Advanced Cell Technology

LEADING
REGENERATIVE
MEDICINE

Bio CEO & INVESTOR CONFERENCE

February 2014

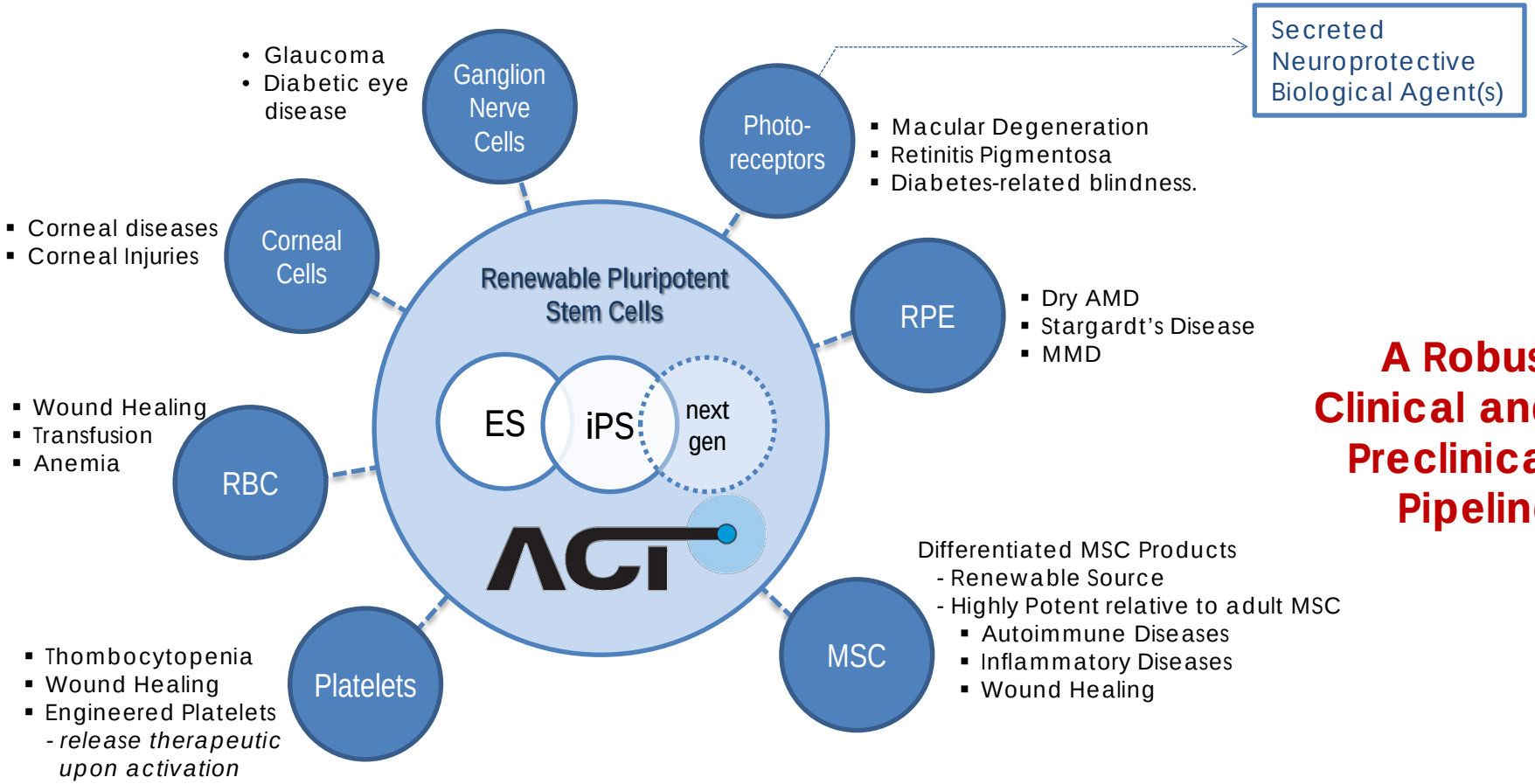
Cautionary Statement Concerning Forward-Looking Statements

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.

Renewable Pluripotent Stem Cell Platform



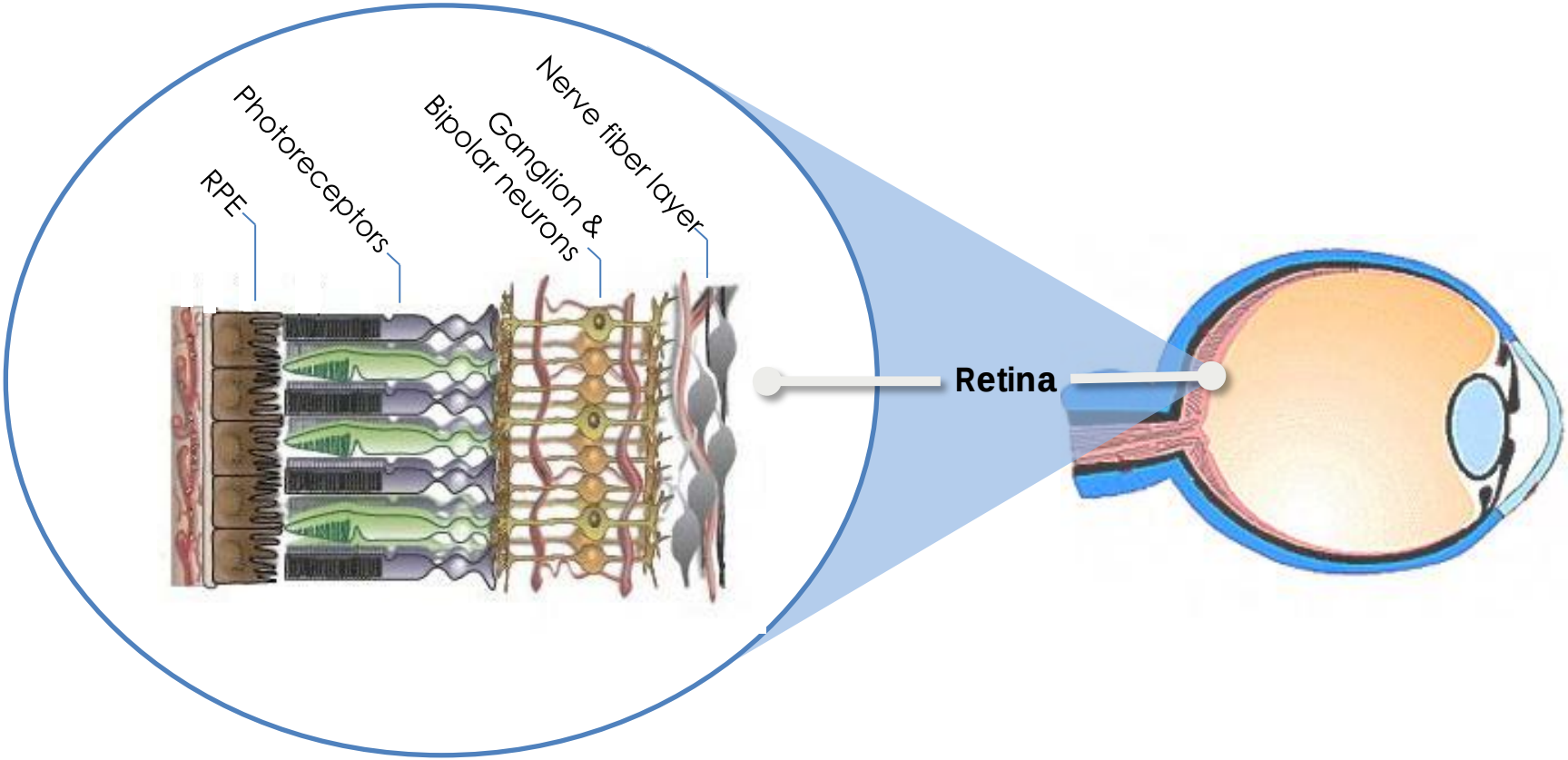
A Robust Clinical and Preclinical Pipeline

