Issuer Free Writing Prospectus dated March 20, 2025
Filed Pursuant to Rule 433
Relating to Preliminary Prospectus Supplement dated March 20, 2025
Registration No. 333-276462

OPUS GENETICS

Market Landscape & Commercial Opportunity

	LCA5	BEST1
Disease Overview	Most early-onset and severe form of all IRDs; severe vision loss during infancy or at an early age	Most common bestrophinopathy; presents in first two decades of life and causes progressive bilateral vision loss
U.S. Prevalence	~200 patients	~9,000 patients
Prognosis	Onset of profound vision loss typically during infancy, with 100% legally blind at an early age	Slow and progressive vision loss, with some progressing to legal blindness
Treatments	None	None (small proportion who develop CNV as a complication are treated with anti-VEGF therapy)
Pipeline	None	None
HCP / Patient Adoption Rate*	99% / 83%	82% / 61%
Suggested Price	~$500K per eye (all cases are bilateral)	~$450K per eye (majority of cases are bilateral)
Coverage Rate	92%; Premium price to Luxturna®, with limited restrictions due to urgent need/small patient population	92%; Limited restrictions, with Luxturna as benchmark for price/coverage

*Based on target product profile suggesting improved vision.
Luxturna® is a registered trademark of Spark Therapeutics, Inc.

BEST1, bestrophin 1; CNV, choroidal neovascularization; IRD, inherited retinal disease; LCA5, Leber congenital amaurosis 5; VEGF, vascular endothelial growth factor.

1. Stone et al. Ophthalmology. 2017;124:1314-1331. 2. Triangle Insights Group market research, conducted August 2023.

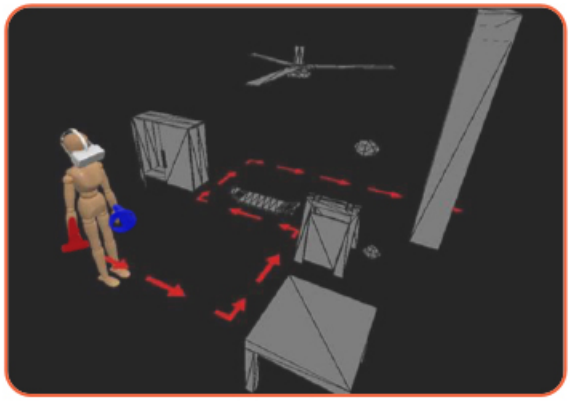
One-year Results from a Phase 1/2 Study of OPGx-LCA5 Gene Therapy for *LCA5*

Alan,
LCA5 patient

LCA5, Leber congenital amaurosis 5.

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)



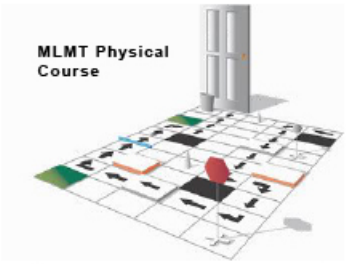
MLoMT, Multi-luminance orientation and mobility test; VR, virtual reality.

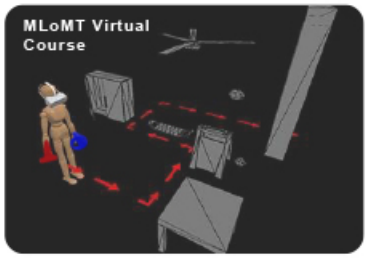
Bennett J, et al. *Transl Vis Sci Technol*. 2023;12:28.

MLoMT Builds Upon the Success of MLMT®

Leverages VR to Provide Flexible Testing with Automatic Scoring

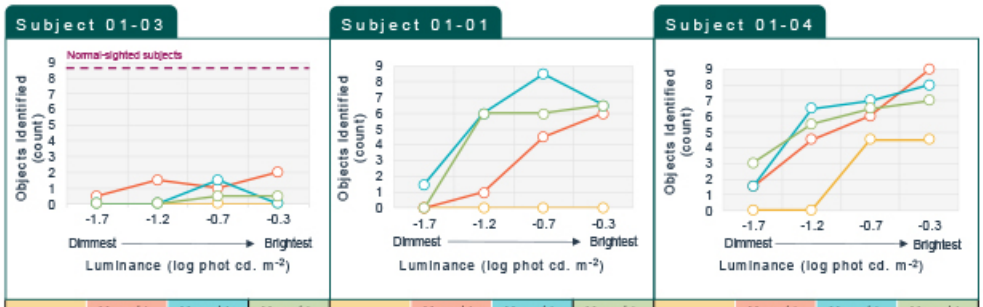
- Automatic randomization of dozens of configurations
- Delivers test in a relatively short time (20 mins)
- Equipment/space affordable
- Easy to deploy and duplicate at multiple sites
- No physical obstacles that could cause harm in a collision
- Attractive to digital-savvy pediatric population
- Quantitative information (timing, direction of gaze, acceleration, deceleration, collisions) captured automatically as digital data
- Data obtained instantaneously and analyzed objectively (no need for reading center)





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

MLoMT: All Treated Subjects Identified More Objects Through 12 Months Compared to Baseline



Luminance	Subject 01-03 BL	Subject 01-03 Month 3	Subject 01-03 Month 6	Subject 01-03 Month 12	Subject 01-01 BL	Subject 01-01 Month 3	Subject 01-01 Month 6	Subject 01-01 Month 12	Subject 01-04 BL	Subject 01-04 Month 3	Subject 01-04 Month 6	Subject 01-04 Month 12
-1.7 (dimmest)	0	0.5	0	0	0	0	1.5	0	0	1.5	1.5	3
-1.2	0	1.5	0	0	0	1	6	6	0	4.5	6.5	5.5
-0.7	0	1	1.5	0.5	0	4.5	8.5	6	4.5	6	7	6.5
-0.3 (brightest)	0	2	0	0.5	0	6	6.5	6.5	4.5	9	8	7

