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SUBRETINAL GENE THERAPY LARU-ZOVA FOR X-LINKED RETINITIS PIGMENTOSA (XLRP)

Pivotal Phase 2/3 VISTA Trial Design and Baseline Demographics

Ashley Simmons, PharmD; JungAh Jung, PhD; Daniel Chung, DO
Beacon Therapeutics, Cambridge, MA

X-linked retinitis pigmentosa (XLRP)

is an early-onset inherited retinal disease (IRD), characterized by the progressive loss of rod and cone photoreceptors[1-5]

There are no treatment options for XLRP

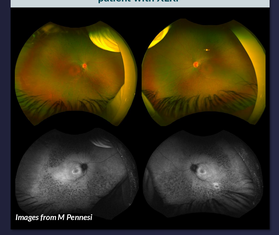
Primarily affecting males, symptoms begin in childhood and progress to central vision loss and legal blindness by median age of 45[3]

Early-Stage: Childhood
- Early changes in peripheral vision
- Night blindness
- Difficulties in low light environments

Mid-Stage: Ages 20–30 yrs
- No longer safe to drive
- Difficulty reading, completing chores, playing sports

Late-Stage: Ages 40–50 yrs
- Tunnel vision; progressive loss of visual acuity
- Loss of reading ability
- Increased difficulty navigating unfamiliar areas

Images from a 12-year old male patient with XLRP



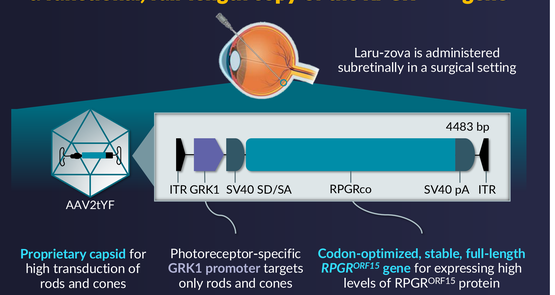
Images from M Pennesi

RPGR gene mutations underlie ≥70% of XLRP cases[2]

- *RGPR*-related XLRP is characterized by early peripheral rod degeneration, followed by later-onset cone dysfunction
- Loss of RPGR function likely disrupts protein transport, impairing phototransduction in the outer segment, ultimately resulting in photoreceptor dysfunction and death[6,7]

Laru-zova (laruparetigene zovaparvovec)

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



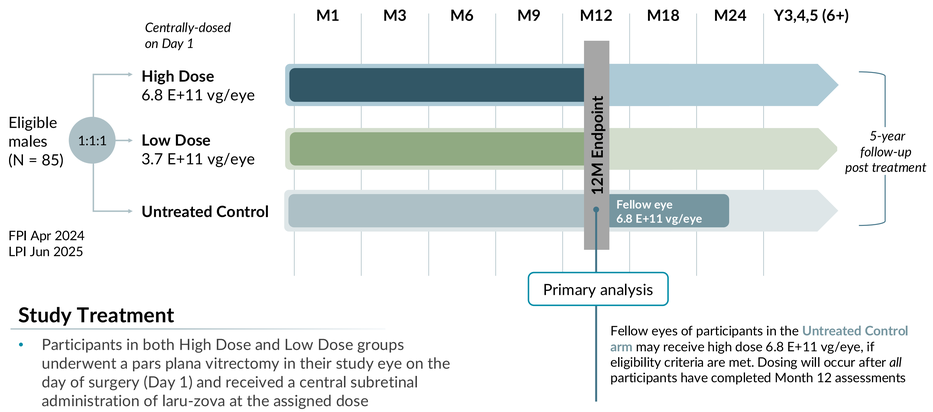
Proprietary capsid for high transduction of rods and cones

Photoreceptor-specific **GRK1 promoter** targets only rods and cones

Codon-optimized, stable, full-length *RPGR*^{ORF15} gene for expressing high levels of RPGR^{ORF15} protein

