LINEAGE
Cell Therapeutics

# Directed Differentiation and Subretinal Delivery of Allogeneic RPE Cells

## OpRegen®

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

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lineagecell.com

# Forward-Looking Statements

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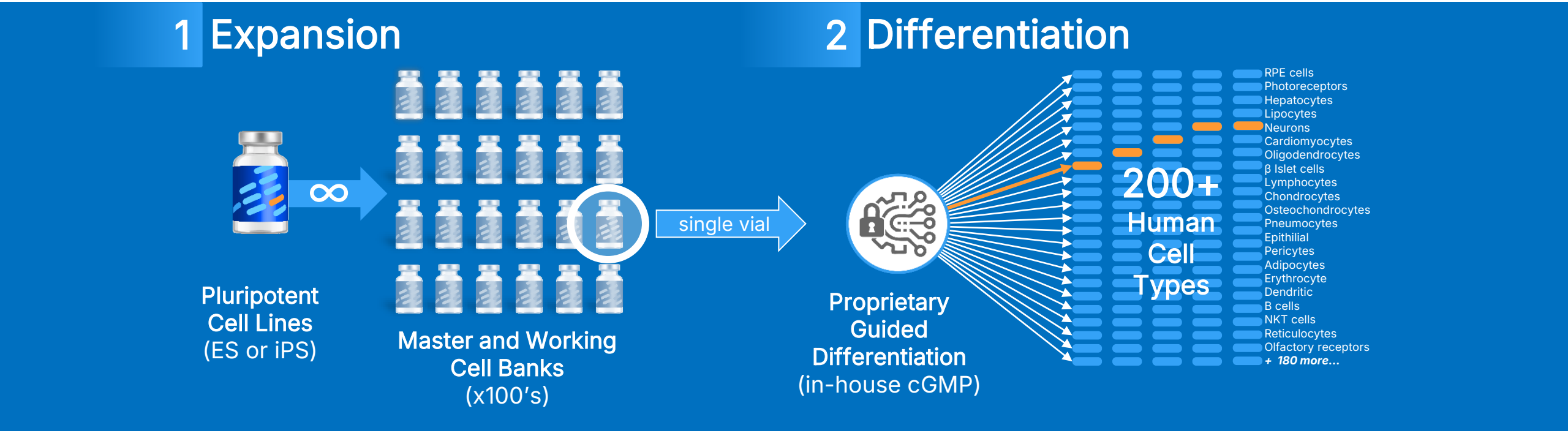
# Neurology Cell Transplant Pipeline – 100% Allogeneic

| FIELD | PROGRAM | PHASE 1 | PHASE 2 | PHASE 3 | |
|---|---|---|---|---|---|
|  Ophthalmology | **OpRegen** Dry AMD with Geographic Atrophy (GA) | 24 patients treated | Enrolling | | Genentech A Member of the Roche Group *Funded Partnership* |
|  Demyelination | **OPC1** Spinal Cord Injury (SCI) | | 30 patients treated | | CIRM CALIFORNIA'S STEM CELL AGENCY *Grant Partner* |
|  Neurotology | **ANP1 *("ReSonance")*** Auditory Neuropathy (Hearing Loss) | *Preclinical* | | | |
|  Ophthalmology | **PNC1** Vision loss; Retinitis Pigmentosa | *Research* | | | |
|  Neurology | **RND1** Undisclosed indications | *Research* | | | eterna *Gene Editing Partner* |

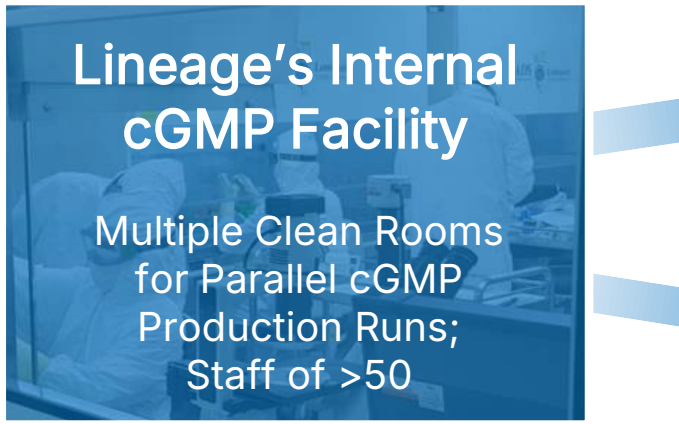
# Lineage Technology: Two-Step Allogeneic Cell Production




- Pluripotent stem cell lines (PSCs) provide an *endless supply* of undifferentiated starting material for all programs
- PSCs can become each of the 200+ cell types of the human body
- No genetic editing is required

- The target cell has been validated by evolution
- Residual pluripotent cells are undetectable
- Generates IP (~375 issued and pending patents)
- Ready to inject formulation (no dose preparation delay)
- One-time treatment – cells integrate without rejection
- Scalable process for clinical and commercial use

# Requirements for a Successful Cell Therapy




## Control (Safety) & Reproducibility

- Source line characterization, cell banking, versatile expansion systems
- Differentiation process development; culture conditions, optimization
- Analytical methods, in-process controls, release criteria

## Purity / Identity

- Clinically compatible post-production processing
- Analytical method development for process control and product release

## Potency

- Functionality and performance testing, reflecting MOA
- Enhancements; genetic modification (optional), various expression systems

## Scalability

- Scale-up modalities, substrates, harvesting protocols
- Clinical and commercial throughputs for drug process and product
- Commercially-attractive cost of goods

LINEAGE
Cell Therapeutics

# OpRegen®

## RPE Cell Transplants to Treat Dry AMD

Improving structure *and* function

# Worldwide Collaboration for OpRegen (RG6501)

— Allogeneic retinal pigment epithelial (RPE) cell transplant to treat ocular disorders (dry AMD with GA)

— Genentech funds development and commercialization

— $50M up front received; eligible for $620M of milestone payments plus double-digit royaltie

—Separate, services agreement signed May 2024

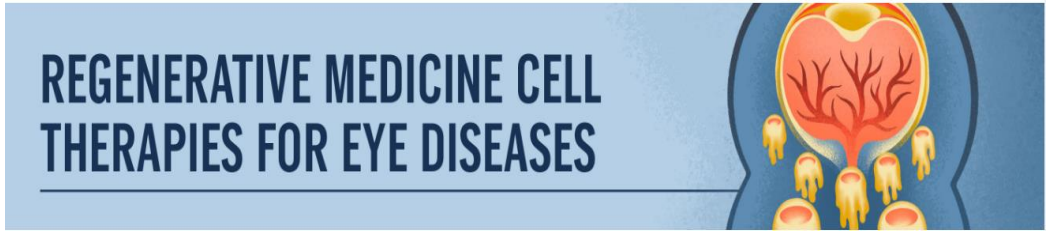
Genentech
A Member of the Roche Group

Roche
125 YEARS
Celebrate Life

"The moment our goal shifted from preservation to restoration"

"Our recent partnership with Lineage Cell Therapeutics…is one of the important routes we are pursuing….The hope is that this treatment could not only slow down progression of the dry form of AMD, but also restore function to the retina."

https://www.celebratelife.roche.com/explore/science/ophthalmology-restoration/




Cell therapy is a powerful approach for turning cells into living medicines

"Cell-based therapies provide the possibility to replace dying or damaged eye cells with new healthy ones. Our aim is to repair the underlying cellular structure of the retina – a thin layer of tissue that lines the back of the eye – to preserve and even restore vision."

