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APAO
Eyes on the Future: Innovating Ophthalmology

Gene Therapy for BEST1 Inherited Retinal Disease

Ash Jayagopal, PhD, MBA

Nargiza,
BEST1 patient

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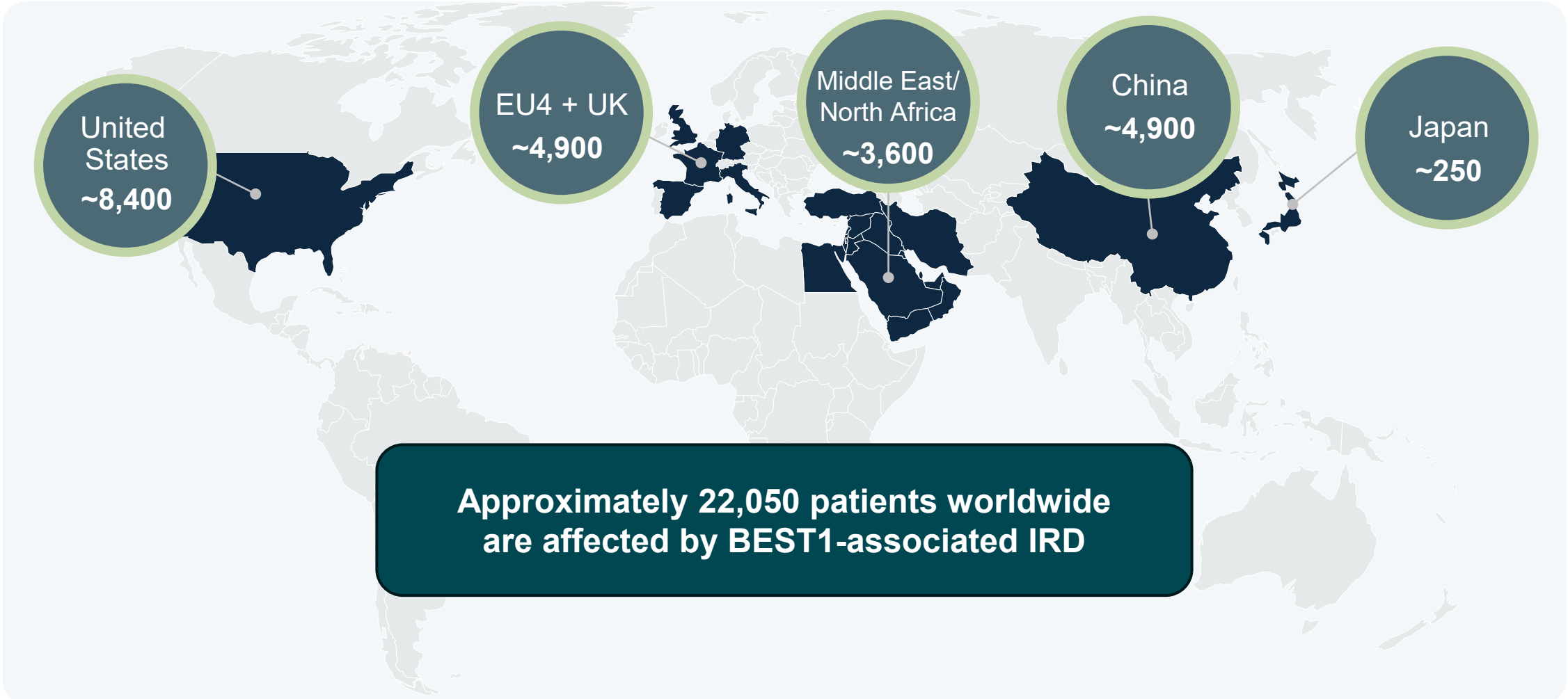
Disclosure

- Ash Jayagopal, PhD, MBA is the Chief Scientific and Development Officer at Opus Genetics

