



LEADING  
REGENERATIVE  
MEDICINE

presented at:



# Cautionary Statement Concerning Forward-Looking Statements

*This presentation is intended to present a summary of ACT's ("ACT", or "Advanced Cell Technology Inc.", or "the Company") salient business characteristics.*

*The information herein contains "forward-looking statements" as defined under the federal securities laws. Actual results could vary materially. Factors that could cause actual results to vary materially are described in our filings with the Securities and Exchange Commission.*

*You should pay particular attention to the "risk factors" contained in documents we file from time to time with the Securities and Exchange Commission. The risks identified therein, as well as others not identified by the Company, could cause the Company's actual results to differ materially from those expressed in any forward-looking statements.*

# Robust Clinical and Preclinical Programs

## Ophthalmology

Transplantable  
RPE Cells

Transplantable  
Photoreceptor Progenitors

Transplantable  
Ganglion Nerve Progenitors

DSEK Corneal Transplant Tissue

Neuroprotective/Neuroregulatory  
Biologics

## Autoimmune/ Inflammation

Lupus

Multiple Sclerosis

Alzheimer's Disease

Inflammatory Bowel Disease

Sepsis

Wound Healing

## Drug Delivery

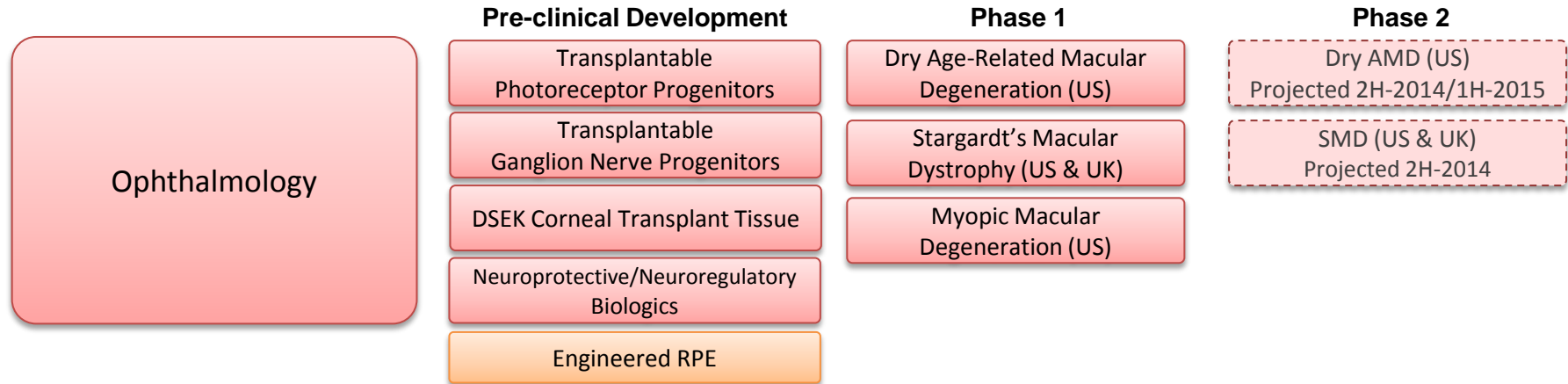
Engineered Platelets & MK

- Factor XIII • Wound Healing
- Anti-cancer

Engineered RPE

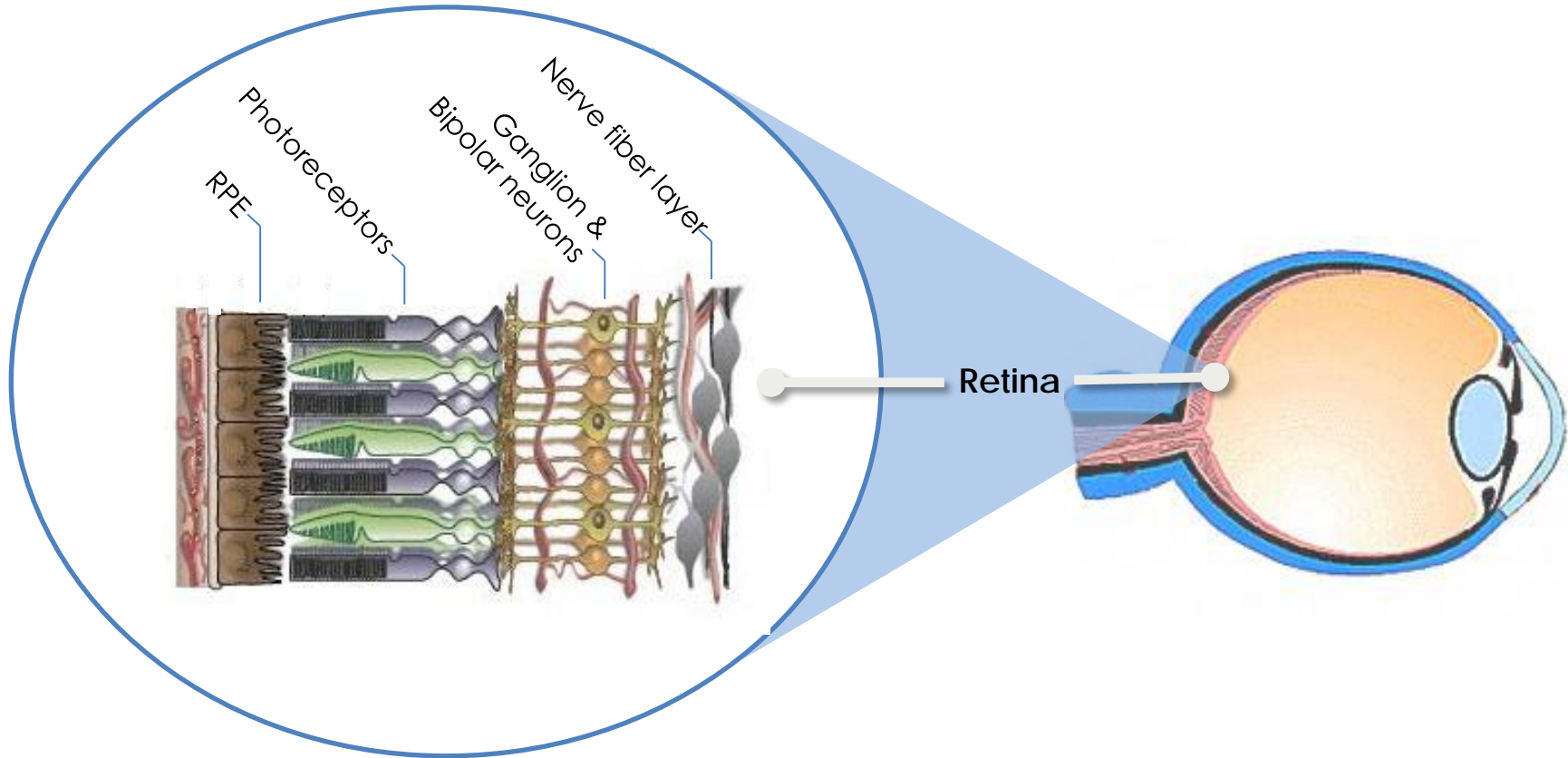
Engineered Photoreceptors

# Robust Clinical and Preclinical Programs



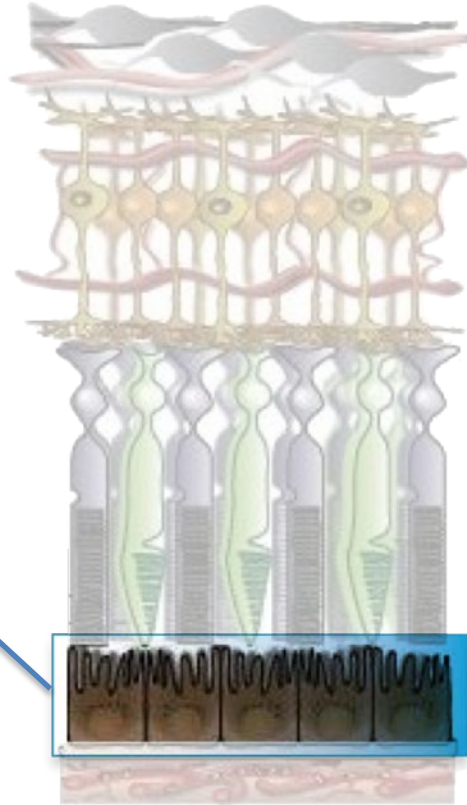
Advanced Cell Technology's  
**Regenerative Ophthalmology™** Programs  
focus on preserving and repairing  
neurosensory retina and cornea function

# Structure of the Retina



# Life Support to Photoreceptors

RPE Layer has  
**multiple  
critical roles**  
in the  
**health and  
function**  
of photoreceptors and  
the retina as a whole.



