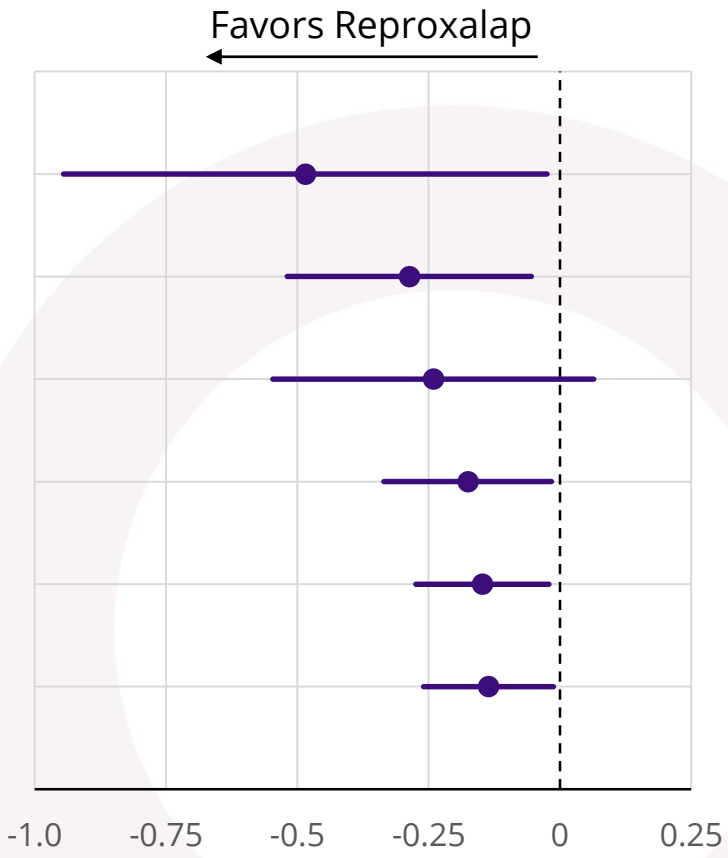
*p<0.05
BL = Baseline; W = Week
MMRM = Mixed Effect Model Repeated Measures (across 12 weeks)

# Reproxalap Demonstrated Rapid and Broad Staining Improvements in RENEW-Part 1

**Fluorescein Staining Treatment Difference (Reproxalap-Vehicle) Over Weeks 1 to 4***

**0-4 Ocular Staining Regions and Sums**

| | p-value |
|---|---|
| Total Eye Sum | 0.0393 |
| Conjunctival Sum | 0.0157 |
| Corneal Sum | NS |
| Nasal† | 0.0313 |
| Temporal | 0.0223 |
| Inferior | 0.0314 |




Total Eye Sum = All five regions
Conjunctival Sum = Nasal + Temporal
Corneal Sum = Inferior + Central + Superior

## Potential Competitive Advantages†

- Rapid sign improvement supports differentiated product profile.
- Reproxalap demonstrated statistically significant improvements over vehicle in majority of regions over Weeks 1 to 4.
- Reproxalap demonstrated substantial improvements at Week 1, with near-peak difference from vehicle achieved by Week 4.

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†Fluorescein Staining co-primary endpoint assessed in pre-specified patient population having a nasal region baseline score of ≥ 2 (N=179).
Source: RENEW-Part 1 induction-maintenance top-line results

# Reproxalap Was Generally Well Tolerated and No Adverse Findings on Safety Assessments Were Observed in RENEW-Part 1

- No treatment-related serious adverse events were reported.
- The most common treatment-emergent event was mild transient instillation site irritation.
  - The majority of reported adverse events were mild; less than 1% of adverse events were moderate.
  - No taste disturbance or throat irritation was reported.
- No adverse findings on detailed safety assessments were observed.
- Discontinuation rates were consistent with clinical trials of currently approved* dry eye products.
  - In the induction-maintenance regimen, 7.6% of patients discontinued due to adverse events in the reproxalap group, and 0.9% of patients discontinued due to adverse events in the vehicle group.
- Topical ocular reproxalap has now been administered to over 1,100 patients across 12 clinical trials.

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*Restasis® and Xiidra® clinical trial publications and FDA summary basis of approval filings
Source: RENEW-Part 1 induction-maintenance top-line results

