# OpRegen® Retinal Pigment Epithelium (RPE) Cell Therapy for Patients with Geographic Atrophy (GA): Month 24 Results from the Phase 1/2a Trial

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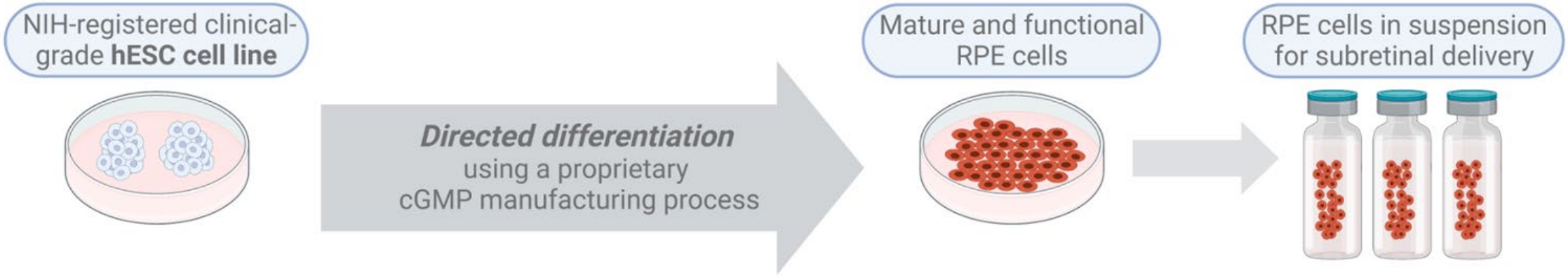
# Disclosures

DT reports the following disclosures:

- **Consultant/ Ad Board:** Abbvie, Alimera, Allergan

# 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.

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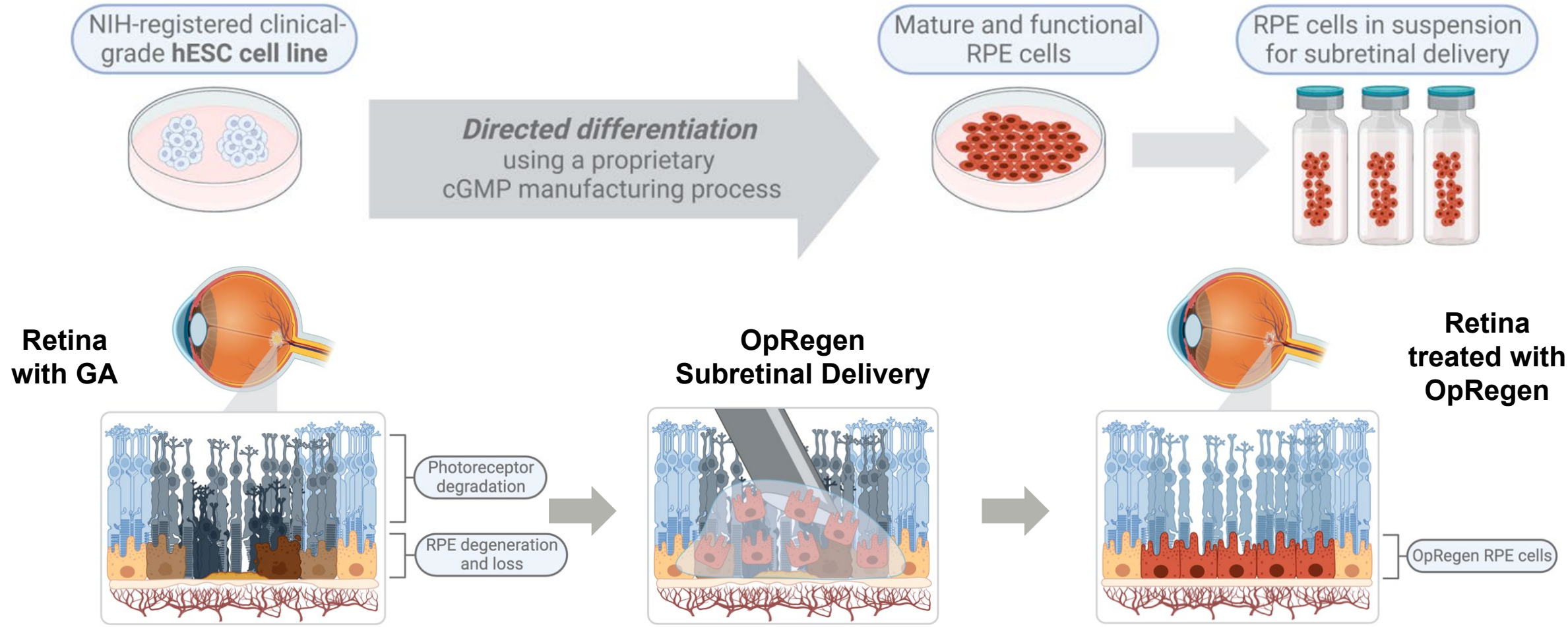


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# Phase I/IIa Study Design (NCT02286089; active)
## *An Open-Label, Single-Arm, Multi-Center, Dose-Escalation Trial*

### Key Enrollment Criteria

Patients with bilateral GA secondary to AMD

**Cohorts 1-3 (n=12):**

- Legally blind (BCVA: ≤20/200)
- GA area: 1.25–17 $mm^2$

**Cohort 4 (n=12):**

- Impaired vision (BCVA: ≥20/250 and ≤20/64)
- GA area: ≥4 and ≤11 $mm^2$

**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

**Subretinal Delivery**

- 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 up to 6 weeks after surgery
Mycophenolate up to 2.0 g daily at least 3 months after surgery

### Key Study Endpoints

- **Primary:** Safety and tolerability of OpRegen following subretinal delivery
- **Secondary:** Potential activity of OpRegen by assessing changes in visual function and retinal structure

AMD, age-related macular degeneration; BCVA, best corrected visual acuity; GA, geographic atrophy; SDS, subretinal delivery system.