**Provides** nutrients and growth factors

- photoreceptors see no blood

**Recycles** Vitamin A

- maintains photoreceptor excitability

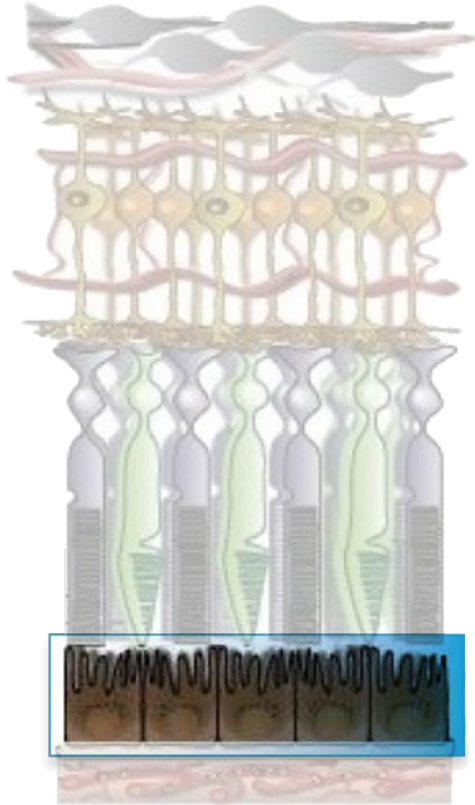
**Detoxifies** photoreceptor layer

**Maintains** Bruch's Membrane

- natural antiangiogenic barrier
- immune privilege of retina

**Absorbs** stray light / protects from UV

# Life Support to Photoreceptors



Failure of RPE cells  
results in many  
degenerative diseases

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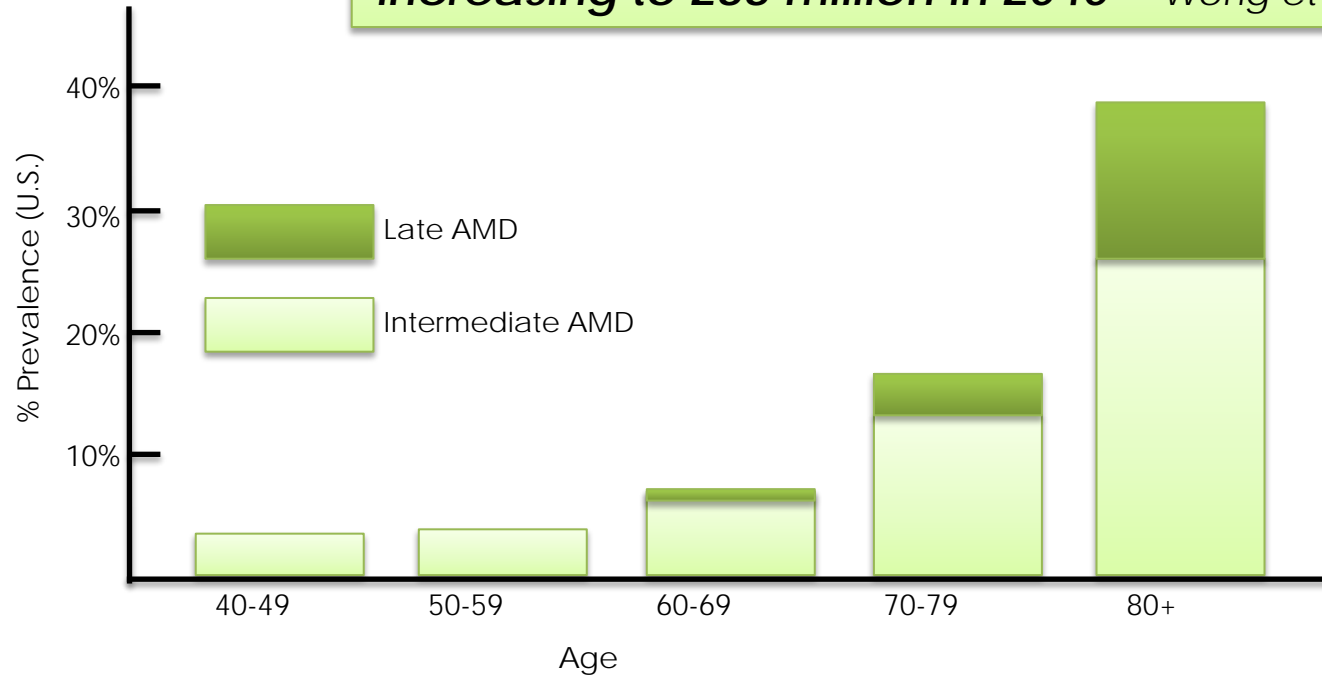
Stargardt's disease (SMD)

Myopic Macular Dystrophy (MMD)

Age-related macular degeneration (AMD)

# Age-Related Macular Degeneration will Soon Take on Aspects of an Epidemic

**The projected number of people worldwide with age-related macular degeneration in 2020 is 196 million, increasing to 288 million in 2040 - Wong et al. Lancet January 2014**



Exponential rise in prevalence and incidence rates with age.

Prevalence rates of late AMD quadruple per decade

Data from <http://www.nei.nih.gov/eyedata/> and U.S. Census Bureau Publication "65+ in the United States", P23-209



# Therapeutic Thesis

**Dissociated RPE Cells** can be injected into the subretinal space and will rebuild functional RPE monolayer where native RPE is compromised or lost.

- RPE layer is surgically accessible -
  - least invasive means to locally deliver cells
- Adult RPE translocation studies included dissociated cell formats
- hESC-derived RPE supported by both In Vitro and In Vivo Studies at ACT and OHSU



Product Cold Chain  
is Easily Scaled for  
Global Sales

- Simple Handling
- Optimized for large scale and centralized manufacturing
- Small Dose Size translates into ACT's ability to manufacture 50,000-100,000 per year in existing facilities.

