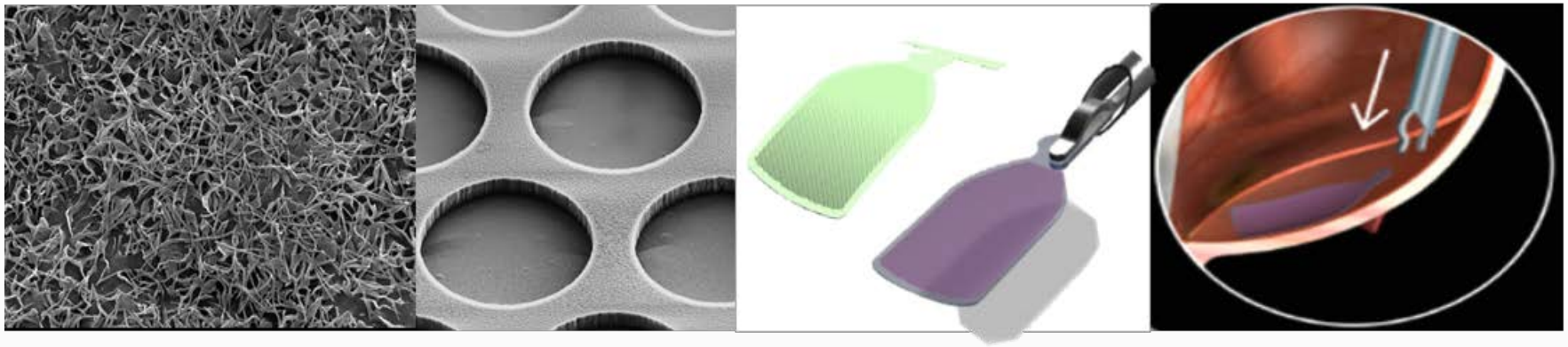

Advancement of a Cryopreserved Bio-Engineered hESC-Derived Retinal Pigmented Epithelial Cell (RPE) Implant for Geographic Atrophy to a Phase IIb Clinical Trial

Jane S Lebkowski Ph.D
President, Regenerative Patch Technologies LLC
December 11, 2025

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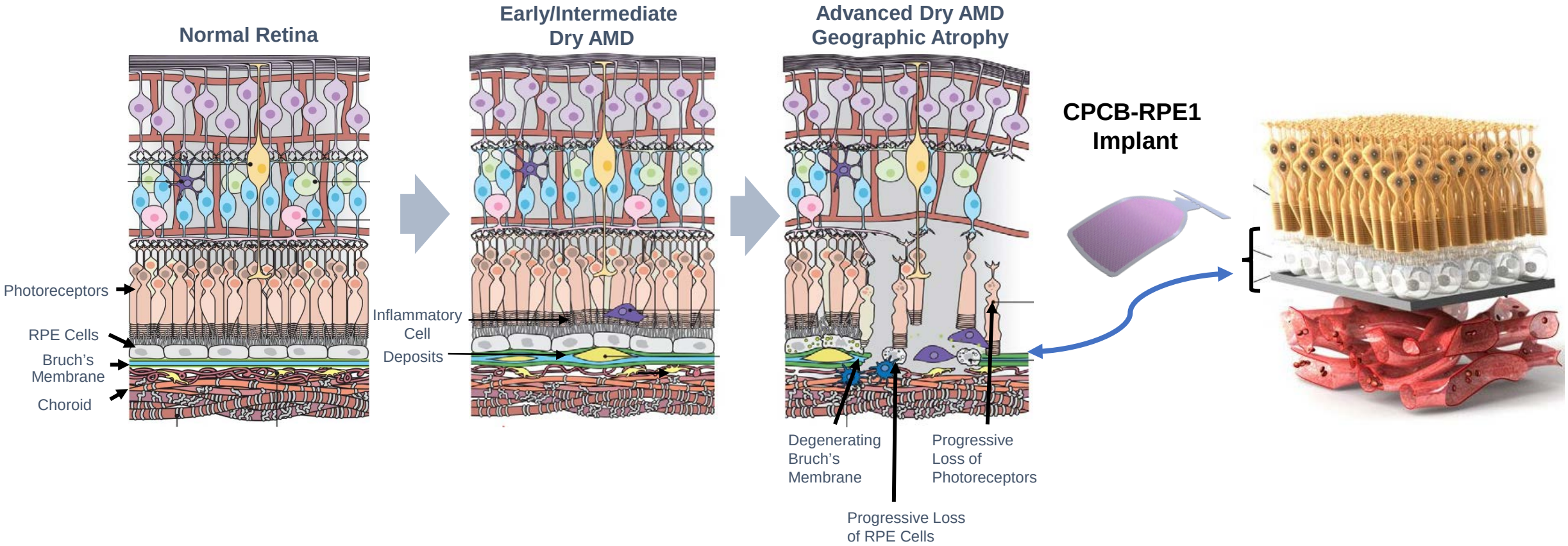
The CPCB-RPE1 Implant Addresses the Disease Pathology in Geographic Atrophy to Potentially Improve Visual Function