*-Tom Zioncheck, Roche*

https://www.gene.com/stories/cell-therapy

# Millions Suffer from Vision Loss due to Dry-AMD

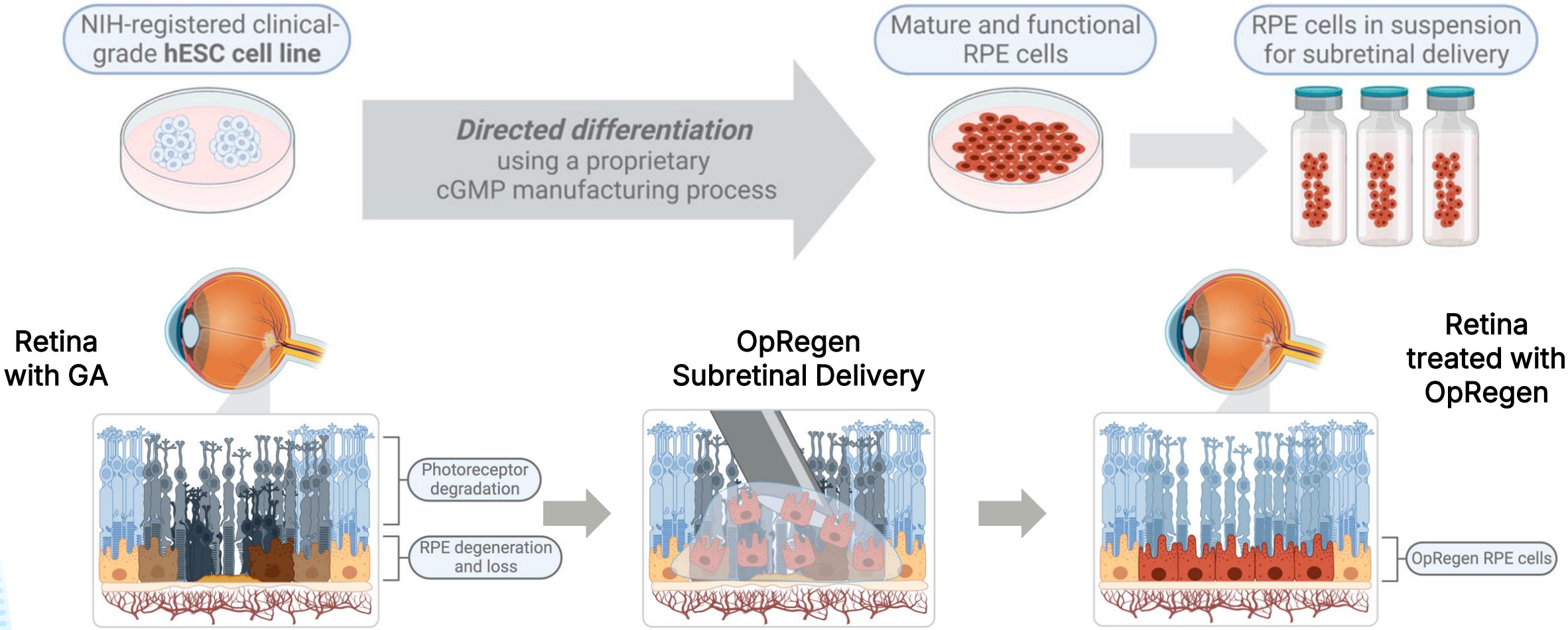
- Age-related macular degeneration (AMD) presents in two forms, wet and dry
- Wet age-related macular degeneration (wet AMD) is usually caused by blood vessels that leak fluid or blood into the macula
- Dry age-related macular degeneration (dry AMD) involves the loss of retinal pigmented epithelium (RPE cells), creating an area of geographic atrophy (GA), causing impaired vision and blindness
- Wet AMD supports >$10Bn[1] in product sales, and dry AMD is eight times more common[2]

*Image courtesy of Macular Society*

*(1) 2018 product sales summary based on publicly reported revenue figures for Lucentis and Eylea.*
*(2) JM Seddon, Epidemiology of age-related macular degeneration. Retina, 3rd ed.;*

# 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.

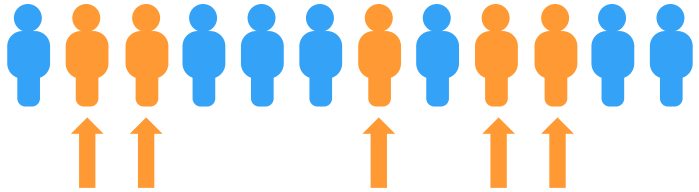
# Phase 1/2a Trial Complete, Long-Term Follow-Up Ongoing

## **Cohorts 1-3** (Dose and Safety)
12 Legally Blind Patients

Generally well-tolerated, no reports of rejection

Cohorts 1-3 (n=12): 12-month gains in visual acuity averaged <5 letters

## **Cohort 4** (Initial Clinical Activity)
12 Impaired Vision Patients



Patients with extensive coverage of atrophic area and foveal center (n=5): **12-month gains in visual acuity averaged +12.8 letters**

**Cohort 4 (n=12): 12-month gains in visual acuity averaged +7.6 letters**

**All patients (n=5) with extensive coverage of their area of atrophy with the OpRegen surgical bleb showed evidence of retinal structure improvement**