# Cell Therapy for RPE, Achievable by a Small Company

## Small dosage size

- less than 200K cells

## Relatively Immune-privileged site

- minimal immunosuppression

## Ease of administration

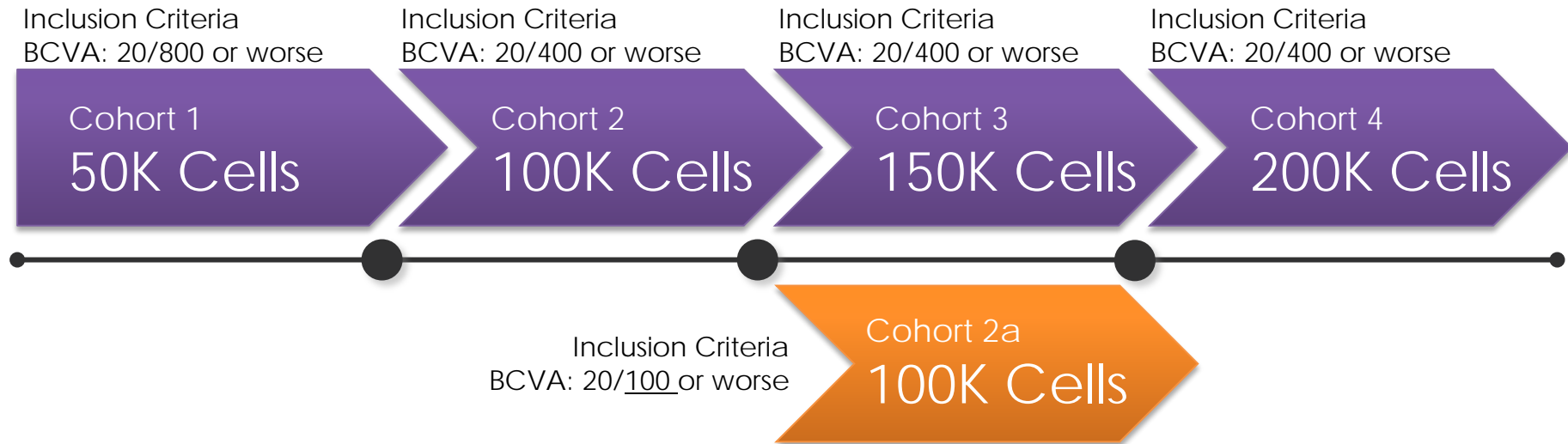
- no separate device approval

## Unique measuring and observation environment

- measurable anatomical and functional endpoints

First Treatments informed a more aggressive strategy to treat “better vision” cohort, could lead to broader label and/or earlier approval

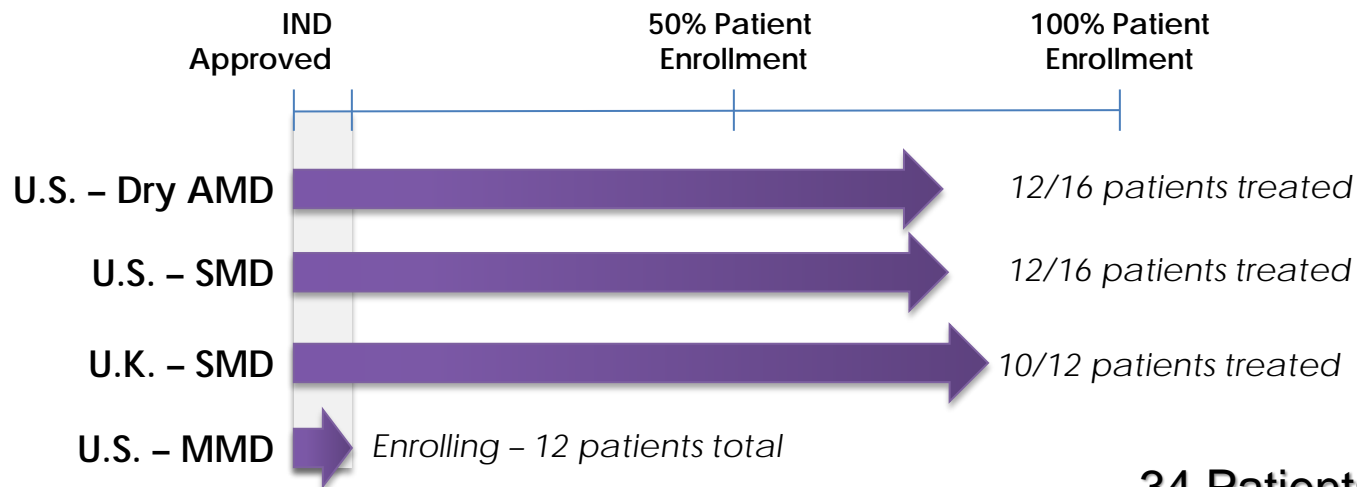
## Initial Trial Design is Ascending Dosage Safety Study 12 Subjects – Four Cohorts of 3 subjects each



Jan 2013: FDA approved additional 4 subject “better vision” cohorts in each trial.

For Cohort 2a – can enroll subjects with vision as good as **20/100**.

