A Multi-Center, Randomized, Double-Masked, Parallel-Group, Vehicle-Controlled Phase 2b Dry Eye Disease Clinical Trial to Evaluate the Safety and Efficacy of Topical Ocular Reproxalap, a Novel RASP Inhibitor.

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Disclosures

- Alcon: Research Grants, Speaker, Advisor
- Aldeyra Pharmaceuticals: Advisory Board, Clinical Research
- Allergan: Research Grants, Speaker, Advisory Board, Media Spokesman
- Bausch & Lomb, Ista, Valeant: Research Grants, Speaker, Advisory Boards
- Abbvie: Research, Advisor, Spokesman
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- EyeRx Research: Clinical Research, Stock Ownership
- Imprimis Pharma: Advisory Board
- Isis Pharmaceuticals: Research, Advisory Board
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- Kala Pharmaceuticals: Research, Advisory Board
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- Senju: Research Grants
- Srathspey Crowne: Investor
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- Tear Lab: Advisory Board, Speaker, Shareholder
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- Topcon: Clinical Research Grant
- Topivert: Consultant
- Vistakon: Advisory Board, Clinical Research
- Xoma, Servier: Clinical Investigator, Advisor
- 1-800-DOCTORS: Advisory Board, Shareholder
- Virginia Eye Consultants & Surgery Center: Owner

Blockade of RASP: A Novel Therapeutic Approach

RASP Binding

- Reproxalap rapidly binds to RASP in a reaction that is essentially irreversible *in vivo*
- Reproxalap out-competes endogenous RASP targets

Adduct Transport

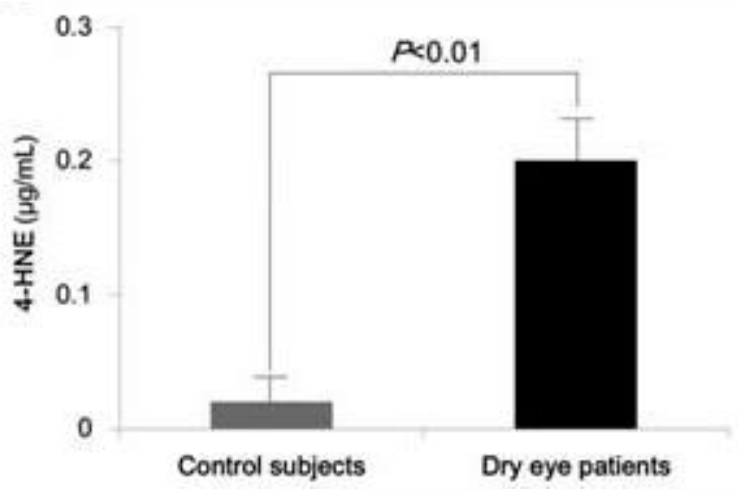
- Reproxalap-RASP adducts are transported inside the cell

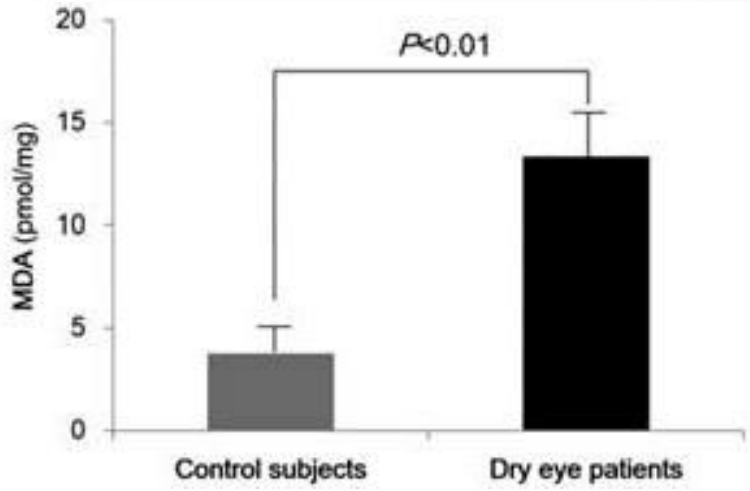
Adduct Degradation

- Reproxalap-RASP adducts are degraded within hours

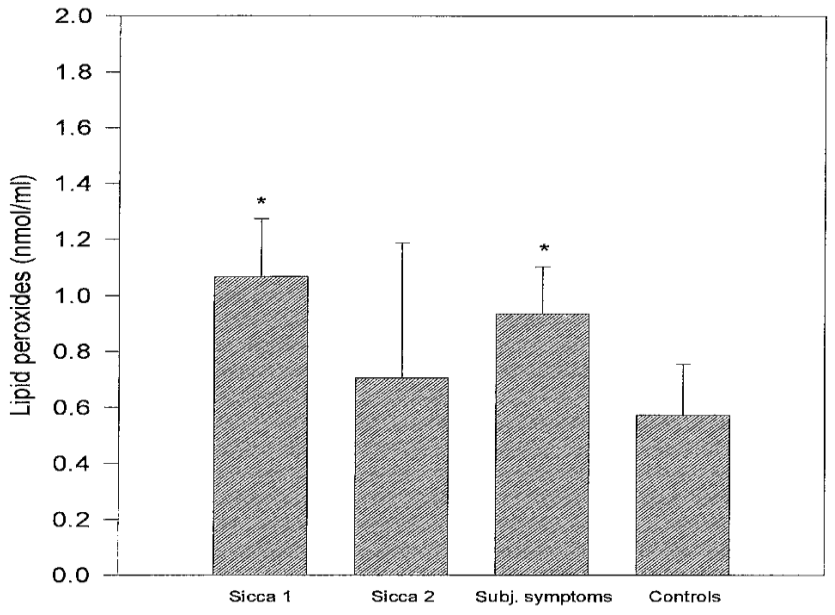
RASP = Reactive Aldehyde Species

RASP Are Elevated in Tears of Dry Eye Disease Patients



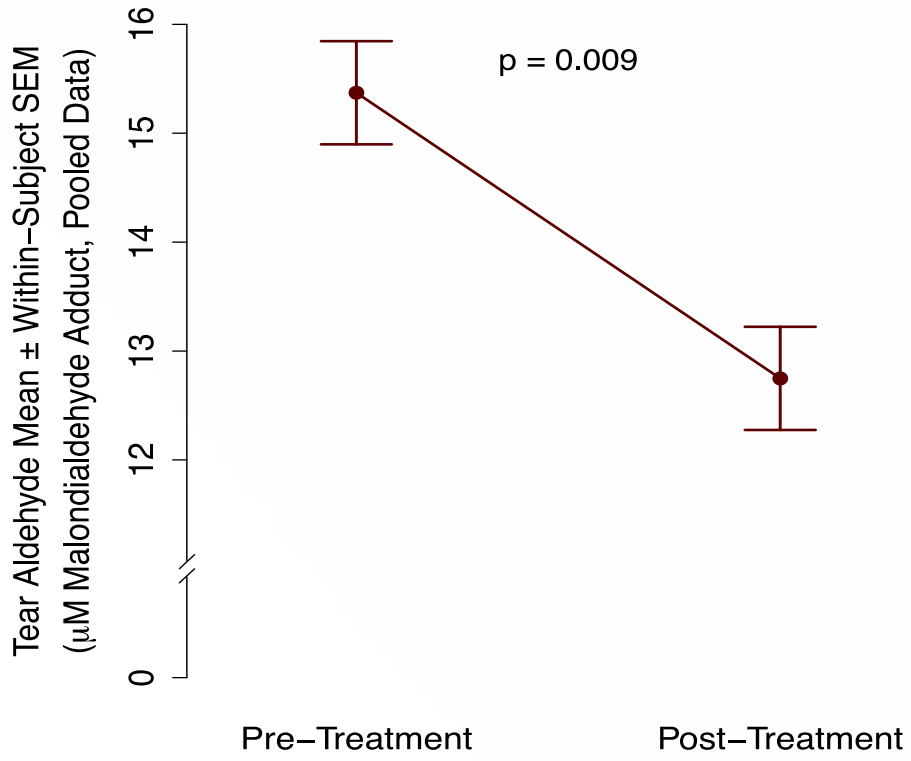


Curr Eye Res. 41:1143-9, 2016.