Advanced Cell Technology

Discovery	Pre-clinical Development	Phase 1	Phase 2
Ophthalmology	Transplantable Photoreceptor Progenitors	Dry Age-Related Macular Degeneration (US)	Dry AMD (US) IN Preparation
	Transplantable Ganglion Nerve Progenitors	Stargardt's Macular Dystrophy (US & UK)	SMD (US & UK) IN Preparation
	DSEK Corneal Transplant Tissue	Myopic Macular Degeneration (US)	
	Neuroprotective/Neuroregulatory Biologics		
Autoimmune/ Inflammation	Lupus	Lupus -TBD-	
	Multiple Sclerosis		
	Alzheimer's Disease		
	Inflammatory Bowel Disease		
	Sepsis		
	Wound Healing		
Blood Components	Platelets		
	Red Blood Cells		
	Immune Cells		
Drug Delivery	Engineered Platelets & MK • Factor XIII • Wound Healing • Anti-cancer		
	Engineered RPE		
	Advance to POC or P1 and Partner		

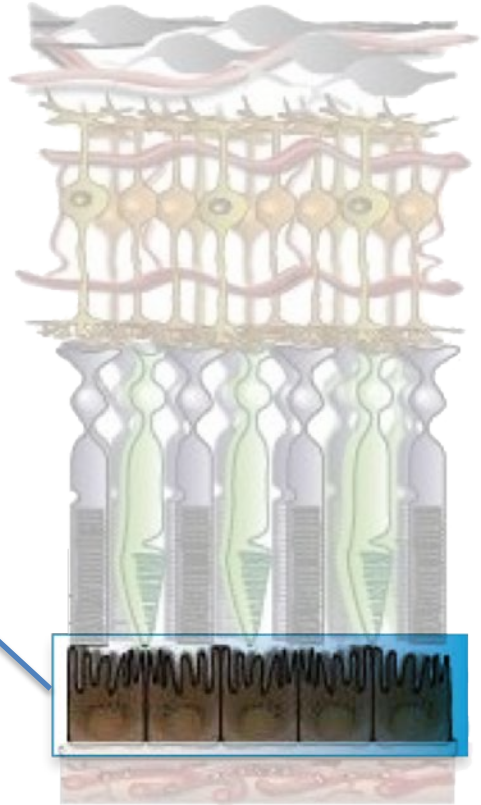
Advanced Cell Technology

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

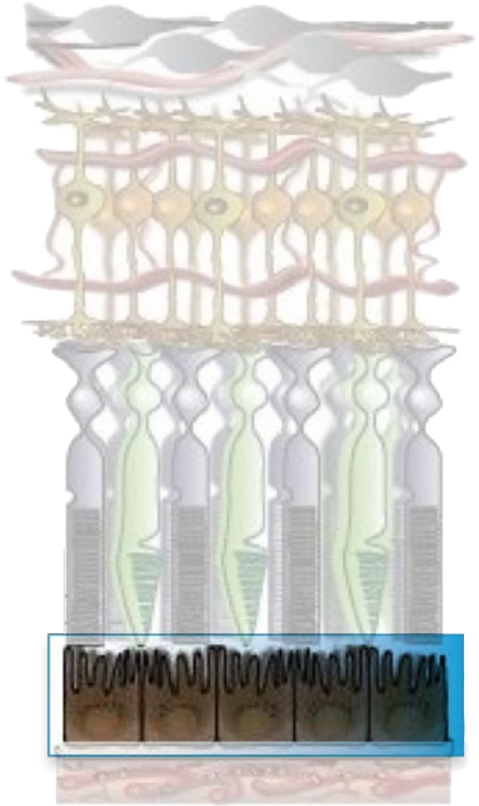
Detoxifies photoreceptor layer

Maintains Bruch's Membrane

- natural antiangiogenic barrier
- immune privilege of retina

Absorbs stray light / protects from UV

Life Support to Photoreceptors

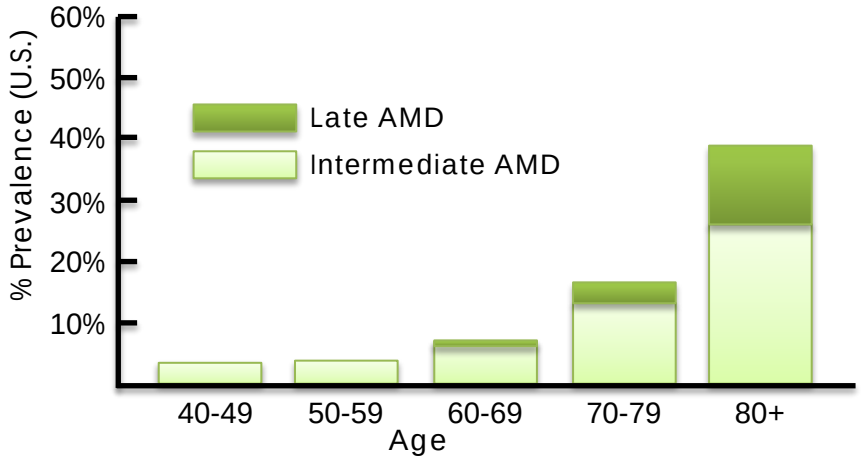


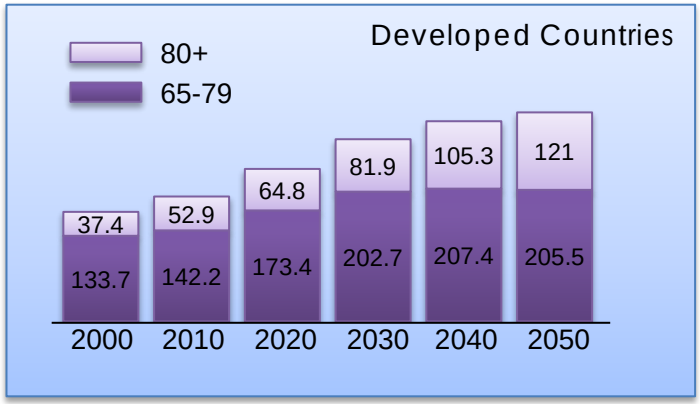
Failure of RPE cells results in many degenerative diseases

