

Subretinal Delivery of OpRegen[®], A Suspension of Allogeneic Retinal Pigment Epithelial (RPE) Cells in Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration (AMD)

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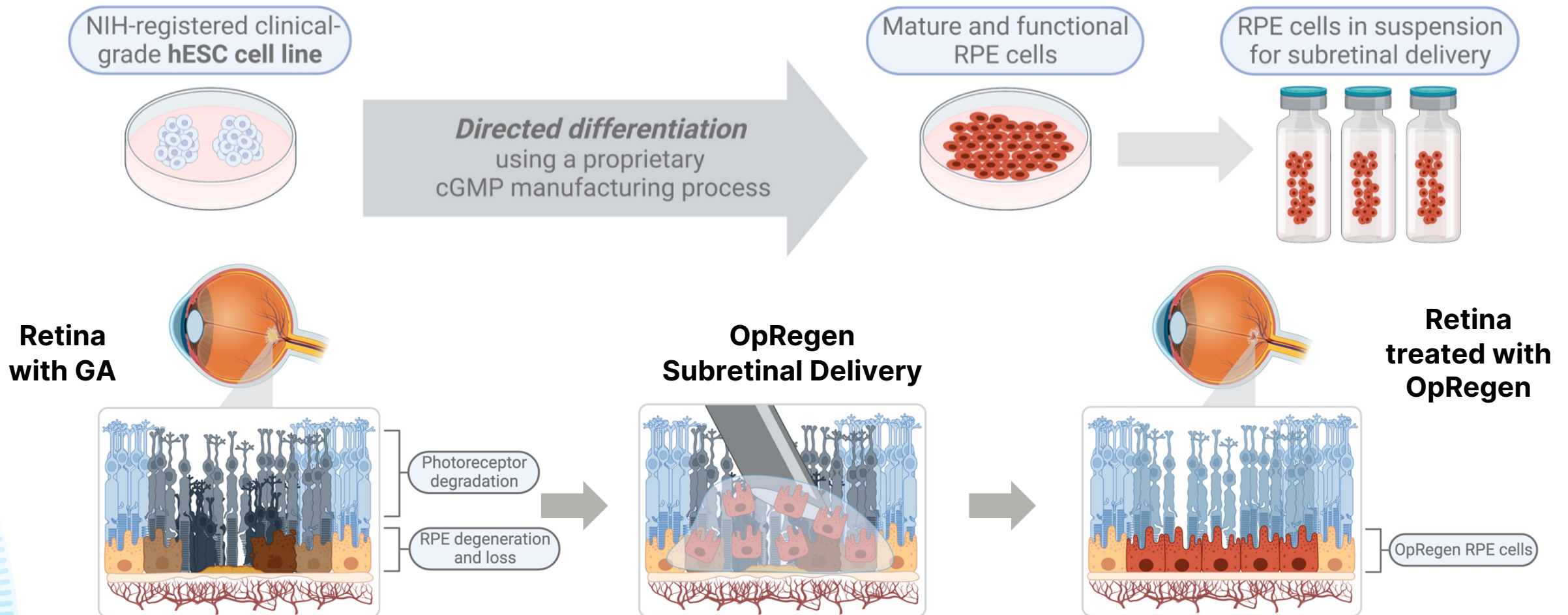
Please refer to www.lineagecell.com for additional details

Disclosures

- Gary S. Hogge is an employee of Lineage Cell Therapeutics, Inc. (Carlsbad, CA, USA)

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. Figures created with BioRender.com.

Phase 1/2a Study Design (NCT02286089)

An Open-Label, Single-Arm, Multi-Center, Dose-Escalation Trial

Key Eligibility Criteria

Patients with bilateral GA secondary to AMD

Cohorts 1-3 (n=12):

- Legally blind (BCVA: $\leq 20/200$)
- GA area: 1.25–17 mm²

Cohort 4 (n=12):

- Impaired vision (BCVA: $\geq 20/250$ to $\leq 20/64$)
- GA area: ≥ 4 and ≤ 11 mm²

Single OpRegen Administration

Cohort 1 (n=3)
50,000 cells

Cohort 2 (n=3)
Up to 200,000 cells

Cohort 3 (n=6)
Up to 200,000 cells

Cohort 4 (n=12)
Up to 200,000 cells



Objectives & Follow-up

Primary and secondary objectives assessed at 12 months following OpRegen subretinal delivery; patients followed for up to 5 years

Primary Objective:

- To evaluate the safety and tolerability of OpRegen following subretinal delivery

Secondary Objective:

- To evaluate the potential activity of OpRegen by assessing changes in visual function and retinal structure

Subretinal Delivery Via:

- Vitrectomy/retinotomy (n=17)
- Suprachoroidal cannula using Orbit SDS™ (Gyroscope Therapeutics) in Cohort 4 only (n=7)

Perioperative Immunosuppressive Regimen:

- Tacrolimus 0.01 mg/kg daily administered until up to 6 weeks post-op
- Mycophenolate up to 2.0 g daily administered until at least 3 months post-op, at discretion of investigator

