Preliminary Results from an Adult Participant in a Phase 1b/2a Clinical Study of OPGx-BEST1 Gene Therapy for the Treatment of BVMD and ARB Due to *BEST1* Mutations

Mark E Pennesi, MD, PhD, FARVO
Chief Medical Officer
Steve and Debbie Gray Inherited Retinal Degeneration Endowed Chair
Director, Inherited Retinal Degeneration Center
Retina Foundation: Dallas, Texas

Adjunct Professor of Ophthalmology
Paul H. Casey Ophthalmic Genetics Division
Casey Eye Institute
Oregon Health & Science University

Coauthors:
Aaron Nagiel, MD/PhD[1]
Kaylie Jones, BS[2]
Rajiv Anand, MD[3]
Charles Wykoff, MD/PhD[4]
Ash Jayagopal, PhD, MBA[5]
Sarah Tuller, JD[5]
Sally Tucker, PhD[5]

[1]Children's Hospital Los Angeles, Los Angeles, CA; [2]Retina Foundation, Dallas, TX; [3]Texas Retina Associates, Dallas, TX, [4]Retinal Consultants of America, Houston, TX,[4]; [5]Opus Genetics, Inc., Durham, NC.

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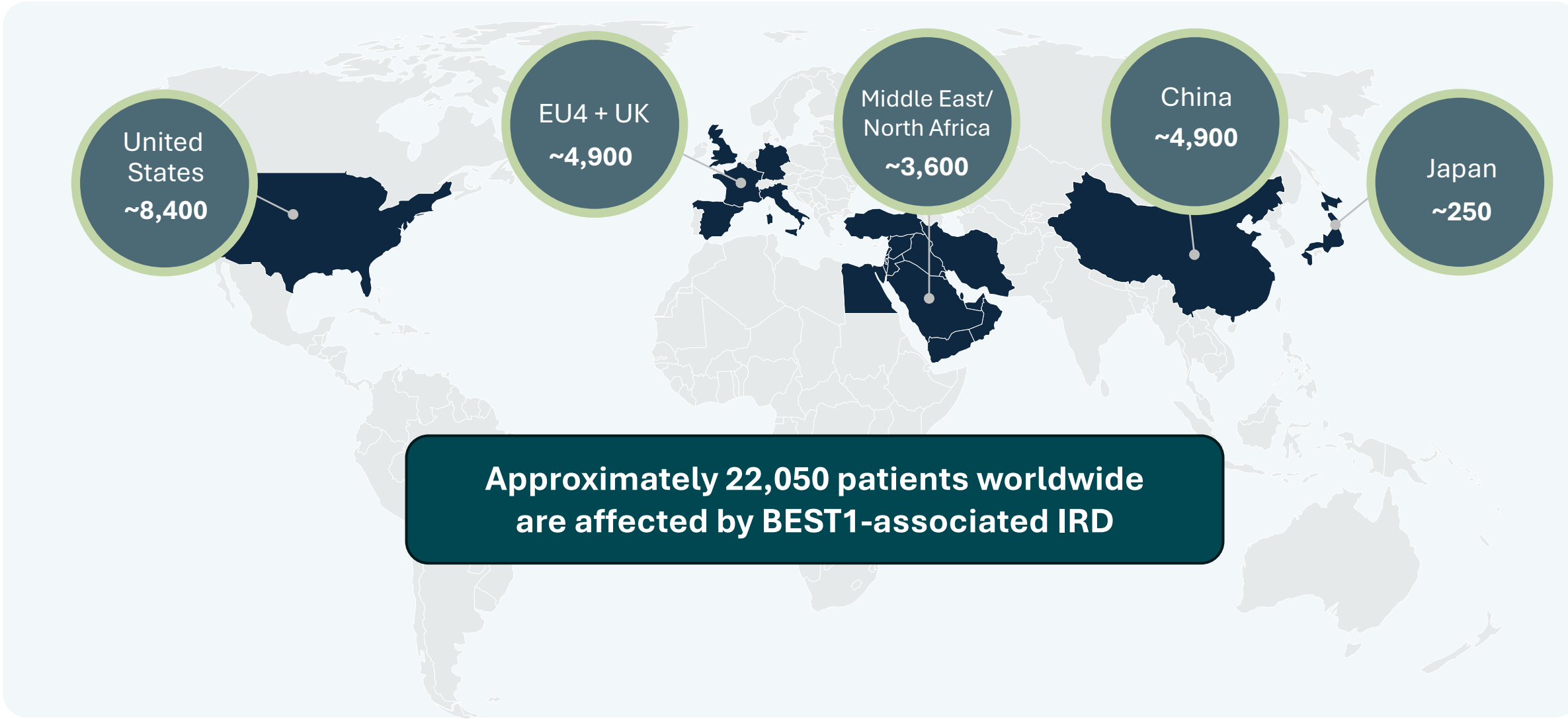
- AJ, S Tucker, S Tuller: Employee, Opus Genetics, Inc.

BEST1-Related Retinopathy Represents One of the Largest IRD Patient Populations Globally



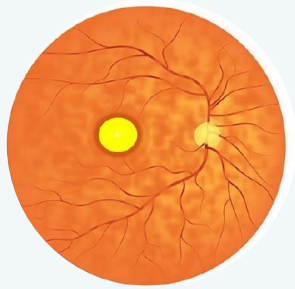
BEST1, bestrophin 1; IRD, inherited retinal disease.