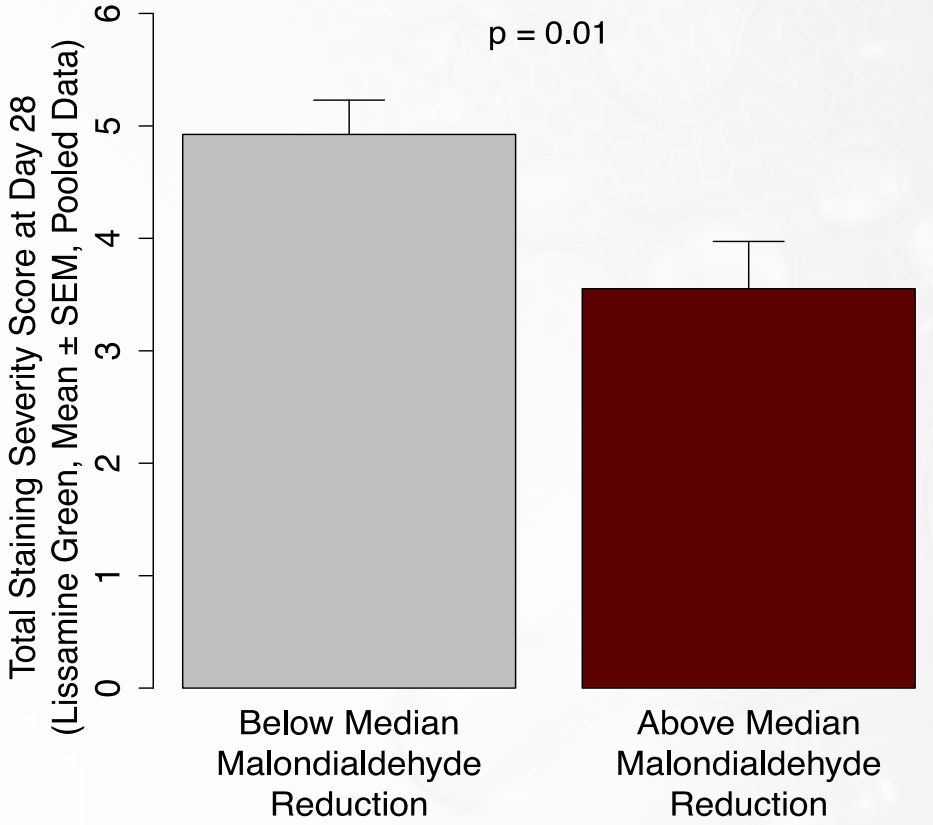


Graefe's Arch Clin Exp Ophthalmol. 233:694-8, 1995.

Reproxalap Demonstrated RASP Reduction in DED Phase 2a Trial Which Correlated with Sign Improvement in Individual Patients

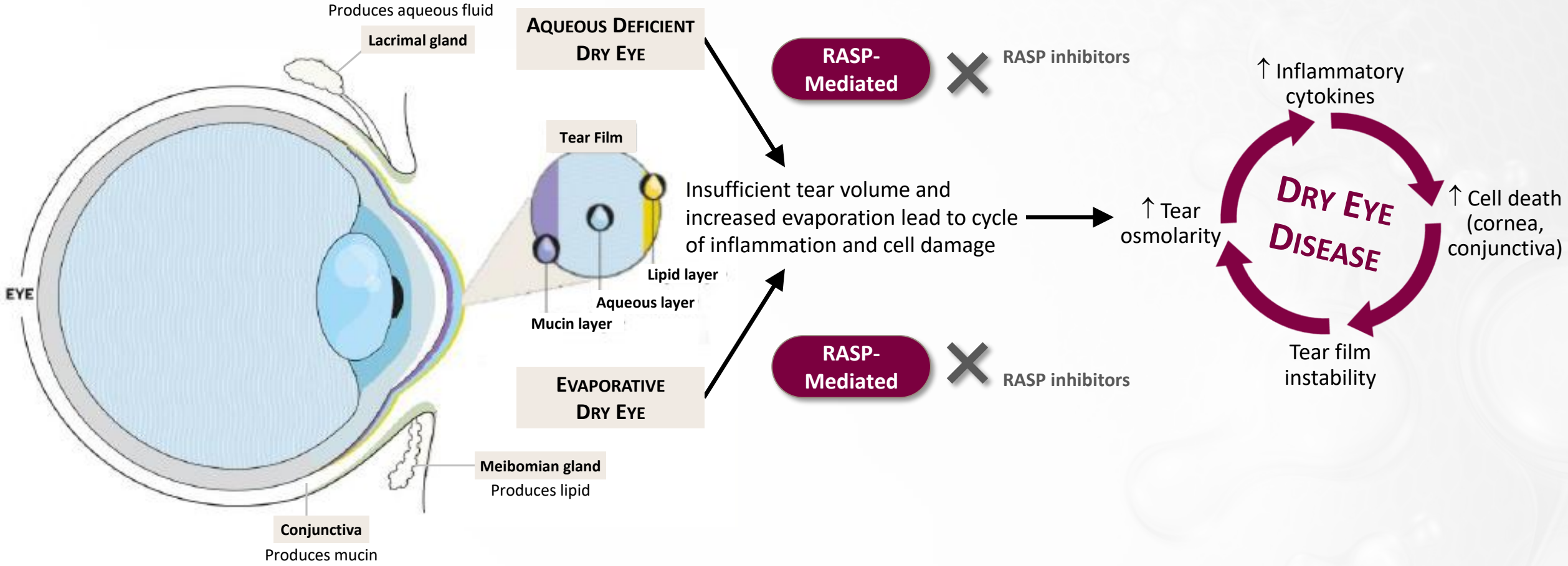


Pre-Treatment = Day 0, Post-Treatment = Day 28.



Pooled data from Phase 2a clinical trial presented at ARVO 2018

Reproxalap's Novel Mechanism of Action has the Potential to Address the Two Major Forms of Dry Eye Disease



RASP = Reactive Aldehyde Species;
Image adapted from Alisdair Macdonald as cited in J Wolffsohn and J Craig, The Pharmaceutical Journal (2017);
RASP activity as shown based on published literature and Aldeyra data on file.

Phase 2b Dry Eye Disease Clinical Trial Design

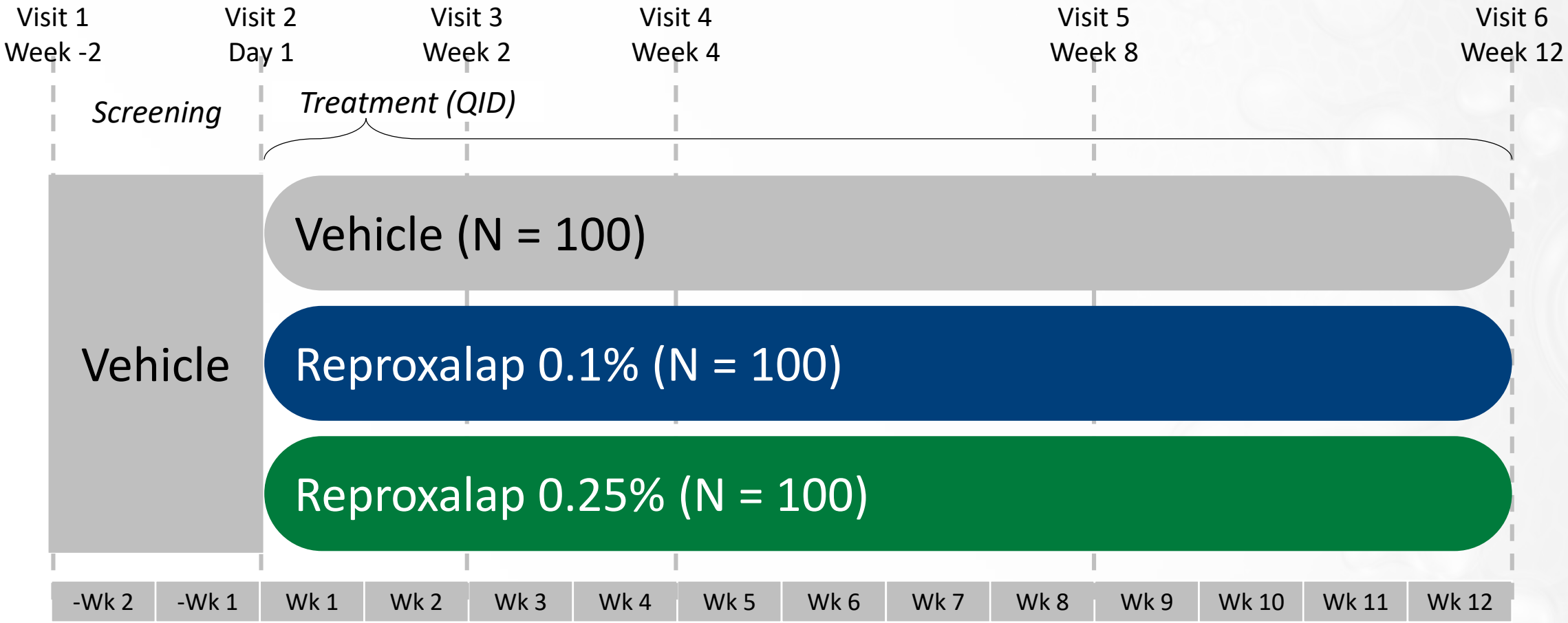
- **Primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solutions vs. baseline and vehicle to **confirm endpoint selection and sample size for Phase 3 clinical trials**

