Key Opinion Leader Event

Phase 1/2 6-month Safety and Efficacy Data of OPGx-LCA5, an Adeno-Associated Virus (AAV)-Based Gene Therapy

December 11, 2024

Braydon,
RDH12 patient

Introductions and Agenda

Ash Jayagopal, PhD, MBA
Chief Scientific and Development Officer, Opus Genetics

Disclosures and Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements concerning expectations regarding our cash runway, data from and future enrollment for our clinical trials, our pipeline of additional indications, expectations of potential growth, and our expectations regarding our recent acquisition of former Opus Genetics Inc. These forward-looking statements relate to us, our business prospects and our results of operations and are subject to certain risks and uncertainties posed by many factors and events that could cause our actual business, prospects and results of operations to differ materially from those anticipated by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those described under the heading "Risk Factors" included in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 filed with the U.S. Securities and Exchange Commission (the "SEC") and in our other filings with the SEC. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this presentation. In some cases, you can identify forward-looking statements by the following words: "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "ongoing," "plan," "potential," "predict," "project," "should," "will," "would," or the negative of these terms, or other comparable terminology, although not all forward-looking statements contain these words. We undertake no obligation to revise any forward-looking statements in order to reflect events or circumstances that might subsequently arise. These forward-looking statements are based upon our current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: our ability to successfully integrate the business of former Opus Genetics Inc. and manage our expanded combined product pipeline; our ability to develop and obtain regulatory approval for newly acquired gene therapies to treat inherited retinal diseases; our ability to obtain and maintain orphan drug designation or rare pediatric disease designation for our current and future product candidates; the success and timing of regulatory submissions and pre-clinical and clinical trials, including enrollment and data readouts; regulatory requirements or developments; changes to or unanticipated events in connection with clinical trial designs and regulatory pathways; delays or difficulties in the enrollment of patients in clinical trials; substantial competition; rapid technological change; our development of sales and marketing infrastructure; future revenue losses and profitability; changes in capital resource requirements; risks related to our inability to obtain sufficient additional capital to continue to advance our product candidates and preclinical programs; domestic and worldwide legislative, regulatory, political and economic developments; our dependency on key personnel; changes in market opportunities and acceptance; reliance on third parties to conduct our clinical trials and supply and manufacture drug supplies; future potential product liability and securities litigation; system failures, unplanned events, or cyber incidents; the substantial number of shares subject to potential issuance associated with our share purchase facility; risks that our licensing or partnership arrangements may not facilitate the commercialization or market acceptance of our product candidates; future fluctuations in the market price of our common stock; the success and timing of commercialization of any of our product candidates; obtaining and maintaining our intellectual property rights; and the success of mergers and acquisitions.

The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive. Readers are urged to carefully review and consider the various disclosures made by us in this presentation and in our reports filed with the SEC that advise interested parties of the risks and factors that may affect our business. All forward-looking statements contained in this presentation speak only as of the date on which they were made. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Today's Agenda

	Topic	Speaker
1	Welcome, Introductions, and Opus Genetics Updates	Ash Jayagopal, PhD, MBA
2	Overview of *LCA5*-IRD and Multi-Luminance orientation and Mobility Test	Jean Bennett, MD, PhD
3	6 Month Results of Phase 1/2 Study of OPGx-LCA5	Tomas S. Aleman, MD
4	Panel Discussion and Q&A	**Moderator:** Arshad M. Khanani, MD, MA, FACS **Panelists:** Christine Kay, MD; Jean Bennett, MD, PhD; Tomas S. Aleman, MD; Ash Jayagopal, PhD, MBA

LCA5, Leber congenital amaurosis 5; IRD, inherited retinal disease.

Meet Our Speakers

Ash Jayagopal, PhD, MBA
Chief Scientific & Development Officer,
Opus Genetics

Jean Bennett, MD, PhD
F.M. Kirby Emeritus Professor of
Ophthalmology, University of Pennsylvania

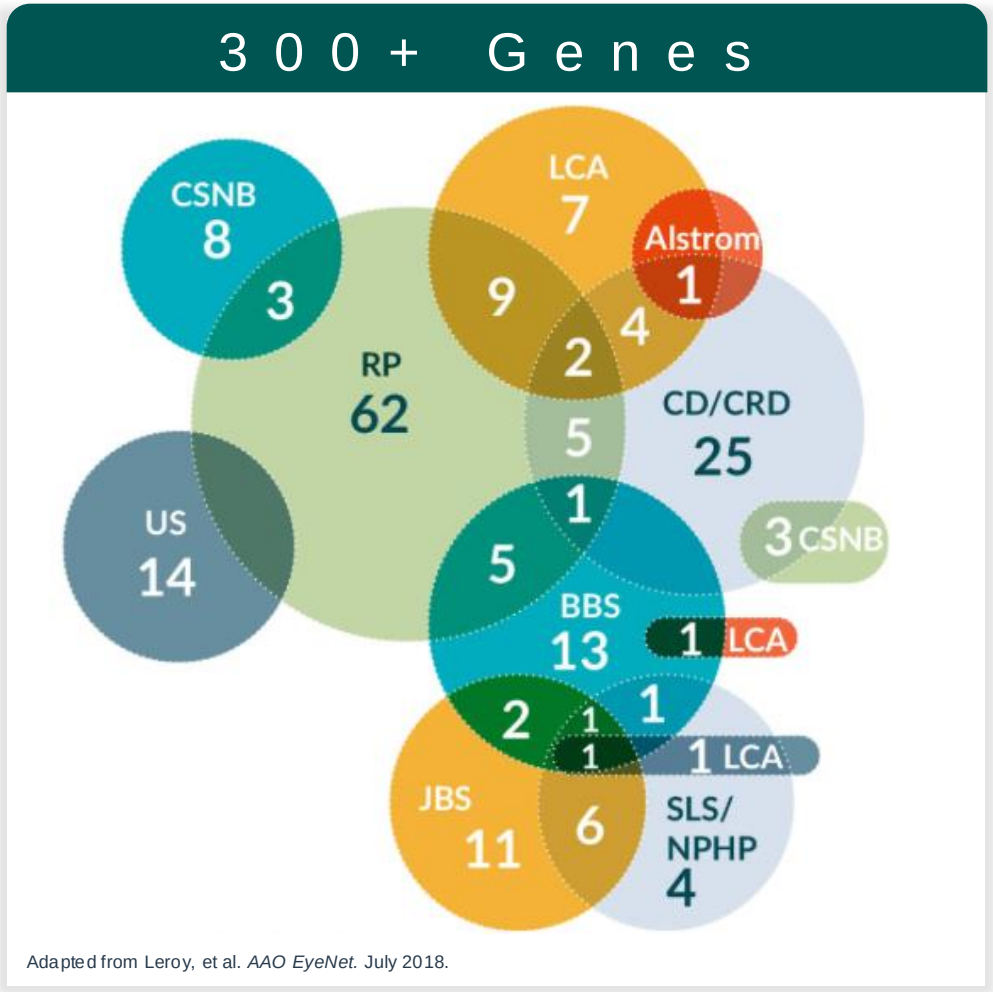
Tomas S. Aleman, MD
Irene Heinz-Given and John LaPorte Research
Professor, University of Pennsylvania

Arshad M. Khanani, MD, MA, FASRS
Managing Partner, Sierra Eye Associates
Clinical Professor, University of Nevada

Christine Kay, MD
Vitreo Retinal Associates
Affiliate Assistant Professor, University of South
Florida

Limited Treatment Options Despite Key Advances in Gene Therapy

- Over 300 genes are known to cause inherited retinal diseases (IRDs), which severely affect vision in more than 180,000 people in the United States*[1,2]
- Almost all IRDs lack treatment to halt progression and rescue vision[2]
- Luxturna® is the only FDA-approved IRD gene therapy and targets the *RPE65* gene mutation[2]



Adapted from Leroy, et al. *AAO EyeNet.* July 2018.

