July 22, 2021

Eyecelerator@ASCRS

Reproxalap: A Novel Treatment Approach for Anterior Segment Inflammatory Disease

Nasdaq: ALDX

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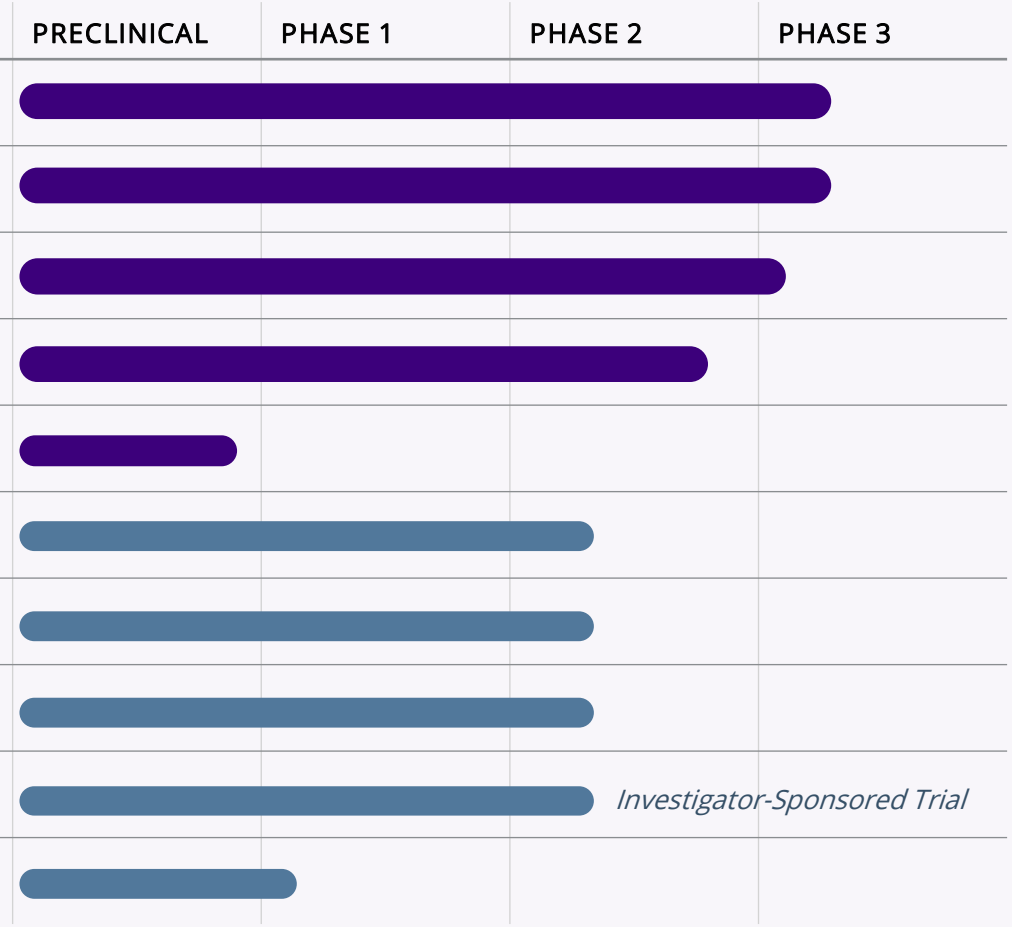
Deep and Innovative Immunology Pipeline

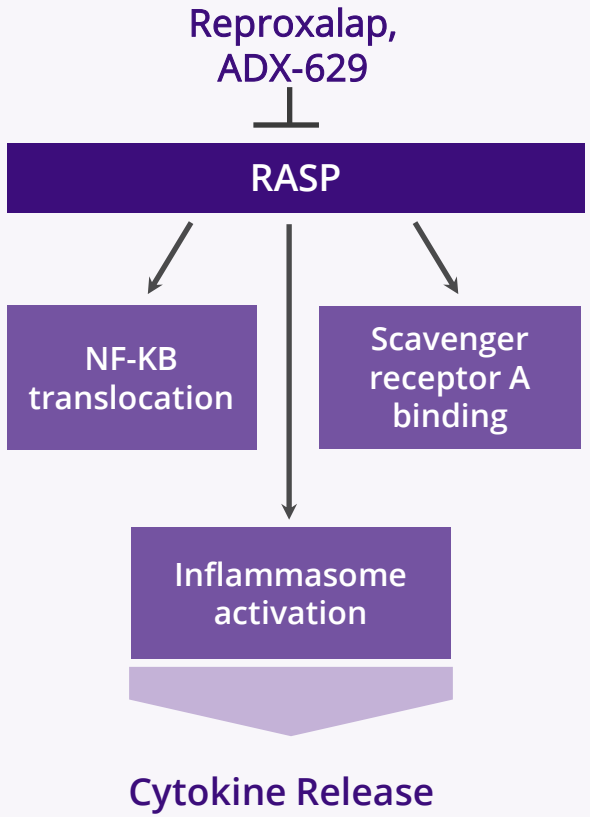
Multiple Phase 3 Clinical Trials in Ocular Disease

DISEASE AREA	COMPOUND	MECHANISM	INDICATION
Ocular Diseases	Reproxalap	RASP	Dry Eye Disease
			Allergic Conjunctivitis
	ADX-2191	DHFR	Proliferative Vitreoretinopathy
			Primary Vitreoretinal Lymphoma
	ADX-103/10X	RASP	Retinal Disease
Systemic Diseases	ADX-629	RASP	Cytokine Release Syndrome (COVID-19)
			Allergy (Atopic Asthma)
			Autoimmune Disease (Psoriasis)
	ADX-1612	CHP	Ovarian Cancer
			SARS-CoV2 Antiviral (COVID-19)



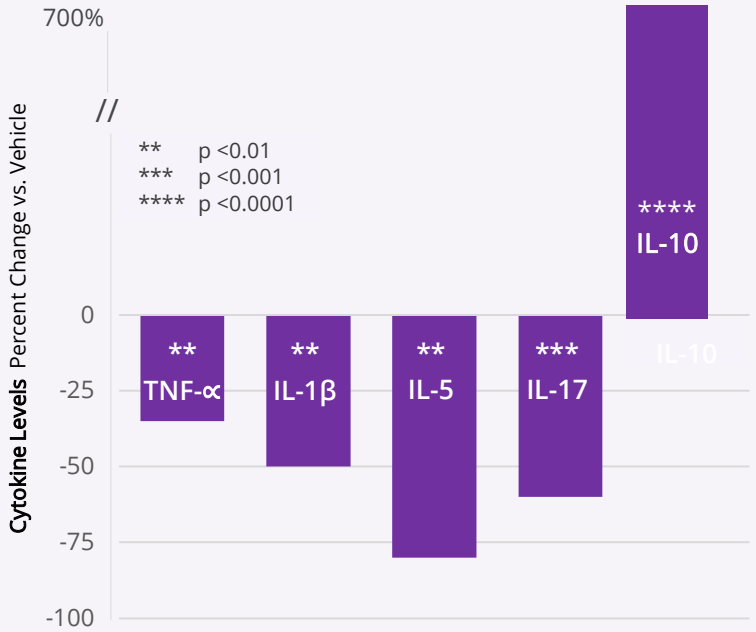
RASP Mechanism = Reactive Aldehyde Species Inhibitor DHFR Mechanism = Dihydrofolate Reductase Inhibitor CHP Mechanism = Chaperome Inhibitor

RASP Inhibition is a Pre-Cytokine, Systems-Based Approach that Has Been Clinically Validated in Late-Stage Trials



Preclinical Broad-based Cytokine Reduction

LPS Animal Model of Cytokine Storm

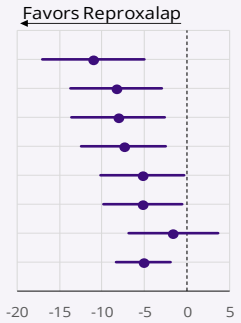


Broad-based Symptom Reduction

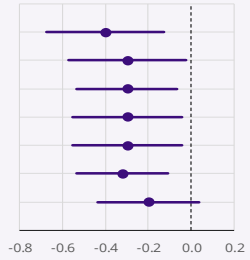
RENEW-Part 1 Phase 3 Dry Eye Disease Trial

