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

Phase 1/2 HORIZON 5-Year Safety Results

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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

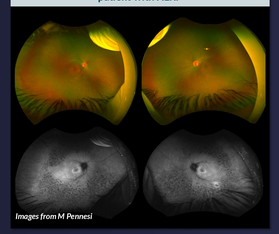
Primarily affecting males, symptoms begin in childhood and progress to central vision loss and legal blindness by median age of 45[3]

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



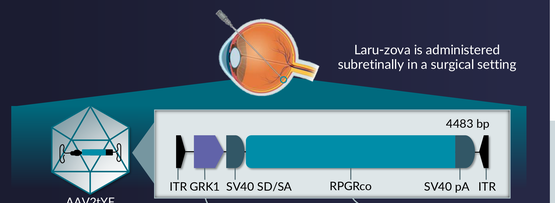
Images from M Pennesi

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

Year 5 Final Safety Results

HORIZON Followed Participants for 5 Years

- HORIZON enrolled a total of 29 participants, all of whom had mutations in the ***RPGR* gene, with 55% in the *ORF15* gene**
- Two participants in Group 4 were <18 years old; all other participants were ≥18 years of age
- At 36 months, laru-zova was generally well-tolerated, with mostly mild or moderate AEs that were associated with the subretinal injection procedure or concomitant medications, and resolved during the post-treatment convalescent period[8]
- 3 participants did not complete the Year 5 visit because they rolled over into the open-label, fellow eye dosing DAWN study. 1 participant voluntarily withdrew from the study before the Year 5 visit

Summary of Ocular AEs Reported in the Study Eye at Year 5

	Group 2 Centrally Dosed (N=2)	Group 4 Centrally Dosed (N=7)	Group 5 Centrally Dosed (N=7)	Group 6 Centrally Dosed (N=4)	All Centrally Dosed (N=21*)	All Peripherally Dosed (N=8)	All Participants (N=29)
At least 1 AE	2 (100%)	7 (100%)	7 (100%)	4 (100%)	21 (100%)	8 (100%)	29 (100%)
At least 1 SAE	1 (50%)	2 (29%)	0	0	4 (19%)	3 (38%)	7 (24%)
At least 1 ocular AE related[a] to							
Surgical procedure	2 (100%)	7 (100%)	7 (100%)	4 (100%)	21 (100%)	8 (100%)	29 (100%)
Laru-zova	1 (50%)	3 (43%)	4 (57%)	3 (75%)	12 (57%)	3 (38%)	15 (52%)

*Statistics presented: n (%) of participants. Multiple events of the same category in a participant are counted only once. *Including n=1 in Group 1.*
[a] Related AEs were scored as possibly, probably, or definitely related to surgical procedure or laru-zova.

- All participants experienced ≥1 ocular AE in the study eye, the majority were non-serious
- **No SUSARs or endophthalmitis** reported
- Overall, the safety profile was consistent between the primary 36-month analysis and the final 5-year analysis

25 of 29 participants completed the Year 5 follow up visit
No participants terminated the study early due to an AE

Ocular AEs deemed related to laru-zova were all non-serious, and mostly Grade 1–2 in severity

Grade ≥3 Ocular AEs Reported in the Study Eye at Year 5

MedDRA Preferred Term	Group 2 Centrally Dosed (N=2)	Group 4 Centrally Dosed (N=7)	Group 5 Centrally Dosed (N=7)	Group 6 Centrally Dosed (N=4)	All Centrally Dosed (N=21*)	All Peripherally Dosed (N=8)	All Participants (N=29)
Any Grade ≥3 Ocular AE	1 (50%)	2 (29%)	1 (14%)	1 (25%)	5 (24%)	4 (50%)	9 (31%)
Retinal detachment[a]	1 (50%)	0	0	0	1 (5%)	3 (38%)	4 (14%)
Glaucoma[a]	0	1 (14%)	1 (14%)	0	2 (10%)	0	2 (7%)
Cataract nuclear	0	0	0	0	0	1 (13%)	1 (3%)
Conjunctival hyperemia	0	1 (14%)	0	0	1 (5%)	0	1 (3%)
Lens disorder	0	1 (14%)	0	0	1 (5%)	0	1 (3%)
Retinal depigmentation[b]	0	0	0	1 (25%)	1 (5%)	0	1 (3%)
Visual acuity reduced[a]	0	1 (14%)	0	0	1 (5%)	0	1 (3%)