BEST1 Represents One of the Largest IRD Patient Populations Globally

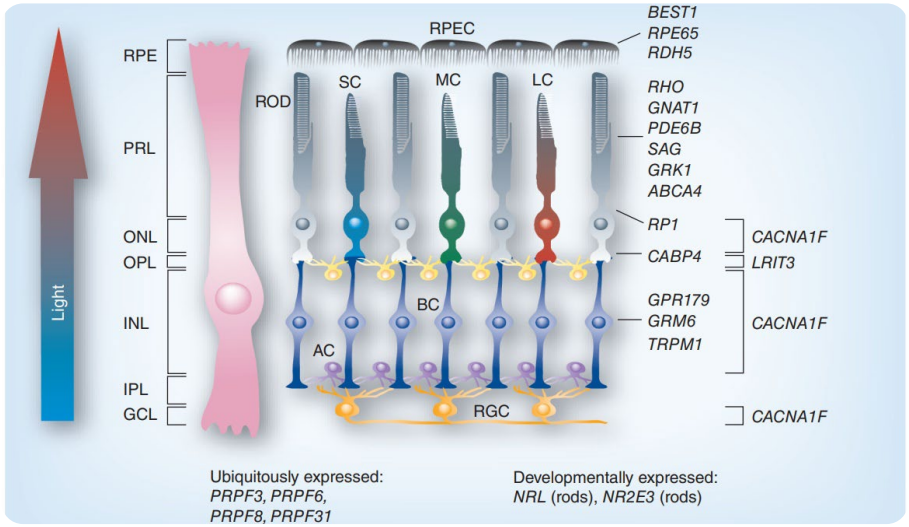


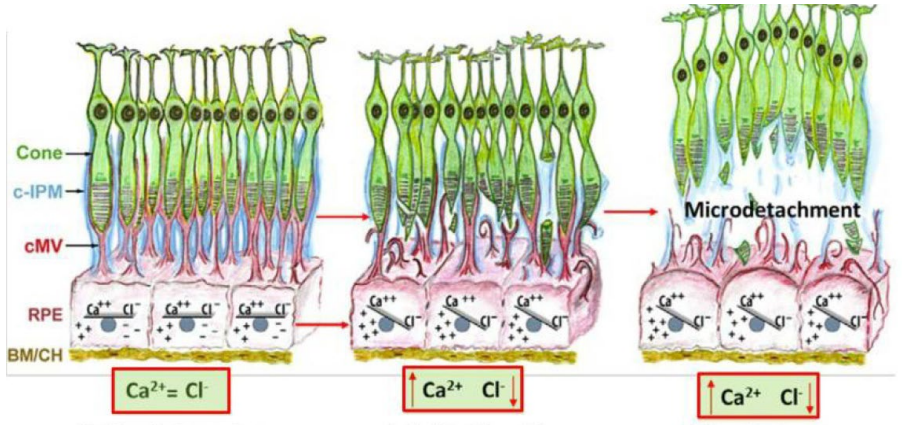
BEST1, bestrophin 1; IRD, inherited retinal disease.
Triangle Insights Epidemiology Support for IRDs, conducted January-February 2026.

BEST1 Disease Biology

- BEST1 gene encodes for Bestrophin-1 (basolateral RPE)
- 585 AA homo-**pentameric** transmembrane protein (5 BEST1 monomers are required for full length BEST1 channel)
- Ca2+-activated Chloride channel (CaCC)
  - Transepithelial ion transport of intracellular calcium
  - RPE cell volume
  - Homeostasis of subretinal space / IP matrix

The BEST1 protein is a pentamer that assembles as a complex of five identical monomers

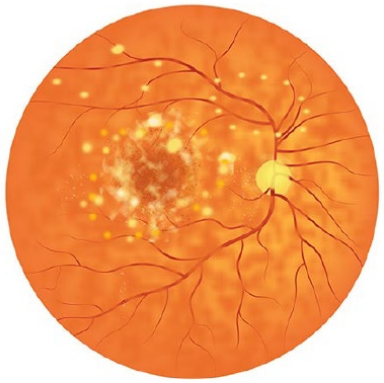




BEST1, bestrophin 1; IP, interphotoreceptor; IRD, inherited retinal disease; RPE, retinal pigment epithelium.

BEST1 IRDs: Clinical Staging and Pathology of Two Main Phenotypes

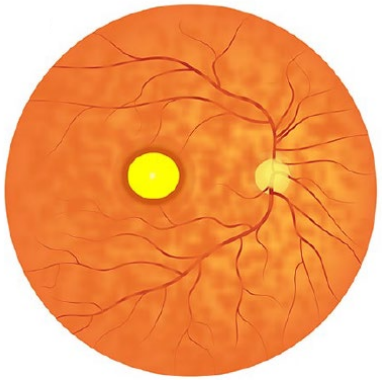
ARB



ARB prevalence: 1:1,000,000

- Severe, multifocal degeneration beginning in childhood

BVMD



BVMD Prevalence: 1:60,000

- Macular dystrophy similar to AMD with teen onset
- 20/60 and worse BCVA observed beginning at Stage 3 disease, leading to choroidal neovascularization, retinal detachment, chorioretinal atrophy

BVMD Stages

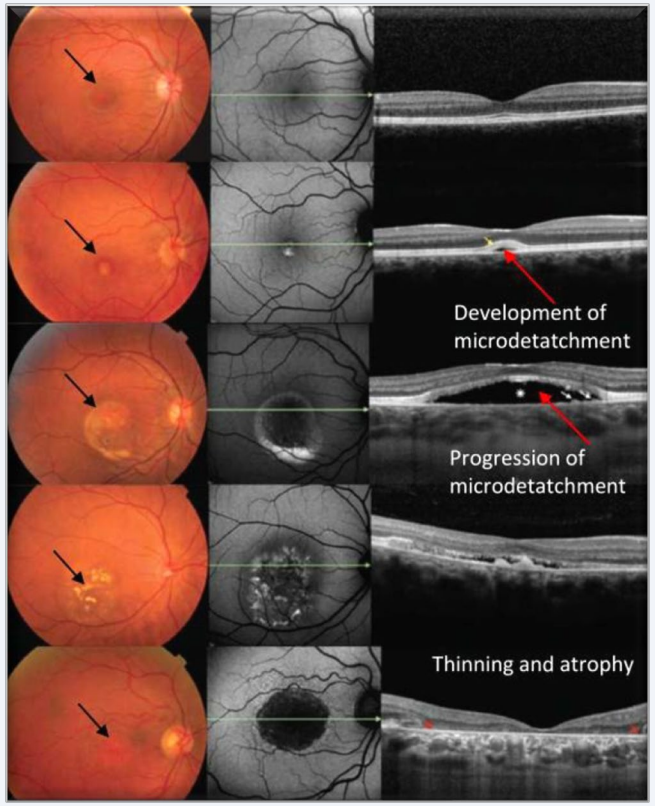
Stage 1: Pre-vitelliform

Stage 2: Vitelliform

Stage 3: Pseudohypopyon

Stage 4: Vitelliruptive

Stage 5: Atrophy/Fibrosis



BVMD, best vitelliform macular dystrophy; ARB, autosomal recessive bestrophinopathy; AMD, age-related macular degeneration; BCVA, best-corrected visual acuity; IRD, inherited retinal disease; OCT, optical coherence tomography.