*Based on 2019 estimates
Luxturna® is a registered trademark of Spark Therapeutics, Inc.
FDA, Food and Drug Administration; IRD, inherited retinal disease; RPE65, retinal pigment epithelium 65 kDa protein.

1. RetNet Retinal Information Network. 2024. Accessed on November 25, 2024. https://retnet.org/summaries#a-genes
2. Gong J, et al. *Clin Ophthalmol.* 2021;15:2855-2866.

There are Multiple Barriers to the Clinical Translation of IRD Gene Therapies

Small addressable market: Cost/benefit justification is challenging for low prevalence IRDs

Small patient population poses challenges for patient recruitment

Manufacturing geared to high volume production, not IRD gene therapies

Clinical, scientific, and regulatory excellence is required to have success in treating IRDs

IRD, inherited retinal disease.

The Opus Approach Overcomes These Challenges

Building a robust IRD-focused gene therapy pipeline

- Multiple assets for unaddressed IRDs to balance risk across programs
- Favorable competitive landscape

Partnering with patient networks and advocacy organizations

- Significant relationships with key patient advocacy groups
- Strategic partnerships to access global IRD patient registries and natural history studies

Focusing on small-scale, high-quality production

- Favorable COGS with high-quality gene therapy vectors
- Dedicated production lines tailored for IRDs (100s to 10,000s of patients)

Establishing strong partnerships and leveraging synergies between programs enables:

- Natural history and interventional trials at IRD centers of excellence with high-resolution readouts of safety and efficacy
- Harmonization across programs to streamline manufacturing and regulatory processes
- Development of shared biomarkers/endpoints across multiple IRD indications

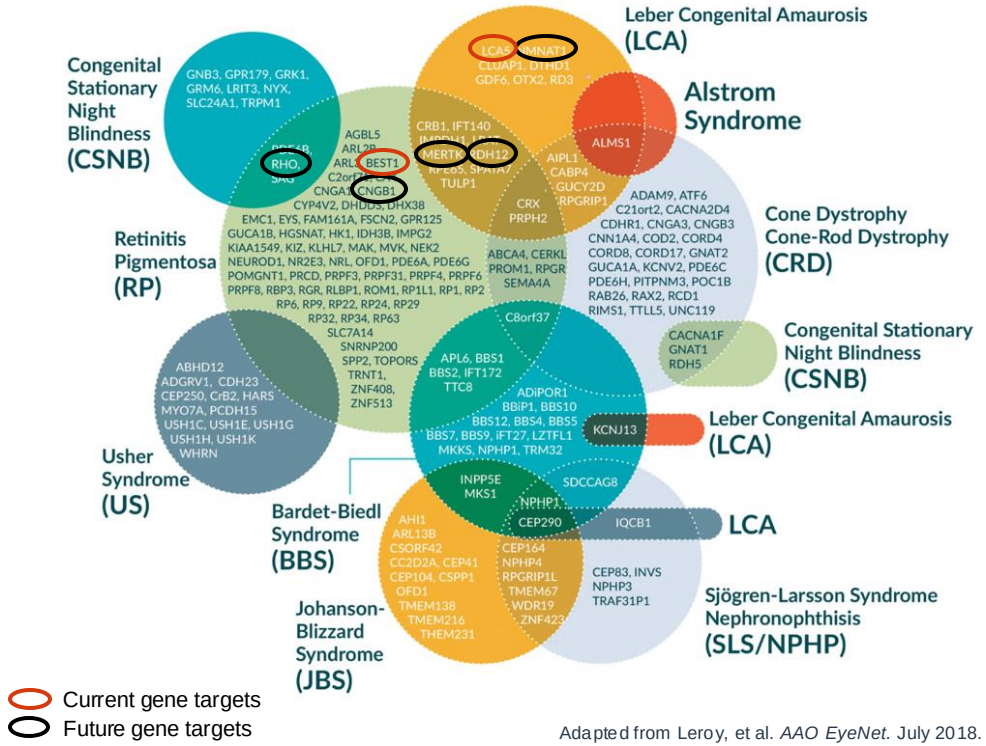
COGS, cost of goods sold; IRD, inherited retinal disease.

One of the Largest Dedicated IRD Portfolios and an Established Blueprint for Development

Our Foundational Roadmap

- Clinically derisked AAV technology
- Rigorous prioritization of two clinical-stage gene therapies
- Strategic optionality to advance new candidates into development in additional IRD indications

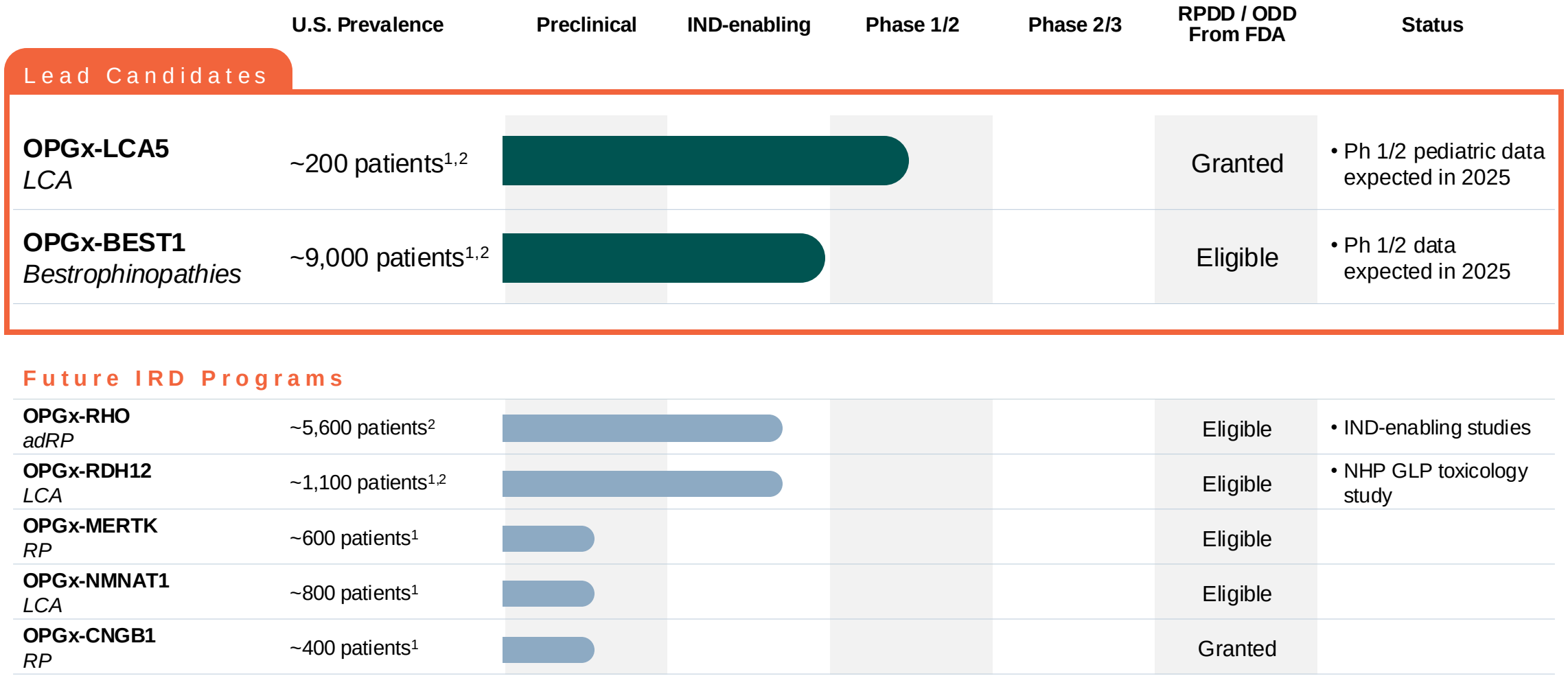
Gene targets selected based on clinical derisking and commercial value



Adapted from Leroy, et al. *AAO EyeNet.* July 2018.

