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# First-in-Human Study of Urcosimod to Treat Neuropathic Corneal Pain (NCP) Shows Clinically Meaningful Pain Reduction and Quality-of-Life Improvement in NCP Patients

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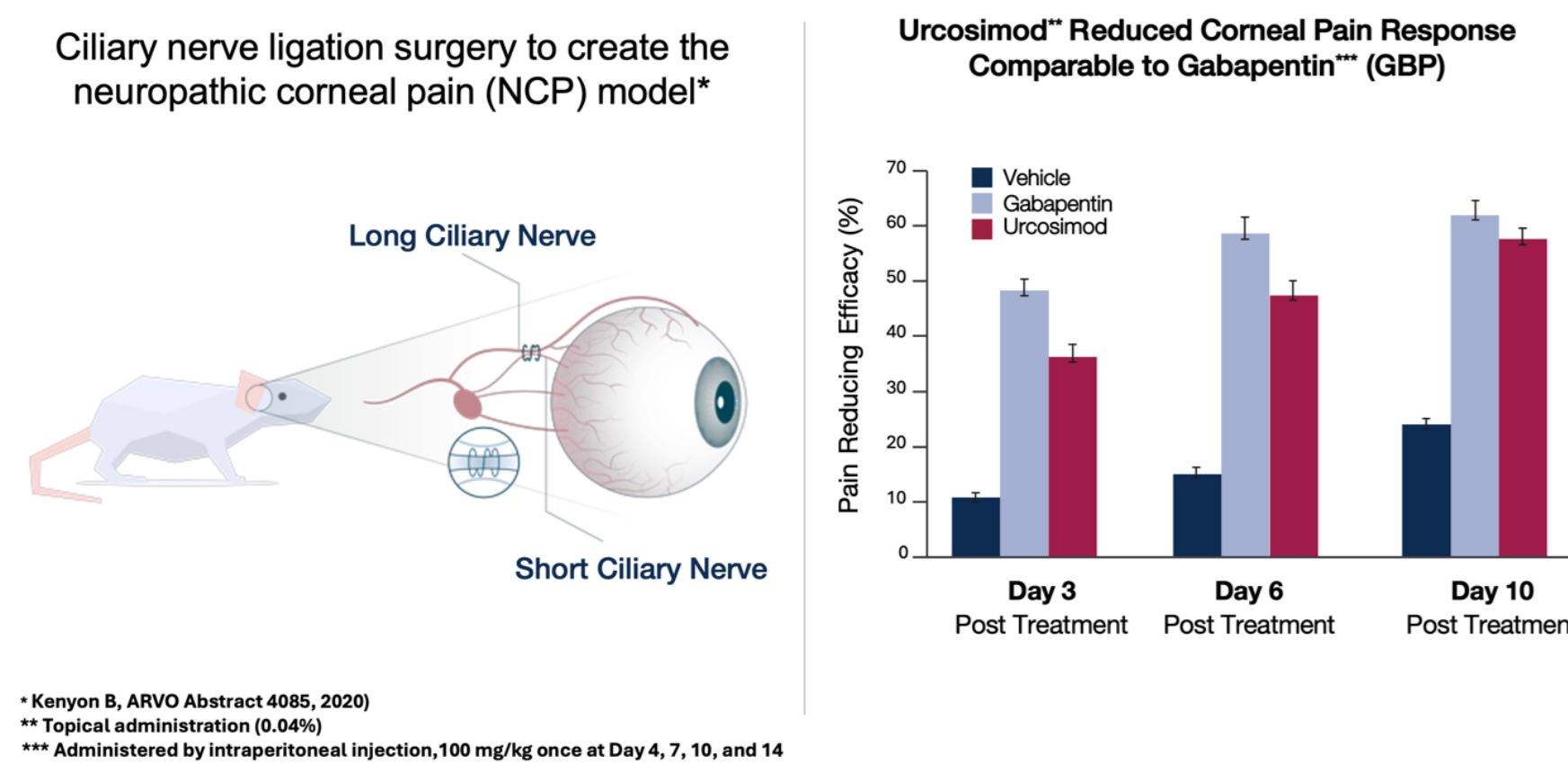
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## BACKGROUND