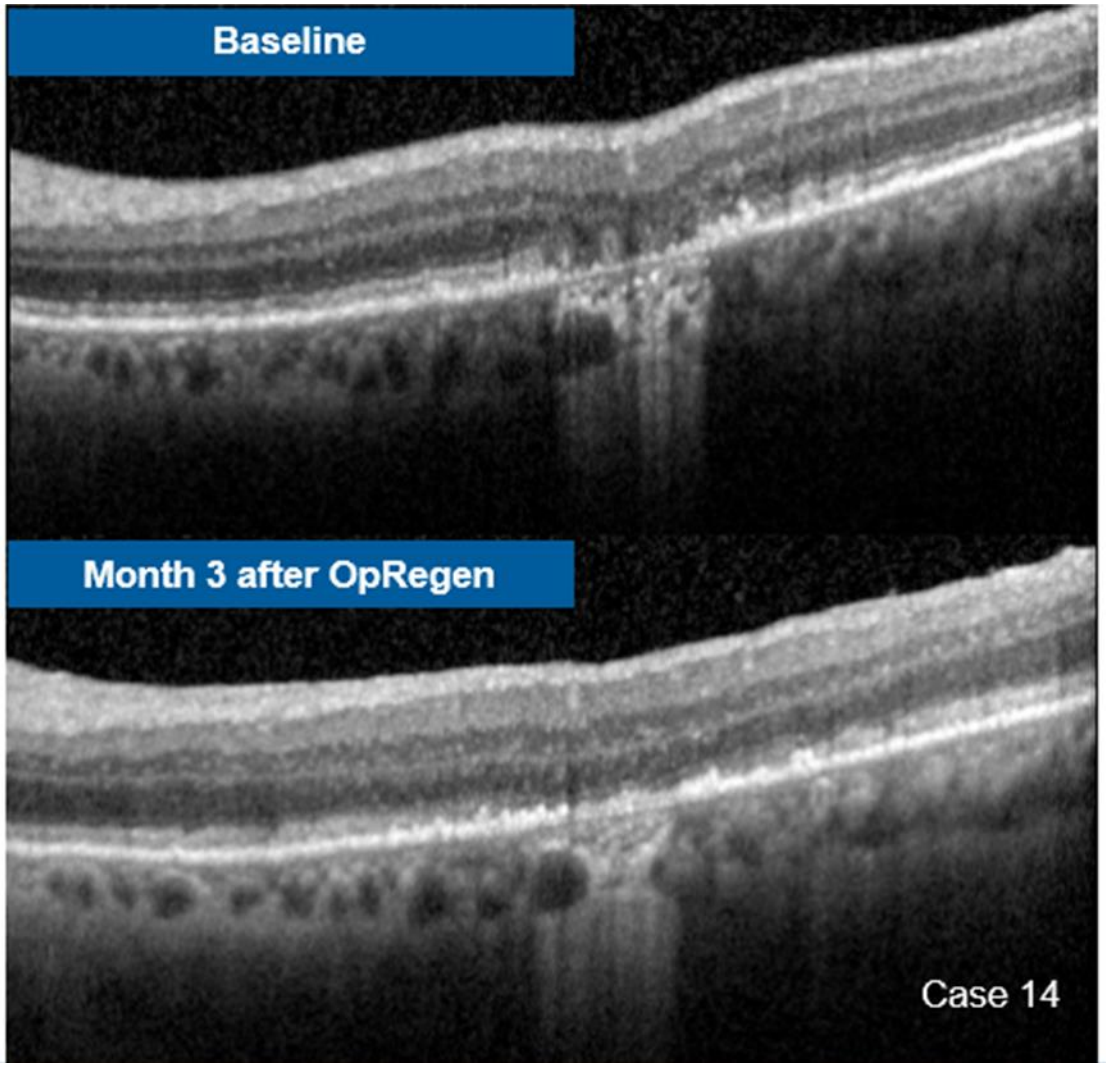
# Exploratory Objective: Onset of Structural Improvement

*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[a]:

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




[a] 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.

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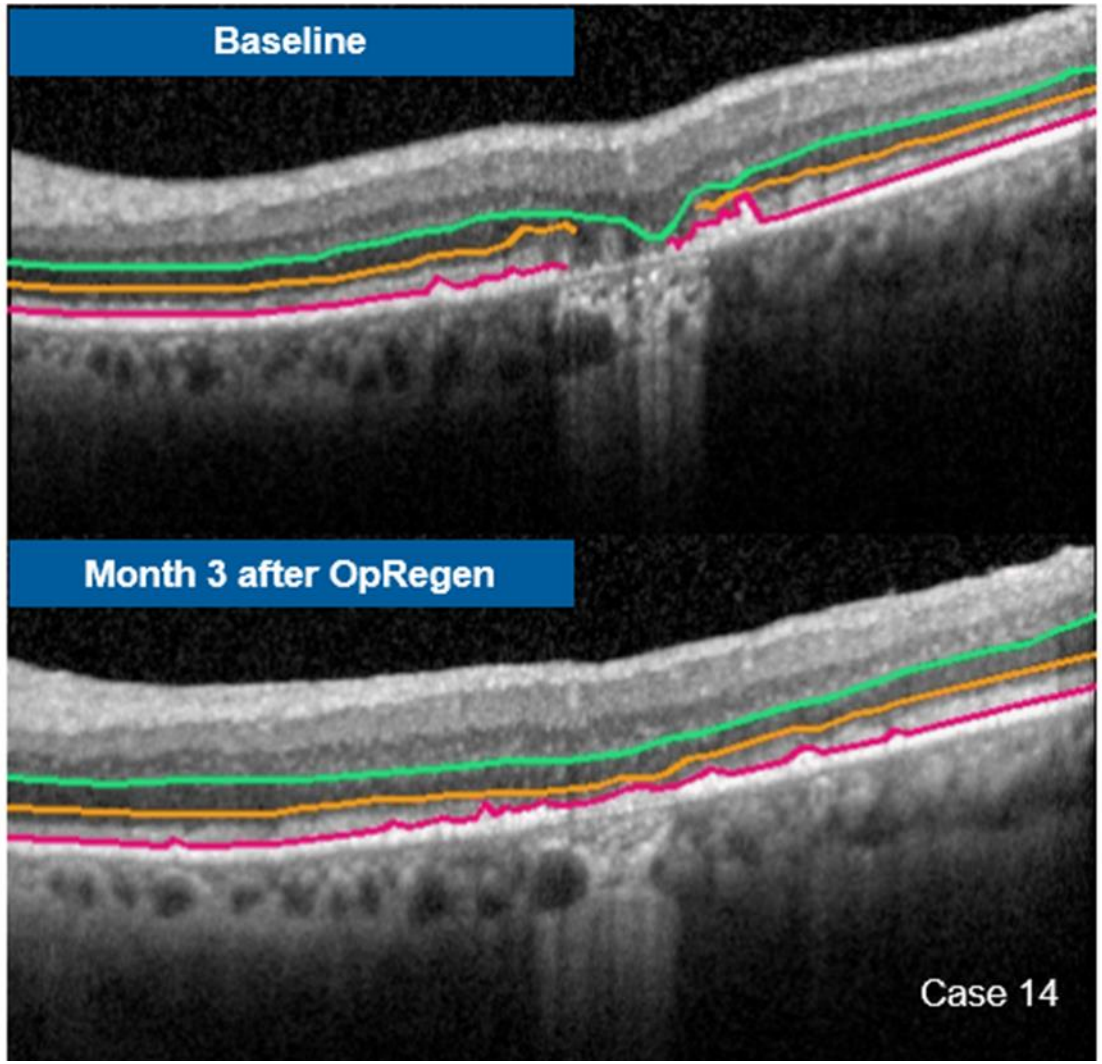


