

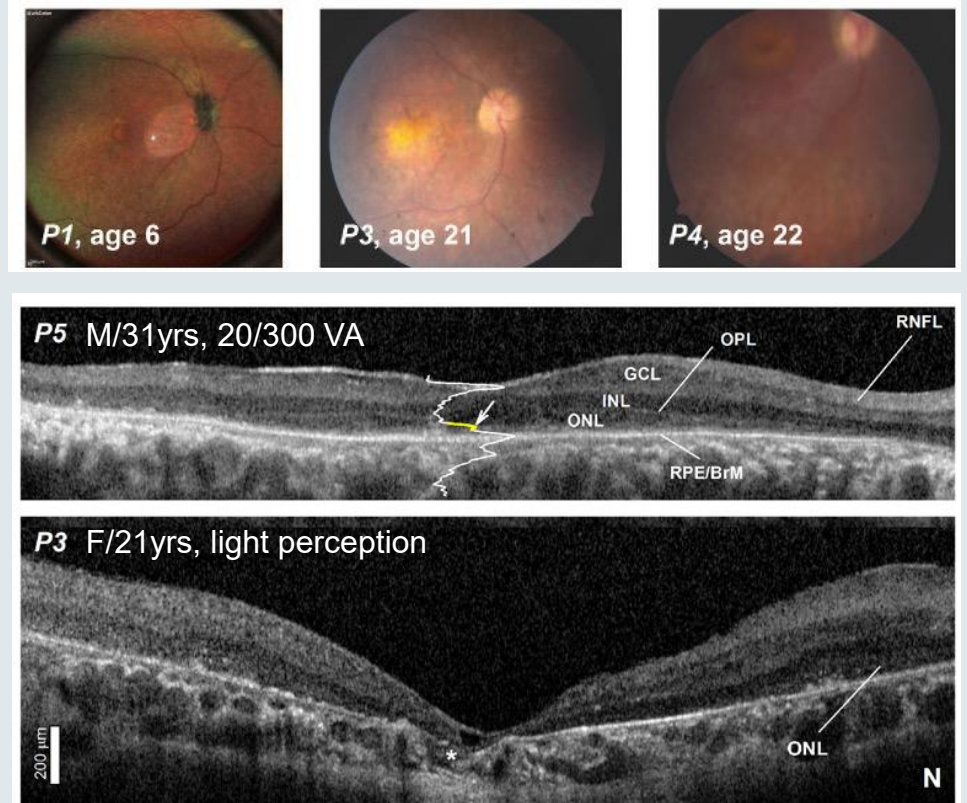
Gene Therapy For Congenital Leber Amaurosis (LCA5)

Dr. Rodrigo Jorge
Ribeirão Preto Medical School
University of São Paulo - Brazil

LCA5: Early-onset, Severe IRD with Early Vision Loss

Overview & prevalence	• Very early onset severe disease typically presenting in infancy or early childhood¹ • LCA5 represents ~2% of all LCA cases¹ • Global prevalence*: ~3,240 patients² • U.S. prevalence: ~170 patients²
Clinical features ^{1,3}	• Pigmentary retinopathy • Macular atrophy • Photoreceptor structure often preserved
Symptoms ^{1,3}	• Vision loss (typically starting in infancy); often limited to hand motions or light perception • Nystagmus • Hyperopia • Severe and early photoreceptor loss results in severely abnormal or non-detectable visual fields

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



*Global prevalence estimate includes United States, EU4 (France, Spain, Germany, & Italy), UK, Middle East/North Africa, and China.

LCA, Leber congenital amaurosis; VA, visual acuity.

1. Boldt K, et al. *J Clin Invest*. 2011;121(6):2169-2180. 2. Triangle Insights Group Analysis, February 2026. 3. Uyhazi KE, et al. *Invest Ophthalmol Vis Sci*. 2020;61:30.

