

# Randomized, Controlled, Phase 3 Studies of Phentolamine Solution in Keratorefractive Patients with Low Mesopic Vision and Photic Complaints

---

**Presenter:** Jay S. Pepose MD, PhD, ABO<sup>1</sup>

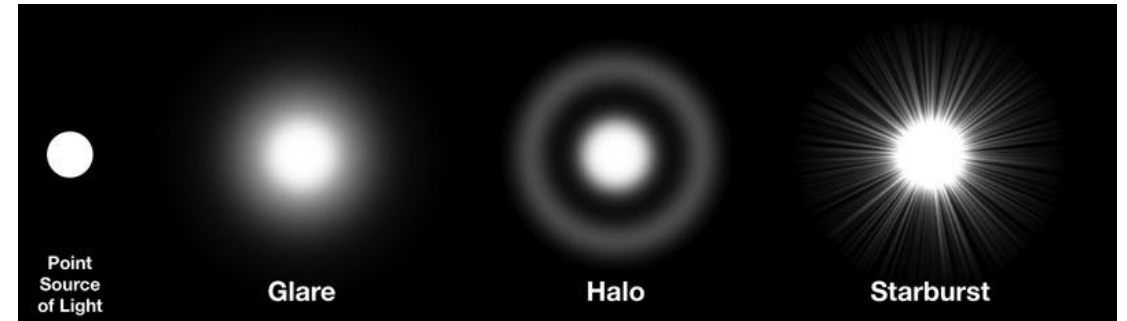
**Co-authors:** Marguerite McDonald, MD, FACS, James Katz, MD, Konstantinos Charizanis, PhD, Mitchell G Brigell, PhD

**Financial Disclosures:** <sup>1</sup>American Genomics (A, SO), Bausch + Lomb (C), BRIM Biotech (C), OKYO Pharma (A, SO), Opus Genetics (A, SU, SO), Laurent Pharma (C), Mimetogen (A, SO), Stuart Pharma (C, SO), Thea Pharma (C)

**Disclaimer:** Phentolamine is not an FDA-approved product for keratorefractive subjects with reduced mesopic vision and photic phenomena

# Large Unmet Need in Dim Light Disturbances (DLD)

- Peripheral, unfocused rays of light are unmasked when pupils enlarge in dim light, causing **reduced mesopic low contrast vision**<sup>1,2</sup>
  - **Glare:** Light that appears bright and intense
  - **Ghosting:** Faint, partial, monocular double image
  - **Starburst:** Radial or regular radiating scatter of light from a point source
- DLD may be caused by **keratorefractive surgery, keratoconus, and cortical cataracts**<sup>1</sup>
- **Symptoms cannot be properly corrected by glasses**



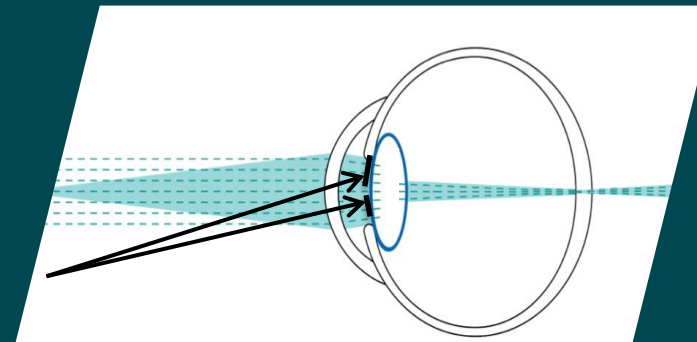
No Commercially-Available  
Treatment for Dim Light  
Disturbances<sup>1</sup>

# Night Vision Disturbances

- **Glare reduces several aspects of nighttime visual performance in older subjects**, and is associated with decreased mesopic visual function<sup>1</sup>
- Previous versions of LASIK, prior to laser flaps and wavefront-guided and optimized treatments, **were associated with decreased night driving performance**<sup>2-4</sup>



Effects of DLD can be mitigated when a **smaller pupil blocks unfocused, peripheral aberrant rays of light**, selectively allowing passage of more centrally focused rays



DLD, dim light disturbances; LASIK, laser assisted in situ keratomileusis.

1. Kimlin, JA, et al. *Invest Ophthalmol Vis Sci*, 58(5), 2796-2803. 2. Schallhorn SC, et al. *Ophthalmology*. 2009;116:702-9. 3. Bidgoli, S., & Alio, J. L. (2018). Alio, J., Azar, D. (eds) *Management of Complications in Refractive Surgery*. Springer, Cham. 4. Martinez CE, et al. *Arch Ophthalmol*, 116, 1053-1062.