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# Baseline Characteristics, Follow-up, & Safety Summary[a]

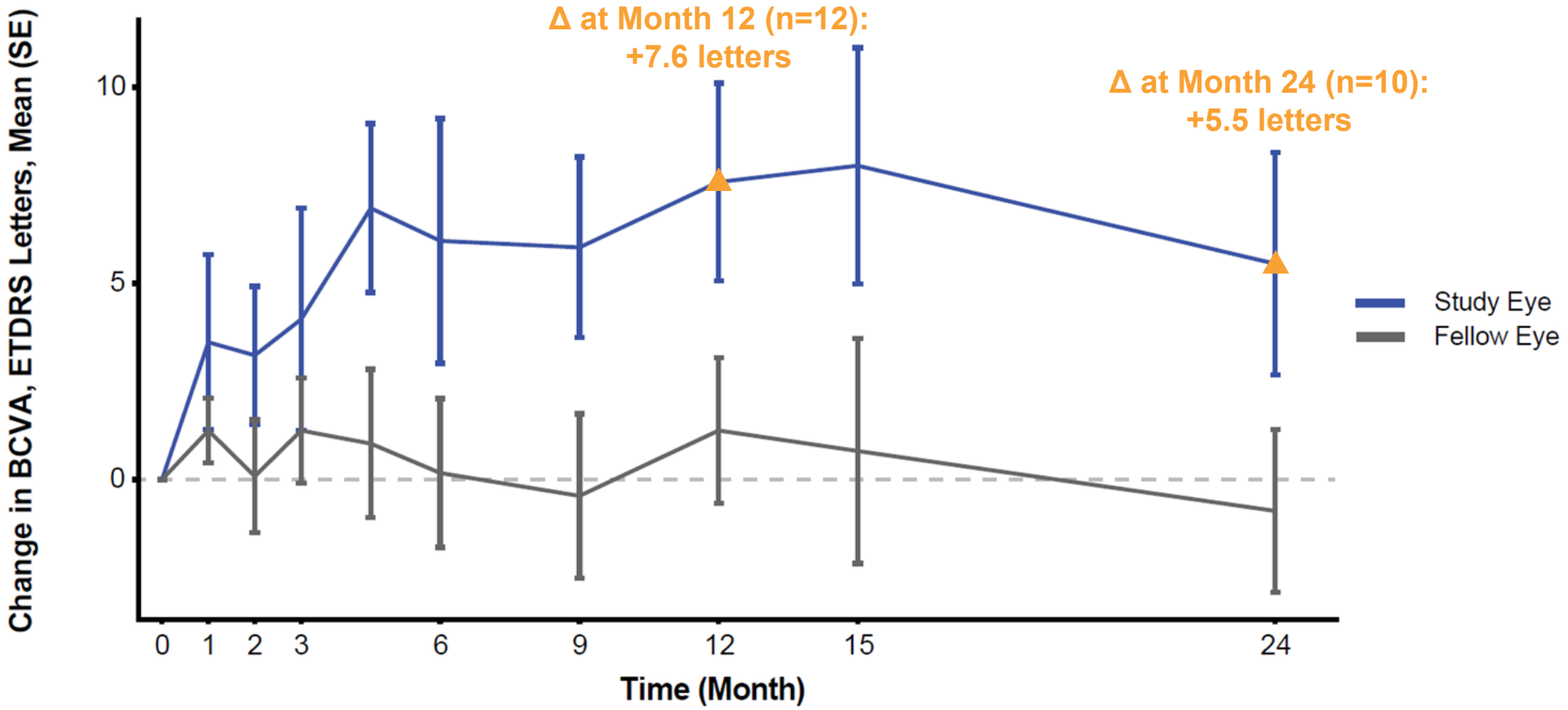
- The most frequent ocular AEs reported in all patients on study were conjunctival hemorrhage/hyperemia (71%) and ERM (67%)[d]
- Most AEs reported following OpRegen administration were mild (87%)
- No reported cases of:
  - Rejection following OpRegen delivery
  - Acute or delayed intraocular inflammation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

| 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) | 45.0 (10.0–56.8) | 36.4 (11.5-56.5) |

[a]Safety data previously presented (Ho AC et al. ARVO 2022. https://iovs.arvojournals.org/article.aspx?articleid=2780049)
[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.
ERM, epiretinal membrane.

Data cutoff: 30 Oct 2023.