*Statistics presented: n (%) of participants. Multiple events of the same category in a participant are counted only once. *Including n=1 in Group 1. [a] Reported as SAE. [b] Reported as related to laru-zova, not associated with any visual sequelae. Group 6 dose not moving forward with clinical development.*

- In Group 6, one non-serious Grade 3 AE of retinal depigmentation related to laru-zova was reported, and **not associated with any visual sequelae**
- One new event of nuclear cataract was reported in a Group 2 peripherally-treated participant between Month 36 and Year 5

Grade ≥3 ocular AEs **related to surgical injection procedure** include retinal detachment, conjunctival hyperemia, nuclear cataract, retinal depigmentation, and reduced visual acuity

Ocular SAEs Reported in the Study Eye at Year 5

	MedDRA Preferred Term	Group 2 Centrally Dosed (N=2)	Group 4 Centrally Dosed (N=7)	Group 5 Centrally Dosed (N=7)	Group 6 Centrally Dosed (N=4)	All Centrally Dosed (N=21*)	All Peripherally Dosed (N=8)	All Participants (N=29)
Related to surgical procedure	Retinal detachment	1 (50%)	0	0	0	1 (5%)	3 (38%)	4 (14%)
	Cataract subcapsular	0	0	0	0	1 (5%)	0	1 (3%)
	Visual acuity reduced	0	1 (14%)	0	0	1 (5%)	0	1 (3%)
Related to concomitant medication	Glaucoma[a]	0	1 (14%)	0	0	1 (5%)	0	1 (3%)

*Statistics presented: n (%) of participants. Multiple events of the same category in a participant are counted only once. *Including n=1 in Group 1.*
[a] Increased intraocular pressure secondary to peri-operative corticosteroids.

- Seven ocular SAEs were reported in 7 participants
- SAEs of retinal detachment, cataract subcapsular, and reduced visual acuity were deemed related to the surgical injection procedure
- One SAE of glaucoma was deemed related to the peri-operative corticosteroids
- No new ocular SAEs were reported between Month 36 and Year 5

All ocular SAEs were deemed related to surgical injection procedure or prophylactic corticosteroid regimen

Subretinal laru-zova was well tolerated, with AEs consistent with subretinal injections and corticosteroid treatment

Learnings from HORIZON Phase 1/2 Trial Informed Future Trial Designs

Maximum Tolerated Dose

- Although evidence of effect through Month 36 was observed in Group 6, findings suggest an increased incidence of retinal pigmentary changes. Based on the overall benefit–risk assessment, **Group 5 was selected as the MTD**

Peripheral Versus Central Dosing

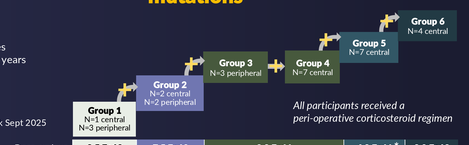
- Peripheral dosing was complicated by risk of retinal detachment
- **Greater potential for therapeutic benefit with central dosing**

Established Initial Safety Profile of Laru-zova and the Surgical Procedure

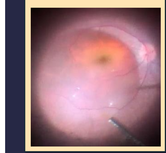
- Cumulative 5-year follow-up results show laru-zova was **generally well-tolerated** when administered once via subretinal injection

HORIZON

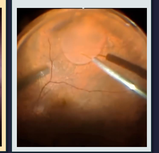
is a first in human, phase 1/2, open-label, dose-escalation study evaluating safety of subretinal laru-zova in males with XLRP caused by *RPGR* gene mutations