# Reduced Mesopic Vision and Photic Phenomena Associated with Keratorefractive Surgery

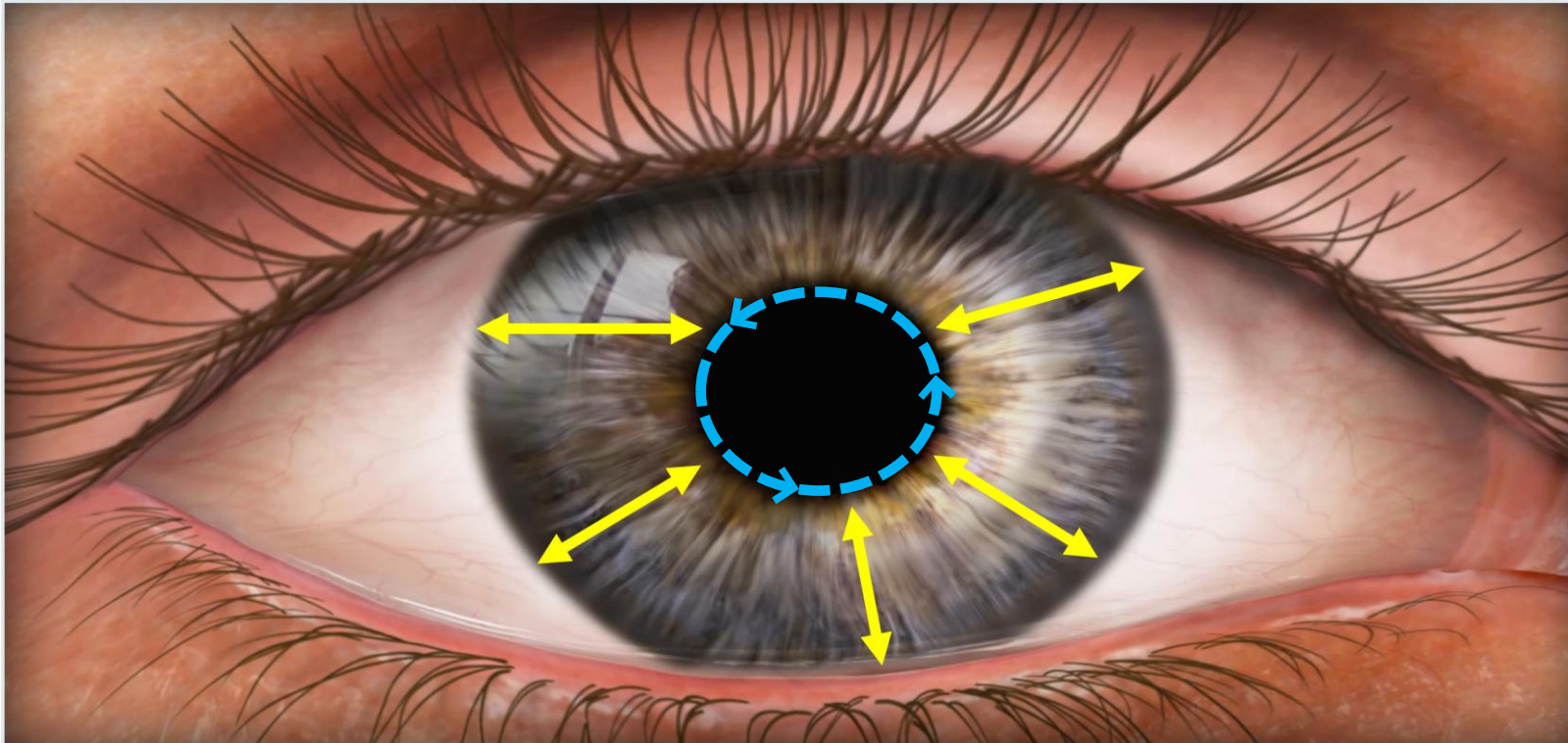
**800K - 1.4M**  
**PRK and LASIK**  
procedures performed  
annually in the U.S.<sup>1</sup>

**~40M**  
**keratorefractive**  
procedures performed  
each year globally<sup>1</sup>

- Keratorefractive surgery has evolved since the approval of PRK in 1995 and LASIK in 1999<sup>2-4</sup>
- Substantial number of patients who underwent legacy keratorefractive procedures have **debilitating reduced mesopic best spectacle corrected low contrast vision and photic phenomena** and are **more likely to be involved in motor vehicle collisions**<sup>2-4</sup>
- Data from Summaries of Safety and Effectiveness of 12 excimer lasers FDA-approved 1998-2004 for LASIK revealed<sup>5</sup>:
  - **19.3% reported worsening night driving problems**, ranging up to 34.8% with some laser systems
  - **19.7% reported glare**, ranging up to 36.6% with some laser systems
  - **17.5% reported halos**, ranging up to 25.4% with some laser systems

# Potential Treatment Option: Phentolamine Ophthalmic Solution 0.75%

- Differentiated iris dilator inhibition MOA for functional vision improvement
- Phentolamine is the active ingredient in POS, a non-selective  $\alpha_1$  antagonist



Phentolamine blocks  $\alpha_1$  receptors on the **iris dilator muscle**



Decreases pupil size (moderately) **without affecting the iris sphincter or ciliary muscles**



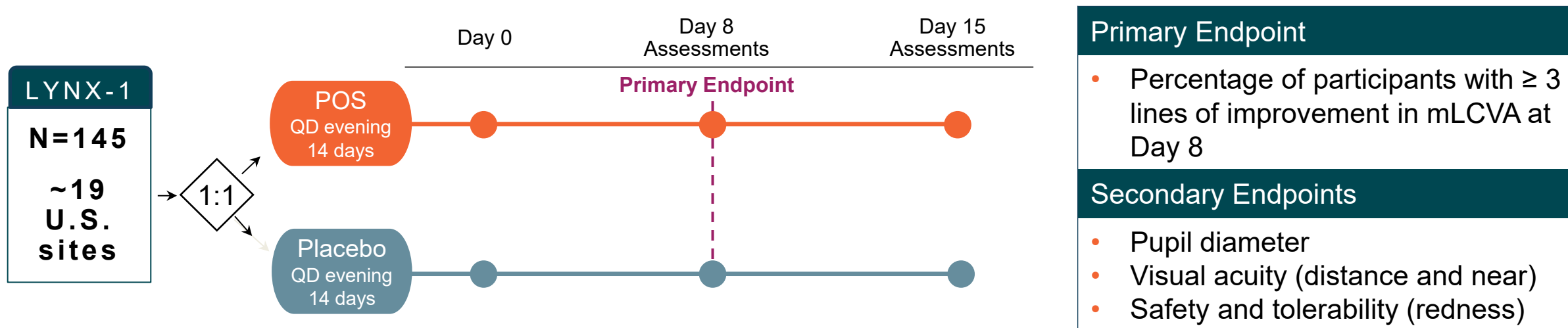
Allows for 3 indications: **Reversal of pharmacologically induced mydriasis, presbyopia, and DLD**

