Subretinal Gene Therapy Laru-zova (AGTC-501) for X-linked Retinitis Pigmentosa (XLRP): Phase 2 DAWN Safety and Efficacy Update

Andreas K. Lauer, MD[1]; Mark E. Pennesi, MD, PhD[1,2]; David Birch, PhD[2]; Rajiv Anand, MD[2,3]; Robert A. Sisk, MD[4]; Anne Fulton, MD[5]; Efren Gonzalez, MD[5]; Sandeep Grover, MD[6]; Aleksandra Rachitskaya, MD[7]; Paul Yang, MD, PhD[1]; Daniel Chung, DO[8]

[1]OHSU Casey Eye Institute, Portland, OR; [2]Retina Foundation of the Southwest, Dallas, TX; [3]Texas Retina Associates, Dallas, TX; [4]Cincinnati Eye Institute, Cincinnati, OH; [5]Boston Children's Hospital, Boston, MA; [6]University of Florida, Jacksonville, FL; [7]Cleveland Eye Institute, Cleveland, OH; [8]Beacon Therapeutics, Cambridge, MA

Presented at the Association for Research in Vision & Ophthalmology Annual Meeting, May 3–7, 2026 | Denver, CO

Laru-zova is an investigational product; it has not been approved by the FDA. Conclusive evidence of efficacy and safety of laru-zova will require further investigation in additional clinical trials. Beacon Therapeutics, Inc. was the sponsor of the study and provided funding for third-party writing support by Nancy Nguyen, PharmD, of Koahana, Inc.

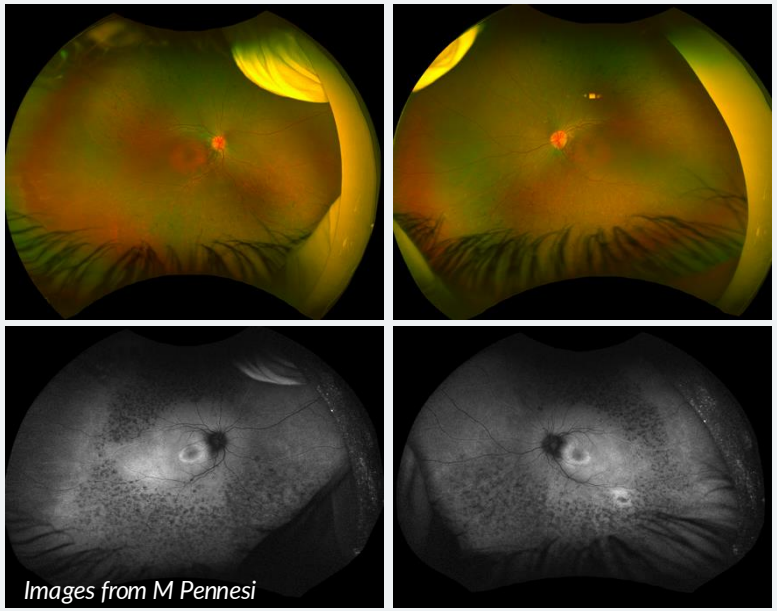
X-Linked Retinitis Pigmentosa (XLRP)

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

- Primarily affecting males, ***RPGR* gene mutations underlie ≥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

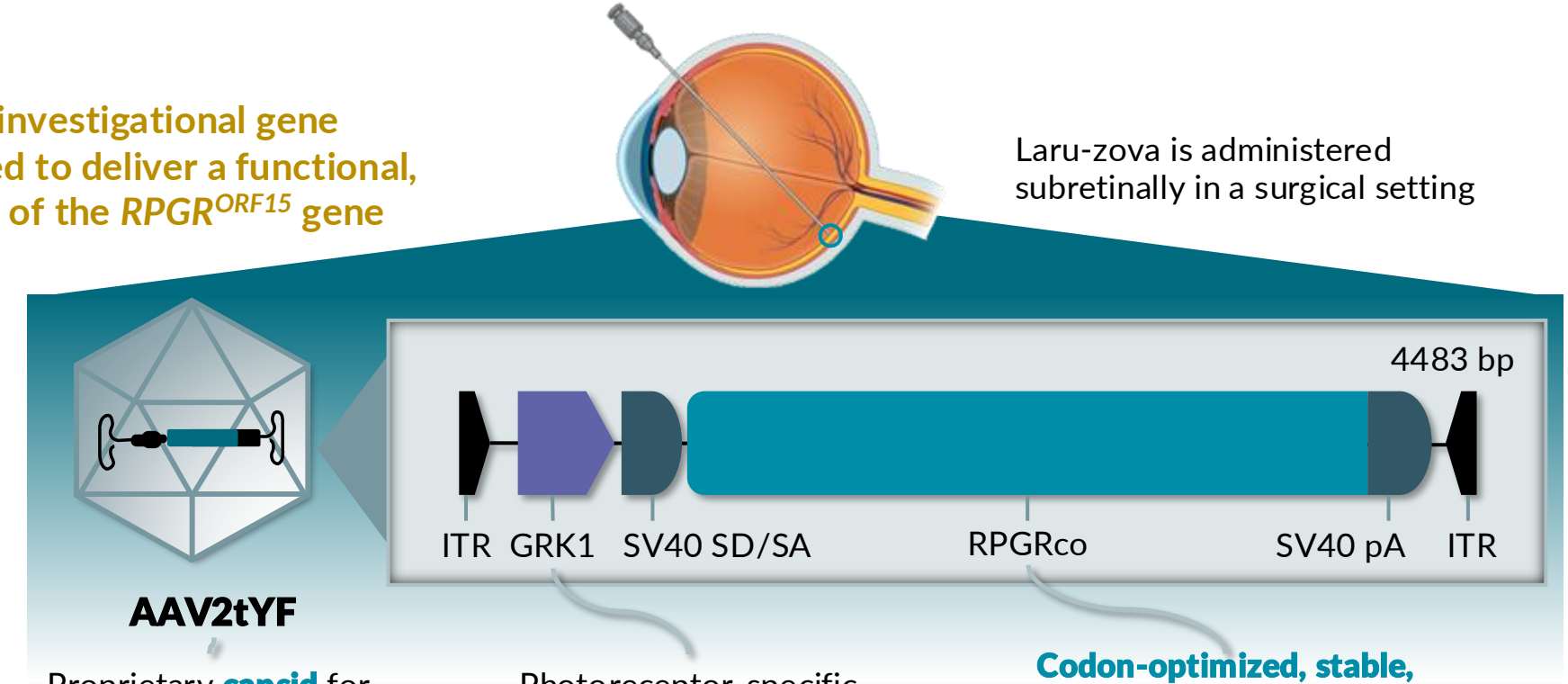
Images from a 12-year old male patient with XLRP