- **Inclusion/exclusion highlights:**
  - History of dry eye disease for at least 6 months, and history of use or desire to use eye drops for dry eye symptoms within 6 months
  - Moderate to severe dry eye disease
    - ≥ 2 on OD & 4-Symptom Questionnaire (in at least one symptom score)
    - Schirmer's Test ≤ 10 mm and ≥ 1 mm
    - Tear Film Break-Up Time ≤ 5 sec
    - Corneal fluorescein staining score of ≥ 2 in at least one region (e.g., inferior, superior, or central)
    - Sum corneal fluorescein staining score of ≥ 4
    - Total lissamine green conjunctival score of ≥ 2
    - Demonstrate Controlled Adverse Environment (CAE) response

OD = Ocular Discomfort
QID = four times daily
Source: Reproxalap DED Phase 2b clinical trial protocol

Phase 2b Dry Eye Disease Clinical Trial Design

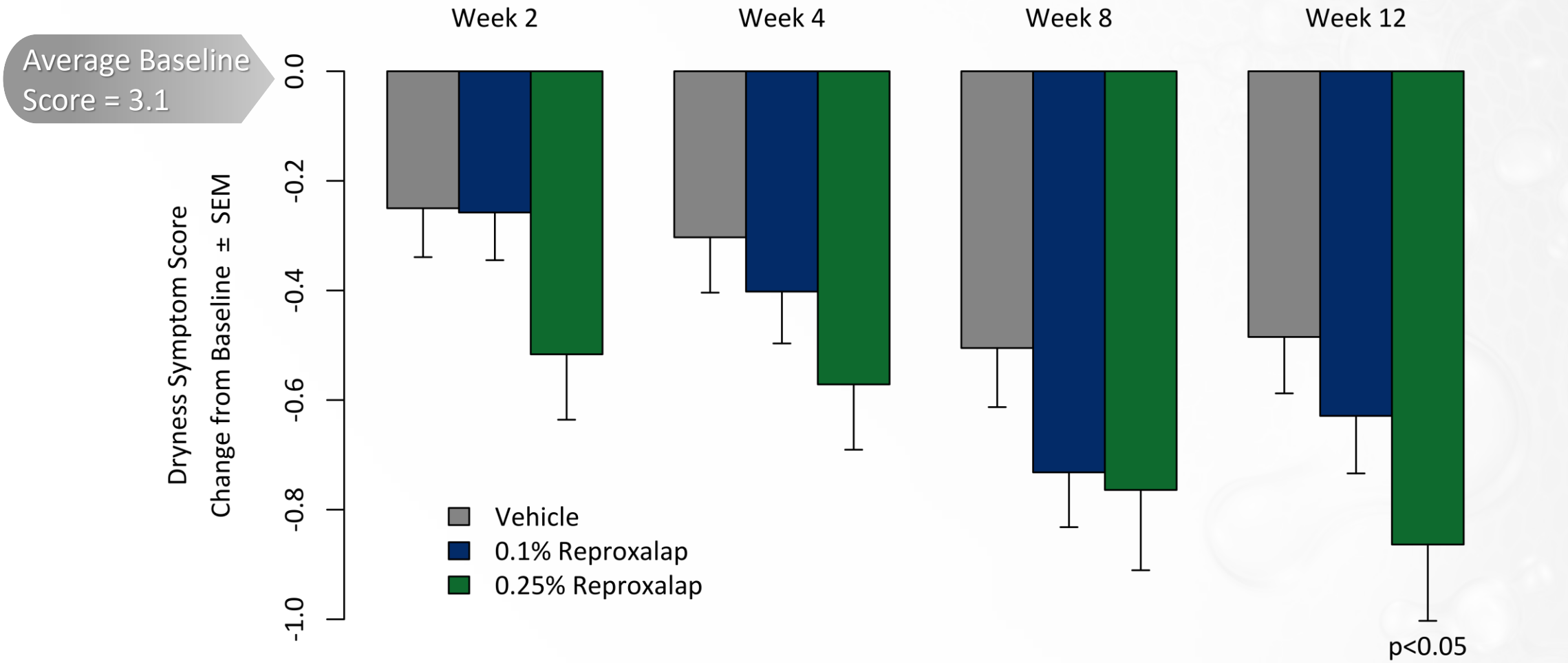
Phase 2b Dry Eye Disease Clinical Trial



Reproxalap Improved Ocular Dryness vs. Vehicle

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

ITT Population with Observed Data Only



p values subject to change based on quality control analysis

Source: Reproxalap DED Phase 2b clinical trial results

OD = Ocular Discomfort

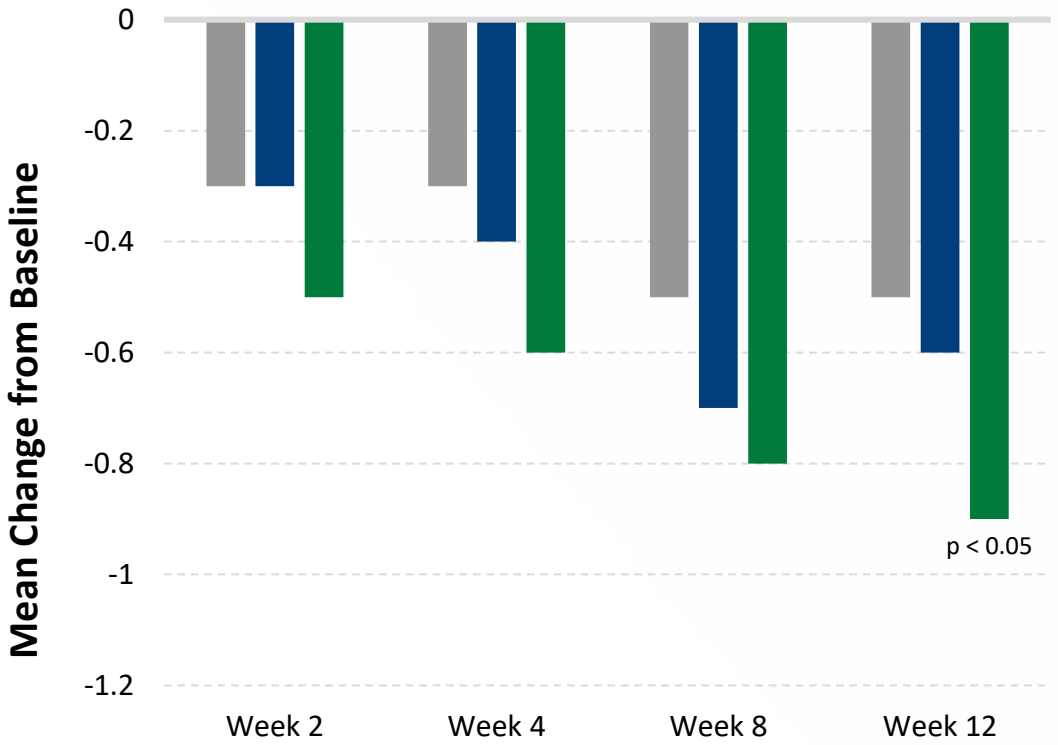
Drug Potency Supported by Ocular Dryness Improvement vs. Vehicle in Higher Baseline Patients

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

Total Population (N=100|100|100)

ITT Population with Observed Data Only

Total Population Average Baseline Score = 3.1

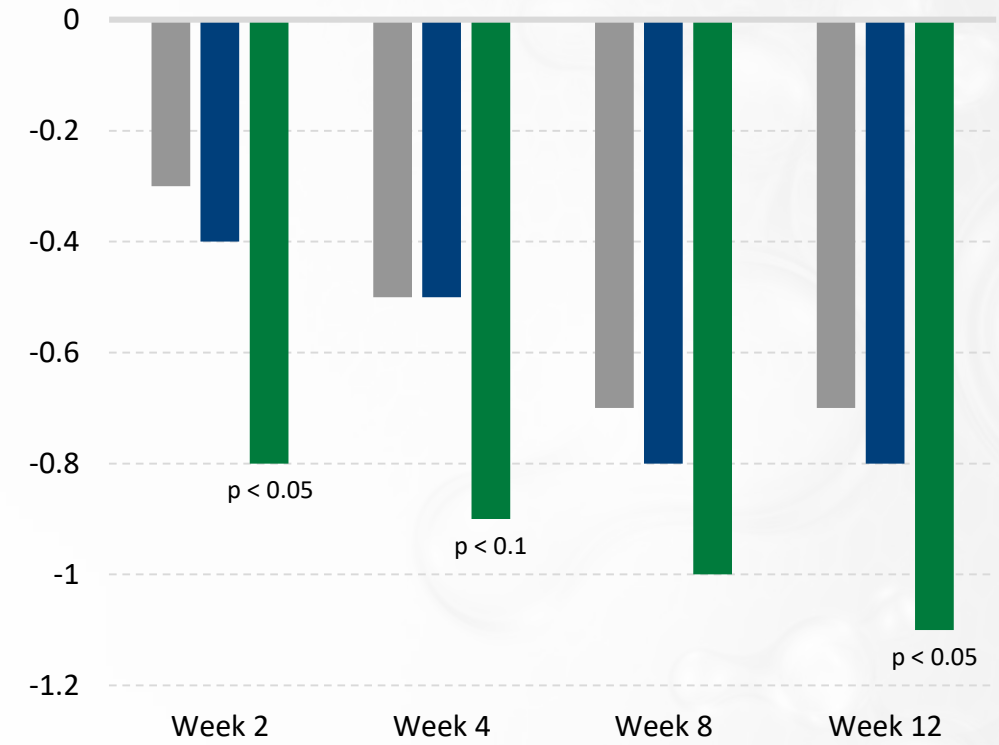


vs.