Progression of Dry AMD

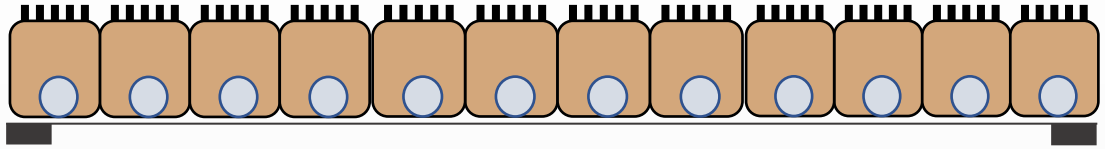
Problem: There are no native mechanisms in the eye to replace degenerating RPE cells. Transplantation of these cells is required.

The Approach: Insert Implant of RPE Cells on a Synthetic Bruch's Membrane to Provide Metabolic and Structural Support for Photoreceptors



The CPCB-RPE1 Implant: A Composite RPE Cell-Parylene Membrane Implant

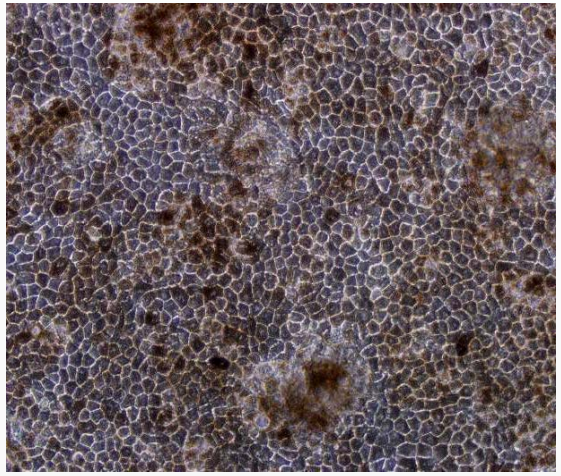
Implant Called CPCB-RPE1



Polarized Healthy RPE Cells:
Replace Dysfunctional RPE Layer in AMD Retina

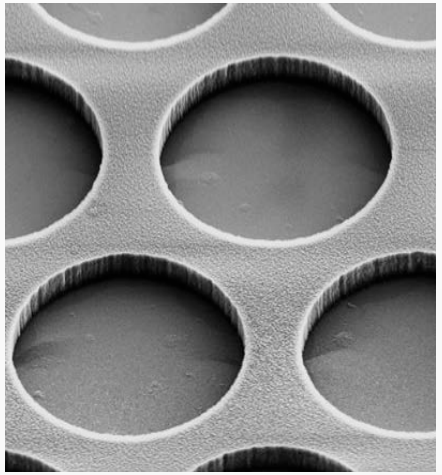
Ultrathin Diffusible Parylene Membrane:
Replace Degenerating Bruch's Membrane

RPE Cells Produced from Pluripotent Stem Cells



+

Ultrathin Parylene Membrane



CPCB-RPE1 Implant

Implant Body

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Phase I/IIa Clinical Trial Designed to Establish Safety and Potential Activity of the Implant in Patients with Advanced Disease

Study Design and Population	
Design	Single Arm Open Label Study
Indication	Advanced, Dry Age-Related Macular Degeneration with Significant Geographic Atrophy Involving the Central Fovea
Number of Subjects	16 Subjects
Visual Acuity of Treated Subjects	BCVA ≤20/200; Worst Eye Treated; All Treated Eyes Legally Blind
Dose	One Implant
Primary Endpoint	Test the Safety and Tolerability of CPCB-RPE1 at 1 Year Post Implantation
Secondary Endpoint	Assess Visual Acuity Retinal Function After CPCB-RPE1 Administration
Immunosuppression	68-Day Immunosuppression Protocol Using Tacrolimus

Phase I/IIa clinical trial designed to test:

- The safety and feasibility of administration of the implant
- The safety of the implant
- The immunosuppression regimen
- Possible signals of efficacy

Very late-stage, legally blind, subjects selected for first-in-human clinical trial due to novelty of product and approach