Neuropathic corneal pain (NCP), also referred to as corneal neuralgia, is a chronic disorder of the somatosensory nervous system characterized by persistent ocular pain that is often disproportionate to clinical findings.<sup>1</sup> It is a challenging and relatively uncommon condition arising from diverse etiologies and involving both peripheral and central sensitization.<sup>2</sup> Patients typically present with severe eye pain, burning, foreign body sensation, dryness, and photophobia, often with minimal or no observable signs. NCP may develop following ocular trauma, refractive or other ocular surgery, infections, or in association with ocular surface diseases such as dry eye disease. Its underlying pathophysiology includes corneal nerve sensitization and central pain processing abnormalities, contributing to persistent and potentially debilitating pain symptoms. Currently, there are no FDA-approved therapies specifically for NCP.

Urcosimod (formerly OK-101) is a lipidated chemerin peptide and a potent agonist of the ChemR23 chemerin receptor, which is expressed on inflammatory, epithelial, and neuronal cells, including those in the cornea and pain pathway.<sup>3,4</sup> Activation of ChemR23 has been shown to produce both anti-inflammatory and anti-nociceptive effects, although endogenous ligands such as resolvin E1 and chemerin are limited by short half-lives. In preclinical neuropathic pain models, urcosimod demonstrated prolonged analgesic activity lasting up to 24 hours, outperforming resolvin E1.<sup>5</sup> It also reduced ocular pain in a ciliary nerve ligation mouse model of neuropathic corneal pain, comparable to intraperitoneally administered gabapentin, whereas urcosimod was administered topically.<sup>6</sup>

### Urcosimod Reduced Neuropathic Corneal Pain in a Mouse Model



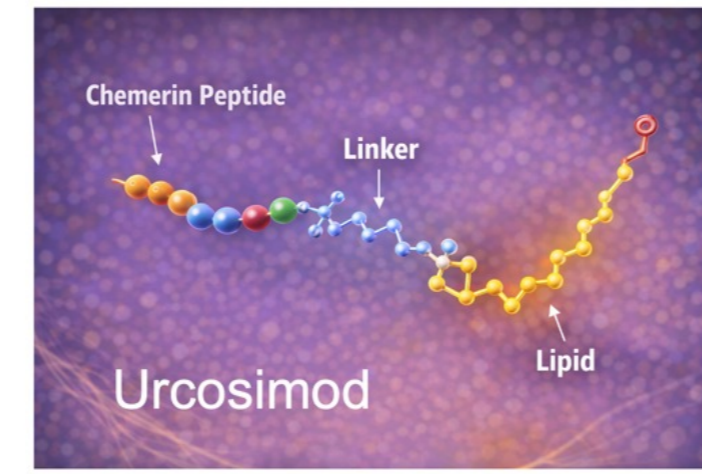
## PURPOSE

The purpose of this study was to evaluate clinical efficacy and safety of urcosimod ophthalmic solution compared with placebo for treatment of NCP, a significant unmet need with no FDA-approved therapy, in a randomized, double masked, placebo-controlled Phase 2 trial conducted at a single site in US. Enrollment used clinical inclusion/exclusion criteria and confirmation of NCP diagnosis by in vivo confocal microscopy.