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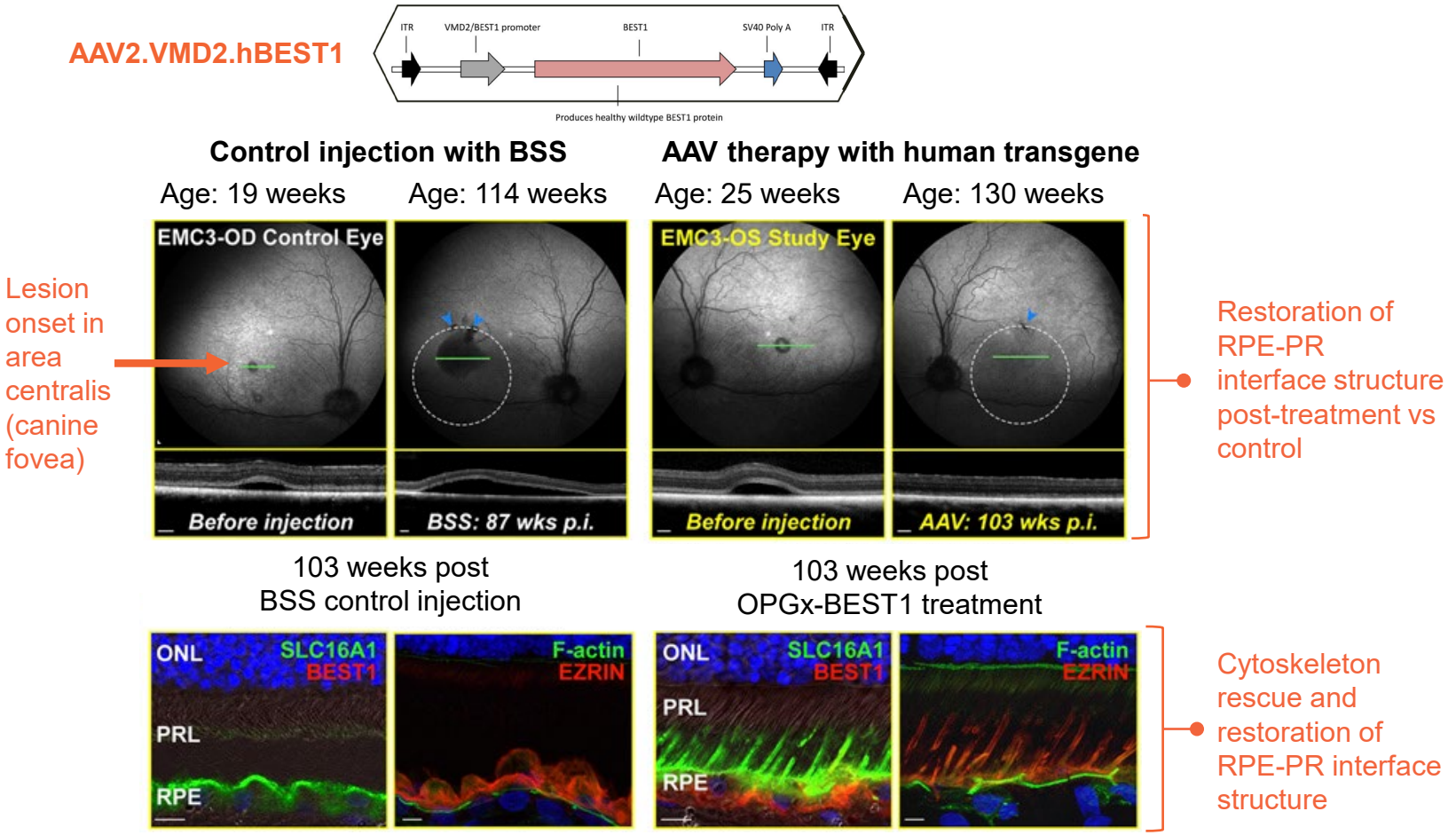
Proof-of-concept Study of OPGx-BEST1 AAV2 in Canine Model of ARB

- Robust restoration of RPE-photoceptor interface demonstrated in canine models of ARB
- 9 dogs treated with low dose (1.4E9 vg/eye) and high dose (4.5E9 vg/eye); 16-108 weeks
- De-risked AAV2 capsid, with AAV2.VMD2 clinical precedent (MERTK) with no known safety issues
- Treated cBEST1 models exhibit **reversal of lesions and retinal microdetachments, which are hallmarks BEST1 disease**
- Regression of lesions and dose-dependent ERG improvement with favorable safety profile supporting clinical dosing