Stargardt's disease
Myopic Macular Dystrophy
Age-related macular degeneration (AMD)

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

Exponential rise in prevalence and incidence rates with age, with prevalence rates of late AMD quadrupling per decade





"macular degeneration will soon take on aspects of an epidemic"

- former Director of the National Eye Institute Dr Carl Kupfer

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

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

There are currently >30 Million American and European AMD patients. This is projected to exceed 50 Million patients by 2025

Wong et al. Lancet January 2014

The projected number of people worldwide with age-related macular degeneration in 2020 is 196 million, increasing to 288 million in 2040.

Pursuing Therapy for AMD/SMD has Attributes that Make it Appealing to a Large Pharma Co, but Attainable by an Emerging Biotech

Small dosage size – fewer than 200k cells per eye

- Capable of 50k – 100k doses/year in our current GMP facility

Immune-privileged site – may make this therapy available to all patients

- Use of immune-suppression drugs in PI, under evaluation for PII

Ease of administration – very common surgery, ~90 seconds per eye

- Trial being run by KOL's but lack of special devices makes this therapy scale-able to the high volume clinicians

Unique measuring and observation environment – gives us clear endpoints

- Observation at the cellular level enables clear understanding of impact

Significant unmet medical need – AMD is approaching epidemic status

GMP Process

GMP process for differentiation and purification of RPE

- Virtually unlimited supply from stem cell source
- Optimized for large scale manufacturing
- Centralized Manufacturing
- Robust Release Assays
- Simple Handling

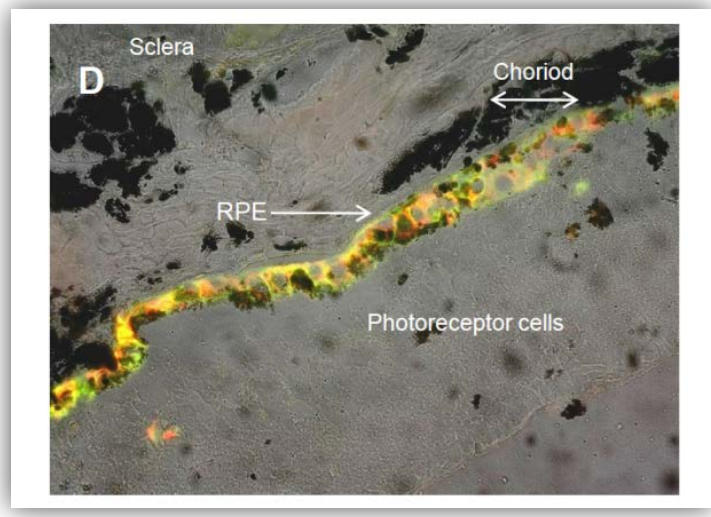
A single 6-well plate can generate 50-100 doses

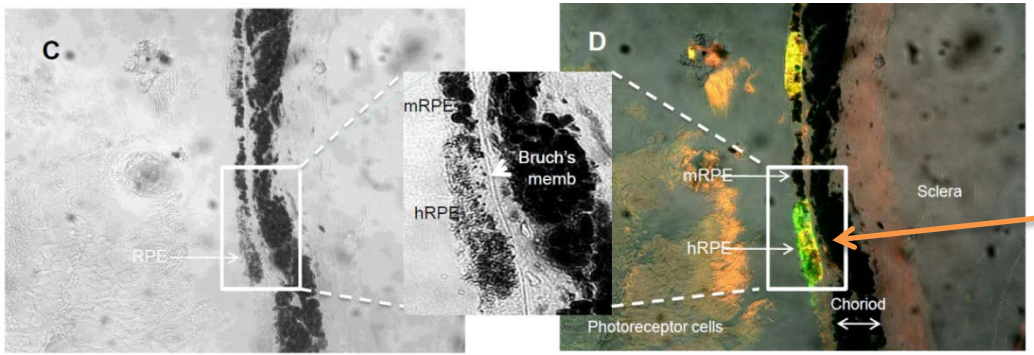
Product Cold Chain is Easily Scaled for Global Sales

- Small Dose Size translates into ACT's ability to manufacture 50,000-100,000 per year in existing facilities.

Preclinical Models

Transplanted cells **engraft** and form **correct anatomical** structure





ELOVL4 Mouse model for macular degeneration

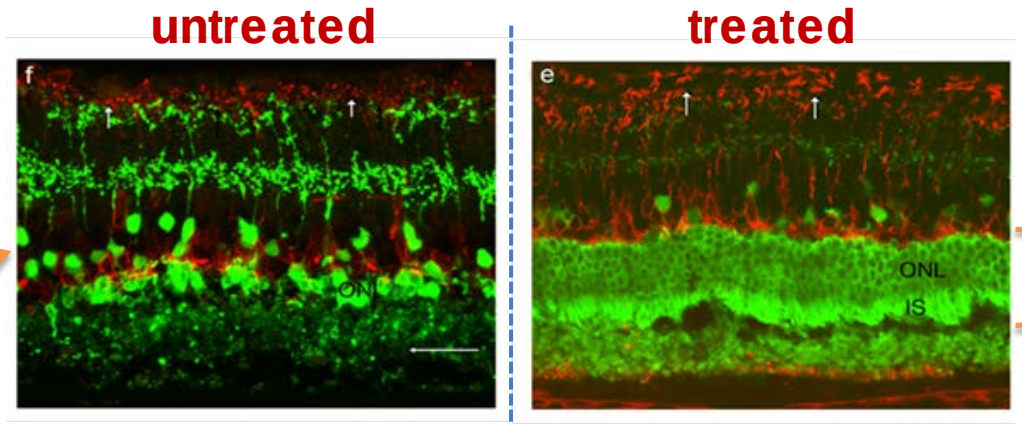
Injected human RPE cells repair monolayer structure in eye