**Yellow arrows - iris dilator muscle (alpha antagonists e.g., phentolamine, brimonidine)**

**Blue circle - iris sphincter muscle (cholinergic agonists e.g.; pilocarpine, carbachol, aceclidine)**

# LYNX-1: DLD Phase 3 Design & Eligibility Criteria

Randomized, Double-Masked, Placebo-Controlled, Multicenter, Two-Week Trial



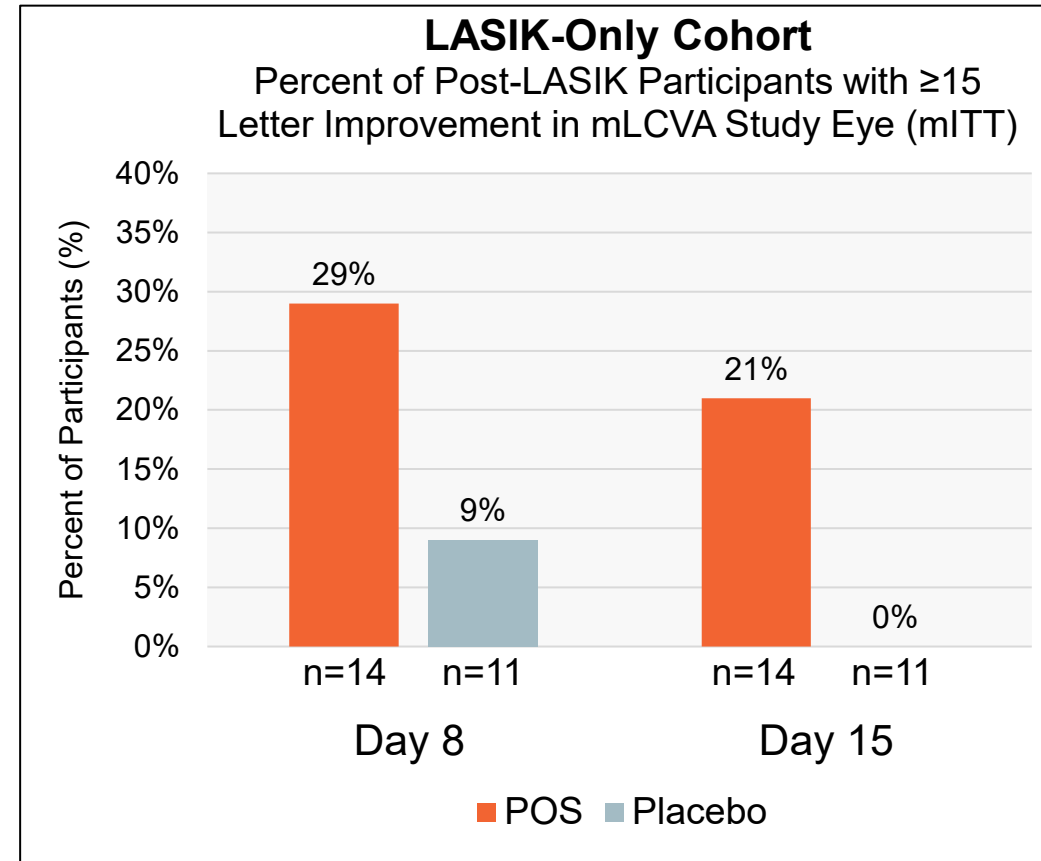
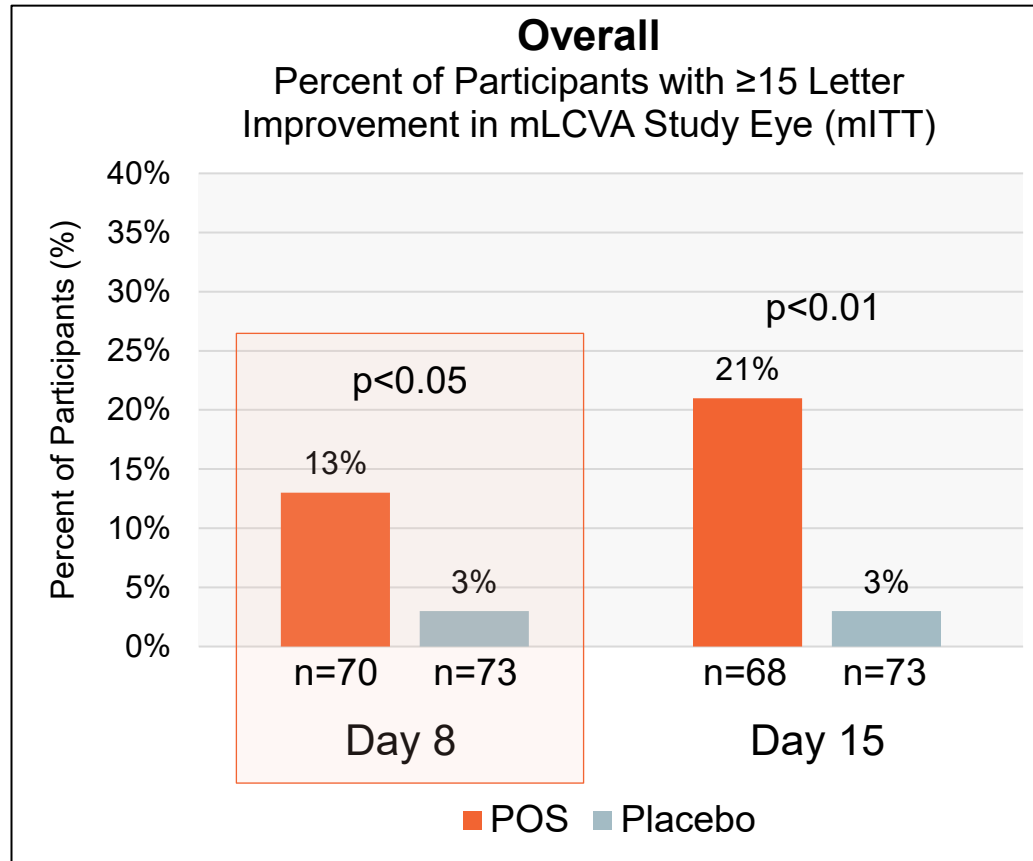
## Eligibility Criteria

- Males or females  $\geq 18$  years of age
- Participant self-reported DLD (participants with history of multifocal IOLs, LASIK, corneal scars, and keratoconus)
- Baseline mLCVA impairment (Snellen 20/63 or worse) in at least one eye
- $\geq 10$  letters improvement in mLCVA during illumination of contralateral eye with a BAT system
- PD  $\geq 5$ mm under mesopic conditions in at least one eye
- Participants with no recent (6 months) ocular procedures or clinically significant ocular disease

BAT, brightness acuity tester; DLD, dim light disturbances; IOL, intraocular lens; LASIK, laser assisted in situ keratomileusis; mLCVA, mesopic low contrast distance visual acuity; PD, pupil diameter; POS, phentolamine ophthalmic solution 0.75%; QD, once daily.