1. Triangle Insights Epidemiology Support for IRDs, conducted January-February 2026.

BEST1 Mutations are Associated with Retinal Degeneration

- *BEST1* mutations are associated with at least five clinically distinct retinal degenerative diseases[1]
- Characterized by retinal lesions, with symptoms including dimness of vision, metamorphopsia, or scotoma[2]
- Mutations, depending on impact on *BEST1* function, may lead to serous retinal detachment, vitelliform lesions, macular atrophy, and loss of central vision[1]
- Exhibits slow rate of decline and central photoreceptors usually remain viable for decades, providing a wide therapeutic window

Three Main *BEST1* Phenotypes



BVMD

- Prevalence – 1:60,000
- Dominant Inheritance
  - Haploinsuffiency
  - Dominant Negative
- Macular dystrophy
- Occult MNV within Vitelliform Material

ARB

- Prevalence ~ 1:1,000,000
- Recessive – Loss of Function
- Severe, multifocal degeneration beginning in childhood

ADVIRC

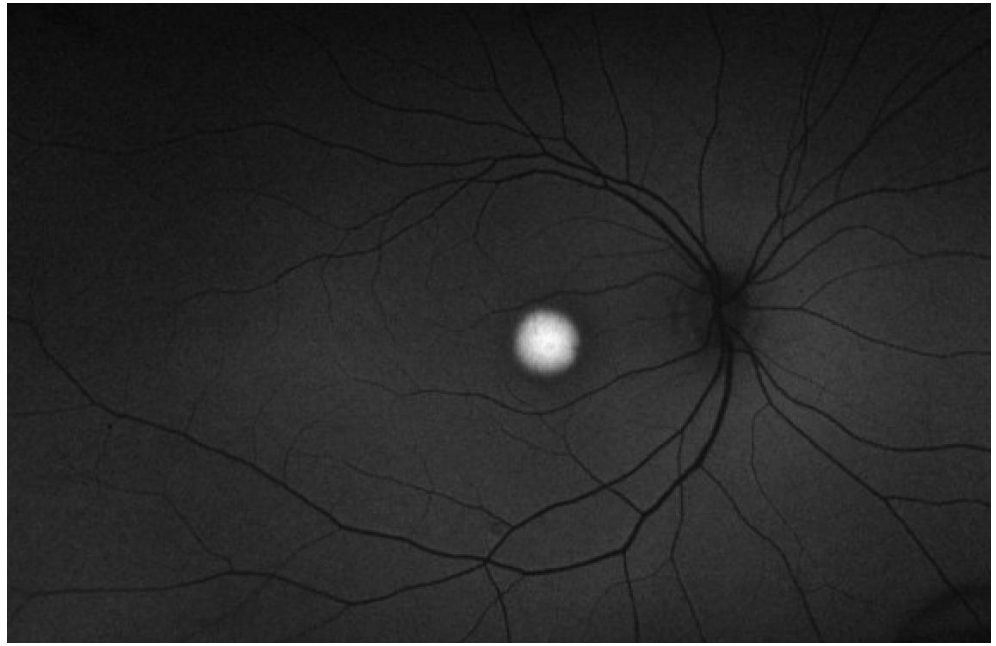
- Very rare < 1:1,000,000
- Dominant – Gain of Function
- Short Axial Length
- Peripheral Pigmentation with distinct boundary

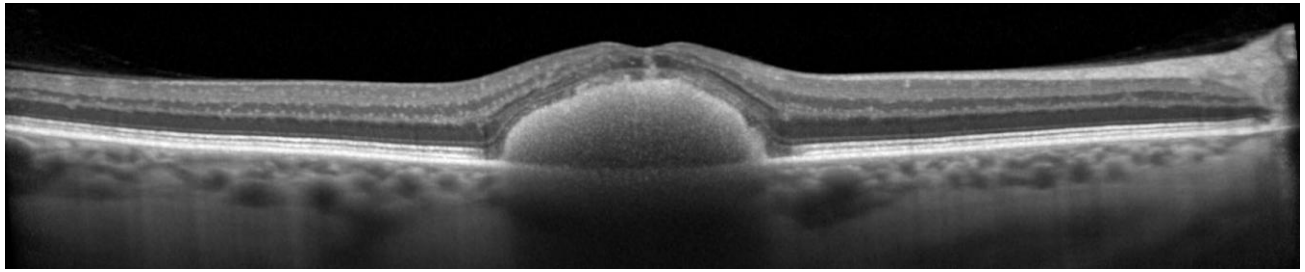
ARB, autosomal recessive bestrophinopathy; AMD, age-related macular degeneration; BCVA, best-corrected visual acuity; BEST1; bestrophin-1; BVMD, best vitelliform macular dystrophy; CNV, choroidal neovascularization.

1. Johnson AA, et al. Prog Retin Eye Res. 2017;58:45-69. **2.** Tripathy K, et al. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.