Above Median Baseline Population (N=79|69|69)

ITT Population with Observed Data Only

Above Median Population Average Baseline Score = 3.6



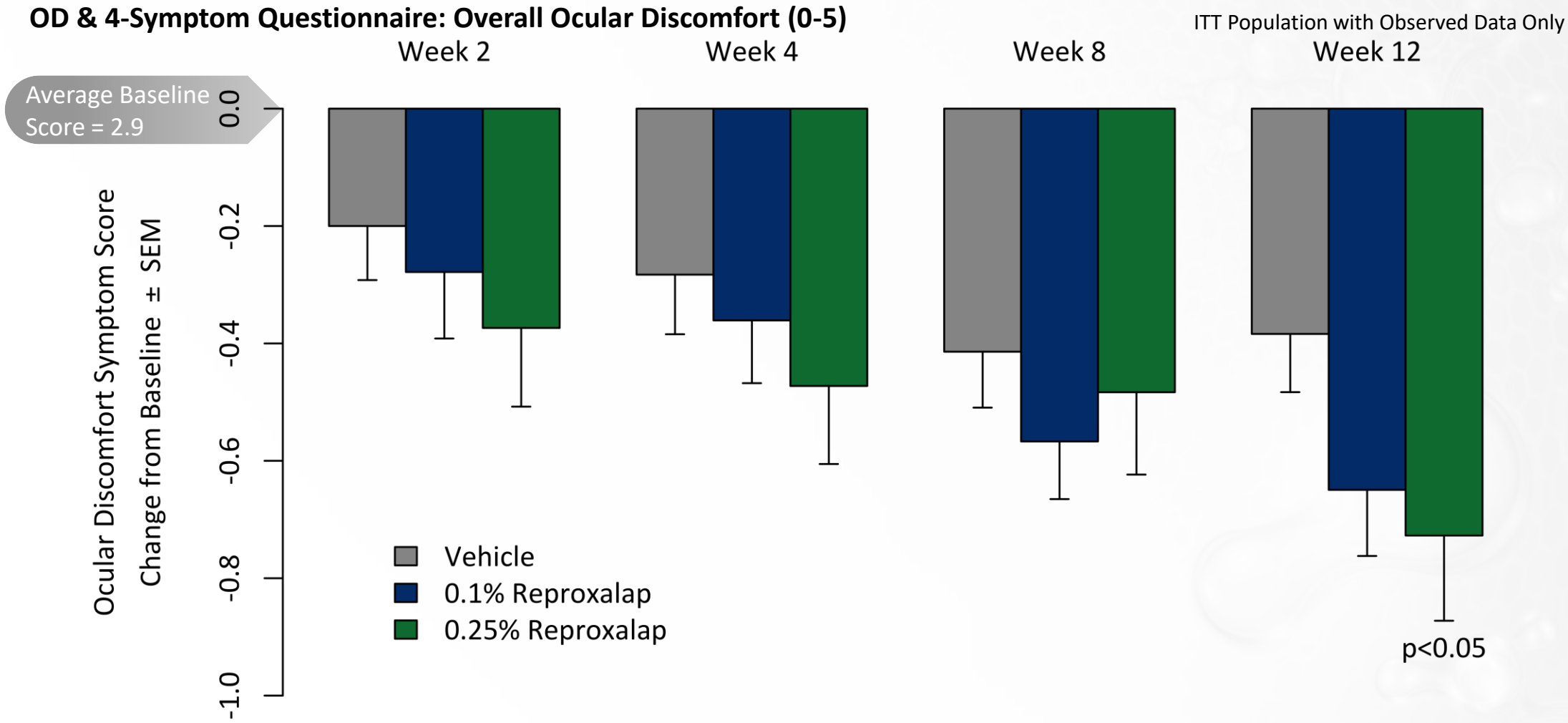
Vehicle | Reproxalap (0.1%) | Reproxalap (0.25%)

p values subject to change based on quality control analysis

Source: Reproxalap DED Phase 2b clinical trial results

OD = Ocular Discomfort

Ocular Discomfort Symptom Results Support Observed Improvement in Ocular Dryness Score



p values subject to change based on quality control analysis

Source: Reproxalap DED Phase 2b clinical trial results

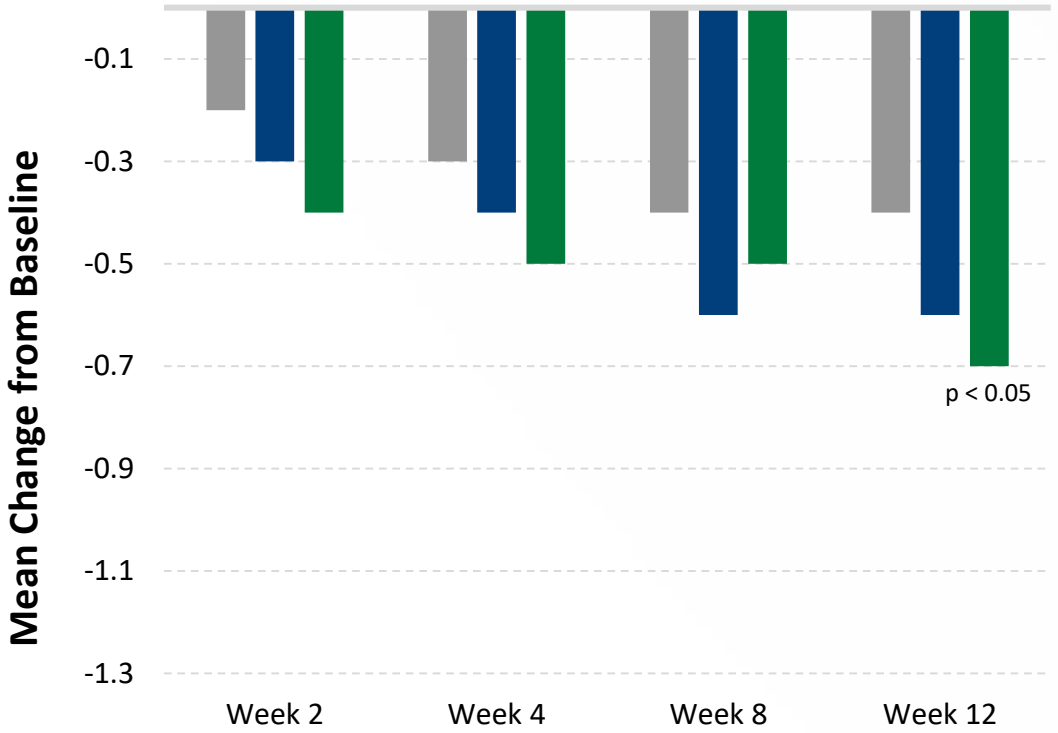
OD = Ocular Discomfort

Drug Potency Supported by Ocular Discomfort Improvement vs. Vehicle in Higher Baseline Patients

OD & 4-Symptom Questionnaire: Overall Ocular Discomfort (0-5)