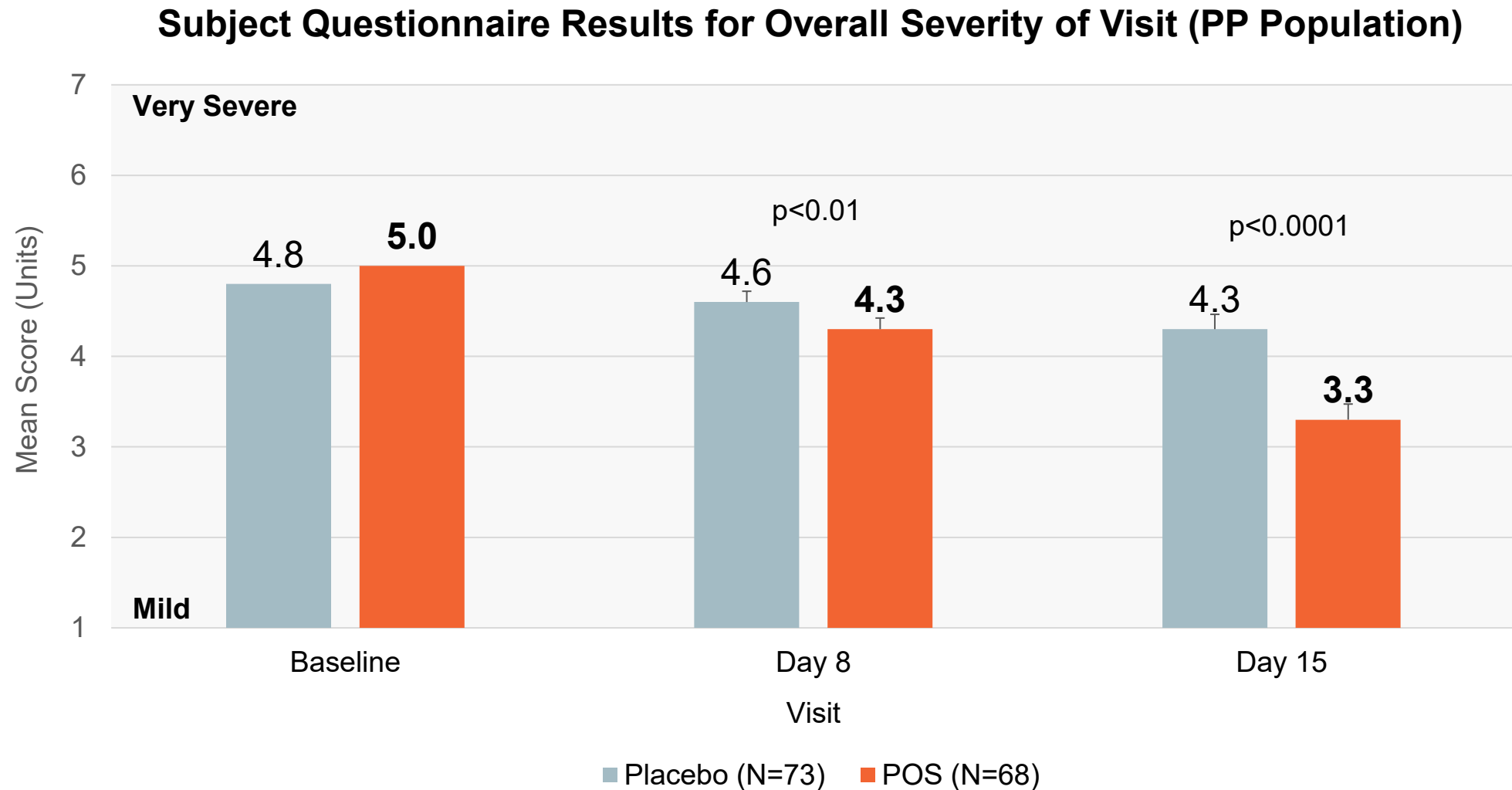
Source: Data on File, Opus/Viatris.

# POS Met Primary Endpoint Overall and Showed Favorable Results in Post-LASIK Patients



# Overall Severity of DLD

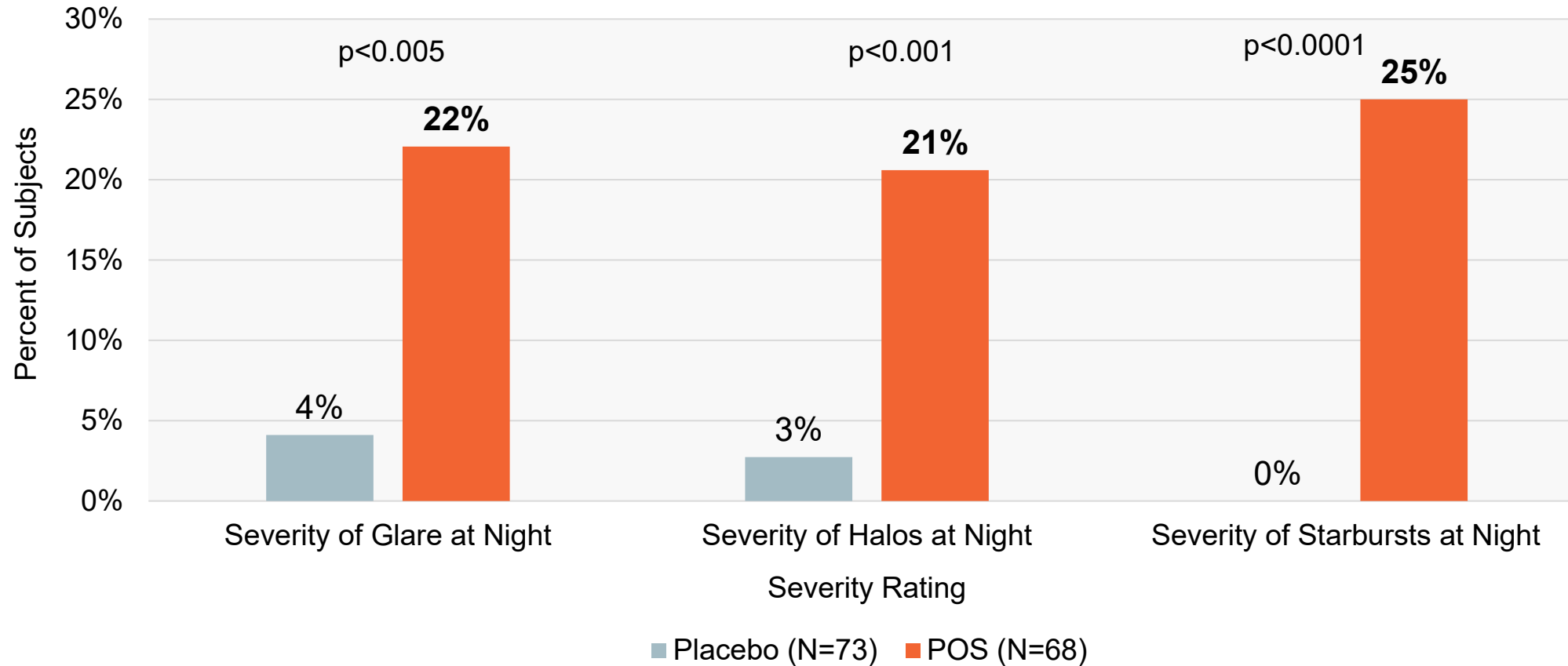
*POS Treatment Significantly Reduced Subjective Severity of DLD*