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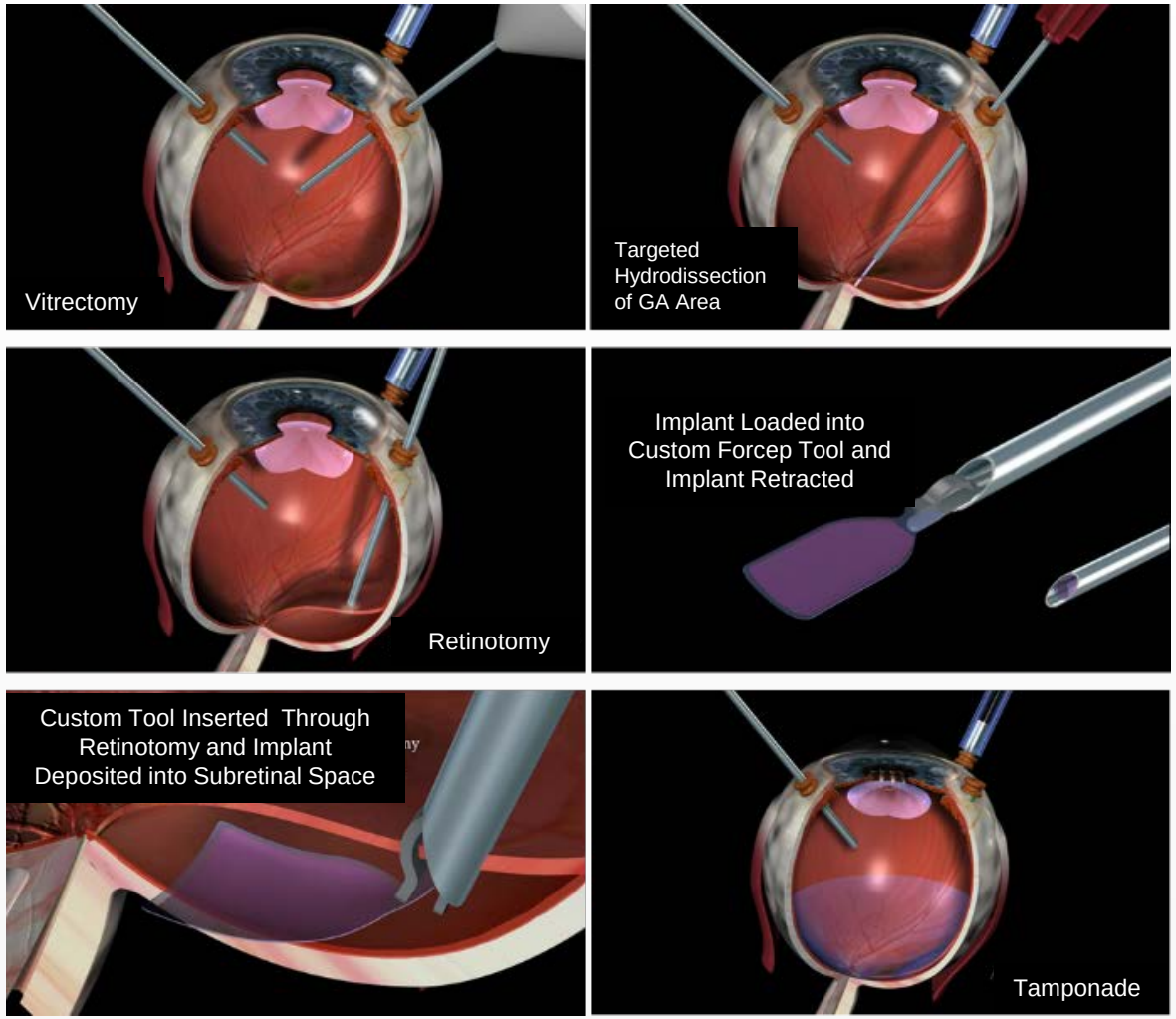
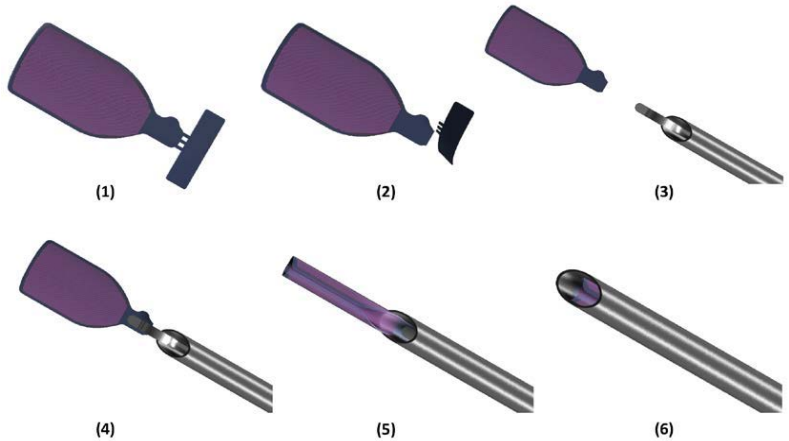
Implant Surgical Delivery: Uses Established Retinal Surgery Procedures





Custom surgical tool and ability to fold membrane enables delivery through 1.5mm Peripheral Retinopathy

- Uses Established Retinal Surgery Procedures
- Administered as Outpatient Surgery