Baseline Characteristics, Follow-up, & Safety Summary^a

Baseline Characteristic	Cohorts 1-3 (n=12) Legally Blind	Cohort 4 (n=12) Impaired Vision
Age, years, mean (SD / min–max)	78.1 (±8.2 / 64.8–92.2)	75.7 (±8.0 / 60.1–87.6)
Sex, female male, n	7 5	6 6
Study Eye BCVA ^b , letters, mean (SD / min–max)	23.5 (±11.7 / 0–39) 24 letters ≈ 20/320	44.8 (±7.5 / 28–54) 45 letters ≈ 20/125
Study Eye GA Area ^c , mm ² , mean (SD / min–max)	12.7 (±6.7 / 6–30)	7.4 (±2.9 / 1.6–10.9)
Study Follow-up, months, mean (min–max)	41.4 (9.3–56.8)	18.4 (10.9–35.1)

- The most frequent ocular AEs reported in all patients on study were conjunctival hemorrhage/hyperemia (71%) and ERM (67%)^d
- Most AEs reported following OpRegen administration were mild (87%)
- No reported cases of:
 - Rejection following OpRegen delivery
 - Acute or delayed intraocular inflammation
 - Sustained intraocular pressure increase
 - Discontinuation due to a related AE
- No cluster of AEs related to immunosuppressive regimen were reported

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

^b The worse eye based on BCVA was selected for OpRegen subretinal delivery

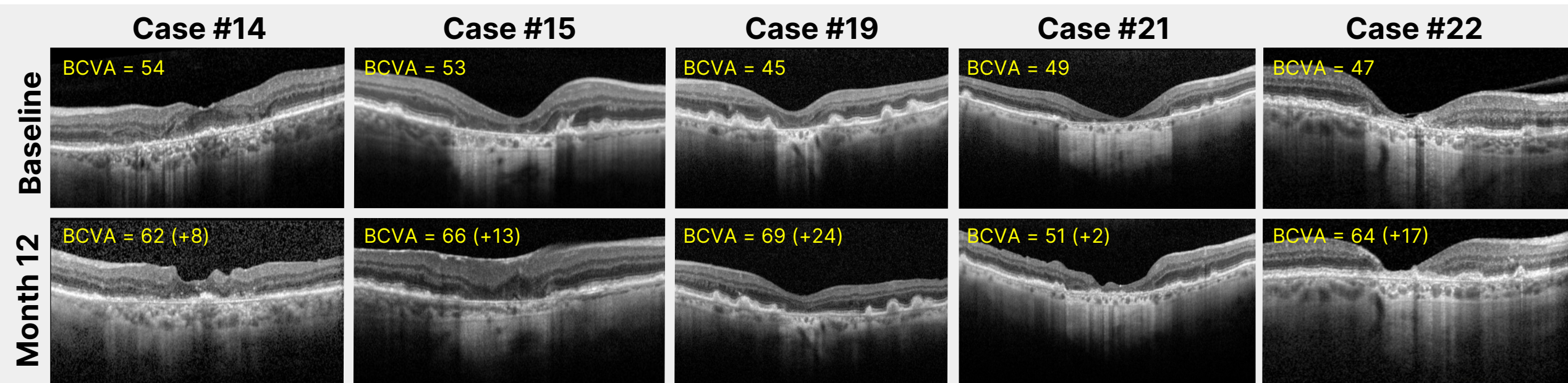
^c Based on central grading of fundus autofluorescence imaging.

^d 6/10 patients with a reported ERM AE in Cohorts 1-3 and 2/6 patients in Cohort 4 had pre-existing ERM; 3 patients had clinically significant ERM requiring surgical intervention.

Subretinal Delivery of OpRegen to GA Area and Fovea

Greater Visual Function Gains With Areas of Outer Retinal Structure Improvement

- Five patients in Cohort 4 had OpRegen delivered to most or all of the GA area, including the fovea
 - These 5 patients had greater gains in visual function (average +12.8 letter gain), with evidence for regions of apparent improvement of outer retinal structure as assessed by SD-OCT