Total Population (N=100|100|100)
ITT Population with Observed Data Only

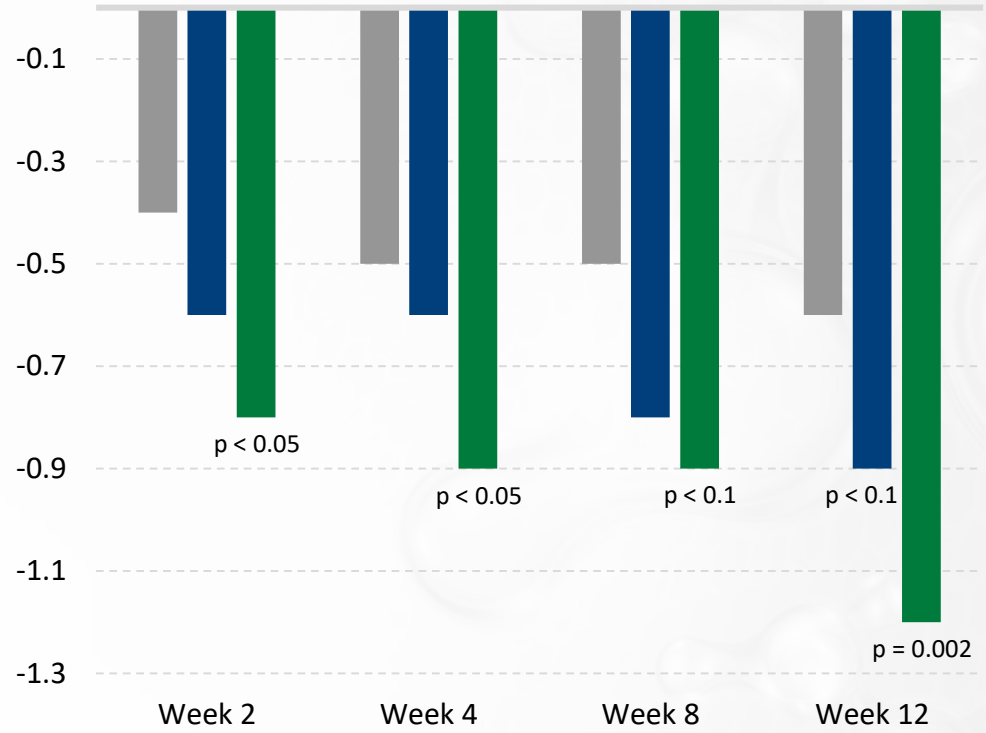
Total Population Average Baseline Score = 2.9



vs.

Above Median Baseline Population (N=69|65|64)
ITT Population with Observed Data Only

Above Median Population Average Baseline Score = 3.4



Vehicle | Reproxalap (0.1%) | Reproxalap (0.25%)

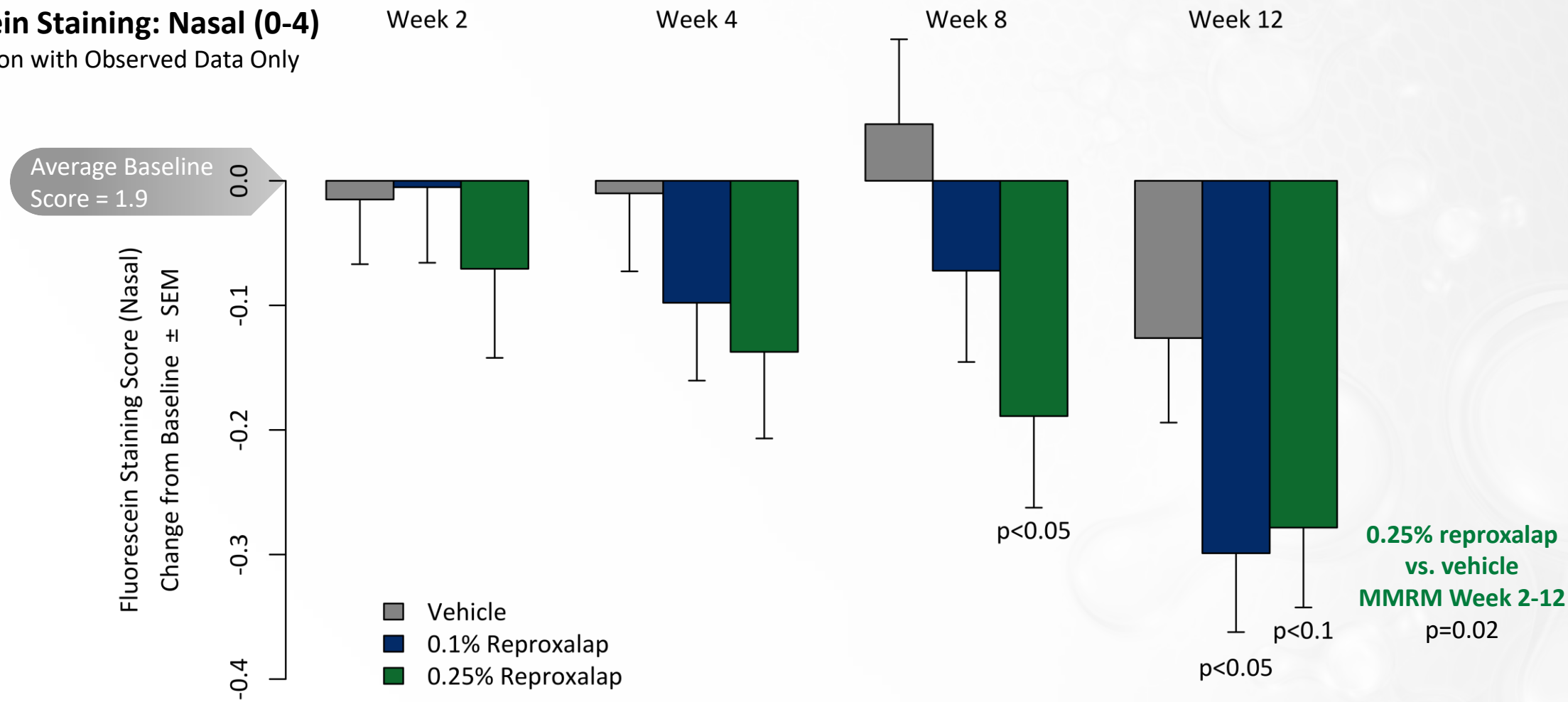
p values subject to change based on quality control analysis
Source: Reproxalap DED Phase 2b clinical trial results

OD = Ocular Discomfort

Reproxalap Improved Ocular Staining vs. Vehicle

Fluorescein Staining: Nasal (0-4)

ITT Population with Observed Data Only



p values subject to change based on quality control analysis

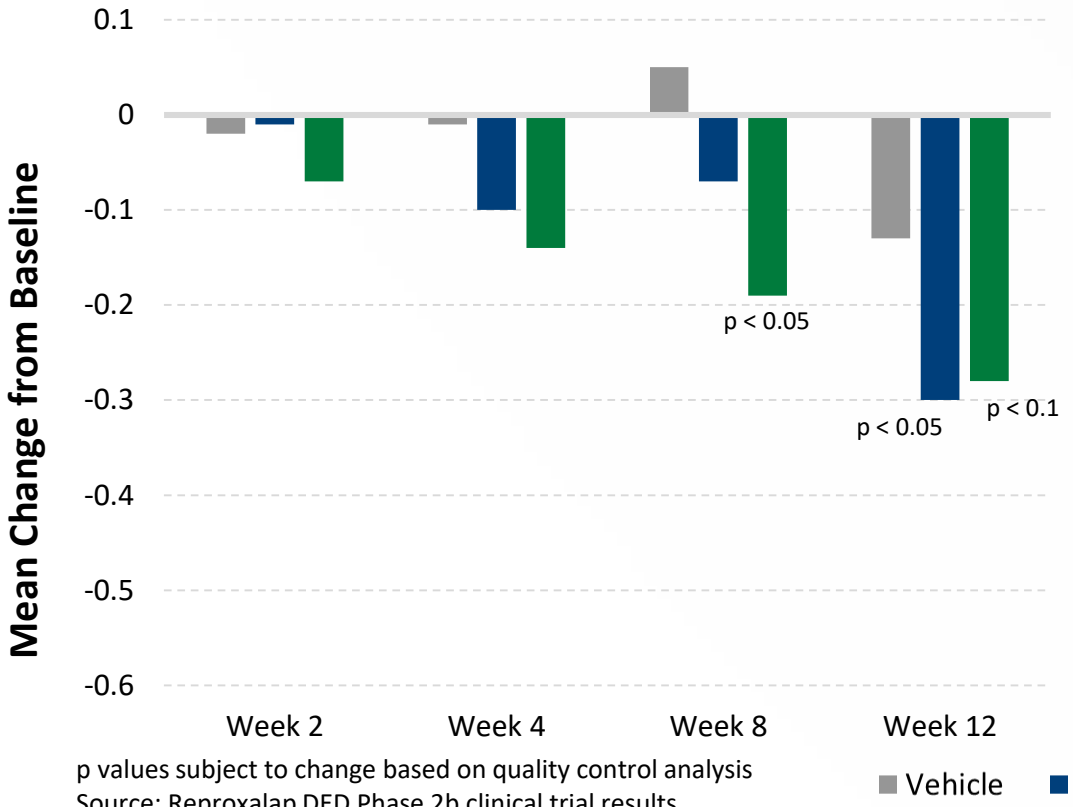
Source: Reproxalap DED Phase 2b clinical trial results