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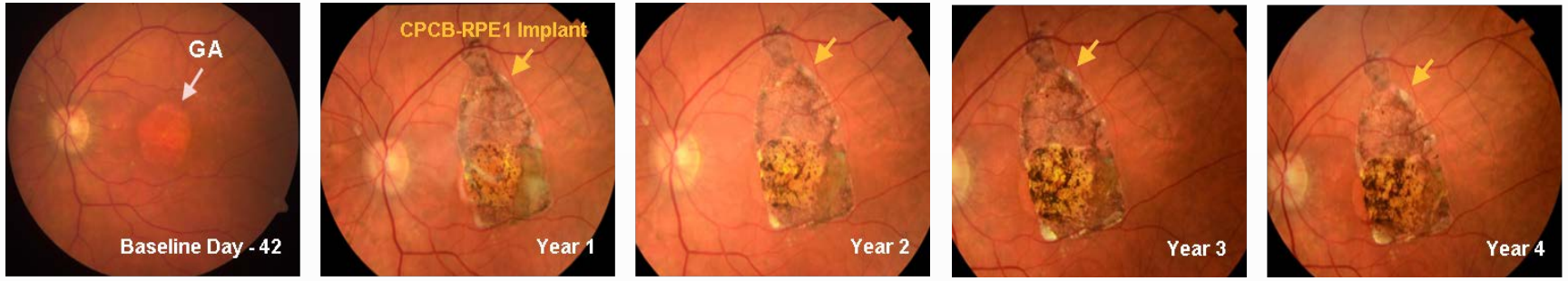
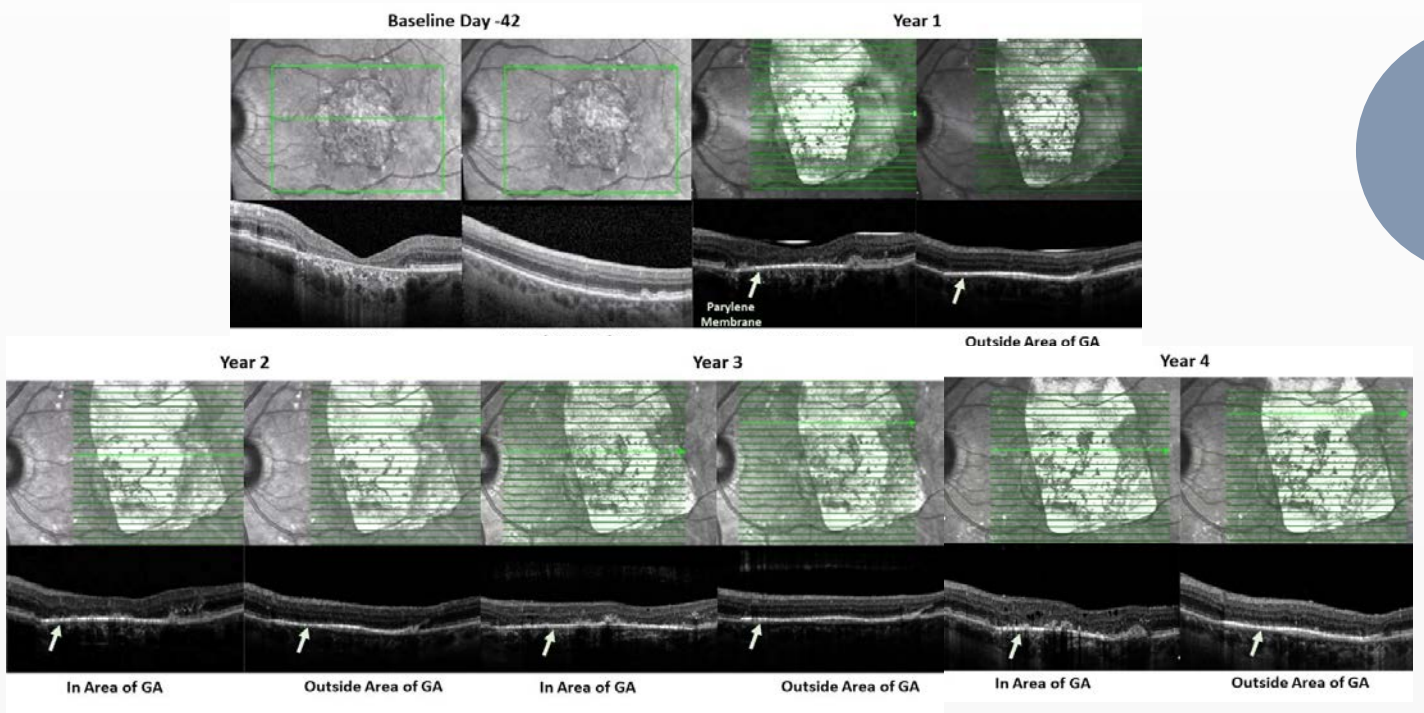
CPCB-RPE1 Implant Delivery Safe and Positioned Over Area of Geographic Atrophy





- The surgical procedure is feasible and safe in the outpatient setting
- Refined implantation procedure to minimize hemorrhage and fibrinous debris
- Implant stably positioned over area of GA in all patients
- Stable position of implant over time
- No evidence of implant degradation
- Good preservation of retinal architecture even in areas of intact RPE layer

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Increased Stable or Improved Best Corrected Visual Acuity Over Time