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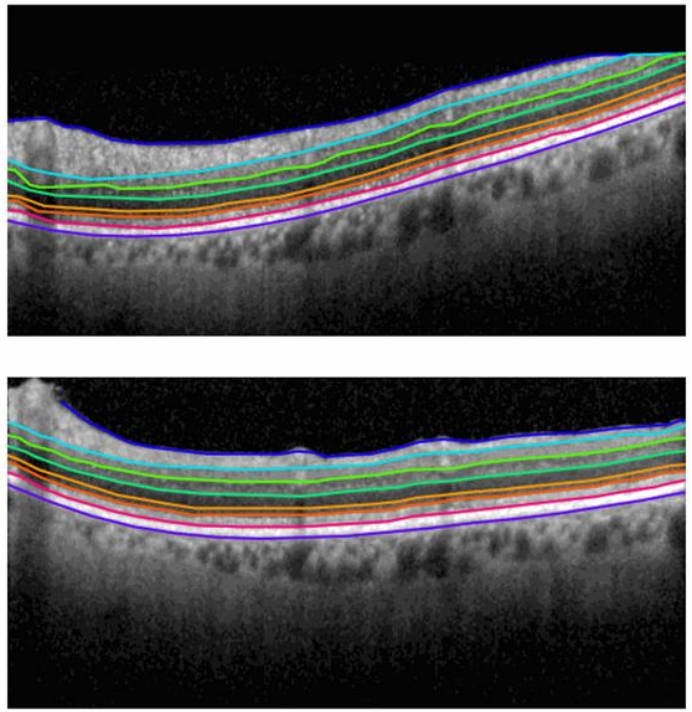
# Quantitation of RPEDC and ELM Area Shows Cases of Improvement Between Baseline and 24 Months Post Treatment

## SD-OCT segmentation[a]

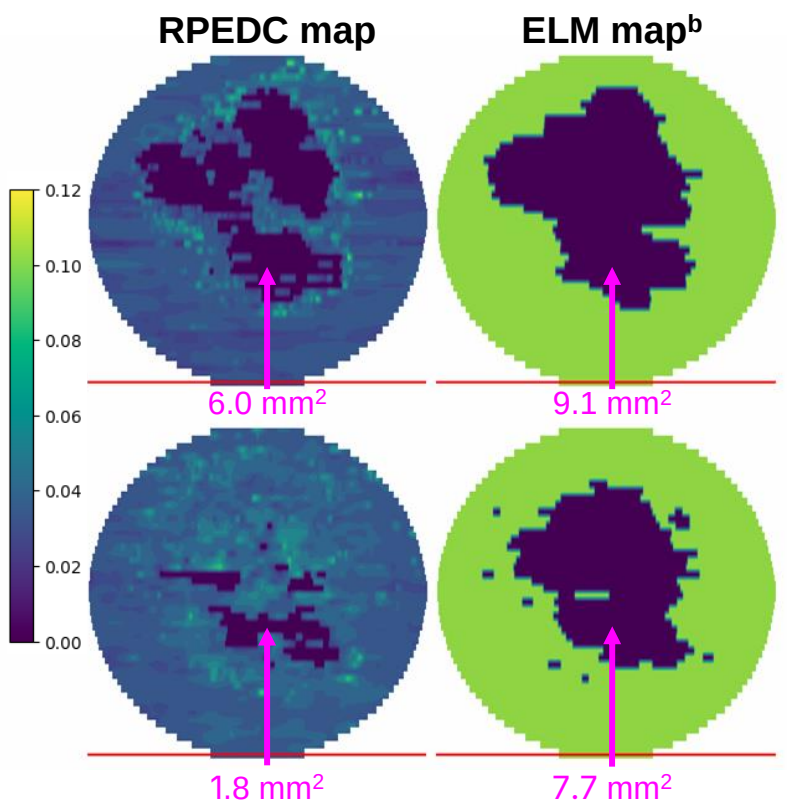
Baseline

Month 24

ILM
oRNFL
oIPL
oOPL
iELM
iEZ
iRPE
BM



## Quantification



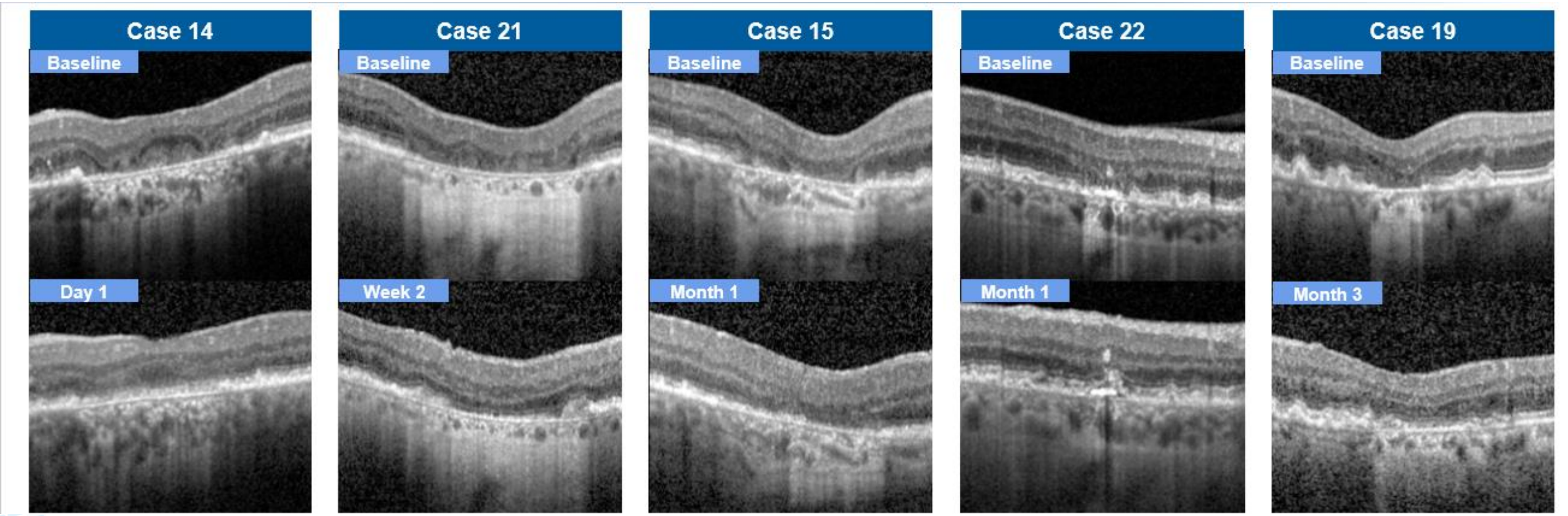

Baseline

Month 24

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.