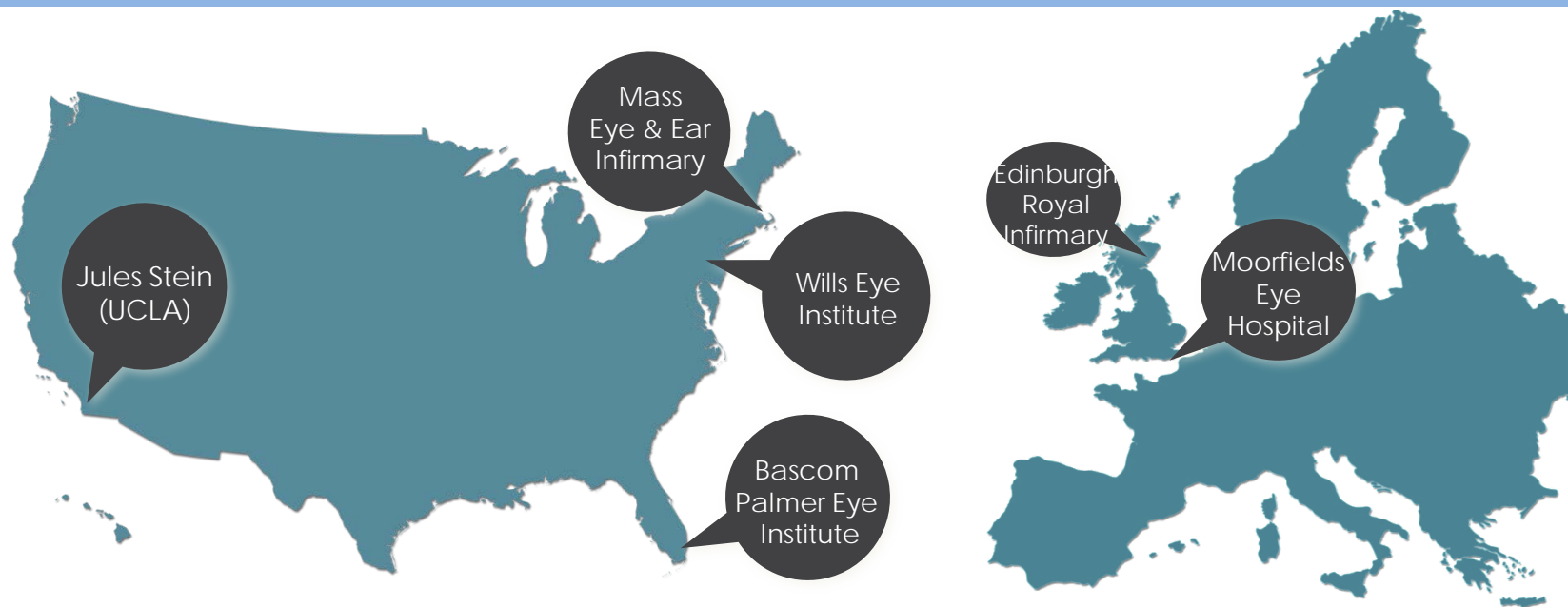
# Current Status of P1 Trials enables Planning for P2



**34 Patients Treated to Date**

Early Hypothesis Developed for PII,  
Vetted with Investigators, Dialoging with MHRA and FDA

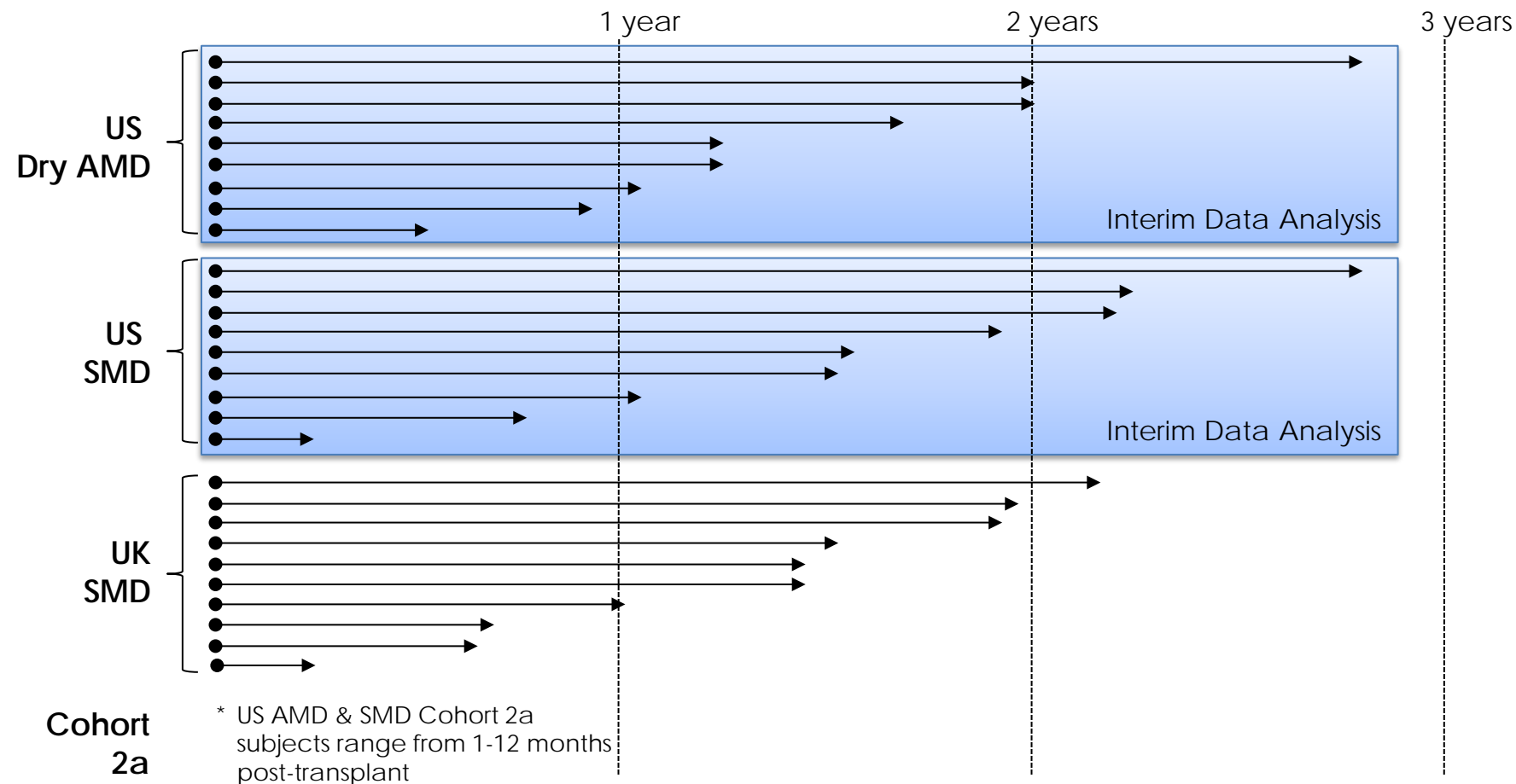
# Clinical Trials being led by World Leaders in Ophthalmology