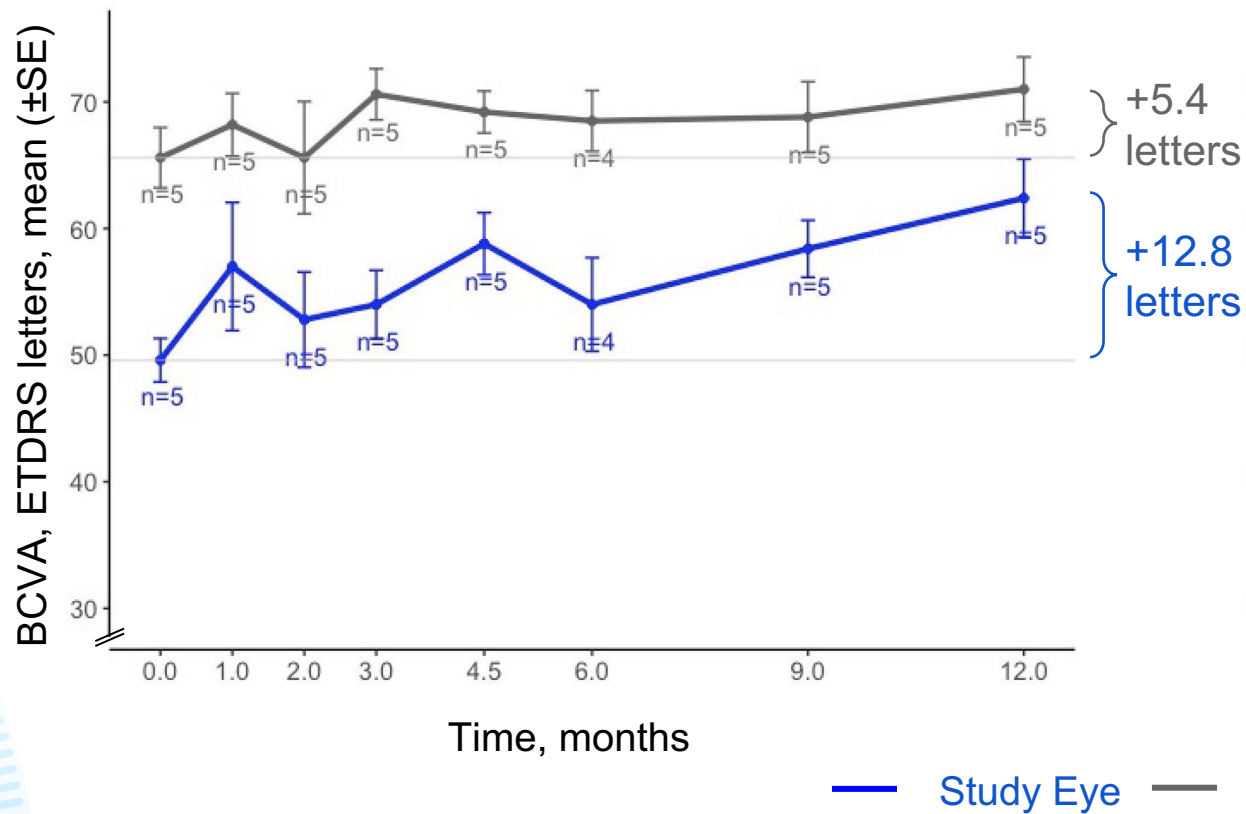


SD-OCT, spectral domain optical coherence tomography. BCVA measured by ETDRS letter score.

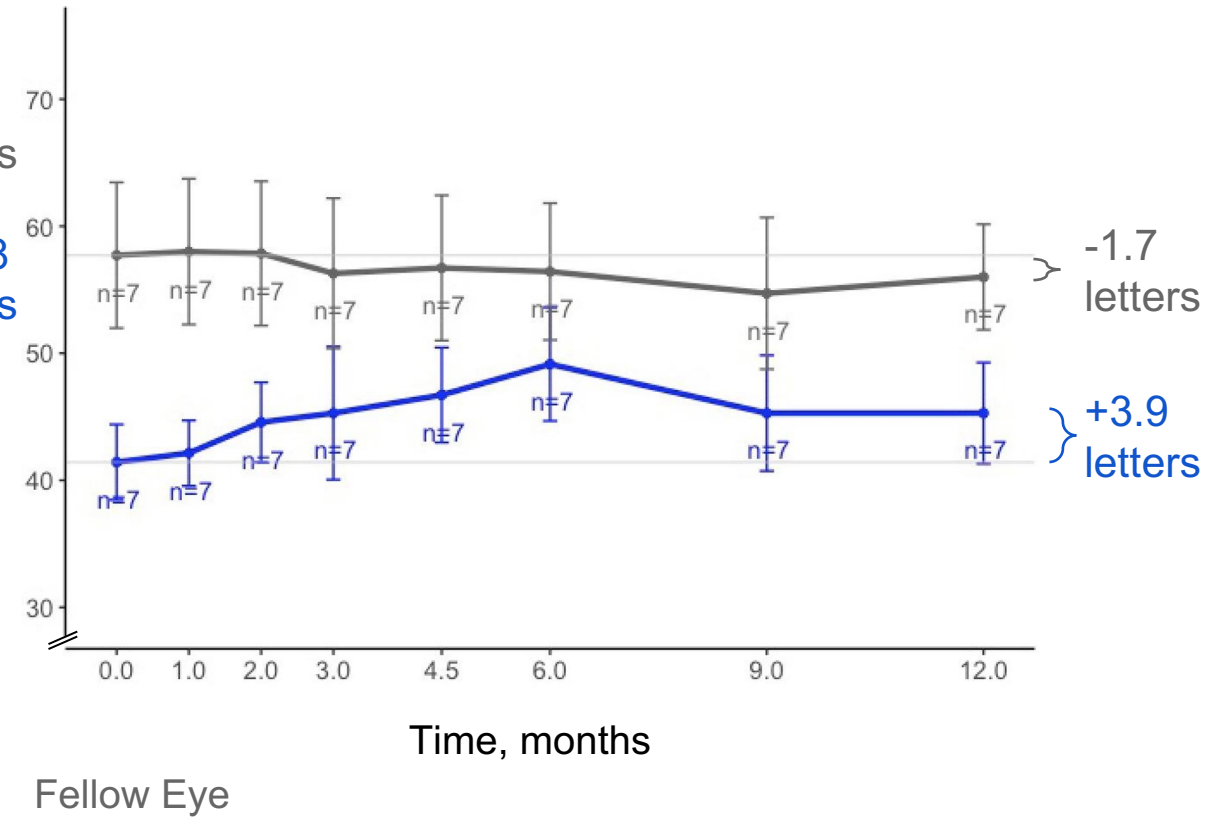
BCVA Change by Extent of OpRegen Bleb Coverage in Cohort 4