Example of Central Dosed Bleb



Example of Peripheral Dosed Bleb



Primary Outcome

Number and proportion of participants experiencing Grade ≥3 ocular or systemic AEs within 36 months

Secondary Outcomes

Change from baseline in:
- Microperimetry, BCVA (ETDRS), FST, OCT
- Static perimetry (light and dark adapted)
- QoL questionnaires

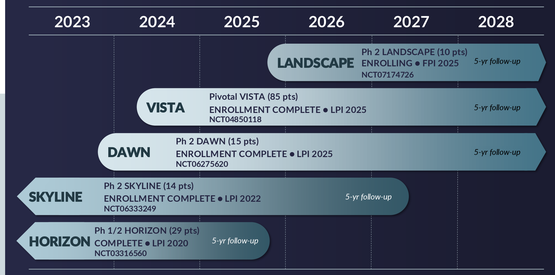
HORIZON Safety Results Summary

Laru-zova was generally safe and well-tolerated

- No SUSARs or endophthalmitis were reported, and majority of AEs were non-serious at Month 36 and was similar through Year 5
- All ocular SAEs were deemed related to surgical injection procedure or prophylactic corticosteroid regimen

Clinical Development Program

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



HORIZON results support continued development of laru-zova; 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. *Clinicoocon 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.** Beacon Therapeutics (USA), Inc. AGTC-RPGR-001 (HORIZON) Clinical Study Report. 2026.

Abbreviations

AAV2tYF, AAV2 capsid variant with three surface tyrosine residues changed to phenylalanine; **AE,** adverse event; **BCVA,** best-corrected visual acuity; **bp,** base pair; **DSMC,** Data and Safety Monitoring Committee; **ETDRS,** Early Treatment Diabetic Retinopathy Study; **FPI,** first patient in; **FST,** full-field stimulus threshold; **GRK1,** G protein-coupled receptor kinase 1; **H,** half; **IRD,** inherited retinal disease; **ITR,** inverted terminal repeat; **LPI,** last patient in; **MTD,** maximum tolerated dose; **OCT,** optical coherence tomography; **pA,** polyadenylation signal; **QoL,** quality of life; **RPGR^{ORF15},** retinitis pigmentosa GTPase regulator (open reading frame 15); **RPGRco,** codon-optimized human RPGR complementary DNA; **SA,** splice acceptor; **SD,** splice donor; **SV40,** simian virus 40; **SAE,** serious adverse event; **SUSAR,** suspected unexpected serious adverse reactions; **XLRP,** X-linked retinitis pigmentosa; **yrs,** years.

Study Disclosures

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 (USA), Inc. was the sponsor of the study and provided funding for third-party writing support by Nancy Nguyen, PharmD, of Koahana, Inc.

Author Disclosures

PY: 4D Molecular Therapeutics (F), AAVantgarde Bio (C), Adverum (C), Astellas (C), Ascidian Therapeutics (F), Atsena (F), Beacon Therapeutics (USA), Inc. (C,F), Biogen (F), BlueRock Therapeutics (C), Editas (F), Endogena (C), Foundation Fighting Blindness (C, F), Janssen (C), Kalaris (C), Lexitas (C), MeiraGTx (C), Nanoscope Therapeutics (C), Ocugen (F), PYC (F), Sanofi (F), Sepul Bio (F), Sparing Vision (F), Spark (F), SpliceBio (F), TeamedOn (C); **DB:** Nacuity (C), Beacon Therapeutics (USA), Inc. (C), 4D Molecular Therapeutics (C); **RA:** Beacon Therapeutics (USA), Inc. (C); **RAS:** Ascidian (C); Beacon Therapeutics (USA), Inc. (C), RegenxBio (C); **AL:** Beacon Therapeutics (USA), Inc. (C, F); SparingVision (C,F); SpliceBio (C, F); TeamedOn (C); **DC:** Beacon Therapeutics (USA), Inc. (E)