

Subretinal Gene Therapy laru-zova for X-linked Retinitis Pigmentosa (XLRP): Pivotal VISTA Trial First-time Results

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On Behalf of the VISTA Investigator Group

Presented at the American Academy of Ophthalmology Retina Subspecialty Day Meeting

October 10, 2026 | New Orleans, Louisiana

Laru-zova is an investigational product; it has not been approved by the FDA. Beacon Therapeutics, Inc. was the sponsor of the study.

Speaker Disclosures

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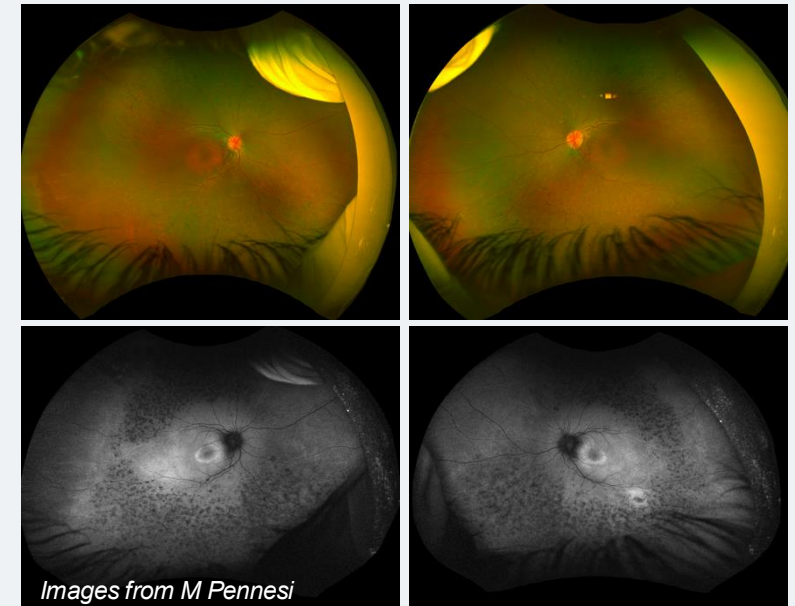
X-Linked Retinitis Pigmentosa (XLRP)

Rare inherited retinal disease characterized by progressive photoreceptor degeneration that leads to blindness with no treatment options

- Primarily affecting males, ***RPGR* gene mutations underlie $\geq 70\%$ of XLRP cases**^{1,2}
- Early symptoms include night blindness and peripheral vision loss, progressing to central vision loss and **legal blindness by median age of 45**¹

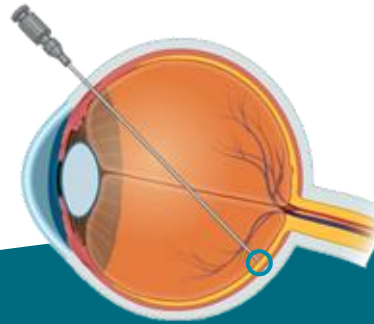
Early ³ Childhood	Mid-Stage ^{1,4} 20–30s	Late Stage ^{1,4–6} 40–50s
- Early changes in peripheral vision - Night blindness - Difficulties in low light environments	- No longer safe to drive - Difficulty reading, completing chores, playing sports	- Tunnel vision; progressive loss of central visual acuity - Loss of reading ability - Increased difficulty navigating unfamiliar areas