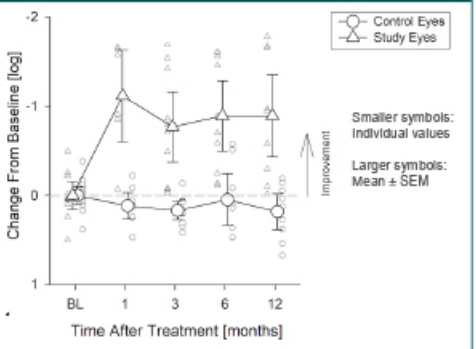
Count of Objects Identified (Max=9)

Average CFB to 6 months at -0.7 luminance was 4 objects identified;
This will be the possible primary endpoint in the FDA registrational study

6 CFB, change from baseline; FDA, Food and Drug Administration; MLoMT, Multi-Luminance orientation and Mobility Test.

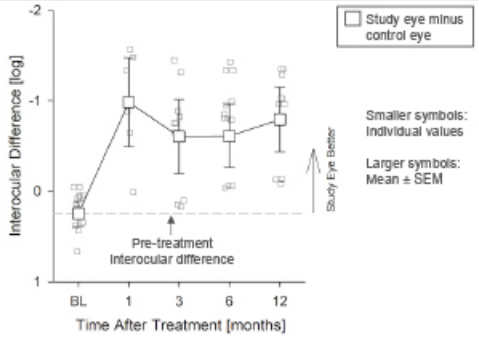
Full-field Stimulus Testing: Demonstrated an Overall Improvement in Vision in Treated Eyes

Mean CFB in FST



- **Mean CFB:** 0.86 log improvement in study eyes vs 0.16 in control eyes
- Study eyes showed larger change from baseline, demonstrating improvement in vision

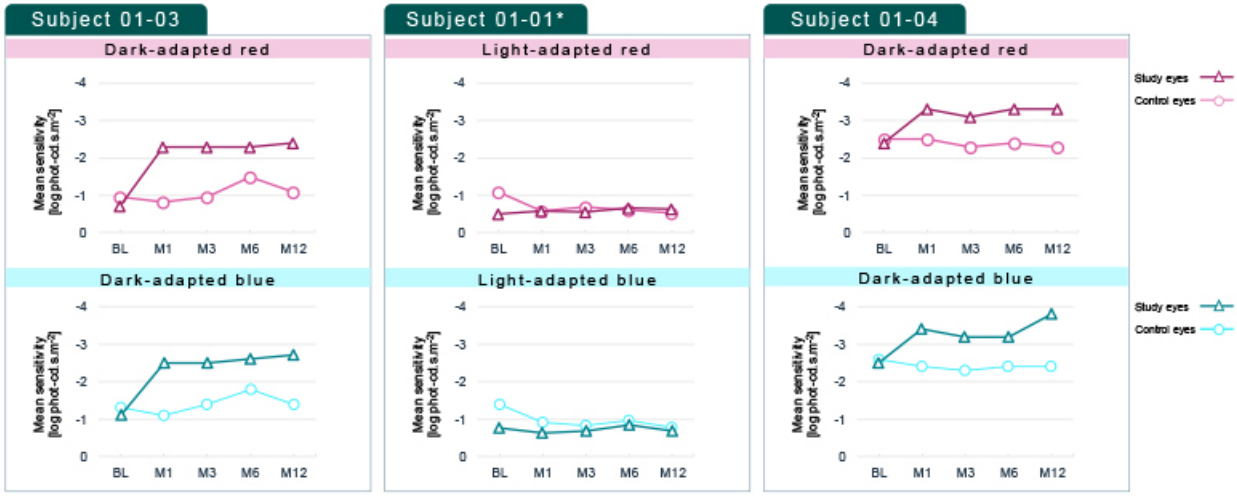
Mean IOD in FST



- **Baseline:** IOD average of 0.3 log better sensitivity in control eyes
- **Post-treatment:** IOD switched, with average of 0.7 log better sensitivity in study eyes

BL, baseline; CFB, change from baseline; FST, full-field stimulus testing; IOD, interocular difference; SEM, standard error of the mean.

FST: Retinal Sensitivity Gains Comparable to Adult Patients Treated with Luxturna



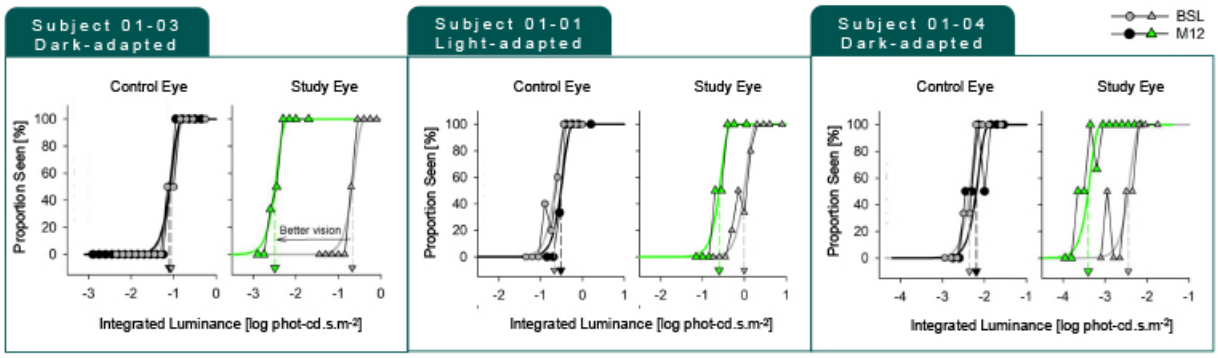
*Subject 01-01 was measured in light-adapted conditions; Remaining rod function was strong enough that it interfered with measuring cone function; to isolate and measure cone responses, rods had to be desensitized by adapting the eye to white light

Note: Subject 01-03 and 01-04 are cone-mediated disease and Subject 01-01 is rod-mediated disease.