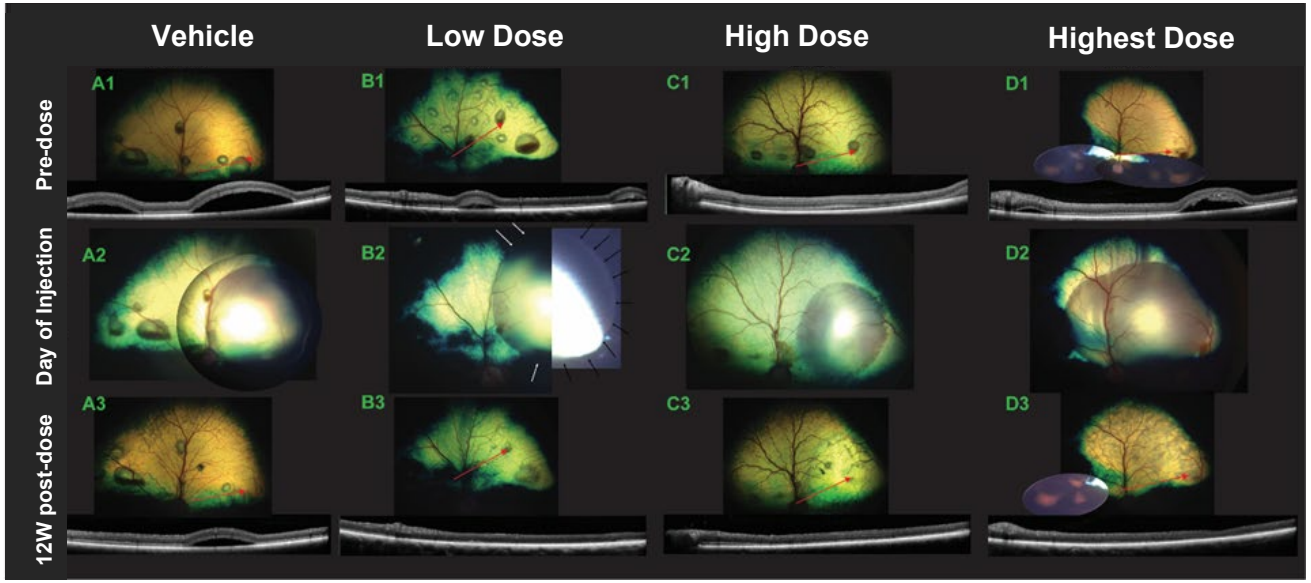


BSS, balanced salt solution; ERG, electroretinogram; MERTK, MER proto-oncogene, tyrosine kinase; RPE, retinal pigment epithelium.
Guziewicz, et al. *PNAS.* 2018;115:E2839–E2848.

IND-enabling Efficacy and Toxicity Study of AAV2/2-BEST1 in BEST1 Mutant Dogs

- 12 BEST1-mutant dogs received single subretinal injection of AAV2/2-BEST1 (OS)
- Contralateral eye (OD) remained untreated
- Age range: 17-194 weeks
- Study duration: 13 weeks

		Dose Level		
Dose	Number of Animals	Vector Concentration (vg/mL)	Total Dose (vg per eye)	Injection Volume (mL)
Vehicle	3	0	0	~ 0.15
Low	3	9.5×10^9	1.4×10^9	~ 0.15
High	3	3.0×10^{10}	4.5×10^9	~ 0.15
Highest	3	3.0×10^{11}	4.5×10^{10}	~ 0.15