Average +12.8 Letter Gain in Study Eye with Extensive Bleb Coverage

Eyes with **Extensive** Bleb Coverage (n=5)



Eyes with **Limited** Bleb Coverage (n=7)

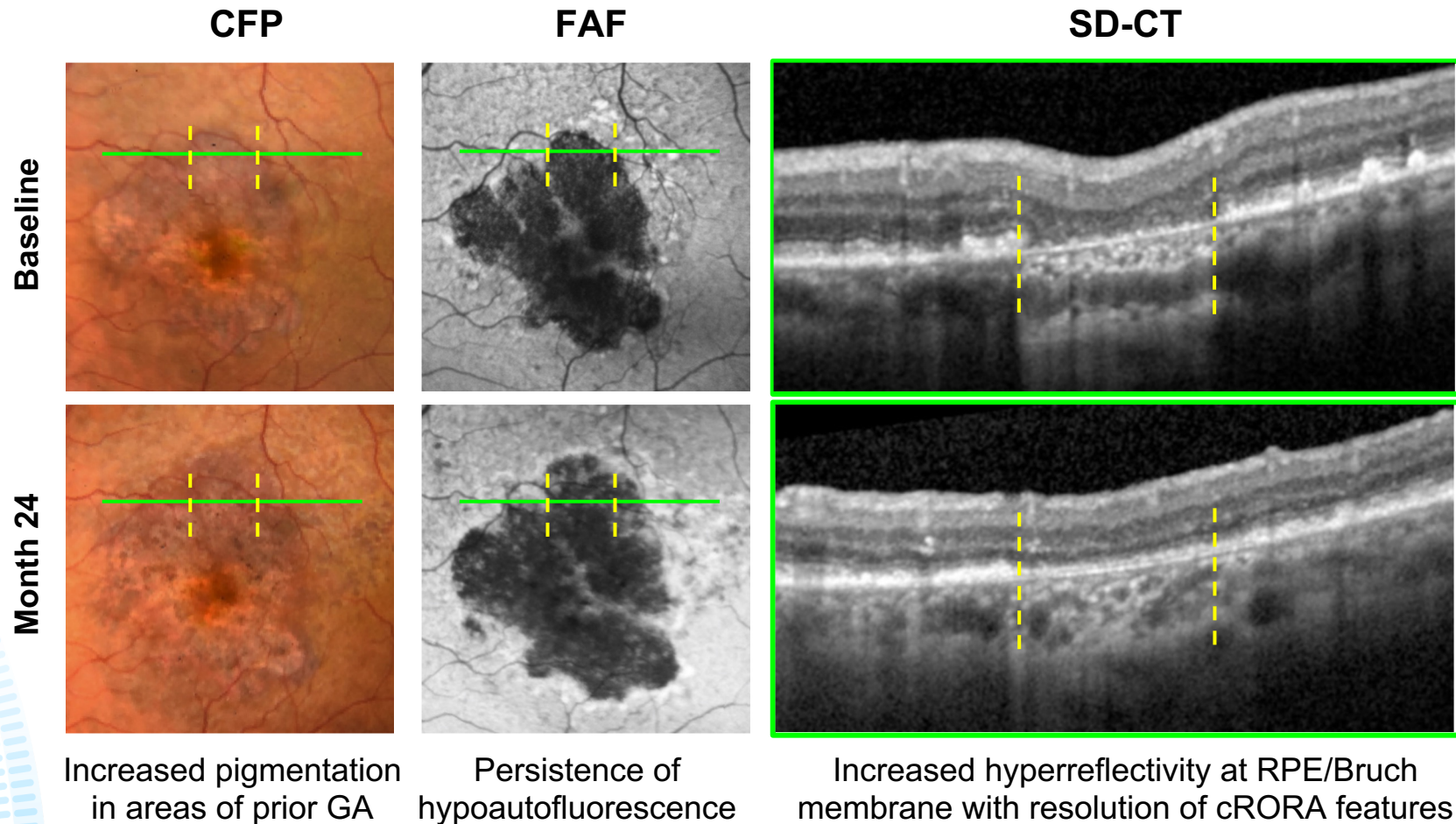


Data cutoff: 18 Jan 2022.

Reubinoff B, et al. Presented at the International Society for Stem Cell Research Annual Meeting. Boston, MA, USA. June 14-17, 2023.

