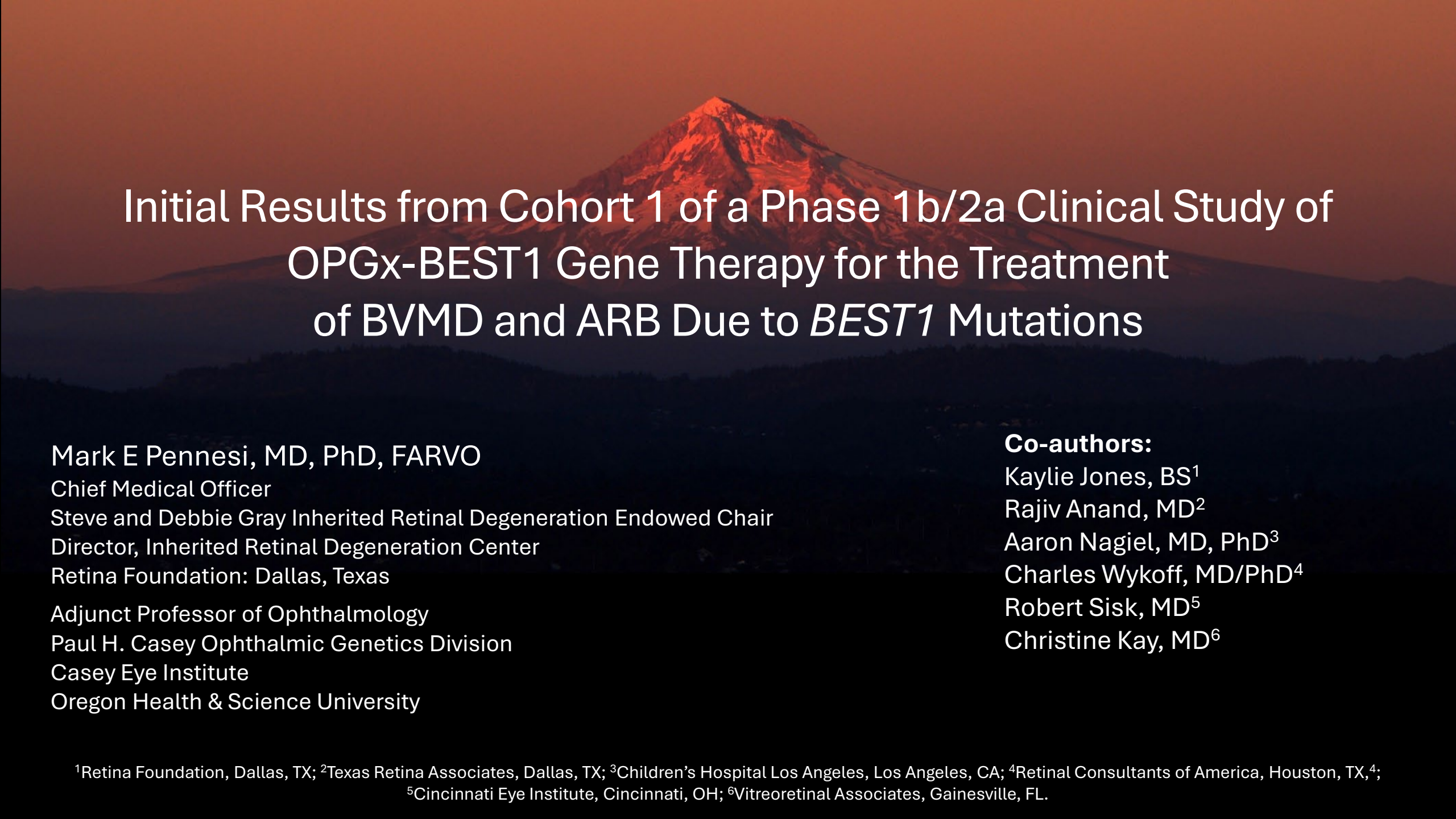




Initial Results from Cohort 1 of a Phase 1b/2a Clinical Study of OPGx-BEST1 Gene Therapy for the Treatment of BVMD and ARB Due to *BEST1* Mutations

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

Co-authors:

Kaylie Jones, BS¹

Rajiv Anand, MD²

Aaron Nagiel, MD, PhD³

Charles Wykoff, MD/PhD⁴

Robert Sisk, MD⁵

Christine Kay, MD⁶

¹Retina Foundation, Dallas, TX; ²Texas Retina Associates, Dallas, TX; ³Children's Hospital Los Angeles, Los Angeles, CA; ⁴Retinal Consultants of America, Houston, TX; ⁴;

⁵Cincinnati Eye Institute, Cincinnati, OH; ⁶Vitreoretinal Associates, Gainesville, FL.