Advanced Cell Technology

Preclinical Models

RCS Rat model for macular degeneration

photoreceptor layer is lost



Photoreceptor layer

Transplanted RPE cells

protect photoreceptors and

prevent loss of vision

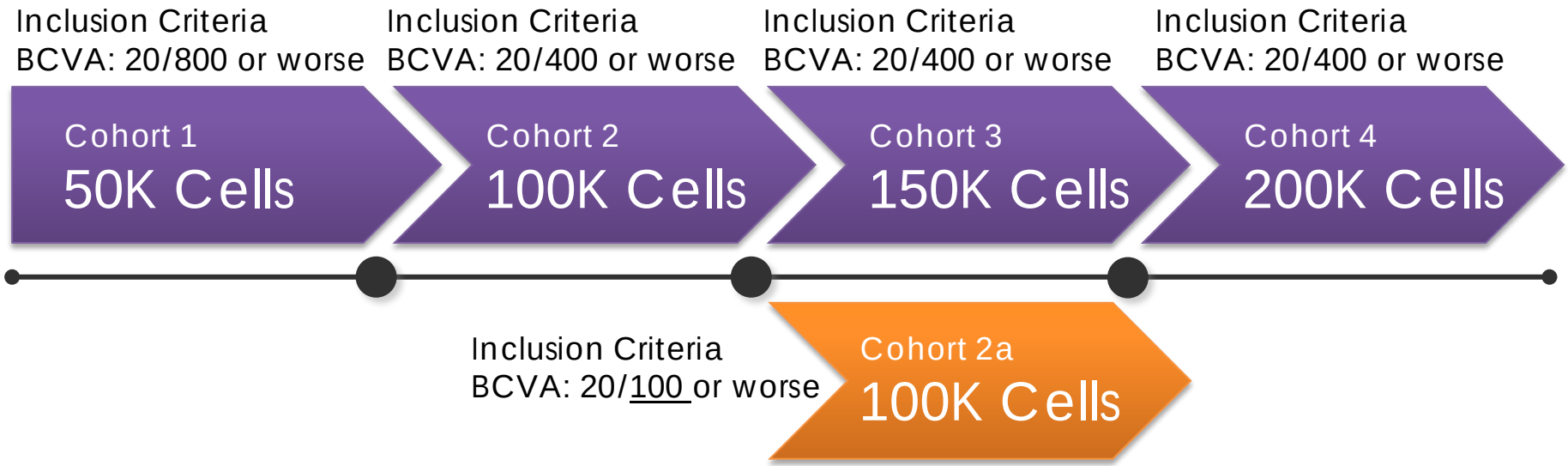
- ***Untreated animals go blind***
- ***Treated animals maintain 70-80% of normal vision***

Advanced Cell Technology

Initial Trial Design is Ascending Dosage Safety Study
12 Patients – Four Cohorts of 3 patients each

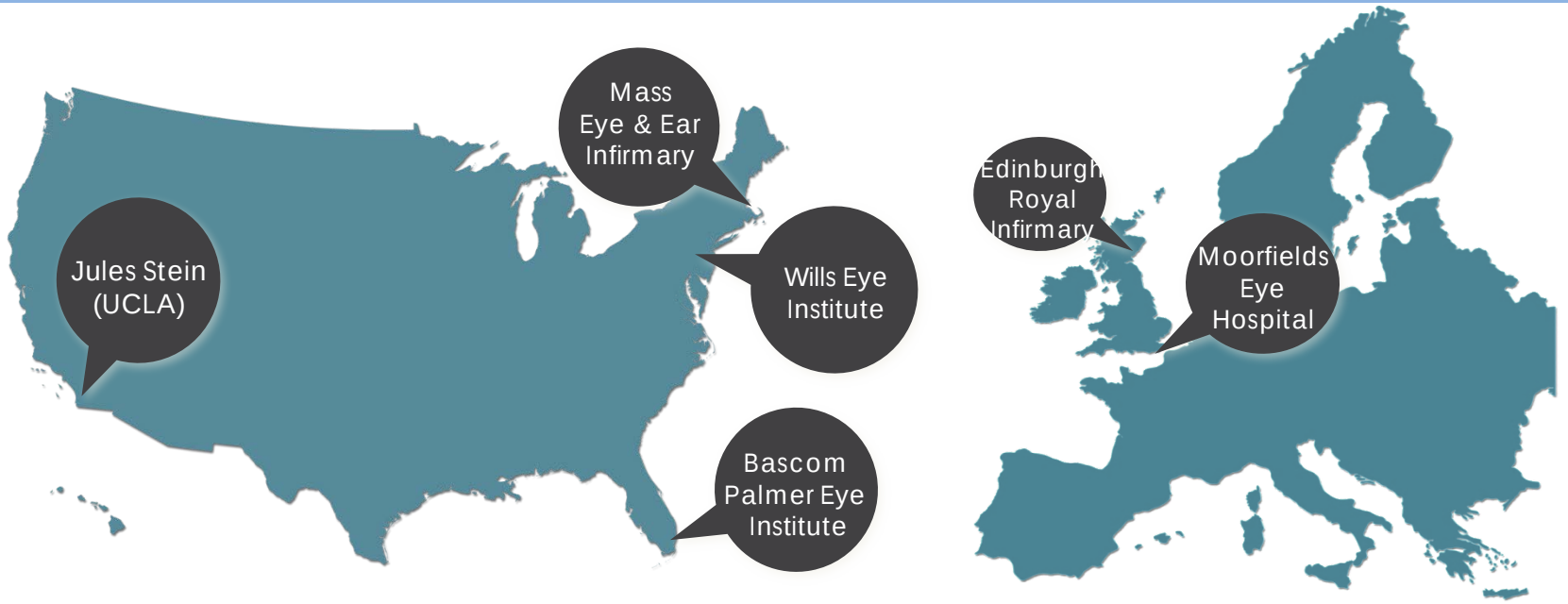
January 2013: FDA approved additional 4 patient "better vision" cohorts in each trial.

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



Advanced Cell Technology

Clinical Trials being led by World Leaders in Ophthalmology



World renowned leadership to help us navigate the clinical path and ultimately support market launch