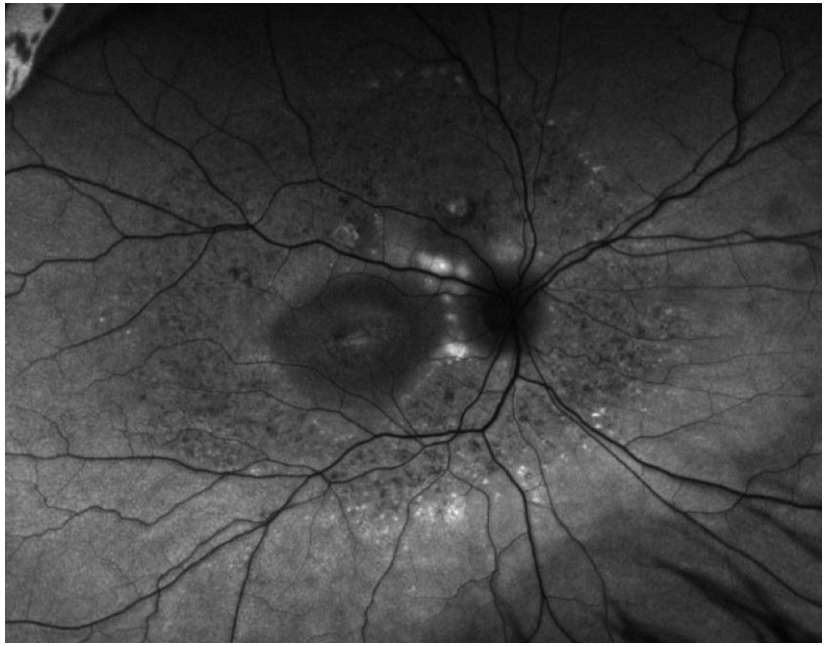
AF and OCT Findings in ARB and BVMD

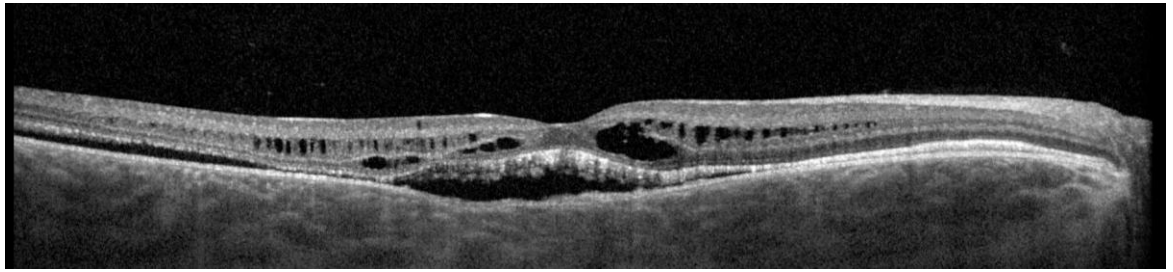
Best Vitelliform Macular Dystrophy





Autosomal Recessive Bestrophinopathy

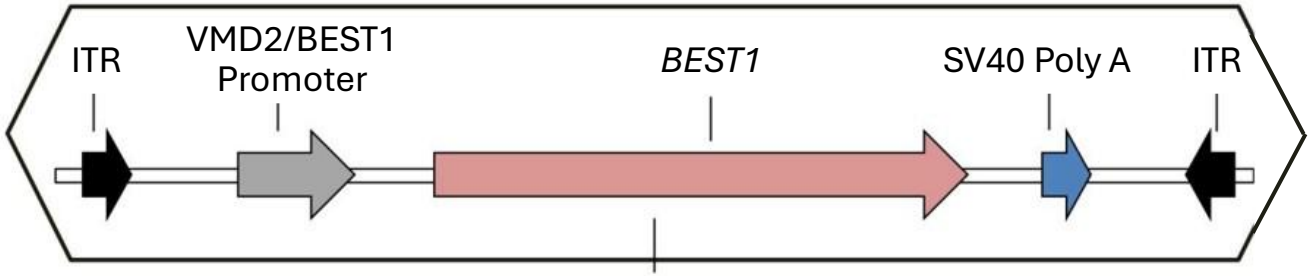




OPGx-BEST1 Gene Therapy

- Leverages AAV2 capsid (employed in voretigene) to deliver functional copy of BEST1 gene
- RPE-specific promoter
- Approach aims to augment the mutated gene and restore normal function of RPE cells

AAV2.VMD2.hBEST1 Vector



Produces healthy wildtype BEST1 protein

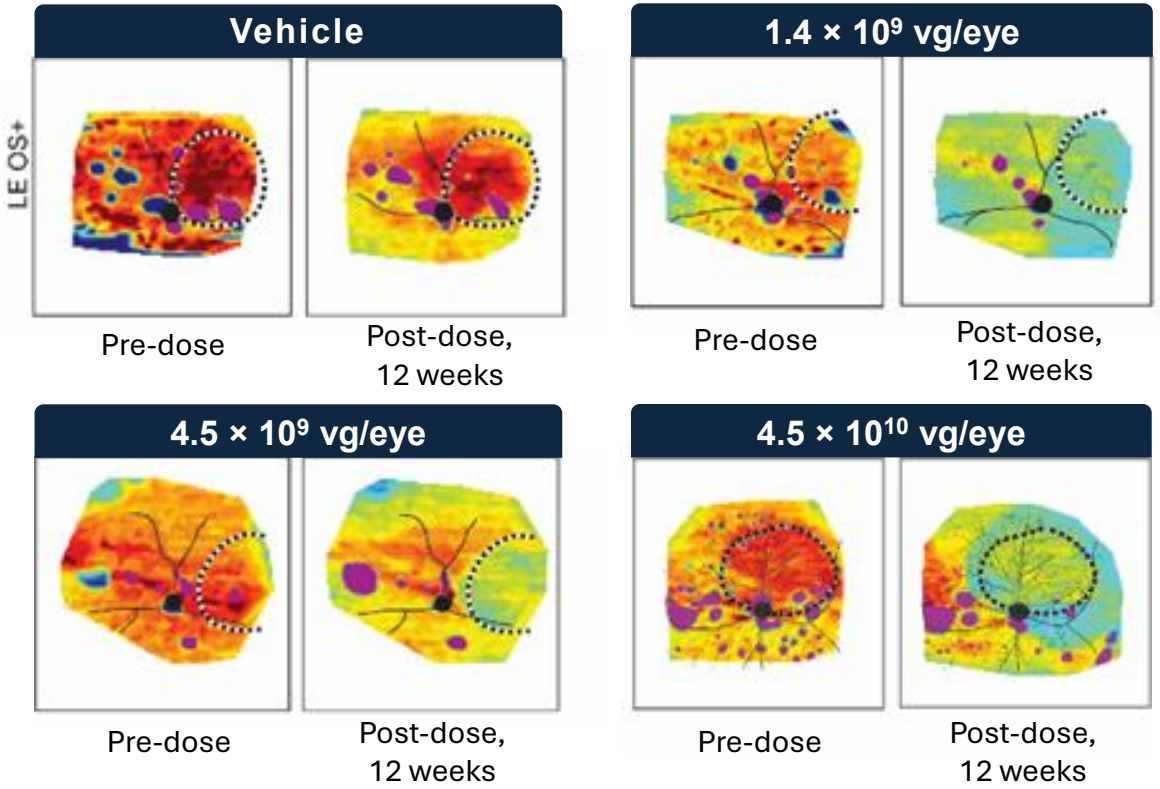
Administered as a one-time subretinal injection and designed to restore retinal ion homeostasis, ameliorating retinal structural and functional deficits