	One Year Post-Implantation		As of Last Follow-up (mean 37.4 months, median 36.9 months, range 12 to 54 months)	
% Subjects With	**Treated Eye % (n/15 Implanted Subjects)**	**Untreated Eye % (n/15 Implanted Subjects)**	**Treated Eye % (n/15 Implanted Subjects)**	**Untreated Eye % (n/15 Implanted Subjects)**
% Subjects with Improved BCVA (>5 Letter Gain)	27% (4/15)	7% (1/15)	27% (4/15)	7% (1/15)
% Subjects with Improved (>5 Letter Gain) or Stable BCVA (+/- 5 Letters from Baseline)	67% (10/15)	47% (7/15)	53% (8/15)	20% (3/15)
% Subjects with Worse BCVA (>5 Letter Loss)	33% (5/15)	53% (8/15)	47% (7/15)	80% (12/15)

Improvements Ranged from 7-16 letters

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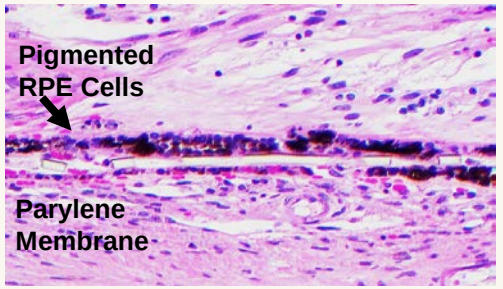
No Class I or Class II HLA Matching Performed Between Donor RPE Cells and Recipient Subject: Genotyping Performed

- Genotyping performed on 16 HLA Class I and Class II alleles to determine extent of mismatches*
- All subjects have more than 50% of alleles mismatched
- Best match is 7 of 16 HLA alleles
- No peripheral blood antibody responses to donor cell MHC molecules

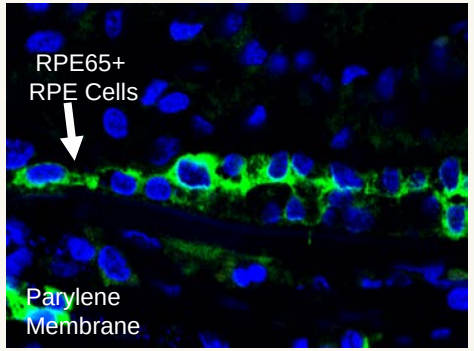
Subject	# Mismatched HLA Alleles	Subject	# Mismatched HLA Alleles
204	9 of 12	**401**	13 of 16
125	14 of 16	**216**	12 of 16
128	9 of 16	**403**	12 of 16
303	11 of 16	**404**	13 of 16
304	10 of 16	**606**	13 of 16
305	12 of 16	**502**	13 of 16
130	11 of 16	**607**	12 of 16
501	13 of 16		

*Genotyping performed at UCLA Immunogenetics Lab

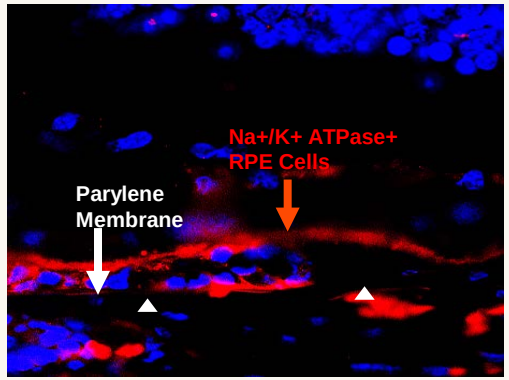
The Fully Allogeneic RPE Cells Survive at Least 2 Years with Only a Short Course of Immunosuppression



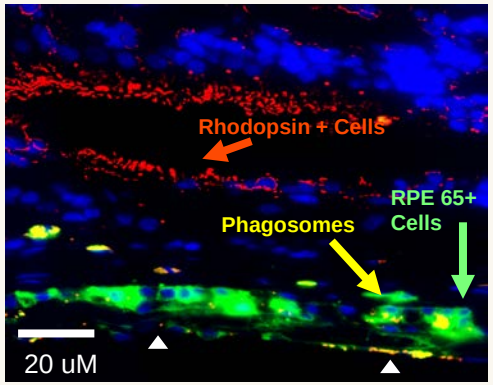
- Pigmented RPE Cells Survive on the Parylene Membrane at Least 2 Years



- Implanted RPE Cells Express RPE65, a Visual Function Protein



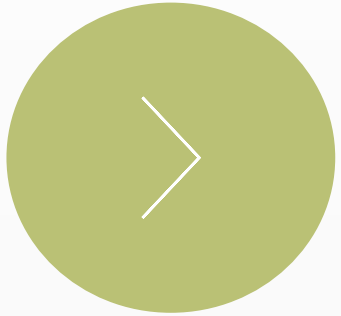
- Implanted RPE Cells Have Apical Expression of Na+/K+ATPase, Suggesting Polarized Mature Function.



- Spared Rhodopsin + Rosettes Over Implant
- Presence of Phagosomes Suggests Functional Integration of Implant RPE Cells

CPCB-RPE1 CMC Development for Advanced Clinical Trials and Eventual Commercialization

Develop Methods to Provide a Shelf Stable Product that Can Be Distributed Globally to Meet the Global Market



- Develop a long-term, stable storage formulation for the CPCB-RPE1 implant
- Scale RPE production to support registration trials and eventual commercialization.
- Scale implant production to support registration trials and eventual commercialization.
- Incorporate automation processes
- Optimize COGs and distribution to support an affordable therapeutic product compatible with reimbursement policies.