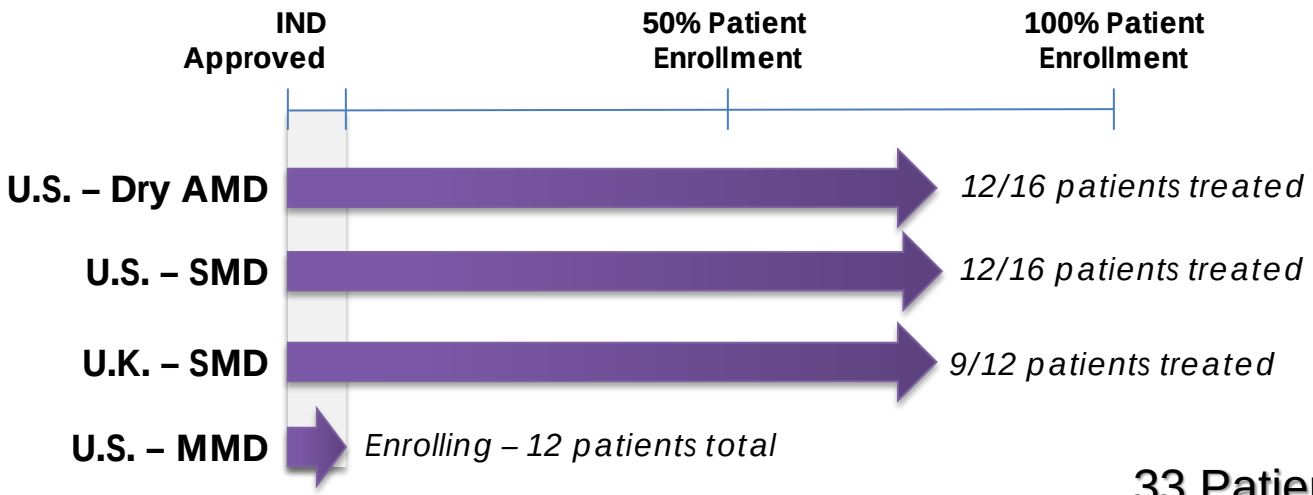
ACT Advanced Cell Technology

Surgical Overview

Procedure:

- 25 Gauge Pars Plana Vitrectomy
- Posterior Vitreous Separation
- Subretinal hESC-derived RPE cells injection
- Bleb Confirmation
- Day Surgery/Sedation only

Current Status of P1 Trials enables Planning for P2



33 Patients Treated to Date

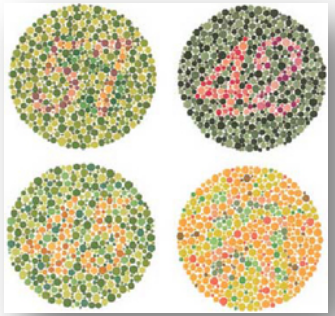
Early Hypothesis Developed for PII, Currently Vetting with Investigators, Meeting with FDA Planned for Q2

Advanced Cell Technology

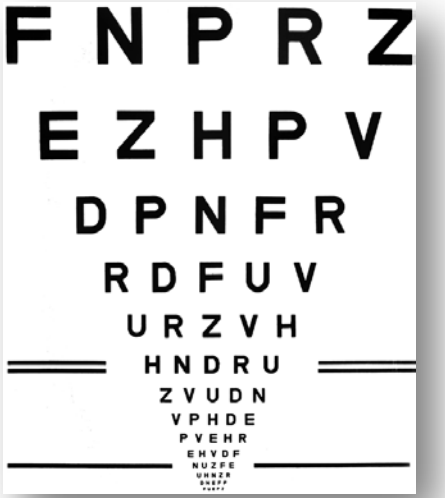
Phase I Trials Exceeding Expectations – No Safety Issues and Persistence of Cells

- **Excellent Safety Profile**
- **Persistence of cells**
- **Impact on Acuity**

Recorded functional visual improvements in majority of patients.



- Increased letters on ETDRS Charts
- Color perception
- Contrast
- Low light vision



ACT Advanced Cell Technology

Preliminary Results

Recorded **functional visual improvements** in both patients.

- SMD Patient: Best corrected visual acuity improved from hand motions to 20/800 and improved from 0 to 5 letters on the ETDRS visual acuity chart in the study eye.
- Dry AMD Patient: Vision improved in the patient with dry age-related macular degeneration (21 ETDRS letters to 28).

33 Patients - Up to 2 years of Follow-Up Visits

- **Measurable Improvements in Visual Acuity**
- **Gains in Visual Acuity Generally Persist**

SMD Patient #1

	BCVA	ETDRS (number of letters)
Fellow eye		
Baseline	Hand motion	0
1 week	Hand motion	0
2 weeks	Hand motion	0
3 weeks	Hand motion	0
4 weeks	Hand motion	0
6 weeks	Hand motion	0
8 weeks	Hand motion	0
12 weeks	Hand motion	0
Operated eye		
Baseline	Hand motion	0
1 week	Counting fingers	0
2 weeks	Counting fingers	1
3 weeks	Counting fingers	3
4 weeks	20/800	5
6 weeks	20/800	5
8 weeks	20/800	5
12 weeks	20/800	5

Visual acuity gains have persisted for more than 2 years

ACT Advanced Cell Technology

Expanding Clinical Programs

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:

- **7th** in the United Sates
- **4th** in Hong Kong
- **2nd in mainland China and Japan**

January 2013 - FDA Approved MMD Phase I/II study

Jules Stein Eye Institute (UCLA) and ACT

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-angiogeneic 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 β-amyloid agents**
  Drusen deposits resemble amyloid deposits.
- **Anti-Inflammatory agents**
  IL-1, IL-2, IL-3, and TNF-α 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 <u>any</u> 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

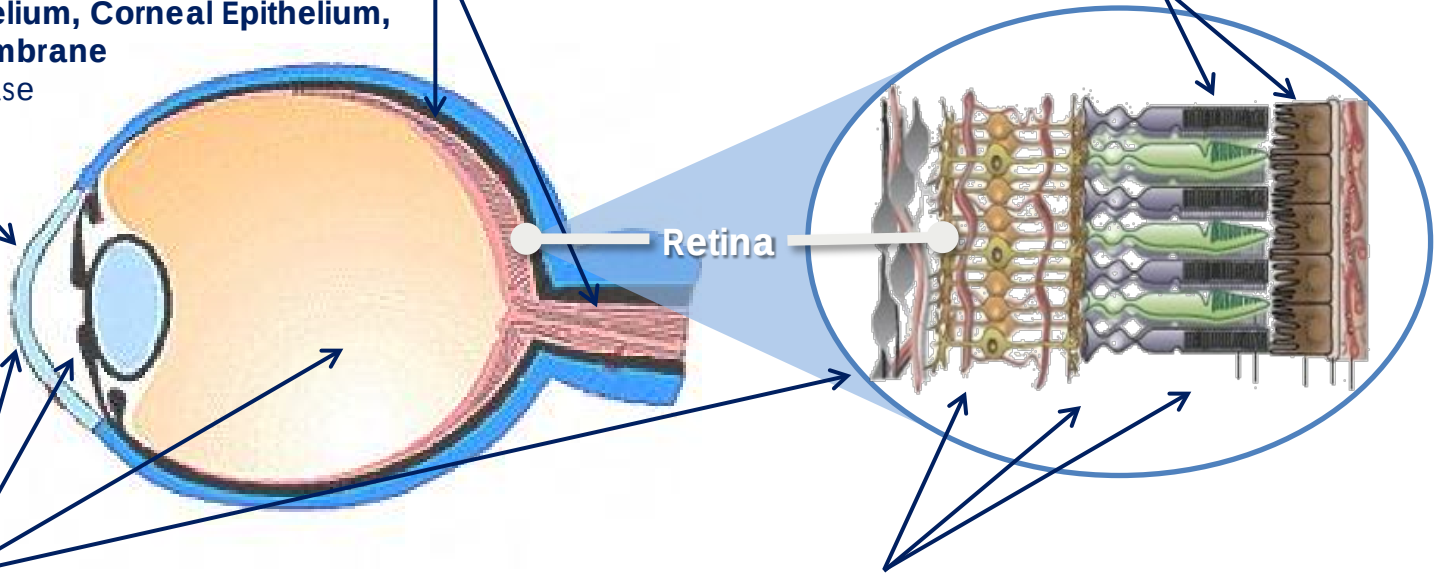
ACT Advanced Cell Technology

Therapeutic Pipeline - Other Ocular Programs

Hemangioblast cells
- Ischemic retinopathy
  - diabetic retinopathy, vascular occlusions