AAV, adeno-associated virus; BEST1; bestrophin-1; ITR, inverted terminal repeats; RPE, retinal pigment epithelium.

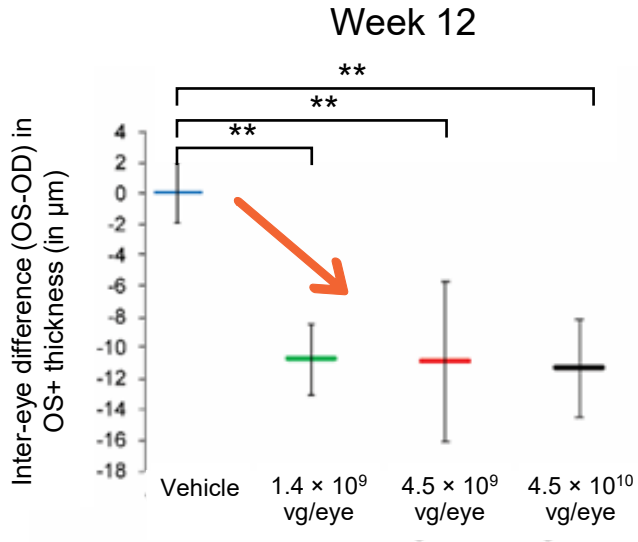
OPGx-BEST1 Reduces Outer Retinal Thickness in a Canine Model

OS+ thickness is a collective measurement of pathologies; Reduction in retinal thickness indicates resolution of vitelliform deposits, edema, and detachments

OS+ Thickness of Treated Eye (OD) Pre-dose and 12 Weeks Post-dose (one eye from one canine):



Significant Reduction in Retinal Thickness in Treated Eye Compared to Untreated Eye



Dashed circle = SR bleb

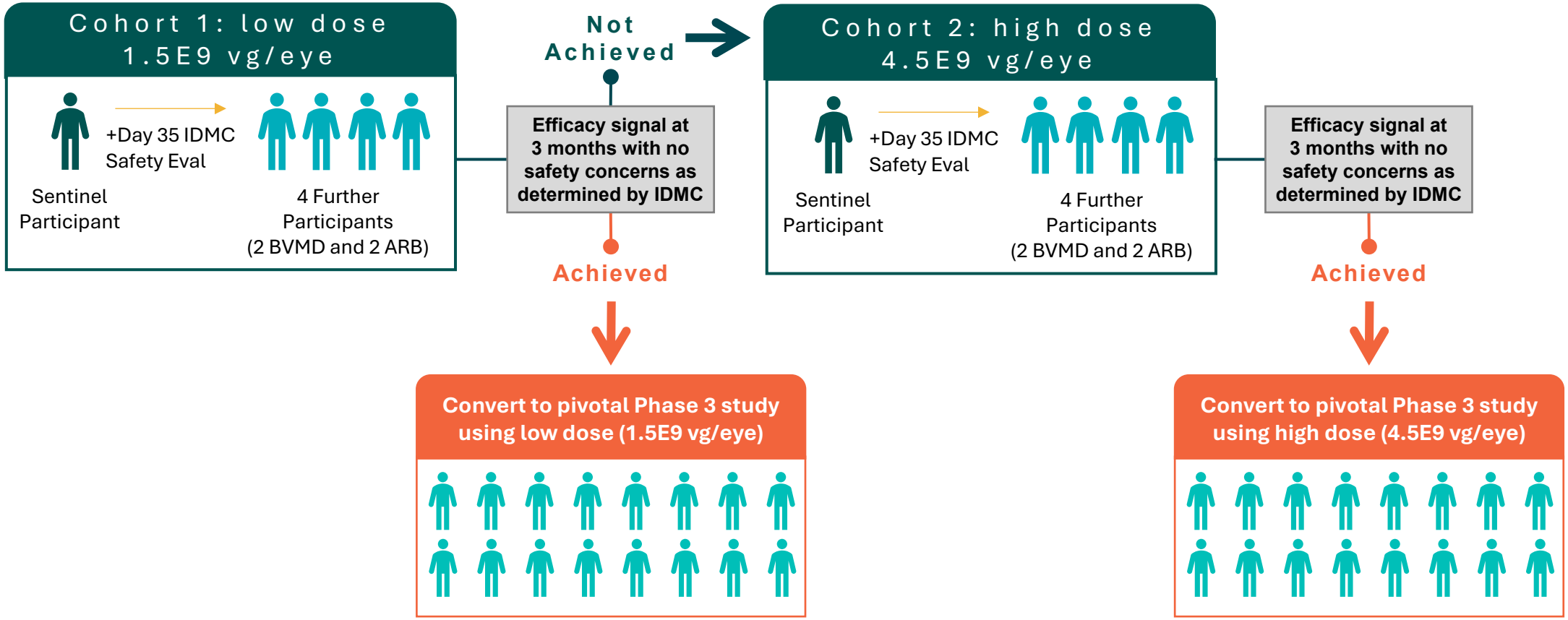
Treatment boundaries are based on fundus photographs of the bleb taken at the time of the injection (dotted lines). Optic nerve and major blood vessels (black) are overlaid.