## STUDY DESIGN AND SAFETY

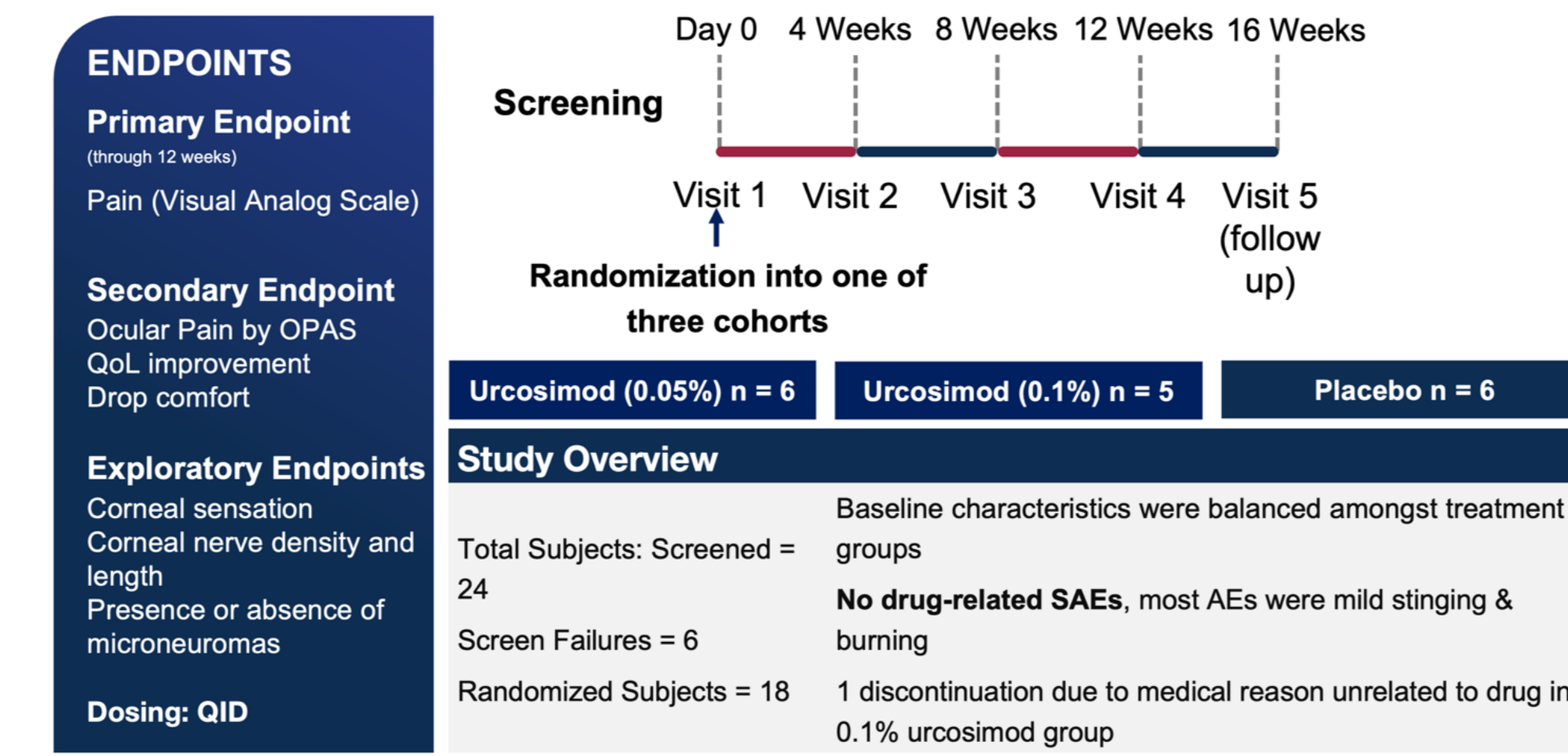
### Urcosimod: Lipid-Conjugated Chemerin Peptide

- First-in-Class chemerin receptor agonist** that modulates neuro-immune cross-talk
- Dual mechanism of action:** Targets both immune-driven inflammation and neuronal/glial-driven pain, delivering a dual hit where it matters most
- Topically active peptide** designed for enhanced potency and corneal retention
- Preservative-free, EDTA-free, and isotonic formulation**, optimized for sensitive eyes and chronic use



**Targeting ChemR23** (GPCR Receptor)  
**Receptor localization**  
Expressed on immune and neuronal cells, linking inflammation and pain signaling  
**Endogenous ligand**  
Chemerin: 136 aa peptide