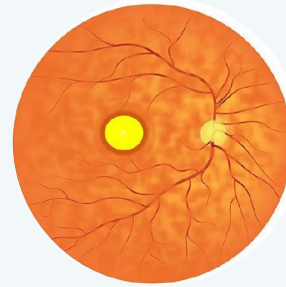
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BEST1 Mutations are Associated with Retinal Degeneration

- *BEST1* mutations are associated with at least five clinically distinct retinal degenerative diseases¹
- Characterized by retinal lesions, with symptoms including dimness of vision, metamorphopsia, or scotoma²
- Mutations, depending on impact on *BEST1* function, may lead to serous retinal detachment, vitelliform lesions, macular atrophy, and loss of central vision¹
- Exhibits slow rate of decline and central photoreceptors usually remain viable for decades, providing a wide therapeutic window

Three Main *BEST1* Phenotypes



BVMD

- Prevalence – 1:15,000
- Dominant Inheritance
 - Haploinsufficiency
 - 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

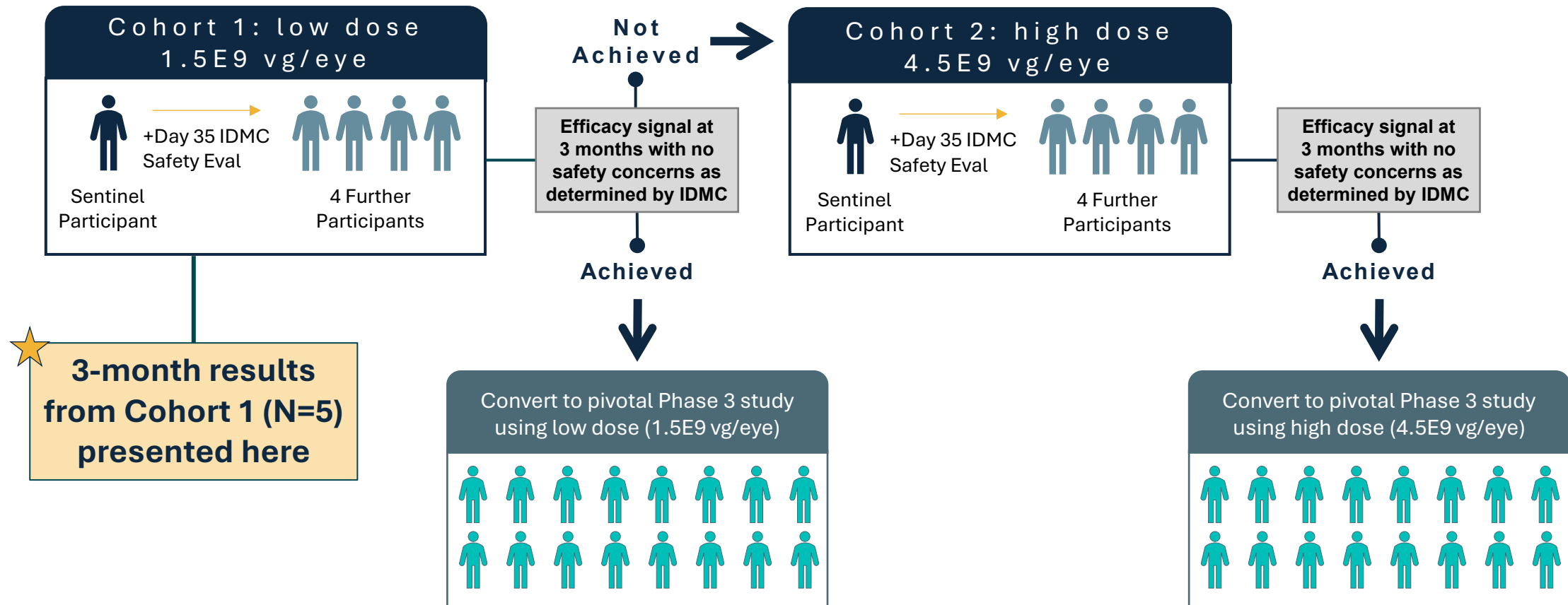


ADVIRC

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

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

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



Participant Demographics: Cohort 1, Low-dose (1.5x10⁹ vg/eye)