World Renowned Leadership to help us navigate the Clinical Path and Ultimately Support Market Launch



# Elapsed Time Since Transplant – as May 2014



# Overview of Interim Data

Manuscript detailing interim data under review at impactful journal  
*Co-authored by participating surgeons and company*

- Clean safety profile
- Evidence of engraftment and persistence of transplanted RPE cells
- Persisting Improvement of Visual Acuity for many patients

*A number of patients with clinically significant improvements in BCVA*

**Exemplars of  
Patients With  
Improved  
Visual Acuity**

AMD-207 improved 20/400 to 20/40

- Improvement has persisted through follow-up visits (> 1 year)

SMD-001 improved from HM to 20/500

- Improvement (with further gains) has persisted through follow-up visits (>2 year)

**Based on advice from all 5 clinical trial sites and participating surgeons, as well as input from regulators, we are advancing to phase 2 studies**

- › Active dialog with MHRA and FDA
- › Anticipate P2 commencement in 2H2014



Myopia creates a higher risk of permanent vision loss due to **Myopic Macular Degeneration** (MMD)

- Severe near-sightedness causes elongation of the eyeball -- which can cause fissures in RPE layer.



As the cause of legal blindness, MMD is ranked:

- **7<sup>th</sup>** in the United States
- **4<sup>th</sup>** in Hong Kong
- **2<sup>nd</sup>** in mainland China and Japan

Jules Stein Eye (UCLA) and ACT to Initiate Phase I/II Study

# Second Generation RPE Cell Therapy Products

By engineering the master stem cell bank used to manufacture RPE cells, the transplanted RPE cells can express

- **Anti-angiogenic agents**

Reduce occurrence of choroidal neovascularization (wet AMD).

- **Complement factor D, Factor C5 and/or Factor C3 Inhibitors**

Activation of alternative complement pathway implicated in disease progression for certain patients

- **Anti  $\beta$ -amyloid agents**

Drusen deposits resemble amyloid deposits.