# Cohort 4 (Less advanced GA) BCVA gains in study eyes are sustained through Month 24

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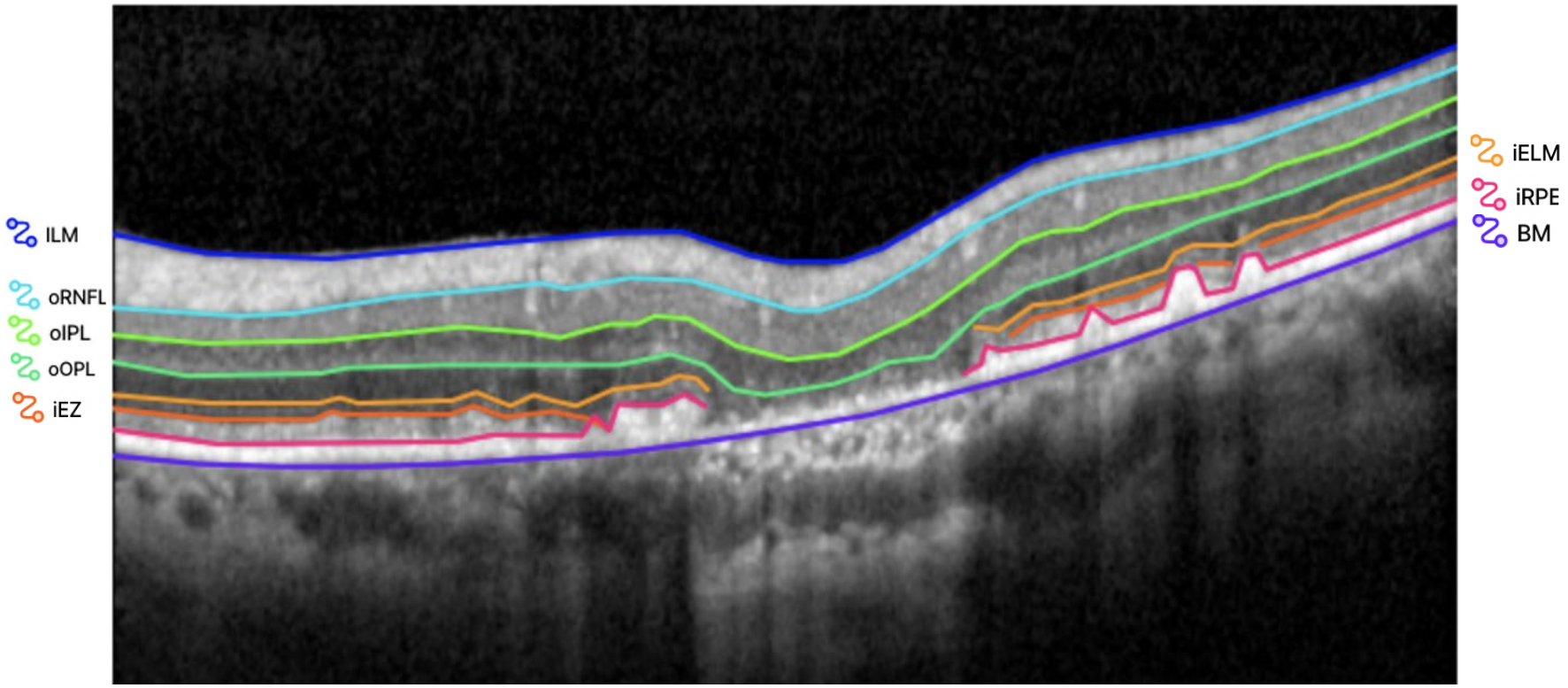
# Outer retinal structure analyzed using EyeNotate OCT segmentation algorithm in Cohort 4 patients




**ELM (external limiting membrane):**
Graded as present or absent (orange line).

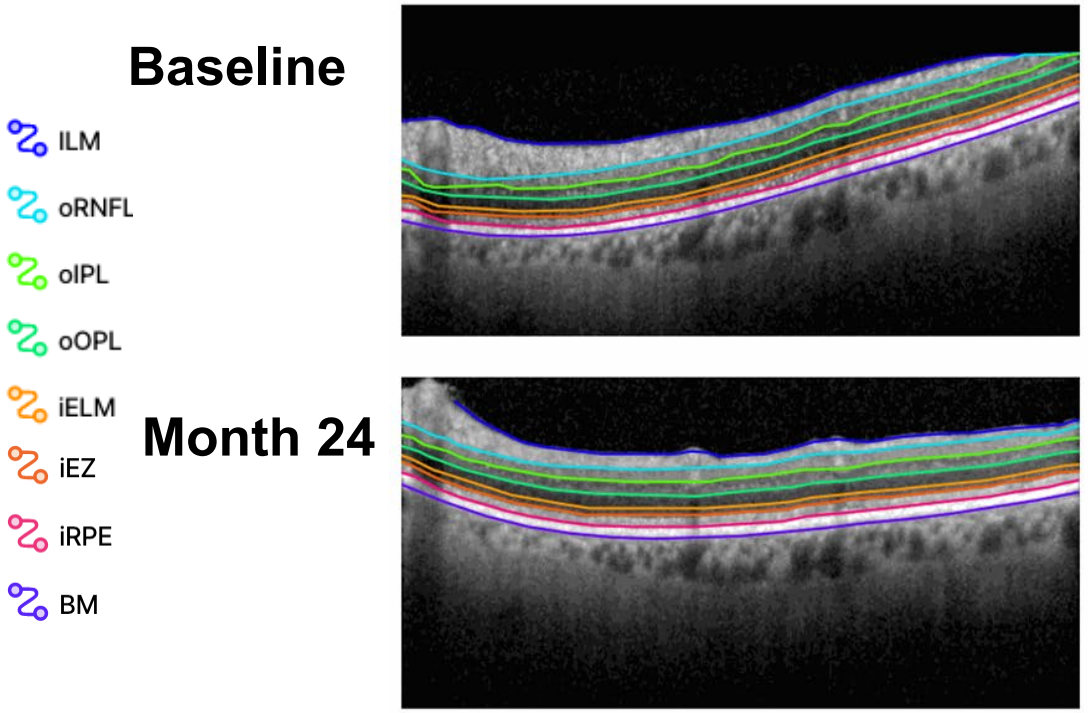
**RPEDC (retinal pigment epithelium drusen complex):**
The thickness between the hyper-reflective bands representing inner border of RPE (red line) and **BM (purple line)** when RPE is present.