AAV, adeno-associated virus; IRD, inherited retinal disease.

Efficient IRD Pipeline with Multiple Near-Term Value Inflection Points Anticipated



adRP, autosomal dominant retinitis pigmentosa; BEST1, bestrophin 1; CNGB1, cyclic nucleotide-gated channel β1; FDA, Food and Drug Administration; GLP, Good Laboratory Practice; IND, Investigational New Drug; IRD, inherited retinal disease; LCA, Leber congenital amaurosis; MERTK, MER proto-oncogene tyrosine kinase; NHP, nonhuman primate; NMNAT1, nicotinamide mononucleotide adenylyltransferase 1; ODD, Orphan Drug Designation; RDH12, retinol dehydrogenase 12; RHO, rhodopsin; RP, retinitis pigmentosa; RPDD, Rare Pediatric Disease Designation.

1. Stone et al. *Ophthalmology.* 2017;124:1314-1331. **2.** Triangle Insights Group market research (compilation of prevalence studies), conducted August 2023.

Overview of *LCA5*-LCA and Multi-Luminance orientation and Mobility Test (MLoMT)

Jean Bennett, MD, PhD
F.M. Kirby Emeritus Professor of Ophthalmology
University of Pennsylvania

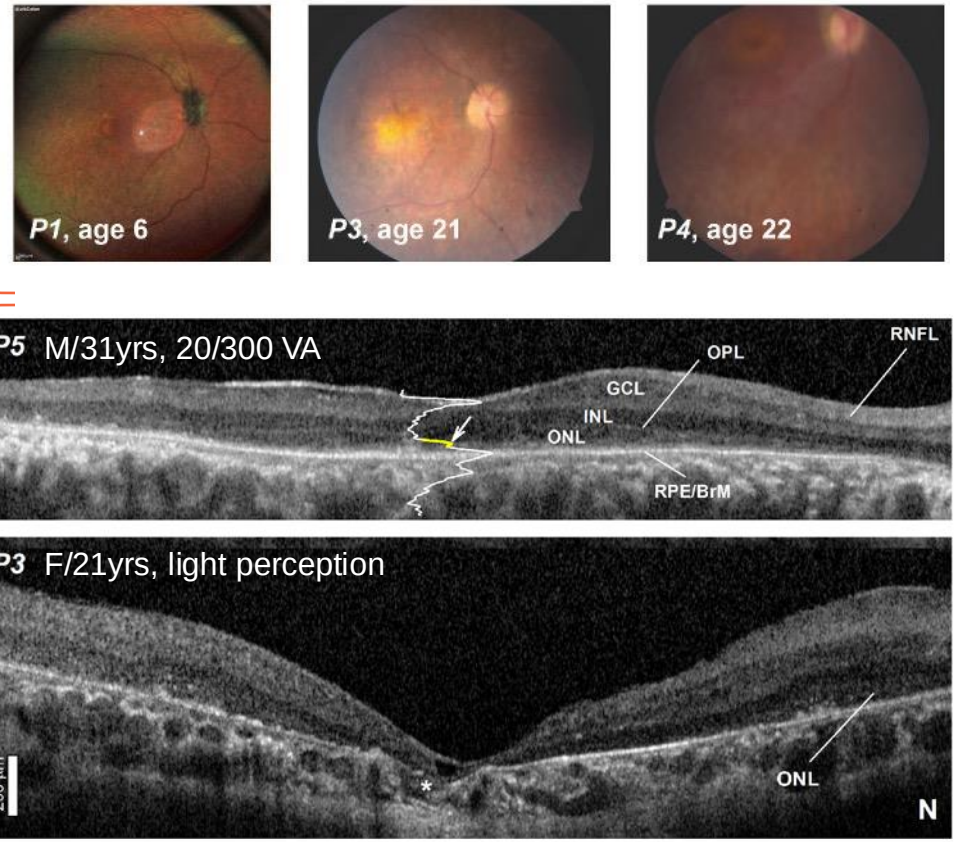
LCA, Leber congenital amaurosis; LCA5, Leber congenital amaurosis 5.

LCA5 is an Early-Onset, Severe Hereditary Retinal Degeneration

- Presentation in 1st year of life with nystagmus and vision loss[1,2]
- Severe and early photoreceptor loss results in severely abnormal or non-detectable visual fields[1,2]
- Visual acuity often limited to hand motions or light perception[1,2]
- Fundus photography exhibits pigmentary retinopathy with areas of RPE and photoreceptors[1]
- OCT demonstrates spared photoreceptors (ONL) and inner/outer segments (*P5*), even at a severe disease stage (*P3*)[1]

Structure-function disassociation creates favorable pathobiology for AAV gene replacement

LCA5 patients exhibit preserved photoreceptors in the central retina in adulthood despite disease severity and early onset

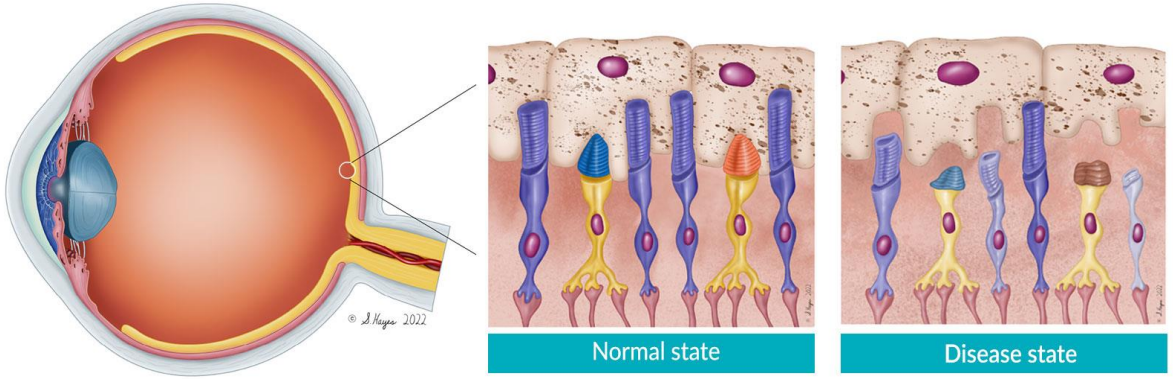


AAV, adeno-associated virus; LCA5, Leber congenital amaurosis 5; OCT, optical coherence tomography; ONL, outer nerve layer; RPE, retinal pigment epithelium; VA, visual acuity.

1. Uyhazi KE, et al. *Invest Ophthalmol Vis Sci.* 2020;61:30. **2.** Boldt K, et al. *J Clin Invest.* 2011;121(6):2169-2180.

