

A photograph of a hiker with a backpack standing on a rocky mountain trail. The hiker is silhouetted against a bright sun that creates a rainbow in the sky. The landscape is rugged with green grass and rocky terrain.

# Directed Differentiation and Subretinal Delivery of Allogeneic RPE Cells

## OpRegen<sup>®</sup>

A Suspension of Allogeneic Retinal Pigment Epithelial (RPE) Cells in Patients with Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration (AMD)

Brian M. Culley, Chief Executive Officer

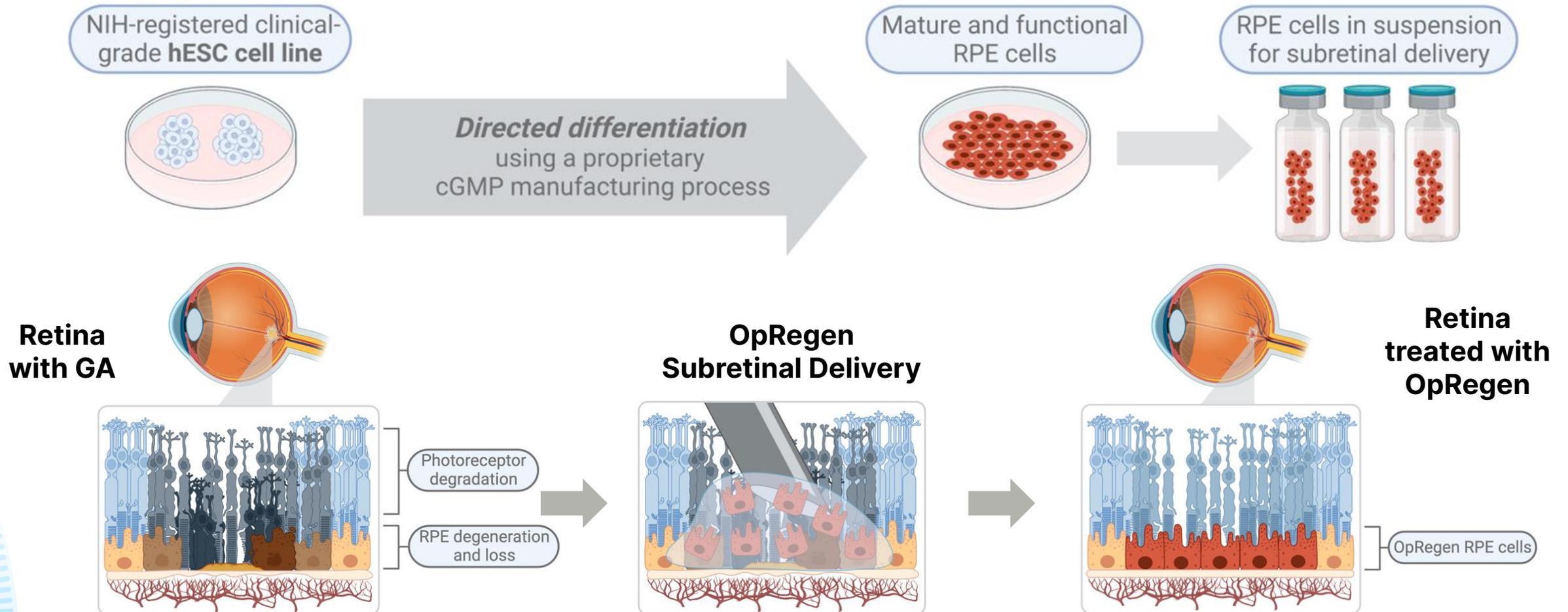
# Forward-Looking Statements

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# OpRegen – A Suspension of Allogeneic RPE Cells

*With the Potential to Counteract RPE Cell Dysfunction & Loss in GA*



cGMP, current Good Manufacturing Practice; hESC, human embryonic stem cell; RPE, retinal pigment epithelium.  
NIH registry for hESC cell line HAD-C 102 available at [https://grants.nih.gov/stem\\_cells/registry/current.htm?id=428](https://grants.nih.gov/stem_cells/registry/current.htm?id=428). Figures created with BioRender.com.