RPGR, retinitis pigmentosa GTPase regulator; **VA,** visual acuity; **XLRP,** X-linked retinitis pigmentosa. **1.** Chivers M, et al. *Clinicoecon Outcomes Res*. 2021;13:565-572. **2.** Nguyen XT, et al. *Int J Mol Sci.* 2020;21(3):835. **3.** Churchill JD, et al. *Invest Ophthalmol Vis Sci*. 2013;54(2):1411-1416. **4.** Senthil MP, et al. *Eye (Lond)*. 2017;31(5):741-748. **5.** Di Iorio V, et al. *Invest Ophthalmol Vis Sci*. 2020;61(14):36. **6.** O'Neal TB, et al. Retinitis Pigmentosa. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519518.

Laru-zova (laruparetigene zovaparvovec)

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

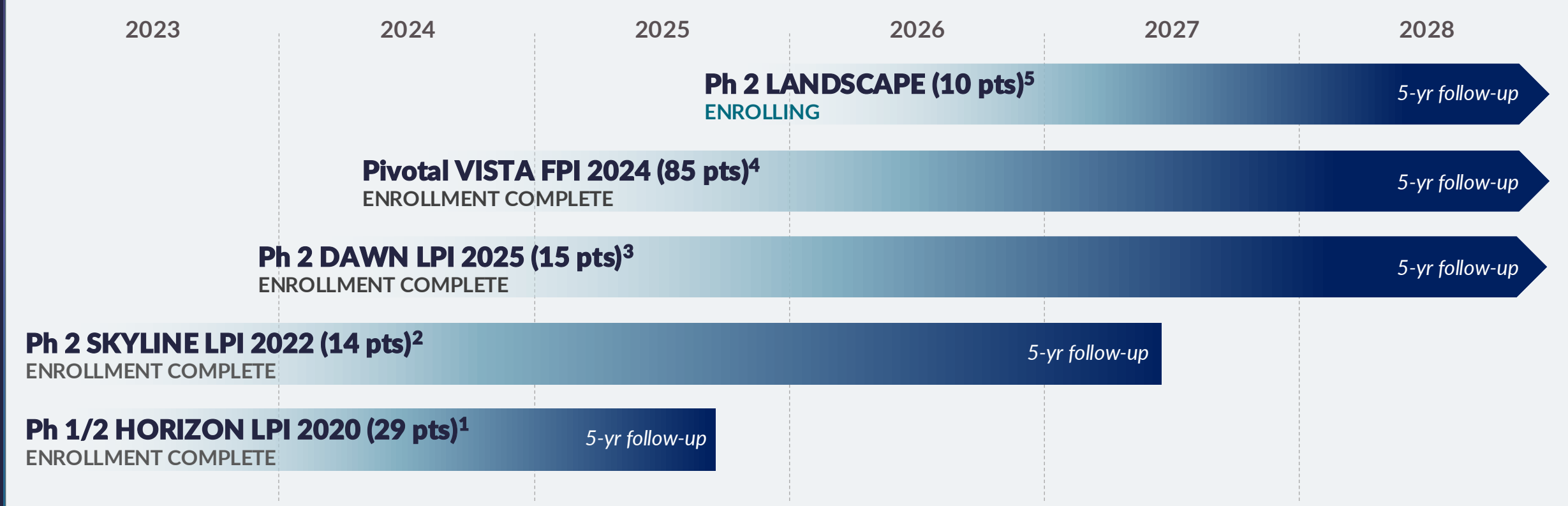


Laru-zova has the potential to restore the natural function of both rods and cones in XLRP caused by *RPGR* mutations

AAV2tYF, AAV2 capsid variant with three surface tyrosine residues changed to phenylalanine; **bp,** base pair; **GRK1,** G protein-coupled receptor kinase 1; **ITR,** inverted terminal repeat; **pA,** polyadenylation signal; **rAAV,** recombinant adeno-associated virus; **RPGR,** retinitis pigmentosa GTPase regulator; **RPGRco,** codon-optimized human RPGR complementary DNA; **SA,** splice acceptor, **SD,** splice donor; **SV40,** simian virus 40; **XLRP,** X-linked retinitis pigmentosa. Data on file. Beacon Therapeutics (USA), Inc.

Laru-zova Clinical Development Program

Comprehensive program to deliver a potential first-in-class therapy to patients with XLRP

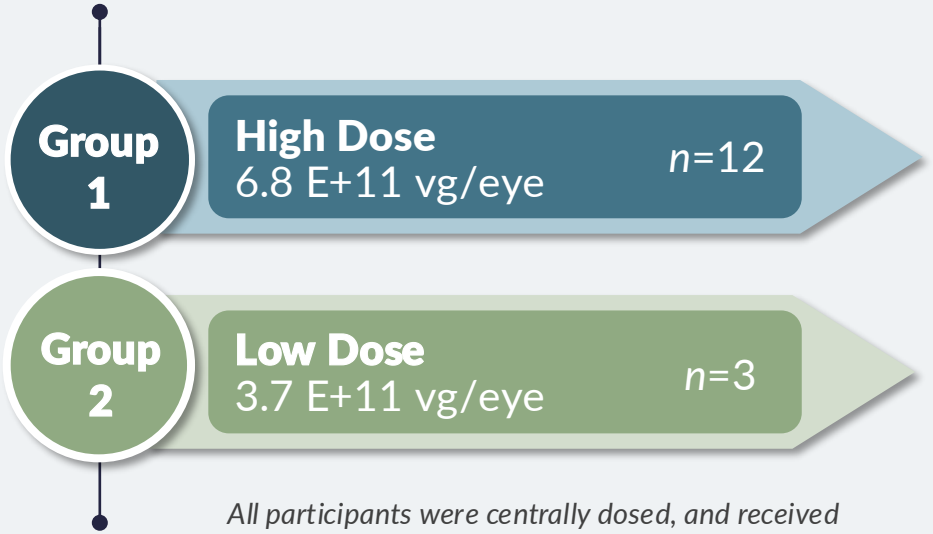


FPI, first participant in; **LPI,** last participant in; **ph,** phase; **pts,** participants; **XLRP,** X-linked retinitis pigmentosa.