OPGx-LCA5 Restores Structure and Function in Photoreceptors

- Lebercilin is a ciliary protein critical for the function of photoreceptor inner and outer segments[1]
- In *LCA5*-LCA patients, photoreceptor function is severely impaired due to a lack of functioning lebercilin[1]
  - However, photoreceptors can survive through the third decade of life, suggestive of a broad window for therapeutic intervention[2]



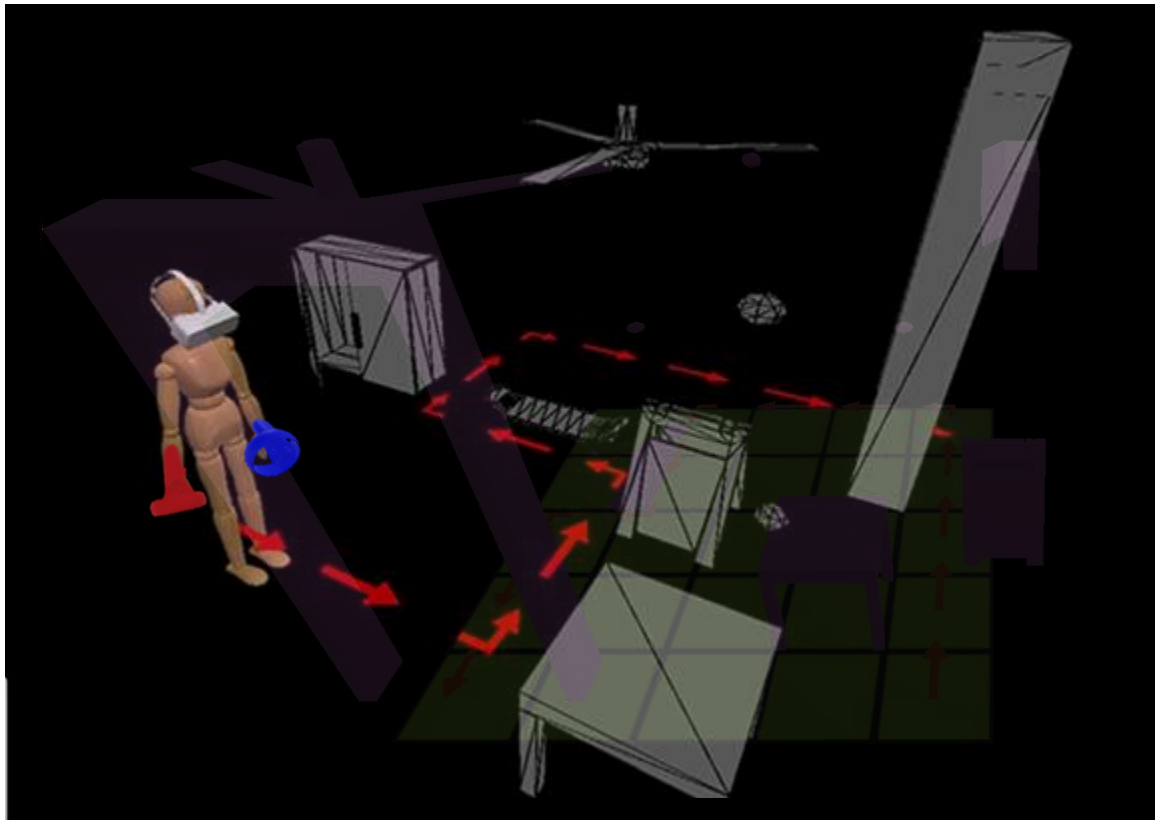
- **OPGx-LCA5 is designed to address mutations in the *LCA5* gene, which encodes for the lebercilin protein**
  - Clinically derisked AAV8 vector delivers a functional *LCA5* gene directly to photoreceptor cells
  - Same promoter technology as Luxturna
  - Validated surgical delivery method via subretinal injection

AAV, adeno-associated virus; LCA, Leber congenital amaurosis; LCA5, Leber congenital amaurosis 5.

1. Uyhazi KE, et al. *Invest Ophthalmol Vis Sci*. 2020;61:30. **2.** Song JY, et al. *Mol Ther.* 2018;26:1581-1593.

Easing the Answer to a Regulatory Need: Functional Vision Assessment with a Multi-Luminance orientation and Mobility Test (MLoMT)

- MLoMT utilizes a **readily available VR headset** with body trackers to navigate a virtual course
- Household objects are presented at increasing illumination while the subject follows a path of red arrows
- Subject identifies and “touches” obstacles while following the path
- Establishes a "threshold" of functional vision that may be used to assess impact of disease and treatments
- Enormous amount of data automatically collected
- Relates well with clinical readouts (visual acuity, visual fields, and visual sensitivity)

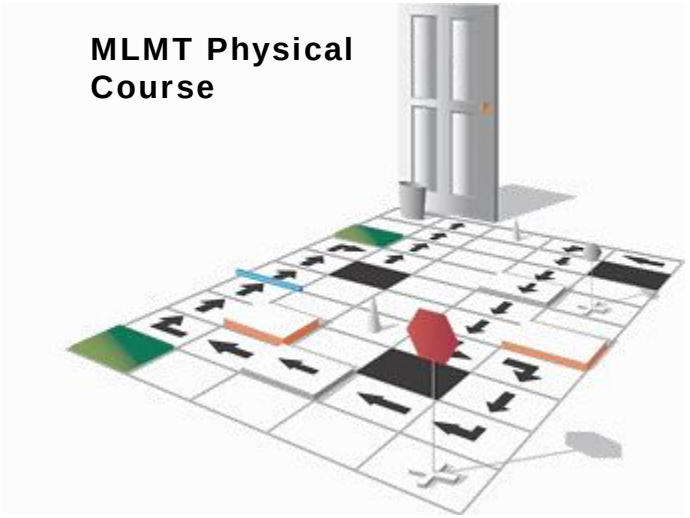


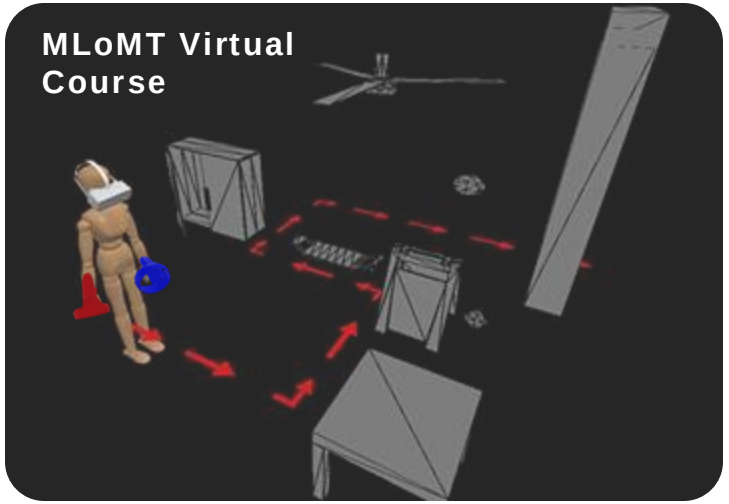
VR, virtual reality.

Bennett J, et al. *Transl Vis Sci Technol.* 2023;12:28.

MLoMT Builds Upon the Success of MLMT®

- Allows automatic randomization of dozens of configurations
- Extends operating range (>3 log units)
- Can be tailored to different diseases by altering variables (light intensities, wavelength, contrast, color, motion, etc.)
- Delivers test in a relatively short time (20 mins)
- Equipment/space affordable
- Easy to deploy and duplicate at multiple sites
- No physical obstacles that could cause harm in a collision
- Can test one eye at a time or both eyes
- Can adjust to subject's height
- Attractive to digital-savvy pediatric population
- Quantitative information (timing, direction of gaze, acceleration, deceleration, collisions) captured automatically as digital data
- Data obtained instantaneously and analyzed objectively (no need for reading center)
- No personal identifiers





MLMT® and Multi-Luminance Mobility Test® are registered trademarks of Spark Therapeutics, Inc.
MLoMT, Multi-luminance orientation and Mobility Test; MLMT, Multi-Luminance Mobility Test.