Symptom Treatment Difference‡ (Reproxalap-Vehicle) Weeks 2 -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
OSDI (Total)	0.0020



0-4 & 0-5 Ocular Symptom Scales	
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



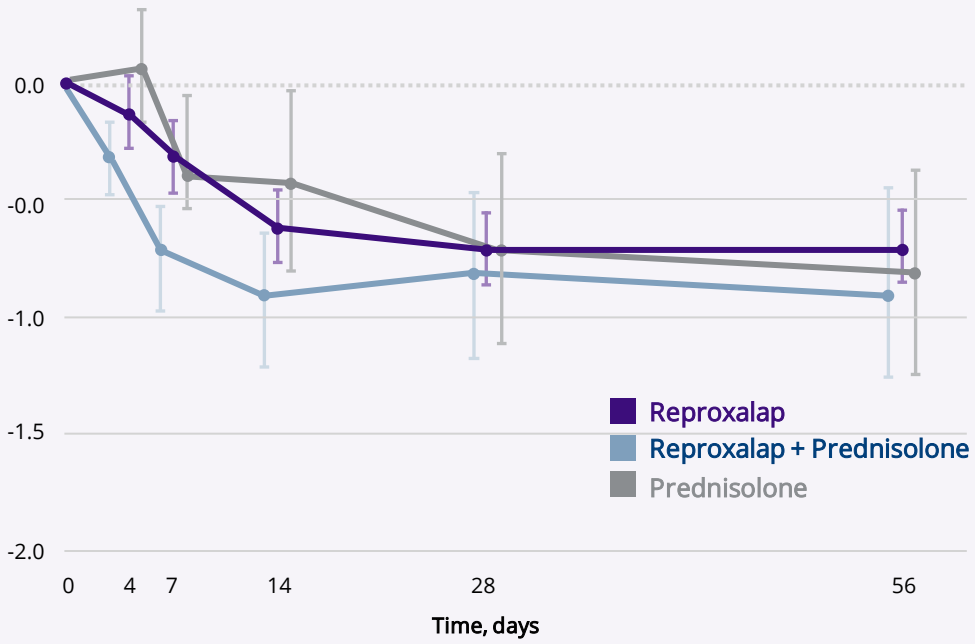
‡Treatment Difference of induction-maintenance dosing, defined as the difference between the changes from baseline for the evaluated drug vs. vehicle (LS Mean Difference ± 95% CI). Ocular Dryness Score co-primary endpoint assessed in pre-specified patient population having an OD4S dryness baseline score of ≥ 3 (N=170). Sources: Cullen, et al. The Small Molecule Aldehyde Trap NS2 Exhibits Potent Anti-Inflammatory Activity in Three Murine Models of Inflammation [abstract]. In: The Journal of Allergy and Clinical Immunology. Volume 135, Issue 2, AB384, Feb 2015; ; Reproxalap RENEW-Part 1 clinical trial results. RASP = Reactive Aldehyde Species VAS = Visual Analog Scale OSDI = Ocular Surface Disease Index NS = Not Significant OD4S = Ocular Discomfort & 4-Symptom CAC = Conjunctival Allergen Challenge

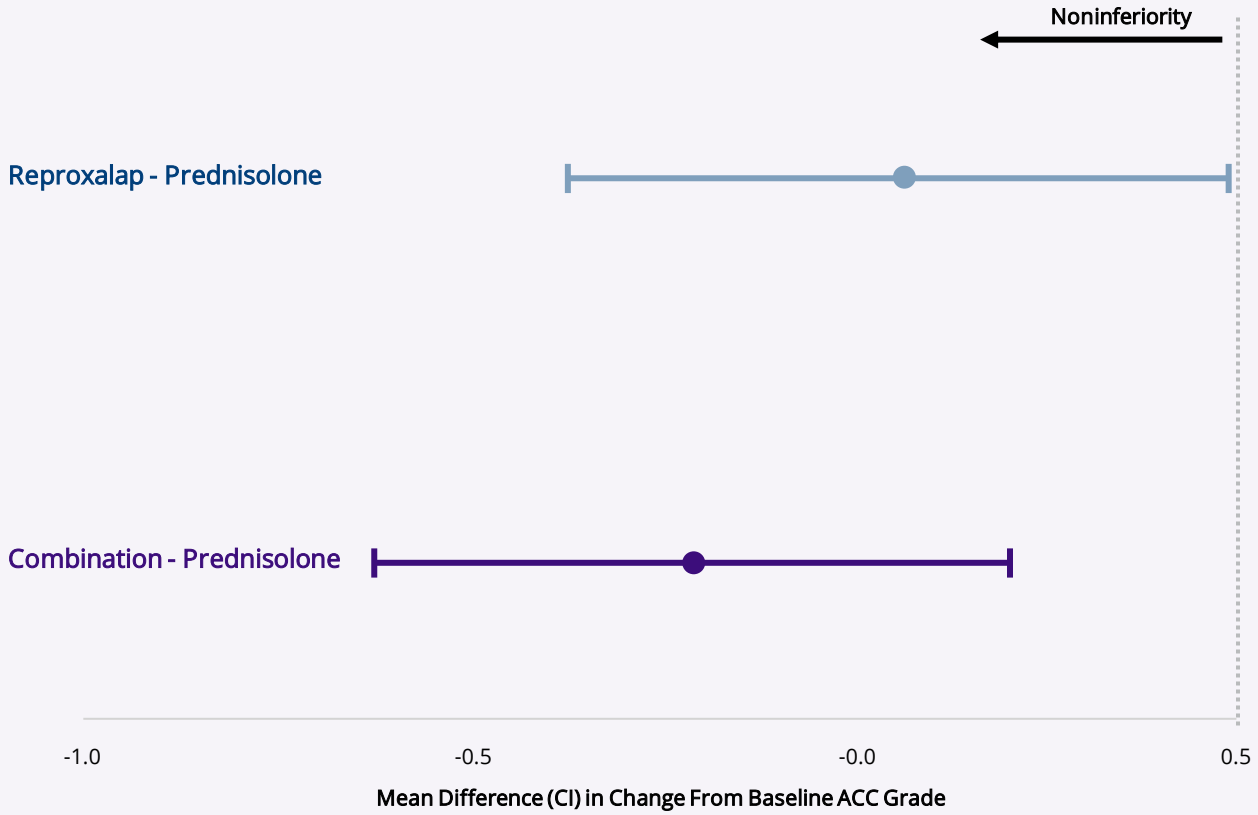
Reproxalap Activity in Ocular Inflammatory Diseases is Supported by Marquee Peer-Reviewed Publications

Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Reproxalap Reduced Anterior Cell Count in Patients with Noninfectious Anterior Uveitis