# Exploratory Objective: Onset of Structural Improvement

*In Study Eyes with Extensive OpRegen Bleb Coverage (n=5)*

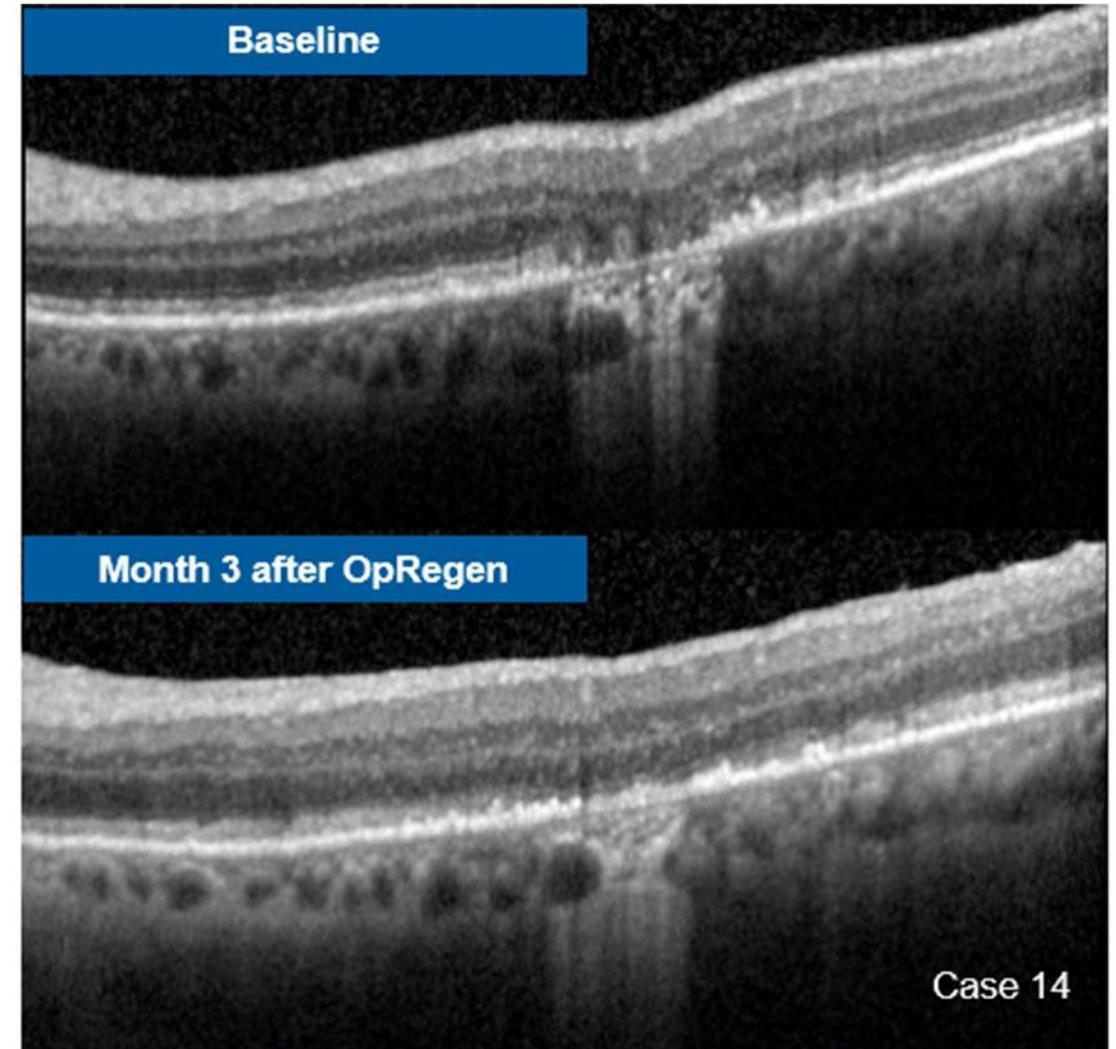
Structural improvement was assessed by 3 independent expert reviewers and based on meeting all of the following pre-specified criteria<sup>a</sup>:

- a. Reduction in outer plexiform layer and/or inner nuclear layer subsidence**
- b. Reappearance of external limiting membrane**
- c. Increased hyperreflectivity of RPE and/or Bruch's membrane or reduction of hypertransmission**

Cases were assessed to have structural improvement if determined by at least 2 of the 3 reviewers

<sup>a</sup> On at least two non-adjacent B scans; the onset of improvement may be confounded by surgical bleb resolution.

Follow-up mode was turned on during acquisition of these OCT scans to enforce longitudinal registration. Registration was verified manually by comparing choroidal patterns. There may be slight offset of inner retina blood vessels due to eye orientation difference during acquisition.