1. NCT03316560. ClinicalTrials.gov. Last Updated May 20, 2024. https://clinicaltrials.gov/study/NCT03316560 **2.** NCT06333249. ClinicalTrials.gov. Last Updated August 12, 2024. https://clinicaltrials.gov/study/NCT06333249 **3.** NCT06275620. ClinicalTrials.gov. Last updated October 30, 2024. https://clinicaltrials.gov/study/NCT06275620. **4.** NCT04850118. ClinicalTrials.gov. Last updated April 7, 2024. https://clinicaltrials.gov/study/NCT04850118 **5.** NCT07174726. ClinicalTrials.gov. Last updated February 19, 2026. https://clinicaltrials.gov/study/NCT07174726.

Phase 2 DAWN Study Design: Fellow Eye Treatment in Previously-treated Participants

Non-randomized, open-label, multicenter study comparing two dose levels of laru-zova in the fellow eye of previously-treated male participants with XLRP caused by mutations in the *RPGR* gene



All participants were centrally dosed, and received a peri- and post-operative corticosteroid regimen

Primary outcome

- **Number and proportion of Grade 3 or higher ocular or non-ocular treatment-emergent AEs or SAEs**

Secondary outcomes

- Changes from baseline to Month 12 in visual function and functional vision measures, including low luminance visual acuity (LLVA), mean sensitivity via microperimetry, and mobility course scores

FPI: November 2023; 5-year follow-up post treatment[1]

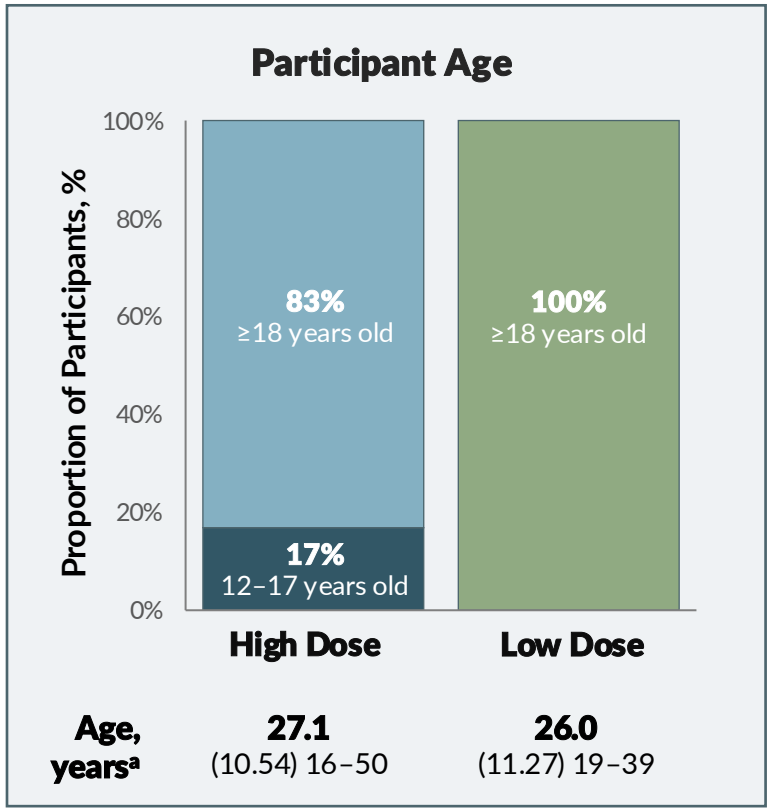
FPI, first participant in; **LLVA,** low luminance visual acuity; **RPGR,** retinitis pigmentosa GTPase regulator; **(S)AE,** (serious) adverse event; **XLRP,** X-linked retinitis pigmentosa.

1. NCT06275620. ClinicalTrials.gov. Last updated October 30, 2024. https://clinicaltrials.gov/study/NCT06275620.

DAWN ClinicalTrials.gov Identifier: NCT06275620.

Most participants were previously treated with laru-zova in Phase 1/2 HORIZON and Phase 2 SKYLINE studies

DAWN enrolled 15 male participants, averaging ≈26.9 years old



	Group 1 High Dose 6.8 E+11 vg/eye (*n*=12)		Group 2 Low Dose 3.7 E+11 vg/eye (*n*=3)	
Previous trial participation, n				
Phase 1/2 (HORIZON)	8		0	
Phase 2 (SKYLINE)	3		3	
Biogen XIRIUS trial	1		0	
Time between doses, months[a]	**54.0[b]** 28.7–74.7		**31.6** 29.9–32.6	
Baseline Vision, ETDRS letters[a]	**Study Eye**	**Fellow Eye[c]**	**Study Eye**	**Fellow Eye[c]**
BCVA	**67.7** (6.20) 57–76	**69.4** (8.21) 54–80	**74.7** (1.15) 74–76	**78.3** (6.35) 71–82
LLVA	**46.7** (12.54) 24–62	**55.1** (9.47) 40–70	**53.3** (5.77) 50–60	**66.3** (6.03) 60–72
LLD	**21.0** (8.53) 12– 38	**14.3** (5.05) 5–22	**21.3** (4.62) 16–24	**12.0** (2.65) 10–15
MAIA mean sensitivity (whole grid), dB[a]	**2.91** (2.13) 1.3–8.8	**4.04** (2.44) 0.6–9.2	**2.46** (1.06) 1.7–3.7	**4.56** (0.68) 4.1–5.4