OS+, outer segment; SR, subretinal.

Data on file.

BIRD-1: Phase 1/2 Study of OPGx-BEST1 Subretinal Gene Therapy is Ongoing

Adaptive, open-label, dose-escalation, safety and tolerability study of a subretinal injection of OPGx-BEST1 in adult (≥18 years old) participants with autosomal dominant BVMD or autosomal recessive ARB



ARB, autosomal-recessive bestrophinopathy; BVMD, best vitelliform macular dystrophy; DAC, dark-adapted chromatic; EOG, electro-oculogram; IDMC, Independent Data Monitoring Committee; OCT-A, optical coherence tomography angiography; SD-OCT, spectral domain optical coherence tomography.

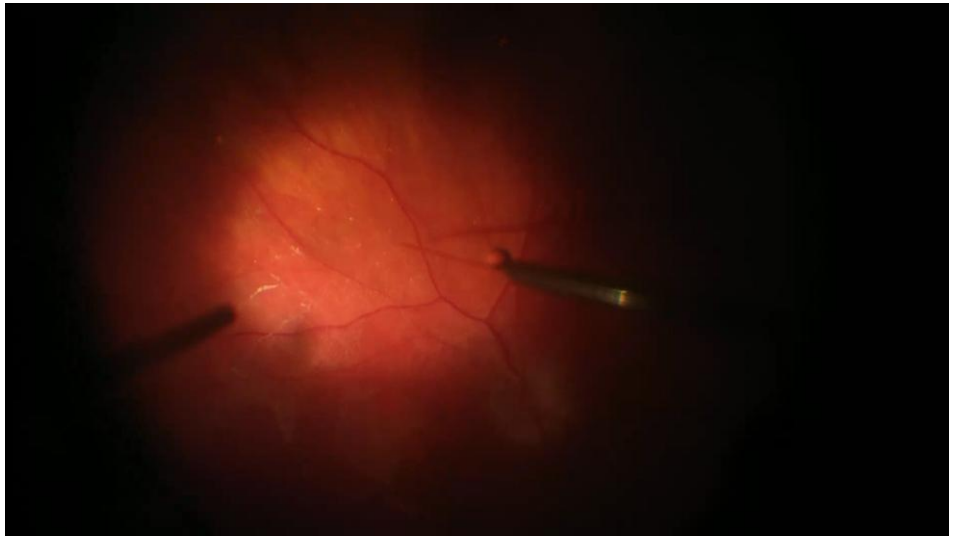
Demographics of Sentinel Participant

Age	63
Sex	Female
Diagnosis year	2015
BEST phenotype	ARB
Study (treated) eye	OS
VA at Baseline (OS)	LogMAR 1.66 (CF)
CST at Baseline (OS)	Atrophic macula
Follow-up duration	3 months (to date)

Worse eye deemed study (treated) eye.
ARB, autosomal recessive bestrinopathy; BL, baseline; CF, counting fingers; OCT, optical coherence tomography; OS, left eye; VA, visual acuity.

Sentinel Participant: Surgical Notes

- 2 major blebs created that surgeon believed were connected
- Estimated >80% of macula was treated with SR blebs
- Areas of chorioretinal atrophy did not elevate intraoperatively, but were adjacent to the blebs above and below
- 2-3 clock hours of macula between ONH & fovea was not elevated intraoperatively



ONH, optic nerve head; SR, subretinal.