- **Anti-Inflammatory agents**

IL-1, IL-2, IL-3, and TNF- $\alpha$  antagonists

Recombinant Lipocortin – a potent anti-inflammatory protein

# Intellectual Property – RPE Program

## Dominant Patent Positions in Major Markets for **Platform Technology and Treatments**

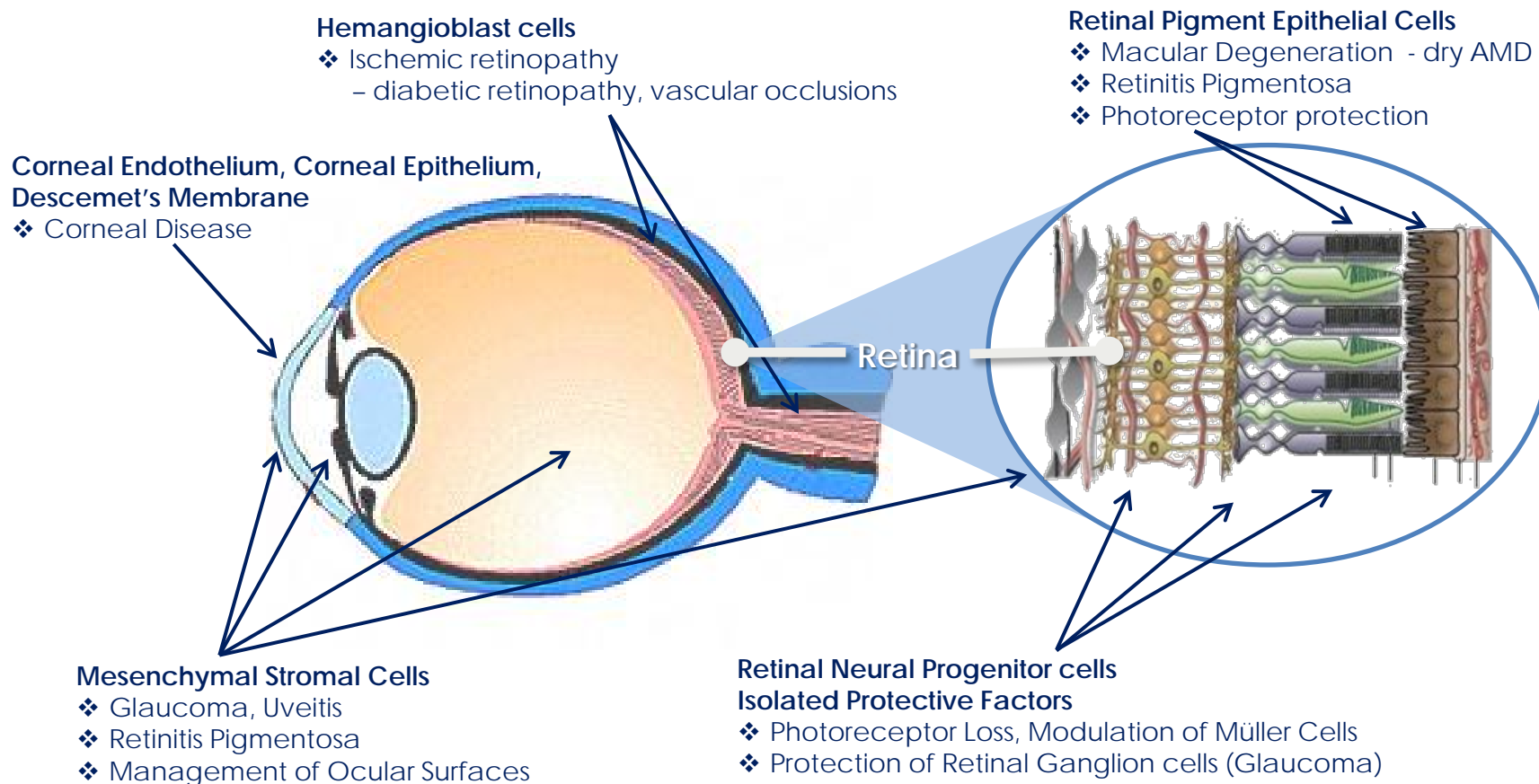
- Broad Coverage for Manufacturing RPE Cells
- Broad protection of pharmaceutical preparations of RPE cells
  - Every practical formulation format for use in human patients
    - Covers RPE cell suspensions for injection
    - Covers scaffolded RPE layers for implantation
    - Covers polarized monolayers of cells
- Covers RPE Cells derived from any pluripotent stem cell source
  - From hESC to iPS cells to pluripotent stem cells yet to be invented

**First Mover and First-in-Clinic Efforts  
Translate into Broad First-to-File Patents**



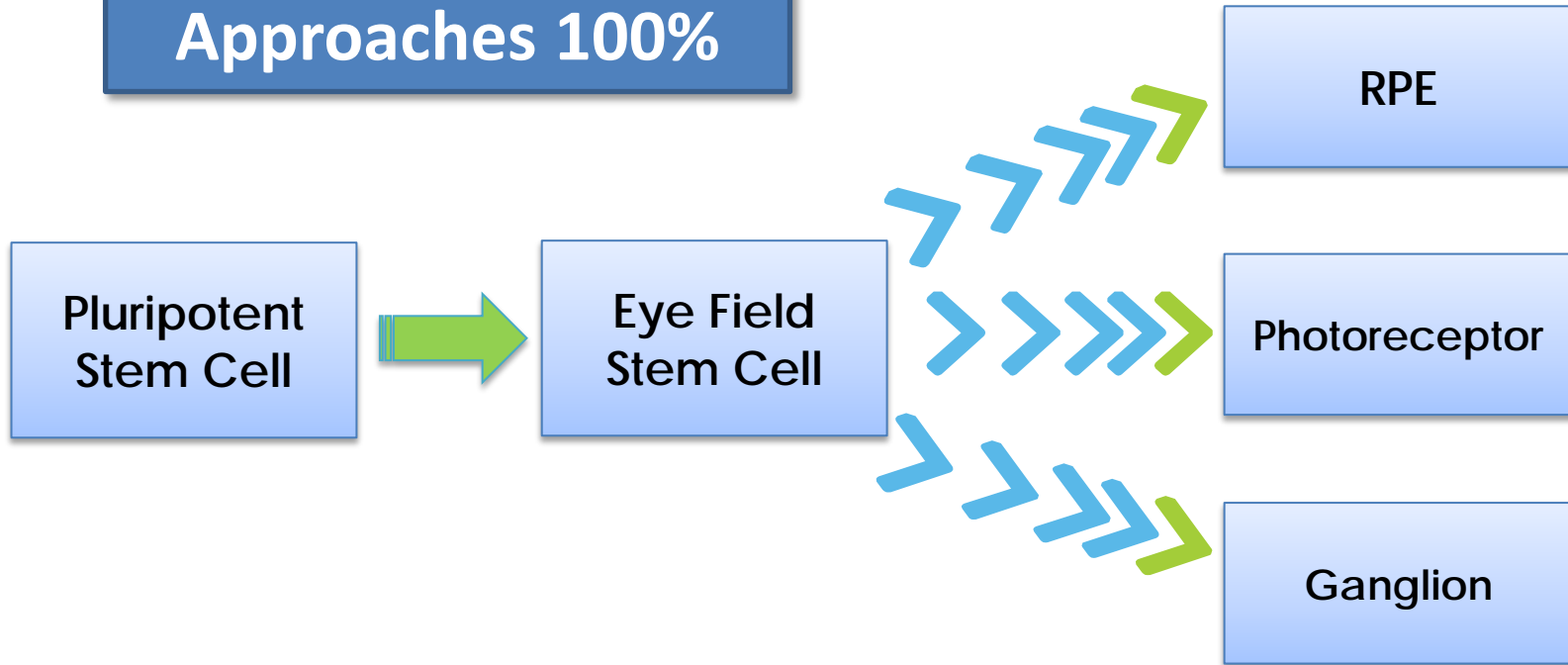
# Therapeutic Pipeline - Other Ocular Programs