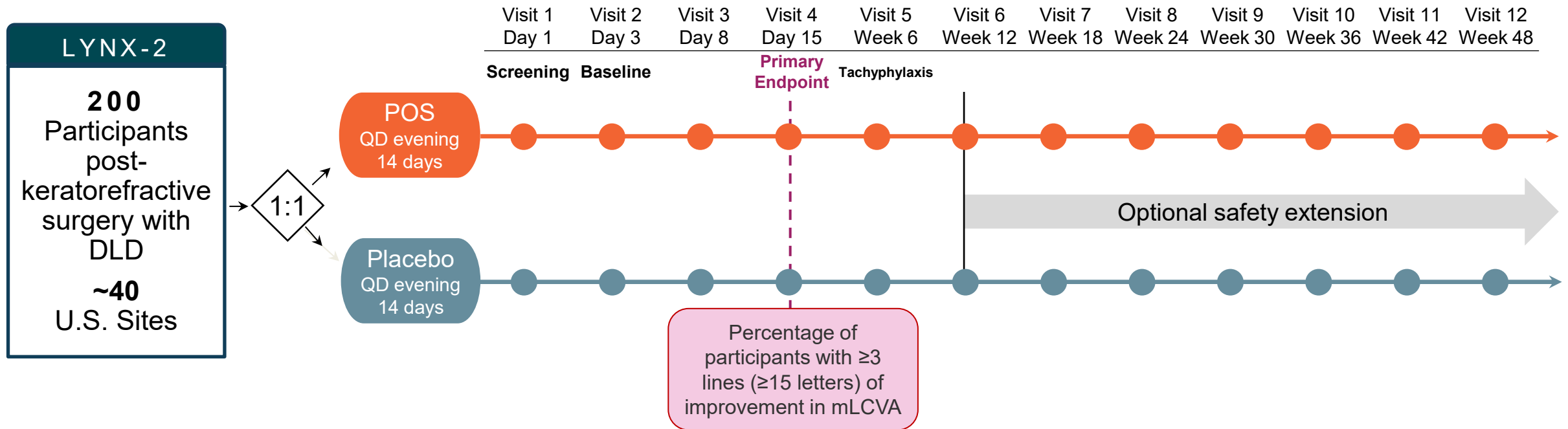
DLD, dim light disturbances; POS, phentolamine ophthalmic solution 0.75%; PP, per protocol.  
Source: Data on File, Opus/Viatris.