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

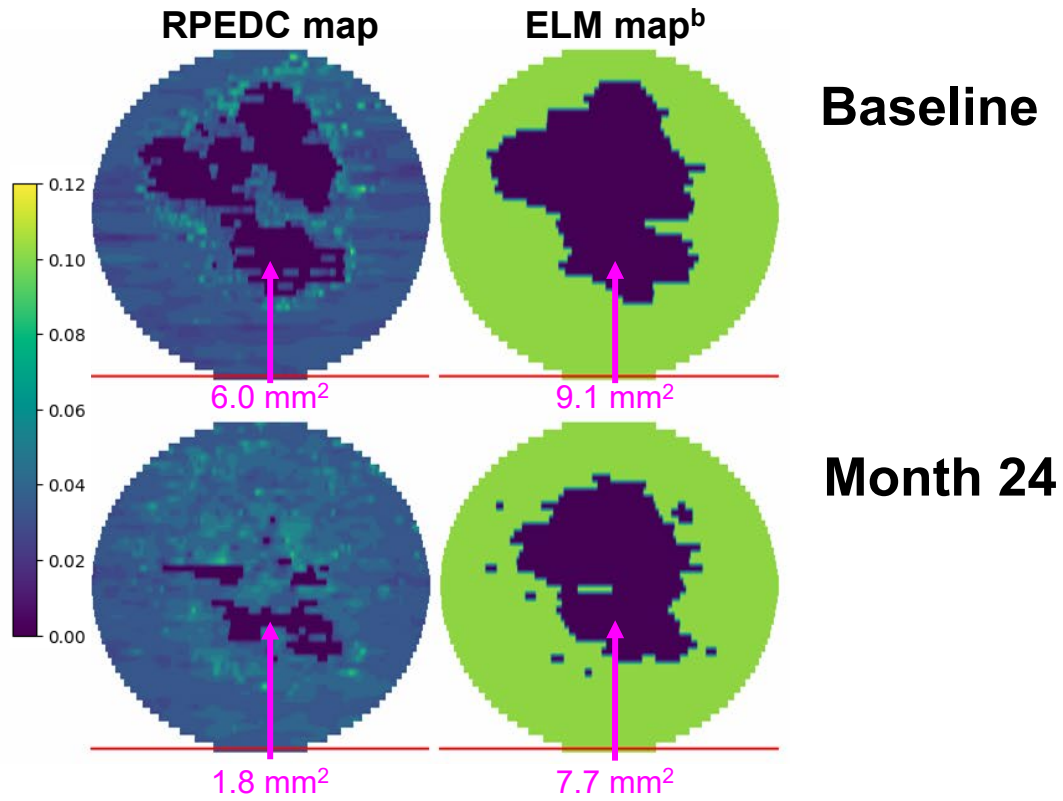
BM, Bruch's membrane; EZ, ellipsoid zone; i-, inner boundary of layer; ILM, internal limiting membrane; IPL, inner plexiform layer; o-, outer boundary of layer; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer.

# Quantitation of RPEDC and ELM area shows cases of improvement between Baseline and Month 24

## SD-OCT segmentation[a]




## Quantification

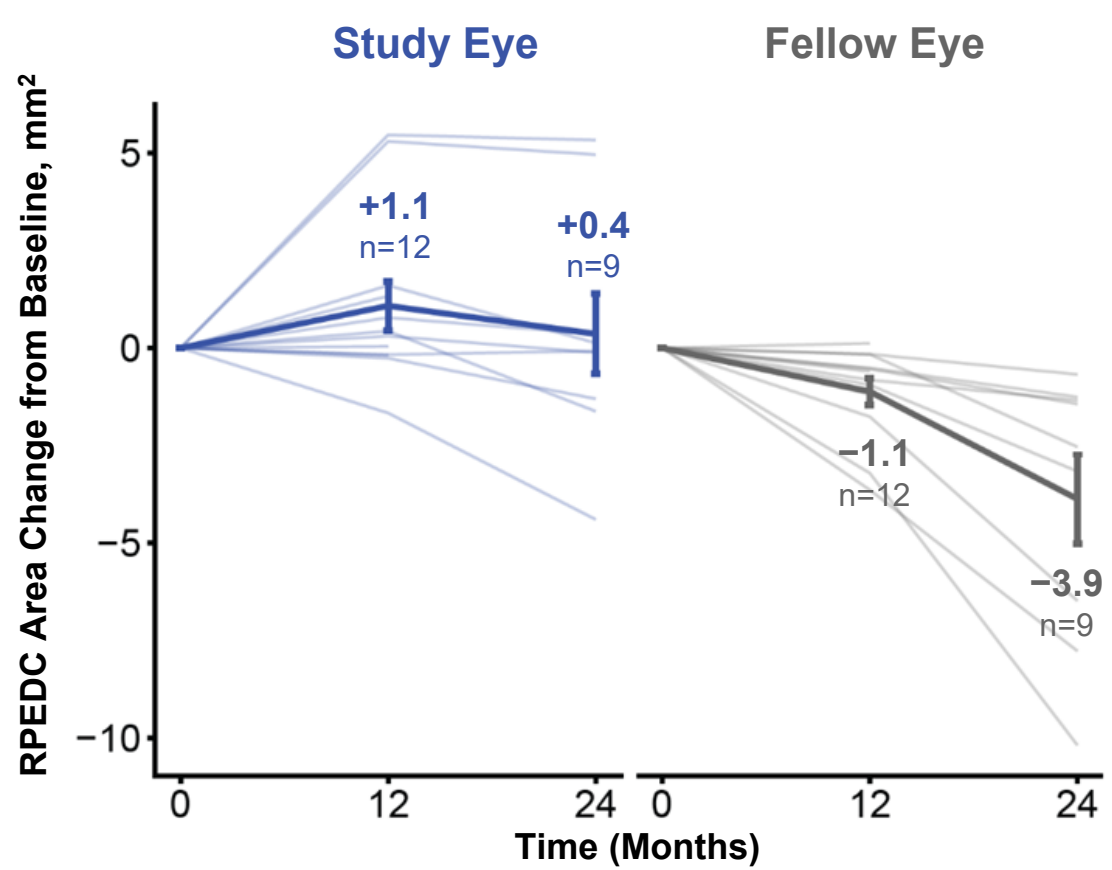



ELM, external limiting membrane; RPEDC, retinal pigment epithelium drusen complex.
[a]Segmentation result is generated by Genentech EyeNotate OCT segmentation algorithm, reviewed and corrected by a single masked expert grader.
[b]ELM map, binary external limiting membrane presence/absence map, green when ELM is present, dark blue when ELM is absent.