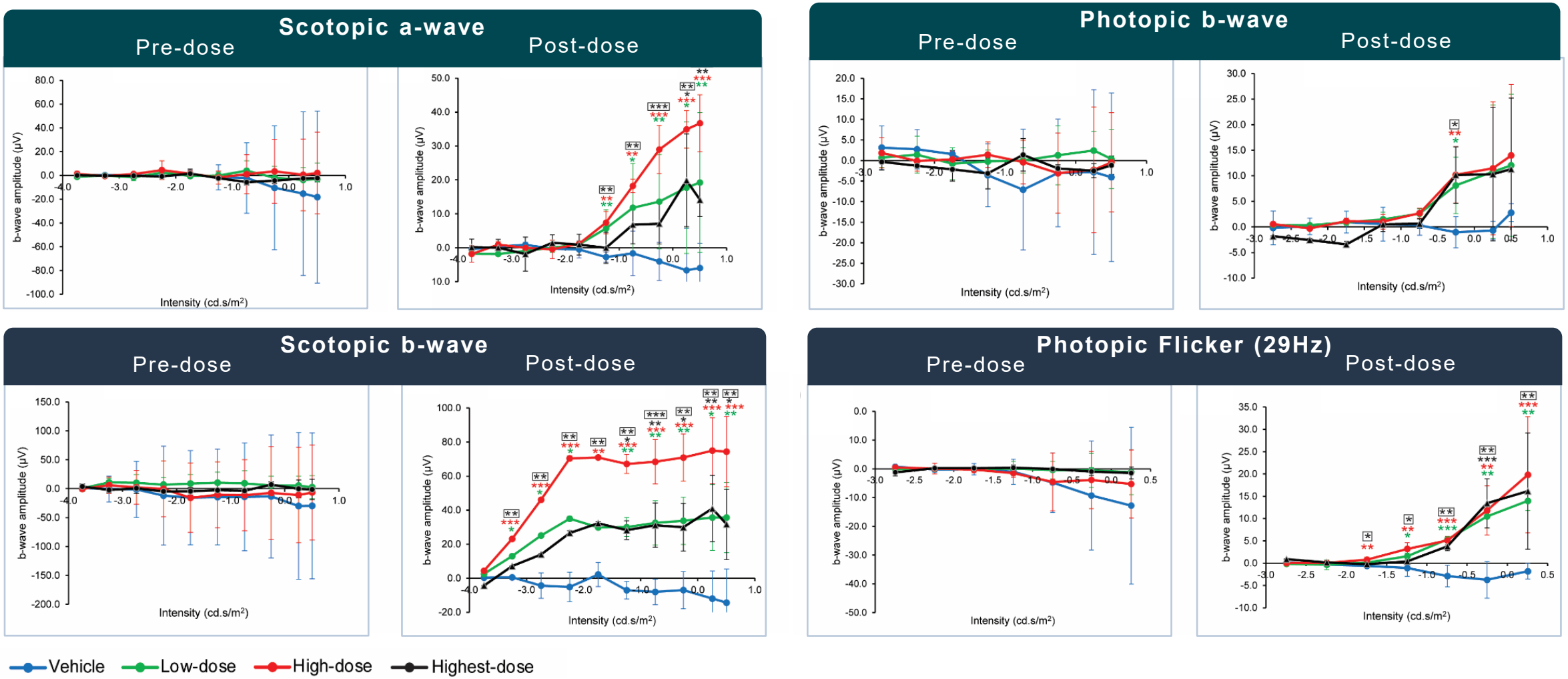


Retinal imaging illustrates location and appearance of the treated area

All treatment groups displayed multiple Stage II/III lesions

BEST1, Bestrophin-1; OD, right eye; OS, left eye.
Data on file.

Dose-dependent Statistically Significant Difference in Mean Inter-ocular ERG Differences at 11 Weeks Post-dose



Boxed asterisks represent p values from the one-way ANOVA
Colored asterisks represent p value of Bonferroni post-hoc analysis: *= p< 0.05, **= p ≤ 0.01, and ***= p ≤ 0.001

Data on file.

Potential Treatment-Associated BEST1 Lesion Improvement Observed at Week 12

BEST1 Lesion(s)	Pre-dose	Week 12
Non-Treated Eyes		
Stage II- Vitelliform	2/12	4/12
Stage III-Pseudohypopion	6/12	6/12
Treated Eyes (Treated Area)		
Vehicle		
Stage II- Vitelliform	1/3	1/3
Stage III-Pseudohypopion	1/3	0/3
Low Dose (1.4×10^9 vg/eye)		
Stage II- Vitelliform	0/3	1/3
Stage III-Pseudohypopion	**1/3**	**0/3**
High Dose (4.5×10^9 vg/eye)		
Stage II- Vitelliform	0/3	0/3
Stage III-Pseudohypopion	**1/3**	**0/3**
Highest Dose (4.5×10^{10} vg/eye)		
Stage II-Vitelliform	**1/3**	**0/3**
Stage III-Pseudohypopyon	**2/3**	**0/3**

Non-Treated and Vehicle Treated Eyes:
Demonstrated persistent BEST1 lesions

Treated Eyes:
Demonstrated potential efficacy

- **Low Dose:** A stage III lesion reverted into a stage II lesion at Week 12 in one dog
- **High Dose:** A single focal stage III was no longer detectable at Week 12 in one dog
- **Highest Dose:** One dog presented with a stage II lesion that resolved at Week 12; Two dogs presented with stage III lesions that resolved at Week 12

BEST1, Bestrophin-1; OD, right eye; OS, left eye.
Data on file.

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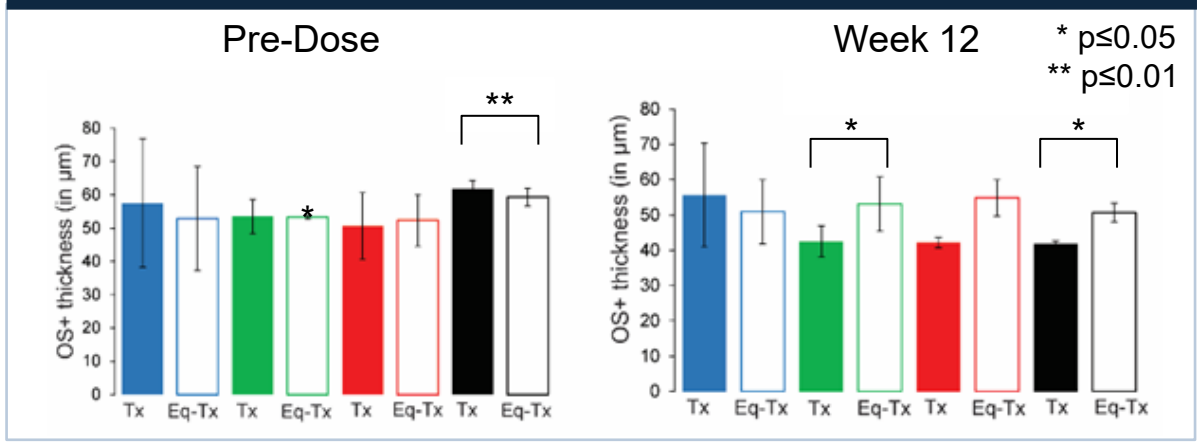
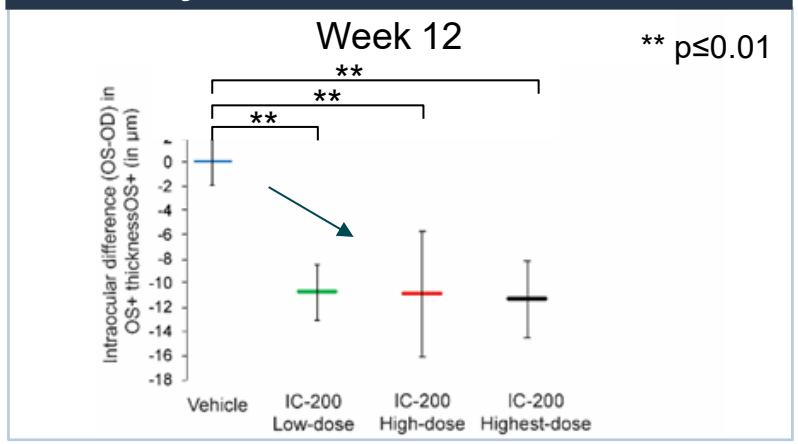
Outer Segment and Outer Nuclear Layer Thickness Pre-dose and at Week 12