Anterior Chamber Cell Count Grade Mean (SE) Change From Baseline

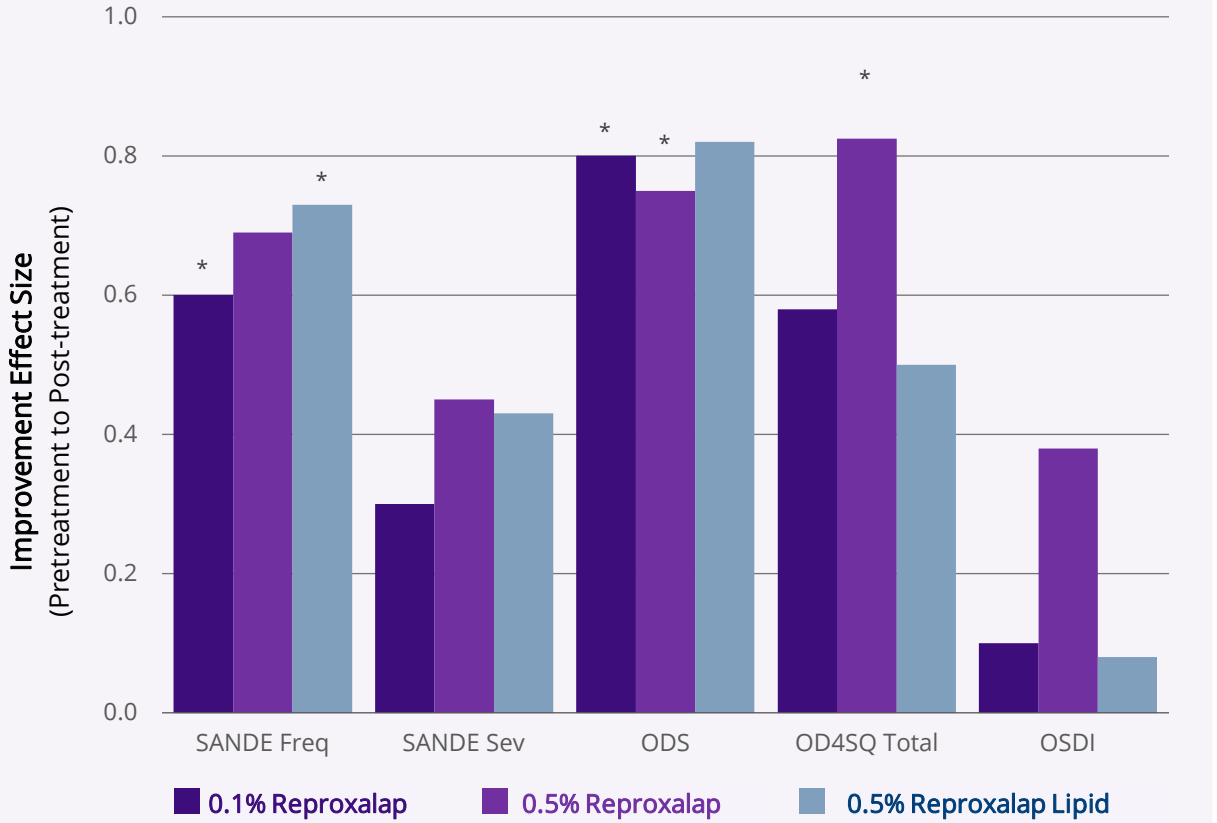


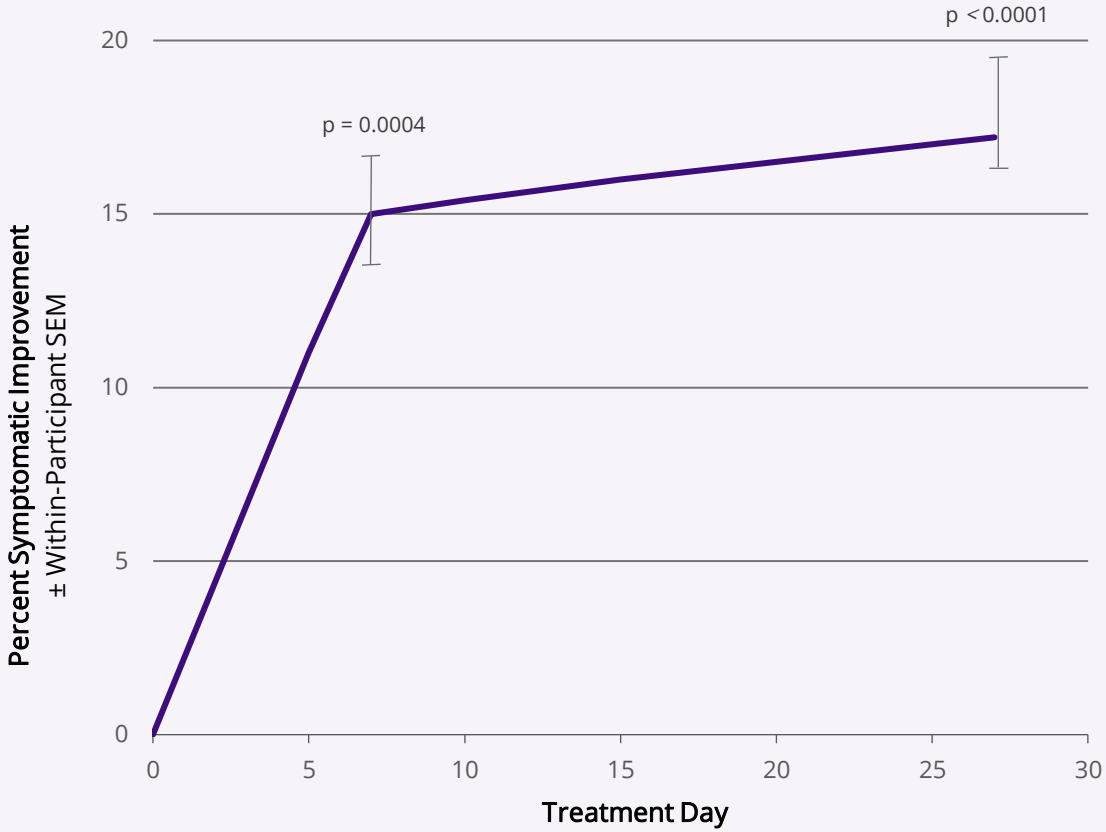


Mandell KJ, Clark D, Chu DS, Foster CS, Sheppard J, Brady TC. Randomized Phase 2 Trial of Reproxalap, a Novel Reactive Aldehyde Species Inhibitor, in Patients with Noninfectious Anterior Uveitis: Model for Corticosteroid Replacement. J Ocul Pharmacol Ther. 2020;36(10):732-739.

Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Reproxalap Generated Early Onset and Clinically Relevant Improvements in Dry Eye Disease Symptoms in Phase 2a Trial





Clark D, Sheppard J, Brady TC. A Randomized Double-Masked Phase 2a Trial to Evaluate Activity and Safety of Topical Ocular Reproxalap, a Novel RASP Inhibitor, in Dry Eye Disease. J Ocul Pharmacol Ther. 2021 May;37(4):193-199. doi: 10.1089/jop.2020.0087. Epub 2021 Jan 15. PMID: 33450164; PMCID: PMC8106247.

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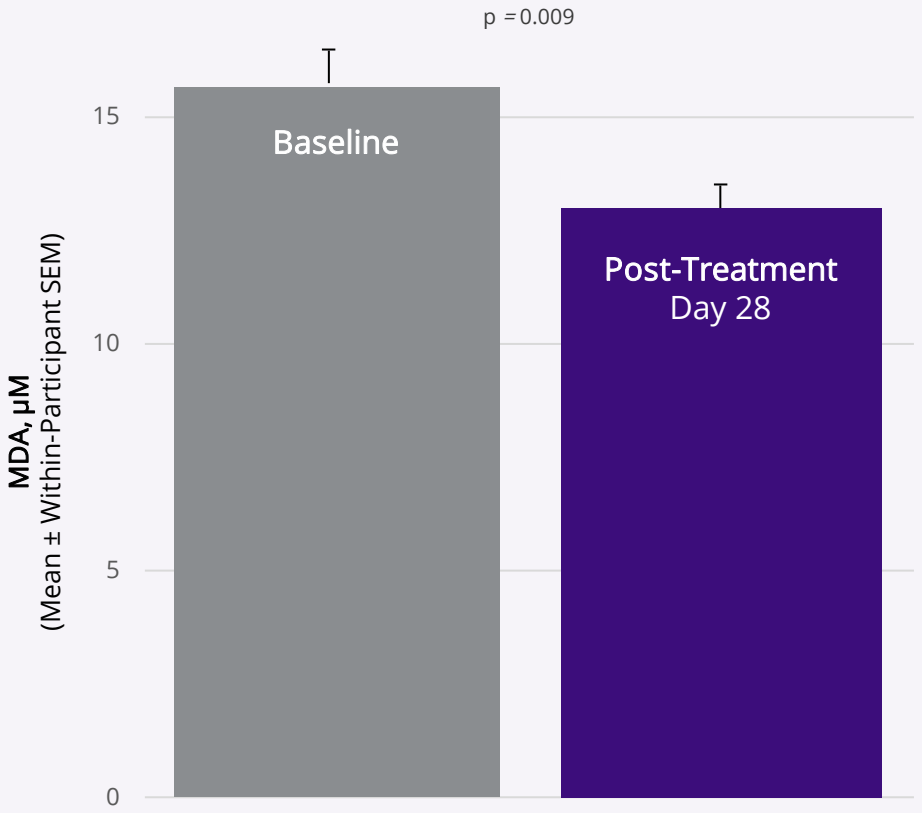
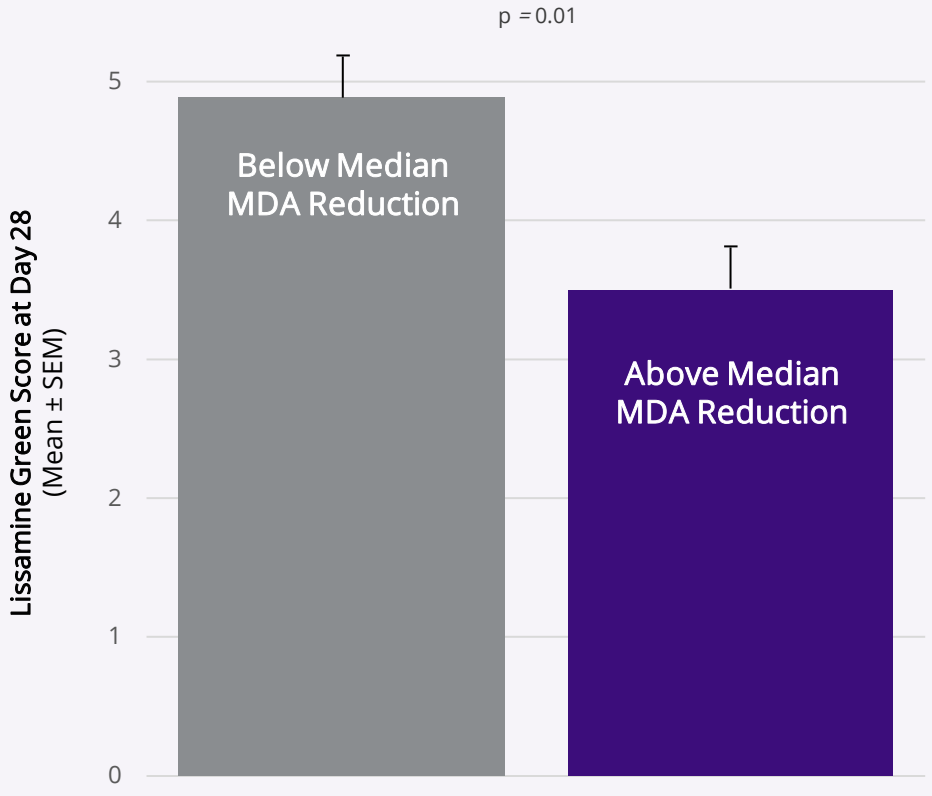
Reproxalap Reduced Tear RASP Levels in Phase 2a Trial