OPGx-LCA5 Gene Therapy is Designed to Restore a Key Protein of the Visual Cycle

- Lebercilin is a ciliary protein critical for function of photoreceptors¹
- In *LCA5* patients, photoreceptor function is severely impaired due to a lack of functioning lebercilin¹
- 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, using same promoter technology as LUXTURN[®] (voretigene neparvovec-rzyl)

OPGx-LCA5 Gene Therapy	
Vector	AAV8
Delivery	Single subretinal injection
Status	• Phase 1/2 ongoing • Phase 3 run-in ongoing • Phase 3 dosing initiation expected Q4 2026

Clinical development timelines are based on current estimates and are subject to change.

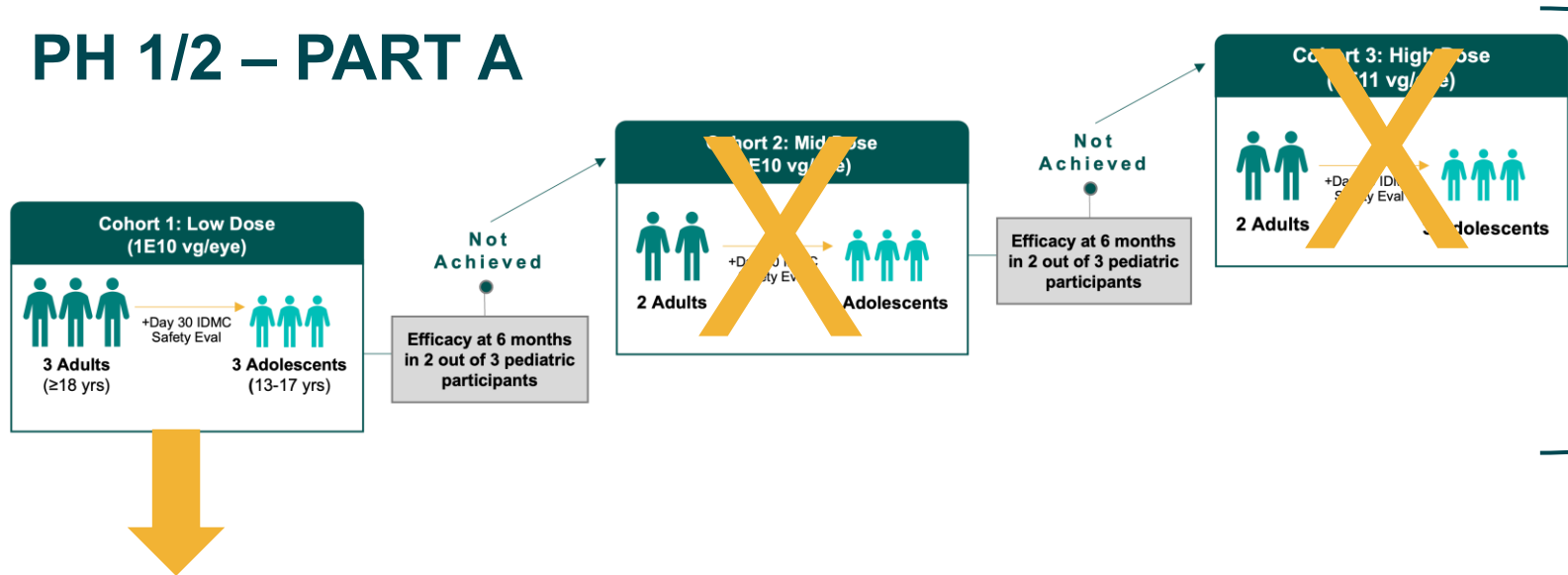
LUXTURN[®] is a registered trademark of Spark Therapeutics, Inc.

AAV8, adeno-associated virus serotype 8; 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.

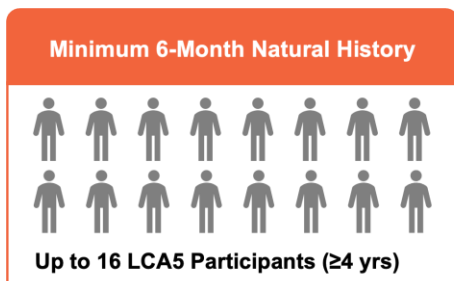
Clinical Development Status

PH 1/2 – PART A



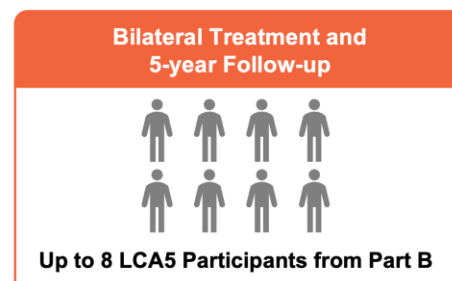
- Ongoing follow-up
- No dose-escalation needed
- Advanced to Ph 3 using low dose