### Urcosimod Phase 2a NCP Trial Design



### Demographics: Intent-to-Treat Population

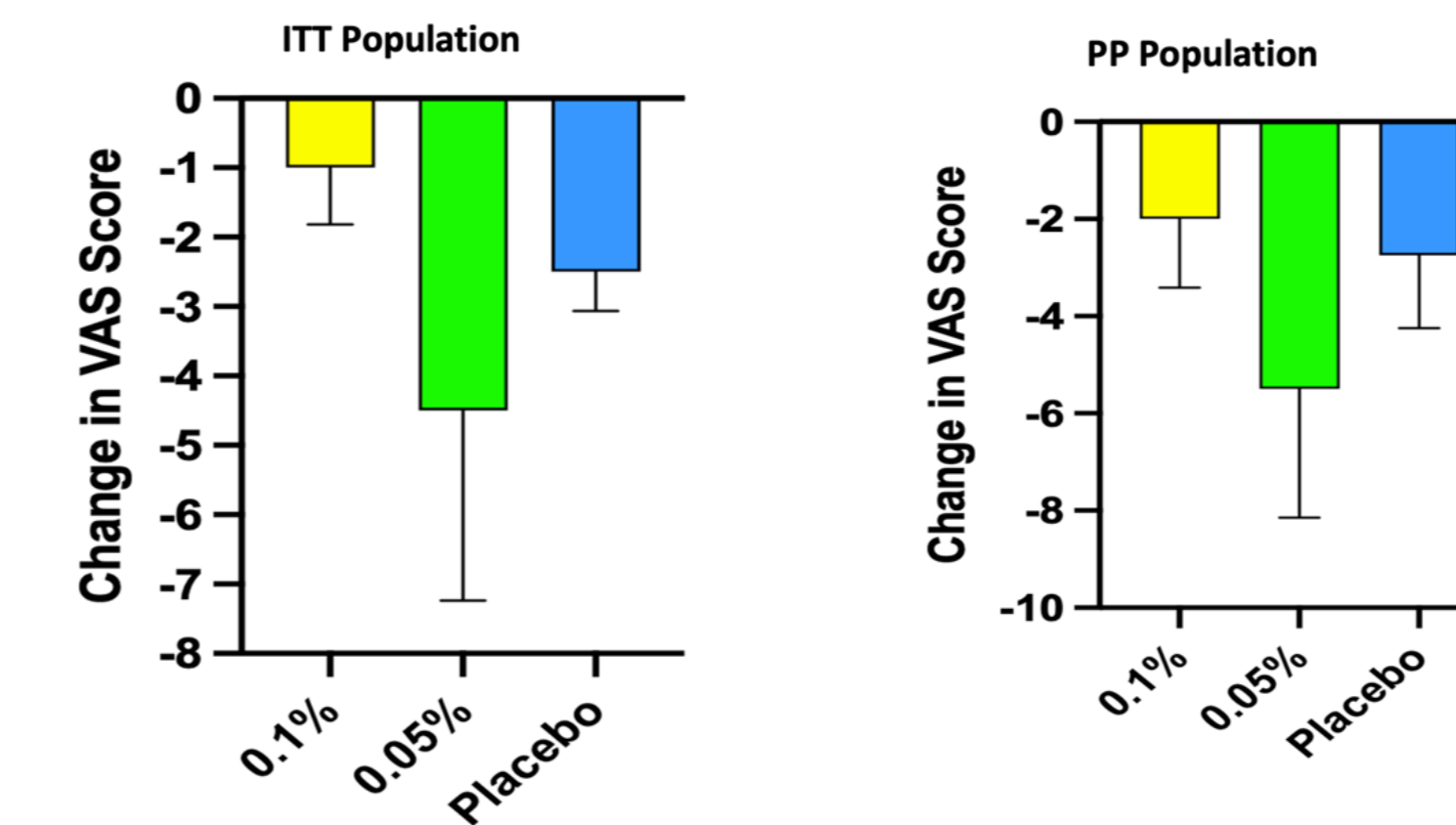
	0.1% Group (n=6)	0.05% Group (n=6)	Placebo (n=6)
<b>Age</b>			
Mean ± Standard Deviation	40.0 ± 18.06	46.5 ± 13.75	46.5 ± 13.28
Median (Range)	31.5 (28-75)	52.0 (26-58)	46.5 (33-63)
<b>Sex</b>			
Female	4	6	4
Male	2	0	2
<b>Race</b>			
White	6	5	6
Asian	0	1	0
<b>Baseline VAS</b>	6.33 ± 1.86	7.17 ± 1.60	6.00 ± 2.28