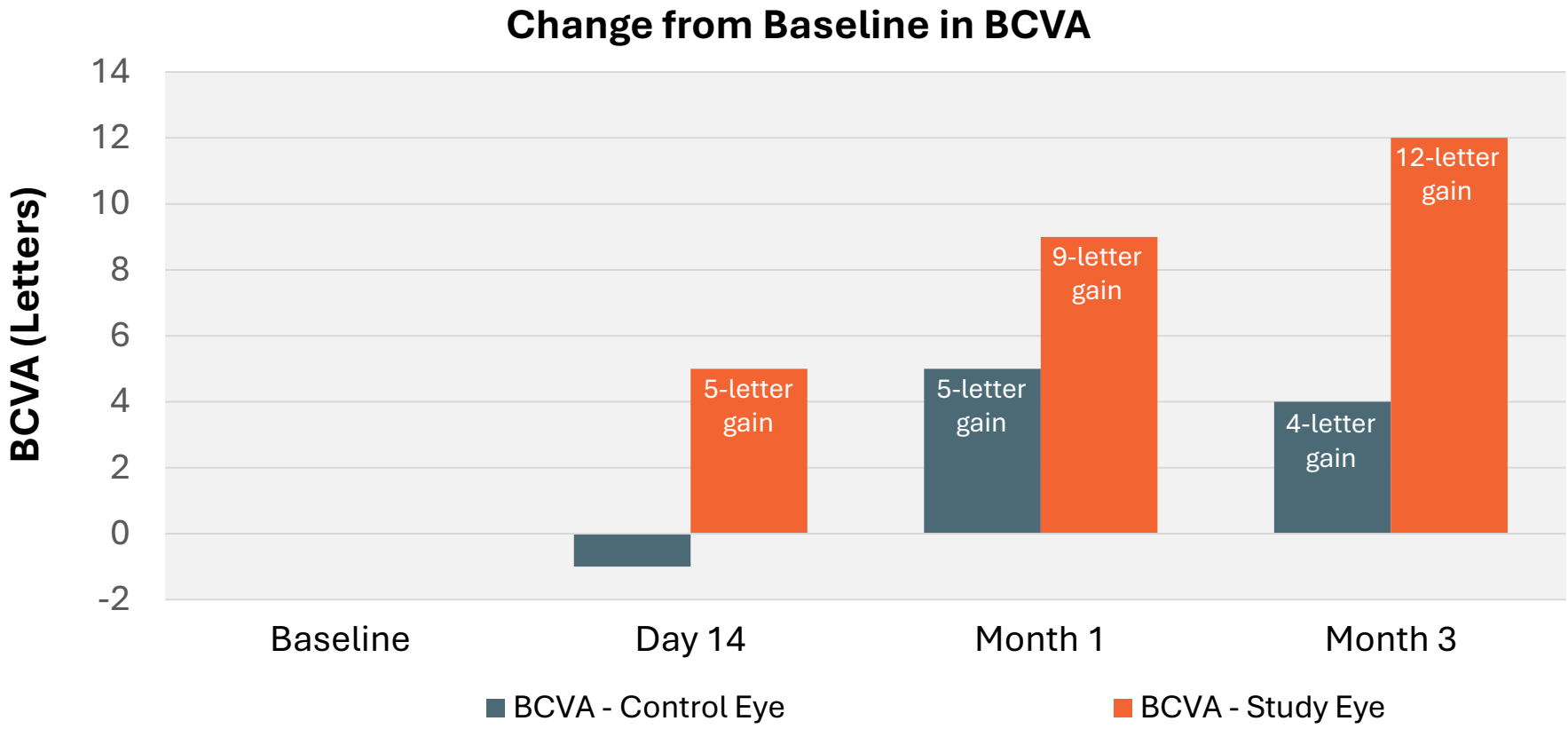
Sentinel Participant: Preliminary Safety Summary

- **Day 14**
  - Few pigmented cells in vitreous
  - No AC inflammation
  - Steroid taper initiated
- **Postop Month #1**
  - No ocular inflammation
  - No ocular AEs
  - No treatment-related AEs or DLT
- **Postop Month #3**
  - No ocular inflammation
  - No ocular adverse events
  - Steroid taper complete

The Independent Data Monitoring Committee (IDMC) meeting resulted in the unanimous consensus to dose remaining participants in low dose cohort

AC, anterior chamber; AE, adverse event; DLT, drug limiting toxicities.

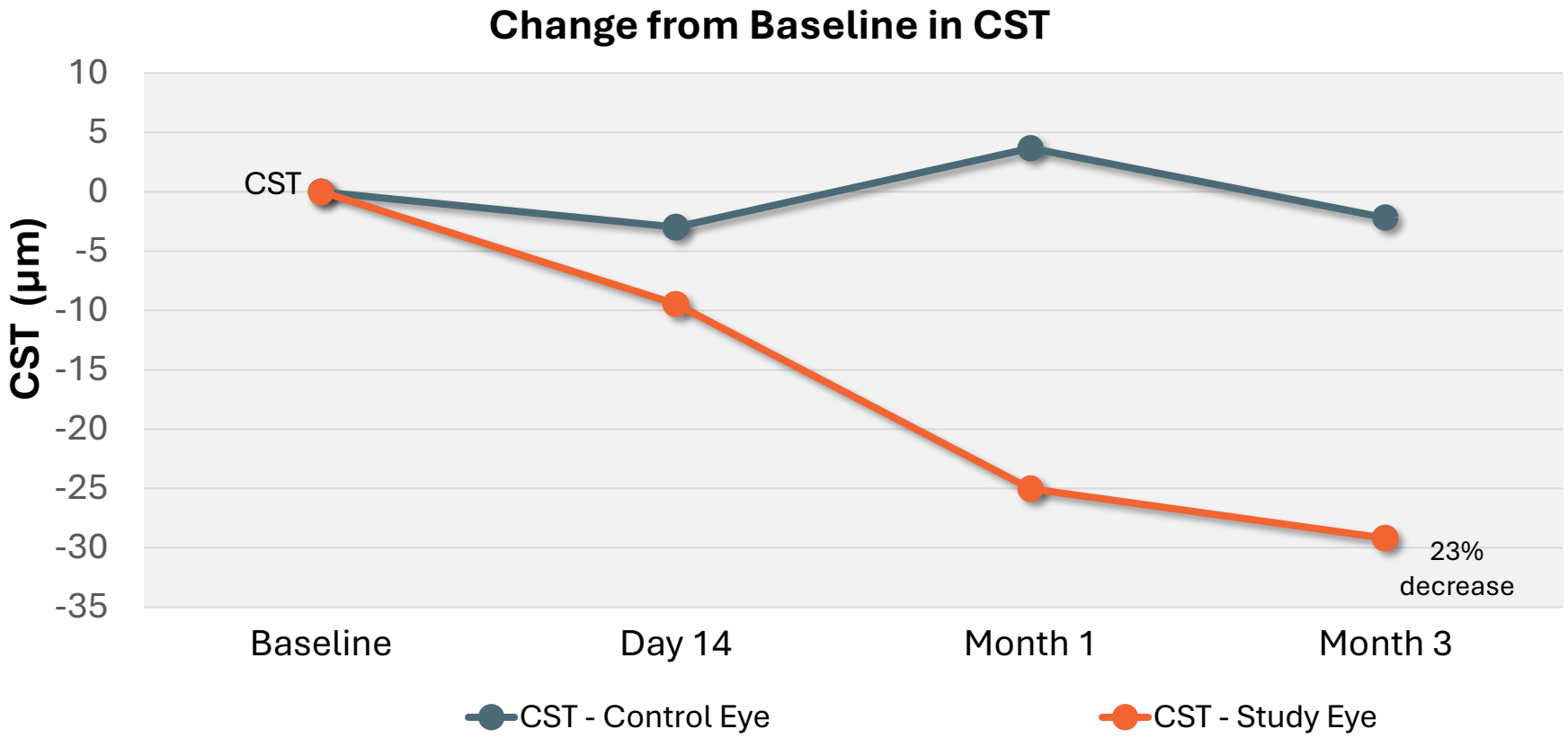
BCVA in the Treated Eye Improved Over 3 Months