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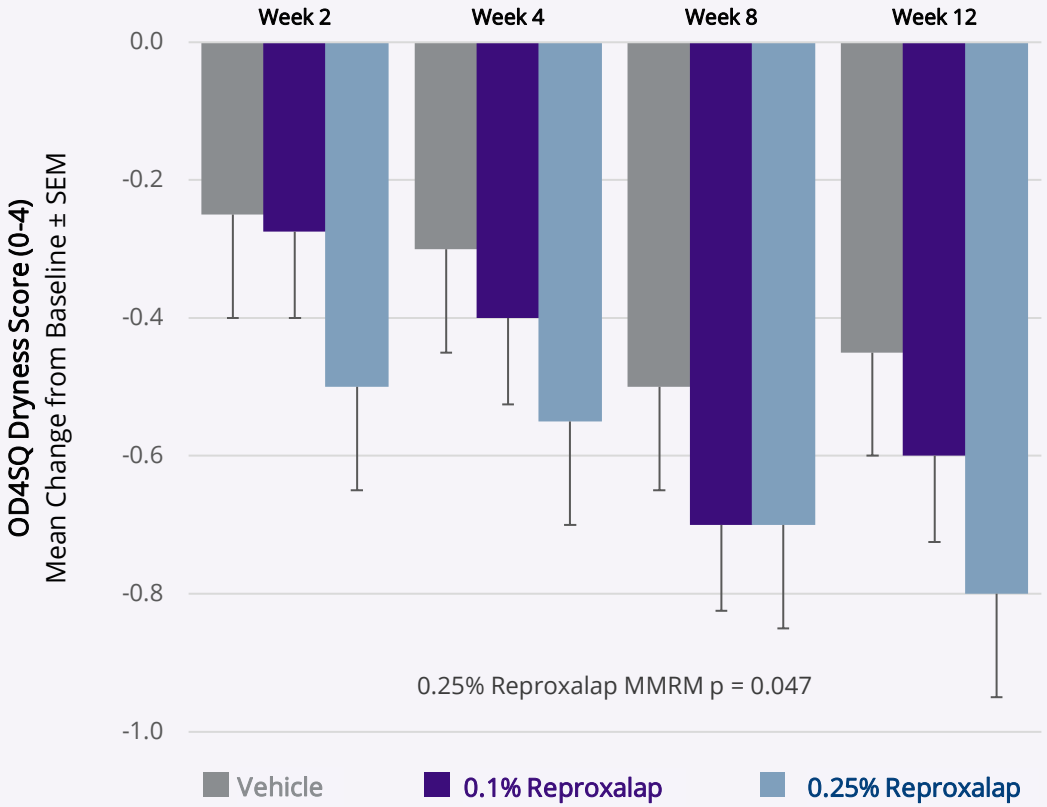
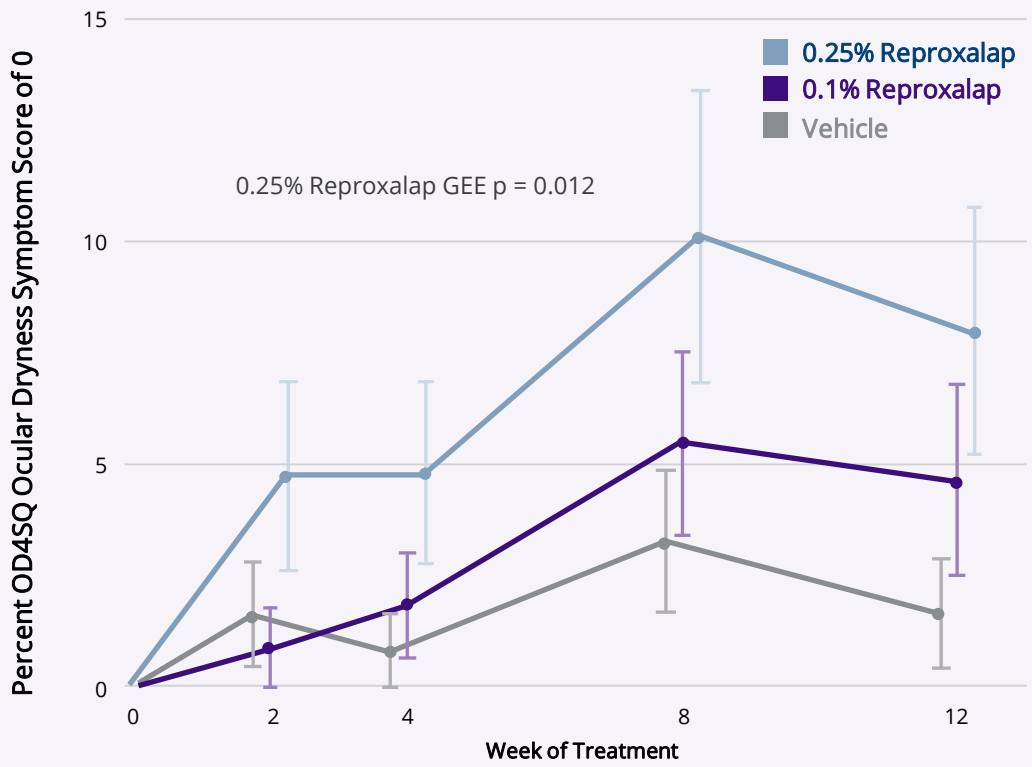
Reproxalap Generated Clinically Relevant Improvements in Dry Eye Disease Symptoms in Phase 2b Trial





Clark D, Tauber J, Sheppard J, Brady TC. Early Onset and Broad Activity of Reproxalap in a Randomized, Double-Masked, Vehicle-Controlled Phase 2b Trial in Dry Eye Disease [published online ahead of print, 2021 Jan 30]. Am J Ophthalmol. 2021;226:22-31. doi:10.1016/j.ajo.2021.01.011