Assessment of GA Following OpRegen Delivery (Case #14)

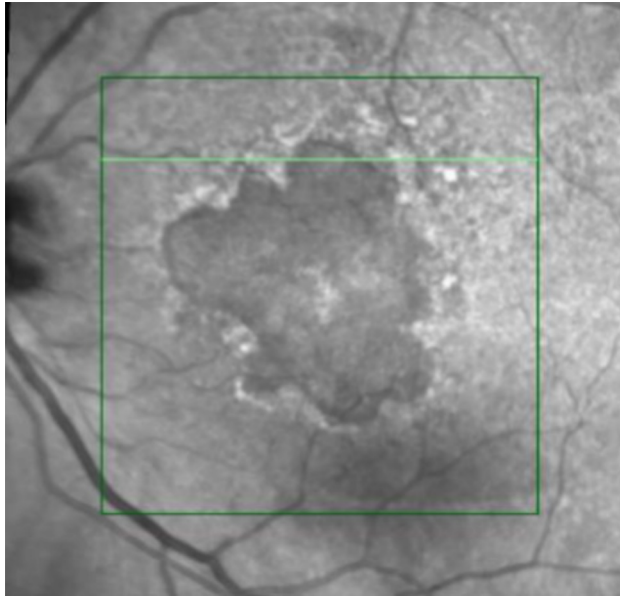
Advantages of SD-OCT versus Fundus Autofluorescence (FAF) Imaging



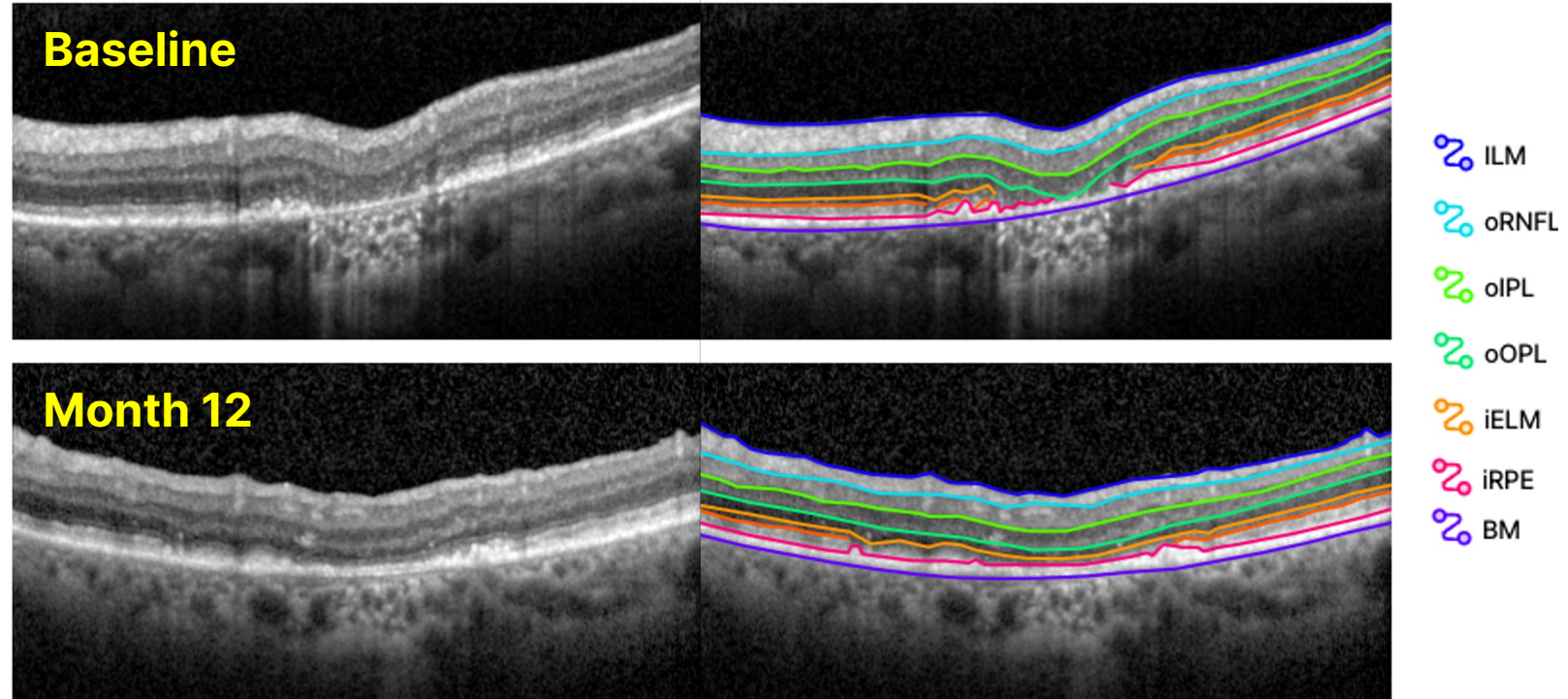
- The allogeneic hESC-derived RPE cells in OpRegen are young and have low lipofuscin content
- Therefore, OpRegen RPE cells are not expected to be readily detectable by standard FAF following subretinal delivery and are actually hypo-AF
- OCT imaging may thus be better suited to study retinal structure and define atrophy following transplantation

Resolution of cRORA Near Borders of Baseline GA (Case #14)

In Cases With Extensive OpRegen Bleb Coverage of Area of GA



Case #14



- Features of cRORA no longer present
- Greater hyperreflectivity at the level of RPE/BM
- Less choroidal hypertransmission

