LYNX-1 Phase 3 Trial of the Safety and Efficacy of Phentolamine Ophthalmic Solution for the Treatment of Reduced Mesopic Low Contrast Vision: A Subset Analysis of Keratorefractive Subjects

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Kostas Charizanis, PhD, MBA[1]; Mitchell G Bridgell, PhD[1]; Jay S Pepose, MD, PhD, FARVO[1]

[1]Opus Genetics, Inc., Durham, NC, United States

Purpose

- There are no current on-label treatments for reduced mesopic vision in keratorefractive patients with photic complaints.[1-3]
- LYNX-1 was a randomized, double-masked, placebo-controlled study of the safety and efficacy of 0.75% phentolamine ophthalmic solution (POS) in participants with dim light disturbances (DLD) of various etiologies.
- A subset analysis of 25 keratorefractive participants in LYNX-1 with reduced mesopic low contrast visual acuity (mLCVA) and photic complaints was conducted to inform patient population selection for future Phase 3 studies.

Methods

- In the LYNX-1 study (NTC04638660), 145 participants with self-reported DLD and photic phenomena were randomized 1:1 to receive 14 nighttime doses of POS or placebo.
- Inclusion criteria included baseline mLCVA impairment (≤20/63) in at least one eye, ≥10 letters improvement in mLCVA during illumination of contralateral eye, pupil diameter (PD) ≥5mm under mesopic conditions in at least one eye, and no recent ocular procedures or clinically significant ocular disease.
- The primary efficacy outcome was percentage of subjects with ≥3-line improvement in mLCVA at Day 8, with secondary analysis of PD, visual acuity measures, patient reported outcomes (PROs), and safety and tolerability at Days 8 and 15.
- Keratorefractive participants were defined as subjects that had undergone laser-assisted in situ keratomileusis (LASIK) at least 6 months prior to screening.

Results

- Of the 25 post-LASIK participants, 21% (3/14) POS vs 0% (0/11) placebo showed a 3-line improvement from baseline in mLCVA at Day 15 (p=0.23); **Figure 1, left**.
- This improvement was numerically similar to the statistically significant improvement in ≥3-line gain of mLCVA at Day 15 in the entire 143 participant cohort, with 21% (14/68) POS vs 3% (2/73) placebo (p<0.01); **Figure 1, right**.
- In the post-LASIK participants at Day 15, the POS group gained a mean of 10.1 letters in mLCVA vs 5.1 in placebo (p=0.04), with a statistically significant reduction in halos (p=0.02) and starburst (p=0.03) in the POS group.
- Percentage of participants who showed improvement of ≥2 grades on the PRO scale for most measures was statistically significant in both the overall and post-LASIK populations (p<0.05); **Figure 2**

Figure 1

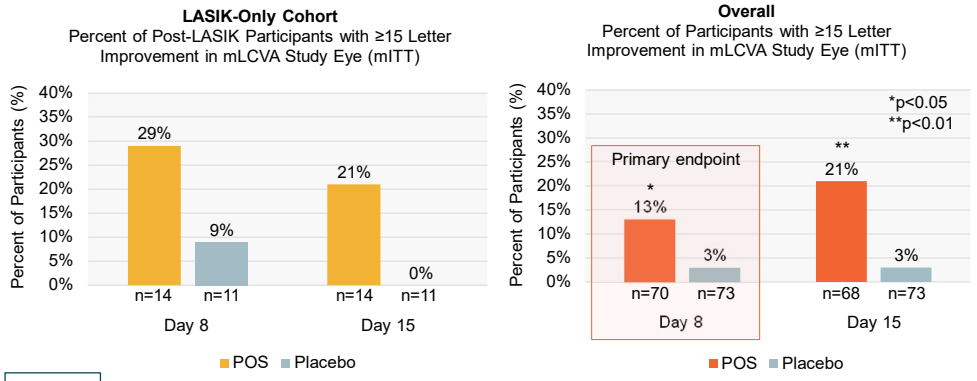
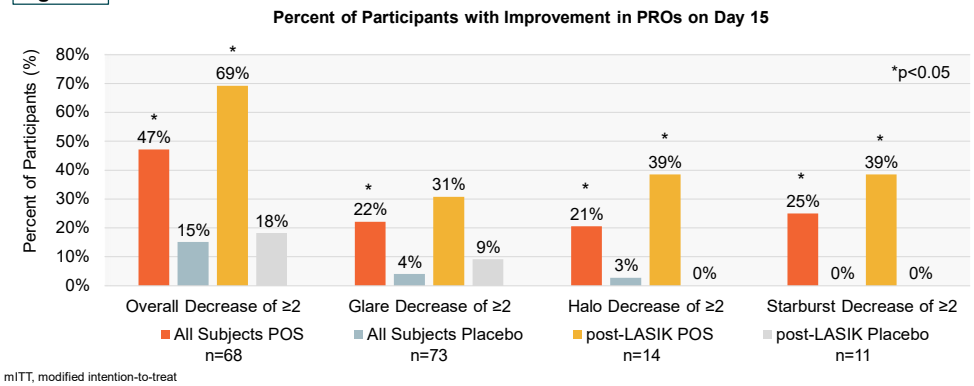


Figure 2



mITT, modified intention-to-treat

Conclusions

- POS met the primary endpoint of participants gaining ≥15 letters of mLCVA compared to placebo on Day 8 (p<0.05) and showed increased efficacy after 14 days of evening dosing.
- A similar trend was seen in the post-LASIK POS subset as the full DLD cohort for clinically meaningful ≥3-line improvement in mLCVA.
- In the post-LASIK POS population, a statistically significant improvement was also seen in both mean mLCVA and subjective reports of photic phenomena.
- In both the overall and subset POS populations, a statistically significant improvement was seen in most of the patient reported outcome measures of photic phenomena (glare, halos, and starbursts).
- No serious adverse events (AEs) observed; treatment-emergent AEs were uncommon and limited to mild and transient conjunctival hyperemia, instillation site discomfort, and dysgeusia.
- These findings support additional Phase 3 trials of POS in keratorefractive participants with reduced mLCVA and photic complaints.
- The LYNX-2 Phase 3 trial is ongoing to support an sNDA submission for POS in keratorefractive particiapants with reduced mesopic vision and photic phenomena.

References

1. Pepose J, Brigell M, Lazar E, et al. *BMC Ophthalmol.* 2022;22:402.
2. Tahzib NG, et al. *J Cataract Refract Surg.* 2005;31:1943-1951.
3. Bailey MD, Zadnik K. *Cornea.* 2007;26:246-254.

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

Disclosures: Kostas Charizanis, PhD, MBA (C); Mitchell G Bridgell, PhD (C); Jay S Pepose, MD, PhD, FARVO (C) of Opus Genetics, Inc.

Direct all inquiries to kcharizanis@opusgtx.com

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