

LEADING REGENERATIVE MEDICINE

October 2012



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.

Company Overview

ACT is a publicly-traded biotechnology company

- Develop cellular therapies for the treatment of diseases and conditions that impact hundreds of millions of people worldwide
- Cell therapies are traditionally derided for being high cost, high touch and having lack of scalability. Not our approach at all
- Premier scientific and research development team

About ACT:

- Ticker ACTC
- Market Capitalization: \$170 million
- Principal lab and GMP facility: Marlborough, MA
- Corporate HQ: Santa Monica, CA
- Only hESC-derived tissue trials ongoing worldwide
- Nearly completed corporate turnaround from disastrous financial and legal decisions



Multiple Pluripotent Cell Platforms

Single Blastomere-derived Embryonic Stem Cell Lines

Generating hESC lines

---- WITHOUT DESTRUCTION OF EMBRYO



Utilizes a

SINGLE CELL BIOPSY

Final Product Definition: hESC-derived products will be manufactured using a cell line made in 2005 from single cell isolated without the destruction of any embryos

Induced Pluripotency Stem Cells (iPS)

- Early Innovator in Pluripotency (before iPS was even a term!)
- Controlling Filings (earliest priority date) to use of OCT4 for inducing pluripotency





RPE Clinical Program



Structure of 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



Dry AMD

Loss of RPE cells Build up of toxic waste Loss of photoreceptors

Degenerating photoreceptors

Drusen



Wet AMD

Bruch's Mem. dehiscence Choroidal neovascularization

Degenerating photoreceptors

Choroldal neovascularization

- Rupture of Bruch's membrane



RPE Therapy- Rationale





North America & Europe alone have more than 30 million dry AMD patients who should be eligible for our RPE cell therapy



Dry AMD represents more than 90% of all cases of AMD



<u>What if</u> we could **replace** missing RPE cells?

RPE Therapy- Rationale

- Massive unmet medical need
- Unique measuring and observation environment
- Easy to identify aids manufacturing
- Small dosage size less than 200K cells
- Immune-privileged site minimal/no immunosuppression
- Ease of administration no separate device approval

RPE cell therapy may impact over 200 retinal diseases





RPE Therapy- Rationale



ACT'S RPE Cell Therapy should address the full range of dry AMD patients:

Halt progression of vision loss in early stage patients

Restore some visual acuity in later stage patients



GMP Manufacturing

GMP process for differentiation and purification of RPE

- Virtually unlimited supply from stem cell source
- Optimized for manufacturing

Product Cold Chain is Easily Scaled for Global Sales

Ideal Cell Therapy Product

- Centralized Manufacturing
- Small Doses
- Easily Frozen and Shipped
- Simple Handling by Doctor



Preclinical - Examples



Injected human RPE cells repair monolayer structure in eye





Phase I - Clinical Trial Design

SMD and dry AMD Trials approved in U.S., SMD Trial approved in U.K.

Regular Monitoring - including high definition imaging of retina





Participating Retinal Surgeons



Jules Stein Eye Institute

Steven D. Schwartz, MD Chief, Retina Division Ahmanson Professor of Ophthalmology Director, Diabetic Eye Disease and Retinal Vascular Center Director, Ophthalmic Photography Clinical Laboratory

Wills Eye Institute

Carl D. Regillo, MD Director, Retina Service Professor of Ophthalmology, Jefferson Medical College





Bascom Palmer Eye Institute

Byron L. Lam, MD Director, Clinical Visual Physiology Professor of Ophthalmology



Participating Retinal Surgeons



Massachusetts Eye and Ear Infirmary

Dean Eliott, MD Associate Director, Retina Service Professor, Harvard Medical School

Moorfields Eye Hospital

James Bainbridge, MA MB BChir PhD FRCOphth Professor of Retinal Studies, UCL Institute of Ophthalmology