Images from a 12-year old male patient with XLRP

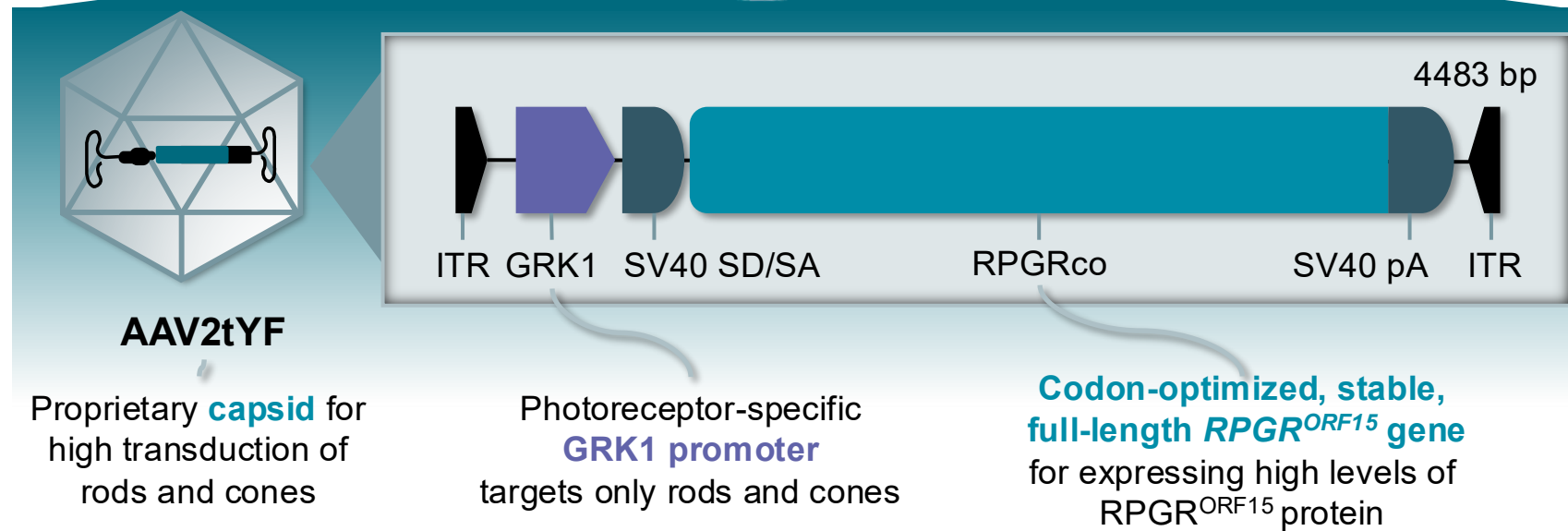


Laru-zova (laruparetigene zovaparvovec)

Laru-zova is an investigational gene therapy designed to deliver a functional, full-length copy of the *RPGR*^{ORF15} gene



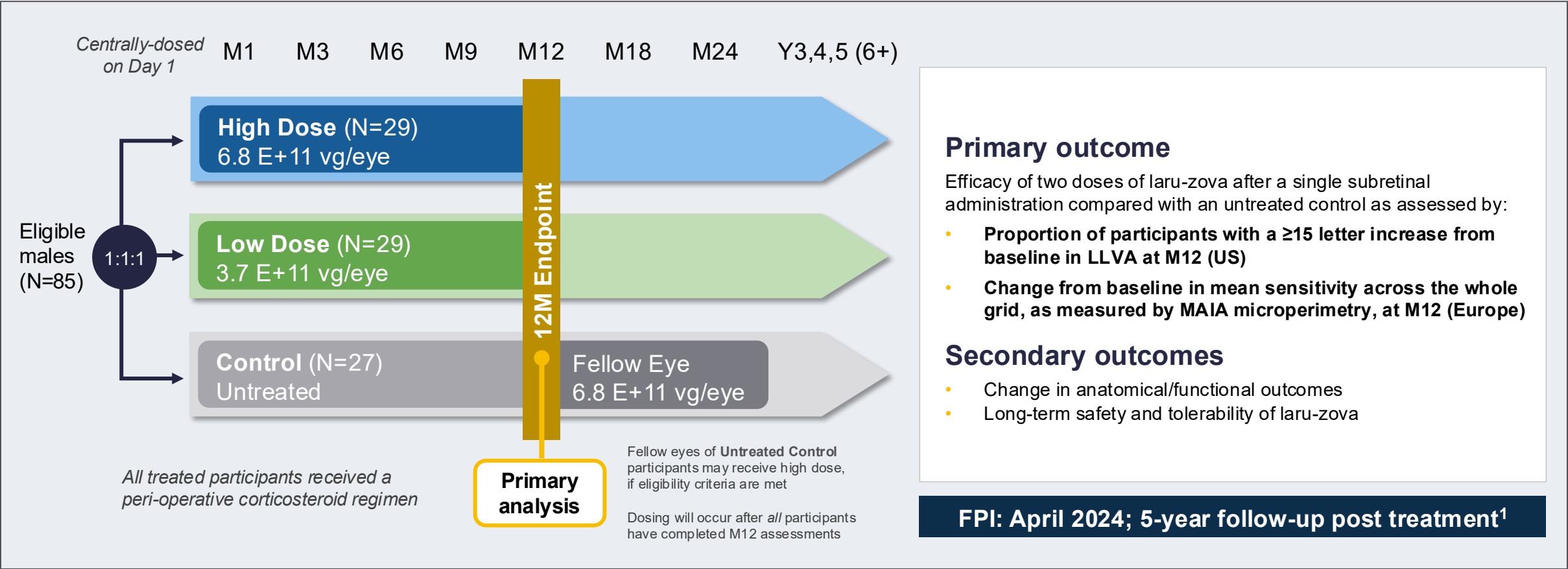
Laru-zova is administered subretinally in a surgical setting



Laru-zova is designed to restore the natural function of both rods and cones in XLRP caused by *RPGR* mutations

Phase 2/3 VISTA Study Design

Randomized, Controlled, Masked, Multicenter Study Evaluating the Efficacy, Safety, and Tolerability of Two Dose Levels of Laruzovab compared to Untreated Control Group in Male Participants with XLRP caused by Mutations In The RPGR Gene



FPI, first participant in; LLVA, low luminance visual acuity; M, month; MAIA, macular integrity assessment; RPGR, retinitis pigmentosa GTPase regulator; XLRP, X-linked retinitis pigmentosa; Y, year. 1. NCT04850118. ClinicalTrials.gov. Last updated April 7, 2026. <https://clinicaltrials.gov/study/NCT04850118>. VISTA ClinicalTrials.gov Identifier: NCT04850118