# Significantly Higher Percent of POS-Treated Subjects Had Improvements in Glare, Halo, and Starburst Severity

**Percent of Subjects With  $\geq 2$  Grade Reduction in DLD Symptom Severity from Baseline to Day 15**



# LYNX-2 Phase 3 Pivotal Study Design

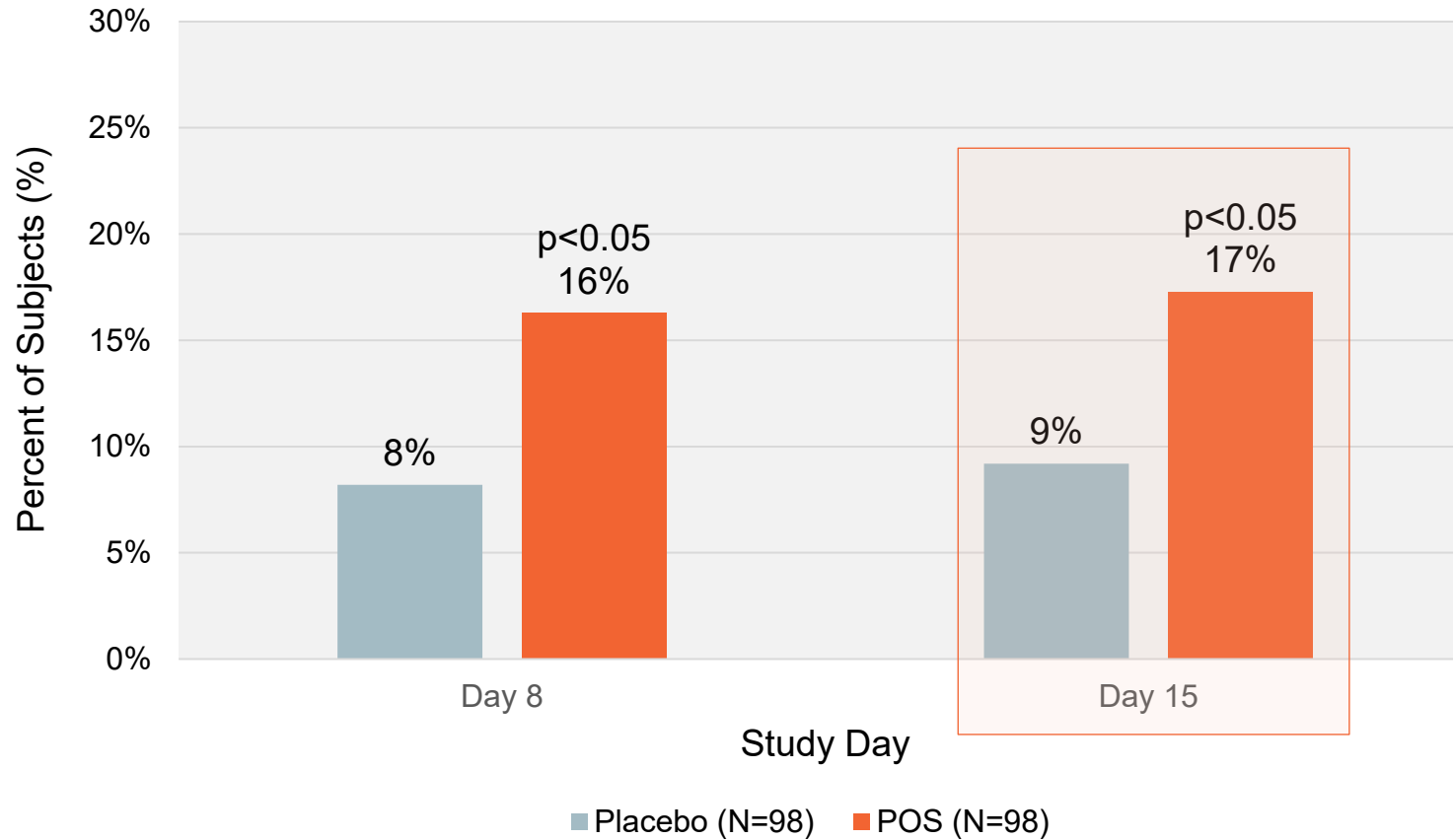


- Conducted under SPA agreement with FDA
- Fully recruited
- Topline results expected mid-2025
- FDA Fast Track Designation granted for POS as treatment of significant chronic night driving impairment in keratorefractive patients with reduced mesopic vision

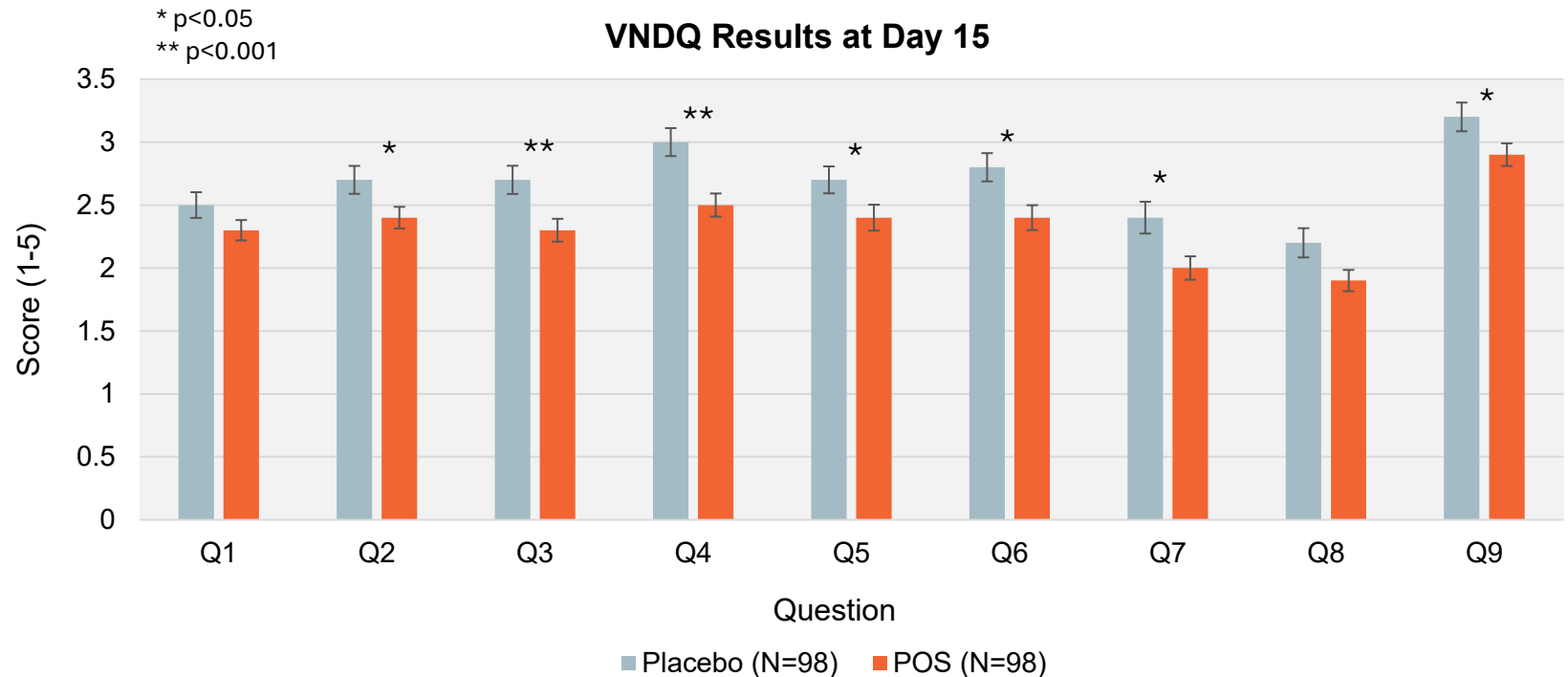
DLD, dim light disturbances; FDA, Food and Drug Administration; mLCVA mesopic low contrast best-corrected distance visual acuity; QD, once daily; SPA, Special Protocol Assessment.  
Source: Clinicaltrials.gov ID: NCT06349759