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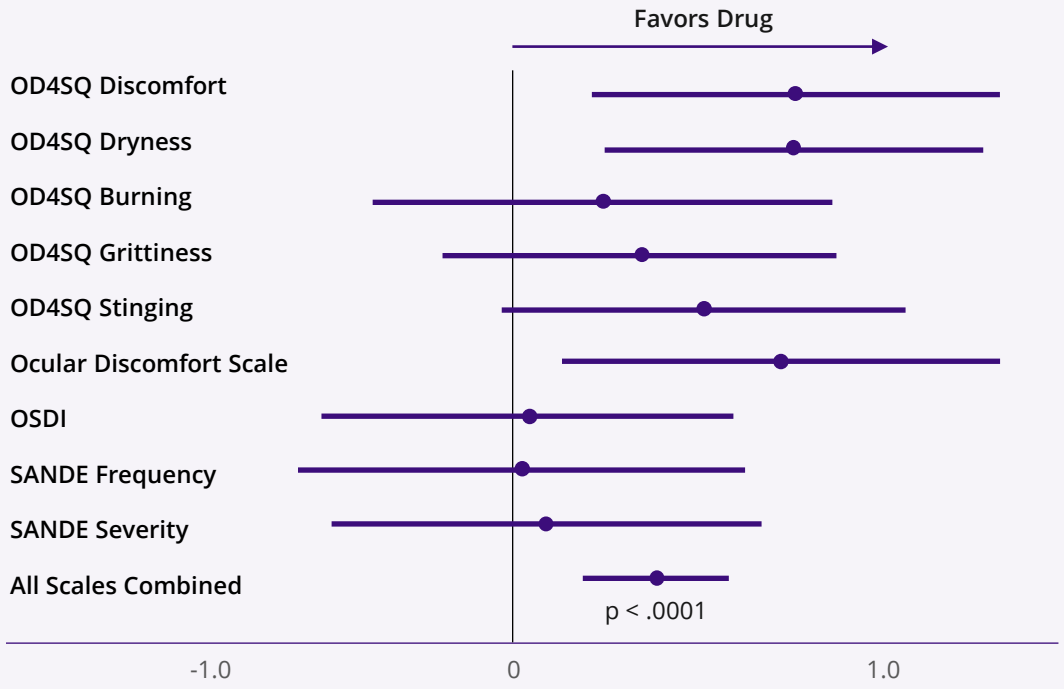
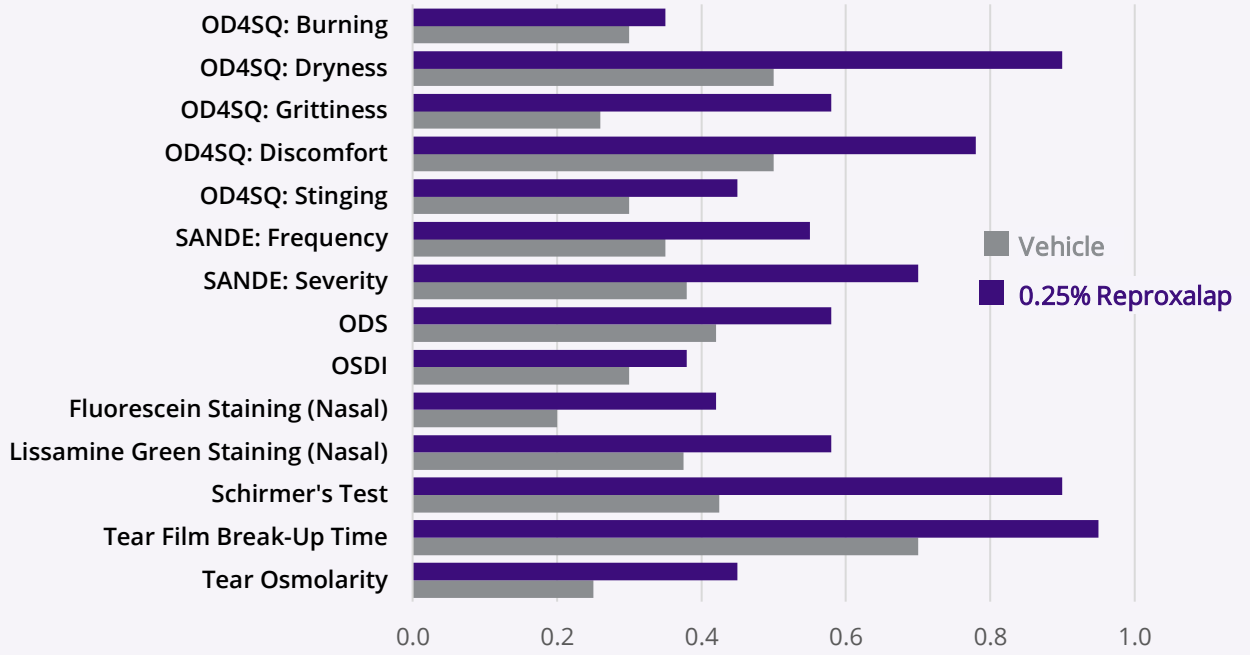
Reproxalap Generated Broad Activity Across Symptoms and Signs in Phase 2b Trial



Improvement Effect Size (Reproxalap – Vehicle)



Improvement Effect Size

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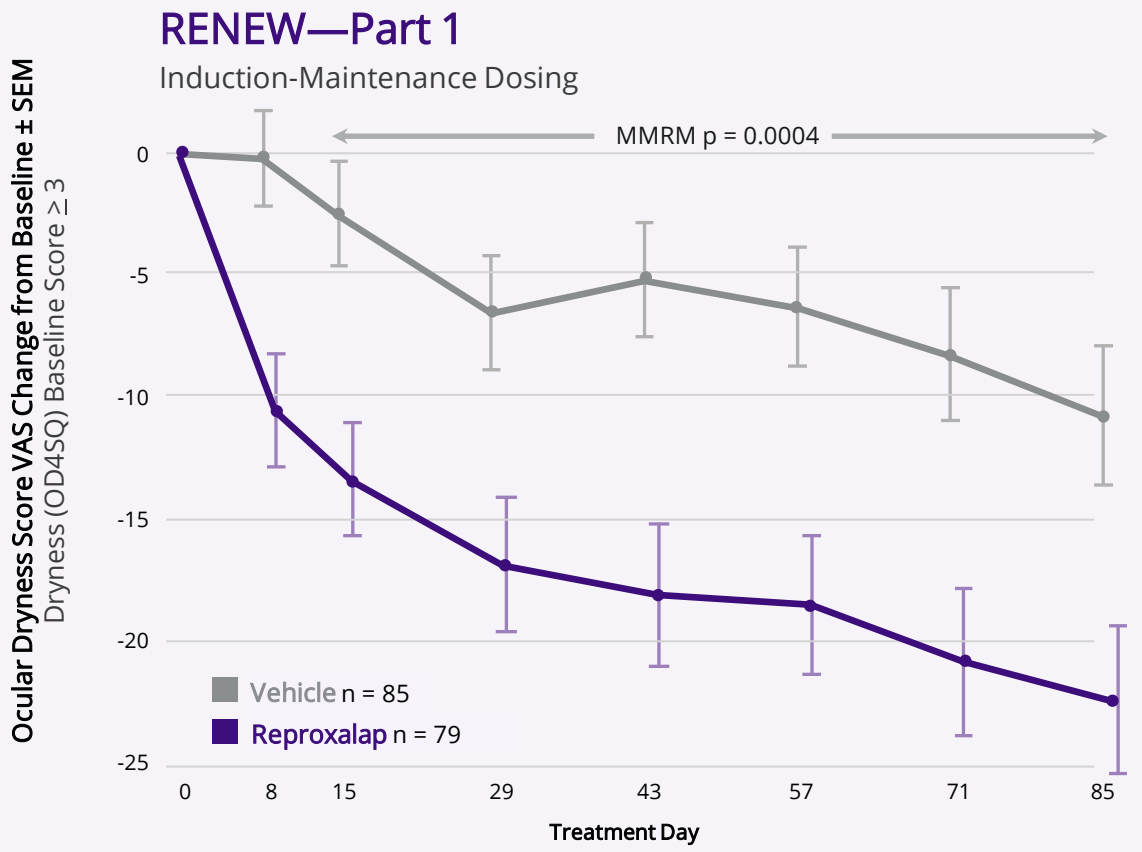
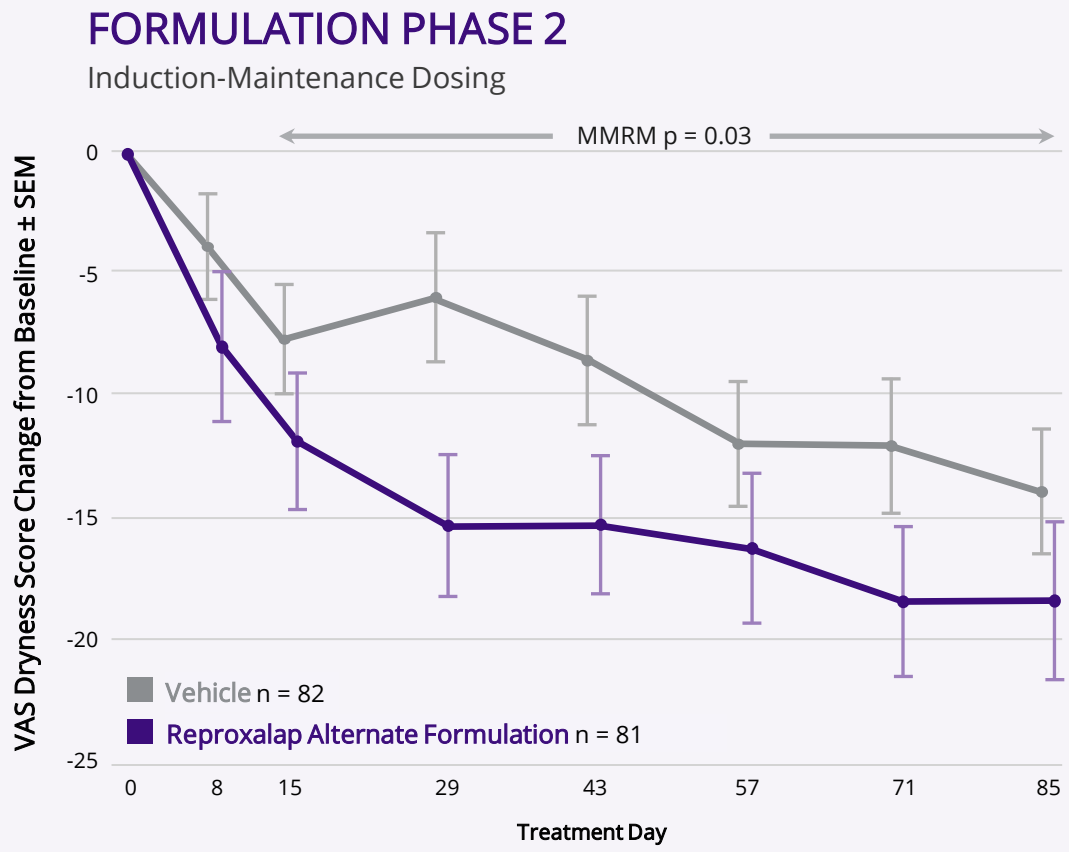
Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials

Reproxalap Met 12-Week (Chronic) Dryness Symptom Primary Endpoint in RENEW-Part 1 and Formulation Phase 2 Clinical Trials



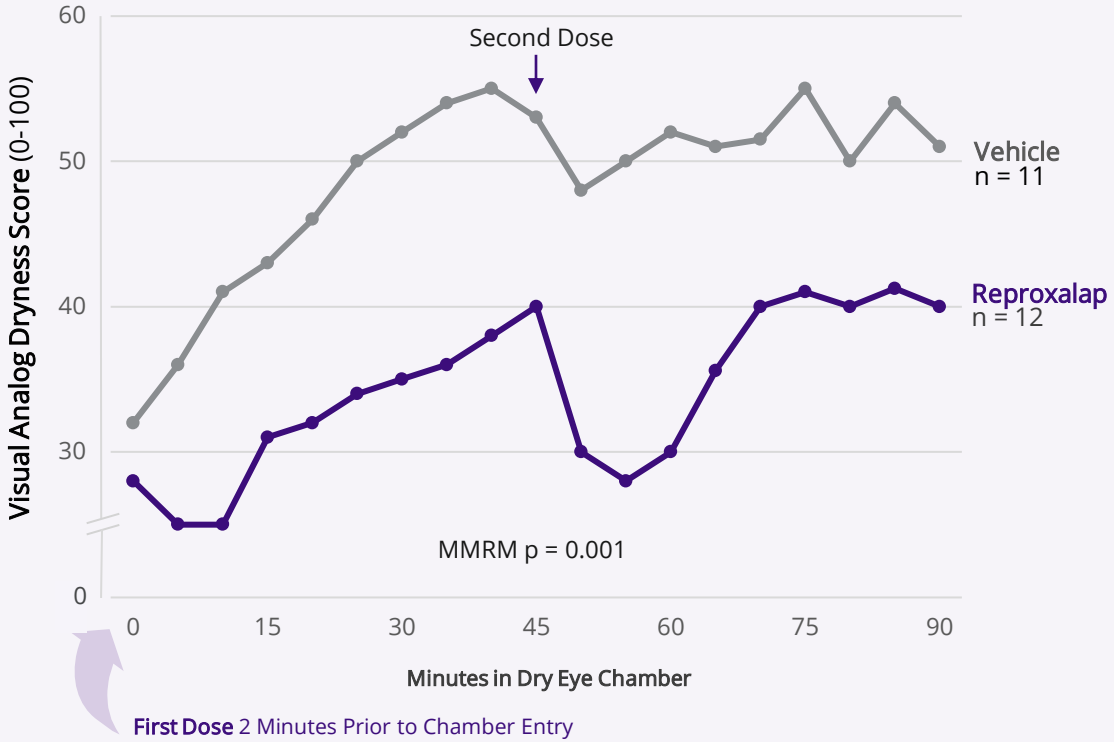


Sources: Reproxalap RENEW-Part 1 and Formulation Phase 2 DED clinical trial results. OD4SQ = Ocular Dryness 4-Symptom Questionnaire VAS = Visual Analog Scale MMRM = Mixed Effect Model Repeated Measures

Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Phase 3 TRANQUILITY Trial Run-In Cohort: Symptom and Sign Activity Demonstrated within Minutes in a Dry Eye Chamber

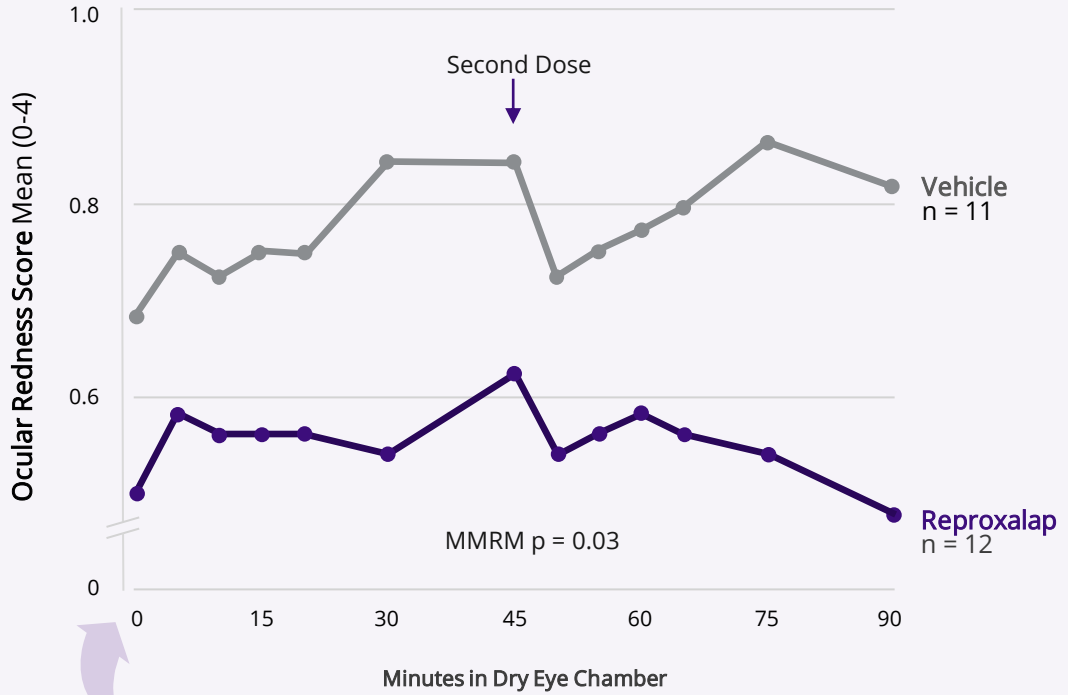
Visual Analog Dryness Score



First Dose 2 Minutes Prior to Chamber Entry

Ocular Redness Score

Redness is an FDA-approvable objective sign of dry eye disease.