Drug Potency Supported by Ocular Staining Improvement vs. Vehicle in Higher Baseline Patients

Fluorescein Staining: Nasal (0-4)

Total Population (N=100|100|100)
ITT Population with Observed Data Only

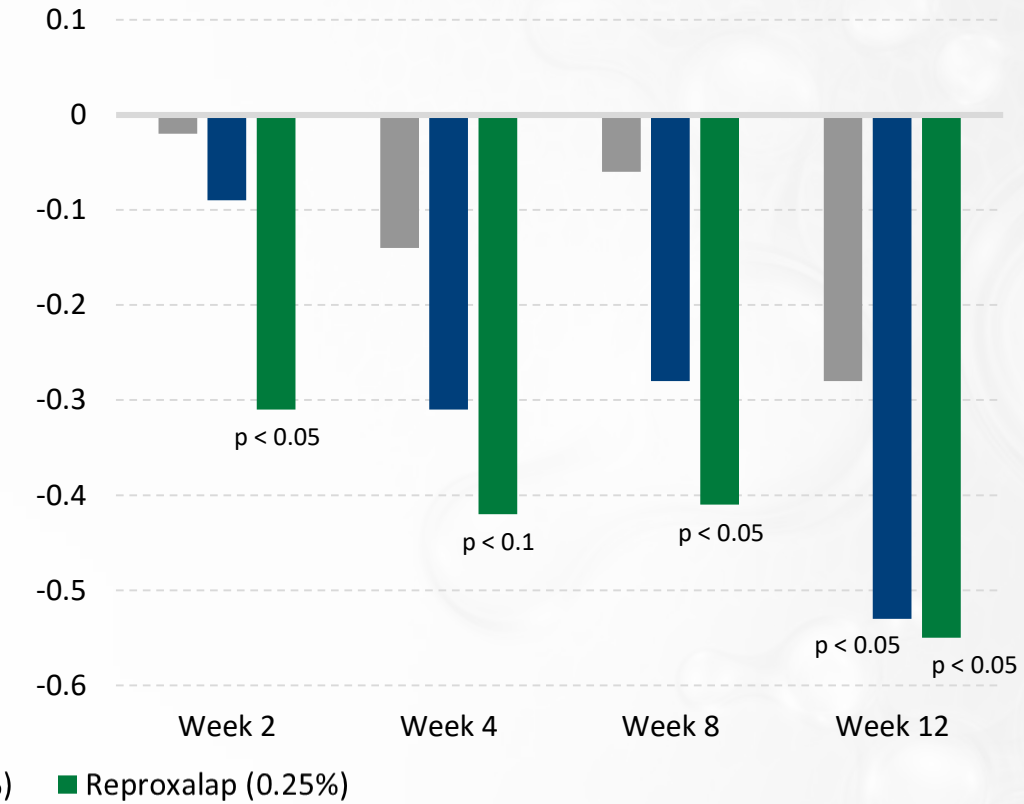
Total Population Average Baseline Score = 1.9



vs.

Above Median Baseline Population (N=59|56|62)
ITT Population with Observed Data Only

Above Median Population Average Baseline Score = 2.3



Vehicle Reproxalap (0.1%) Reproxalap (0.25%)

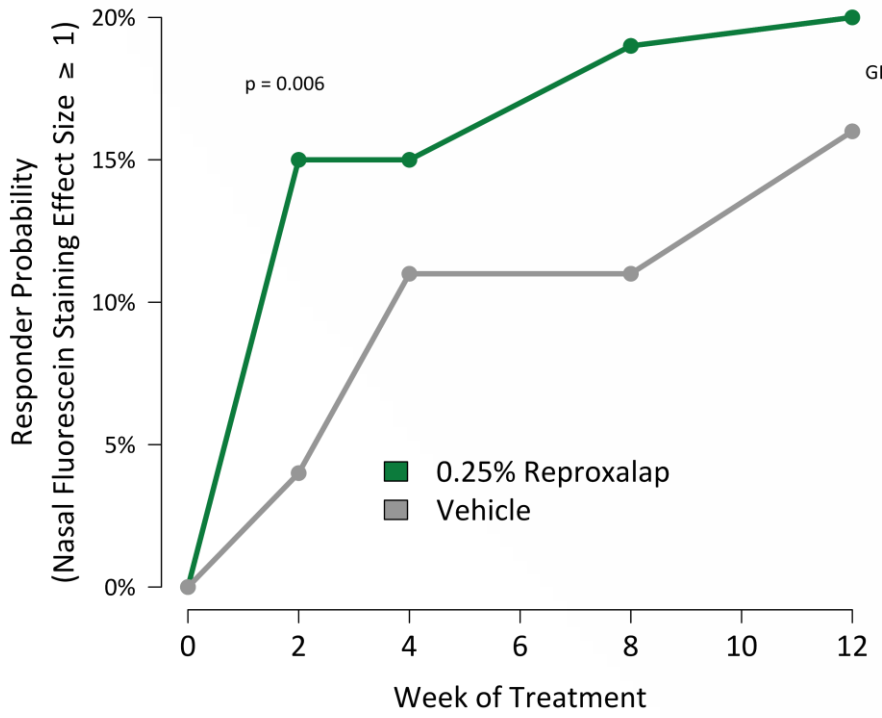
p values subject to change based on quality control analysis
Source: Reproxalap DED Phase 2b clinical trial results

Ocular Staining Responder Analyses Demonstrate Statistical Superiority of Reproxalap over Vehicle

Fluorescein Staining (Nasal)

ITT Population with Observed Data Only

Probability of Response for Staining

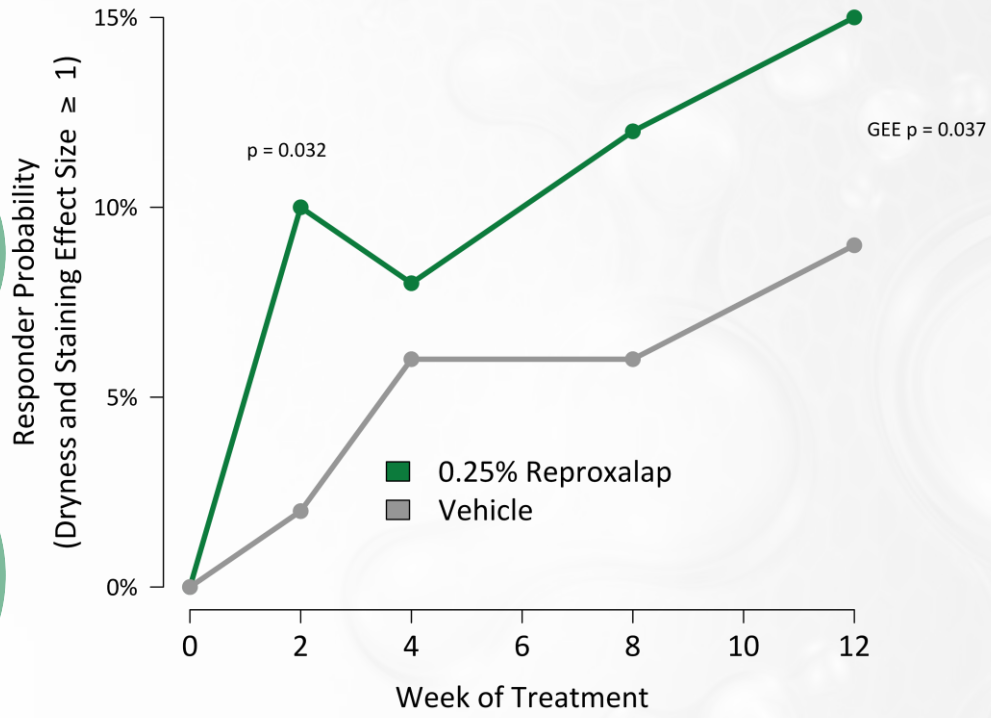


- ✓Clinically significant response in 2 weeks
- ✓Statistically significant response in symptom and sign vs. vehicle

OD&4S: Ocular Dryness and Fluorescein Staining (Nasal)

ITT Population with Observed Data Only

Probability of Response for both Ocular Dryness and Staining



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

OD&4S = Ocular Discomfort & 4 Symptom
Effect Size = Change from Baseline / Standard Deviation at Baseline