[a] Statistics are presented as mean (SD), range. [b] Excludes one participant in Biogen trial. [c] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein.
BCVA, best corrected visual acuity; **ETDRS,** Early Treatment of Diabetic Retinopathy Study; **LLD,** low luminance deficit; **LLVA,** low luminance visual acuity; **MAIA,** Macular Integrity Assessment; **XLRP,** X-linked retinitis pigmentosa.
Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Ocular TEAEs were Generally Mild or Moderate in Severity

Participants with ocular TEAE, n	Group 1 High Dose 6.8 E+11 vg/eye (*n*=12)		Group 2 Low Dose 3.7 E+11 vg/eye (*n*=3)	
	Study Eye	Fellow Eye[a]	Study Eye	Fellow Eye[a]
At least 1 ocular TEAE	12	6	3	2
Mild	6	4	1	1
Moderate	5	2	1	1
Severe	1	0	1	0
At least 1 ocular SAE	1	0	1	0
At least 1 AESI	3	0	1	0
At least 1 ocular TEAE related to:				
Surgical procedure	12	1	3	0
Protocol-required corticosteroids	8	1	2	1
Laru-zova	3	0	0	0

Majority were related to the surgical procedure or corticosteroid regimen and have resolved

[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. **AESI,** adverse event of special interest; **SAE,** serious adverse event; **TEAE,** treatment emergent adverse event.
Based on March 27, 2026 data cutoff. All patients received a peri- and post-operative corticosteroid regimen. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Majority of Ocular TEAEs were Non-serious

	Preferred term	Group 1 High Dose 6.8 E+11 vg/eye (*n*=12)		Group 2 Low Dose 3.7 E+11 vg/eye (*n*=3)	
		Study Eye	Fellow Eye[a]	Study Eye	Fellow Eye[a]
Ocular SAEs	Glaucoma[b]	1	0	1	0
Ocular TEAEs occurring in >2 participants overall	Glaucoma[b]	8	0	2	1
	Conjunctival haemorrhage	8	0	2	0
	Conjunctival hyperaemia	7	0	0	0
	Ocular discomfort	7	0	0	0
	Cataract subcapsular	4	4	2	0
	Eye pain	4	2	2	0
	Anterior chamber cell	4	1	1	0
	Metamorphopsia	4	0	1	0
	Vitreal cells	4	0	1	0
	Dry eye	3	2	1	0
	Epiretinal membrane	4	0	0	1
	Vision blurred	3	1	1	0
	Eye irritation	3	0	0	0
	Eyelid ptosis	2	0	1	0
	Injection site atrophy	2	0	1	0

No SUSARs, retinal detachments, or endophthalmitis reported

[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. [b] Reported as steroid-induced increase in intraocular pressure. **AESI,** adverse event of special interest; **SAE,** serious adverse event; **SUSAR,** suspected unexpected serious adverse reactions; **TEAE,** treatment emergent adverse event.
Based on March 27, 2026 data cutoff. All patients received a peri- and post-operative corticosteroid regimen. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Adverse Events of Special Interest and Adverse Events of Ocular Inflammation

		Group 1 High Dose 6.8 E+11 vg/eye (*n*=12)		Group 2 Low Dose 3.7 E+11 vg/eye (*n*=3)	
	Preferred term	**Study Eye**	**Fellow Eye[a]**	**Study Eye**	**Fellow Eye[a]**
AESIs	Injection site atrophy	2	0	1	0
	Iridocyclitis	1[b]	0	0	0
Ocular Inflammation	Vitreal cells	4	0	1	0
	Anterior chamber cell	4	1	1	0
	Punctate keratitis	1	1	1	0
	Uveitis	1	0	0	0
	Iridocyclitis	1[b]	0	0	0
	Vitritis	1	0	0	0
	Sub-retinal inflammation[c]	1	0	0	0
	Iritis	0	1	0	0

Majority of ocular inflammation was mild and transient in nature

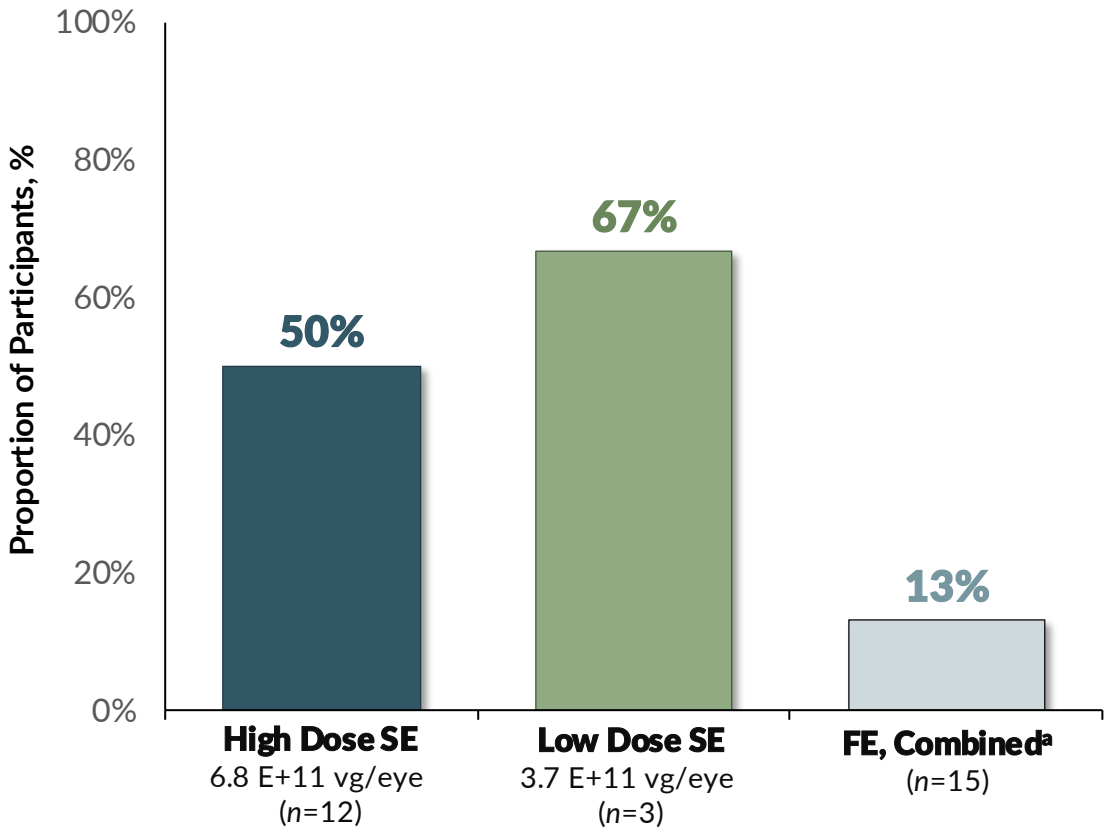
[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. [b] Represents the same adverse event. [c] Reported term, event under review. **AESI,** adverse event of special interest.
Based on March 27, 2026 data cutoff. All patients received a peri- and post-operative corticosteroid regimen. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Improvement in LLVA at Month 12