Key Eligibility Criteria

General	Study Eye Ocular Criteria
• Males aged 12–50 years • At least 1 documented pathogenic or likely pathogenic variant in the <i>RPGR</i> gene within exons 1–14 and/or <i>ORF15</i> • Clinical diagnosis of XLRP	• BCVA 34–78 ETDRS letters • LLVA ≤64 letters, with LLD >10 letters • Detectable baseline mean macular sensitivity measured by MAIA microperimetry (1–12 dB), with fixation loss ≤20% at screening • Detectable foveal EZ line on SD-OCT

BCVA, best-corrected visual acuity; **dB**, decibels; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **EZ**, ellipsoid zone; **LLD**, low luminance deficit; **LLVA**, low luminance visual acuity; **MAIA**, macular integrity assessment; **ORF15**, open reading frame 15; **RPGR**, retinitis pigmentosa GTPase regulator; **SD-OCT**, spectral domain optical coherence tomography; **XLRP**, X-linked retinitis pigmentosa.
VISTA ClinicalTrials.gov Identifier: NCT04850118

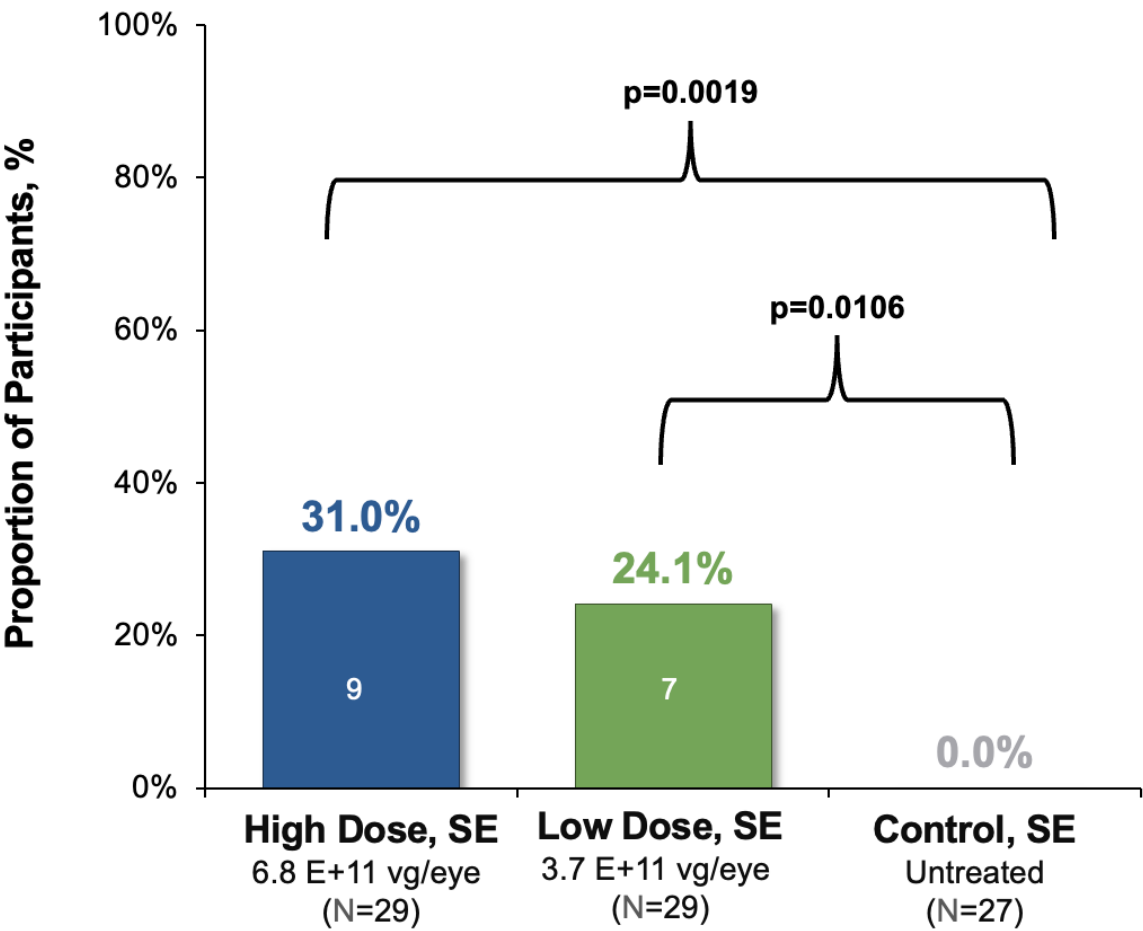
Baseline Characteristics and Demographics Were Well Matched Between Treated and Control Groups