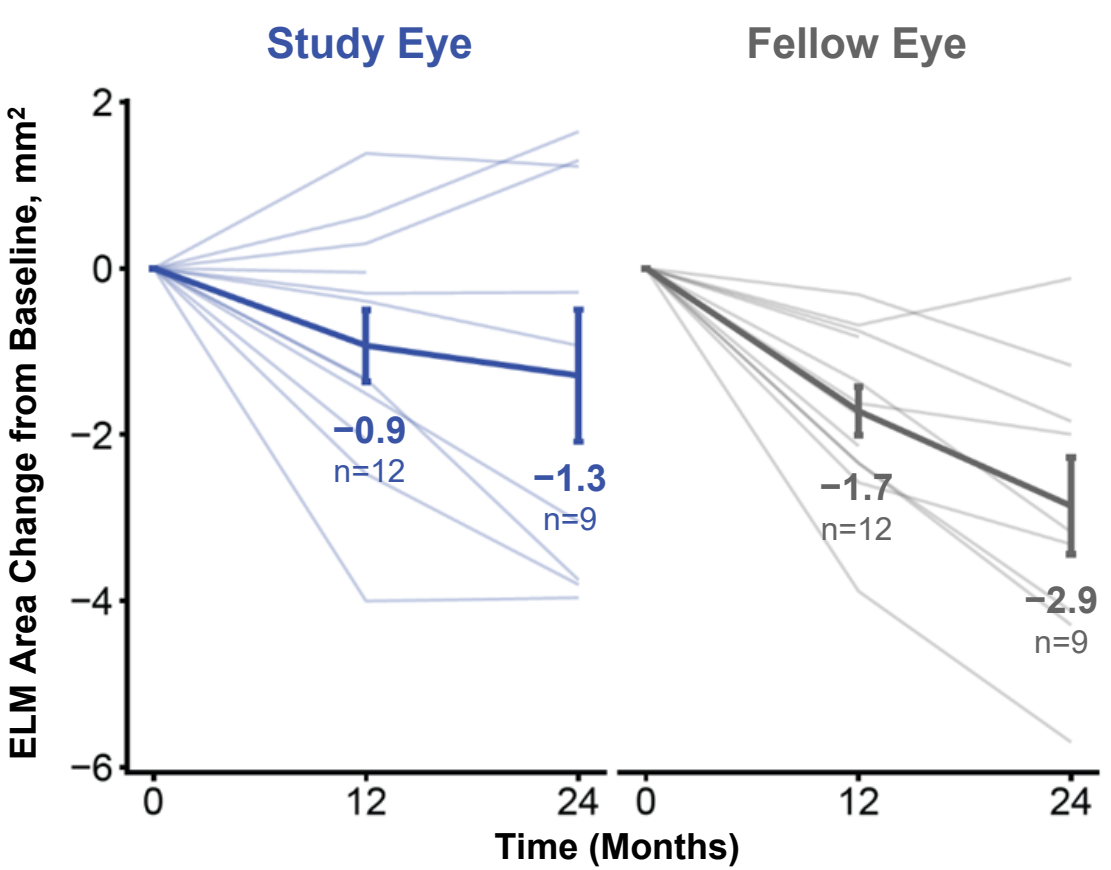
**Case #14**

# Change in RPEDC and ELM area in Cohort 4 (All patients)

## Area of RPEDC Change




## Area of ELM Change

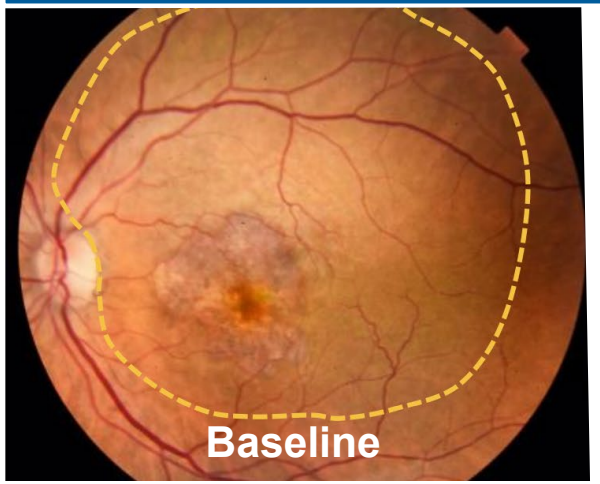


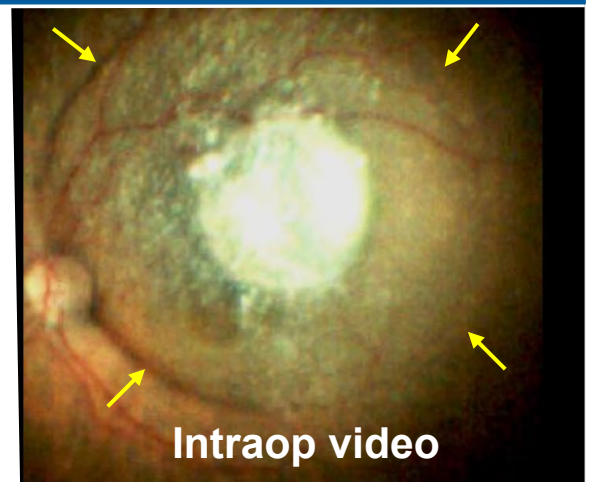

RPEDC, retinal pigment epithelium drusen complex.
Thick lines represent the mean and error bars represent standard error.
Data cutoff: 30 Oct 2023.

# Subgroup analysis in Cohort 4: Functional and anatomic outcomes in eyes with and without delivery of OpRegen to central GA

## Extensive bleb coverage (n=5)

Extensive bleb coverage of GA (including fovea)