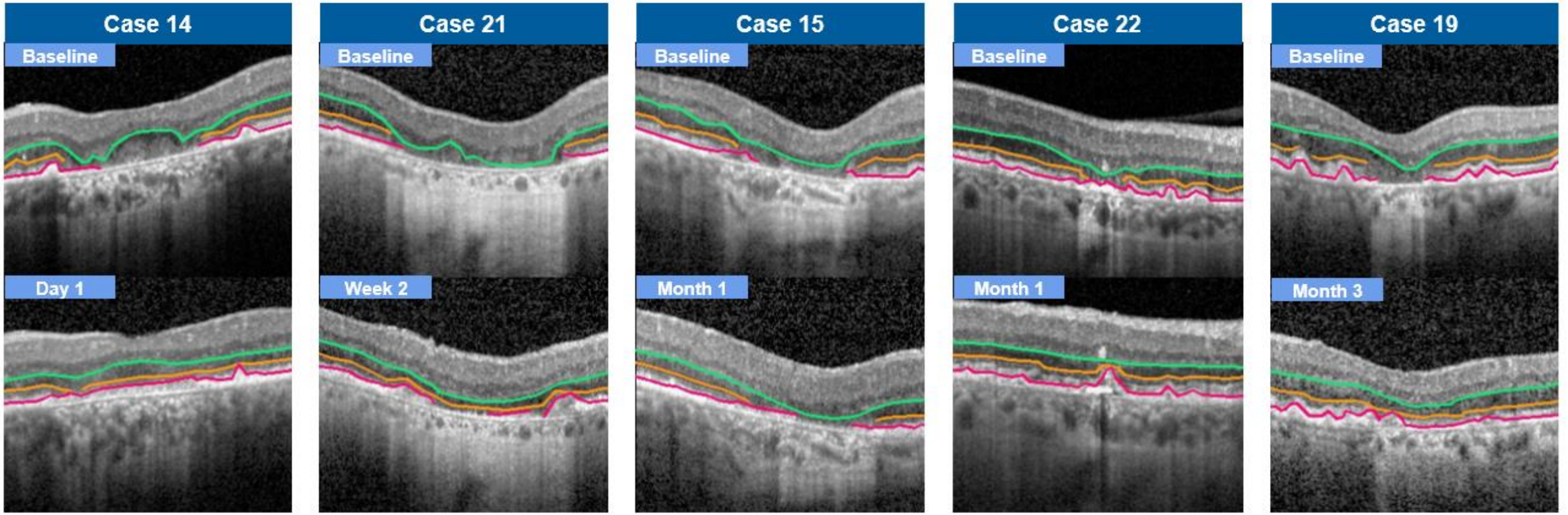
**Case #14**

# 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

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

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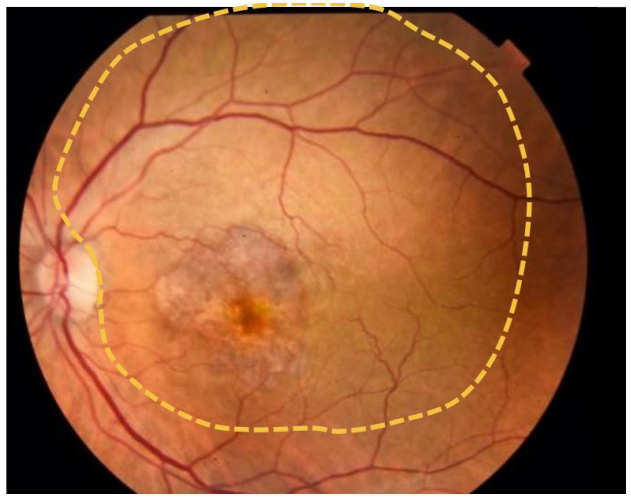
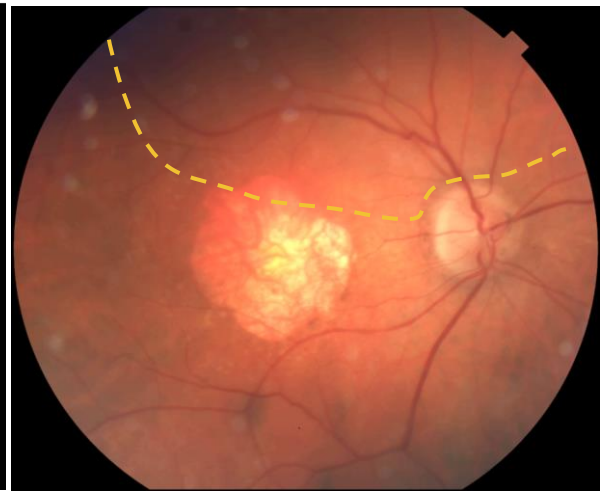
# Greater Visual and Structural Improvements in 5 Patients in Cohort 4 with Extensive Bleb Coverage