BL, baseline; FST, full-field stimulus testing; M, month.

FST: Improvement in Cone-mediated Vision in Treated Patients

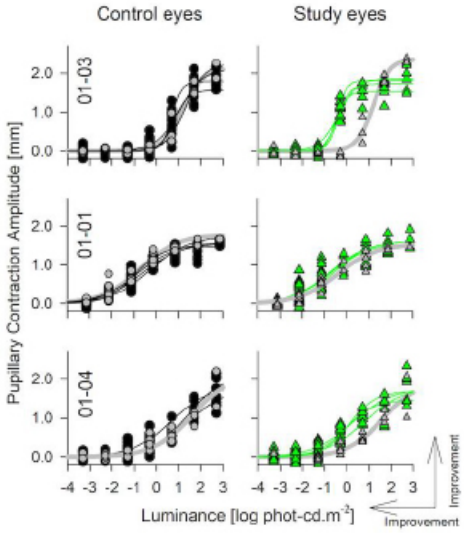
FST data with red stimuli at Baseline and Month 12:



- Study eyes: At 12 months, the proportion of stimuli seen shifted left toward lower luminance in all treated eyes, demonstrating better vision
- Control eyes: Minimal to no change

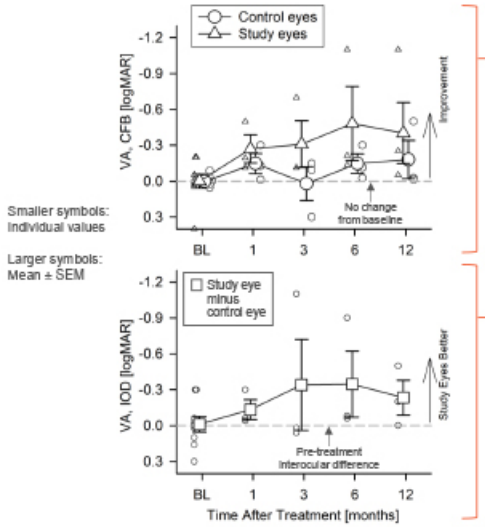
9 BSL, baseline; FST, full-field stimulus testing; M, month.

Pupillary Light Reflex: Results Supportive of Improved Cone-Mediated Vision Through 12 Months



- Pupil responses were larger in study eyes (green lines) compared to control eyes (black lines) and baseline (gray lines)
- Treated eyes demonstrated a shift toward dimmer intensities compared to baseline
  - Subjects 01-03 and 01-04 showed clear shift to the left confirming sensitivity gains

Visual Acuity: Overall Improvements in Treated Patients



CFB in Visual Acuity

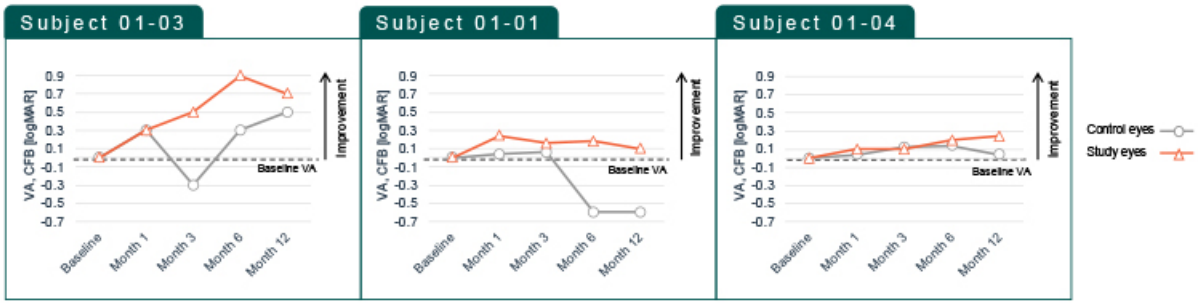
- Study eyes improved to 0.48 logMAR (~5 lines on VA chart) at 6 months
- Control eyes fluctuated within 0.18 logMAR, with no improvement

Mean IOD in Visual Acuity

- Symmetry / no difference between eyes at baseline
- Post-treatment IOD favored study eyes by average of 0.3 logMAR

11 CFB, change from baseline; IOD, interocular difference; logMAR, logarithm of the minimum angle of resolution; VA, visual acuity.