More study eyes had 2- and 3-line improvements compared to previously-treated fellow eyes

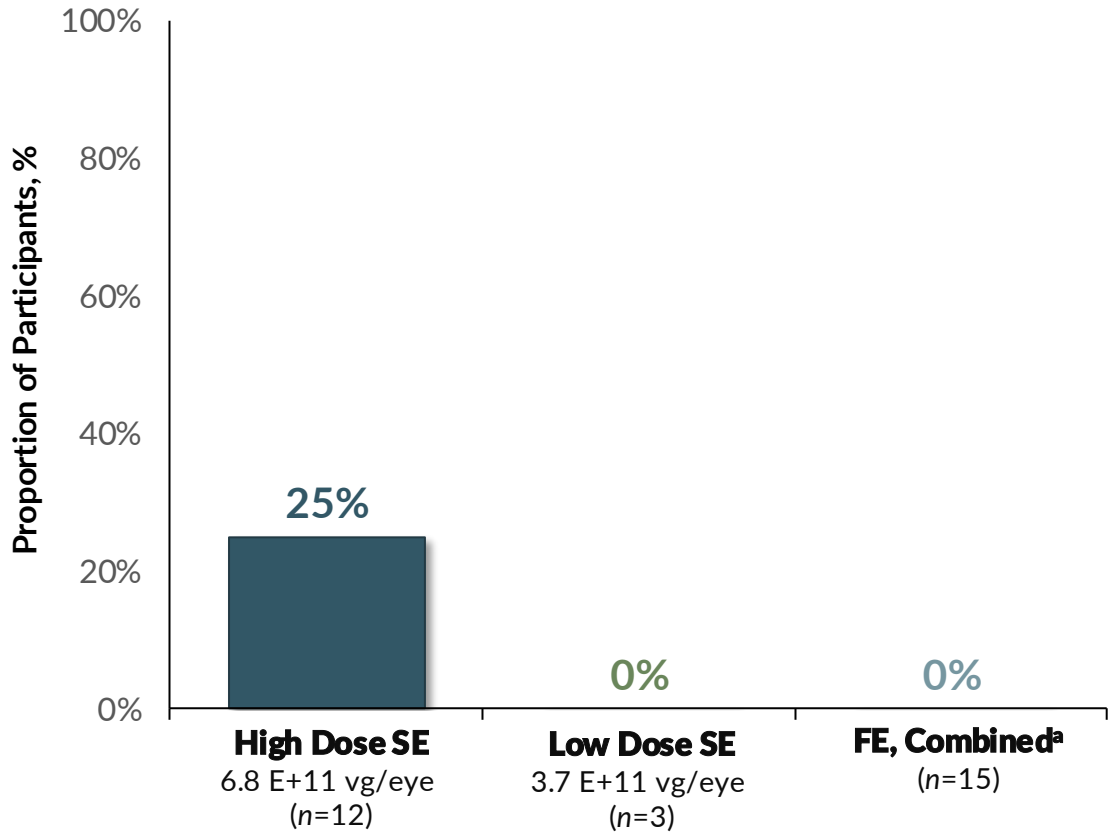
2-line LLVA Response

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



3-line LLVA Response

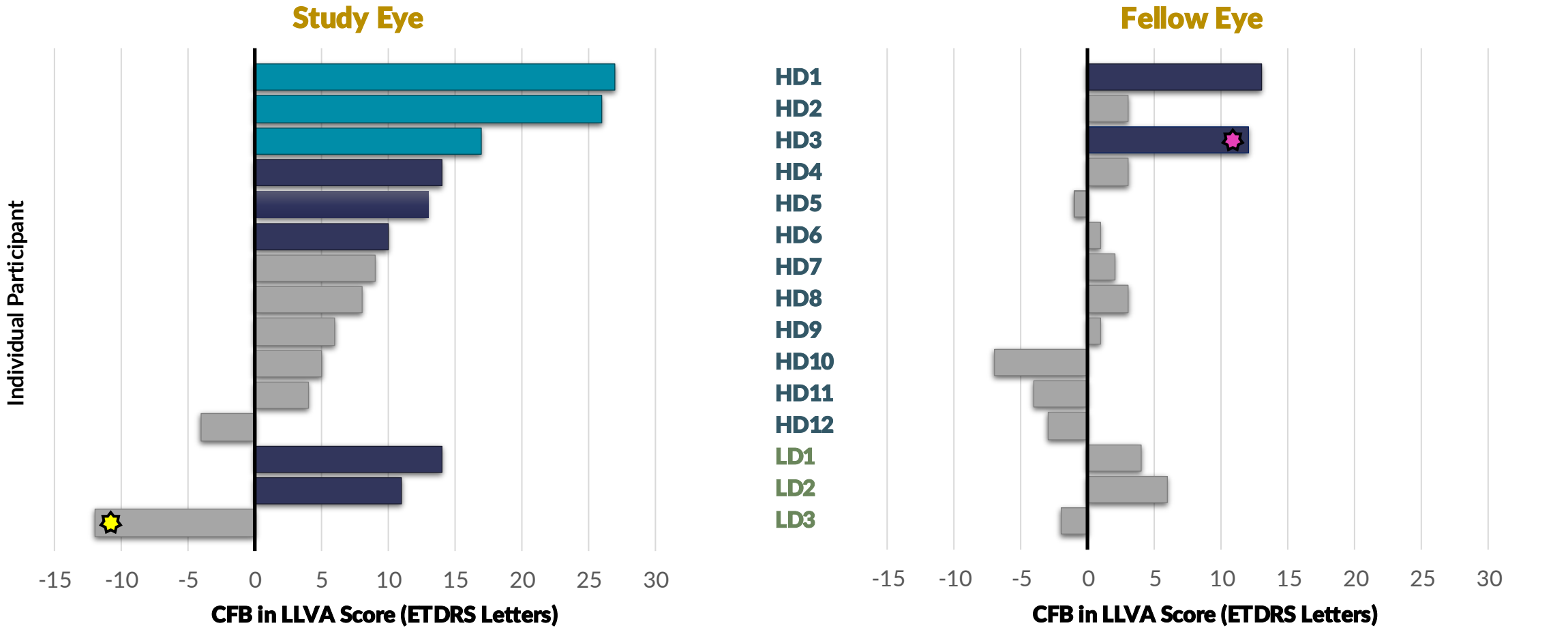
At least **3-line (15+ ETDRS letters)** improvement from baseline