### Summary of Adverse Events

	OK-101, 0.1% (N=5)	OK-101, 0.05% (N=6)	Placebo (N=6)
Number of AEs	17	30	43
Number of Treatment-Emergent AEs	13	16	35
Number of Subjects with any, n (%)	5 (100%)	6 (100%)	6 (100%)
Number of Subjects with any SAE, n (%)	0 (0%)	0 (0%)	0 (0%)
Number of Subjects with TEAEs by Maximal Severity <sup>1</sup>			
Mild	0 (0%)	3 (50.0%)	3 (50.0%)
Moderate	3 (60.0%)	0 (0%)	1 (16.7%)
Severe	1 (20.0%)	3 (50.0%)	2 (33.3%)
TEAEs by Relationship to Study Drug <sup>2</sup>			
Definitely Related	0 (0%)	0 (0%)	0 (0%)
Probably Related	1 (20.0%)	0 (0%)	0 (0%)
Possibly Related	3 (60.0%)	3 (50.0%)	4 (66.7%)
Unlikely Related	0 (0%)	1 (16.7%)	1 (16.7%)
Not Related	0 (0%)	1 (16.7%)	1 (16.7%)
Unclassified	0 (0%)	1 (16.7%)	0 (0%)

## RESULTS: EFFICACY ANALYSIS

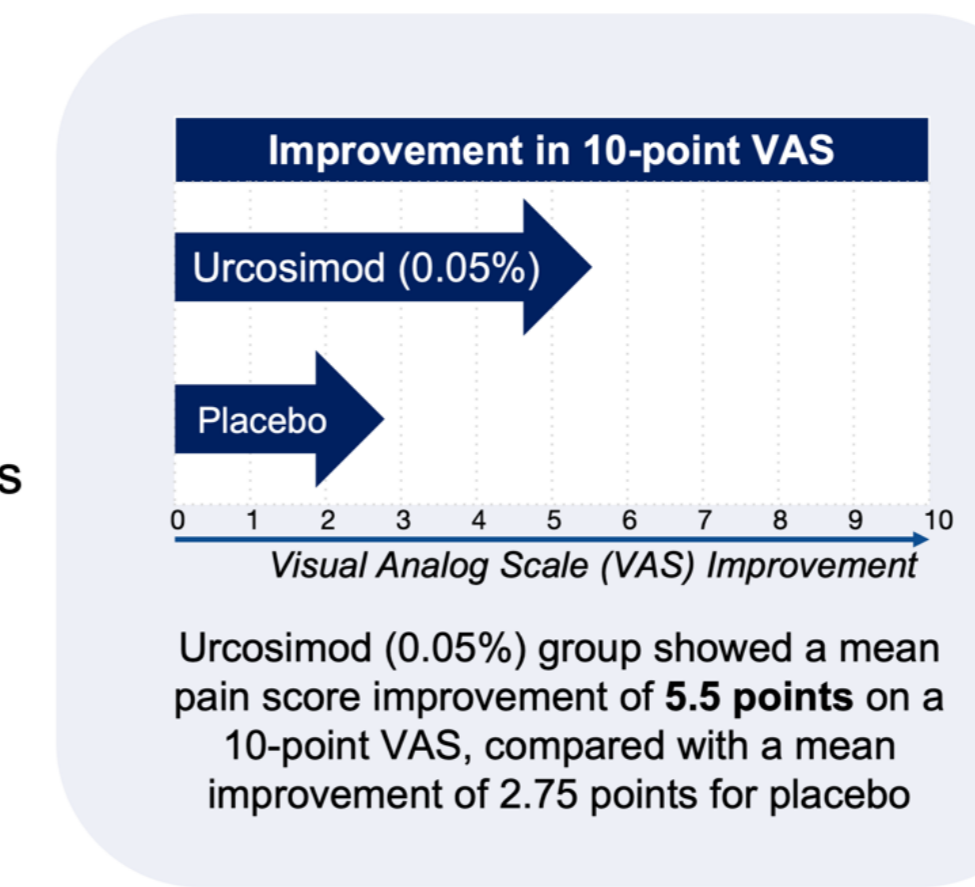
### Mean VAS Change from Baseline (Week 12)