Visual Acuity: Improvements from Baseline Demonstrated in Two Patients Over 12 Months

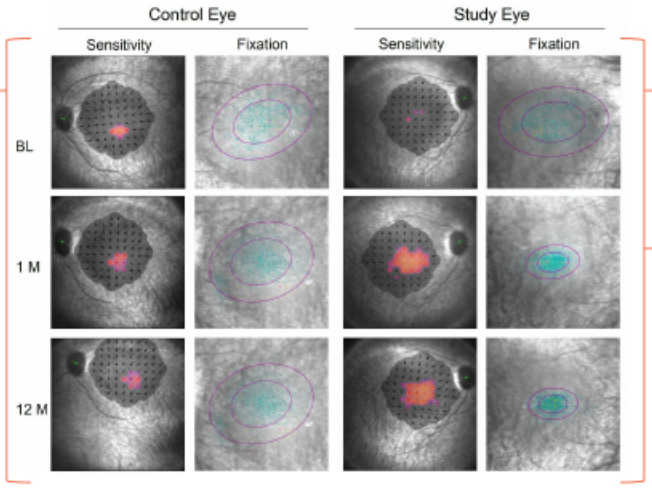


- VA improvements over 12 months in patients 01-03 and 01-04
- Formed vision possible for the first time in the most severely affected patient (most advanced disease), 01-03

12 CFB, change from baseline; VA, visual acuity.

Microperimetry Confirms Foveal Improvement: Subject 01-04 had Greater than 18-Fold Improvement in Macular Sensitivity

Control Eye
Small area of severely reduced sensitivities at 5 points with no change through 12 months



Study Eye

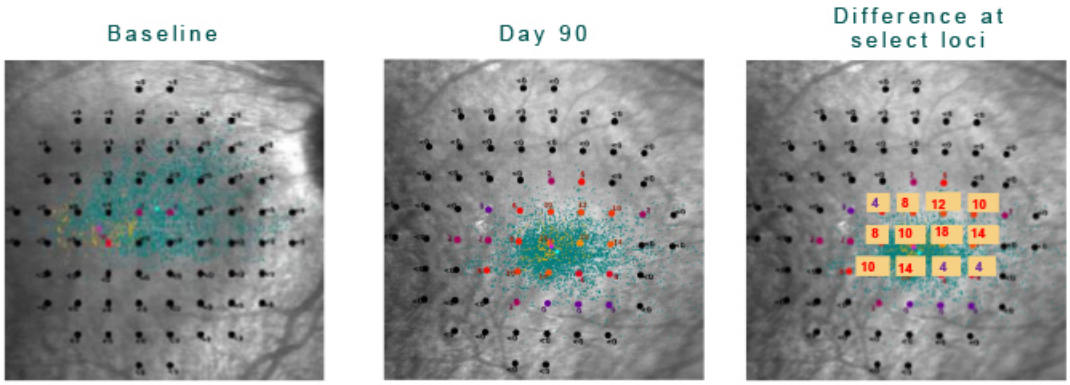
Baseline: Measurable only in scattered points of barely detectable sensitivity; Fixation unsteady, over area of ~10 degrees

1 Month: Improvement with detectable sensitivities in 19 points over area of ~15 degrees

Fixation stabilized and shifted toward foveal center, suggesting improved central vision

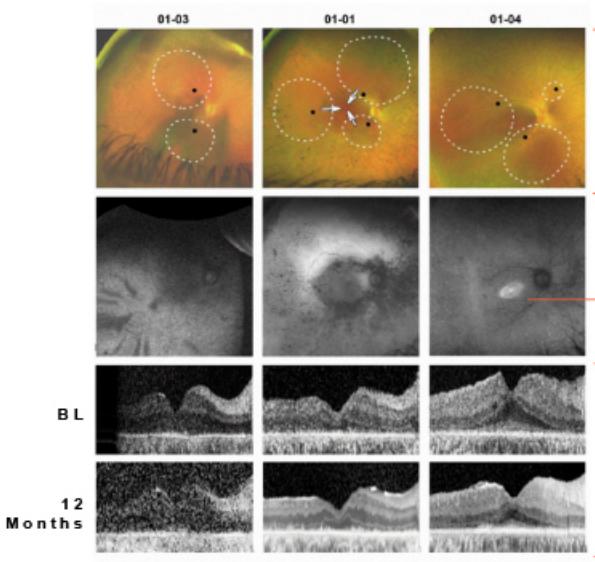
13 Note: Microperimetry only possible in one subject; Two subjects could not fixate.

Possible FDA Registrational Endpoint



7dB difference in the same 5 prespecified loci at two or more timepoints may be a standalone registrational endpoint

Uneventful Subretinal Injections and Unchanged Retinal Structure



- Uneventful subretinal injections
  - Unilateral injection; 300 µl volume
  - Retinotomies (black dots) and resulting subretinal blebs (white dashes)
  - Blebs coalesced near foveal center (arrows)
- Functional retinal pigment epithelium
- No major changes in retina post-treatment
  - Retina reattached post-injection
  - OCT images through foveal center of treated eye at BL and 1 year after procedure

15 BL, baseline; OCT, optical coherence tomography.

OPGx-LCA5 was Safe and Well-Tolerated Through One Year

- No dose-limiting toxicities
- No serious adverse events
- Anticipated adverse events were mild and unrelated to treatment
  - Mostly related to use of systemic steroid or with surgical procedure
- All early AEs resolved within 30 days of the procedure

 AE, adverse event; LCA5, Leber congenital amaurosis 5.

Independent Data Safety Monitoring Committee Recommendation

- Data from first three adult patients presented to IDSMC
  - Compelling data demonstrating efficacy
  - Signal akin to Luxturna
- No toxicity
  - OPGx-LCA5 low dose = 1E10 vg/eye
  - Luxturna dose = 1.5E11 vg/eye, with some cases of post-approval inflammation
- Unanimous recommendation to push for a seamless 1/2/3 design with data-driven dose escalation

IDSMC, Independent Data Safety Monitoring Committee; LCA5, Leber congenital amaurosis 5.

A Patient's Journey in the OPGx-LCA5 Trial: Helping Others and Life-changing Moments

"I initially agreed to participate in trial to **help people, including a child in our own neighborhood who also has *LCA5*.** I wanted this research to advance understanding and treatments that could make a difference for him and so many others.