Case 14

# Exploratory Objective: Onset of Structural Improvement

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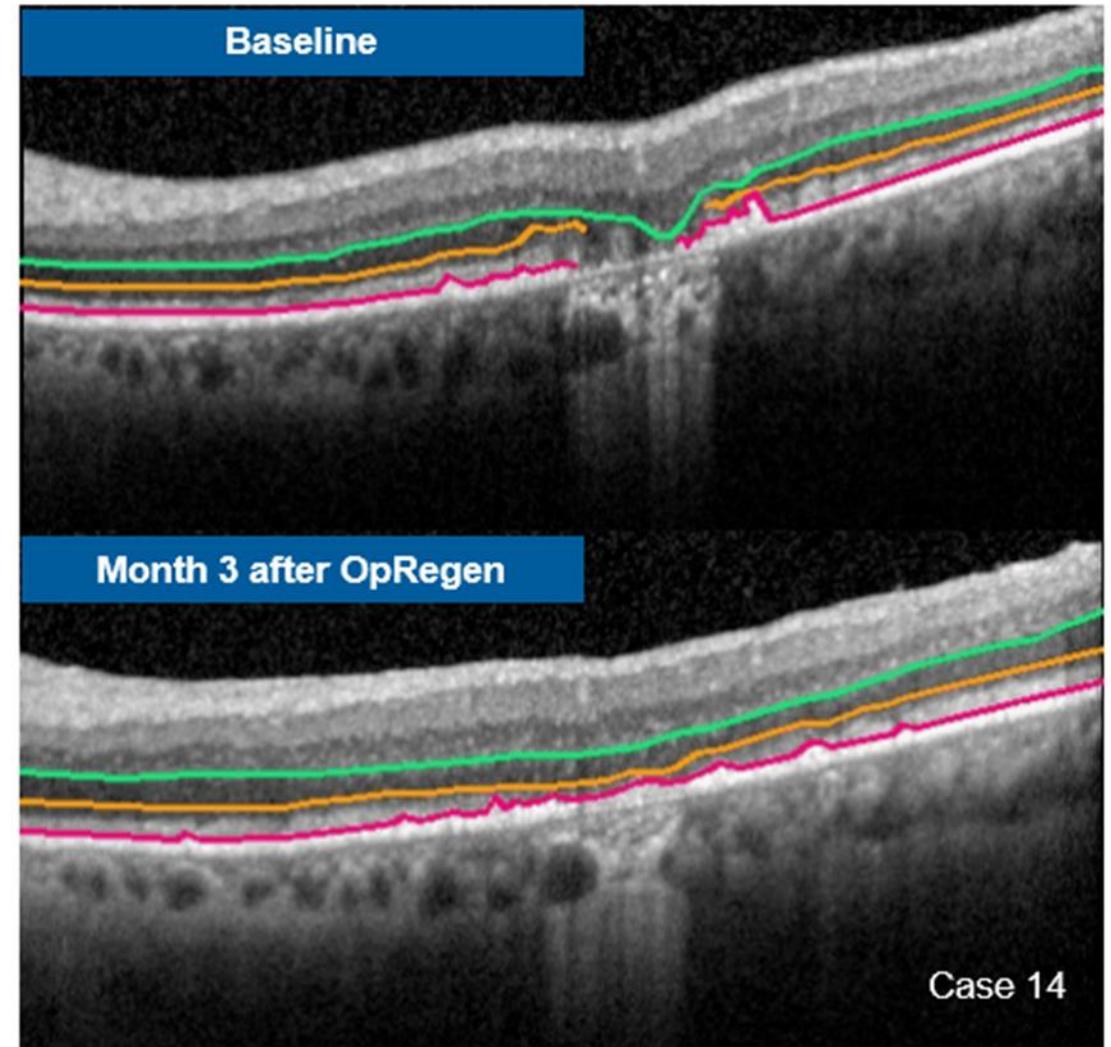
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