	101-101	101-104	102-101	102-102	101-106
Age	63	59	50	45	31
Sex	Female	Female	Male	Male	Male
BEST phenotype	ARB	ARB	BVMD	BVMD	BVMD
Severity of disease	End-stage with significant atrophy	End-stage with significant atrophy	End-stage with sub-foveal, sub-RPE scar	Advanced stage vitello-eruptive with some scarring	Earlier stage without significant atrophy or scarring
ETDRS VA* (study eye [†])	1	50	49	61	47
ETDRS VA* (fellow eye)	43	65	68	72	56
Follow-up duration	6 months	6 months	3 months	3 months	3 months

*ETDRS letters equivalent calculated from logMAR.

[†]Worse eye deemed study eye.

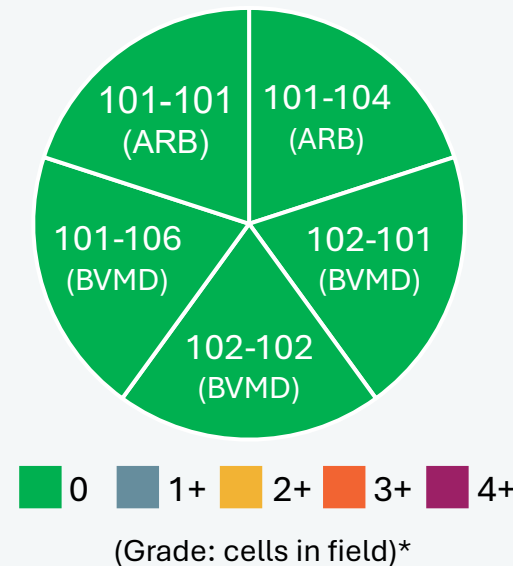
ARB, autosomal recessive bestrophinopathy; BEST, bestrophin; BVMD, best vitelliform macular dystrophy; ETDRS, Early Treatment Diabetic Retinopathy Study; RPE, retinal pigment epithelium; VA, visual acuity.

OPGx-BEST1 Demonstrated a Favorable Safety Profile

OPGx-BEST1 was well-tolerated in all 5 participants:

- No anterior chamber or vitreous cells
- No serious AEs
- No dose-limiting toxicities
- No treatment-related systemic AEs
- All ocular treatment-related AEs were mild/moderate in severity
- No vital sign issues or safety lab findings of note

No anterior chamber or vitreous cells observed in any patient at any study visit



*Based on the SUN Working Group Grading Scheme.

AE, adverse event; ARB, autosomal recessive bestrophinopathy; BVMD, best vitelliform macular dystrophy; .