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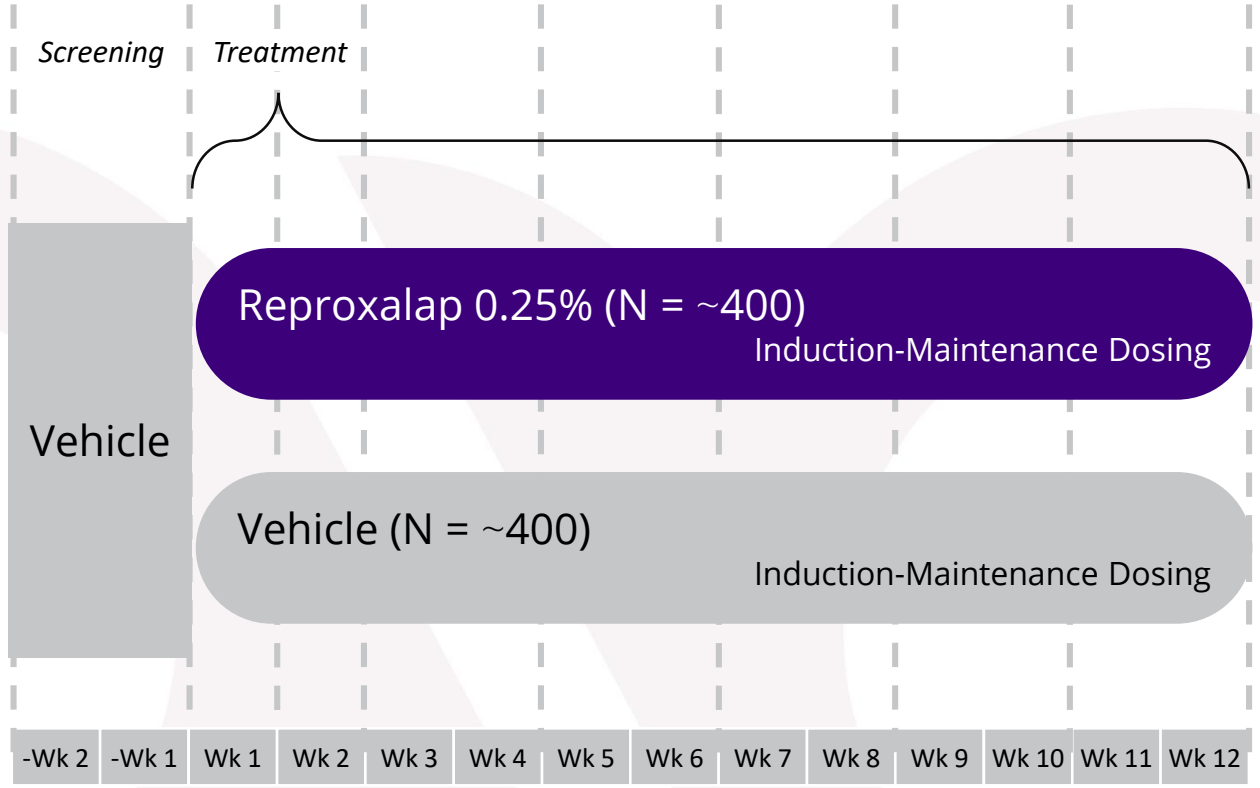
# RENEW-Part 2 Clinical Trial Design*

- **RENEW-Part 2 primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle for the symptoms and signs of dry eye disease
- **RENEW-Part 2 inclusion/exclusion criteria:**
  - Same as used for RENEW-Part 1
  - Moderate to severe dry eye disease
- **RENEW co-primary endpoints:**
  - Ocular dryness score (0-100mm VAS)
  - Fluorescein nasal region staining
- **RENEW analysis strategy:**
  - Mixed Model Repeated Measures (MMRM)
  - Pre-specified patient populations
    - Ocular dryness score (OD4S): baseline score of $\geq$ 3
    - Fluorescein nasal region staining: baseline score $\geq$ 2

**Expected to initiate H1 2020**

**RENEW Phase 3 Dry Eye Disease Clinical Trial: Part 2**

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# A New Paradigm for the Treatment of Ocular Diseases: A Potential Single Treatment for Dry Eye Disease and Allergic Conjunctivitis*

## Dry Eye Disease

**Reproxalap 0.25%**

Rapid and consistent symptom and sign improvements in RENEW-Part 1 top-line results

Broad symptom and sign improvements in RENEW-Part 1 top-line results

**DED trials in >950 patients**

**RENEW-Part 2 Phase 3 Initiation H1 2020**

## Allergic Conjunctivitis

**Reproxalap 0.25%**

Clinically significant and durable symptom response in allergen chamber trial

Active in post-histaminic allergy, for which no drug is approved

**AC trials in >650 patients**

**INVIGORATE Phase 3 Initiation H1 2020**

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

# Upcoming and Recently Achieved Reproxalap Topical Ocular Development Milestones:*

- **Positive** reproxalap allergic conjunctivitis **allergen chamber trial top-line results**
- **Positive** reproxalap allergic conjunctivitis **ALLEVIATE Phase 3 trial results**
- **Primary objective met** in reproxalap dry eye disease **RENEW Phase 3-Part 1 top-line results**
- Reproxalap allergic conjunctivitis **INVIGORATE Phase 3 initiation H1 2020**
- NEW Reproxalap dry eye disease **RENEW Phase 3-Part 2 initiation H1 2020**

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