After surgery and recovery, I've found the trial and treatment has also helped me find more joy in the little things—**now I'm able to see fireworks light up the sky and appreciate the food on my plate**—and improve my ability to do daily tasks that those without retinal diseases may take for granted like **spotting my Uber and using utensils.** I look forward to the possibility of treating my other eye once the trial advances to Phase 2."

- OPGx-LCA5 Clinical Trial Participant"

18 LCA5, Leber congenital amaurosis 5.

OPGx-LCA5 Clinical Development Plan

Alan,
LCA5 patient

LCA5, Leber congenital amaurosis 5.

OPGx-LCA5 Primary and Secondary Endpoints

FDA Discussion /Agreement

- **FDA meeting:** March 3, 2025
- **Final FDA minutes:** April 3, 2025
- **Pre-Type D meeting comments:** FDA open to adaptive Phase 1/2/3 clinical trial design proposed
  - Primary control is change from baseline assessments of MLoMT (6-month run-in compared to 6-month post-treatment)
- FDA open to potentially skipping further dose escalation if 3 adolescent *LCA5* subjects show response of MLoMT ORT of 3 or more

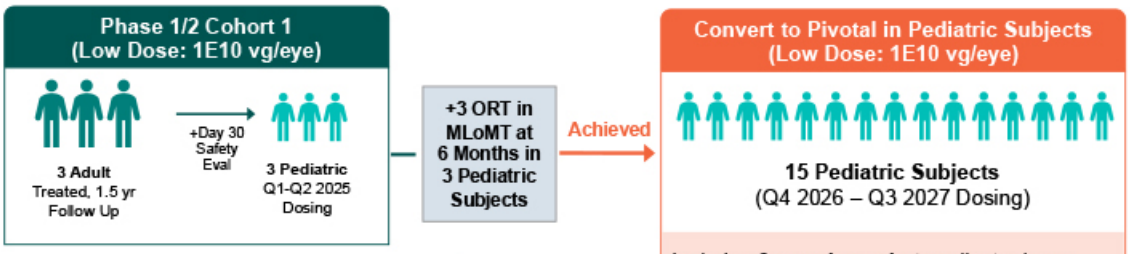
- **Primary endpoint:** MLoMT ORT; Change from baseline in total number of objects recognized
  - FDA pre-meeting feedback indicates **openness to new primary endpoint**
  - **Must provide to IND:** Justification of endpoint relevance in LCA5, tools intended for assessing study outcomes, interview guide for planned cognitive interviews supporting MLoMT measure in LCA5, quantitative assessment of reliability and construct validity for interviews, scoring algorithm, and plans for handling missing data
- **Secondary endpoints:**
  - **Composite MLoMT** measure incorporating orientation, total number of objects recognized, along with luminance
  - **FST** is a key secondary endpoint
  - **Pupillometry** as additional secondary endpoint

FDA, Food and Drug Administration; FST, full-field stimulus testing; IND, Investigational New Drug; LCA5, Leber congenital amaurosis 5; MLoMT, multi-luminance orientation and mobility testing; ORT, object recognition threshold.

Rationale for Adaptive Design for OPGx-LCA5 Clinical Trial

21 LCA5, Leber congenital amaurosis 5.

FDA Approves Adaptive Phase 1/2 Trial Design and Streamlined CMC Package



CMC: Requesting FDA to allow manufacture of only 1 batch

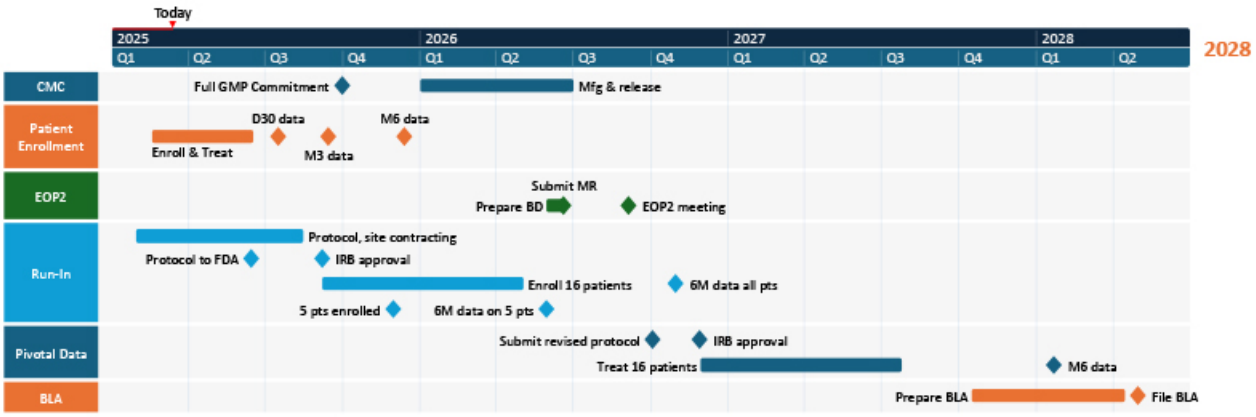
- 1 batch will provide enough vector to treat entire U.S. *LCA5* population
- In Pre-Type D comments, FDA seems open to path to BLA without new batch, batch production may only be for post-approval (commercial) use

Includes **6-month run-in** to collect primary endpoint data, allowing:

- Establishment of an *LCA5*-specific MLoMT reference data set
- Subjects to be used as their own controls

BLA, Biologics License Application; CMC, chemistry, manufacturing, and controls; FDA, Food and Drug Administration; LCA5, Leber congenital amaurosis; MLoMT, Multi-luminance orientation and Mobility Test; ORT, object recognition threshold.