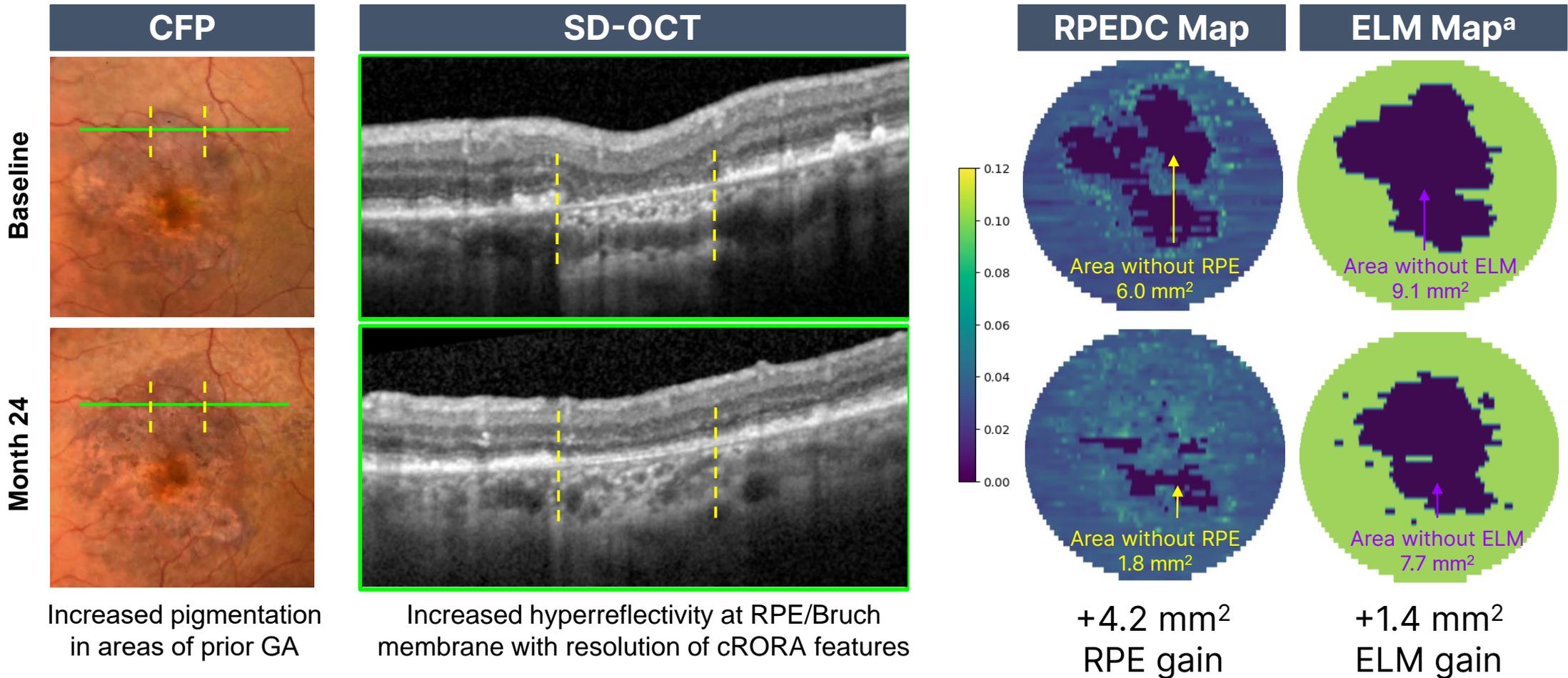
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# Preliminary Evidence of Maintenance of Structural Improvement 24 Months Post-Treatment: A Case Study (Case #14)