First Dose 2 Minutes Prior to Chamber Entry

p values derived from MMRM of change from baseline, where baseline defined as Time 0. MMRM = Mixed Effect Model Repeated Measures Source: TRANQUILITY Run-In Cohort initial results

Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Reproxalap Activity is Also Acute

A single day of dosing led to statistically significant changes in symptoms and Schirmer test.

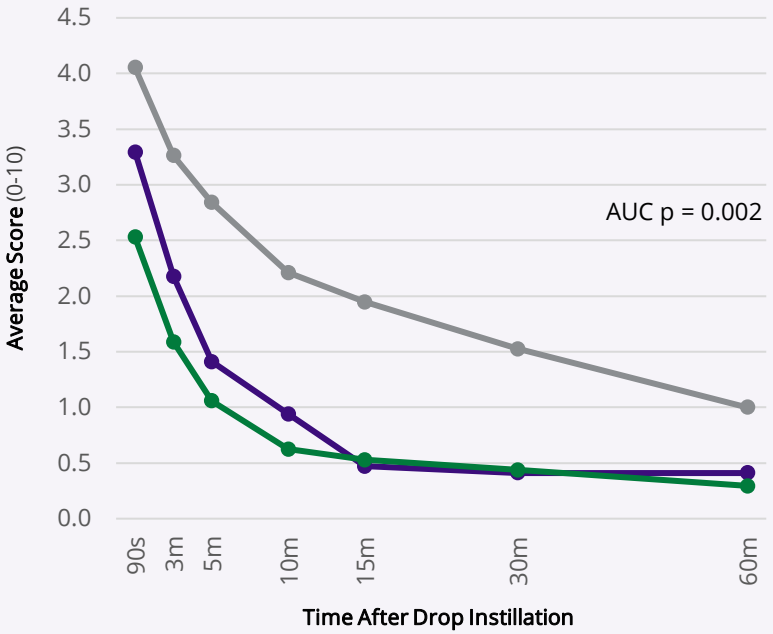
Dry Eye Assessment (Scale) After Environmental Dosing	Change from Baseline		p-Value
	Reproxalap n=12	Vehicle n=11	
VAS Dryness (0-100)	-26	+2	**0.003**
OD4S: Discomfort (0-5)	-0.7	+0.4	**0.003**
OD4S: Dryness (0-5)	-1.2	+0.1	**0.006**
OD4S: Grittiness (0-5)	-1.1	+0.1	**0.006**
OD4S: Burn (0-5)	-0.1	+0.8	0.07
OD4S: Sting (0-5)	-0.1	+0.4	0.23
Ocular Discomfort Scale (0-4)	-0.7	+0.4	0.07
Schirmer's Test (mm)*	+2.9	+0.7	**0.03**

*Schirmer's Test results based on improvement after a second dose of Day 1 relative to screening baseline; all other Day 1 assessments performed over 24 hours after QID dosing. Change from baseline estimates and p values derived from MMRM analyses. Source: TRANQUILITY Run-In Cohort initial results VAS = Visual Analog Scale OD4S = Ocular Discomfort & 4-Symptom Questionnaire QID = Four times daily MMRM = Mixed-effect Model Repeated Measures

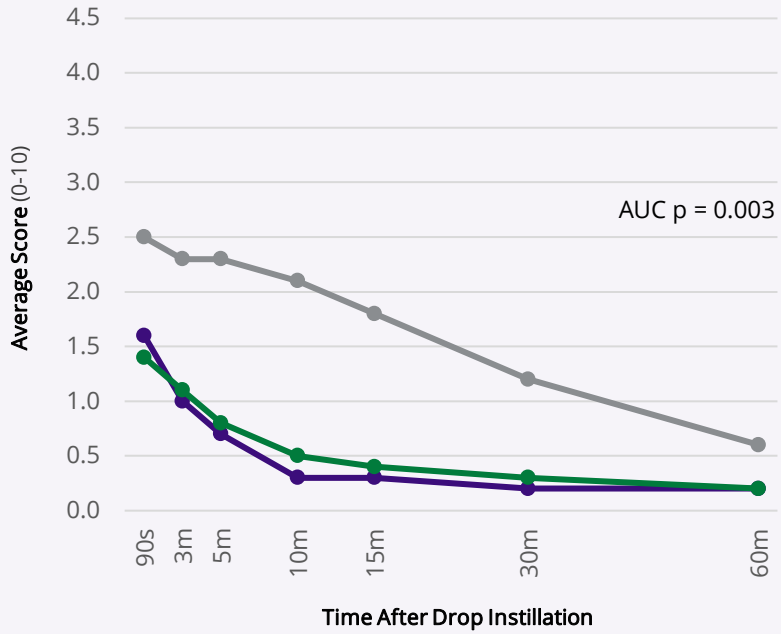
Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

Tolerability of Reproxalap Over One Hour Post-Instillation Significantly Improved vs. Xiidra® in Dry Eye Disease Patients

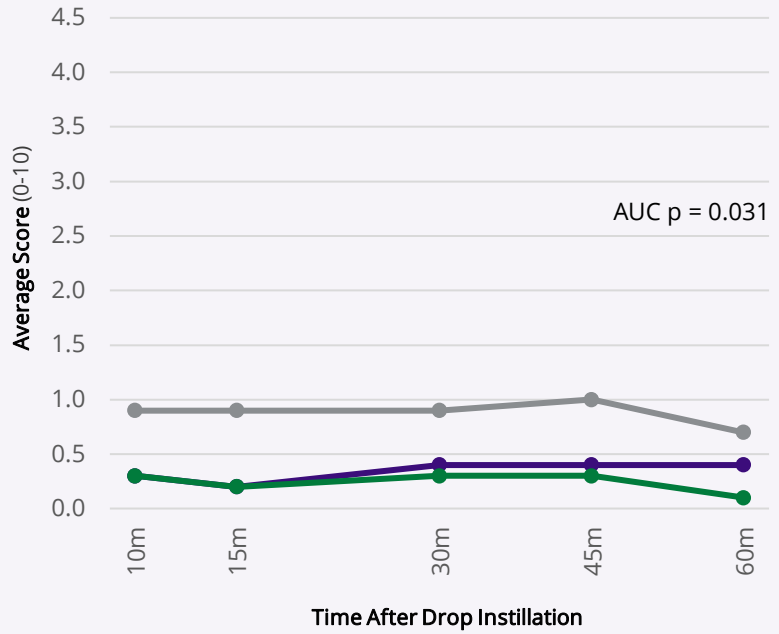
Ocular Discomfort Rating



Blurry Vision Rating



Taste Dysgeusia Rating



Xiidra® Reproxalap Reproxalap Alternate Formulation

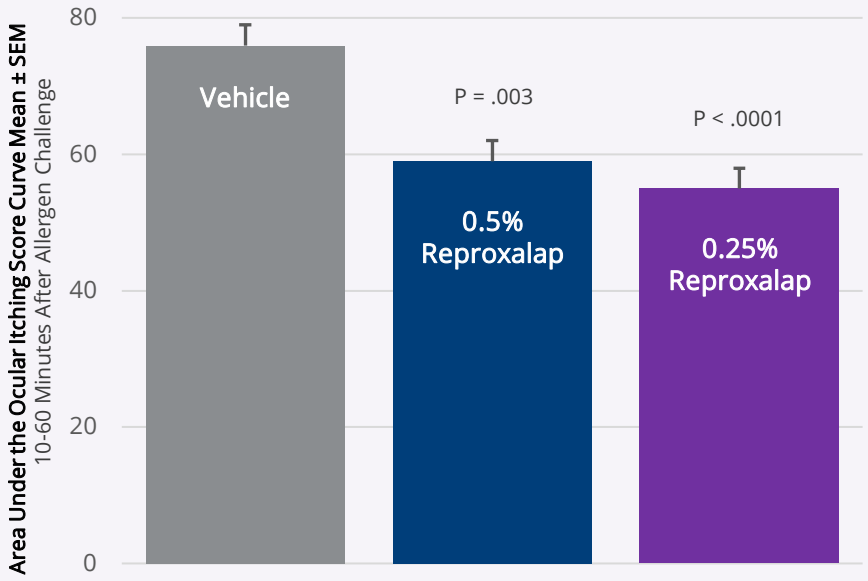
p-values represent MMRM of vehicle AUC vs. pooled Reproxalap AUC. Slide source: Phase Xiidra® HTH Trial results AUC = Area Under The Curve

Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials.