OPGx-LCA5 Timelines



BLA, Biologics License Application; CMC, chemistry, manufacturing, and controls; EOP, end of phase; FDA, Food and Drug Administration; GMP, Good Manufacturing Practices; IRB, Institutional Review Board.

OPGx-LCA5 Use of Funds

Key Program Assumptions	
IND	Complete
Pivotal	FPI (treated): Nov 2026, LPI July 2027
BLA	Q2 2028
CMC	Start analytical work Q3 2025, 1 commercial batch
Other	Nonclinical: Gene expression- and function-based potency assay development (in house + assay transfer and validation at a CRO)

$(000s)		CMC	Pre-/Non-clinical	Clinical	Total
2025	Q1	$0	$25	$244	$269
	Q2	$0	$25	$244	$269
	Q3	$600	$60	$244	$904
	Q4	$1,000	$60	$244	$1,304
	Total	$1,600	$170	$975	$2,745
2026	Q1	$2,600	$30	$368	$2,998
	Q2	$2,600	$30	$368	$2,998
	Q3	$1,600	$30	$368	$1,998
	Q4	$100	$30	$368	$498
	Total	$6,900	$120	$1,470	$8,490
2027	Q1	$125	$30	$352	$507
	Q2	$125	$30	$352	$507
	Q3	$125	$30	$352	$507
	Q4	$125	$30	$352	$507
	Total	$500	$120	$1,410	$2,030
2028	Q1	$125	$0	$309	$434
	Q2	$125	$0	$309	$434
	Q3	$125	$0	$309	$434
	Q4	$125	$0	$309	$434
	Total	$500	$0	$1,235	$1,735
2025-2028 Total		$9,500	$410	$5,090	$15,000

BLA, Biologics License Application; CMC, chemistry, manufacturing, and controls; CRO, contract research organization; FPI, first patient in; IND, Investigational New Drug; LPI, last patient in.

OPGx-BEST1

Phase 1/2-Ready Gene Therapy for *BEST1*-associated Disease

BEST1, bestrophin 1.

OPGx-BEST1 Strategy

OPGx-BEST1 DUO-1001

- **Design:** Phase 1b/2a, open-label, non-randomized, single ascending dose escalation, safety and tolerability study of OPGx-BEST1 in subjects with BVMD or ARB (Basket approach with traditional 3x3 design)
- **Initial dosing:** ARB patients only
- **Up to 3 doses evaluated:** 1.4 E9 vg/eye (cohort 1), 4.5 E9 vg/eye (cohort 2), and 2.25 E10 vg/eye (cohort 3); unilaterally injected

- Traditional 5x3 dose escalation is partially skipped if evidence of full-fluid resolution within 6 months after treatment is seen in Cohort 1 (or Cohort 2)
  - At first occurrence of full fluid resolution in majority (2/3) of a dose cohort, converts to pivotal study extension with 1:1 randomization with crossover (low dose - 1E10 vg/eye)
  - Becomes adaptive Ph 1/2/3 approach like the proposed OPGx-LCA5 adaptive design

 ARB, autosomal recessive BEST1; BEST1, bestrophin 1; BVMD, best vitelliform macular dystrophy.

OPGx-BEST1 Clinical Development Assumptions

Phase 1 / 2

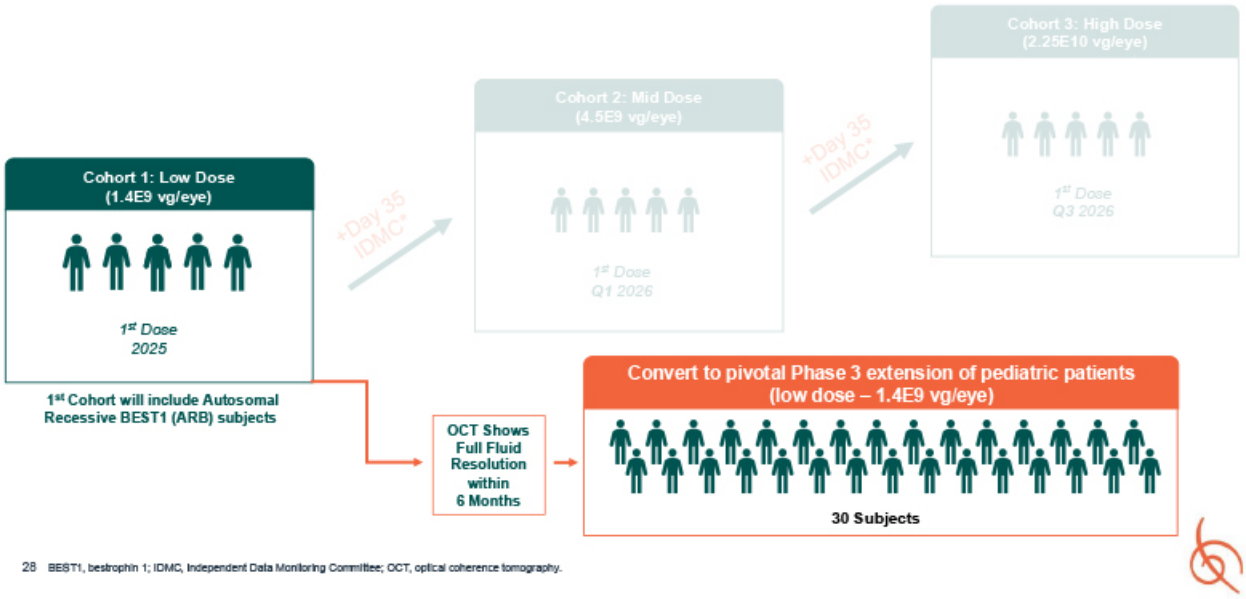
- Subjects: 5 Pediatrics at low dose, no escalation
- Trial sites: 3 (1 EU, 2 US)
- FPI: Oct 2025
- LPI: Jan 2026