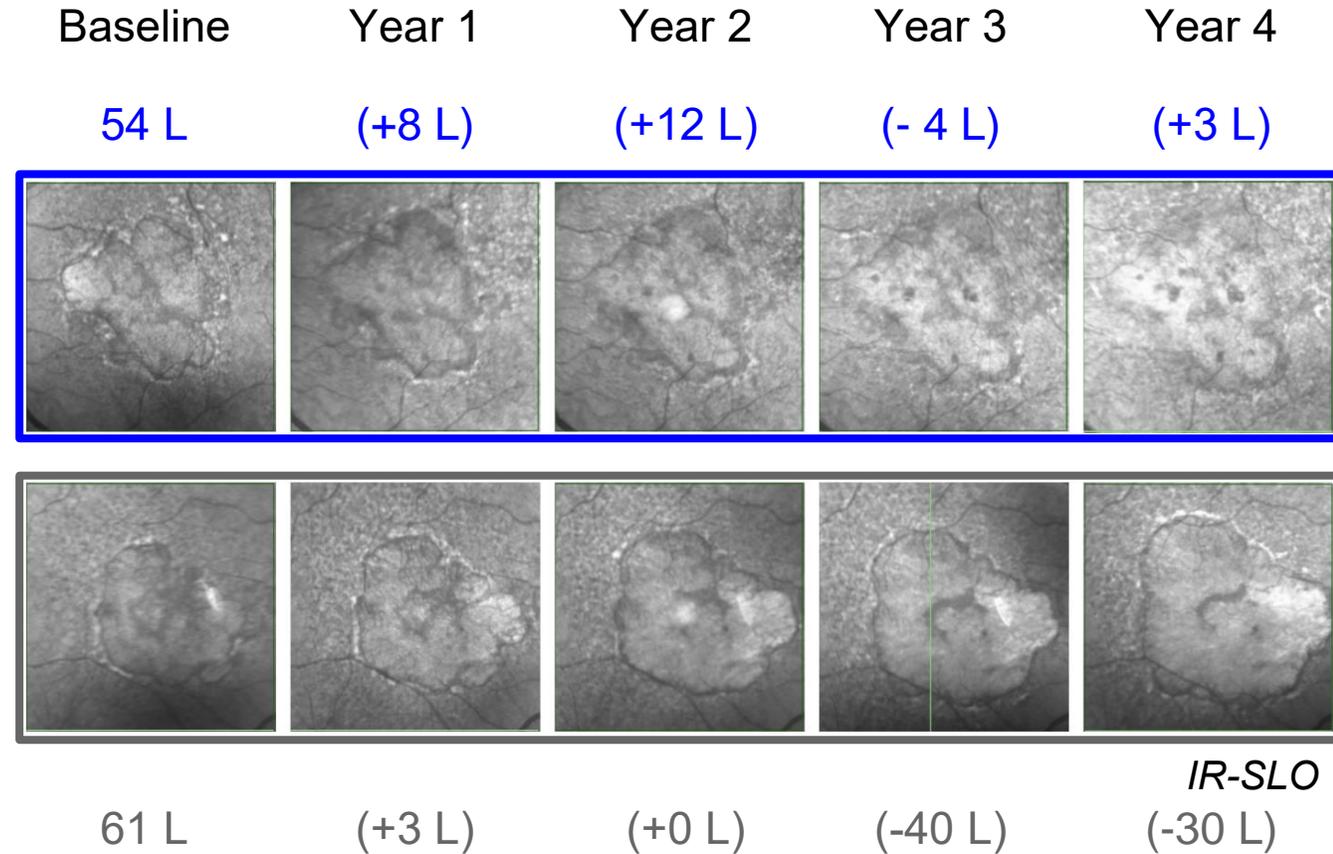
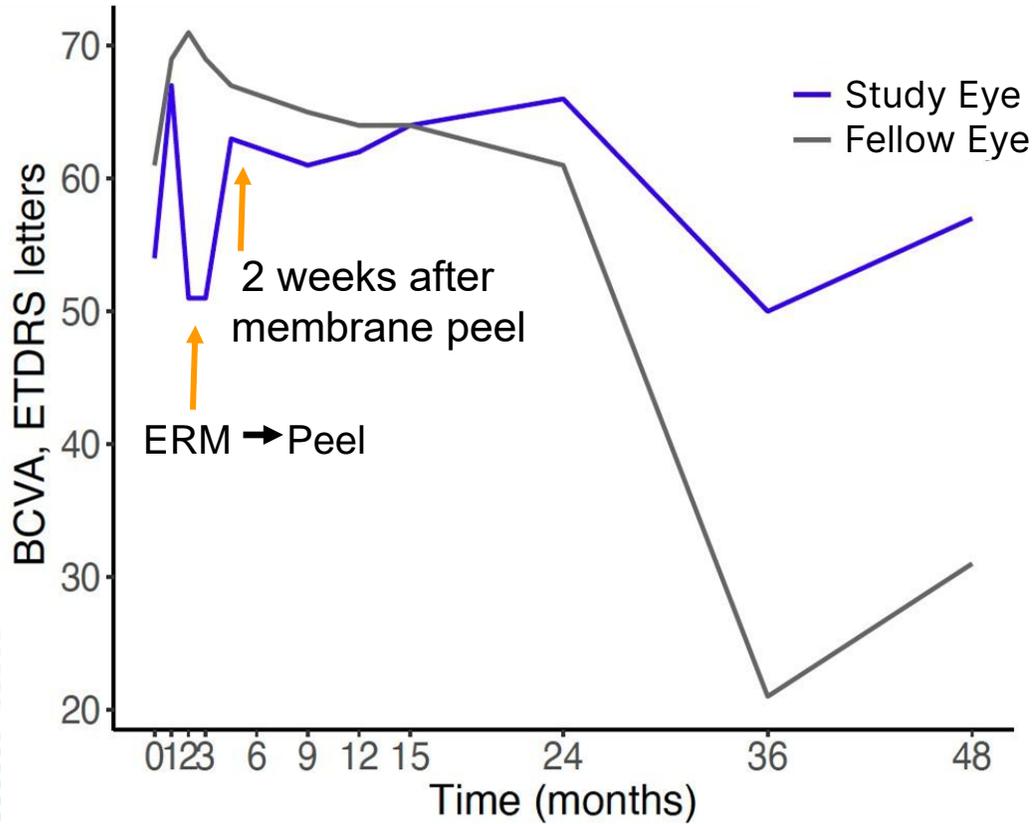
CFP, color fundus photography; cRORA, complete RPE and outer retinal atrophy; RPEDC, retinal pigment epithelium drusen complex