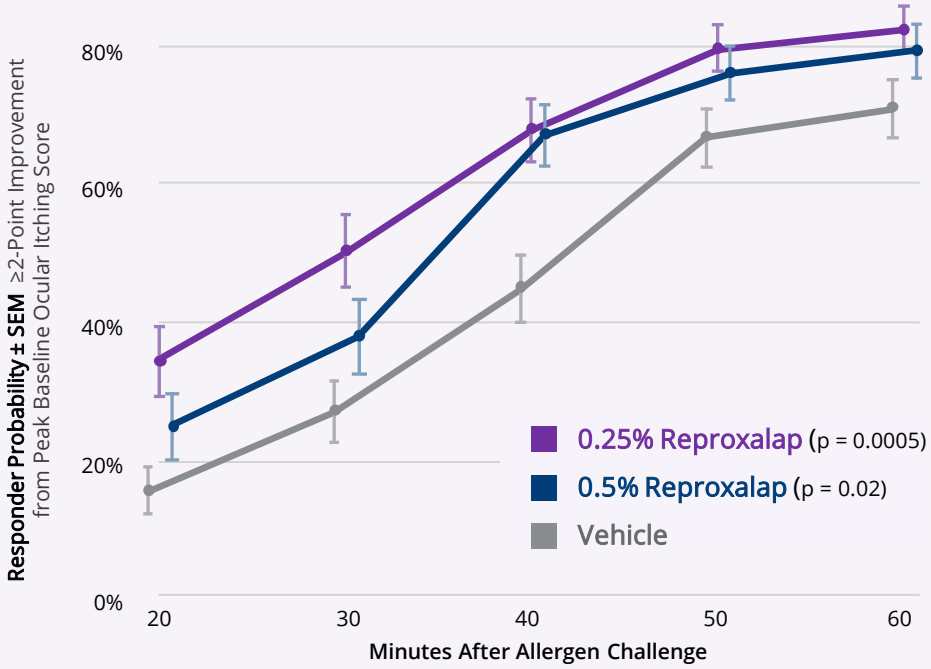
Reproxalap Achieved Primary and Key Secondary Endpoints in ALLEVIATE Phase 3 Trial in Allergic Conjunctivitis

CONJUNCTIVAL ALLERGEN CHALLENGE

Primary Endpoint



Key Secondary Endpoint



Clark D, Cavanagh B, Shields AL, Karpecki P, Sheppard J, Brady TC. Clinically Relevant Activity of the Novel RASP Inhibitor Reproxalap in Allergic Conjunctivitis: The Phase 3 ALLEVIATE Trial. Am J Ophthalmol. 2021 May 1:S0002-9394(21)00222-1. doi: 10.1016/j.ajo.2021.04.023. Epub ahead of print. PMID: 33945820.

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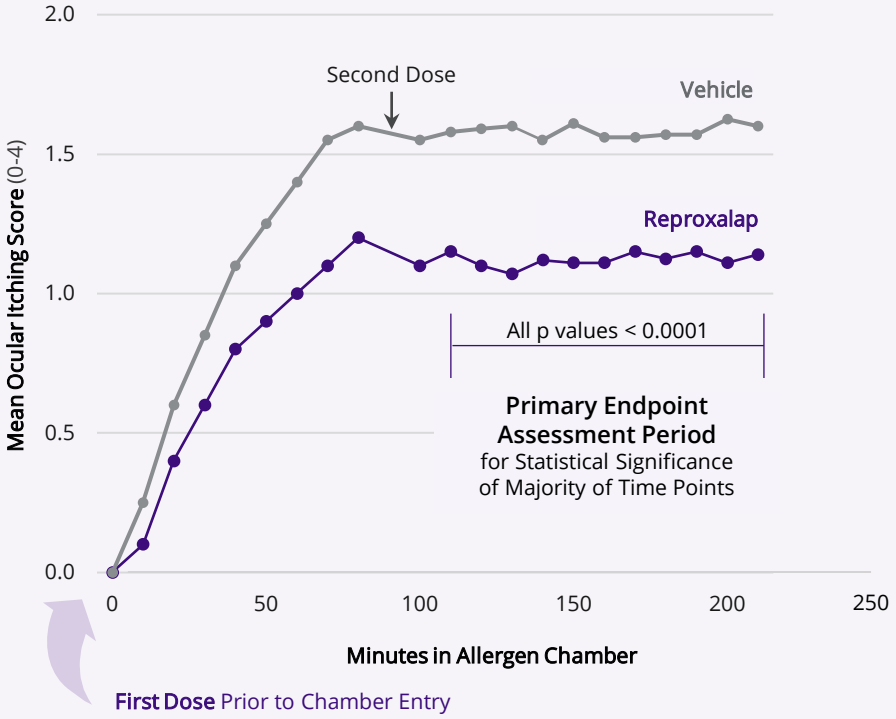
Primary and Key Secondary Endpoints Achieved in Phase 3 INVIGORATE Allergen Chamber Trial

Prophylactic and treatment effects of reproxalap demonstrated

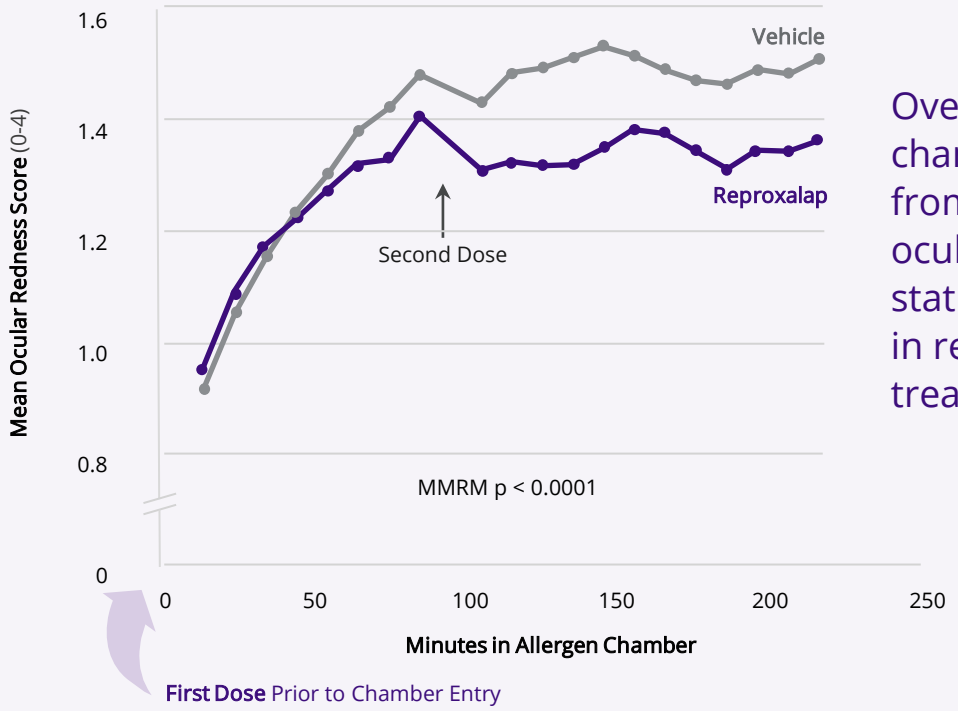
Primary Endpoint

Reduction in Ocular Itching Over Pre-Specified Time Frame



Key Secondary Endpoint

Reduction in Ocular Redness Over the Entire Chamber



Over entire chamber, change from baseline in ocular redness statistically lower in reproxalap-treated subjects

Topical ocular reproxalap has been studied in over 1,200 patients with no observed safety concerns; mild instillation site discomfort is the most commonly reported adverse event in clinical trials. Source: INVIGORATE clinical trial results MMRM = Mixed Effect Model Repeated Measures

Reproxalap Represents a Novel, Rapid Onset Potential Therapeutic Approach in Dry Eye Disease

Potential advantages for patients and healthcare providers could effect a paradigm shift relative to standard of care

Rapid symptom improvement within minutes

Broad symptomatic activity

Acute conjunctival redness control

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