Participant age and baseline characteristics in study eye	High Dose 6.8 E+11 vg/eye (N=29)	Low Dose 3.7 E+11 vg/eye (N=29)	Control Untreated (N=27)
Age, Years, mean (range)	25.4 (13, 47)	24.9 (12, 47)	27.4 (16, 48)
Vision, ETDRS letters, mean (SD)			
BCVA	67.14 (7.234)	68.41 (7.660)	68.48 (6.229)
LLVA	46.93 (11.495)	49.41 (10.189)	49.07 (13.032)
LLD	20.72 (8.514)	18.97 (6.132)	19.52 (9.850)
MAIA mean sensitivity (whole grid), dB, mean (SD)	3.93 (2.712)	4.54 (2.415)	4.15 (2.854)

Statistically Significant Improvement in LLVA at Month 12

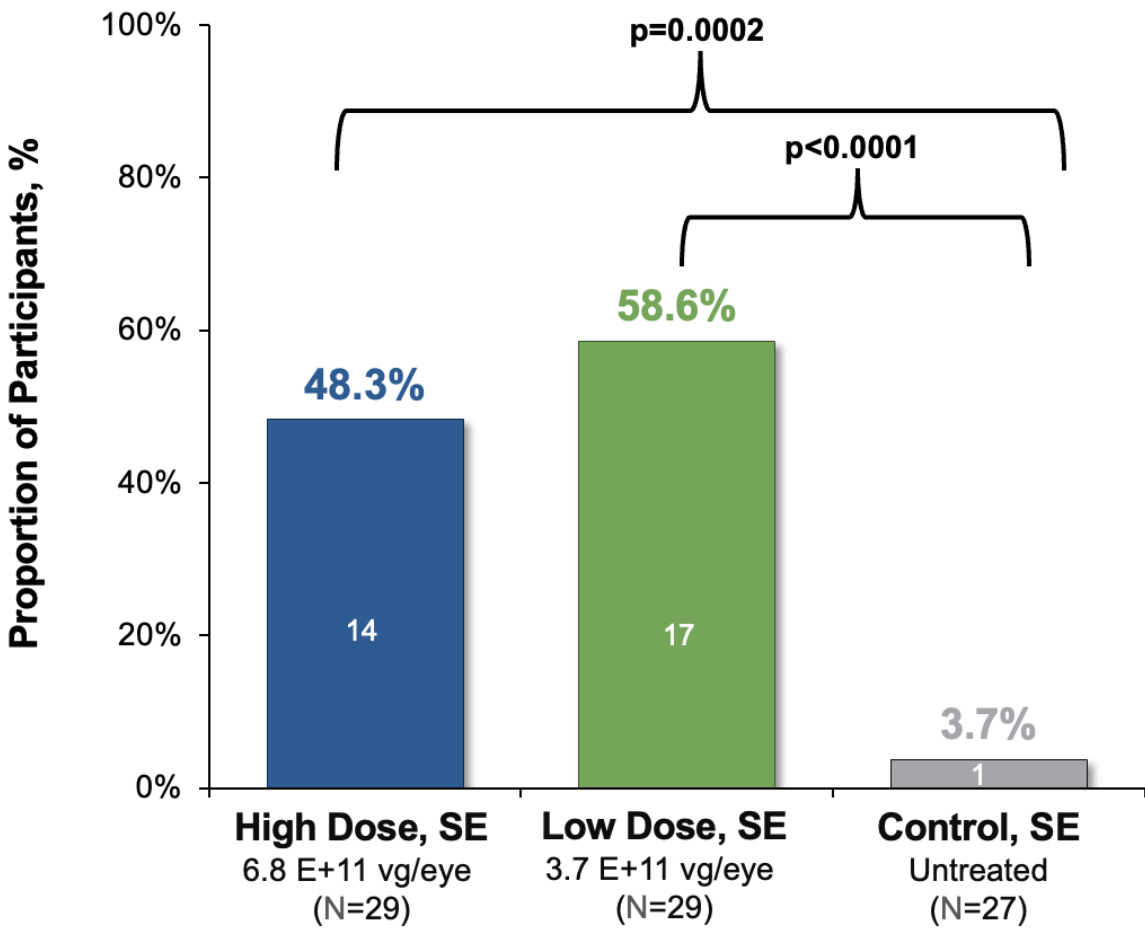
3-line LLVA Response

At least 3-line (15+ ETDRS letters) improvement from baseline



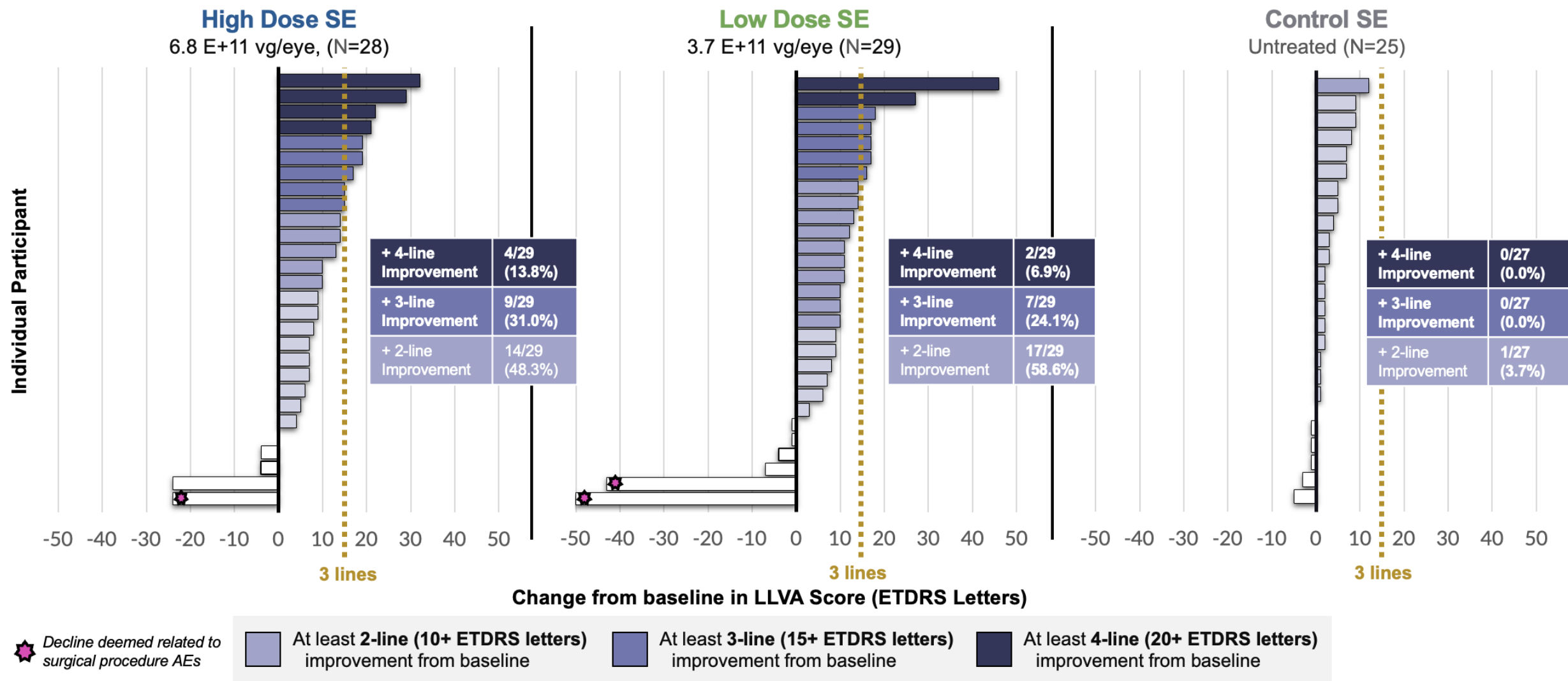
2-line LLVA Response