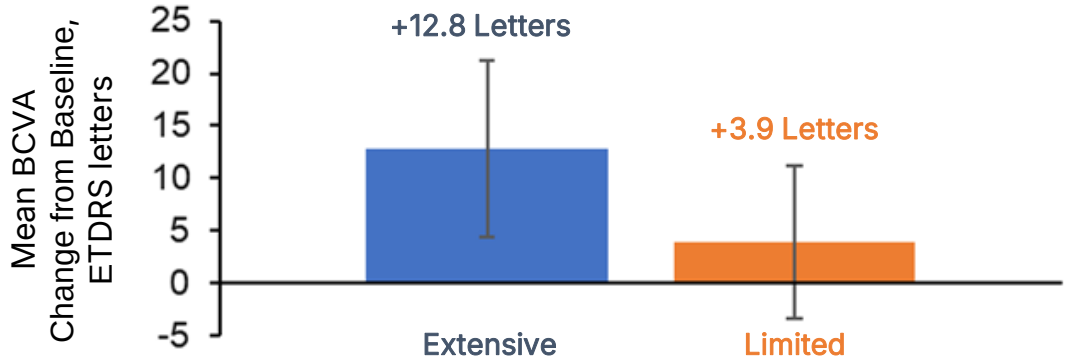


**Extensive**
**Bleb Coverage**
Considerable bleb coverage of GA area (including fovea)
**(n=5)**

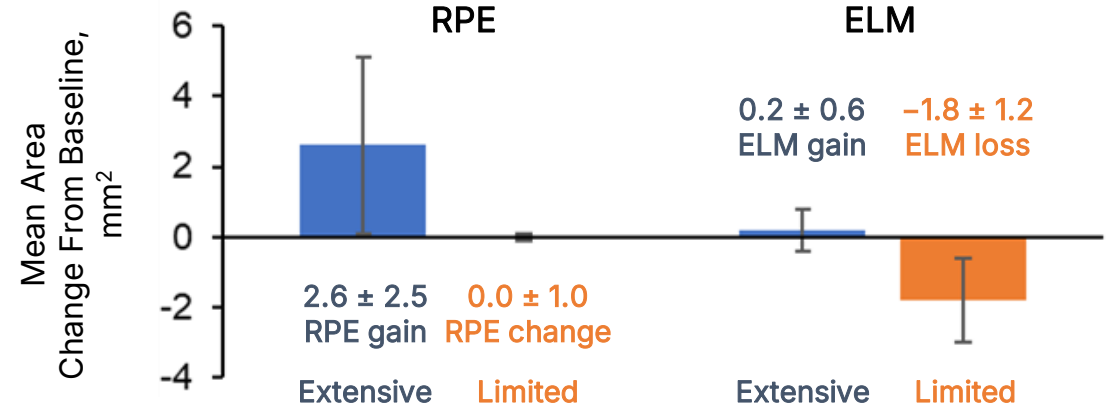


**Limited**
**Bleb Coverage**
Minimal to no bleb coverage of GA area
**(n=7)**

## BCVA Change in Study Eye at Month 12



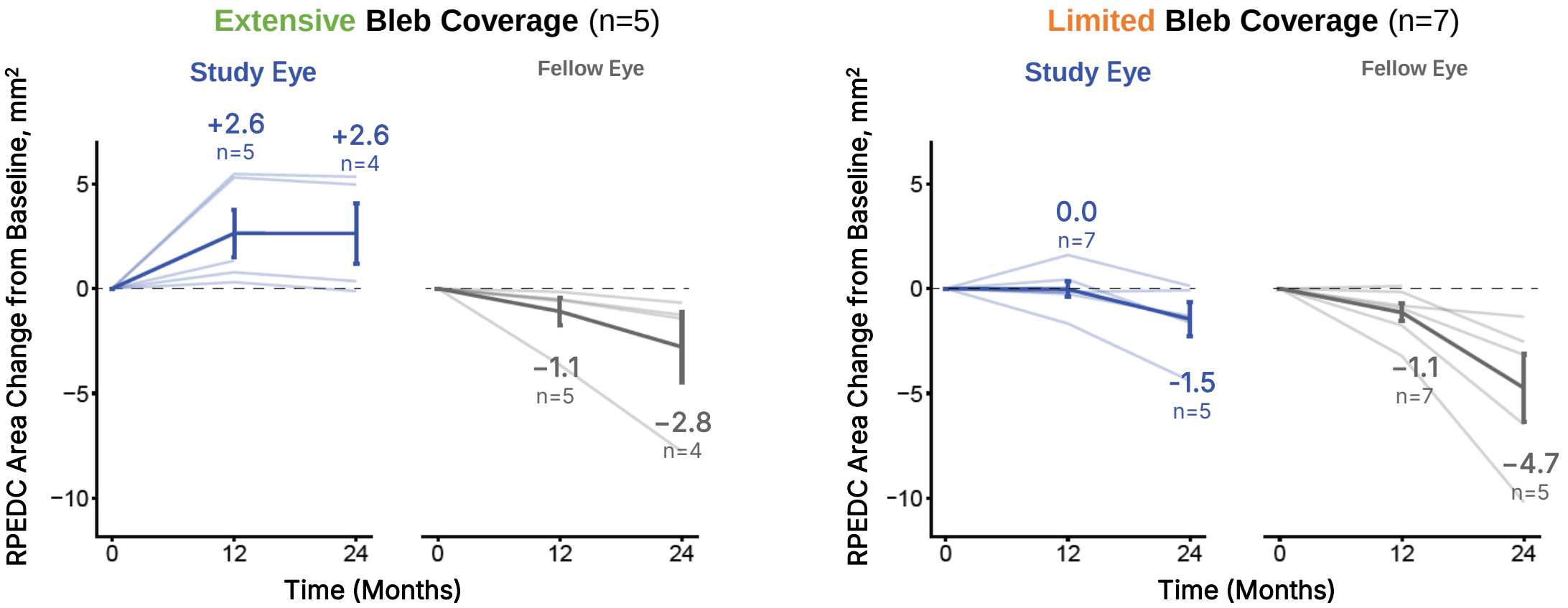

## RPE and ELM Change in Study Eye at Month 12




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