[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. **ETDRS,** Early Treatment of Diabetic Retinopathy Study; **FE,** fellow eye; **LLVA,** low luminance visual acuity; **M,** month; **SE,** study eye (newly treated). Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Individual Change in LLVA at Month 12

More study eyes with 2- and 3-line improvements compared to previously-treated fellow eyes

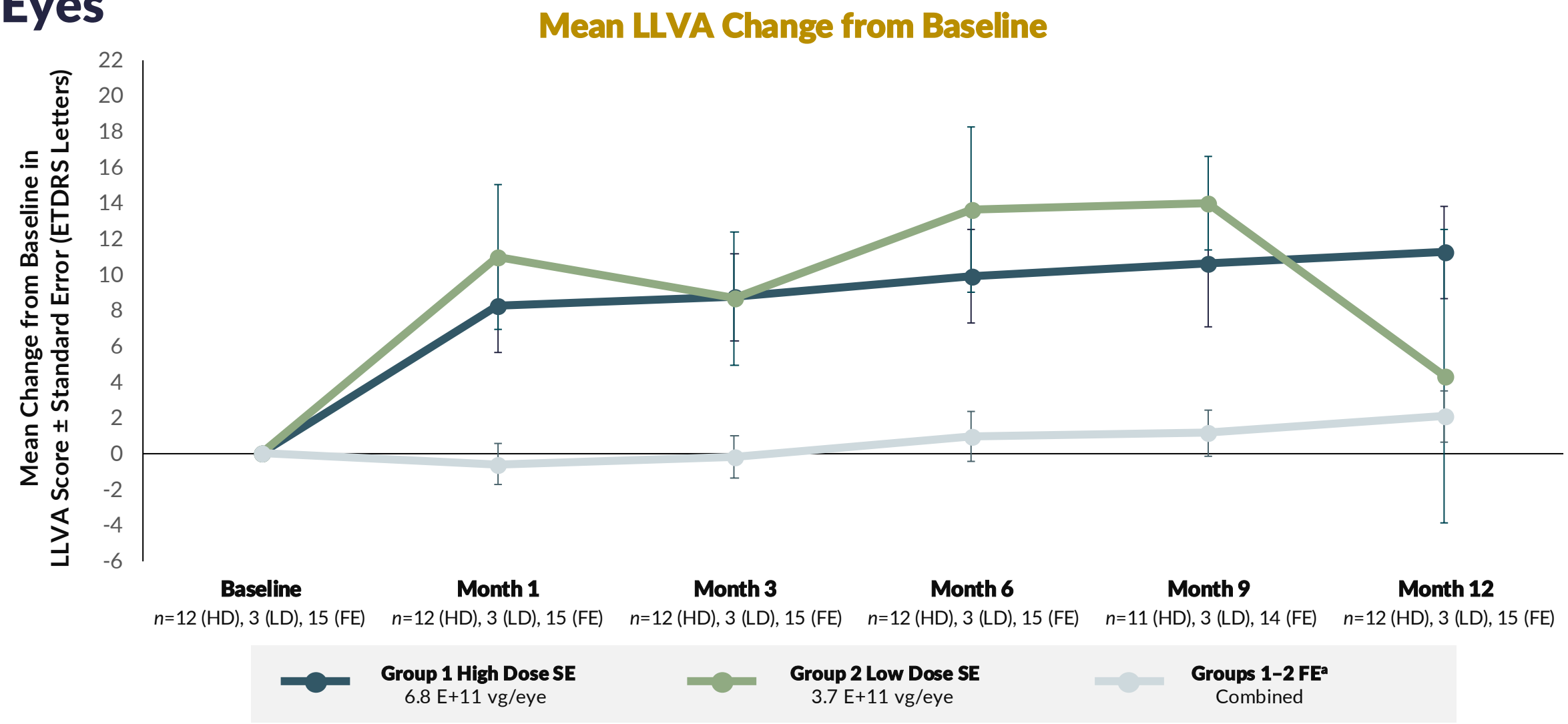


Participant had worsening cataract in study eye; vision declined 3+ lines from prior visit

Participant had cataract surgery in previously treated fellow eye; vision improved 4+ lines from prior visit