Early signal of functional improvement (12 letter gain) observed in the study eye;
Participant commented that their vision was no longer "darkening"

BCVA: equivalent letters
BCVA, best-corrected visual acuity; CST, central subfield thickness.

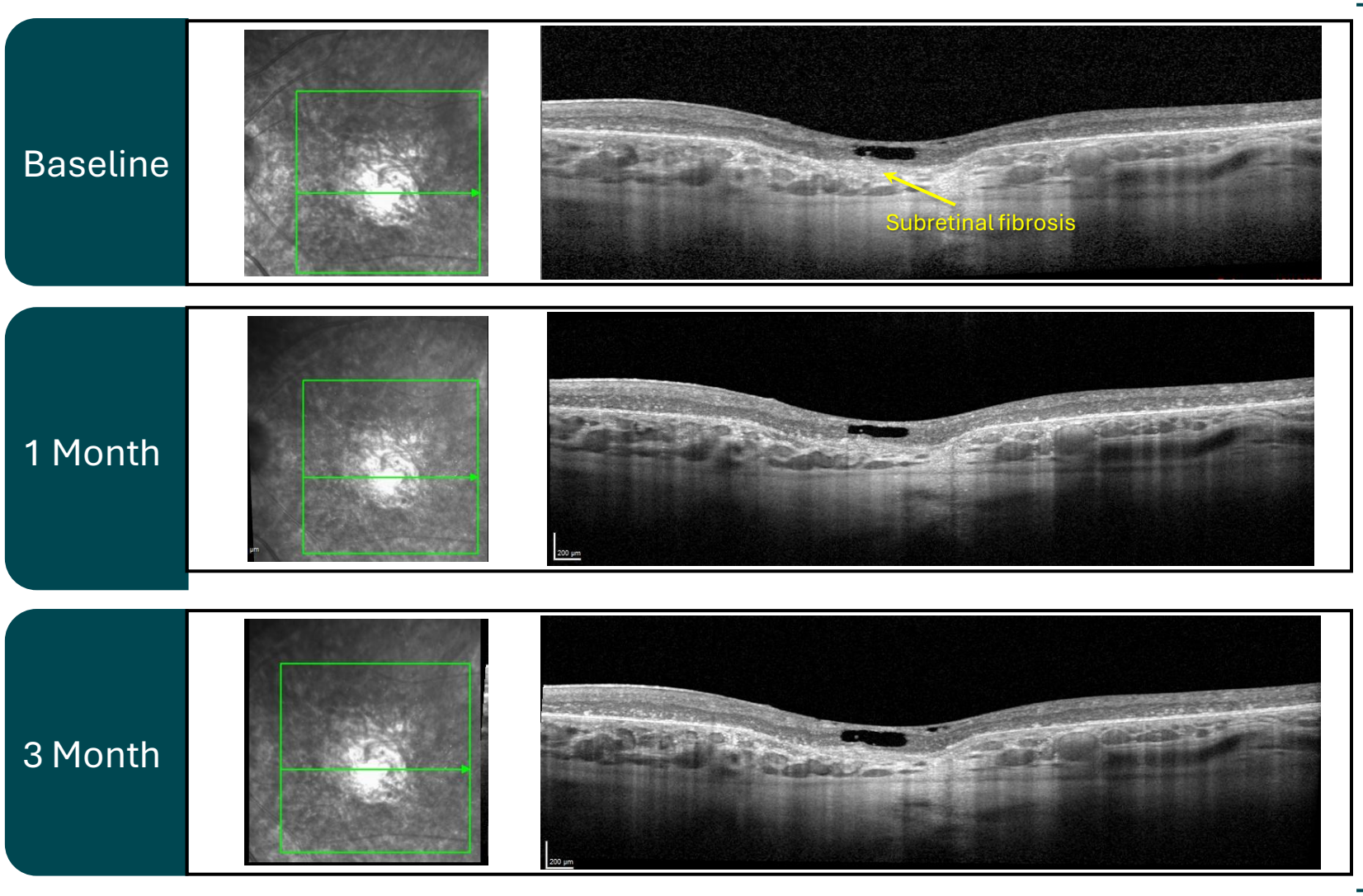
CST in Treated Eye Improved Over 3 Months



Structural improvement (23% decrease) observed in the study eye

BCVA: equivalent letters
BCVA, best-corrected visual acuity; CST, central subfield thickness.