PH 3 - PART B



Fully enrolled

PART C

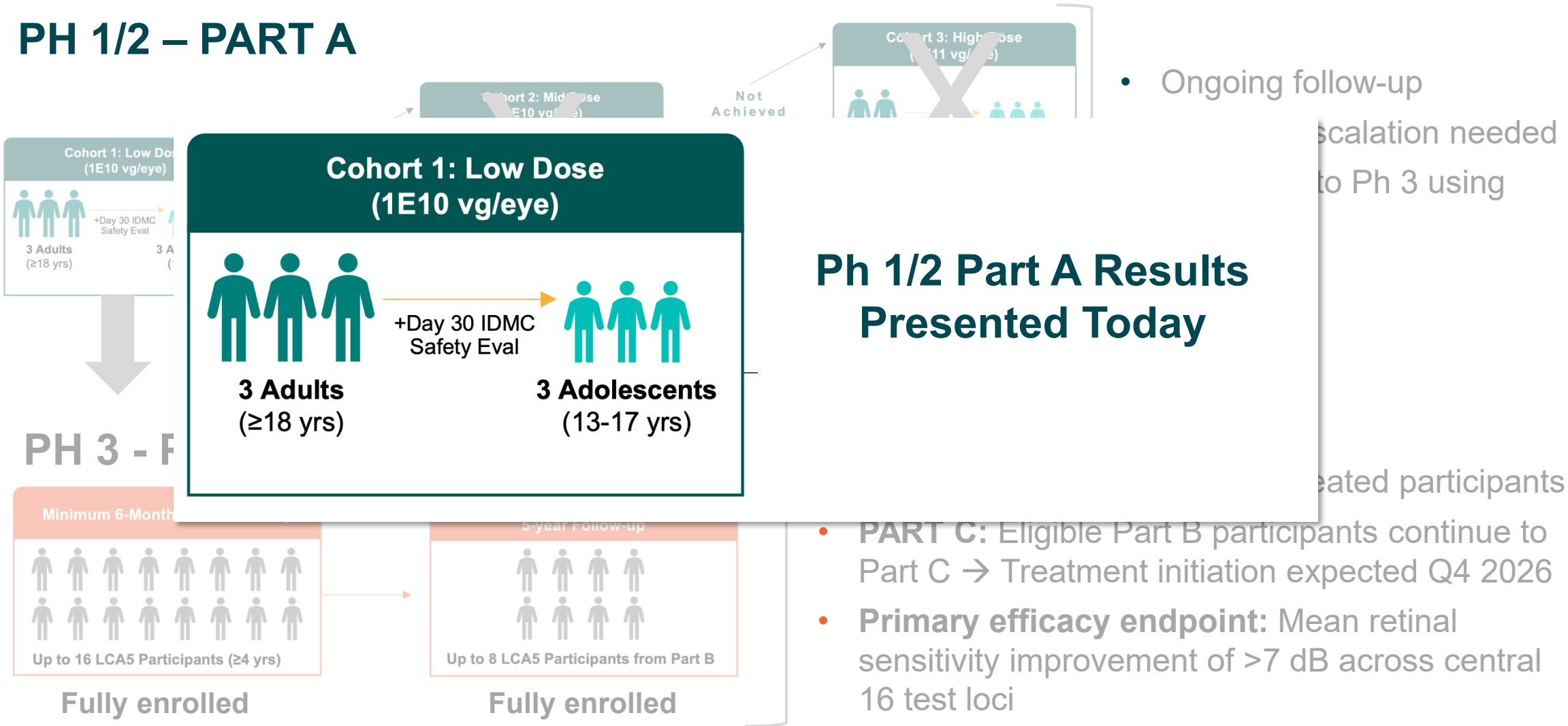


Fully enrolled

- **PART B:** Natural history in untreated participants
- **PART C:** Eligible Part B participants continue to Part C → Treatment initiation expected Q4 2026
- **Primary efficacy endpoint:** Mean retinal sensitivity improvement of >7 dB across central 16 test loci