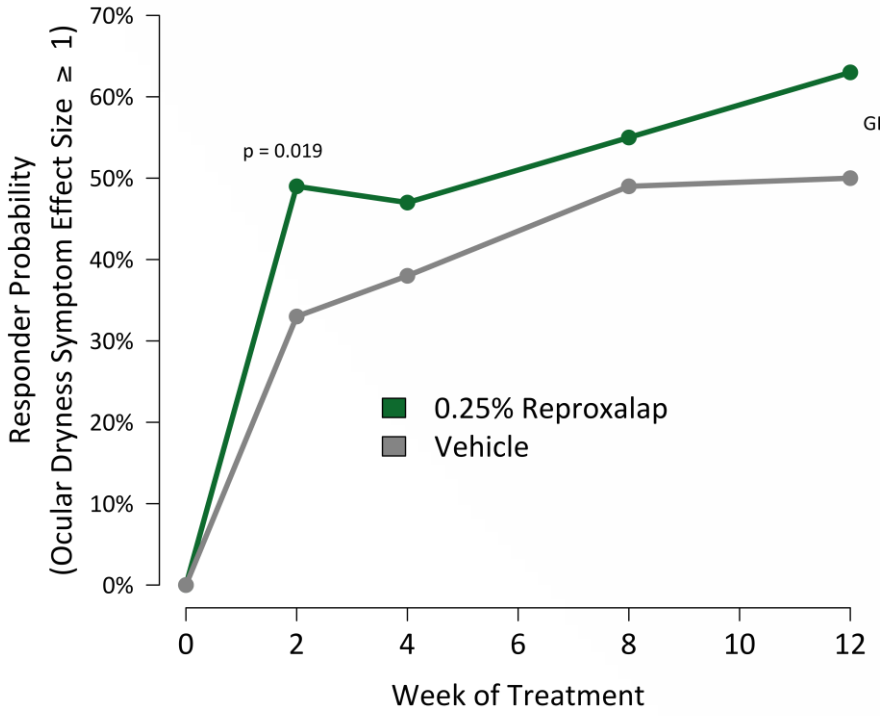
GEE = Generalized Estimating Equations

Reproxalap's Differentiated Product Profile Evidenced by Responder Analyses – Rapid and Symptom-Free (Ocular Dryness)

OD & 4-Symptom Questionnaire: Dryness

ITT Population with Observed Data Only

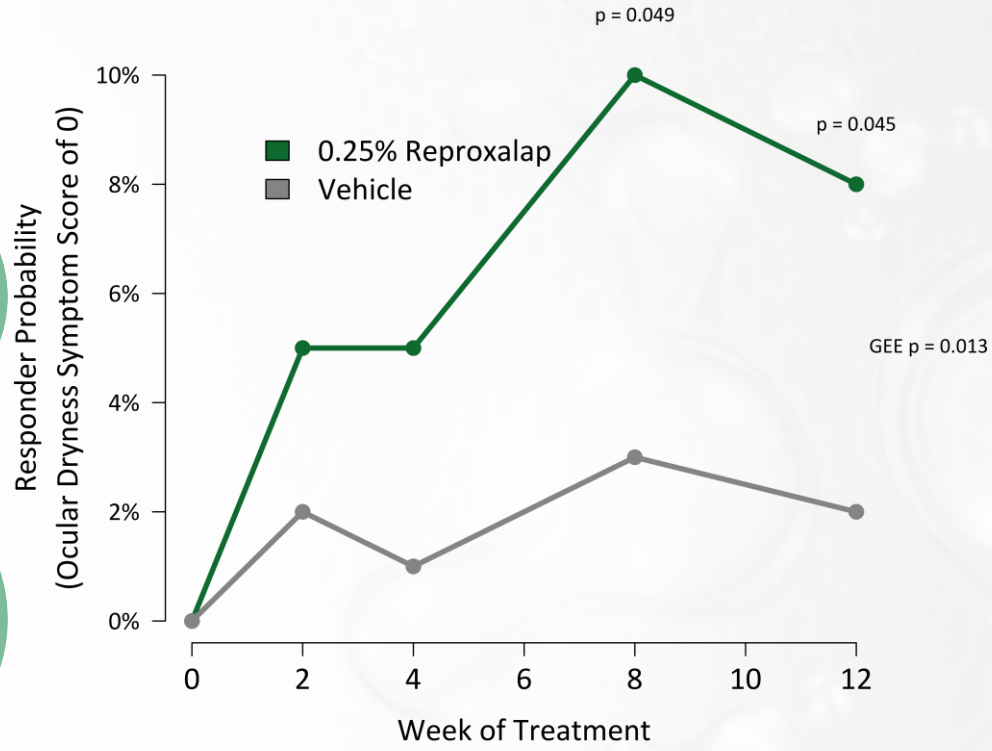
Probability of Response (Improvement Effect Size ≥1)



✓Clinically significant response in 2 weeks

✓Statistically significant symptom-free response vs. vehicle

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



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

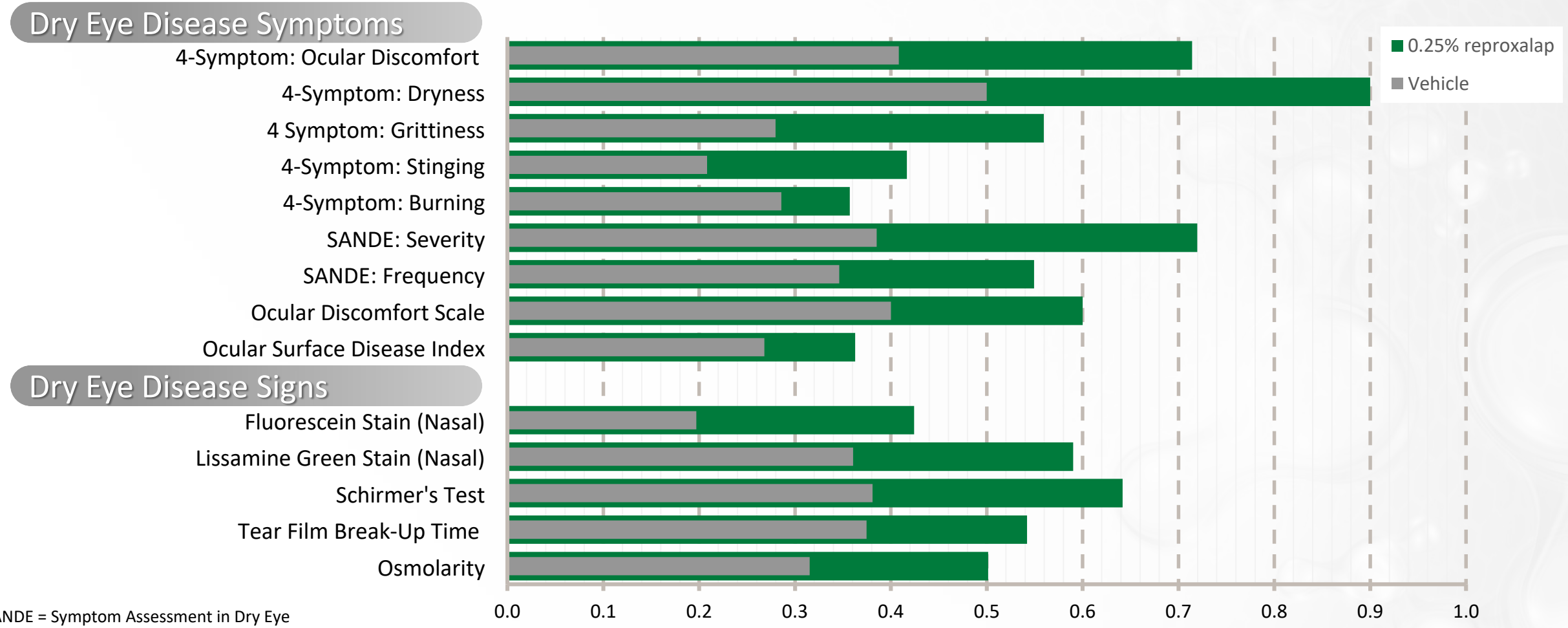
OD = Ocular Discomfort
Effect Size = Change from Baseline / Standard Deviation at Baseline

