

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

**FORM 8-K**

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

Date of Report (date of earliest event reported): **November 4, 2014**

**BioTime, Inc.**

(Exact name of registrant as specified in its charter)

**California**  
(State or other jurisdiction of incorporation)

**1-12830**  
(Commission File Number)

**94-3127919**  
(IRS Employer Identification No.)

**1301 Harbor Bay Parkway**  
**Alameda, California 94502**  
(Address of principal executive offices)

**(510) 521-3390**  
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
  - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
  - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
  - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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## Forward-Looking Statements

Any statements that are not historical fact (including, but not limited to statements that contain words such as “may,” “will,” “believes,” “plans,” “intends,” “anticipates,” “expects,” “estimates”) should also be considered to be forward-looking statements. Additional factors that could cause actual results to differ materially from the results anticipated in these forward-looking statements are contained in BioTime’s periodic reports filed with the SEC under the heading “Risk Factors” and other filings that BioTime may make with the Securities and Exchange Commission. Undue reliance should not be placed on these forward-looking statements which speak only as of the date they are made, and the facts and assumptions underlying these statements may change. Except as required by law, BioTime disclaims any intent or obligation to update these forward-looking statements.

This Report and any accompanying exhibits shall be deemed “furnished” and not “filed” under the Securities Exchange Act of 1934, as amended.

## Section 7 - Regulation FD

### Item 7.01 - Regulation FD Disclosure

On November 4, 2014, we will provide an update on recent developments at BioTime and its subsidiaries to our shareholders following our annual meeting of shareholders in San Francisco, California. The presentation will include the information in the slides attached to this report as Exhibit 99.1.

## Section 9-Financial Statements and Exhibits

### Item 9.01 Financial Statements and Exhibits.

<u>Exhibit Number</u>	<u>Description</u>
99.1	Slide presentation

## SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**BIOTIME, INC.**

Date: November 4, 2014

By: s/Michael D. West  
Chief Executive Officer

<u>Exhibit Number</u>	<u>Description</u>
<a href="#">99.1</a>	Slide presentation



**Shareholder Update**

**The Regenerative  
Medicine Revolution**

November 4, 2014

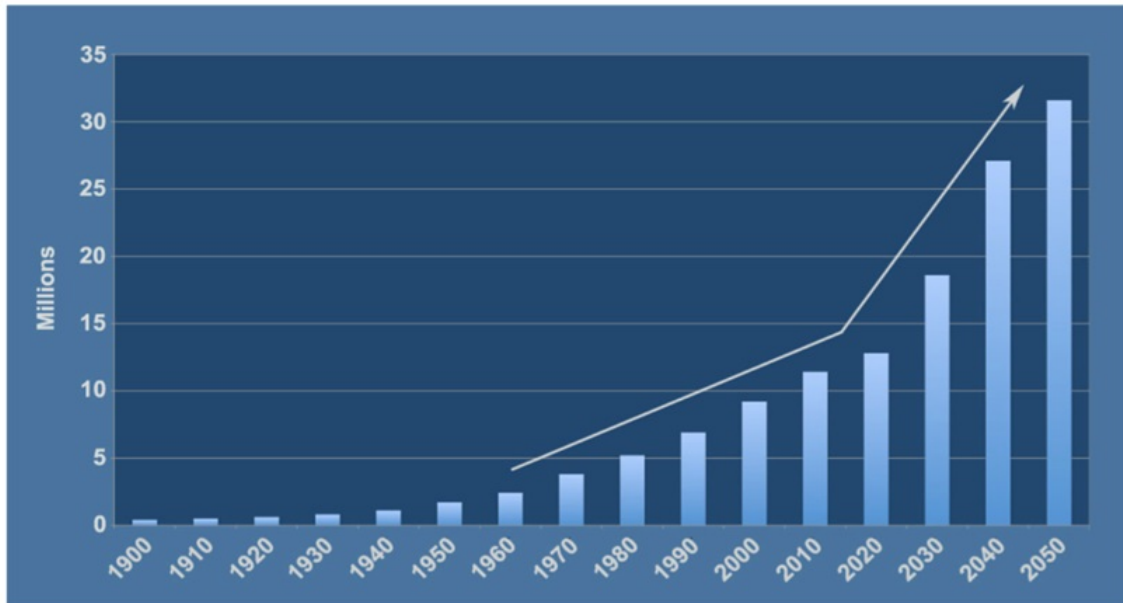


The matters discussed in this presentation include forward looking statements which are subject to various risks, uncertainties, and other factors that could cause actual results to differ materially from the results anticipated. Such risks and uncertainties include but are not limited to the success of BioTime in developing new stem cell products and technologies; results of clinical trials of BioTime products; the ability of BioTime and its licensees to obtain additional FDA and foreign regulatory approval to market BioTime products; competition from products manufactured and sold or being developed by other companies; the price of and demand for BioTime products; and the ability of BioTime to raise the capital needed to finance its current and planned operations. Any statements that are not historical fact (including, but not limited to statements that contain words such as "will," "believes," "plans," "anticipates," "expects," "estimates") should also be considered to be forward-looking statements. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. As actual results may differ materially from the results anticipated in these forward-looking statements they should be evaluated together with the many uncertainties that affect the business of BioTime and its subsidiaries, particularly those mentioned in the cautionary statements found in BioTime's Securities and Exchange Commission filings. BioTime disclaims any intent or obligation to update these forward-looking statements.