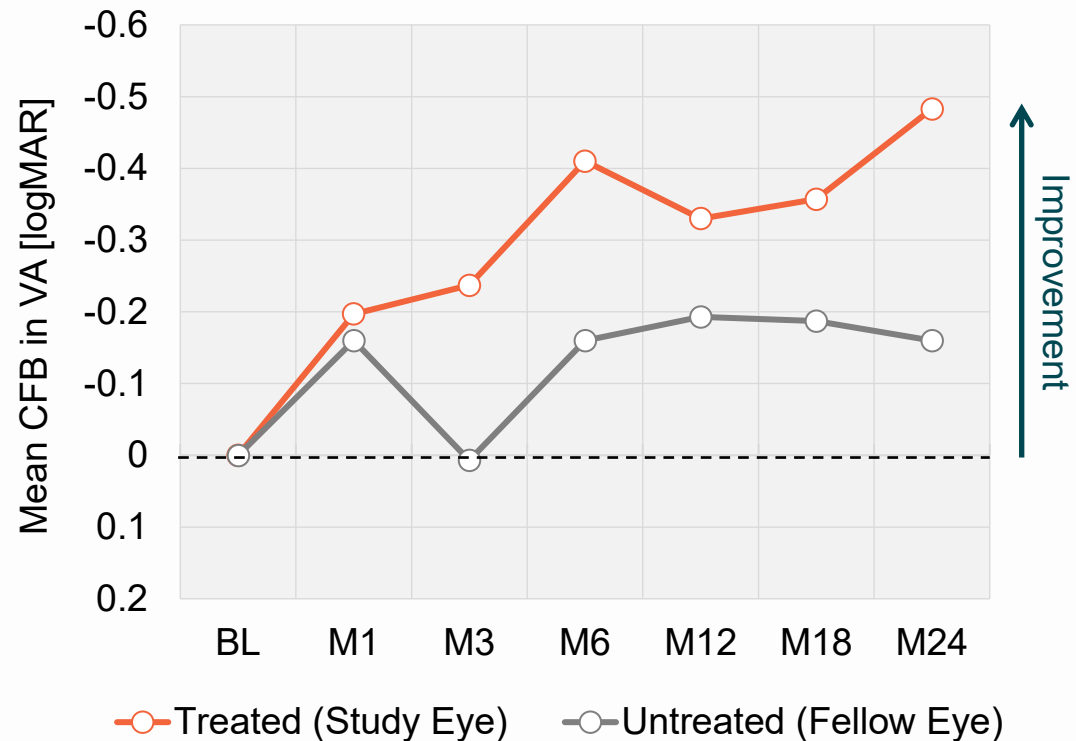
Clinical Development Status

PH 1/2 – PART A

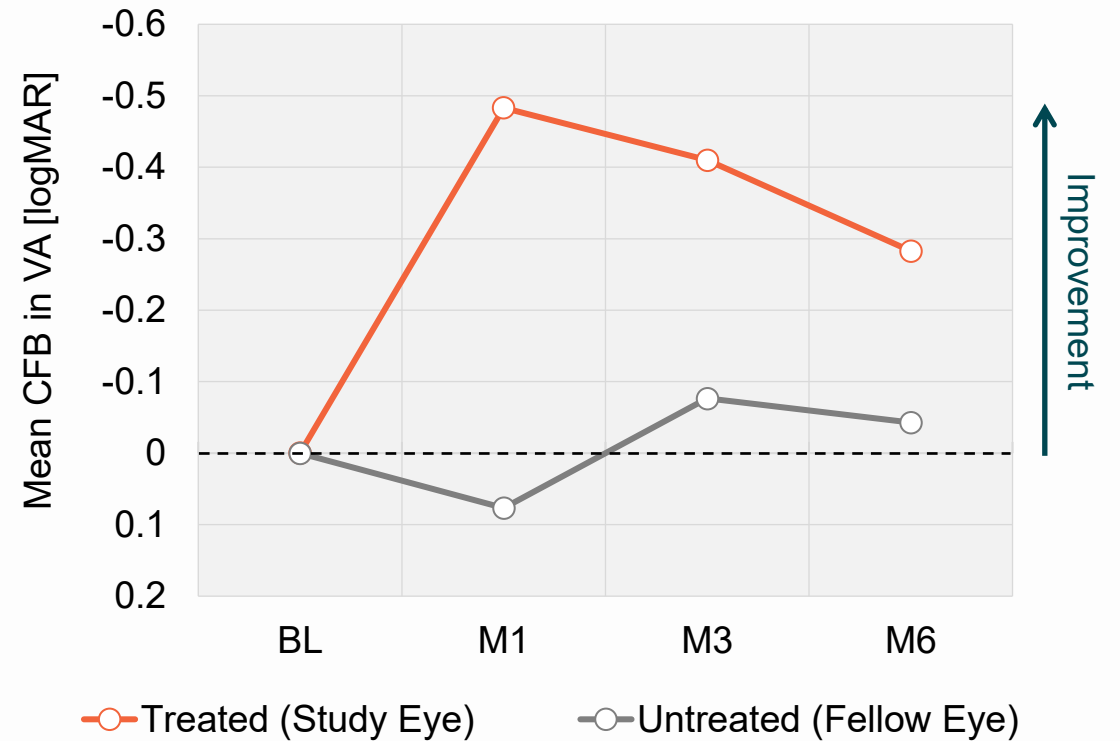


Phase 1/2 Ongoing Study: Visual Acuity Improved in Adults Over 24 Months and in the Pediatric Cohort Over 6 Months

Mean Change from Baseline in VA
Adult Cohort (N=3)



Mean Change from Baseline in VA
Pediatric Cohort (N=3)



Full-field Stimulus Testing (FST)