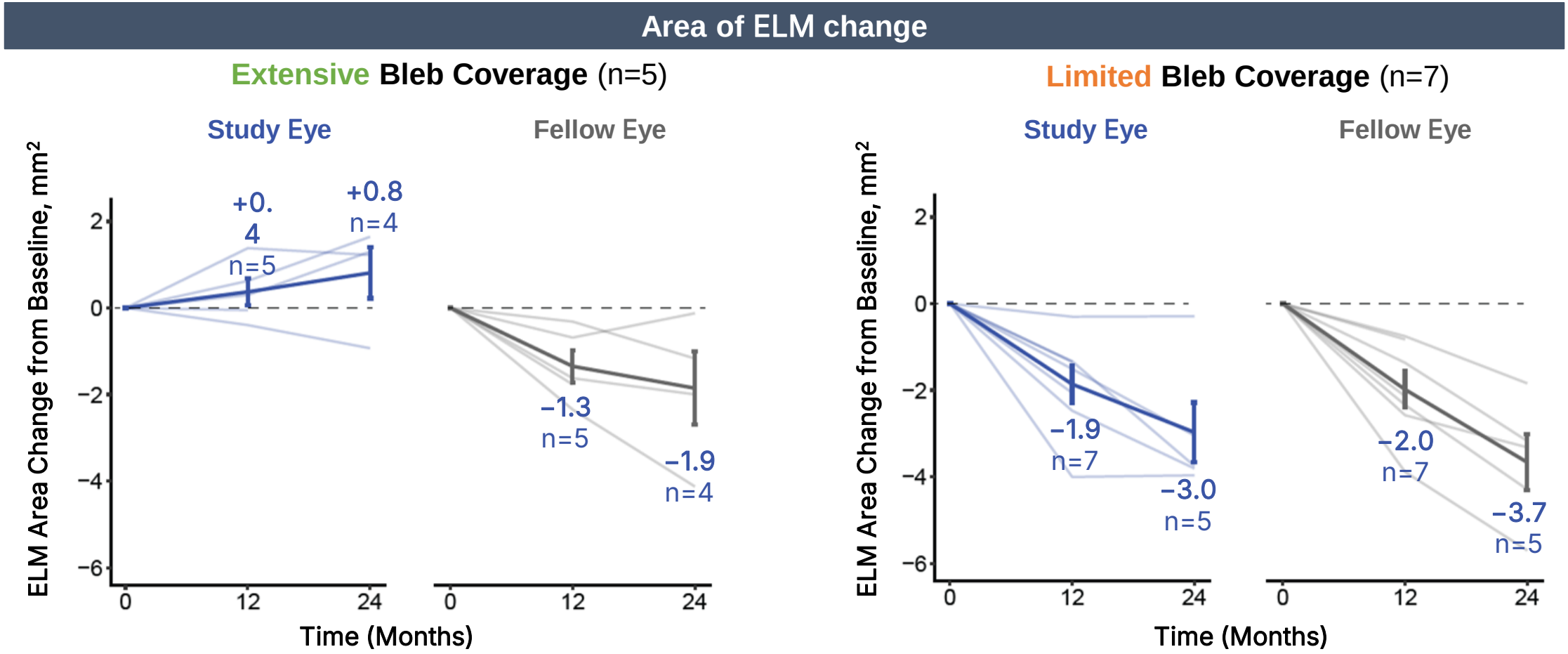
# Maintenance or Improvement of RPEDC Observed in Patients with Extensive OpRegen Bleb Coverage of GA

**Area of RPEDC change**



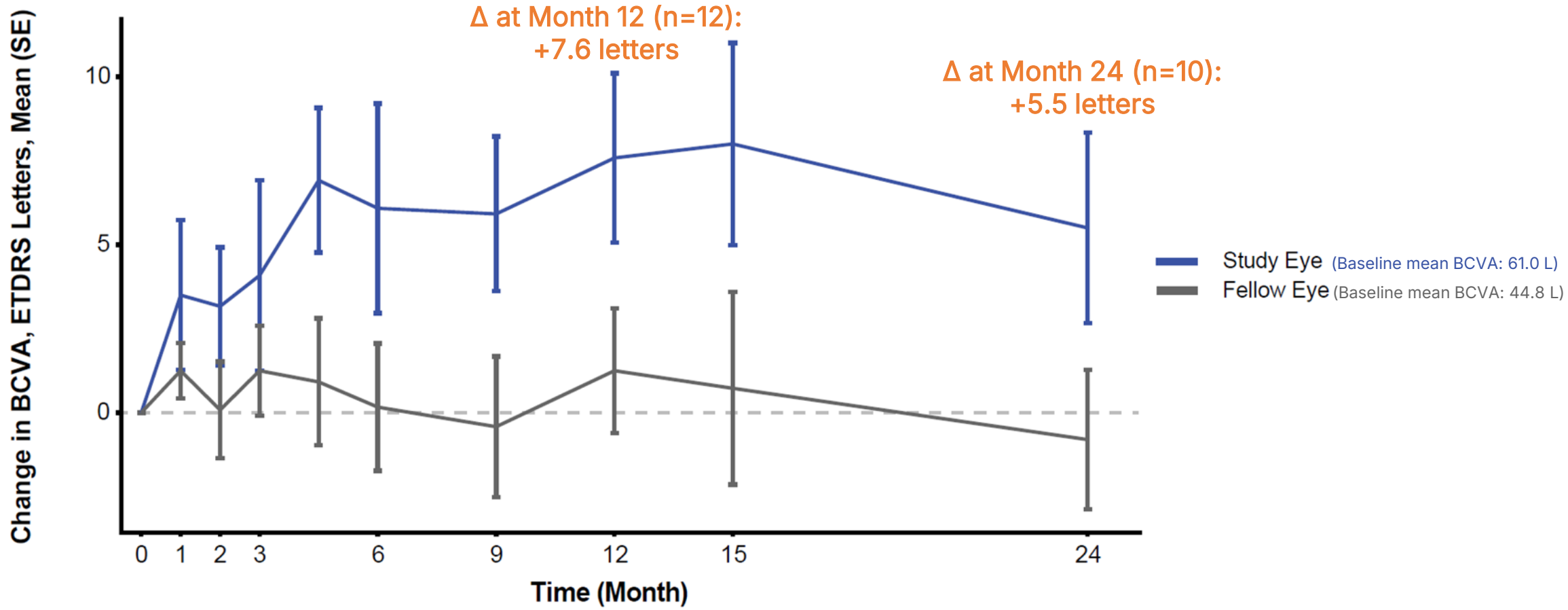

RPEDC, retinal pigment epithelium drusen complex.
Thick lines represent the mean and error bars represent standard error.
Data cutoff: 30 Oct 2023.