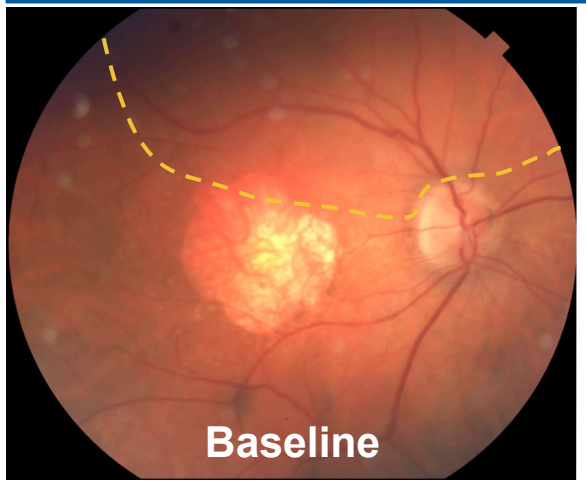


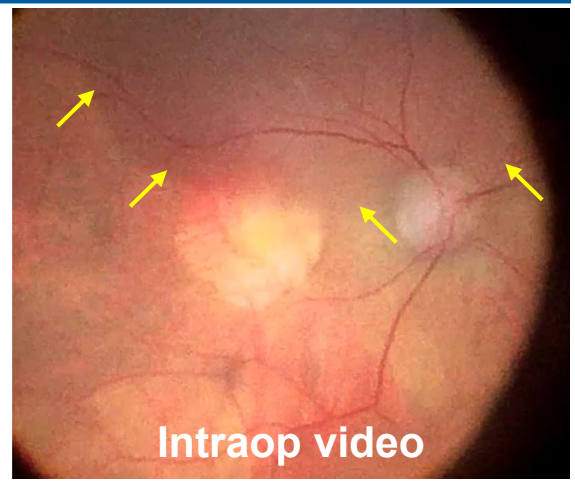




Case #14

## Limited bleb coverage (n=7)

Minimal to no bleb coverage of GA



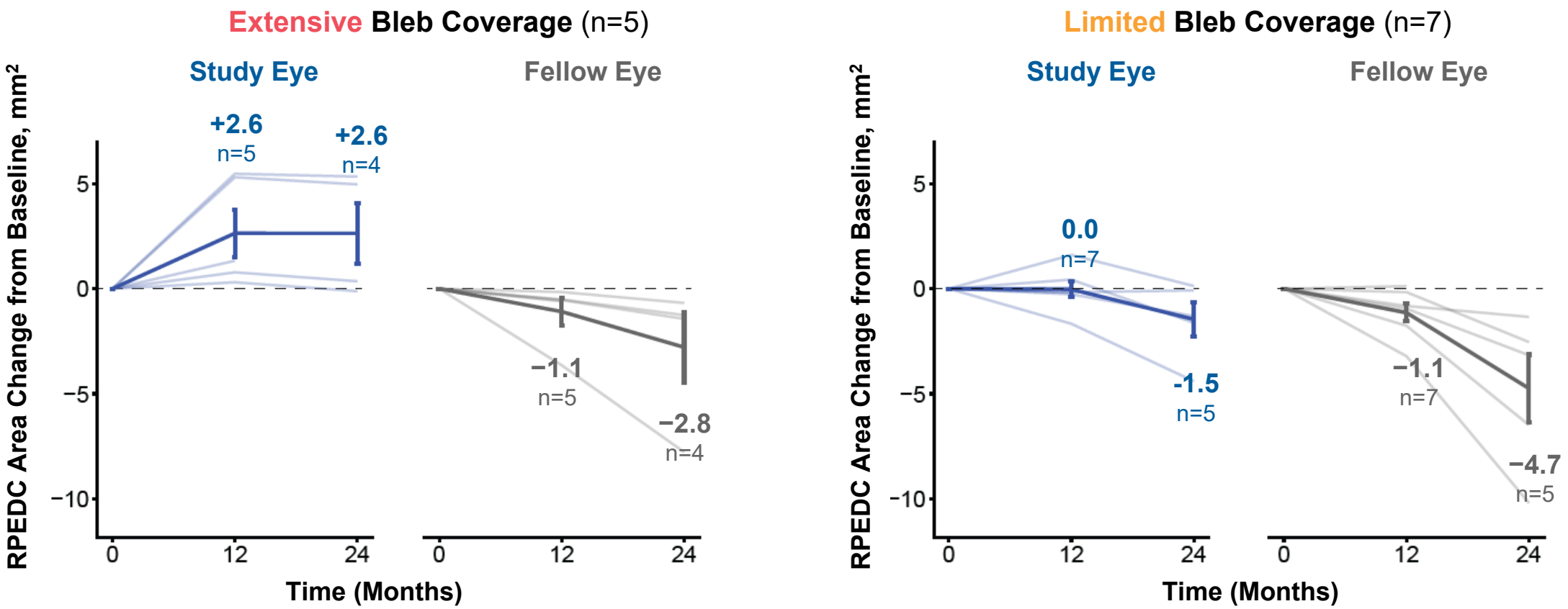




Case #18

OpRegen bleb coverage of GA determined by surgical video for all Cohort 4 cases (n=12)

# Maintenance or improvement of RPEDC was observed in patients with extensive OpRegen bleb coverage of GA

## Area of RPEDC change




RPEDC, retinal pigment epithelium drusen complex.
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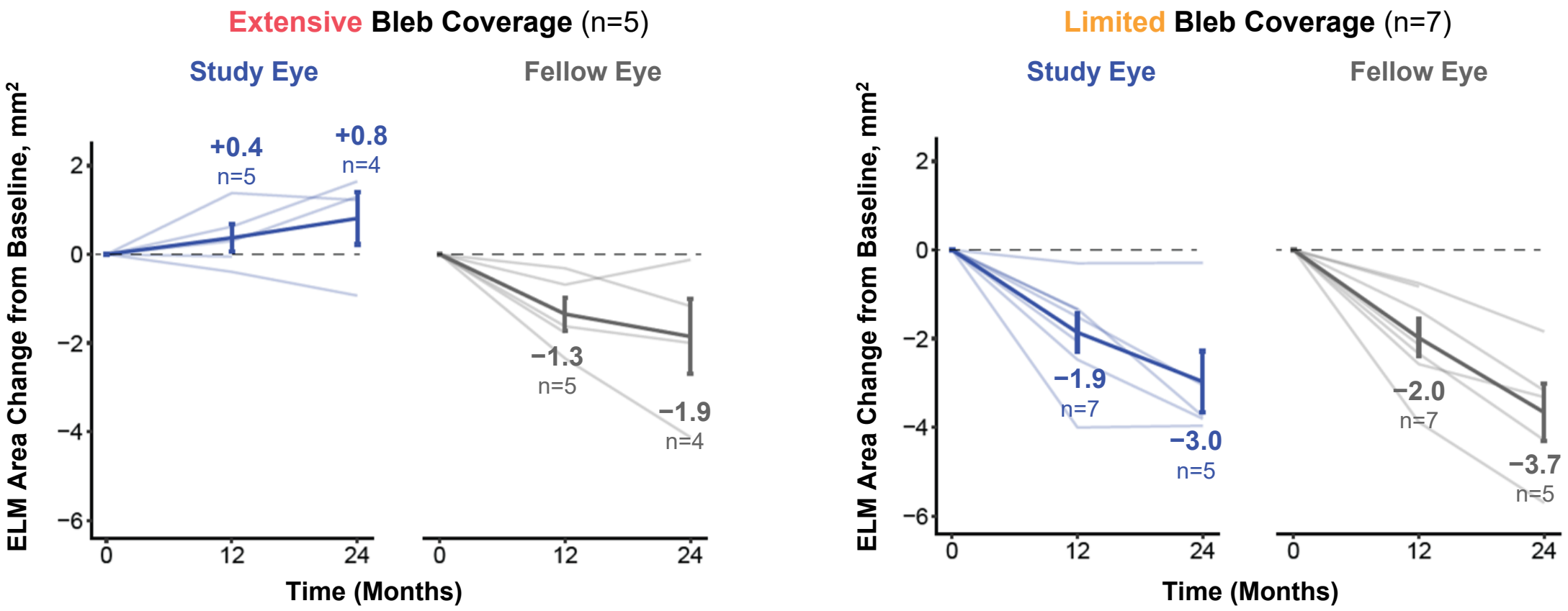
Data cutoff: 30 Oct 2023.