GEE = Generalized Estimating Equations

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

Improvement Effect Size at Week 12

ITT Population with Observed Data Only



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

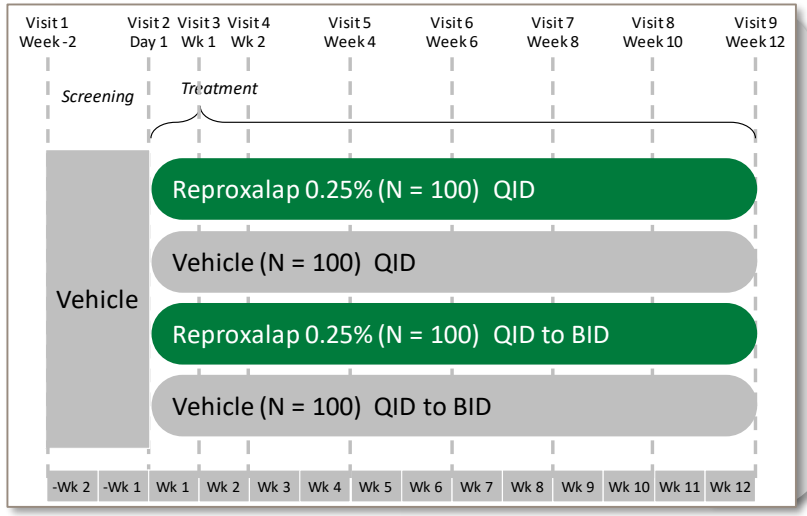
Conclusions

Positive Phase 2b Clinical Trial Results

- **Primary objective achieved:**
  Endpoint selection and sample size powering confirmed for Phase 3 clinical trials
- Reproxalap demonstrated **statistically significant improvements** versus vehicle across multiple symptom and sign measures, consistent with novel and broad mechanism of action
- **Pathway to registration trials confirmed** with ocular dryness symptom score, ocular staining score, and 0.25% reproxalap dose
- **Improvements in symptoms and signs observed as early as two weeks**, consistent with prior reproxalap clinical trial results and supportive of differentiated product profile
- Aldeyra has conducted an EOP2 meeting with the FDA, agreeing on adaptive Phase 3 clinical trial design, primary endpoints and analysis strategy
- **Phase 3 clinical program started in 2019**
- Rigorous clinical data demonstrate the efficacy and safety of reproxalap in **dry eye disease and allergic conjunctivitis**, two medical conditions with considerable overlap

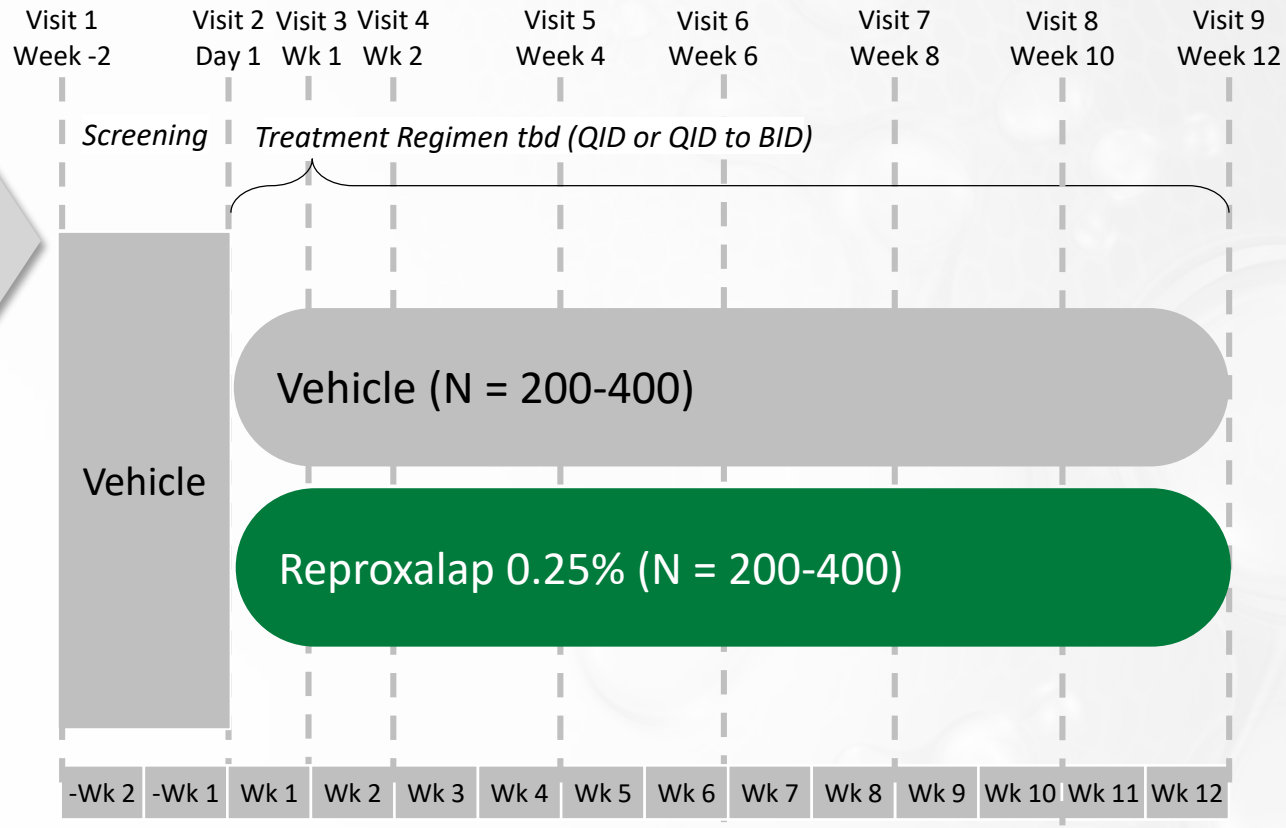
Adaptive Phase 3 Dry Eye Disease Clinical Trial Design

Phase 3 Dry Eye Disease Clinical Trial: Part 1



✓ Confirmed sample size
✓ Confirmed dosing regimen

Phase 3 Dry Eye Disease Clinical Trial: Part 2



Phase 3 Dry Eye Disease Clinical Trial: Part 1 and 2

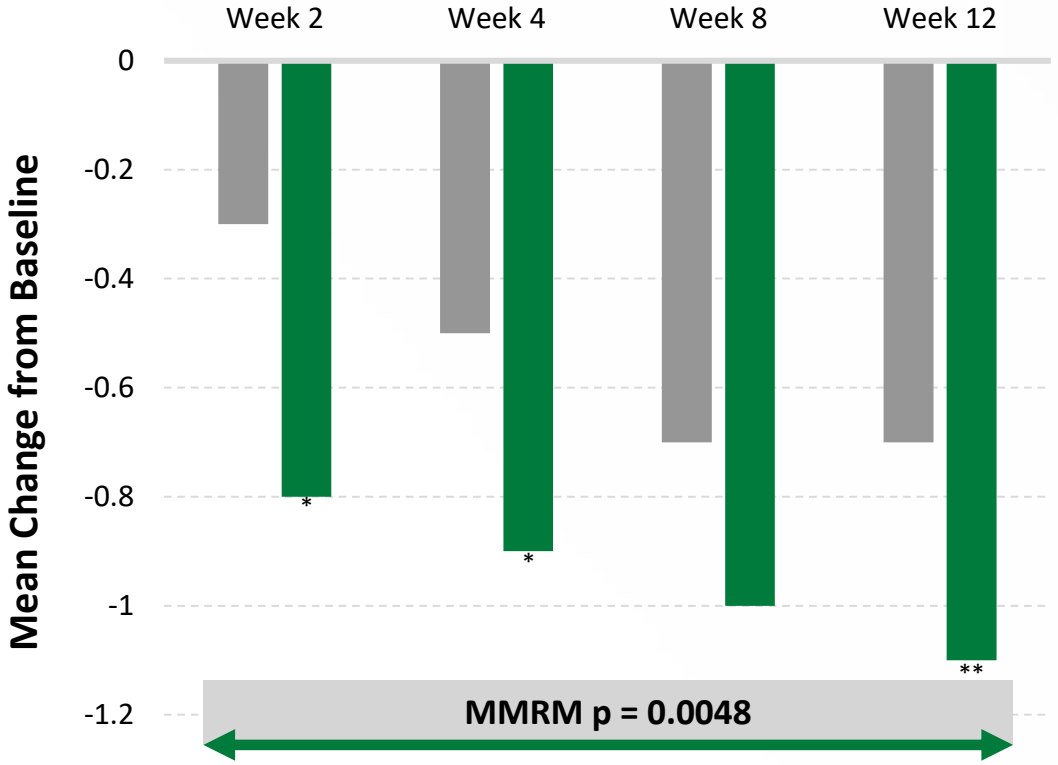
- **Primary objective:**
  Evaluate efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle on co-primary symptom and sign endpoints
- **Population selection and design:**
  Same as used for Phase 2b

Phase 3 Primary Endpoint Strategy: Dry Eye Disease Symptom and Sign Endpoints Achieved in Phase 2b Clinical Trial with MMRM

Primary Symptom Endpoint for Phase 3 DED

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

Baseline Score ≥ 3 (N=69|69)



Primary Sign Endpoint for Phase 3 DED

Fluorescein Staining: Nasal (0-4)

Baseline Score ≥ 2 (N=62|56)

Vehicle Reproxalap (0.25%)

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

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

ALDEYRA THERAPEUTICS™

Thank You

ARVO May 1, 2019 Vancouver, BC