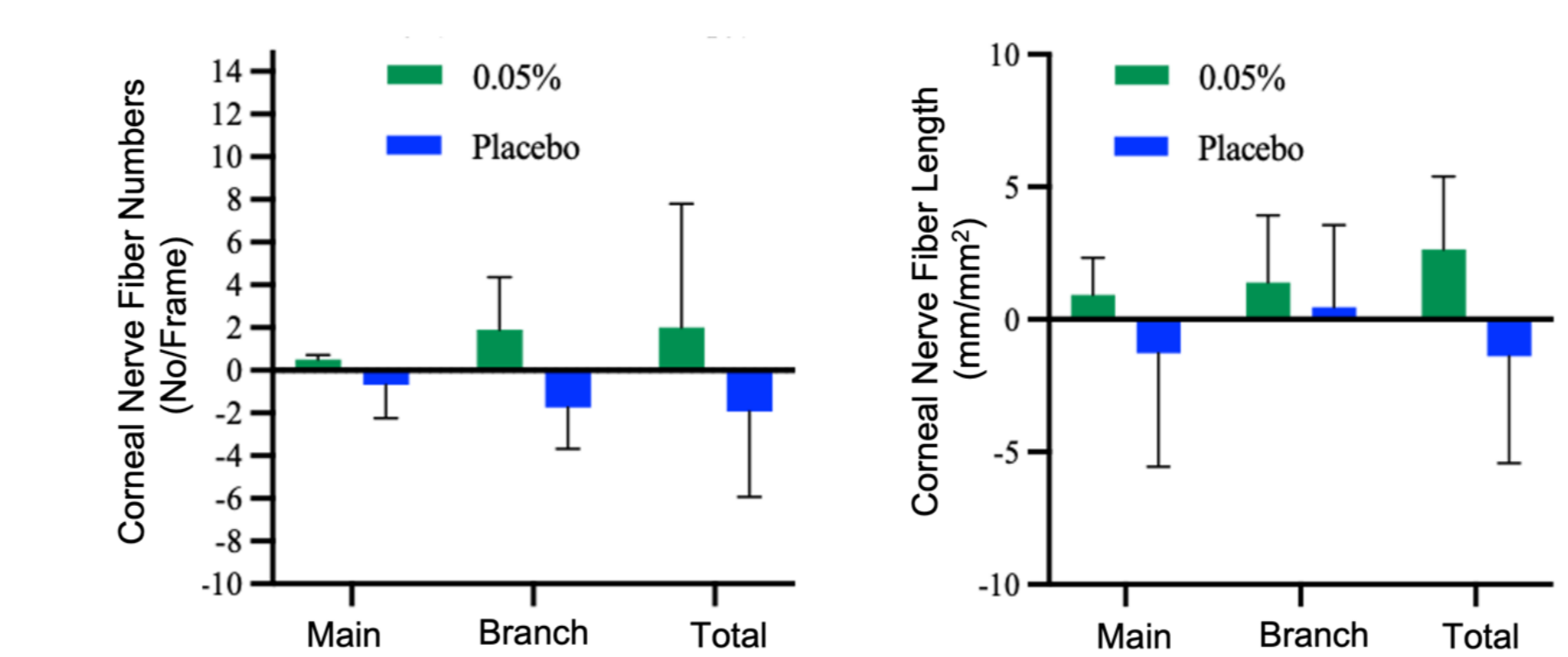
### Urcosimod Shows Clinically Meaningful VAS Improvement

#### STUDY RESULTS

- Greater than 80% reduction in neuropathic corneal pain (VAS) in 75% of per-protocol patients after 12 weeks with 0.05% urcosimod
- Urcosimod (0.05%) reduced pain scores from baseline by Week 4, with sustained efficacy throughout the trial
- All responders had moderate to severe NCP at baseline despite prior maximal medical therapy