At least 2-line (10+ ETDRS letters) improvement from baseline

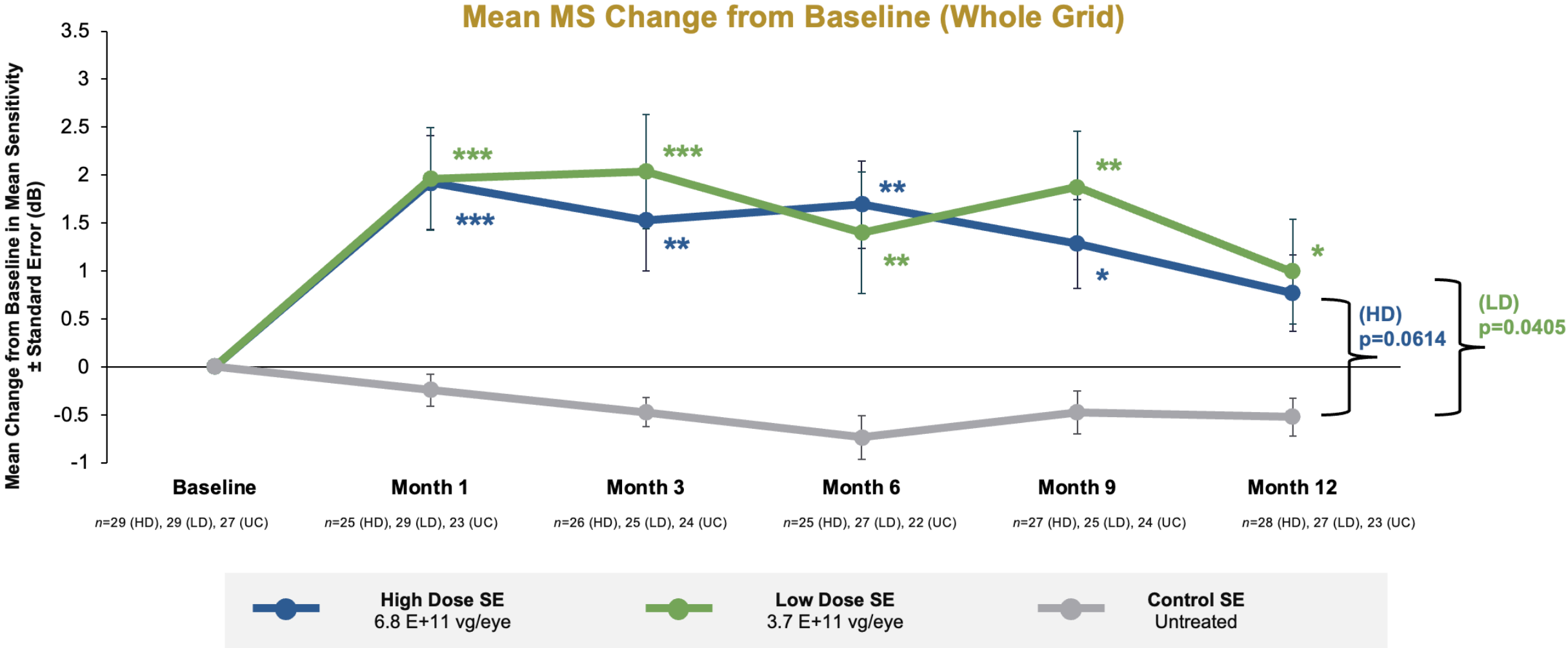


Majority of Participants Gained or Preserved Vision in Both Dose Groups Compared to Control

Individual Change in LLVA at Month 12



Early and Sustained Improvement in Microperimetry Mean Sensitivity Demonstrated with Laru-zova



Intent-to-Treat Population. HD, high dose; LD, low dose; MS, Mean Sensitivity; SE, Study Eye; UC, untreated control.
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* p<0.05; ** p<0.01; *** p<0.001

Participants Excluded from Prespecified Per Protocol Population

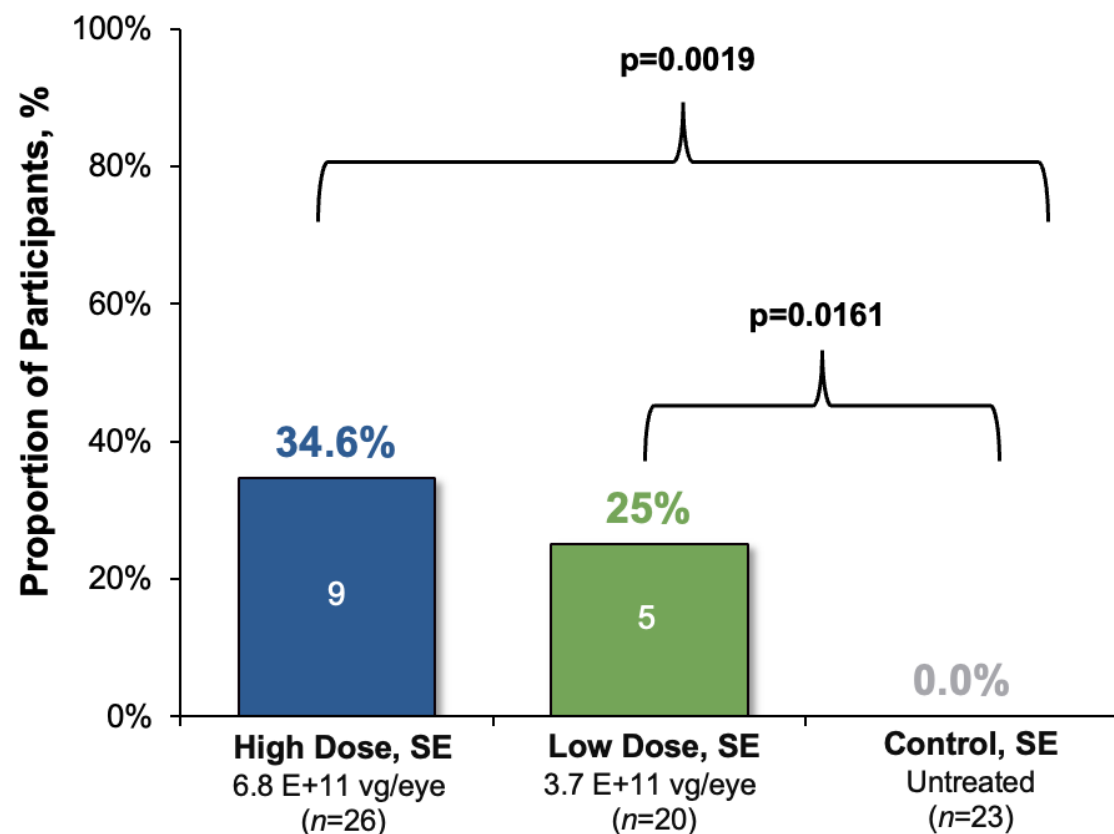
Prespecified Exclusion Criteria	High Dose	Low Dose	Control
No data post-randomization	1	0	2
No treatment due to surgical complication prior to dosing	1	0	NA
Injection volume $\leq 100 \mu\text{L}$	0	4	NA
Visually significant cataract at Month 12 visit ^a	1	1 ^c	0
Surgical complications that resulted in vision loss remaining at Month 12 visit ^b	0	2 ^c	NA
No Month 12 mean sensitivity due to fixation loss $>20\%$	0	3	2
Total Excluded from PP Population	3	9	4
Number of Participants in PP Population	26	20	23

^a Participants who developed a new or worsening cataract which was considered visually significant and was not surgically removed 6 weeks prior to the Month 12 Visit; ^b Participants experienced surgical complications that resulted in vision loss (e.g. retinal detachment and a macular hole); ^c One participant is same participant in both exclusion criteria above
PP, per protocol.