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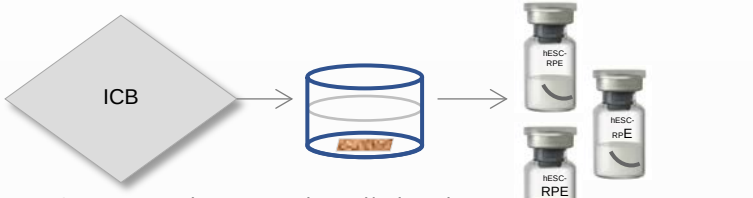
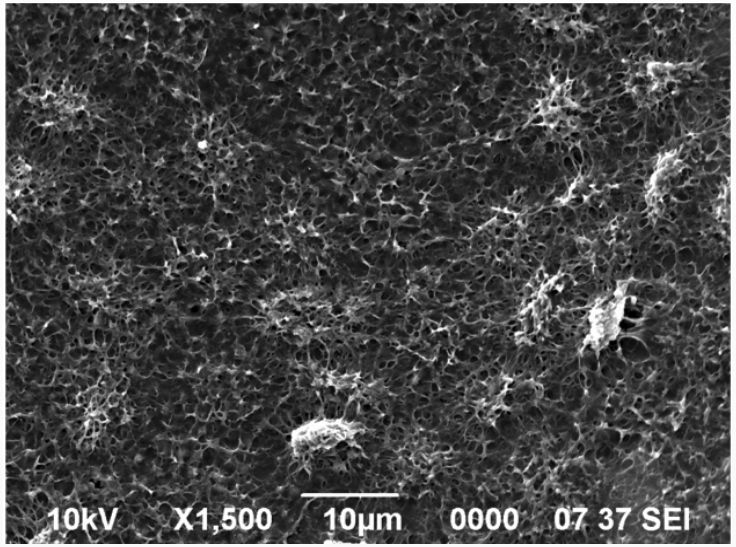
Cryopreserved and Thawed CPCB-RPE1 Implants Form Polarized Cells with Apical and Basal Structures Like the Non-cryopreserved Implant

Production of Implant



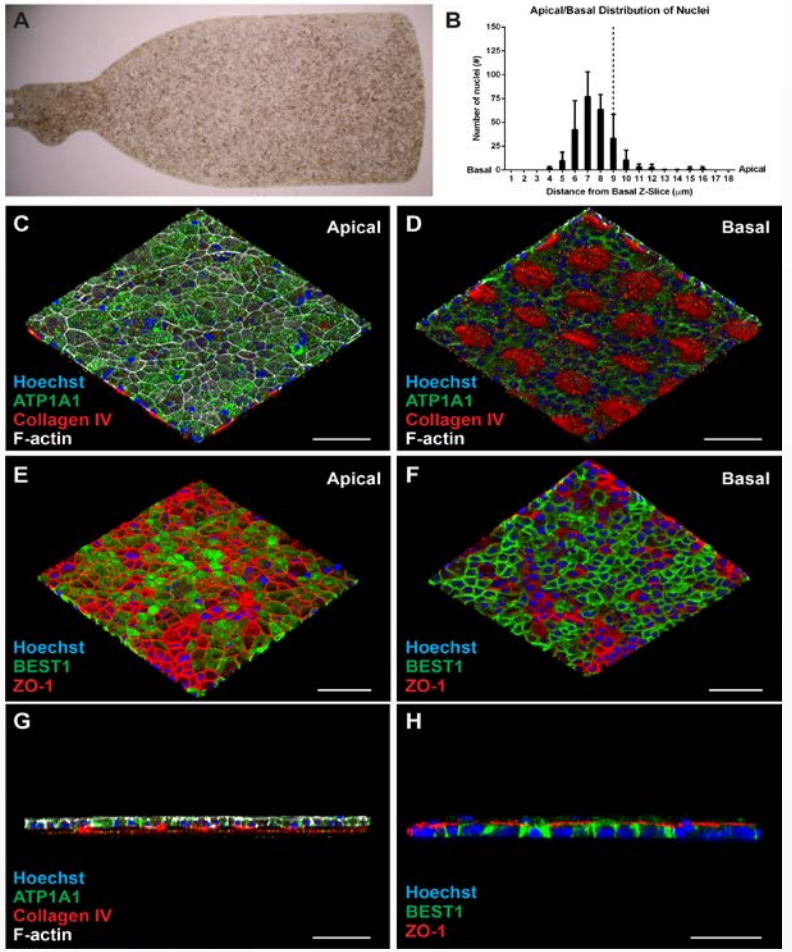
Cryopreserved Long-Term Storage Condition

Develop Apical Villi



Confocal Imaging of Cryopreserved CPCB-RPE1 Showing Cell Polarity Post-Thaw as Assessed for Apical and Basal Markers.