Bascom Palmer Eye Institute

Philip J. Rosenfeld, MD PhD Professor of Ophthalmology

Edinburgh Royal Infirmary

Baljean Dhillon BMed Sci, BM BS, FRCS

Surgeon, Edinburgh Royal Infirmary Surgeon, Lothian University Hospitals NHS Trust Professor of Ophthalmology, University of Edinburgh Professor of Visual Impairment Studies, Heriot Watt University





Surgical Overview



Procedure:

- 25 Gauge Pars Plana Vitrectomy
- Posterior Vitreous Separation (PVD Induction)
- Subretinal hESC-derived RPE cells injection
- Bleb Confirmation
- Air Fluid Exchange





Preliminary Results

No Adverse Events

No signs of hyperproliferation, abnormal growth, rejection or retinal detachment.

Persistence of cells

Anatomical evidence of hESC-RPE survival and engraftment.

Increased pigmentation within the bed of the transplant.

Impact on Acuity

Recorded functional visual improvements in both patients.

THE LANCET

Embryonic stem cell trials for macular degeneration:

a preliminary report

Steven D Schwartz, Jean-Pierre Hubschman, Gad Heilwell, Valentina Franco-Cardenas, Carolyn K Pan, Rosaleen M Ostrick, Edmund Mickunas, Roger Gay, Irina Klimanskaya, Robert Lanza



Preliminary Results – Structural



Engraftment and Survival: SD-OCT image collected at month 3 show survival and engraftment of RPE



Preliminary Results – Structural



Baseline

Month 1

Month 2

SD-OCT confirms RPE engraftment adjacent Bruch's membrane.



Preliminary Results – Functional

Visual Acuity Measurements

- <u>SMD Patient</u>: BCVA improved from hand motions to 20/800 and improved from 0 to 5 letters on the ETDRS visual acuity chart
- <u>Dry AMD Patient</u>: Vision improved in the patient with dry agerelated macular degeneration (21 ETDRS letters to 28)

14 month Follow-up:

- Visual acuity gains remain relatively stable for both patients
- SMD Patient continues to show improvement.
- <u>U.K. SMD01 Patient</u> (at 9 month follow-up)
 - ETDRS: Improved from 5 letters to 10 letters, and stable
 - Subjective: Reports significantly improved ability to read text on TV



Current Safety Profile – Stargardt's Trial

9 SMD Patients Treated (as of 27 October 2012)

3 patients (50K cells cohort) treated at UCLA – US Trial 3 patients (50K cells cohort) treated at Moorfields Eye – UK Trial 2 patient (100K cells cohort) treated at Wills Eye – US Trial 1 patient (100K cells cohort) treated at Moorfields Eye – UK Trial

<u>No</u> reports of any adverse events or complications due to cells per se

- No evidence of inflammation or infiltration
- No evidence of ectopic tissue formation
- No evidence of retinal detachment



Current Safety Profile – Dry AMD Trial

4 dry AMD Patients Treated (as of 27 October 2012)

3 patients (50K cells cohort) treated at UCLA – US Trial 1 patient (100K cells cohort) treated at Wills Eye – US Trial

<u>No</u> reports of any adverse events or complications due to cells per se

- No evidence of inflammation or infiltration
- No evidence of ectopic tissue formation
- No evidence of retinal detachment



RPE Program Milestone Objectives

Key upcoming milestones

- Continue to treat and review patient data
- Define efficacy endpoints and targeted patient visual criteria
- Treat earlier stage disease to determine curative power of dissociated cell injections
- Simplify shipping and cell-prep to enhance scaled distribution platform



Intellectual Property – RPE Program

Treatment Dominant Patent Position for Treating Retinal Degeneration

Manufacturing Broad Coverage for Manufacturing RPE Cells from hESC

- Preparations Claims directed to pharmaceutical preparations of RPE Cells from hESC, including both cell suspensions and scaffolded RPE layers.
 - Sources Issued patents cover RPE Cells derived from other pluripotent stem cells (including iPS cells)

Vigilance Regularly Filing on Improvements

- Extend patent life cycle, with significance to commercialization
- Include composition-of-matter claims (cell preparations, pharmaceutical preparations, etc.)