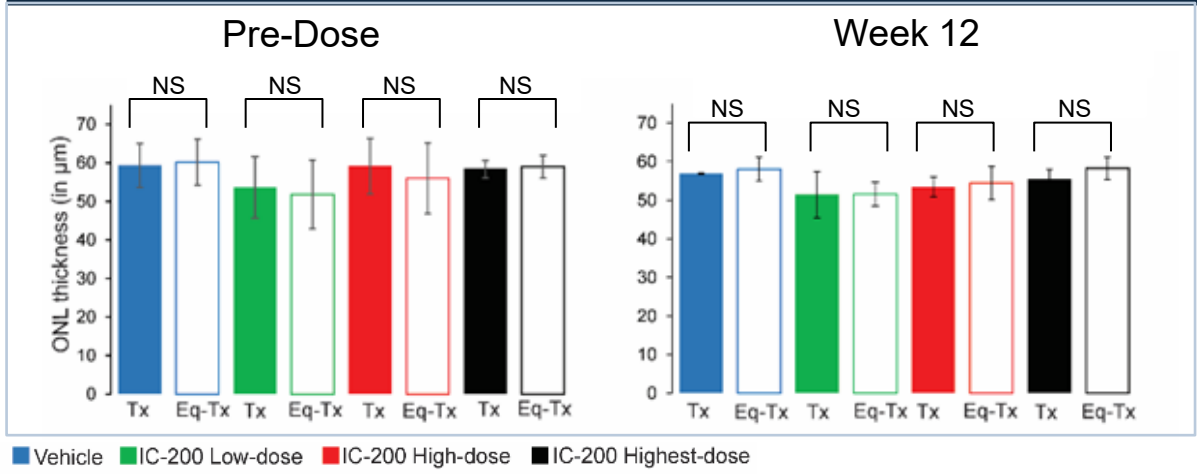
OS+ Thickness



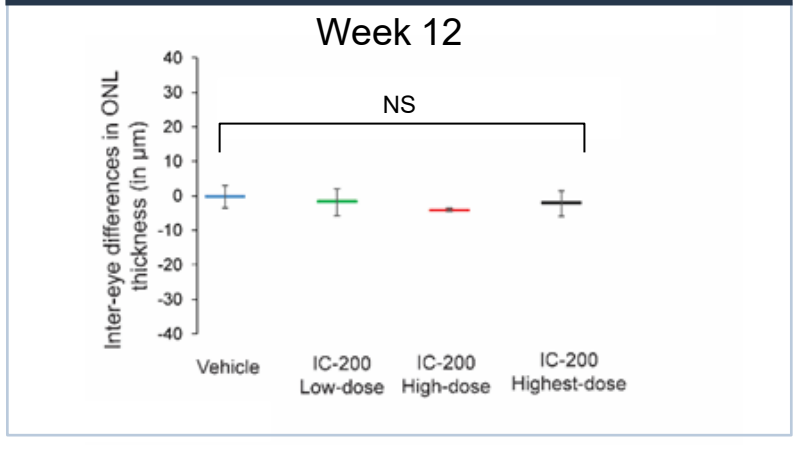
Inter-Eye Difference in OS+ Thickness



ONL Thickness

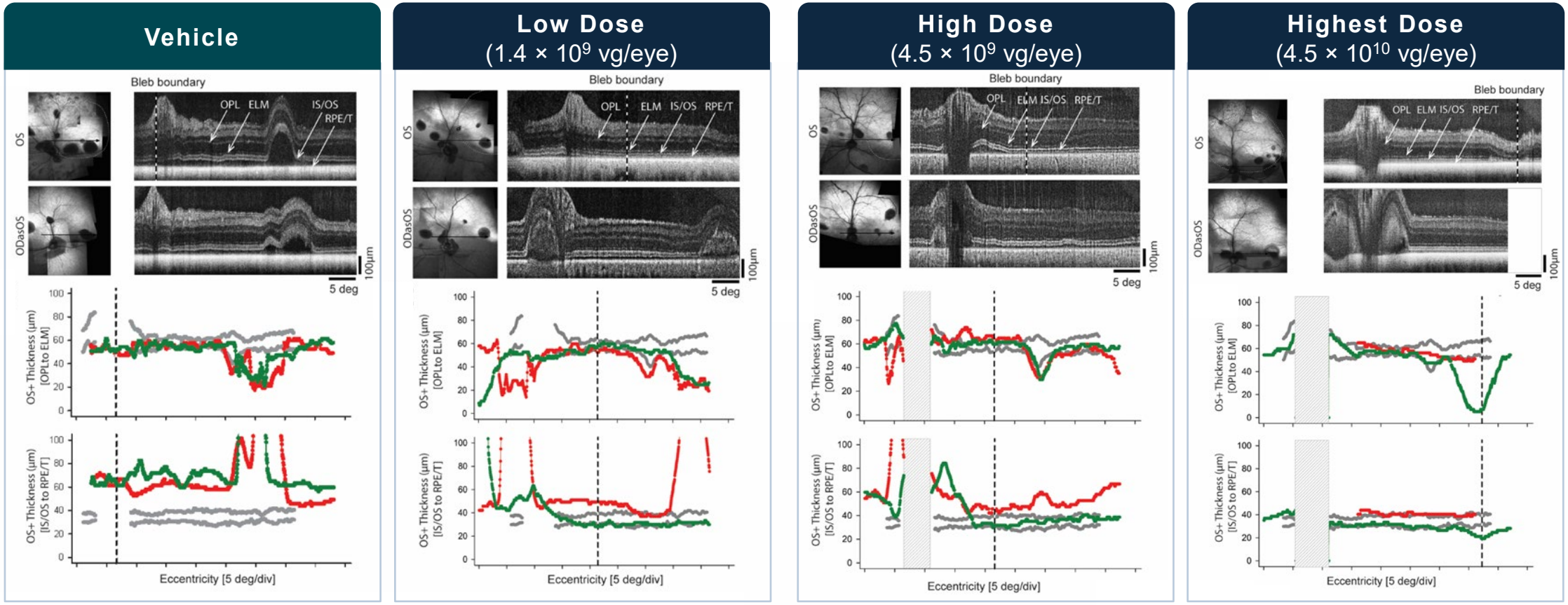


Inter-Eye Difference in ONL Thickness



Eq-Tx, equivalent treatment area in untreated eyes; NS, non-significant; OS+, outer segment; ONL, outer nuclear layer; Tx, treatment area in treated eyes.
Data on file.