Retinal Pigment Epithelial Cells
- Macular Degeneration - dry AMD
- Retinitis Pigmentosa
- Photoreceptor protection

Corneal Endothelium, Corneal Epithelium, Descemet's Membrane
- Corneal Disease



Mesenchymal Stromal Cells
- Glaucoma, Uveitis
- Retinitis Pigmentosa
- Management of Ocular Surfaces

Retinal Neural Progenitor cells
Isolated Protective Factors
- Photoreceptor Loss, Modulation of Müller Cells
- Protection of Retinal Ganglion cells (Glaucoma)

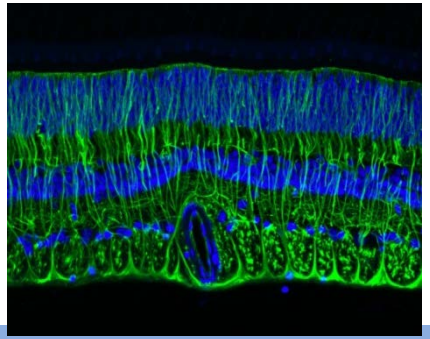
Neurosensory Retina – Photoreceptor Replacement

Until now, photoreceptor transplantation has not been a tractable solution for reversing vision loss…

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.

Encouraging result indicates that the transplanted photoreceptors can function normally.

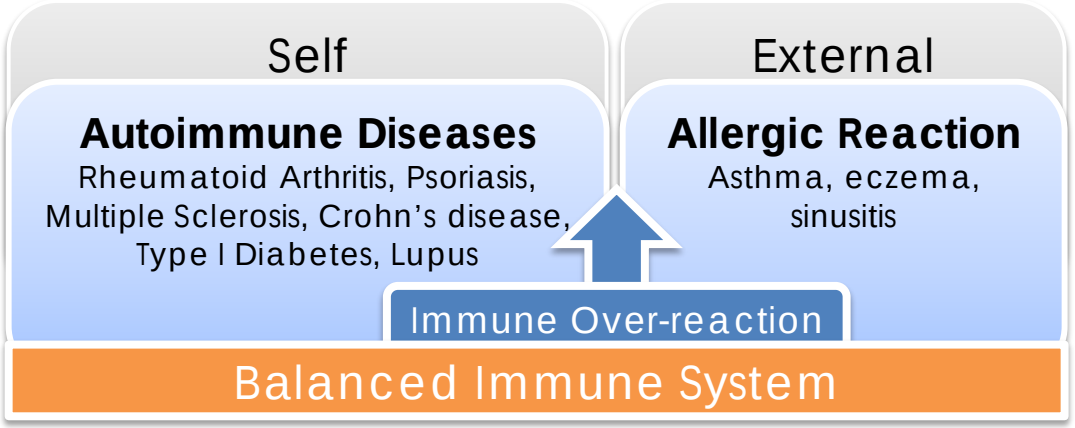
Moving toward POC studies demonstrating utility in models for



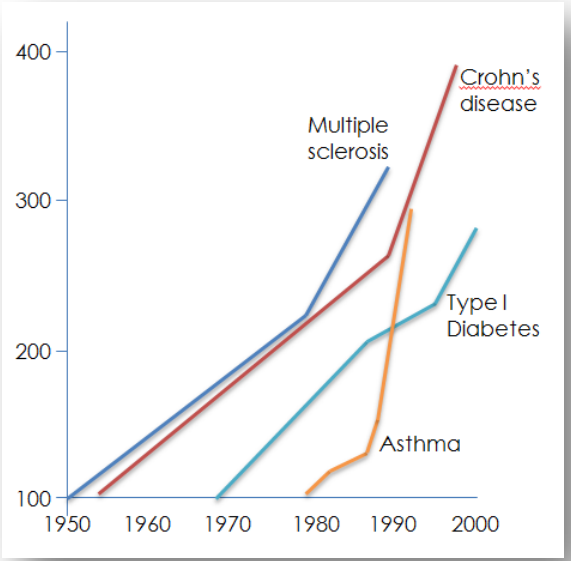
- Late stage macular degeneration
- Retinitis Pigmentosa (RP)
- Night Blindness

Mesenchymal Stem Cell Program

Mesenchymal Stem Cells in Therapy



A rapidly growing health issue (% growth)



Autoimmune Disease Prevalence

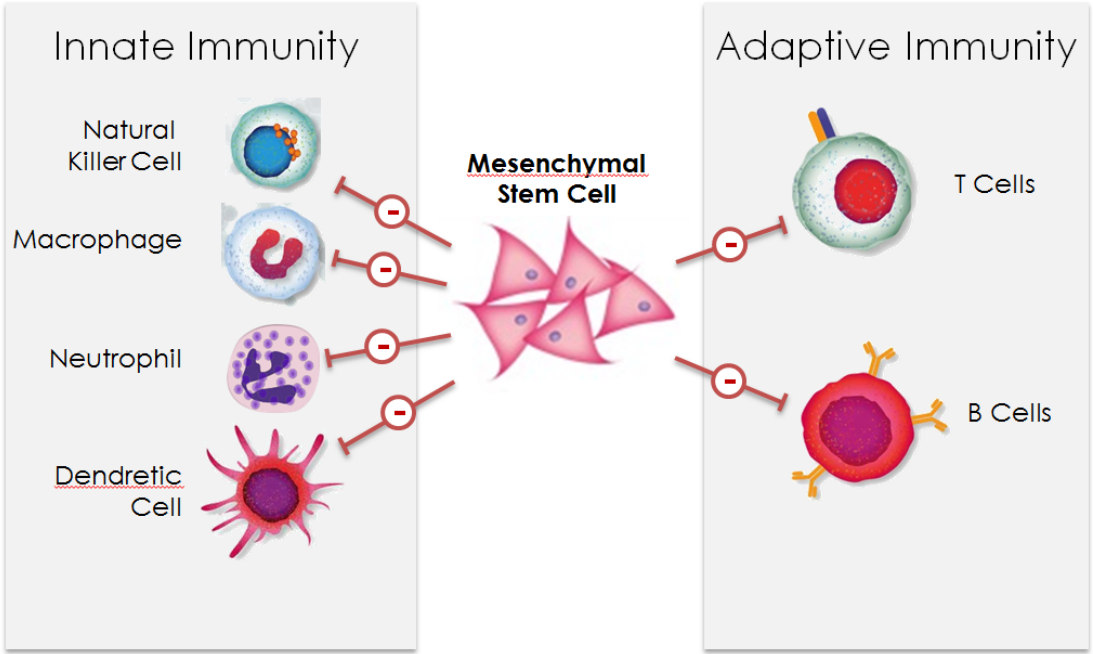
- At least 80 disease affecting every organ system
- Americans spend over **$100B** each year in total healthcare costs associated with autoimmune disease
- In the U.S., **14.7-23.5M people (5%-8%)**
  (for comparison: heart disease (22M), Cancer (9M)