<sup>a</sup>ELM map, binary external limiting membrane presence/absence map, green when ELM is present, dark blue when ELM is absent

RPEDC and ELM maps are generated by Genentech EyeNotate OCT segmentation algorithm; the segmentation results are reviewed and corrected by a single masked expert grader.

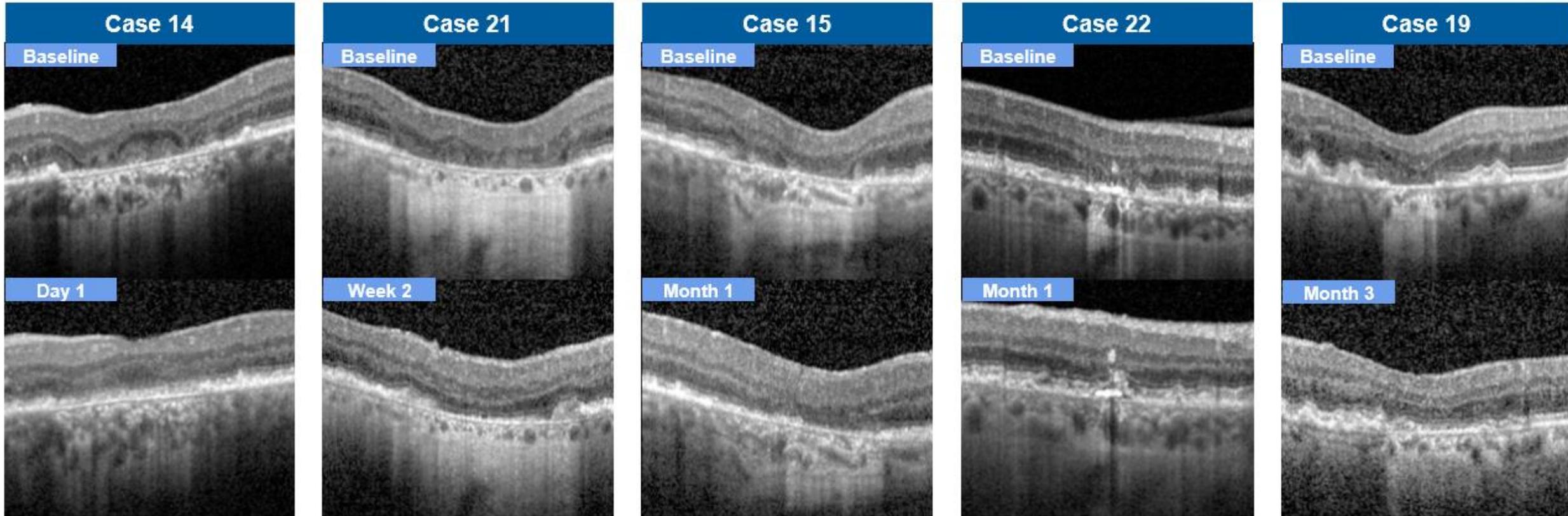
# Long-Term Vision Preservation in Study Eye: A Case Study (Case #14)