Summary of 3-month Safety and Efficacy Results from Low-Dose Cohort 1

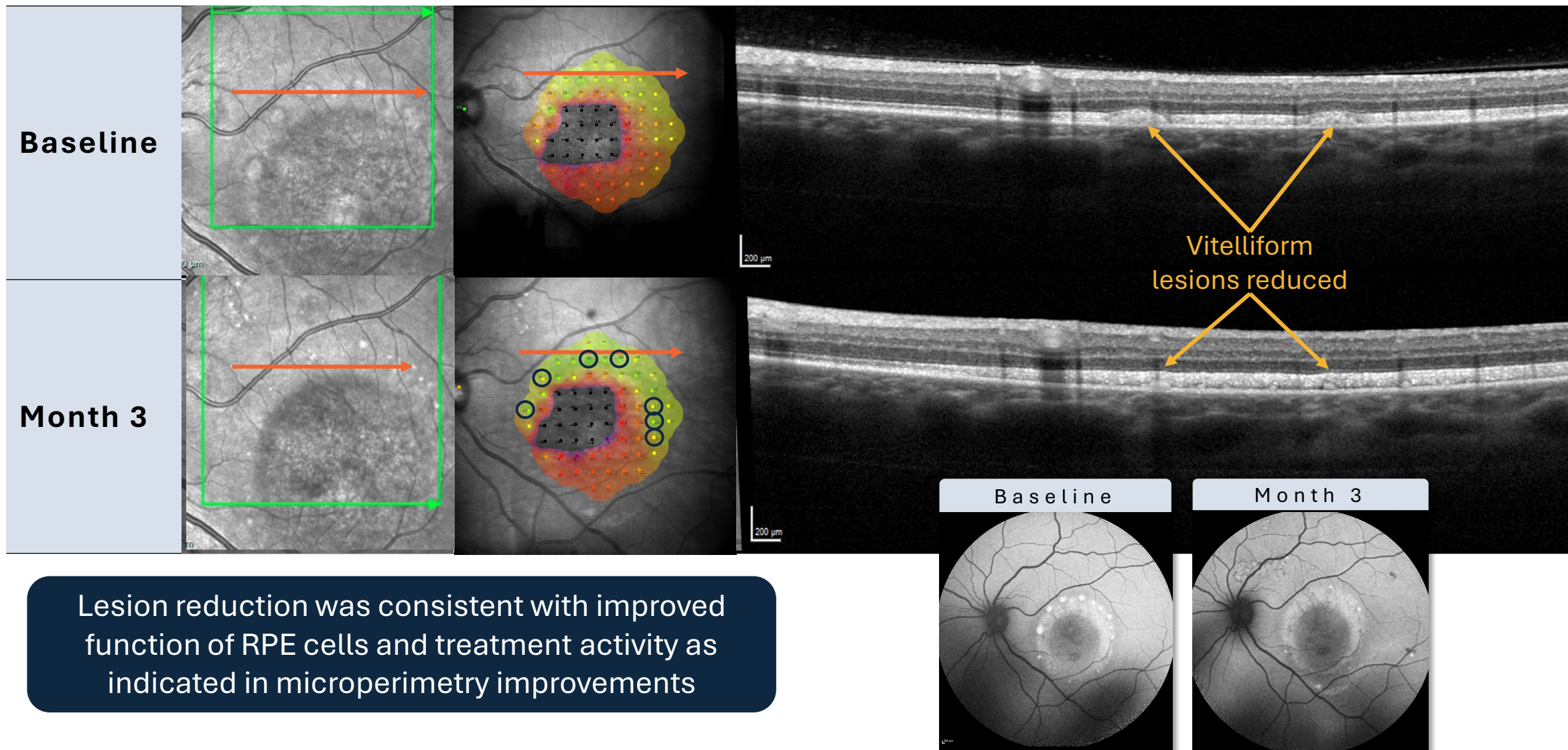
Safety	• OPGx-BEST1 was well-tolerated in 5/5 participants, with no SAEs or DLTs
Structural Endpoints	• 80% of participants (4/5) had structural improvements: • BVMD: 67% of participants (2/3) had a decrease in vitelliform material • ARB: 100% of participants (2/2) had a decrease in intraretinal fluid
Functional Endpoints	• 100% of participants (5/5) had improvements* in at least one functional measure: • Microperimetry – 75% of participants (3/4) improved • BCVA – 60% of participants (3/5) improved • LLVA – 40% of participants (2/5) improved • Contrast Sensitivity – 40% of participants (2/5) improved • Earlier-stage participant (101-106)[†] showed the biggest functional gains, suggesting a potential benefit from earlier treatment

*Improvements defined as: ≥5 letters of improvement from baseline and ≥5 letter improvement from fellow eye in BCVA or LLVA, 0.2 logMAR improvement from baseline in contrast sensitivity, and ≥5 loci cluster improvement by ≥3 decibels in RPE Transitional Zone on microperimetry.