Pivotal

- Design: 1:1 drug vs control (with crossover)
- Subjects: 30, 6-month endpoint to file
- Trial sites: 8 (TBD)
- FPI: Q1 2027
- LPI: Q1 2028
- 6-month data: Q2 2028
- File BLA: Q3 2028

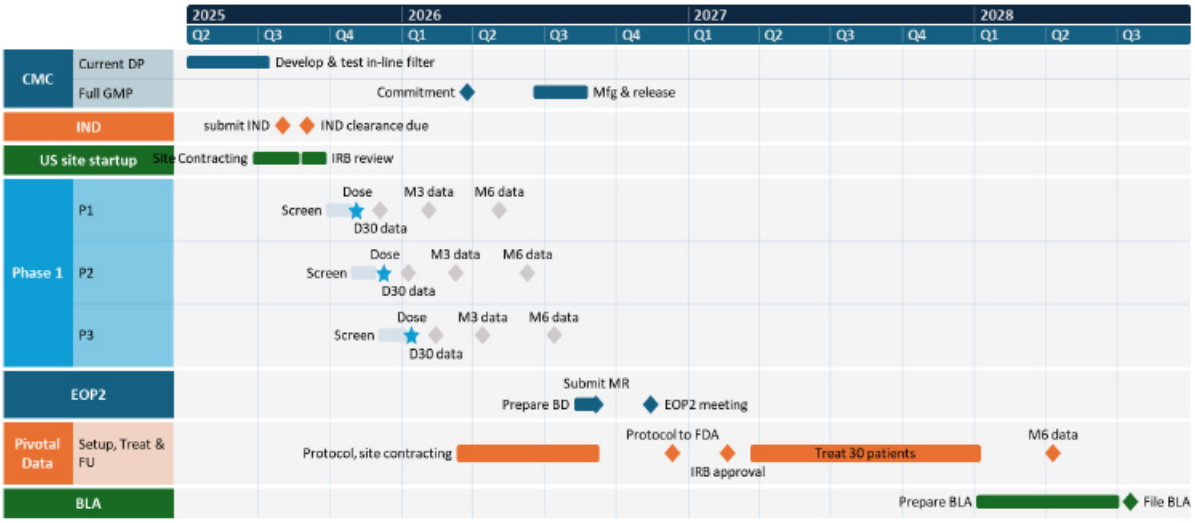
BEST1, bestrophin 1; BLA, Biologics License Application; FPI, first patient in; LPI, last patient in.

OPGx-BEST1 DUO-1001 Clinical Design



28 BEST1, bestrophin 1; IDMC, Independent Data Monitoring Committee; OCT, optical coherence tomography.

OPGx-BEST1 Timelines



BEST1, bestrophin 1; BLA, Biologics License Application; CMC, chemistry, manufacturing, and controls; CRO, contract research organization; D, day; DP, drug product; EOP, end of phase; FDA, Food and Drug Administration; FU, follow-up; GMP, Good Manufacturing Practices; IND, Investigational New Drug; IRB, Institutional Review Board; M, month; P, patient.

OPGx-BEST1 Use of Funds

Key Program Assumptions	
IND	File Aug 2025
Phase 1	FPI: Oct 2025 LPI: Jan 2026
Pivotal	FPI: Q1 2027 LPI: Q1 2028
BLA	Q3 2028
CMC	Initiate full GMP lot after human POC
Other	Nonclinical: gene expression and function-based potency assay development

$(000s)		CMC	Pre-/Non-clinical	Clinical	Total
2025	Q1	$400	$36	$271	$790
	Q2	$200	$36	$271	$590
	Q3	$200	$36	$271	$1,590*
	Q4	$200	$36	$271	$490
	Total	$900	$144	$1,085	$3,129
2026	Q1	$3,000	$30	$476	$3,708
	Q2	$2,200	$30	$476	$2,908
	Q3	$3,600	$30	$476	$4,308
	Q4	$100	$30	$476	$4,058**
	Total	$8,900	$120	$1,903	$14,173
2027	Q1	$100	$30	$443	$693
	Q2	$100	$30	$443	$693
	Q3	$100	$30	$443	$693
	Q4	$100	$30	$443	$693
	Total	$400	$120	$2,293	$2,293
2028	Q1	$100	$0	$412	$647
	Q2	$100	$0	$412	$647
	Q3	$100	$0	$412	$2,147
	Q4	$100	$0	$412	$647
	Total	$400	$0	$1,649	$2,049
2025-2028 Total		$10,600	$384	$6,410	$21,644