1. Bennett J, et al. *Transl Vis Sci Technol.* 2023;12:28; **2.** Aleman et al. *Clin Ophthalmol.* 2021;15:939

6 Month Results of Phase 1/2 Study of OPGx-LCA5

Tomas S. Aleman, MD
Irene Heinz-Given and John LaPorte Professor
Scheie Eye Institute, University of Pennsylvania

OPGx-LCA5-1001 Study to Treat a Severe Photoreceptor Disease

Design

- Phase 1b/2a, open-label of uniocular subretinal injection of OPGx-LCA5
- Nonrandomized, single ascending, dose escalation (**1E10 vg/eye**, 3E10 vg/eye, and 1E11 vg/eye) unilaterally injected
- Minimum of 3 evaluable patients are treated at each dose level
- Preliminary results to Day 180 in three patients

LCA5, Leber congenital amaurosis 5.

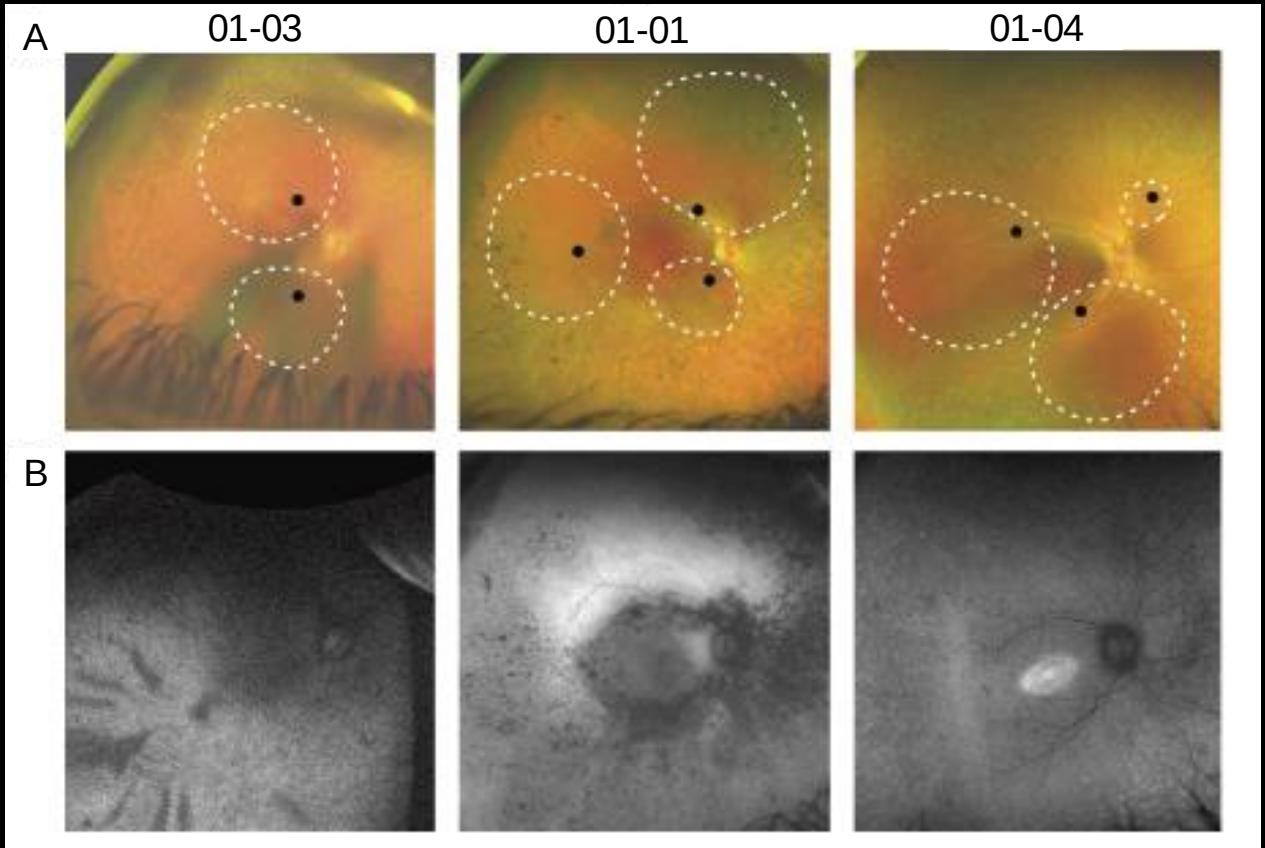
Characteristics of Patients

Study ID	Age*/ Gender	Date IP Administration	Study Eye	LCA5 Variants† Allele 1/Allele 2	Visual Acuity‡		Refraction§		Foveal Thickness [µm]			
									BL		3MO	
					OD	OS	OD	OS	OD	OS	OD	OS
0103	26/M	07Aug2023	OS	Gln279*/Gln279*	HM	HM	+3.00	+3.00	121	NA	136	133.5
0101	34/F	11Sep2023	OS	Arg255Gln/del. Exon 1	20/300	20/400	-1.50	-2.50	123.5	127.1	127.1	119.3
0104	19/F	13Nov2023	OD	Arg255*/Arg255*	20/200	20/200	+2.25	+2.00	232.2	226.5	170.8	205.1

- Null or non-functional proteins
- Poor VA
- Severe photoreceptor loss (thin retinas/foveas)

BL, baseline; HM, hand motion; IP, investigational product; LCA5, Leber congenital amaurosis 5; OD, right eye; OS, left eye;VA, visual acuity.