# Ophthalmology Pipeline Extends Beyond RPE



# Proprietary Methods for Deriving Various Cell Types of the Retina

**Purity of Resulting  
Cell Preparations  
Approaches 100%**



# Highly Reproducible with Various Pluripotent Stem Cell Sources

Cell lines	Percentage of PAX6 + neural stem cells	Percentage of Nestin + neural stem cells
ES lines (N=3)	92%-98%	95%-99%
ES lines, blastomere technology (N=2)	94%-99%	95%-99%
iPS lines, Episomal Vector (N=4)	90%-99.6%	96%-100%
iPS lines, mRNA (N=2)	92%-98%	96%-100%

- Evaluated in multiple hESC and iPS cells lines
- Highly synchronized culture

# Neurosensory Retina – Photoreceptor Replacement

We have demonstrated that subretinally injected hESC- and iPSC-derived photoreceptor progenitors can **migrate to correct anatomical site** in retina, differentiate, and **functionally rescue vision**.

Unique photoreceptor progenitor ("PhRP-x") maintains plasticity to form both rods and cones

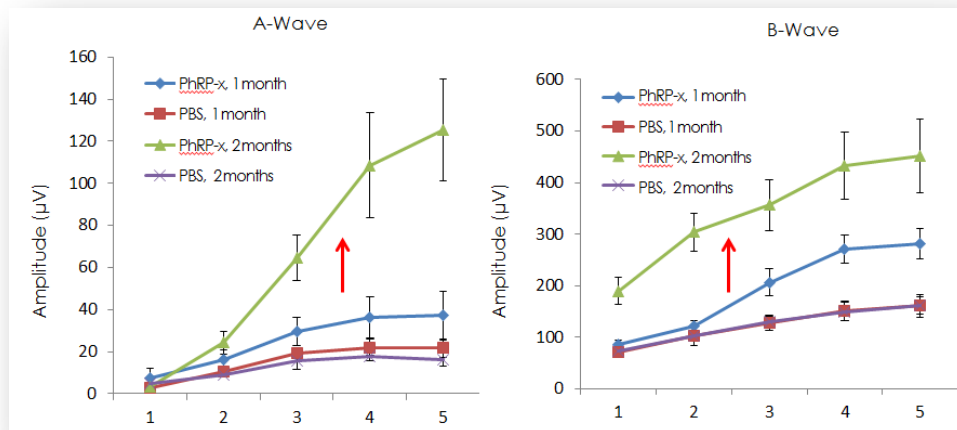
Carrying out disease model POC studies for demonstrating utility in treatment of:



- Late stage macular degeneration
- Retinitis Pigmentosa (RP)
- Night Blindness



# Neurosensory Retina – Neuroprotection



## When delivered systemically

- Scotopic (shown) and Photopic ERG preservation of rod and cone function
- ERG recovery is cell-dependent (CSA removal reverses ERG recovery)
- Also observed preservation of ONL thickness relative to control.

*Only the PhRP-x progenitors have **paracrine neuroprotective activity** – earlier stage high purity retinal progenitors do not.*

## A differentiated functional phenotype

PhRP-x are photoreceptor progenitors which:

- form both rods and cones
- functionally integrate in ONL
- secrete a neuroprotective agent(s)
- have phagocytic activity for OS

# An Experienced and Dedicated Management Team

Edward Myles – Interim President, CFO and EVP of Corp Development

Dr. Matthew Vincent, Ph.D. – Dir., Business Development

Dr. Robert Lanza, MD – Chief Scientific Officer

Dr. Irina Klimanskaya, Ph.D. – Dir., Stem Cell Biology

Dr. Shi-Jiang (John) Lu, Ph.D. – Senior Director of Research

Eddy Anglade, M.D. – EVP, Clinical Development

Dr. Roger Gay, Ph.D. - Senior Director of Manufacturing

**Proven business leaders who can develop and implement corporate strategy and monetize assets to maximize shareholder value**

**World-renowned scientific thought leaders pushing the cutting edge of science to develop important therapies**

**Deep experience in clinical development programs for ophthalmology drug products from early through late-and post-marketing stages**

**GMP manufacturing to ensure the highest quality products are delivered to our patients**

# A World-Class Board of Directors

Michael Heffernan, Chairman	CEO – Collegium Pharmaceuticals
Robert S. Langer, Sc.D.	Institute Professor, MIT
Zohar Loshitzer	CEO – Presbia, Inc., & Principal in Orchard Capital
Greg Perry	EVP & CFO – Eleven Biotherapeutics
Alan C. Shapiro	Finance Professor and Chairman of the Department of Finance and Business Economics (retired) – University of Southern California