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

VISTA Study Design



Study Treatment

- Participants in both High Dose and Low Dose groups underwent a pars plana vitrectomy in their study eye on the day of surgery (Day 1) and received a central subretinal administration of laru-zova at the assigned dose
- All treated participants received a mandatory corticosteroid regimen during their peri-operative period

Fellow eyes of participants in the Untreated Control arm may receive high dose 6.8 E+11 vg/eye, if eligibility criteria are met. Dosing will occur after *all* participants have completed Month 12 assessments

Primary Outcome

Efficacy of two doses of laru-zova after a single subretinal administration compared with an untreated control as assessed by:
- Proportion of participants with a ≥15 letter increase from baseline in LLVA at Month 12 (US)
- Change from baseline in mean sensitivity across the whole grid, as measured by MAIA microperimetry, at Month 12 (Europe)

Safety Outcomes

Ocular and nonocular treatment-emergent adverse events, including relationship to laru-zova, surgical procedure, or peri-operative corticosteroid regimen, to assess safety and tolerability of laru-zova administered by subretinal injection

Secondary Outcomes

Efficacy as assessed by:
- BCVA (ETDRS), LLVA, LLD, MAIA microperimetry, FST, and EZ on SD-OCT
- Ora-VNC™ mobility course score, MObility Standardized Test-Virtual Reality (MOST-VR) mobility course score
- MRDQ Quality-of-life questionnaire

Participants & Baseline Characteristics

Key eligibility criteria

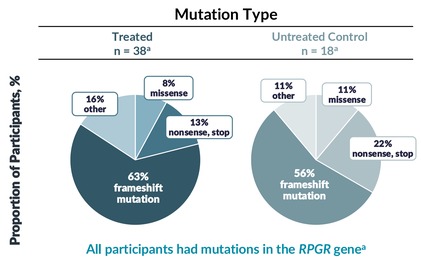
- Age 12–50 years, inclusive
- Male (XY chromosome)
- At least 1 documented pathogenic or likely pathogenic variant in the *RPGR* gene within exons 1–14 and/or *ORF15* from an appropriately certified or accredited laboratory
- Clinical diagnosis of XLRP

Study eye ocular criteria

- BCVA 34–78 ETDRS letters (approximate Snellen equivalent 20/200 to 20/32)
- 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 sub-foveal EZ line on SD-OCT

Baseline characteristics and demographics were well matched between treated and control groups

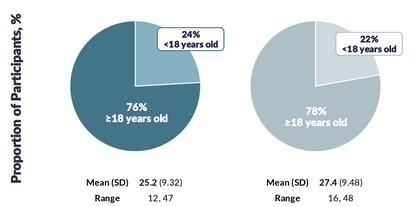
Mutation Type



All participants had mutations in the *RPGR* gene[a]

[a] *Mutation analysis available for 38/58 of treated group eyes and 18/27 of untreated control group eyes as of the November 12, 2025 data cut.*

Age



	Treated N = 58	Untreated Control N = 27
Mean (SD)	25.2 (9.32)	27.4 (9.48)
Range	12, 47	16, 48

Baseline characteristics, mean (SD) range	Treated N = 58 Study Eye	Treated N = 58 Fellow Eye	Untreated Control N = 27 Study Eye	Untreated Control N = 27 Fellow Eye
Vision, ETDRS letters				
BCVA	67.7 (7.48) 44–78	67.3 (11.46) 27–84	68.4 (6.39) 54–77	70.4 (7.64) 40–80
LLVA	47.9 (12.39) 0–64	49.1 (15.67) 1–73	48.9 (13.17) 1–63	52.3 (9.74) 28–67
LLD	20.1 (9.60) 8–67	18.1 (7.79) 3–41	19.7 (9.83) 6–55	18.0 (6.05) 7–37
MAIA mean sensitivity (whole grid),[b] dB	4.3 (2.64) 0.3–11.1	4.2 (2.73) 0.6–11.7	4.1 (2.85) −0.2–11.1	4.9 (3.56) 0.2–16.4