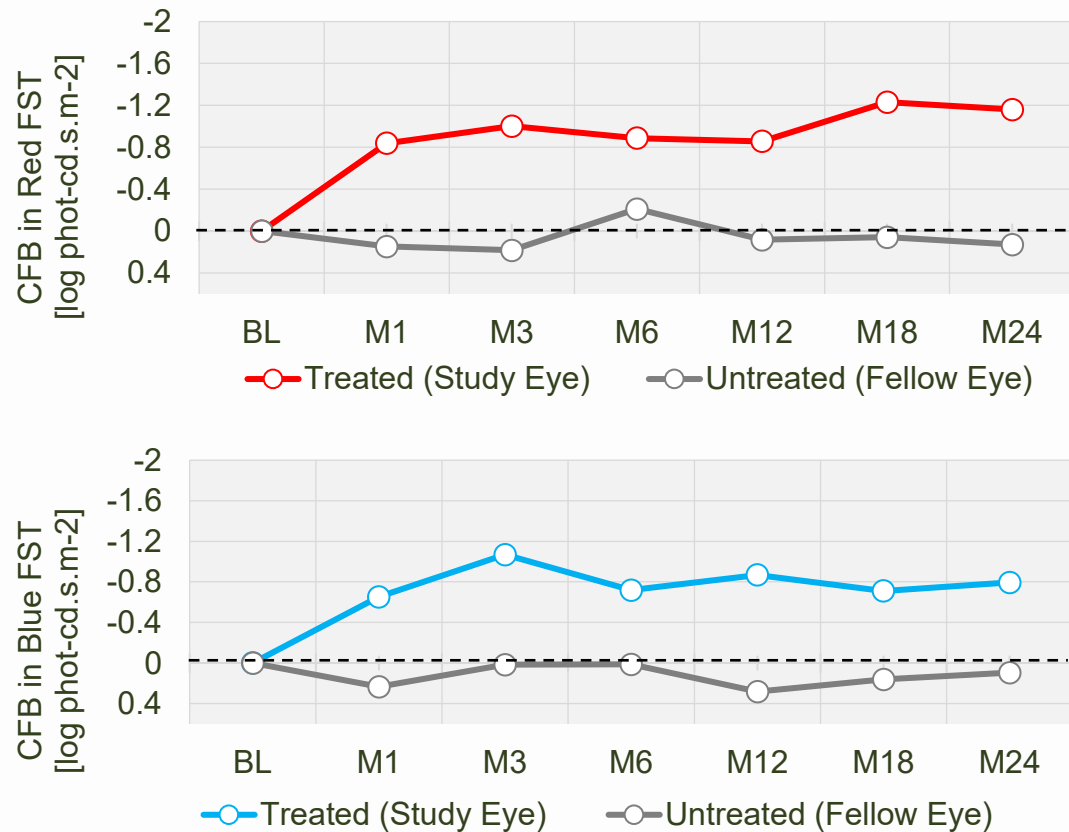


D-FST, Diagnosys LLC, Littleton, MA

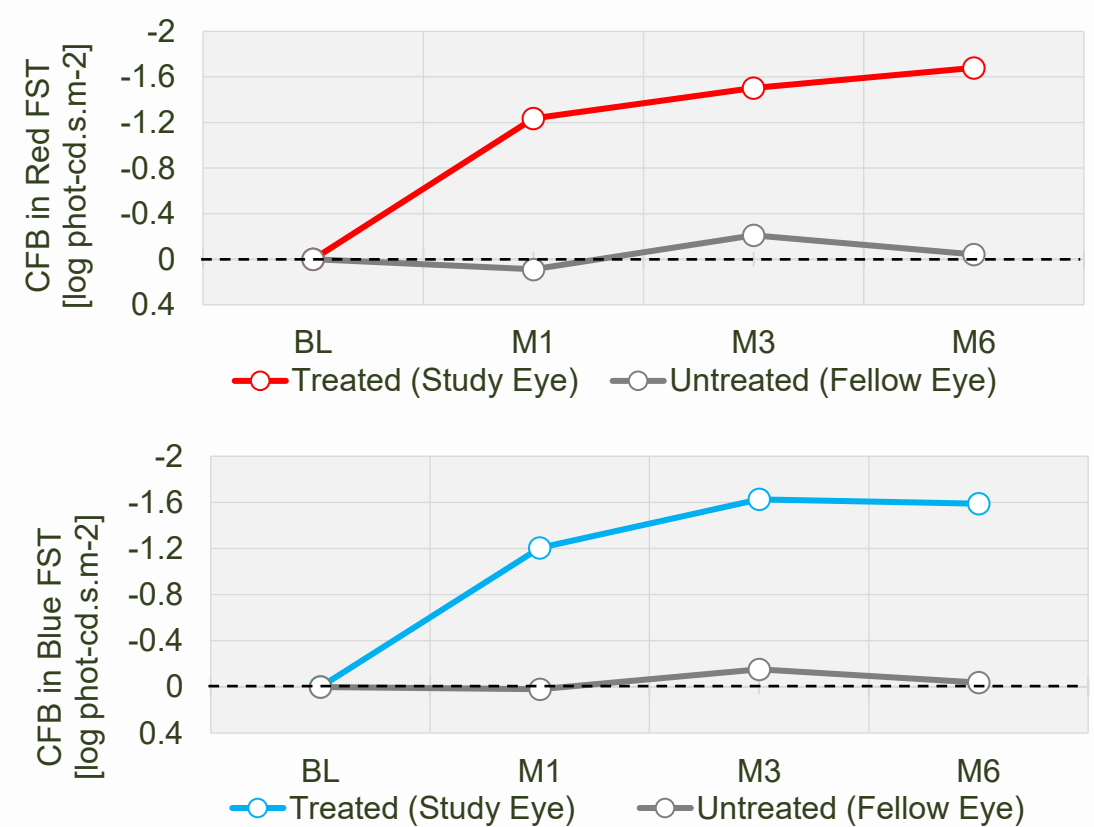
- **Measures** dimmest flash seen across the whole visual field, separating rod and cone sensitivity
- **Setup:** Dilated, dark-adapted eyes (>30 min); one eye tested at a time in a Ganzfeld dome
- **Method:** Forced-choice “seen / not seen” responses to random flashes at varying luminance

Phase 1/2 Ongoing Study: Full-Field Stimulus Test Demonstrated Durable Vision Improvement