## *Vision Loss from GA Progression Over Time in Fellow Untreated Eye*



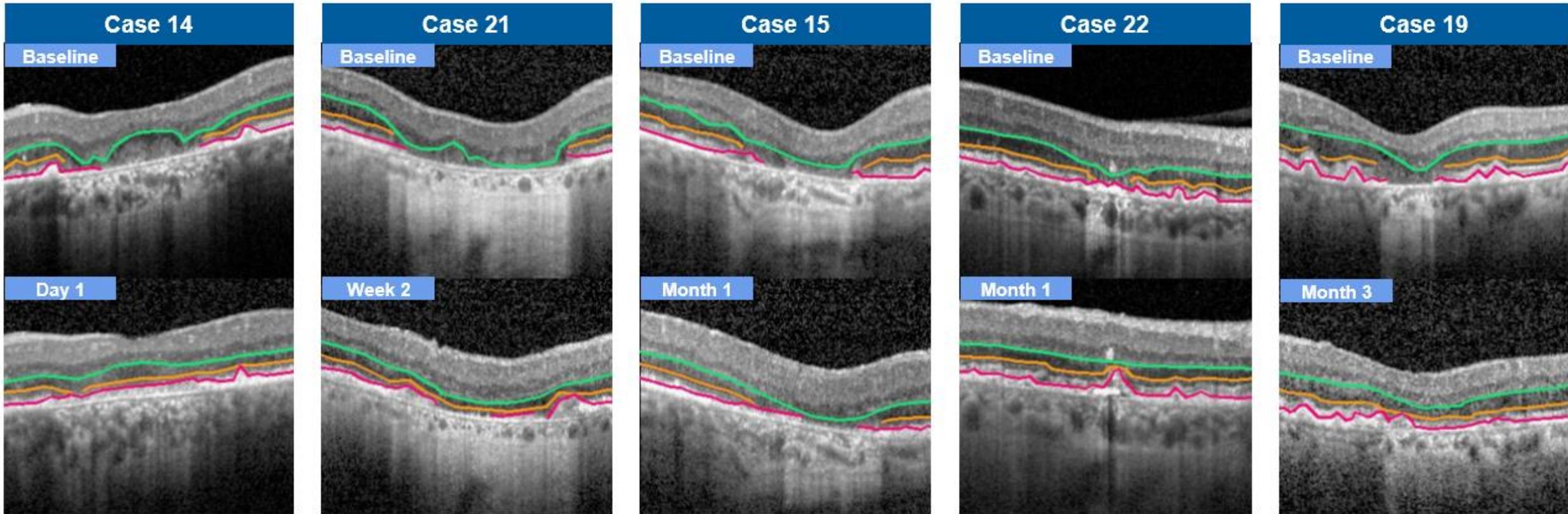
L, letters read

# Onset of Structural Improvement Within 3 Months in All 5 Patients with Extensive Bleb Coverage



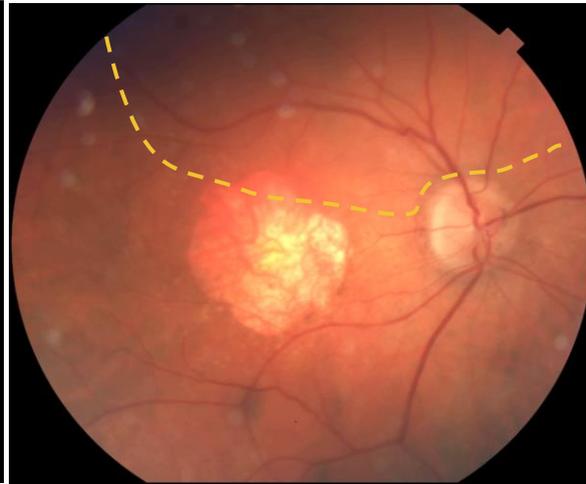
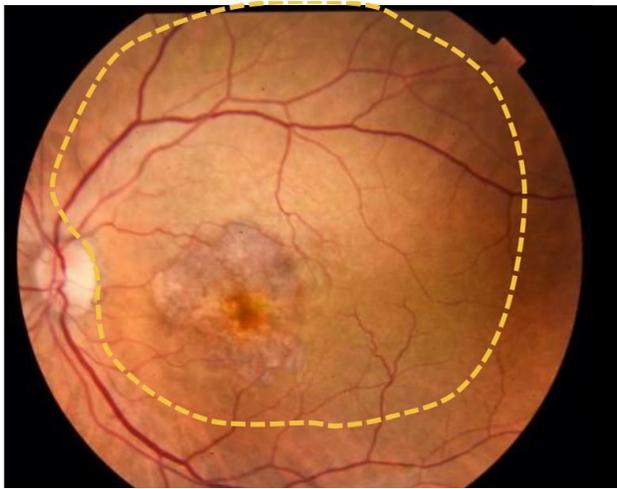
- Structural improvement was only observed within GA lesions covered by surgical bleb
- Maintenance and/or greater structural improvements were observed over time
- These patients also had an average +4.4 letter BCVA gain at Month 3, and +12.8 letter BCVA gain at Month 12