Price Justification

Unmet Therapeutic Need

Efficacy

Patient Prevalence

Pharmacoeconomics

Patient Advocacy

Pricing Justification across all categories of consideration



RPE Program - Investment Thesis

- Immense unmet medical need
- Small Doses
- Immunoprivileged permits central (allogeneic) source of cells
- Noninvasive monitoring of retina

Market potential: More than 50 million patients in major markets.

1% market penetration may represent \$5-10B market opportunity.

Orphan indications are meaningful: Estimating a 10% market penetration with reoccurring treatments every 3-5 years, Stargardt's disease can be a \$100+ million/year product.



Therapeutic Pipeline -Ocular Programs





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)





Mesenchymal Stem Cell Program



Mesenchymal Stem Cells in Therapy

Mesenchymal stem cells (MSCs) regulate immune responses provide therapeutic potential for treating autoimmune or inflammatory diseases.

- Allogeneic without HLA matching.
- Track Record Adult-derived MSCs already in 200+ clinical trials.
 Derived from Bone Marrow and Adipost Tissue

However, allogeneic **adult-derived MSC's** are **limited** by **replicative senescence**, and as it turns out, a relative **lack of potency**



hESC- and iPS – derived MSC

ACT Proprietary Process

- hESC- and iPS-derived MSCs
 - virtually **inexhaustible source** of starting material
 - replicative capacity is more than 33,000 times greater

Advantages for Manufacturing

- Use Single Master Cell Bank
 - Simplifies FDA/regulatory process
 - No need for continually finding and qualifying donors
- Less labor-intensive



hESC- and iPS – derived MSC

Substantially **decreases and reverses** disease conditions in autoimmune models.

- Far more **potent** than adult (BM) derived MSCs.
- Have longer duration of action compared to adult (BM) derived MSCs.





ACT Vascular Program



Hemangioblast Program: Overview

Hemangioblast: common precursor to hematopoietic and endothelial cells.



Multipotent cell produces all cell types in the circulatory and vascular systems



Generation of Blood Products



Process generates large quantities of functional

red blood cells

and

megakaryocytes & platelets



ACT Corporate Overview



Financial Update – Strong Balance Sheet

- Company ended 2012 Q3 with \$42 million in cash or availability of cash through financing commitments
- \$16 million annual cash-burn rate (funded through early 2015)
- Settled nearly all litigation hangover from previous management
- Pending reverse split and NASDAQ listing in coming months



ACT Management Team

Highly Experienced and Tightly Integrated Management Team

Gary Rabin – Chairman & CEO Dr. Robert Lanza, M.D. – Chief Scientific Officer Edmund Mickunas – Vice President of Regulatory Affairs Dr. Irina Klimanskaya, Ph.D. – Director of Stem Cell Biology Dr. Shi-Jiang (John) Lu, Ph.D. – Senior Director of Research Dr. Roger Gay, Ph.D. - Senior Director of Manufacturing Kathy Singh - Controller Rita Parker – Director of Operations Dr. Matthew Vincent, Ph.D. – Director of Business Development Bill Douglass – Dir. of Corporate Communications & Social Media



ACT Leadership

World Class Board of Directors

Gary Rabin: Chairman & CEO

Dr. Robert S. Langer, ScD: Prolific medical inventor; Chair – ACT SAB

Gregory S. Perry: EVP – Immunogen

Michael Heffernan: CEO – Collegium Pharma

Zohar Loshitzer: CEO Presbia; Founder LifeAlert Medical

Dr. Alan C. Shapiro: Renowned business school professor

Highly-regarded Ethics Advisory Board

Dr. Ronald M. Green: Chairman

Dr. Judith Bernstein

Dr. Jeremy B.A. Green

Dr. Robert Kauffman

Dr. Carol A. Tauer





Thank you For more information, visit www.advancedcell.com