[b] *Microperimetry by MAIA; treated study eye/fellow eye, n=57; untreated study eye, n=26; untreated fellow eye, n=25.*

Demographics, % of participants	Treated N = 58	Untreated Control N = 27
Race		
American Indian or Alaska Native	1.7%	0
Asian	0	3.7%
Black or African American	5.2%	0
White	79.3%	88.9%
Not Reported	5.2%	0
Multiple	5.2%	0
Other	3.4%	7.4%
Ethnicity		
Hispanic or Latino	20.7%	18.5%
Not Hispanic or Latino	77.6%	74.1%
Unknown	1.7%	0
Not reported	0	7.4%

VISTA

is a pivotal phase 2/3 randomized, controlled, masked, multicenter clinical trial evaluating 2 dose levels of subretinal laru-zova in male participants with XLRP caused *RPGR* gene mutations

Learnings from a robust early-stage clinical trial program

HORIZON[8]
- Identified maximum tolerated dose of 6.8 E+11 vg/eye and central location for subretinal administration
- Established initial safety profile of laru-zova and surgical procedure

SKYLINE
- Reinforced target dose of 6.8 E+11 vg/eye
- Re-evaluated need for new target low dose for DAWN and VISTA

DAWN
- Process changes to drug manufacturing resulting in improved purity and product quality
- Established a robust surgical training program and a bespoke standardized delivery process
- Establishing safety of fellow-eye treatment in previously-treated participants
- Informed choice of LLVA response as the pivotal study endpoint (US)

HORIZON, SKYLINE, and DAWN efficacy and safety outcomes support a comprehensive laru-zova development program

Clinical Development Program

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

VISTA pivotal results expected H2 2026

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

For more information, please reach out to: medical@beacontx.com

References

1. Birch DG, et al. *Transl Vis Sci Technol*. 2023;12(6):5. **2.** Nguyen XT, et al. *Int J Mol Sci*. 2020;21(3):835. **3.** Chivers M, et al. *Clinicoecon Outcomes Res*. 2021;13:565-572. **4.** Branham K, et al. *Ophthalmic Genetics*. 2025;1-7. **5.** Prem Senthil M, et al. *Eye (Lond)*. 2017;31(5):741-748. **6.** Martinez-Fernandez de la Camara C, et al. *Expert Opin Emerg Drugs*. 2022;27(4):431-443. **7.** Pechnikova NA, et al. *J Clin Med*. 2025;14(3):898. **8.** Yang P, et al. *Am J Ophthalmol*. 2025;271:268-285.

Abbreviations

AAV2tYF, AAV2 capsid variant with three surface tyrosine residues changed to phenylalanine; **AE,** adverse event; **BCVA,** best-corrected visual acuity; **bp,** base pair; **dB,** decibel; **ETDRS,** Early Treatment Diabetic Retinopathy Study; **EZ,** ellipsoid zone; **FPI,** first patient in; **FST,** full-field stimulus threshold; **H,** half; **IRD,** inherited retinal disease; **ITR,** inverted terminal repeat; **LLD,** low luminance deficit; **LLVA,** low luminance visual acuity; **LPI,** last patient in; **M,** month; **MAIA,** macular integrity assessment; **MRDQ,** Michigan Retinal Degeneration Questionnaire; **ORF15,** open reading frame 15; **pA,** polyadenylation signal; **RPGR,** retinitis pigmentosa GTPase regulator; **RPGRco,** codon-optimized human RPGR complementary DNA; **SA,** splice acceptor, **SD,** splice donor; **SV40,** simian virus 40; **SD-OCT,** spectral domain optical coherence tomography; **vg,** vector genome; **VNC,** visual navigation challenge; **XLRP,** X-linked retinitis pigmentosa; **Y,** year.

Study Disclosures

Laru-zova is an investigational product; it has not been approved by the FDA.

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Author Disclosures

All authors are employees (E) of Beacon Therapeutics (USA), Inc.