# Primary Endpoint: Percent of Subjects Gaining $\geq 15$ Letters mLCVA at Day 15

## Percent of Subjects Who Gained $\geq 15$ Letters ( $\geq 3$ Lines) of mLCVA at Day 15



# Patient Reported Outcomes (VNDQ) at Day 15



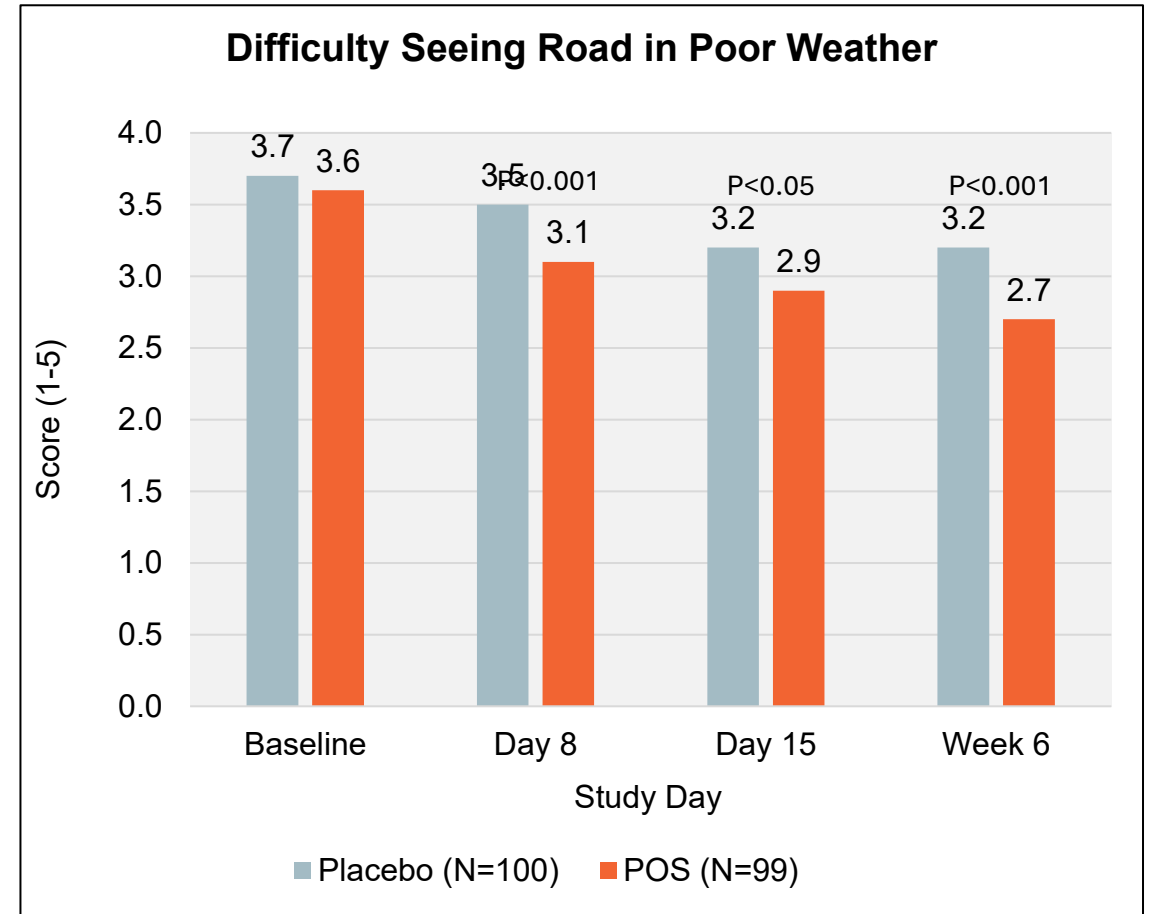
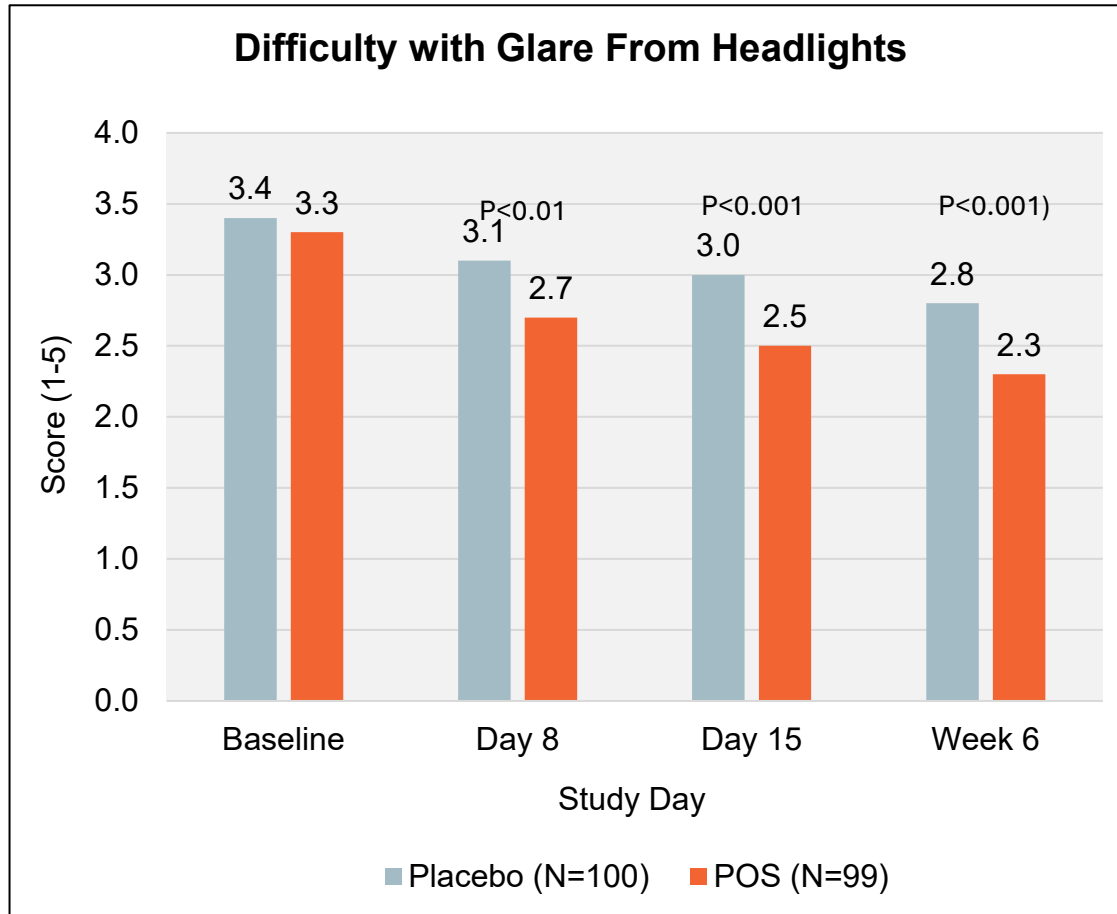
## Score