# Maintenance or Improvement of ELM Observed in Patients with Extensive OpRegen Bleb Coverage of GA



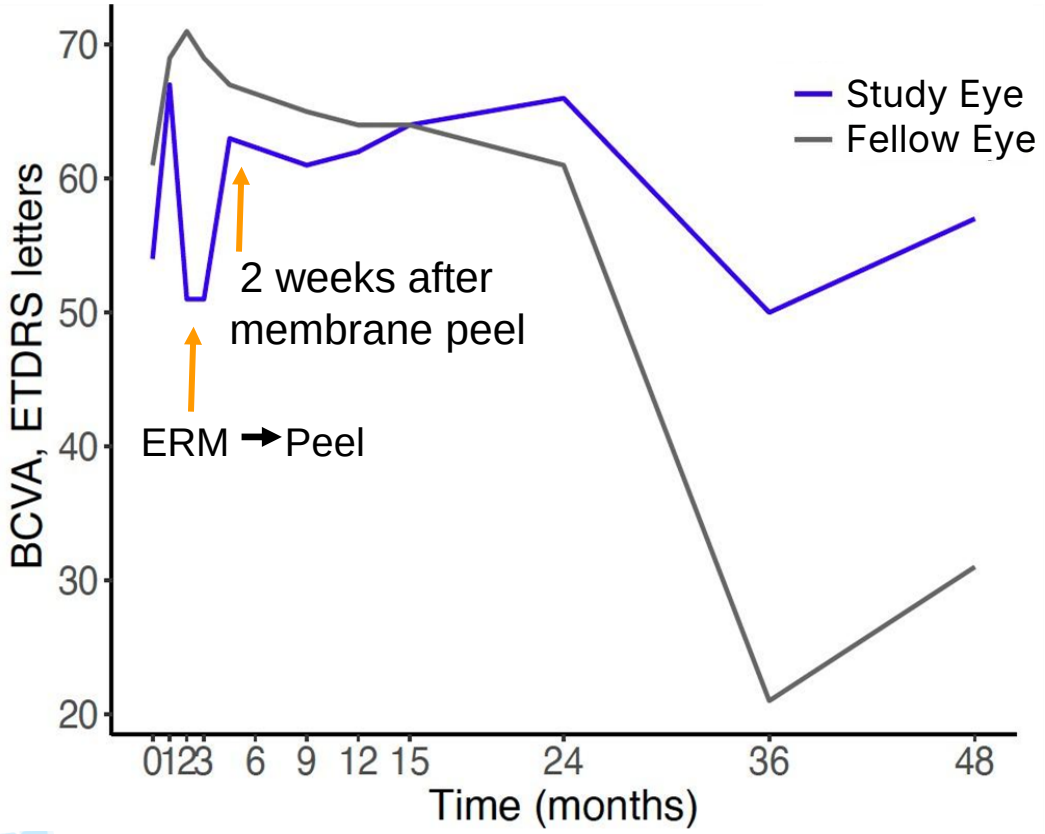

Thick lines represent the mean and error bars represent standard error.
Data cutoff: 30 Oct 2023.

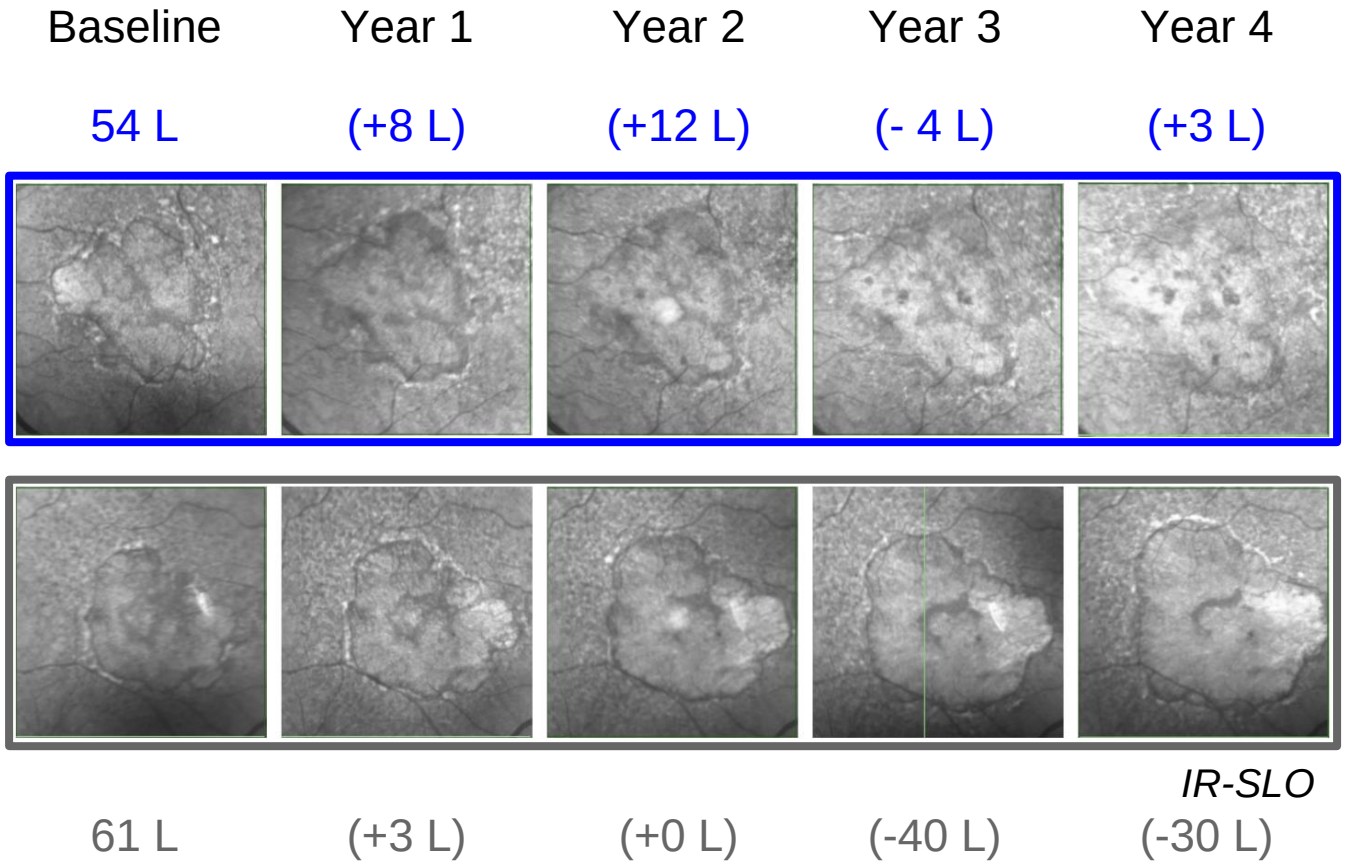
# Cohort 4 (Less advanced GA) BCVA Gains in Study Eyes Sustained 24 Months Post Treatment



# 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

# Safety Summary[1]

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

- All 24 (100%) treated patients reported ≥1 AE and ≥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

[1] 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

Genentech
A Member of the Roche Group

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

- Study sponsored 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 at 6 study sites in U.S. & Israel

(ClinicalTrials.gov: NCT05626114)

# Lineage Cell Therapeutics

#ReplaceAndRestore

## Broad Capabilities

Cell manufacturing and transplant technology

**5**

Cell types in active development

**>200**

Cell types for future targeting

**∞**

Commercial scalability and cell line supply

## Highly Differentiated

Allogeneic product candidates

**2**

Product candidates in active clinical trials

**0**

>50 patients treated with zero cases of rejection

**>$1B**

Addressing multi-billion dollar markets

## Validated Technology

Global partnership for lead asset OpRegen®

**$670M***

Partnership

Genentech
A Member of the Roche Group

**5**

Unprecedented cases of retinal regeneration

**1**

Single administration per patient

** Includes $50M up front payment received Jan 2022, $620M of eligible milestones, plus double-digit royalties on sales*

Thank You to Roche and Genentech, a member of the Roche Group; all participating clinical study sites, study investigators, and the patients.

Brian M. Culley, CEO

bculley@lineagecell.com


# Our Inspiration.

View their stories at
lineagecell.com/media