Statistically Significant Improvement in LLVA at Month 12 in Prespecified Per Protocol Population

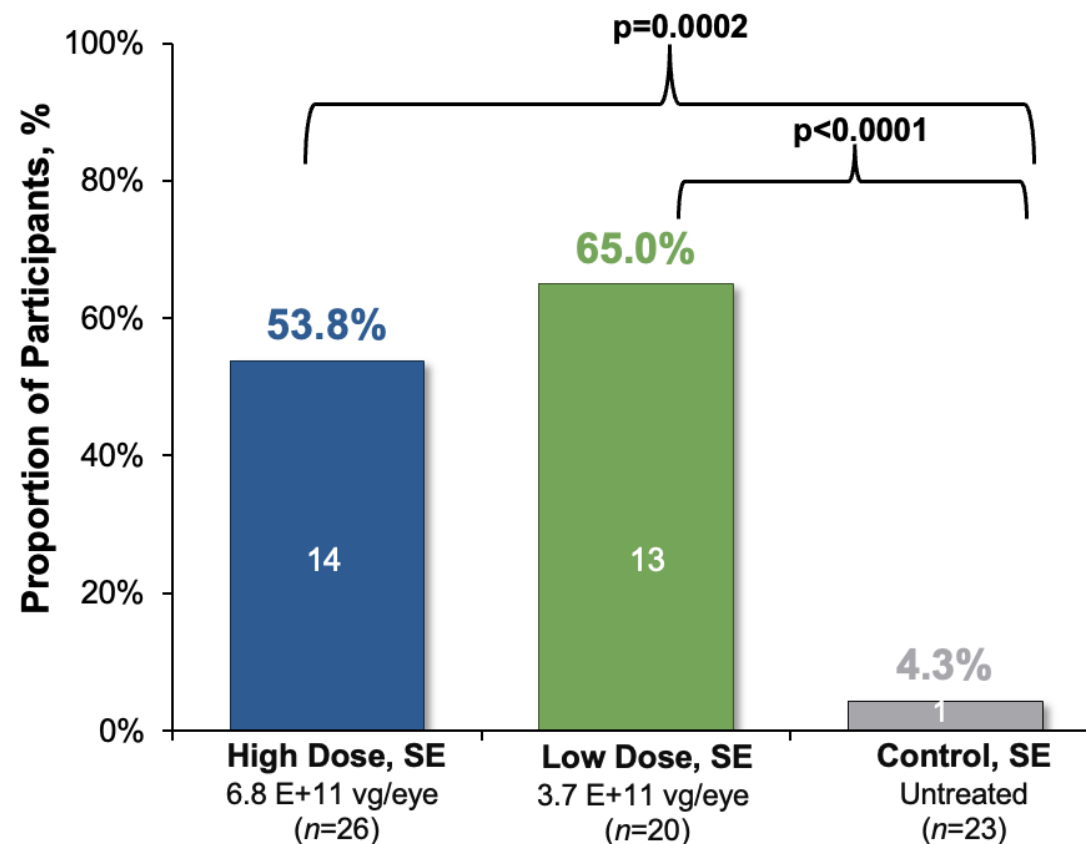
3-line LLVA Response

At least 3-line (15+ ETDRS letters) improvement from baseline

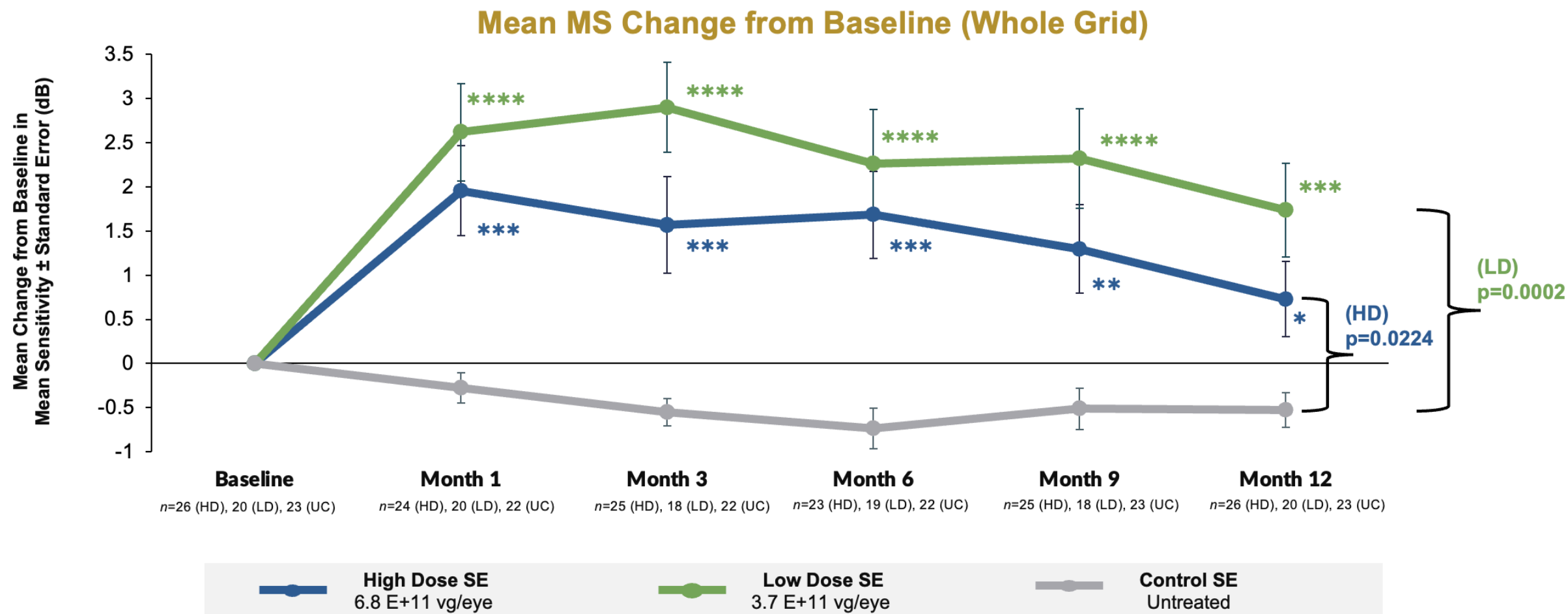


2-line LLVA Response

At least 2-line (10+ ETDRS letters) improvement from baseline



Early and Sustained Improvement in Microperimetry Mean Sensitivity Demonstrated with Laru-zova (PP Population)



PP, Prespecified Per Protocol; MS, Mean Sensitivity, MP, microperimetry. HD, High Dose; LD, Low Dose; SE, Study Eye; UC, Untreated Control.
VISTA ClinicalTrials.gov Identifier: NCT04850118.

* p<0.05; ** p<0.01; ***p<0.001; ****p<0.0001

Laru-zova Demonstrated a Favorable Safety and Tolerability Profile, with Predominantly Mild to Moderate Ocular TEAEs and Only Surgical Procedure-related SAEs

- Ocular TEAEs were balanced across treatment groups and were predominantly mild to moderate in severity with the majority of TEAEs attributed to the surgical procedure.
- Only two ocular SAEs were reported (macular hole and retinal detachment), both occurring in the low-dose cohort (6.9%) and attributed to the surgical procedure.
- Laru-zova-related ocular TEAEs were reported in 25% of participants in the high-dose cohort and ~38% in the low-dose cohort.
- Protocol-required steroid-related ocular TEAEs were reported in ~32% and ~28% of participants in the high-dose and low-dose cohorts, respectively.

Ocular TEAEs Related to Laru-zova and Ocular SAEs

		High Dose 6.8 E+11 vg/eye (N=28)		Low Dose 3.7 E+11 vg/eye (N=29)		Control Untreated (N=25)	