- 1: No difficulty
- 2: A little difficulty
- 3: Moderate difficulty
- 4: A lot of difficulty
- 5: Extreme difficulty

1. Seeing dark cars when driving at night
2. Seeing pedestrians on the roadside when driving at night
3. Reading street signs when driving at night
4. Seeing the road because of oncoming headlights
5. Seeing because of glare when driving at day or dusk
6. Adjusting after passing headlights from oncoming cars

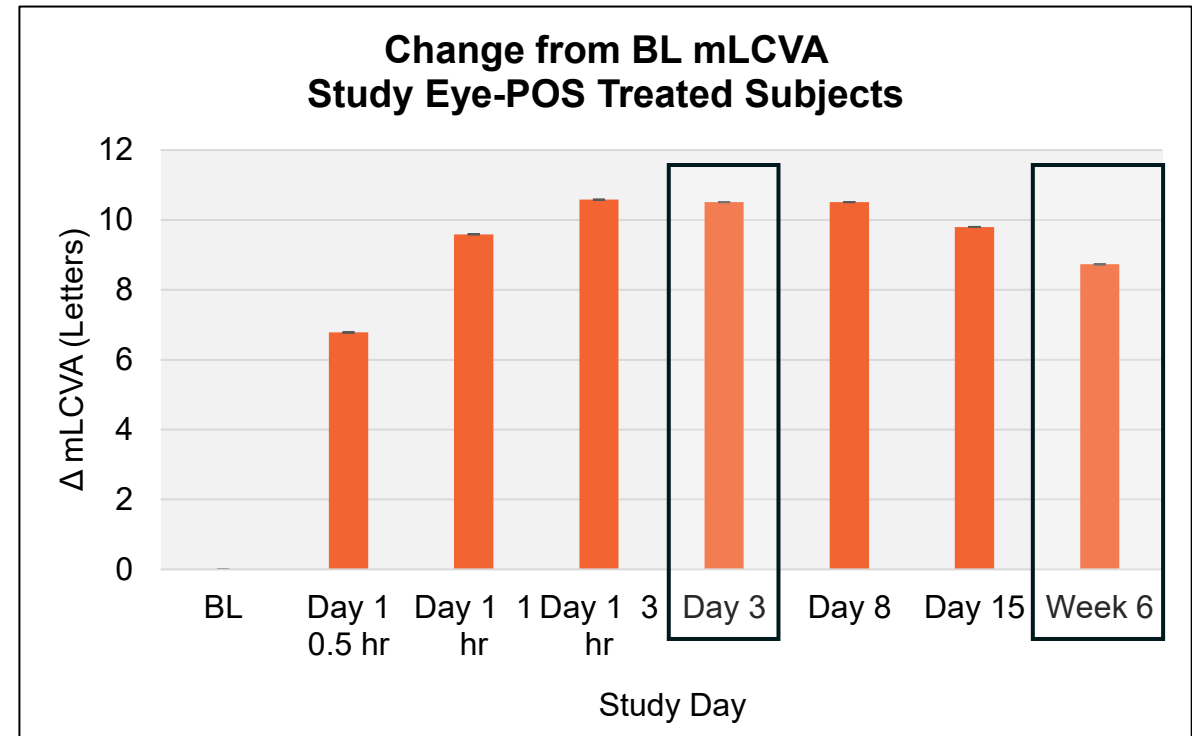
6. Judging the distance to your turnoff or exit while driving at night
7. Judging the distance between you and another moving cars when driving at night
8. Seeing the road in rain or poor weather when driving at night

# Patient Reported Outcomes Over Time (VNDQ)



# Tachyphylaxis Endpoint: Change from Baseline in mLCVA at Week 6 vs Visits Through Day 15 in POS-Treated Study Eyes

- Subjects in the POS group gained 8-11 letters of mLCVA at all time points from 1-hour after the first dose to 6 weeks of daily dosing
- Results do not show evidence of tachyphylaxis
- Difference between best mLCVA (Day 3) and Week 6  $-1.85$  letters
- 95% CI  $-2.73 - -0.97$  does not include the prespecified criterion of  $-5$  letters



# Safety

- Phentolamine Ophthalmic Solution 0.75% was well tolerated with no drug-related serious adverse events reported
- The most common treatment-emergent adverse events ( $\geq 5\%$ ) were mild and consistent with previous studies:
  - Conjunctival hyperemia (35%), instillation site irritation (19%), and dysgeusia (11%)
- Only 1% of POS-treated subjects reported headache

# POS Does Not Impair mLCVA

*No POS treated subject lost a line or more of mLCVA at any timepoint*

	<b>POS (N=99)</b>	<b>Placebo (N=100)</b>
Day 15	98	98
≥15 letters	17 (17.3)	9 (9.2)
≥10 letters	51 (52.0)	42 (42.9)
≥5 letters	83 (84.7)	76 (77.6)
≥-4 to ≤4 letters	15 (15.3)	19 (19.4)
≤-5 letters	0	3 (3.1)
≤-10 letters	0	1 (1.0)
≤-15 letters	0	1 (1.0)

# POS is a Promising Candidate for Keratorefractive Patients with Decreased Mesopic Vision and Photic Complaints

- In LYNX-1, **POS showed a statistically significant and clinically meaningful 15 letter (3-line) and 10 letter (2-line) improvement in mLCVA at Days 8 and 15** compared to placebo with a favorable safety and tolerability profile
  - In the post-LASIK cohort, **POS showed clinically meaningful results in gain of mLCVA and reduced photic complaints**
- In LYNX-2, the primary outcome of the study was met
  - **Significantly more POS treated post-keratorefractive subjects gained  $\geq 15$  letters of mesopic LCVA compared to placebo at Day 15**
- POS treated subjects also had a significant reduction in subjective difficulty with night-time driving discomfort at Day 15 compared to placebo
- No evidence of tachyphylaxis over 6 weeks of repeated dosing
- As with previous studies, POS displayed a favorable safety profile with AEs  $\geq 5\%$  predominantly mild and limited to conjunctival hyperemia, instillation site irritation and dysgeusia
- No POS treated subject lost one or more lines of mLCVA at any timepoint
- **POS has the potential to be a first in class treatment for keratorefractive patients suffering from reduced mesopic vision and halo, glare, and starburst**