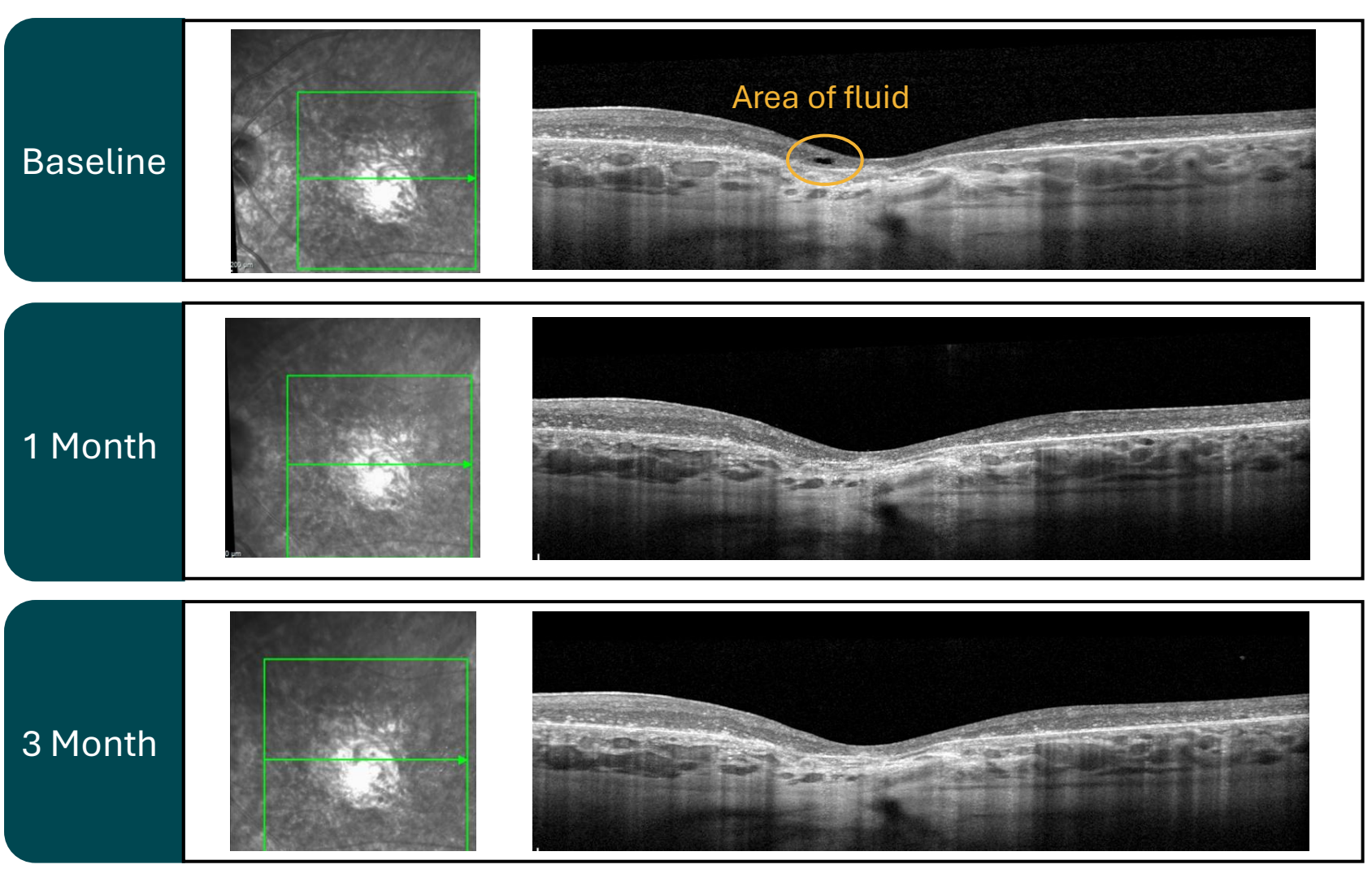
Untreated Area Remained Unchanged Over 3 Months



In areas of absent RPE and severe atrophy outside the bleb, there was no change over time

OCT, optical coherence tomography; OS, left eye; RPE, retinal pigment epithelium.

Treated Area Improved Over 3 Months



Reduction of intraretinal fluid as early as 1 month in areas with less atrophy

OCT, optical coherence tomography; OS, left eye.

Conclusions and Next Steps

- OPGx-BEST1 is a targeted gene augmentation approach designed to restore RPE function and address the underlying cause of BEST1-related IRD
- 3-month results in the sentinel participant show OPGx-BEST1 is well-tolerated with no ocular inflammation, no ocular or treatment-related AEs, and no DLT
- Early Phase 1/2 study results are encouraging with excellent safety data and early signals showing promise for patients with viable RPE
- Second participant has been treated
- 3-month results from the entire Cohort 1 expected in mid-2026

AE, adverse event; BVMD, best vitelliform macular dystrophy; DLT, dose-limiting toxicity; IRD, inherited retinal disease; RPE, retinal pigment epithelium; SAE, serious adverse events.