OCT Confirmed All Doses Resulted in Reduction of OS+ Thickness, with Statistically Significant Reductions in Low and High Dose Groups



Treated eye
Non-treated eye in the same area
Wild type non-treated dog in the same area
Bleb border

OCT, optical coherence tomography; OS+, outer segment.
Data on file.

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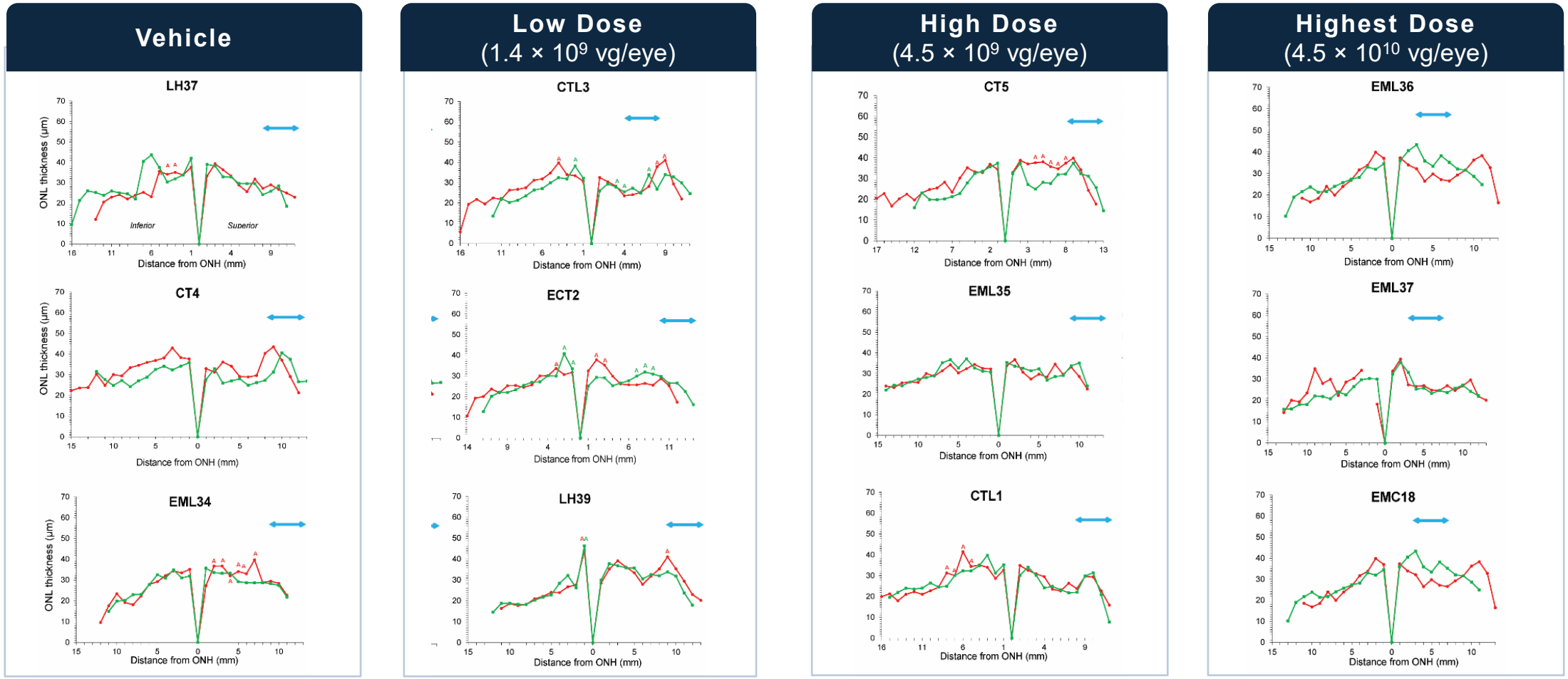
ONL Thickness Quantified by Histology at 13 Weeks Post-Treatment