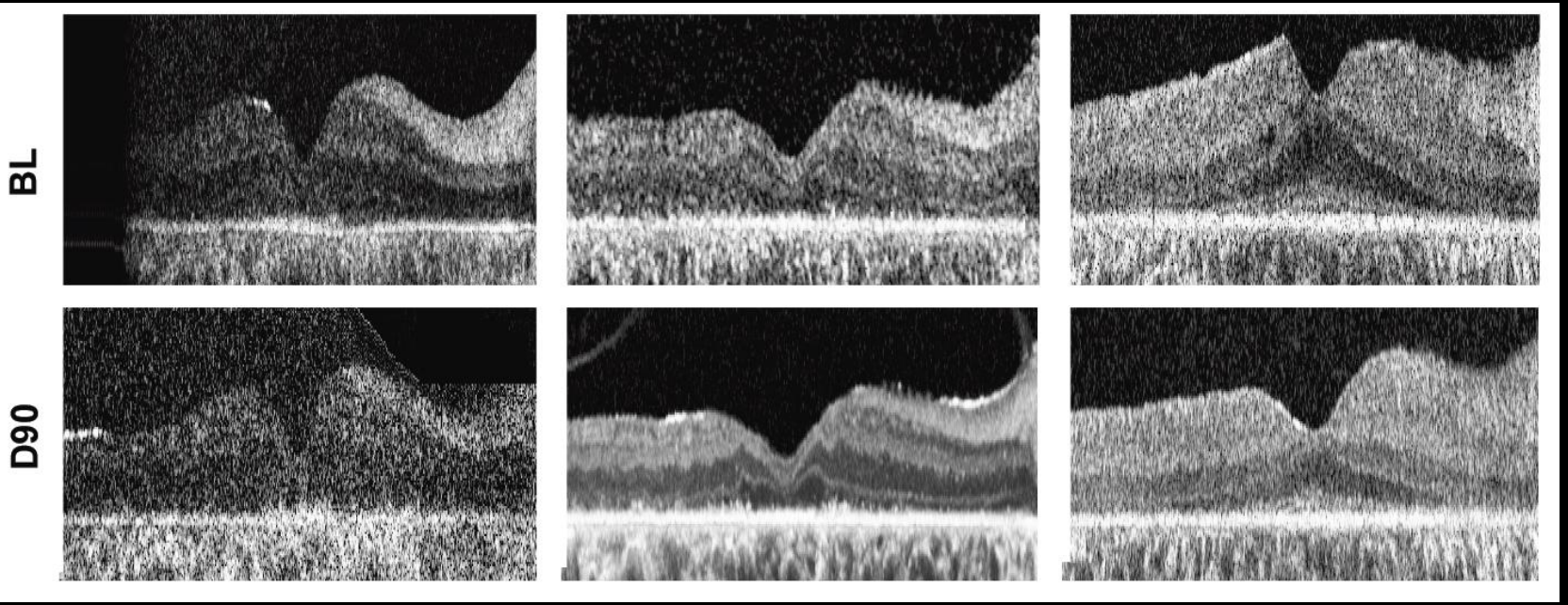
Uneventful Subretinal Injections



- 300 µl volume
- Multiple SR injections extending near the fovea

SR, subretinal.

Safety: Central Retinal Structure



- Retina reattached
- No major changes post-treatment

BL, baseline.

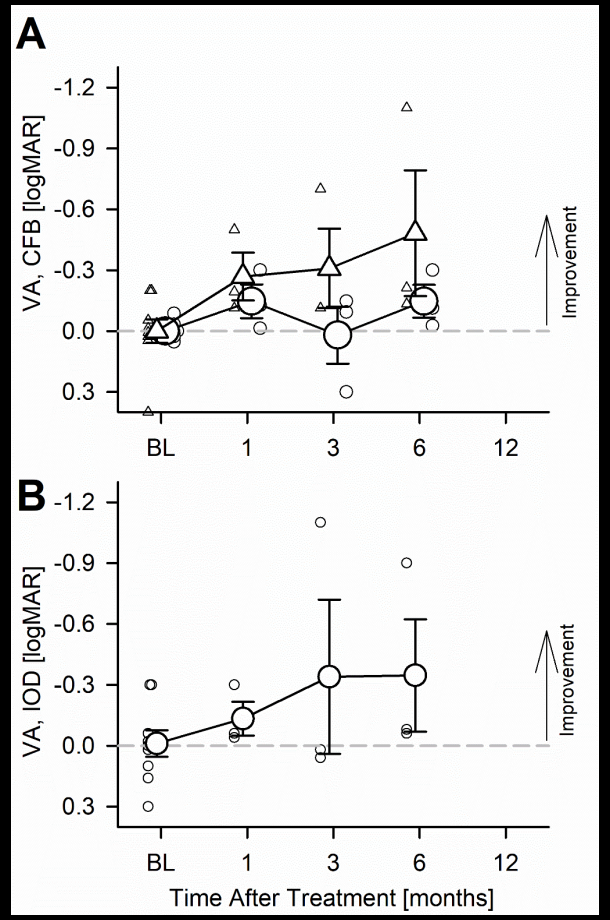
Safety and Tolerability

Subject	Date of onset	Date of Resolution	Diagnosis (if known) or Sign/ Symptoms (list one per AE)	Ocular AE?	Specify eye(s)	Severity	Unexpected	Serious	Frequency	Outcome	Relationship to Investigational Product	Action taken (Add all that apply):
0101	11-SEP-2023	12-SEP-2023	Eye Pain	Yes	Study	Grade 1 - Mild	No	No	Intermittent	Recovered/ Resolved	Unrelated	2 = Con Med (enter on Con Meds Page)
0101	18-SEP-2023	18-SEP-2023	Corneal Abrasion	Yes	Study	Grade 1 - Mild	No	No	Single Episode	Recovered/ Resolved	Unrelated	2 = Con Med (enter on Con Meds Page) 3 = Other
0103	07-AUG-2023	08-AUG-2023	Eye Pain	Yes	Study	Grade 1 - Mild	No	No	Intermittent	Recovered/ Resolved	Unrelated	2 = Con Med (enter on Con Meds Page)
0104	08-AUG-2023	14-NOV-2023	Eye Pain	Yes		Grade 1 - Mild	No	No	Continuous	Recovered/ Resolved	Unrelated	2 = Con Med (enter on Con Meds Page)

- No dose limiting toxicities
- AEs were anticipated, mild, and not related to OPGx-LCA5
- All resolved

AE, adverse event; LCA5, Leber congenital amaurosis.

Visual Acuity Gains

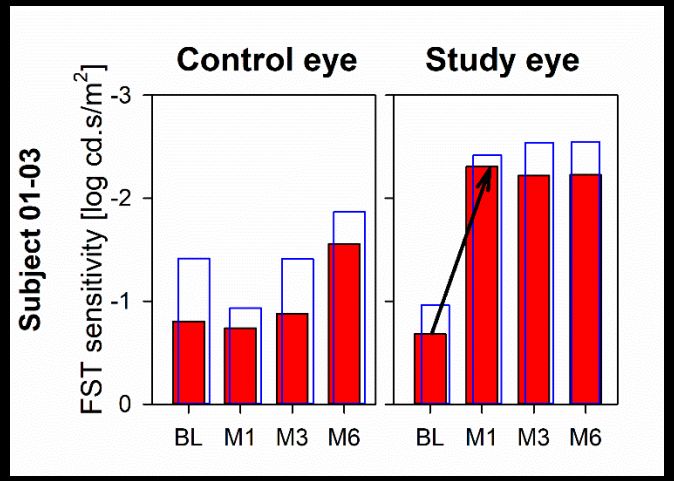


- Formed vision possible for the first time in most affected
- On average, better VAs in treated compared to baseline (BL) and untreated eye

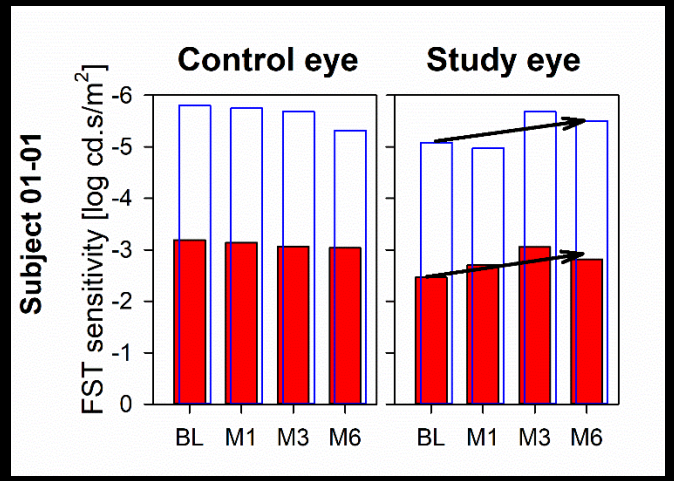
22 VA, visual acuity.