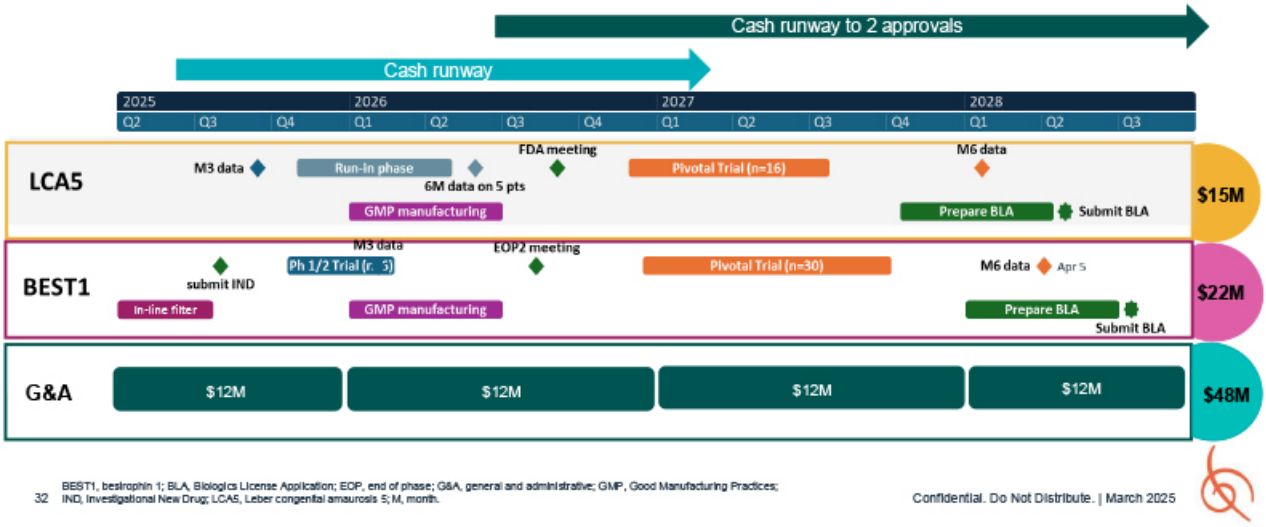
*includes $1,000 license milestone
**includes $3,250 license milestone

BEST1, bestrophin 1; BLA, Biologics License Application; CMC, chemistry, manufacturing, and controls; CRO, contract research organization; FPI, first patient in; GMP, Good Manufacturing Practices; IND, Investigational New Drug; LPI, last patient in; POC, proof of concept.

Timing and Use of Funds
OPGx-LCA5 and OPGx-BEST1

BEST1, bestrophin 1; LCA5, Leber congenital amaurosis 5.

OPGx-LCA5 & OPGx-BEST1 Timing and Use of Funds



BEST1, bestrophin 1; BLA, Biologics License Application; EOP, end of phase; G&A, general and administrative; GMP, Good Manufacturing Practices; IND, Investigational New Drug; LCA5, Leber congenital amaurosis 5; M, month.

Every patient's eyes tell a story

Images of real patients with IRDs.

Confidential. Do Not Distribute. | March 2025

OPGx-LCA5 Phase 1/2 Study: Summary of Patient Demographics

		Subject 01-03	Subject 01-01	Subject 01-04
Age		• 26	• 34	• 19
Sex		• Male	• Female	• Female
Study eye		• OS	• OS	• OD
Date of dosing		• Aug 7, 2023	• Sep 11, 2023	• Nov 13, 2023
LCA5 variants; Allele 1/Allele 2		• Gln279/Gln279	• Arg255Gln/del.Exon1	• Arg255/Arg255
Visual acuity		• OD: HM • OS: HM	• OD: 20/300 • OS: 20/400	• OD: 20/200 • OS: 20/200
Refraction		• OD: +3.00 • OS: +3.00	• OD: -1.50 • OS: -2.50	• OD: +2.25 • OS: +2.00
Foveal thickness (µm)	BL	• OD: 121 • OS: NA	• OD: 123.5 • OS: 127.1	• OD: 232.2 • OS: 226.5
	3M	• OD: 136 • OS: 133.5	• OD: 127.1 • OS: 119.3	• OD: 170.8 • OS: 205.1

Null or non-functional proteins, poor VA, and severe photoreceptor loss (thin retinas/foveas)

34 BL, baseline; HM, hand motion; LCA5, Leber congenital amaurosis 5; OD, right eye; OS, left eye; SRI, subretinal injection.

OPGx-LCA5 Phase 1/2 Study: Study Endpoints

Primary: Safety/Tolerability	Secondary: Efficacy	Exploratory: Efficacy
• DLT events • Procedure-related AEs • Number/severity of AEs • OCT: Changes in total and outer retinal thickness	• Dark-adapted FST • BCVA • Oculomoter control and fixation stability • Dark-adapted TPLR • mVFQ-25 • MLCVA	• Visual function/functional vision • Microperimetry • Kinetic perimetry • VR-O&M test (or DMLMT) • FDT perimetry • LA-TPLR • Additional methods as warranted • Immunogenicity • Neutralizing and binding antibodies to AAV8 • Viral shedding • Antibodies to LCA5 protein • ELISpot assay for T cell responses

AE, adverse event; BCVA, Best corrected visual acuity; DLT, dose-limiting toxicity; DMLMT, digital multi-luminance mobility test; FDT, frequency doubling technology; FST, full-field sensitivity testing; LA-TPLR, light-adapted transient pupillary light reflex; LCA5, Leber congenital amaurosis 5; MLCVA, mesopic, low-contrast visual acuity; mVFQ-25, Modified National Eye Institute Visual Functioning Questionnaire-25; OCT, optical coherence tomography; TPLR, transient pupillary light reflex; VR-O&M, virtual reality orientation and mobility.

OPGx-LCA5 Phase 1/2 Study: Ocular Adverse Events

Subject	Sign or Symptoms	Eye	Unexpected AE	Date of onset	Date of resolution	Surgery related?	Oral steroid-related?/Taper onset	Action taken
01-01	Eye pain	Study (OS)	No	Sep 11	Sep 12	Yes	No	Concomitant medication
	Corneal abrasion	Study (OS)	Yes	Sep 18	Sep 18	No	No	Topical antibiotic and eye patching
01-03	Eye pain	Study (OS)	Yes	Aug 7	Aug 8	Yes	No	Concomitant medication
01-04	Subretinal hyper reflexives	Study (OD)	Yes	Nov 13	Ongoing	Yes	No	Oral prednisone

36 LCA5, Leber congenital amaurosis 5; OD, right eye; OS, left eye.