# Maintenance or improvement of ELM was observed in patients with extensive OpRegen bleb coverage of GA

## Area of ELM change

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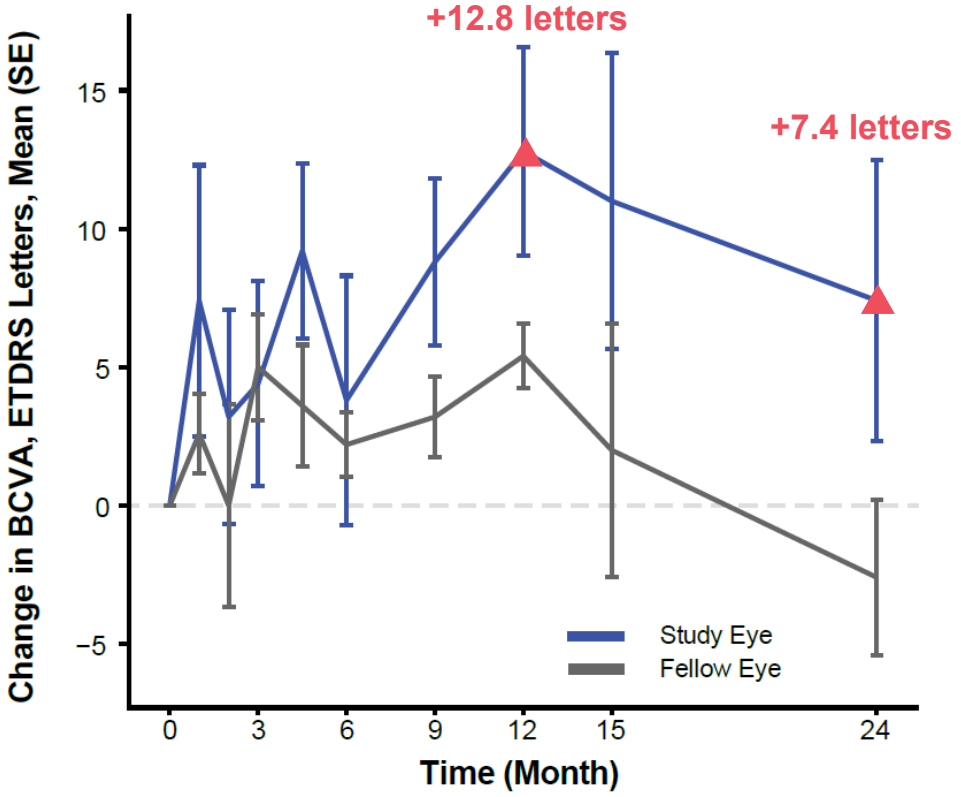
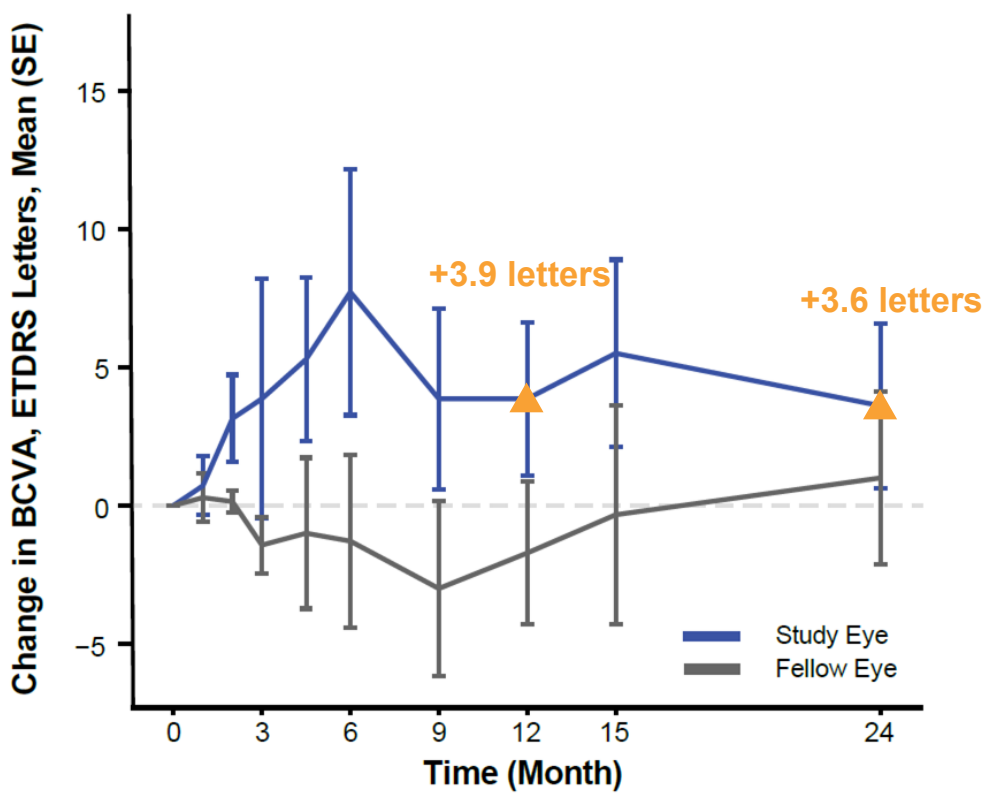
# Greater BCVA gains with extensive OpRegen bleb coverage of GA in Cohort 4 patients through Month 24