Large Sensitivity Gains
Full-field Stimulus Testing

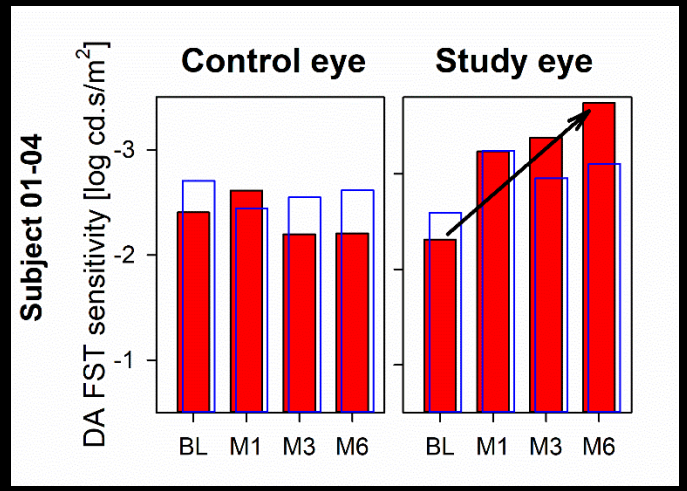
01-03



01-01



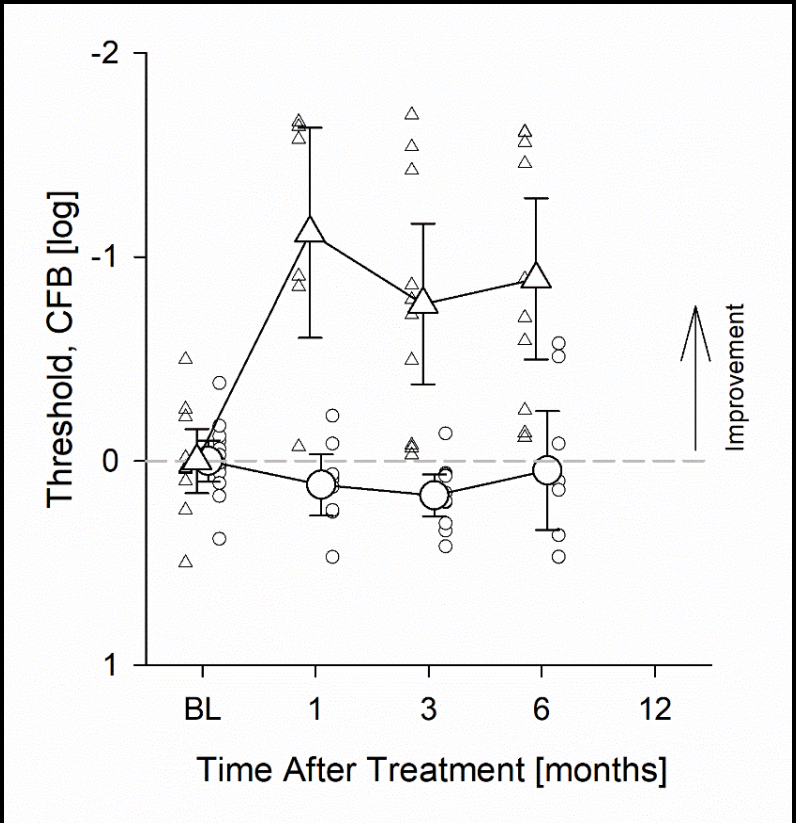
01-04

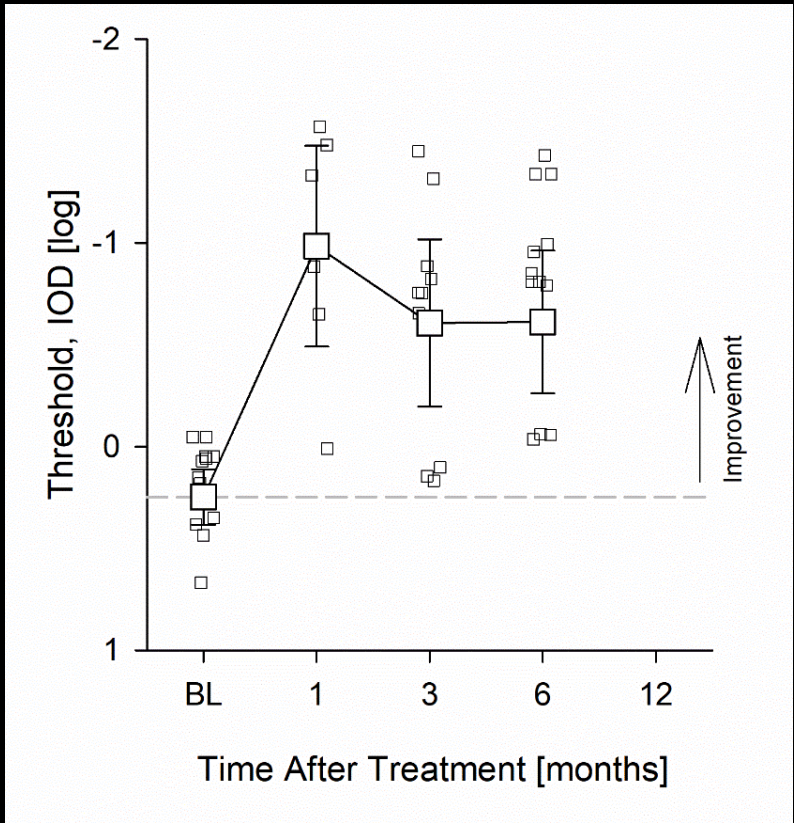


LARGE GAINS IN SENSITIVITIES

- Significant gain (>1.5 log u) in sensitivity compared to contralateral control eye and baseline (BL)
- Results similar for both red (red bars) and blue (blue outlined bars) stimuli in 01-03 and 01-04
- Mechanistically plausible = restoration of function of the cilia

Gains are Mediated by Cones

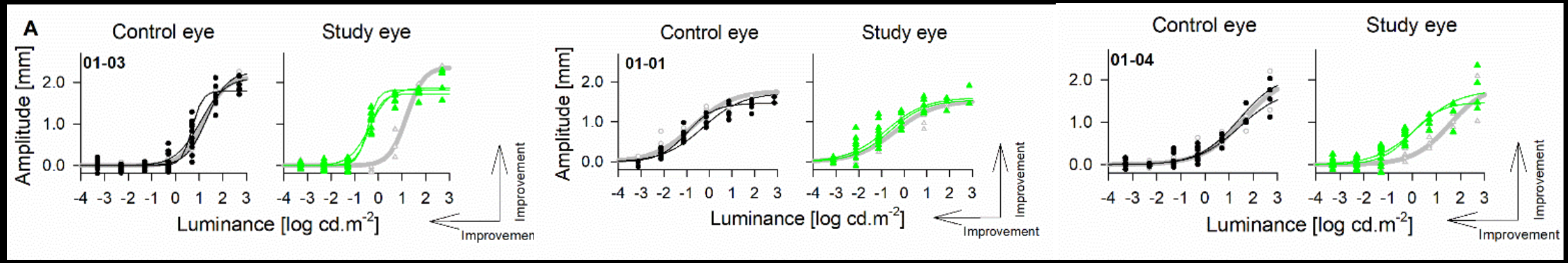




- Gains in cone-mediated sensitivity (light adapted in 01-01) in all three patients compared to baseline (BL) and contralateral control eye