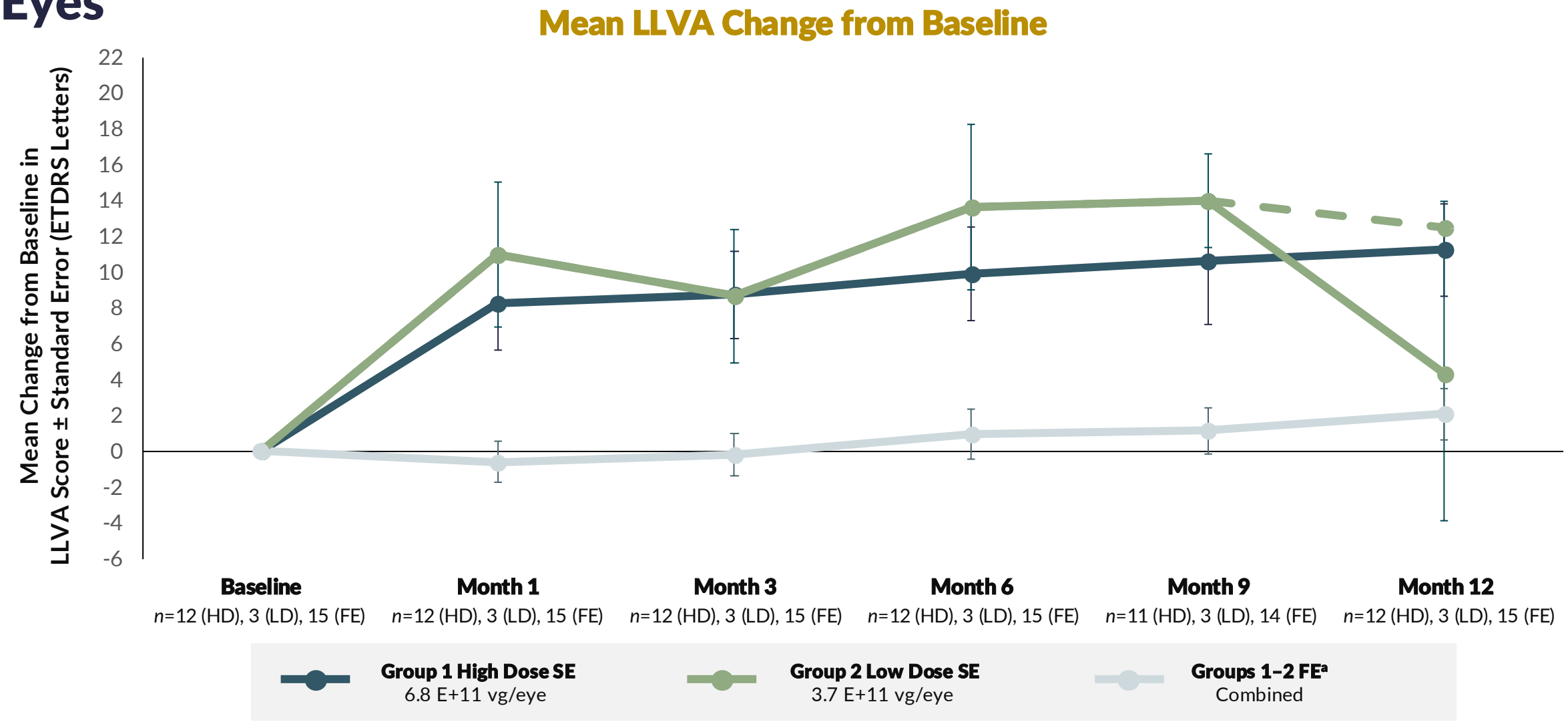
[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. **ETDRS,** Early Treatment of Diabetic Retinopathy Study; **HD,** high dose; **LD,** low dose; **LLVA,** low luminance visual acuity; **M,** month. Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Early and Sustained Improvement in Mean LLVA in DAWN Study Eyes



[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. **ETDRS,** Early Treatment of Diabetic Retinopathy Study; **FE,** fellow eye; **HD,** high dose; **LD,** low dose; **LLVA,** low luminance visual acuity; **SE,** study eye (newly treated).
Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Early and Sustained Improvement in Mean LLVA in DAWN Study Eyes