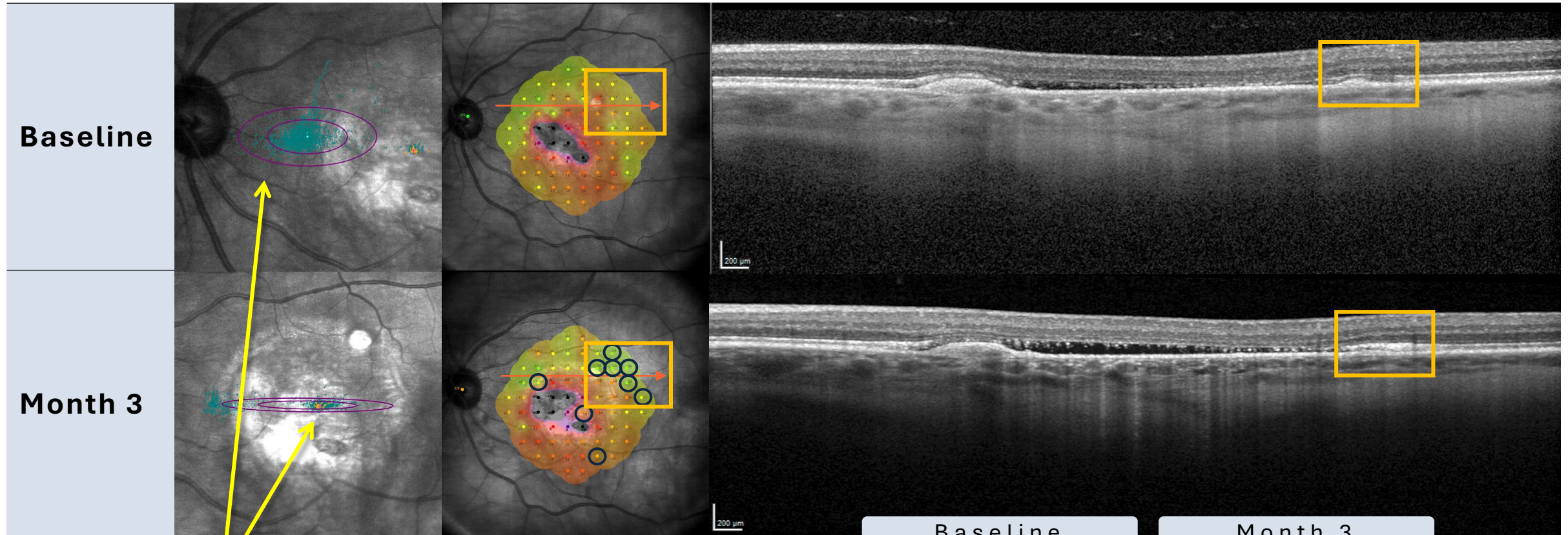
[†]101-106 was the youngest participant with most recent onset of disease and less progressive disease than other participants.

ARB, autosomal recessive bestrophinopathy; BCVA, best-corrected visual acuity; BVMD, best vitelliform macular dystrophy; DLT, dose-limiting toxicity; LLVA, low-luminance visual acuity; logMAR, logarithm of the minimum angle of resolution; RPE, retinal pigment epithelium; SAE, serious adverse event.

Participant 101-106 (BVMD): Vitelliform Material Reduction Co-localized with Microperimetry Improvements

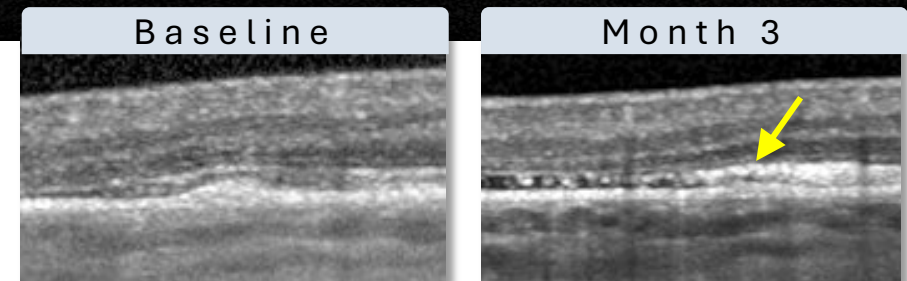


Participant 102-102 (BVMD): Microperimetry Improved in the Treated RPE Transitional Zone