Preferred Term		Study Eye	Fellow Eye	Study Eye	Fellow Eye	Study Eye	Fellow Eye
Ocular SAEs	Macular Hole	0	0	1 (3.4)	0	0	0
	Rhegmatogenous Retinal Detachment	0	0	1 (3.4)	0	0	0
Ocular TEAEs related to laru- zova occurring in >1 participants overall	Cystoid Macular Edema	1 (3.6)	0	2 (6.9)	0	0	0
	Iridocyclitis	1 (3.6)	0	1 (3.4)	0	0	0
	Retinal Degeneration	1 (3.6)	0	1 (3.4)	0	0	0
	Retinal Deposits	1 (3.6)	0	1 (3.4)	0	0	0
	RPE Change	1 (3.6)	0	1 (3.4)	0	0	0
	Uveitis	1 (3.6)	0	1 (3.4)	0	0	0
	Injection Site Atrophy	0	0	2 (6.9)	0	0	0

Both SAEs in the low dose group were attributed to the surgical procedure
All ocular TEAEs related to laru-zova were mild to moderate in severity

Conclusions: Pivotal VISTA Topline Results

- **VISTA met its FDA-endorsed primary endpoint**, demonstrating statistically significant low luminance visual acuity (LLVA) ≥ 15 letter responder rates at Month 12 compared to the untreated control group
- **Laru-zova demonstrated a favorable safety and tolerability profile**, consistent with prior studies
- **VISTA is the first and only pivotal trial in XLRP to achieve its primary endpoint**, further building on the five-year clinical dataset for laru-zova including the prior HORIZON, SKYLINE, and DAWN trials

Based upon these positive topline results, Beacon plans to engage with global regulatory authorities with initiation of a rolling BLA submission planned for later this year

On Behalf of the VISTA Investigator Group

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Thank you to all investigators, surgeons and site staff, along with the study participants and their families in the VISTA study