Pupillometry Objectively Confirms Efficacy

01-03 **01-01** **01-04**

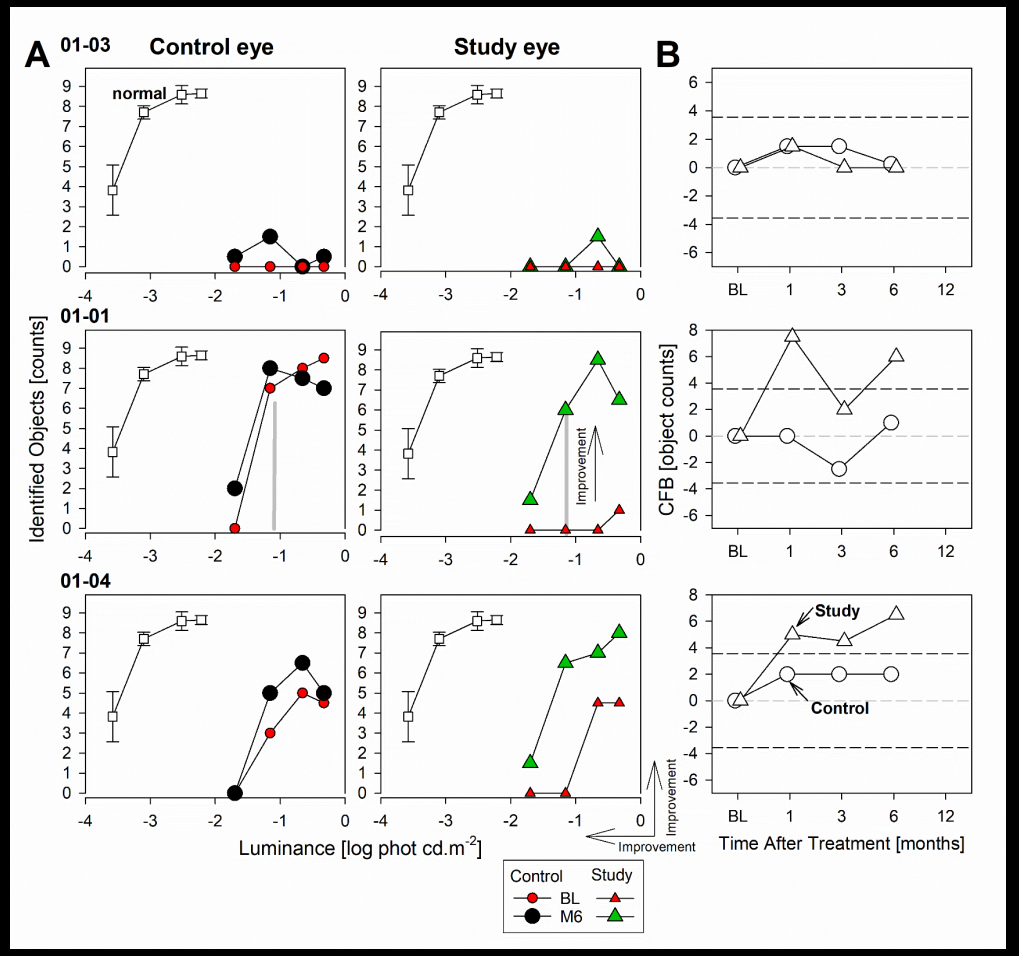


PUPILLOMETRY OBJECTIVELY CONFIRMS EFFICACY/BIOLOGIC ACTIVITY

- Pupil responses are more sensitive (left shifted green symbols) compared to baseline (gray curves) and the contralateral control eye
- Comparable sensitivity change compared to FSTs

FST, full-field stimulus test.

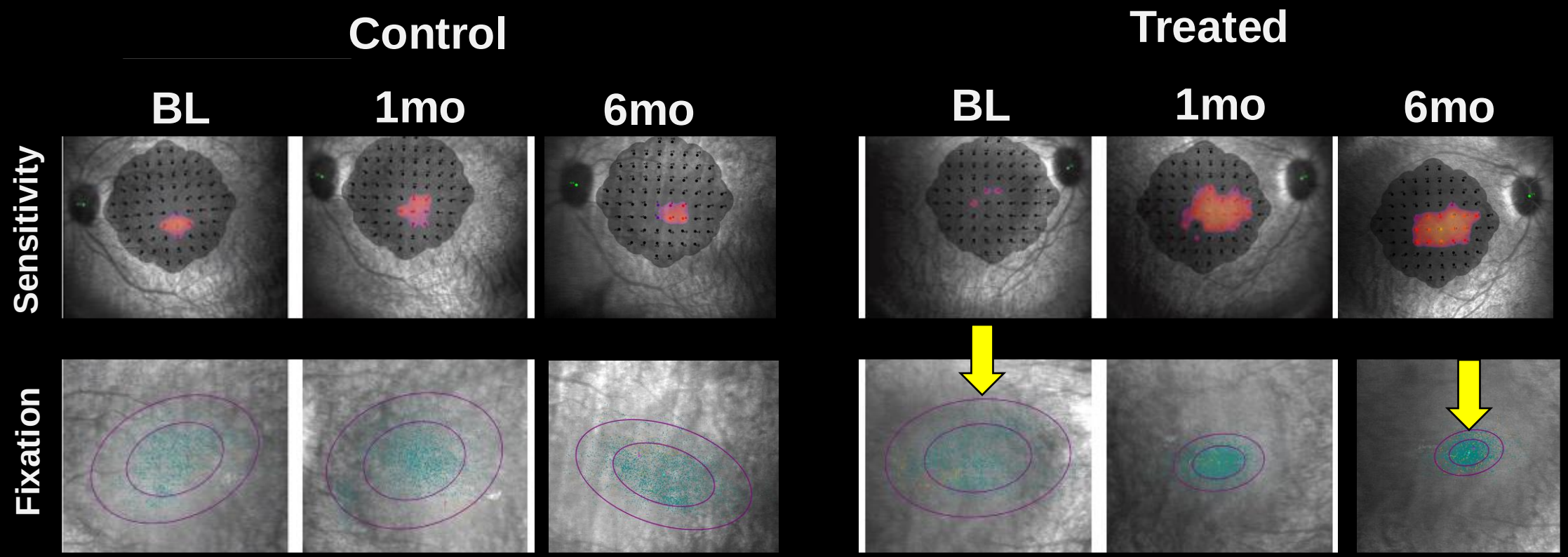
Functional Vision by MLoMT



- Improved orientation and mobility (green up triangles) detected from earliest time point after treatment reproducible to 6 months post-treatment

MLoMT, Multi-Luminance orientation and Mobility Test.

Restoration of the Fovea
Fundus Tracking Perimetry [01-04]



MICROPERIMETRY CONFIRMS FOVEAL IMPROVEMENT

- Microperimetry, possible in one patient, demonstrates sensitivity gain
- Movement of a more stable fixation to the foveal center

BL, baseline.

Conclusions

- Gene augmentation demonstrated robust biologic efficacy in LCA5
- Efficacy corroborated through multiple, mechanistically-driven readouts
- Treatment efficacy is possible in a severe neurodegeneration
- Approach may be used as a template for other severe IRDs
- Inclusion of earlier disease stages in clinical trials is needed

Approved to dose 1st pediatric patient with rolling data readout expected in 2025

IRD, inherited retinal disease; LCA5, Leber congenital amaurosis 5.

Panel Discussion and Q&A

Meet Our Panel

Arshad M. Khanani, MD, MA, FASRS
Managing Partner, Sierra Eye Associates
Clinical Professor, University of Nevada

Moderator

Christine Kay, MD
Vitreo Retinal Associates
Affiliate Assistant Professor, University of South Florida

Jean Bennett, MD, PhD
F.M. Kirby Emeritus Professor of Ophthalmology, University of Pennsylvania

Tomas S. Aleman, MD
Irene Heinz-Given and John LaPorte Research Professor, University of Pennsylvania

Ash Jayagopal, PhD, MBA
Chief Scientific & Development Officer, Opus Genetics

Closing Remarks

Ash Jayagopal, PhD, MBA
Chief Scientific and Development Officer, Opus Genetics

Thank You

Images of real patients with IRDs.