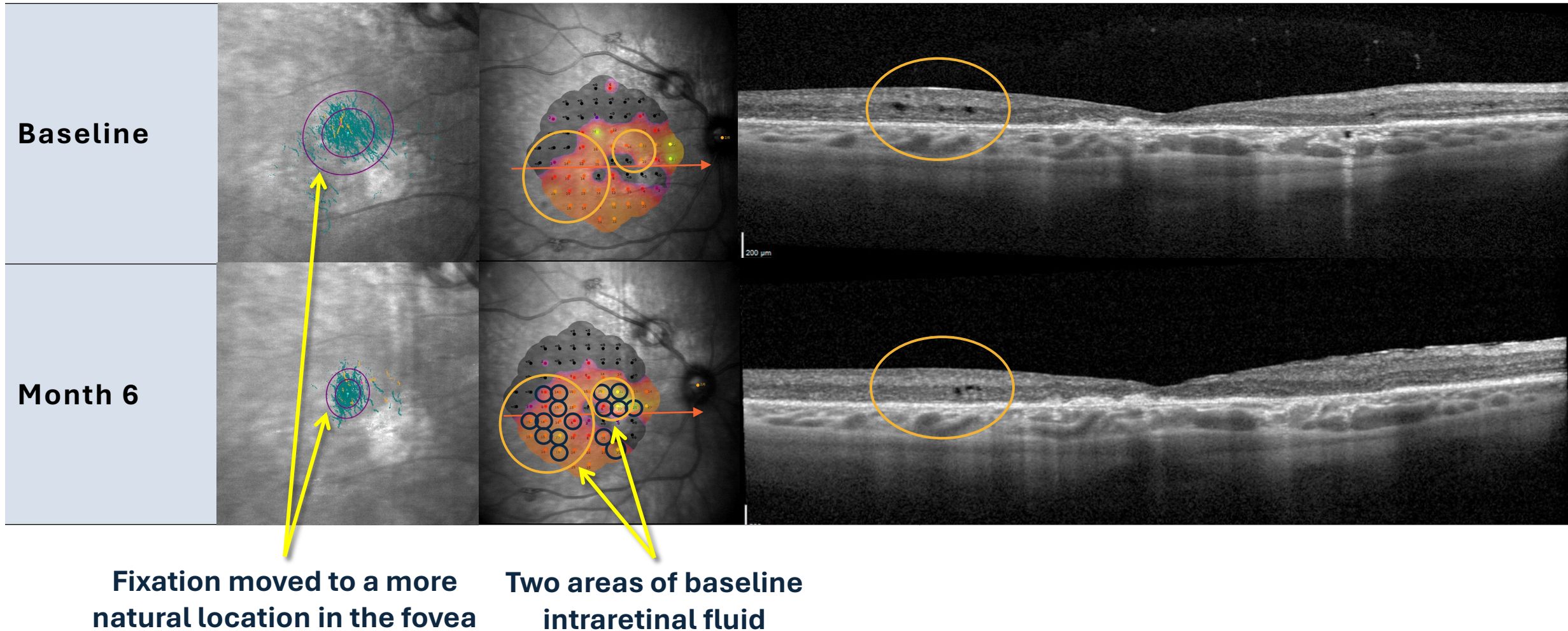


Fixation moved to a more natural location in the fovea

Yellow box represents treated transitional zone.
BVMD, best vitelliform macular dystrophy; RPE, retinal pigment epithelium.



Participant 101-104 (ARB): IRF Improvement Co-localized with Microperimetry Improvement



Yellow circles denote pockets of intraretinal fluid.

Total macular intraretinal fluid volume: Baseline = 19.06 μL , Month 6 = 7.55 μL .

ARB, autosomal recessive bestrophinopathy; IRF, intraretinal fluid.

Summary and Next Steps

- **3-month results in the ongoing, low-dose Cohort 1 (N=5) demonstrated:**
 - OPGx-BEST1 was well-tolerated with with no SAEs, no DLTs, and no intraocular inflammation;
 - Signs of efficacy observed on both functional and structural endpoints
- **IDMC recommended the Phase 1/2 trial advance to Cohort 2 at the higher dose**
 - Over-enrollment of 8 participants with dosing completion expected Q4 2026 and topline 3-month data expected Q2 2027
- **Positive FDA Type C meeting aligned on potential pivotal endpoints**, including use of ≥ 3 dB microperimetry improvement in ≥ 5 prespecified loci area and anchored to a PRO