Advanced Cell Technology

Suppressing Immune Responses gives rise to Therapy

Mesenchymal stem cells (MSCs)

suppress disease-causing immune responses



Promising **therapeutic potential** for treating autoimmune and inflammatory diseases.

However, **adult-derived MSCs** are **limited** by **replicative capacity**

ACT Advanced Cell Technology

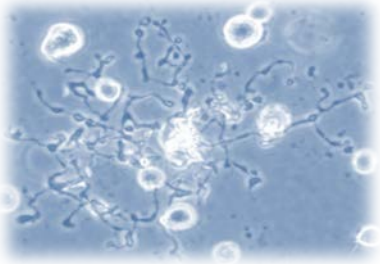
ACT's Breakthrough – Inexhaustible Supply of Very Potent MSC's

ACT Proprietary Process

- Manufacture MSC's from hES and iPS Cell Banks
  - Virtually **inexhaustible source** of starting material
    - Use Single Master Cell Bank
    - Less labor-intensive

A further differentiating feature…

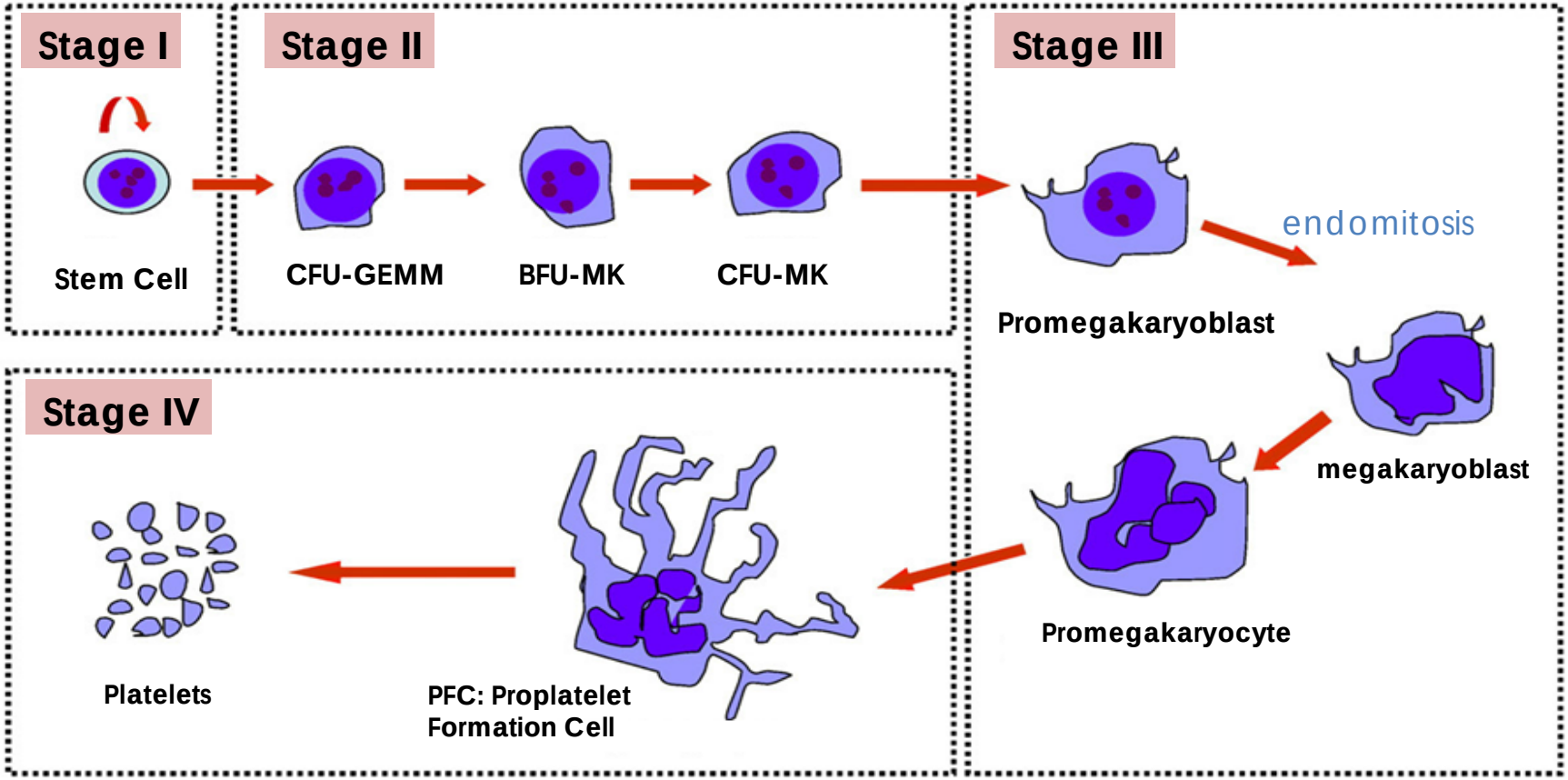
Our MSC's are substantially **more potent** than current sources of cells