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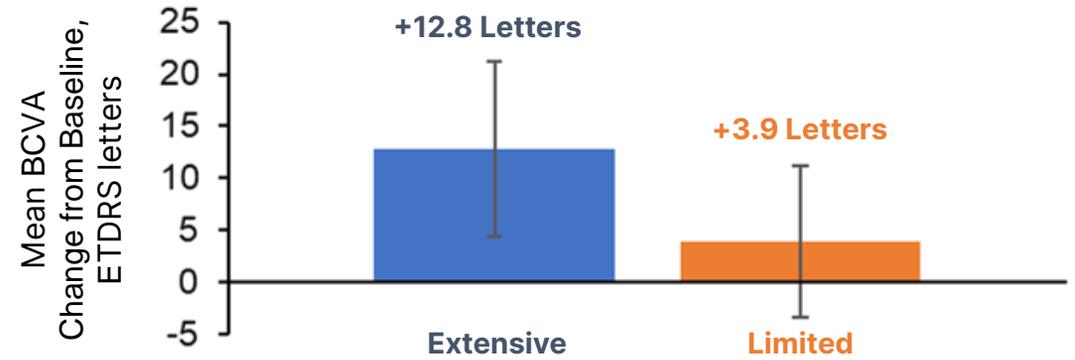
# Greater Visual and Structural Improvements in 5 Patients in Cohort 4 with Extensive Bleb Coverage



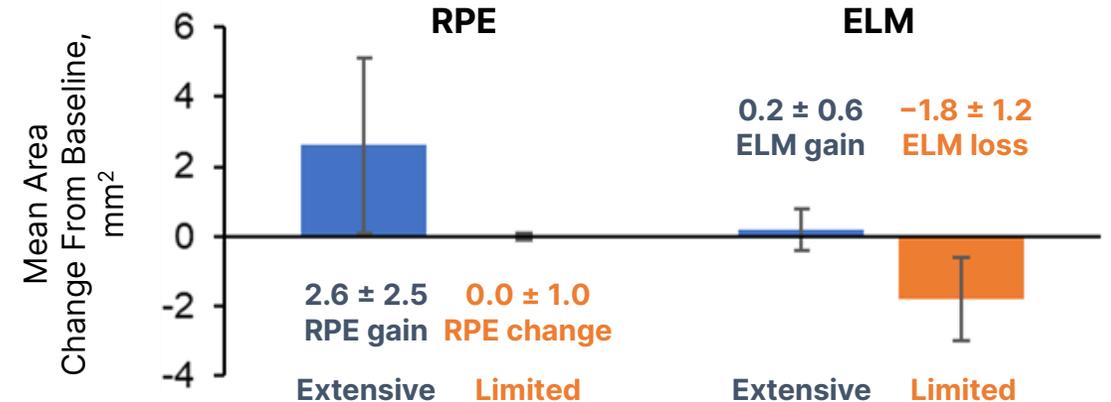
**Extensive Bleb Coverage**  
 Considerable bleb coverage of GA area (including fovea)  
 (n=5)

**Limited Bleb Coverage**  
 Minimal to no bleb coverage of GA area  
 (n=7)

## BCVA Change in Study Eye at Month 12



## RPE and ELM Change in Study Eye at Month 12



ELM, external limiting membrane  
 Error bars represent standard error  
 Data cutoff: 18 Jan 2022

# Safety Summary<sup>1</sup>

## *OpRegen Was Well Tolerated With an Acceptable Safety Profile*

- All 24 (100%) treated patients reported  $\geq 1$  AE and  $\geq 1$  ocular AE
  - Most frequent systemic AE: URTI (n=7)
  - Most frequent ocular AEs: conjunctival hemorrhage/hyperemia (n=17) and ERM (n=16)
  - The majority of AEs reported (Cohorts 1-3, 87%; Cohort 4, 93%) were mild
  - No cluster of AEs related to immunosuppressive regimen were reported
  - One patient discontinued due to an AE (stage IV lung adenocarcinoma unrelated to treatment)
- No cases of rejection have been reported
- No acute or delayed intraocular inflammation, or sustained intraocular pressure increase observed

<sup>1</sup>Ho A, et al. Presented at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting. Denver CO, USA. May 1-4, 2022.

ERM, epiretinal membrane; URTI, upper respiratory tract infection.

Data cutoff: 18 Jan 2022

# Ongoing Development: Phase 2a Trial

A multicenter, open-label, single arm clinical study in patients with geographic atrophy (GA), secondary to age-related macular degeneration

- Study managed and funded by Genentech
- Seeks to evaluate the success and safety of subretinal delivery as well as preliminary activity of OpRegen
- Estimated enrollment up to 60 patients
- Primary objectives:
  - Proportion of patients with subretinal surgical delivery of OpRegen to target regions, and
  - Incidence and severity of procedure-related adverse events at 3 months following surgery
- Secondary objective:
  - Proportion of patients with qualitative improvement in retinal structure, determined by SD-OCT

*Currently enrolling*

*(NCT05626114)*