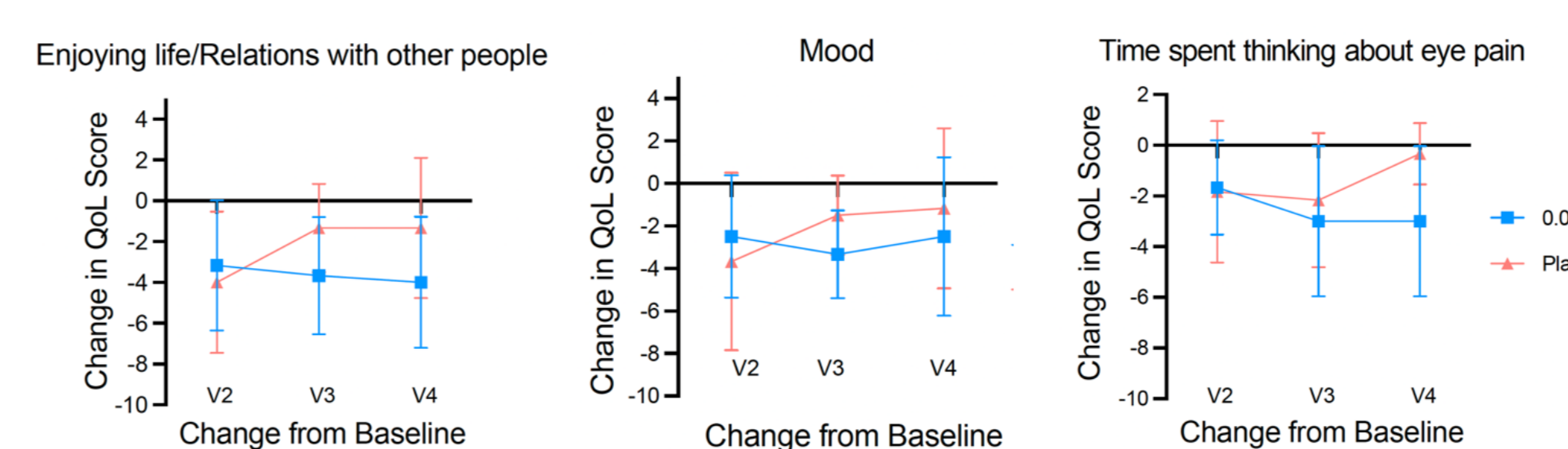


### Urcosimod Shows Potential for Nerve Growth



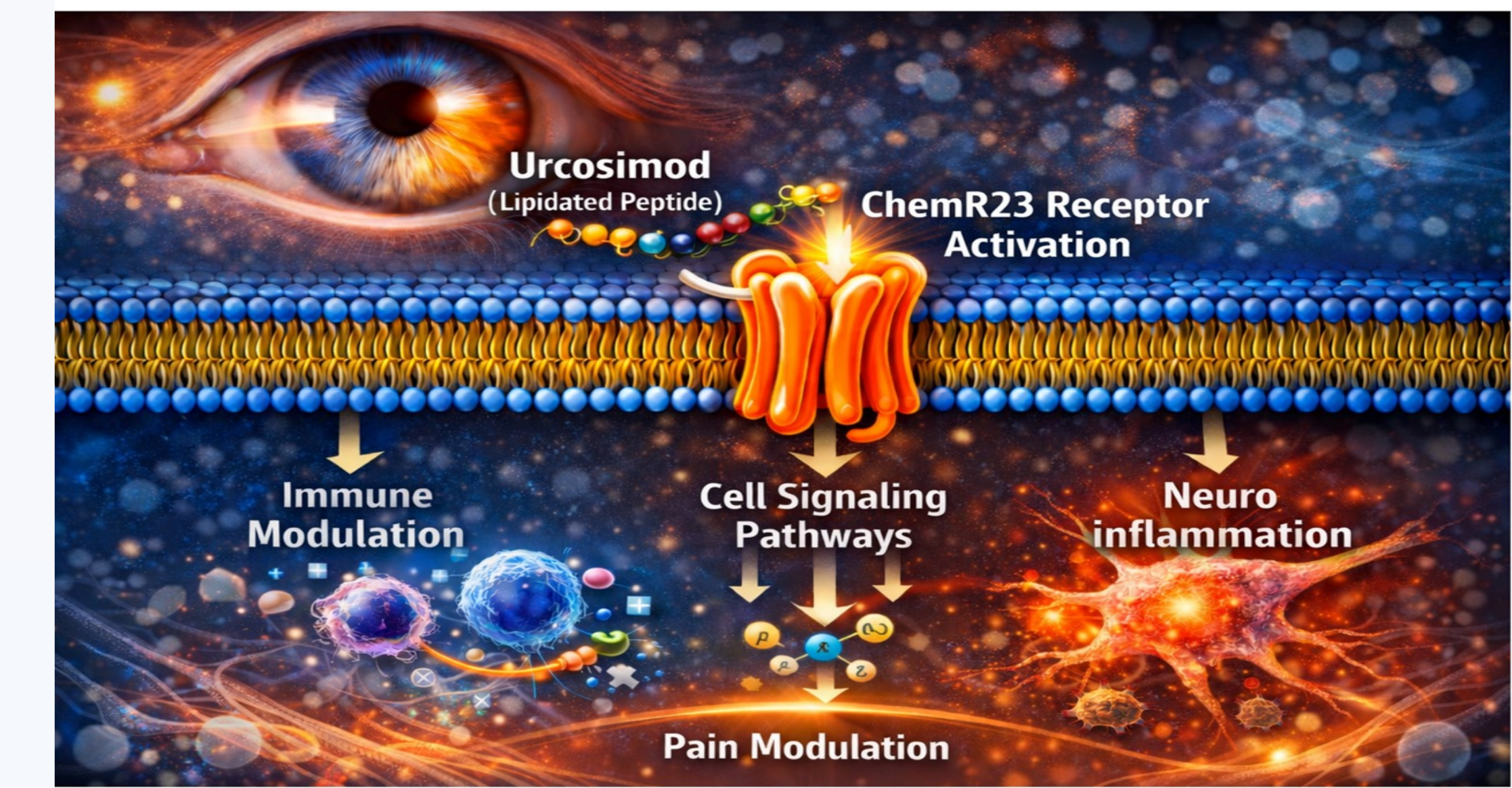
Urcosimod (0.05%) showed a favorable effect on corneal nerve health, indicating corneal nerve restoration.

### Urcosimod Shows a Positive Trend in QoL



Urcosimod (0.05%) demonstrated consistent directional improvement vs. placebo across QoL measures, supporting a meaningful impact on daily functioning.

## MECHANISM



## CONCLUSIONS

- First clinical signal in NCP:** Urcosimod (0.05%), showed clinically meaningful pain reduction in a small patient population with severe chronic NCP
- High responder rate:** 75% of per-protocol patients achieved >80% reduction in pain (VAS) at Week 12
- Rapid and durable effect:** Pain reduction observed as early as Week 4, sustained through 12 weeks
- Potential nerve restoration:** Urcosimod 0.05% showed median increases in corneal nerve fiber count and length, suggesting potential for nerve regeneration
- QoL Improvement Trend:** Urcosimod showed greater improvements across emotional well-being measures, including enjoyment of life/relationships, mood, and reduced time spent thinking about eye pain
- Refractory population:** All responders had moderate-to-severe baseline pain despite prior maximum medical therapy
- Advancing development:** A larger, multicenter Phase 2b/3 trial is planned, with enrollment expected to begin in Q3 2026

## REFERENCES

- Crnej J et al., Corneal Neuropathic Pain: A Review. Survey of Ophthalmology. 2023.
- Dieckmann G et al., Ophthalmology. 2017;124(11 Suppl):S34-S47.
- Herová et al., Journal of Immunology, 2015
- Dickie & Torsney, Molecular Pain, 2014
- Xie et al., Neurosci. Bull. 2021; 37(9):1351-1356.
- Harris DL et al., Invest. Ophthalmol. Vis. Sci. 2022;63(7):1834.

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