## Eyes with extensive bleb coverage (n=5)




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Study Eye | n | 5 | 5 | 4 | 5 | 5 | 5 | 5 |
| Fellow Eye | n | 5 | 5 | 4 | 5 | 5 | 5 | 5 |

## Eyes with limited bleb coverage (n=7)



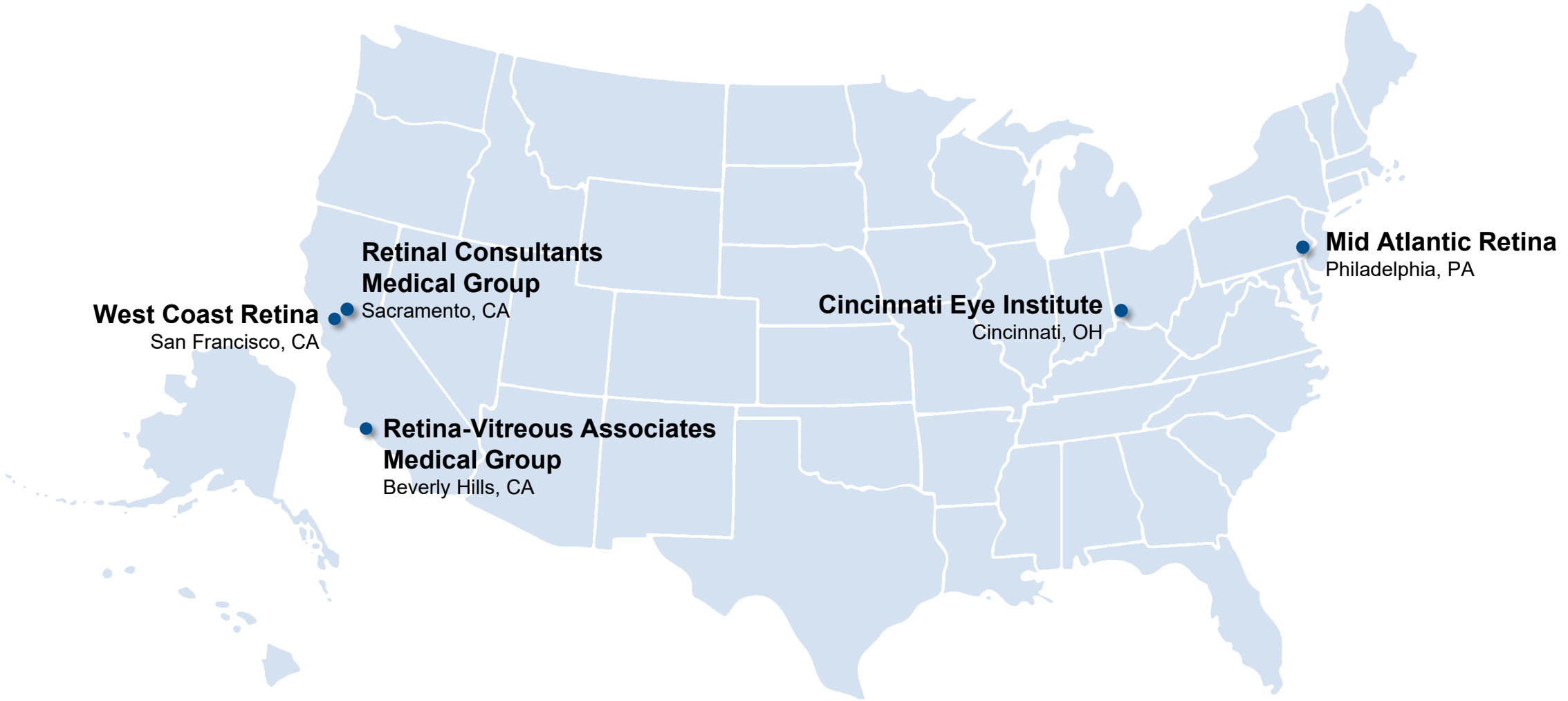

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 7 | 7 | 7 | 7 | 7 | 6 | 5 |
| | | 7 | 7 | 7 | 7 | 7 | 6 | 5 |

Data cutoff: 30 Oct 2023.

# Conclusions

- With extended follow up in a Phase I/IIa study, OpRegen continues to show an acceptable safety profile
- BCVA gains in patients in Cohort 4 (less advanced GA) measured at Month 12 remain evident at Month 24 following subretinal administration of OpRegen
- Improvement in visual acuity and outer retinal structure in patients with extensive OpRegen bleb coverage of their GA area was present through Month 12 (primary endpoint) and persisted through Month 24
- These data suggest that OpRegen RPE cells may counteract RPE cell dysfunction and loss in GA by providing support to the remaining retinal cells within atrophic areas; such effects are durable through at least 24 months after a single administration

# A Phase IIa study evaluating the success of OpRegen delivery to target areas of GA is currently enrolling patients (ClinicalTrials.gov: NCT05626114)



# Investigators, Sites, and Support

## Investigators

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- Richard McDonald, West Coast Retina Group, San Francisco, CA, USA
- Christopher D. Riemann, CEI, Cincinnati, OH, USA
- David Telander, Retinal Consultants Medical Group, Sacramento, CA, USA

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- Avi Ben-Shabat, Lineage Cell Therapeutics, Inc. (Cell Cure Neurosciences, Ltd.), Jerusalem, Israel

## Trial Conduct

- Central Reading Center: Merit CRO (EyeKor), Madison, WI, USA
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- Yumiko Kawai, Lineage Therapeutics, Inc., Carlsbad, CA, USA
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# Thank You to All Patients, Participating Study Sites, and Investigators!