OD, right eye; ONL, outer nuclear layer; OS, left eye.
Data on file.

No Evidence of Toxicity Observed

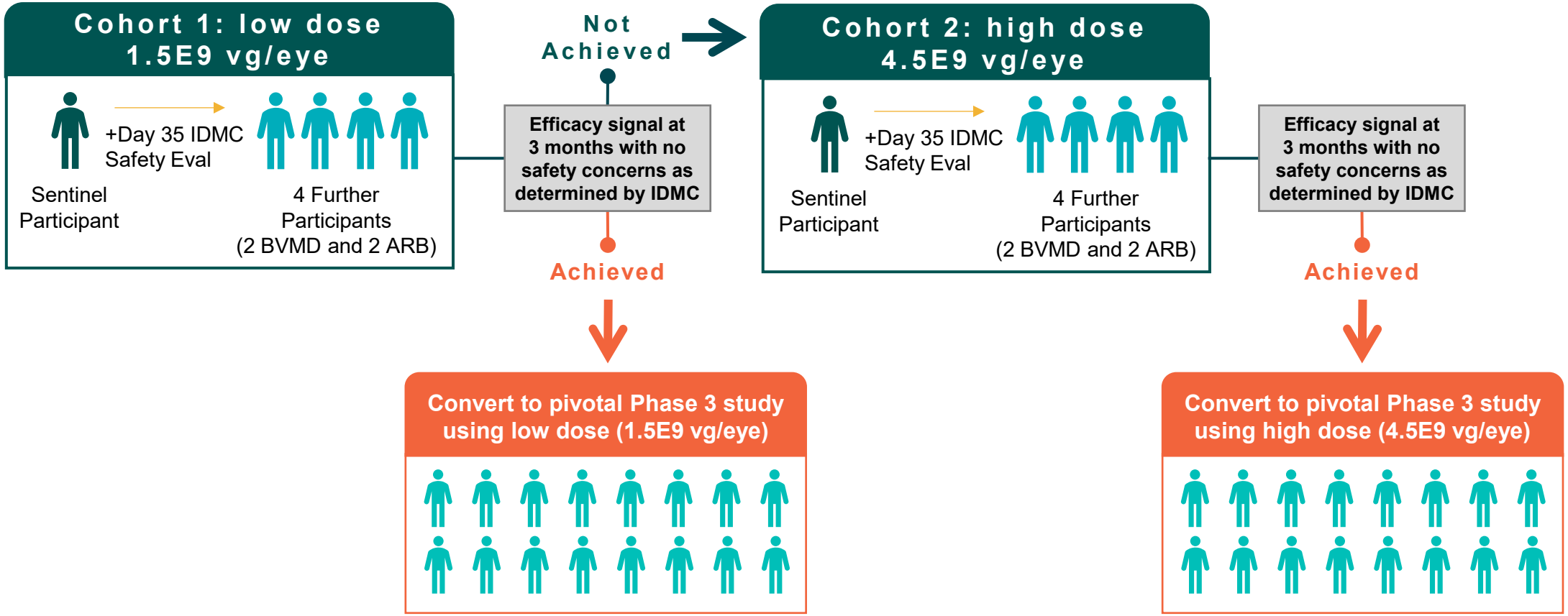
- Subretinal injection of AAV2/2-BEST1 was well tolerated
- No signs of AAV2/2-BEST1 toxicity were detected by histology and clinical pathology
- No adverse findings for up to 13 weeks after subretinal injection in all dosage groups
  - ERG assessments showed no signs of retinal toxicity in the low-dose and high-dose groups
  - Absence of retinal toxicity observed via light microscopy was observed in all dosage groups
- NOAEL determined at 4.5×10^{10} vg/eye based on study results

The U.S. FDA accepted the IND application for OPGx-BEST1 in August 2025 for the treatment of BEST1-related IRD

ERG, electroretinogram; FDA, Food and Drug Administration; IND, investigational new drug; IRD, inherited retinal disease, NOAEL, no-observed-adverse-effect level.
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.

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Thank You

Images of real patients with IRDs.