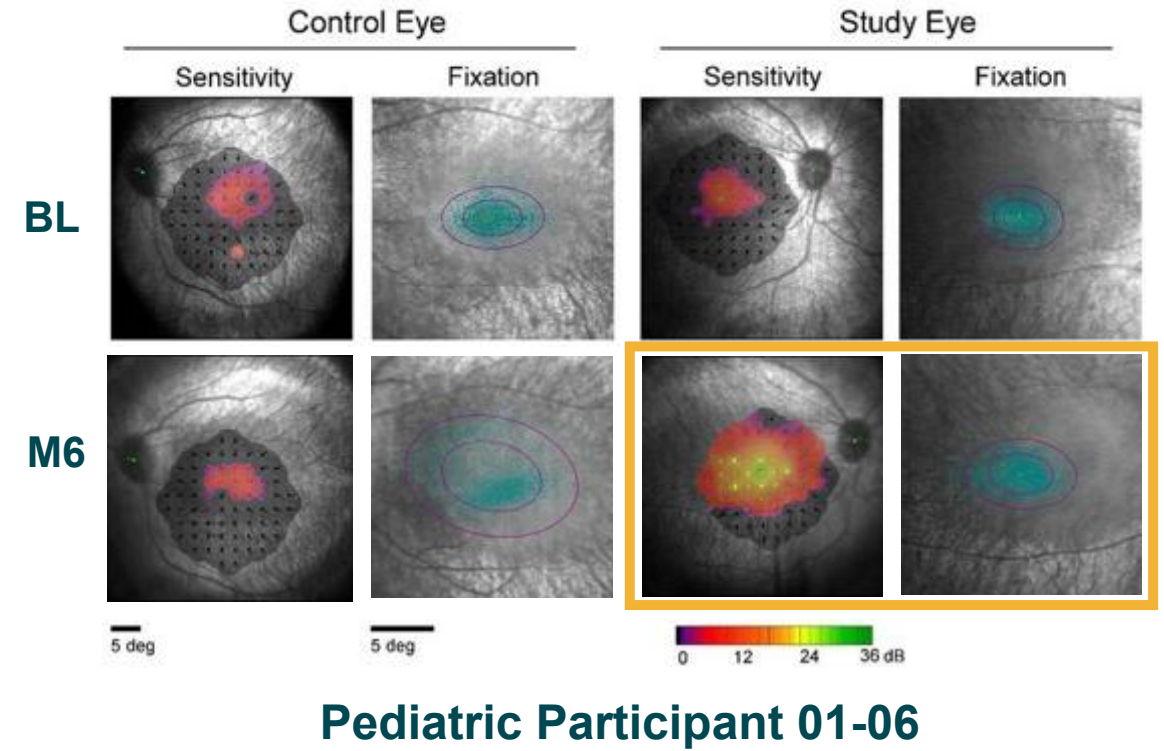
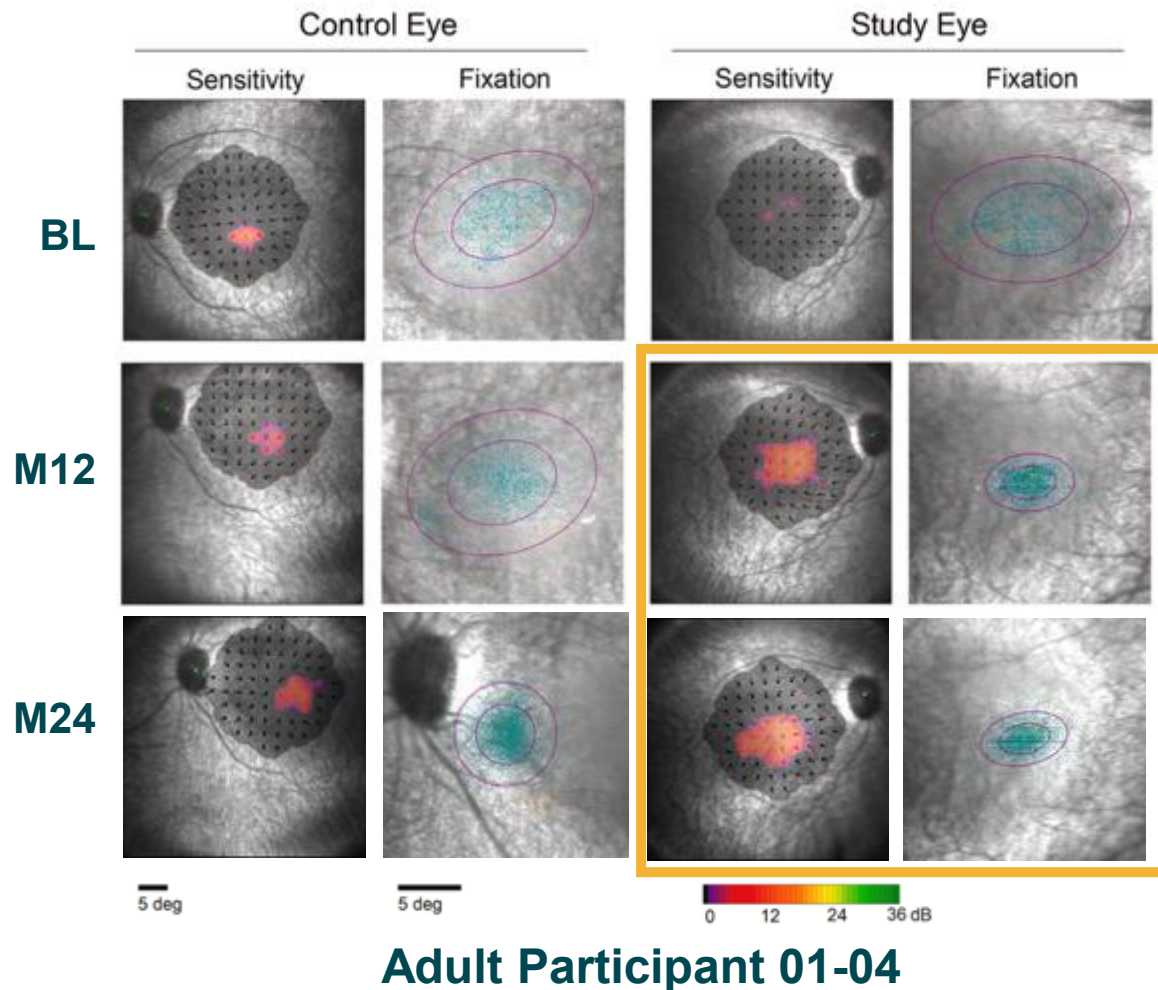
Mean CFB in Red and Blue FST
Adult Cohort (N=3)