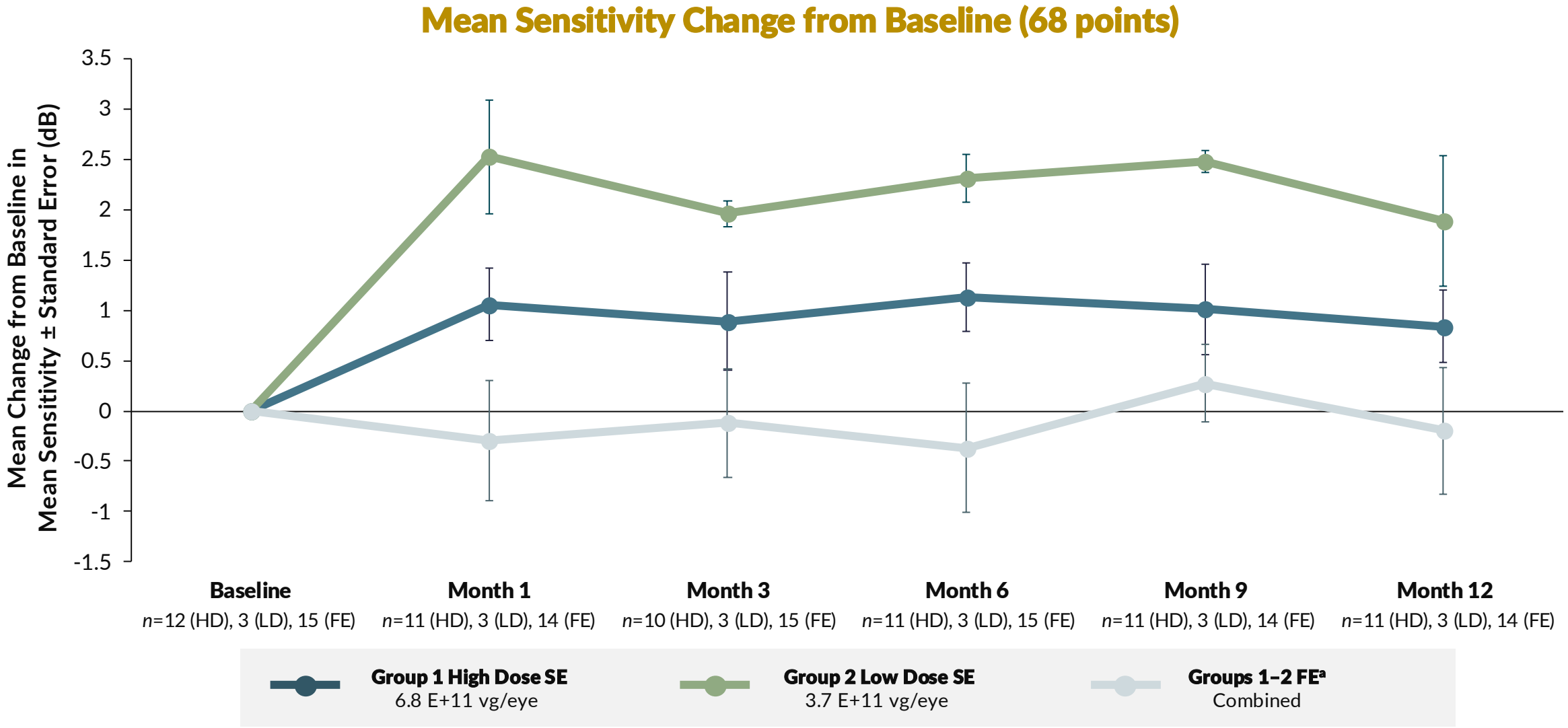


Dotted line excludes 1 eye with visually significant cataracts: Group 2 M12 (–12).

[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. **ETDRS,** Early Treatment of Diabetic Retinopathy Study; **FE,** fellow eye; **HD,** high dose; **LD,** low dose; **LLVA,** low luminance visual acuity; **SE,** study eye (newly treated).

Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Early and Sustained Improvement in Microperimetry Mean Sensitivity



Data was excluded from analysis at an individual timepoint if fixation loss was >20%.

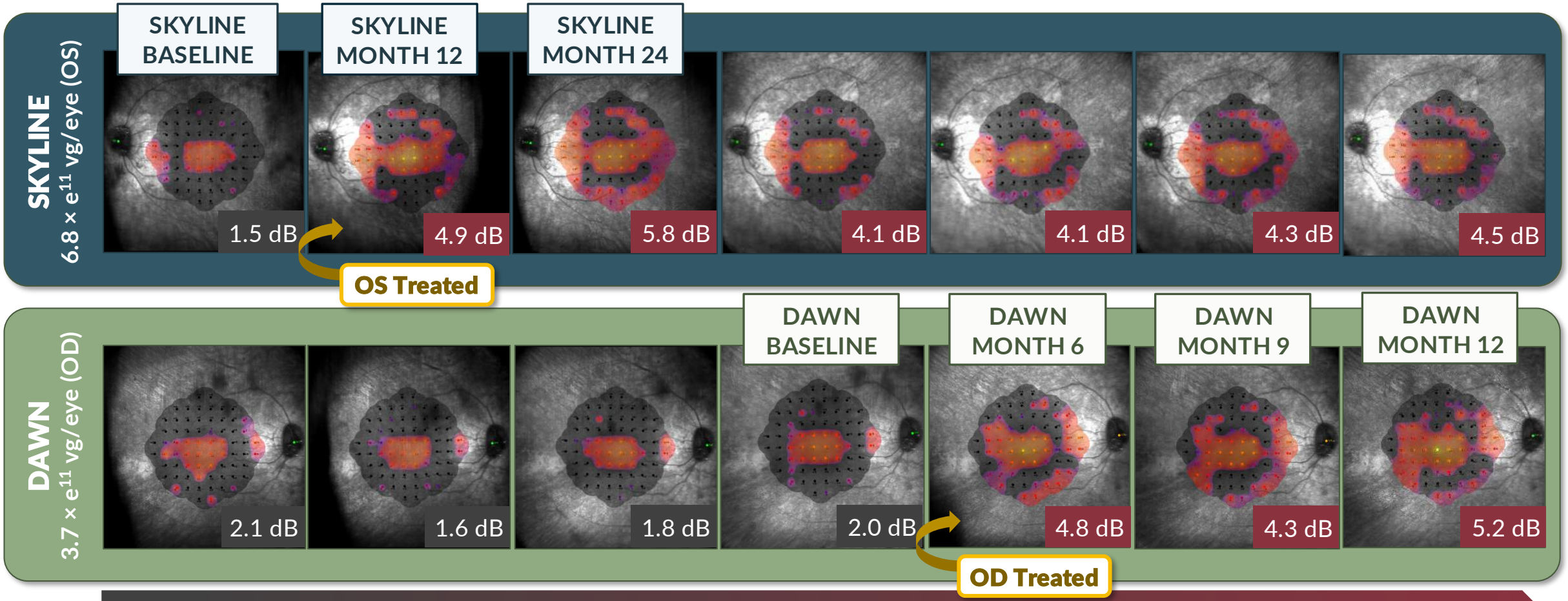
[a] Fellow eyes are eyes previously treated with a full-length AAV vector-based gene therapy targeting RPGR protein. **FE,** fellow eye; **HD,** high dose; **LD,** low dose; **SE,** study eye (newly treated).

Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Case Example: Microperimetry Response Over Time

Age	Laru-zova Dose		
36	SKYLINE	OS	$6.8 \times e^{11}$ vg/eye
	DAWN	OD	$3.7 \times e^{11}$ vg/eye

3+ years follow-up to date across 2 studies



Macular Integrity Assessment (MAIA) Color Scale (dB)

Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

Conclusions: Phase 2 DAWN Safety and Efficacy Update

- To date, subretinal laru-zova has been **generally well-tolerated** in the Phase 2 DAWN study
- Ocular TEAEs were mostly non-serious and mild to moderate in severity, with the majority **consistent with the surgical procedure and corticosteroid regimen**
- Data show promising **early and sustained improvements in LLVA**, a critical measure of visual function

DAWN safety and efficacy data to date support ongoing clinical development of laru-zova for the patients with XLRP caused by *RPGR* mutations

Pivotal VISTA study recently completed enrollment in June 2025, with results expected in second half of 2026

LLVA, low luminance visual acuity; **RPGR,** retinitis pigmentosa GTPase regulator; **TEAE,** treatment-emergent adverse event; **XLRP,** X-linked retinitis pigmentosa.
Based on March 27, 2026 data cutoff. DAWN ClinicalTrials.gov Identifier: NCT06275620.

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