ACT Platelet Program

Advanced Cell Technology

Platelet Production Stages



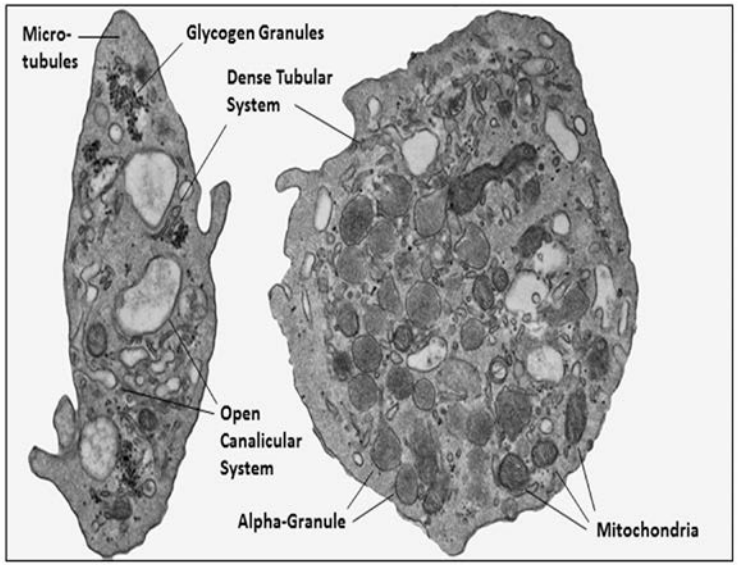
Functional megakaryocytes and platelets

from both human embryonic stem cells (**hESCs**) and induced Pluripotency Stem (**iPS**) cells

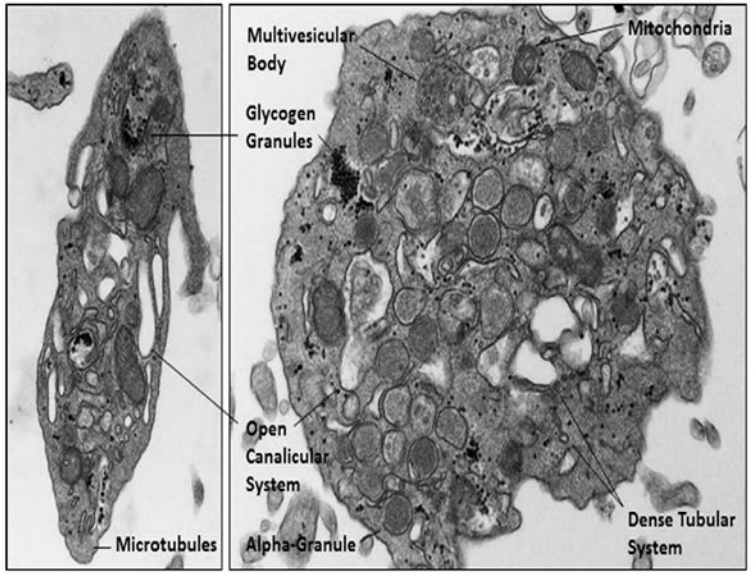
on a large scale.

Comparison of Morphology

Normal Human Blood Platelets

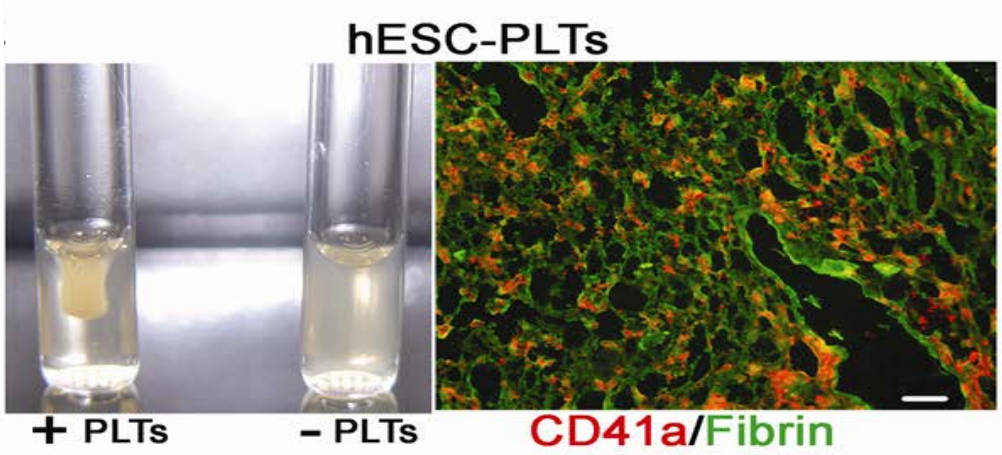


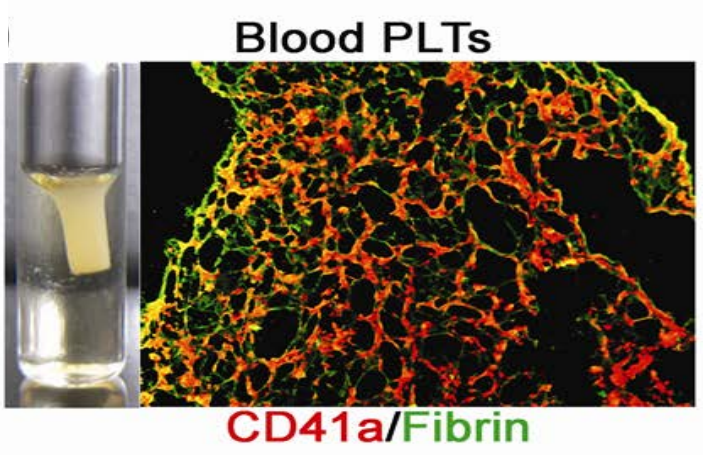
Human PSC-derived Platelets



The morphology and ultrastructure of normal human blood platelets and human iPS-derived platelets are equivalent, as demonstrated by ultrathin-section transmission electron microscopy.

Participation in Clot Formation





hESC- and iPS-derived platelets participate in clot formation and retraction

Second Generation Platelet Products

Engineered master stem cell bank for manufacture of megakaryocytes - resulting platelets can release therapeutic proteins upon activation (i.e., site of a wound, tumor, etc.)

- **α-granule signal sequence has been characterized**
  Can introduce gene into MK cells encoding recombinant fusion proteins which are packaged into α-granules

- **Factor VIII** – treatment of hemophilia by localized delivery of FVIII at site of injury
- **Erythropoietin -** localized delivery accelerates fibrin-induced wound-healing response, such as in the treatment of diabetic ulcers, burns, etc.
- **Insulin-like growth factor 1 (IGF-1); Basic Fibroblast Growth Factor; etc.**

Culture media for megakaryocytes can include therapeutic agent - resulting platelets can provide local and sustained release of drug

- **Anti-cancer Agents**
- **Antithrombotic/Antirestenosis agents for use during angioplasty and thrombolysis procedures.**

An Experienced and Dedicated Management Team

Edward Myles – Interim President, CFO and EVP of Corp Development	**Proven business leaders who can develop and implement corporate strategy and monetize assets to maximize shareholder value**
Dr. Matthew Vincent, Ph.D. – Dir., Business Development	
Dr. Robert Lanza, MD – Chief Scientific Officer	**World-renowned scientific thought leaders pushing the cutting edge of science to develop important therapies**
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	**Deep experience in clinical development programs for ophthalmology drug products from early through late-and post-marketing stages**
Dr. Roger Gay, Ph.D. - Senior Director of Manufacturing	**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

Thank you

For more information, visit www.advancedcell.com