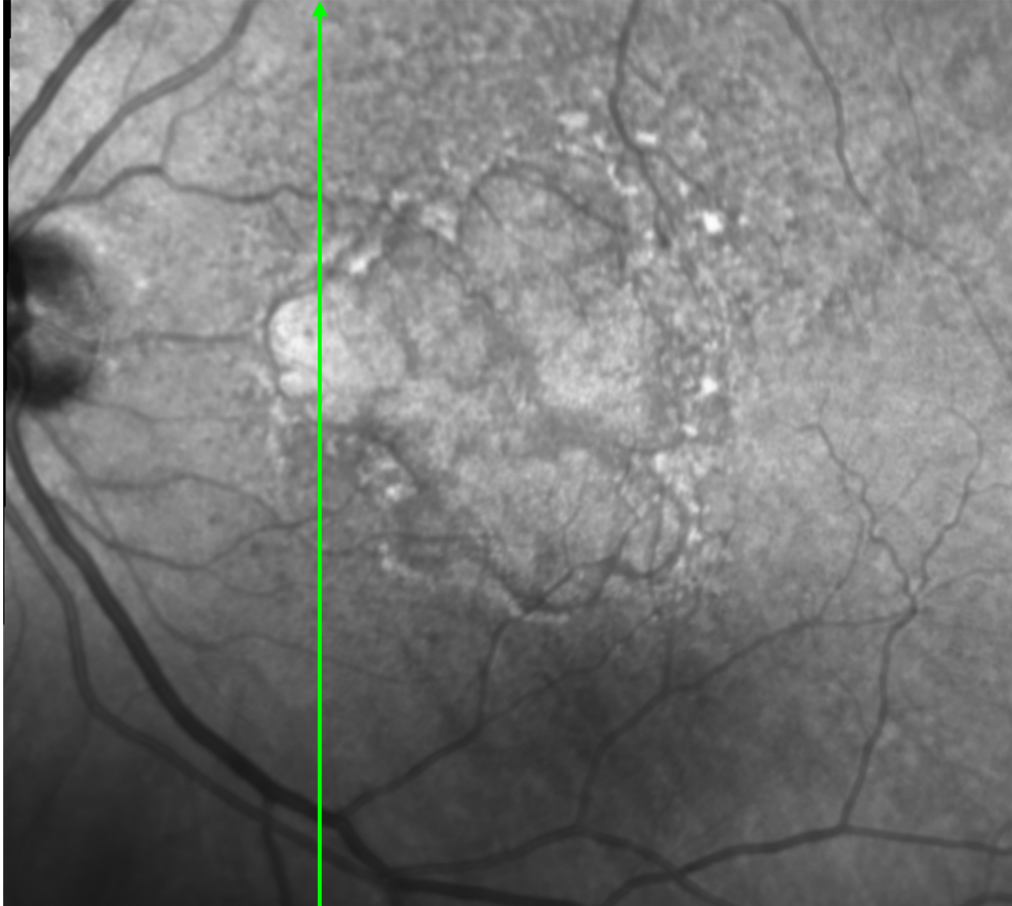
- Resolution of retinal subsidence, with greater continuity of outer retinal layers
- Similar features seen at nasal, superior, and inferior borders of GA

BM, Bruch's membrane; cRORA, complete RPE and outer retinal atrophy; i-, inner boundary of layer; ILM, internal limiting membrane; IPL, inner plexiform layer; o-, outer boundary of layer; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer.

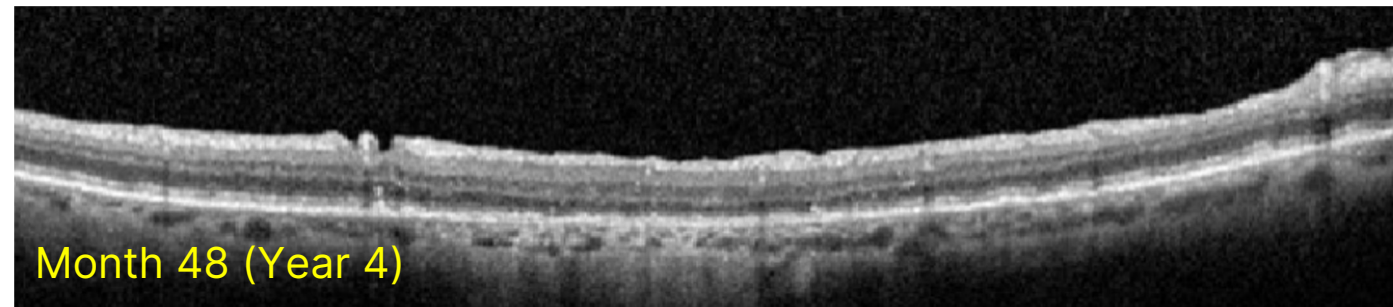
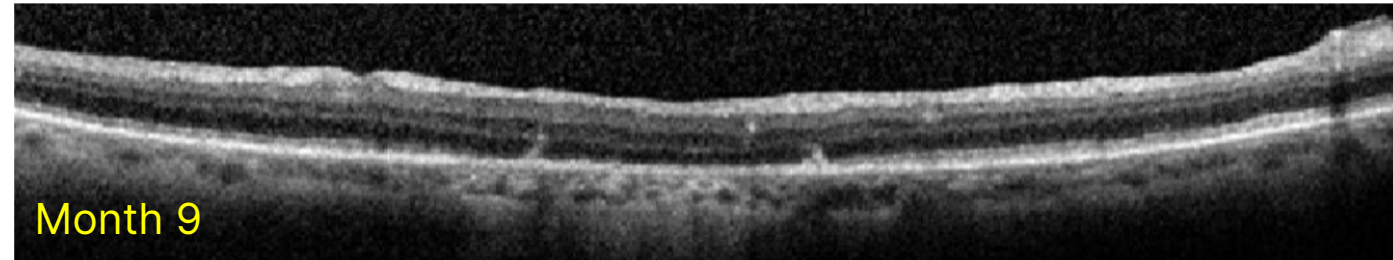
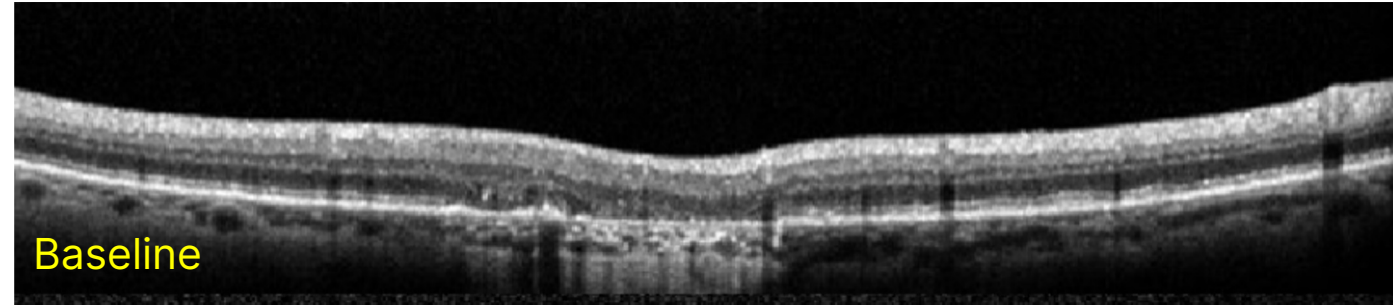
Segmentation result generated by Roche EyeNotate OCT segmentation algorithm, reviewed and corrected by a single masked expert grader