Mean CFB in Red and Blue FST
Pediatric Cohort (N=3)



Phase 1/2 Ongoing Study: Microperimetry Data Provides Evidence of Increased Sensitivity and Movement of Fixation Toward the Fovea



Powerful Participant-Reported Outcomes After OPGx-LCA5 Treatment

Adult Participants

01-01: Able to **identify her children within a larger group** of children one month after surgery, which she previously could not do

01-04*: Since treatment, **no longer requires a cane** and can **navigate urban environments independently**.

01-03: Had no formative vision prior to treatment. Able to **see his newborn niece for the first time and watch his sister get married**.

Able to pour a glass of wine and drink unassisted for the first time in his life.

Able to travel independently and, as a result, acquired a new job, which requires a greater level of independence than he had previously.

Pediatric Participants

01-05: Able to **walk and cook without assistance** of others; treatment has helped in her **writing capabilities**

01-06*: Noticeable **difference in visual brightness** between his treated and untreated eyes

Able to **watch basketball and can see the players and follow the ball** instead of just watching the score ticker and listening.

01-07: Mostly nonvisual prior to treatment. Reported visiting a local zoo, where she was **able to visualize an owl for the first time**, and also reported having to learn colors and what a window was in a hotel

*01-04 and 01-06 were able to complete microperimetry.

Participant-reported outcomes provided in follow up visits in 2025.

A Conversation with Lindsay Rambo, a Patient Living with *LCA5*:

What do you wish people could feel or experience to truly understand the potential impact of this treatment?



Lindsey Rambo

Thank you

Gene Therapy For Congenital Leber Amaurosis (LCA5)

Dr. Jorge Rodrigo

Ribeirão Preto Medical School

University of São Paulo - Brazil