Polarized Phenotype



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Key Objective of Phase IIb Clinical Trial

Phase IIb Clinical Trial

Designed to:

- Assess safety and effectiveness of the CPCB-RPE1 implant in the target GA population with less severe disease intended for registration.
- Verify study procedures to be used in Phase III registration trials including:
  - Use of multiple clinical trial sites for implantation of the CPCB-RPE1 implant
  - Use of the cryopreserved implant to enable widespread distribution.
  - Test outcome measures such as microperimetry that FDA accepts as registration endpoints for licensure.
  - Incorporate randomization and masking schemes that FDA currently requires for registration trials.

Features of Phase IIb Clinical Trial

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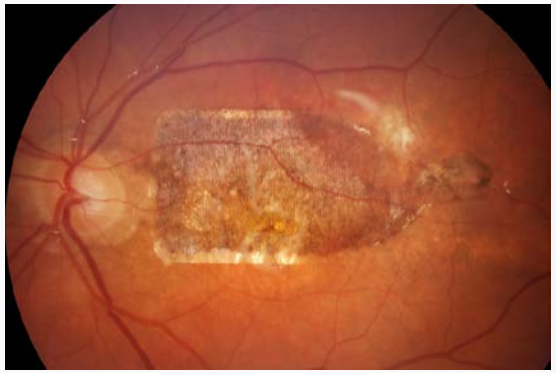
PATCH-AMD

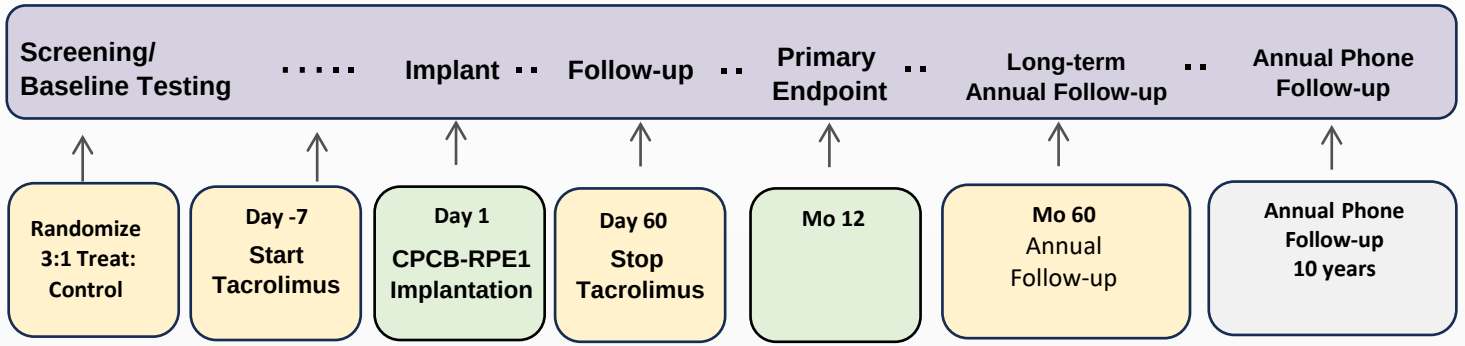


1. **Randomized masked clinical trial**
2. **24** subjects
3. **Less severe patient population** (BCVA ≤20/63-≥20/200; to potentially boost efficacy signal based on Phase 1/2a results
4. **Multiple surgical implantation clinical trial sites** to demonstrate broad feasibility of implantation procedure
5. **FDA approved registration** endpoints including microperimetry
6. Use of **cryopreserved implant**

Currently Enrolling: RPT-14-02 – PATCH-AMD

A Phase IIb, Randomized, Assessor-Masked, Multicenter Clinical Trial to Assess the Safety and Efficacy of Subretinal Implantation of the CPCB-RPE1 implant in Subjects with Advanced, Dry Age-Related Macular Degeneration (Geographic Atrophy)

- **Age 55 to 90**
- **Area of GA involving the fovea**
- **BCVA ≥20/200 to 20/63**
- **No current or history of CNV <u>in either eye</u>**
- **Pseudophakic** in the study eye
- **Able to complete microperimetry**
- **No diabetic retinopathy**



Endpoints

Visual Acuity (BCVA, LLVA)

Retinal Sensitivity (Microperimetry)

Imaging (OCT, Fundus Photos, FAF, FA)

ClinicalTrials.gov NCT06557460

clinicaltrials@regenerativepatch.com

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Clinical Trial Sites Actively Enrolling