Long-Term Assessment of Outer Retina Structure (Case #14)

Outer Retinal Improvement Persisted Over 4 years in Study Eye

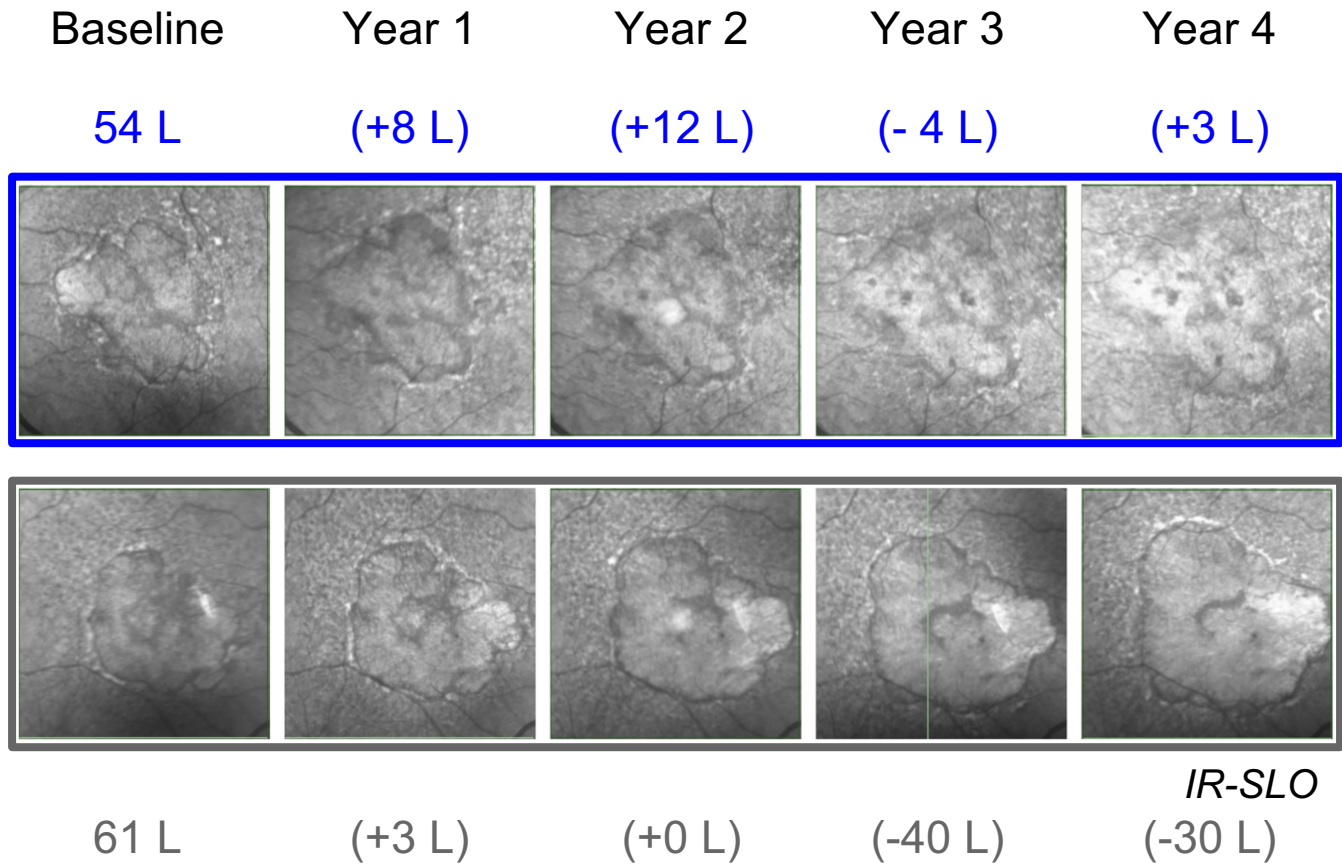
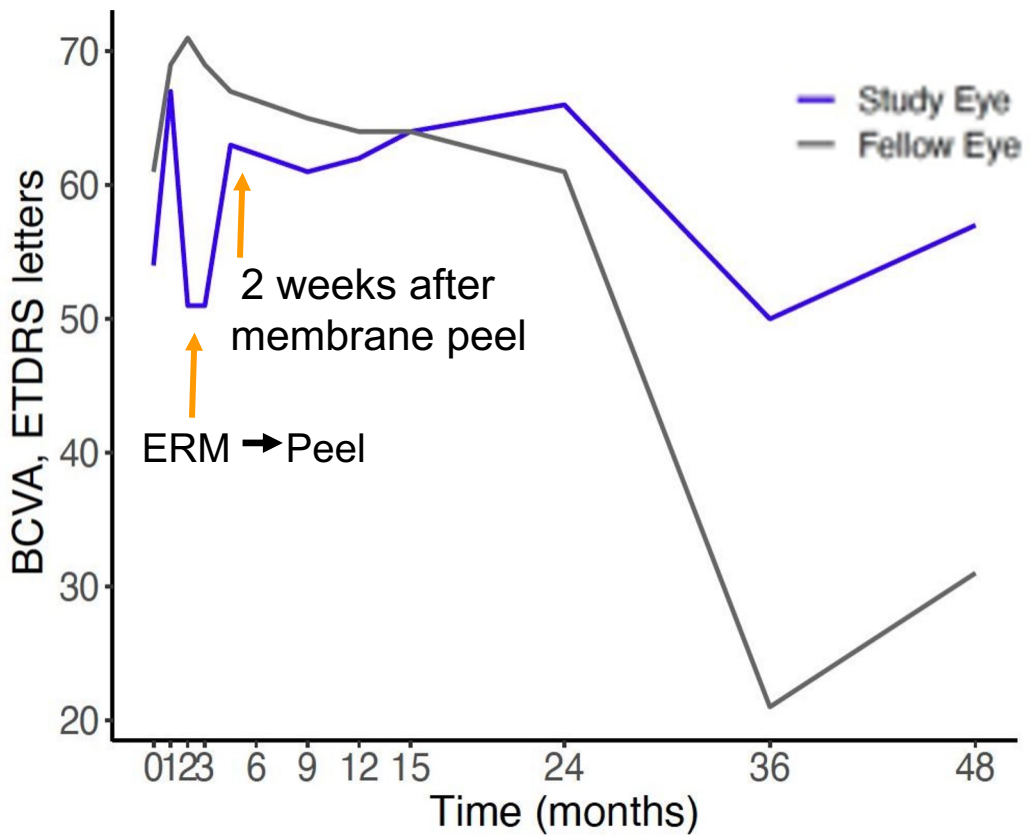


Case #14



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

Vision Loss from GA Progression Over Time in Fellow Untreated Eye



Summary and Future Directions

- Preliminary evidence of outer retinal structure and visual function improvements with OpRegen was observed in patients with GA and impaired vision (Cohort 4 [n=12])
 - The extent of OpRegen bleb coverage may be important to optimize patient outcomes
 - OCT may be more suitable than FAF to assess retinal integrity post-treatment
- These data suggest that OpRegen RPE cells may provide support to the remaining retinal cells within atrophic areas by counteracting RPE cell dysfunction and loss
- Further assessment of the optimal disease stage for intervention and target delivery location of OpRegen in a larger, controlled clinical study is needed to confirm these preliminary findings

Ongoing Development: Phase 2a Trial (NCT05626114)

A Study to Optimize Subretinal Surgical Delivery and to Evaluate Safety and Activity of Opregen in Participants With Geographic Atrophy Secondary to Age-Related Macular Degeneration

- A multicenter, open-label, single arm clinical study
- Study will evaluate the success and safety of subretinal surgical delivery as well as the preliminary activity of OpRegen in participants with GA
- 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 – primary and secondary endpoints
assessed 3 months post surgery**

Thank You to All Participating Study Sites, Investigators, and Patients!

Investigators

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Imaging Analysis

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- OCT and GA progression analyses: Jordi M. Monés, Institut de la Màcula, Barcelona, Spain
- Supplemental OCT Analyses: Brandon Lujan, Lujan Imaging LLC, Portland, OR, USA
- Doheny Image Reading and Research Lab (DIRRL)
- OCT Segmentation and Quantification of Lesions: AI Ophthalmology team, Early Clinical Development, Genentech Inc., South San Francisco, CA, USA,