Dr. Sun Young Lee

Keck School of Medicine of USC

Dr. Hani Salehi-Had

RETINA ASSOCIATES OF SOUTHERN CALIFORNIA
An NVISION® Eye Center

Dr. Meena George

UNIVERSITY RETINA

Dr. Firas Rahhal

Retina-Vitreous Associates Medical Group

Dr. Charles Wykoff

Retina Consultants of Texas™

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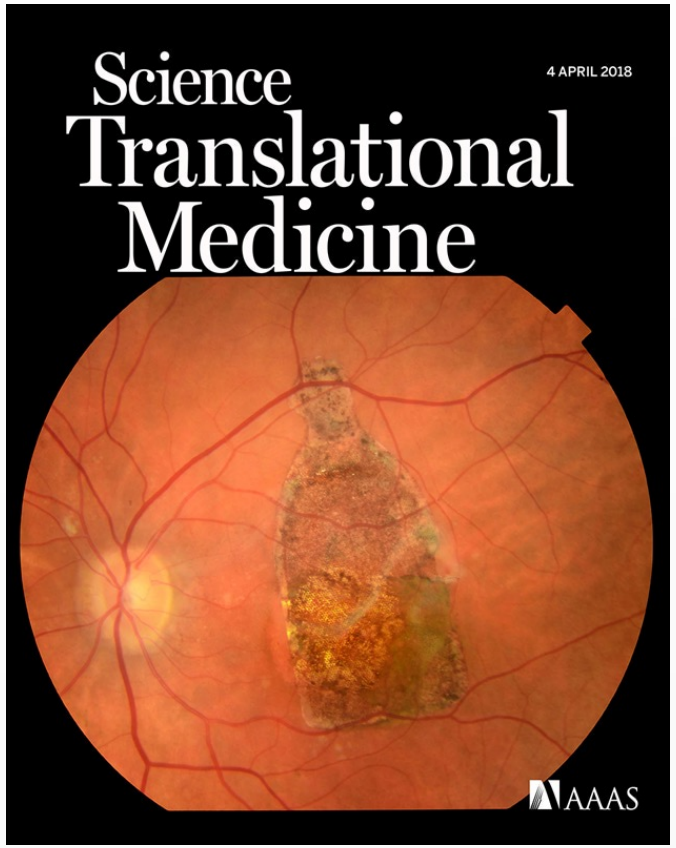
Clinical Trial Data Published



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

RETINAL DISEASE

A bioengineered retinal pigment epithelial monolayer for advanced, dry age-related macular degeneration

Amir H. Kashani,[1]* Jane S. Lebkowski,[2] Firas M. Rahhal,[3] Robert L. Avery,[4] Hani Salehi-Had,[5] Wei Dang,[6] Chih-Min Lin,[6] Debbie Mitra,[1] Danhong Zhu,[7] Biju B. Thomas,[1] Sherry T. Hikita,[8] Britney O. Pennington,[8] Lincoln V. Johnson,[2,8] Dennis O. Clegg,[8] David R. Hinton,[1,7] Mark S. Humayun[1,9]*

Kashani *et al.*, *Sci. Transl. Med.* **10**, eaao4097 (2018) 4 April 2018

Surgical Method for Implantation of a Biosynthetic Retinal Pigment Epithelium Monolayer for Geographic Atrophy: Experience from a Phase 1/2a Study

Amir H. Kashani, MD, PhD,[1] Jeremy Uang, BS,[1] Melissa Mert, MS,[2] Firas Rahhal, MD,[3] Clement Chan, MD,[4] Robert L. Avery, MD,[5] Pravin Dugel, MD,[6] Sanford Chen, MD,[7] Jane Lebkowski, PhD,[8] Dennis O. Clegg, PhD,[9] David R. Hinton, MD,[10] Mark S. Humayun, MD, PhD[1,11]

Ophthalmology Retina 2020; 4:264-273

One-Year Follow-Up in a Phase 1/2a Clinical Trial of an Allogeneic RPE Cell Bioengineered Implant for Advanced Dry Age-Related Macular Degeneration

Amir H. Kashani1, Jane S. Lebkowski2, Firas M. Rahhal3, Robert L. Avery4, Hani Salehi-Had5, Sanford Chen6, Clement Chan7, Neal Palejwala8, April Ingram2, Wei Dang9, Chih-Min Lin9, DebbieMitra10, Britney O. Pennington2,11, Cassidy Hinman2,11,Mohamed A. Faynus2,11, Jeffrey K. Bailey2,11, Sukriti Mohan10, Narsing Rao12, Lincoln V. Johnson2,11, Dennis O. Clegg11, David R. Hinton10,12, and Mark S. Humayun10,13

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Stem Cell Reports

Survival of an HLA-mismatched, bioengineered RPE implant in dry age-related macular degeneration

Amir H. Kashani,1 Jane S. Lebkowski,2 David R. Hinton,3,12 Danhong Zhu,3 Mohamed A. Faynus,2,4 Sanford Chen,5 Firas M. Rahhal,6 Robert L. Avery,7 Hani Salehi-Had,8 Clement Chan,9 Neal Palejwala,10 April Ingram,2Wei Dang,11 Chih-Min Lin,11 Debbie Mitra,12 Juan Carlos Martinez-Camarillo,1 Jeff Bailey,2,4 Cassidy Arnold,2,4 Britney O. Pennington,2,4 Narsing Rao,12 Lincoln V. Johnson,2 Dennis O. Clegg,4 and Mark S. Humayun12,13,*

Stem Cell Reports (2022), https://doi.org/10.1016/j.stemcr.2022.01.001

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