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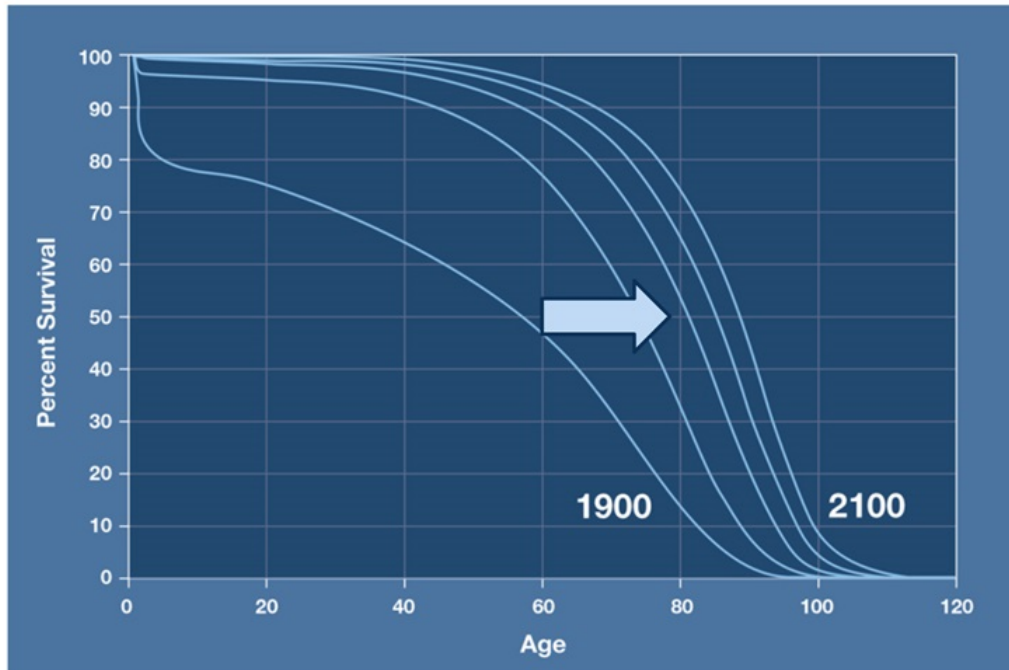
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## The Rise of the Aged Baby Boomers



Source of data on projected growth of US population: US Census Bureau

## Rectangularization of Survivorship Curve



## Aging: The Rogue Wave

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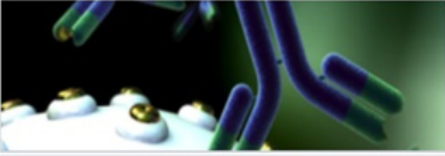

## The Tsunami of Chronic Age-Related Degenerative Disease

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- CDD due to lack of cellular regeneration
- 80% Americans have CDD of aging
- 50% of Americans have two CDDs
- 95% costs in aging is CDD



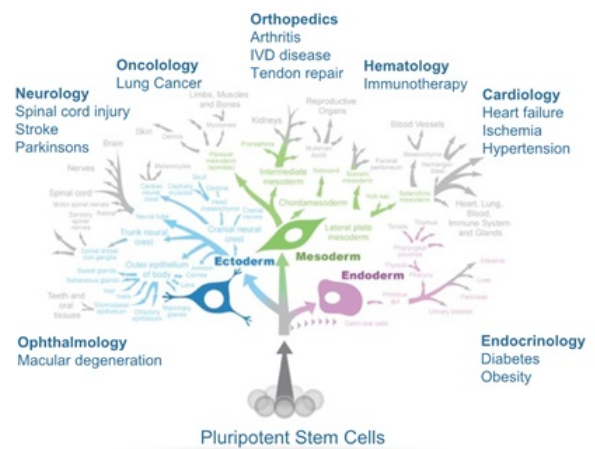
Biotech revolutions often take 15-20 years from conception to commercialization

Recombinant DNA	Monoclonal Antibodies	Regenerative Medicine
		
<p><b>Advent:</b> 1974: Gene cloning technology developed</p> <p><b>Hurdle:</b> 1976: moratorium on rDNA research</p> <p><b>Launch:</b> 1989: EPO is first billion dollar product</p> <ul style="list-style-type: none"> <li>• 2014: products using rDNA technology are ubiquitous</li> <li>• &gt;140 clinical trials</li> <li>• \$75bn current global market</li> </ul>	<p><b>Advent:</b> 1975: Hybridoma technology developed</p> <p><b>Hurdle:</b> HAMA response</p> <p><b>Launch:</b> 1997: Rituximab is first billion-dollar product</p> <ul style="list-style-type: none"> <li>• 2014: 8 of the 20 best-selling biotechnology drugs are therapeutic monoclonal antibodies</li> <li>• &gt;200 clinical trials</li> <li>• \$44bn current global market</li> </ul>	<p><b>Advent:</b> 1998: Isolation of pluripotent stem cells</p> <p><b>Hurdle:</b> 2001: U.S. federal funding restriction (reversed in 2009)</p> <ul style="list-style-type: none"> <li>• 2010: First-in-human trial of OPC1</li> <li>• Future: First billion-dollar product</li> </ul>

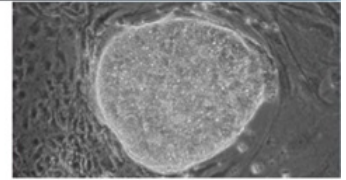
To lead in the application of pluripotent stem cell technology for regenerative therapeutic applications in age-related degenerative disease.

## The Technology Leader in Regenerative Medicine

- Poised to commercialize one of the largest revolutions in medicine
- Targeting large markets in degenerative diseases (\$billion markets)
- Multiple clinical milestones in 2H2014
- Balance of near-term and longer-term products in development
- Leader in core pluripotent stem cell technology with >600 patents/patent applications worldwide
- No approval pathway for generics or biosimilars to our cell therapies



## Two Defining Characteristics of hESCs



Pluripotency

Any functional cell type can be produced  
Permanently functional replacement cells

Not Possible With  
"Tissue Sourced"  
Stem Cells

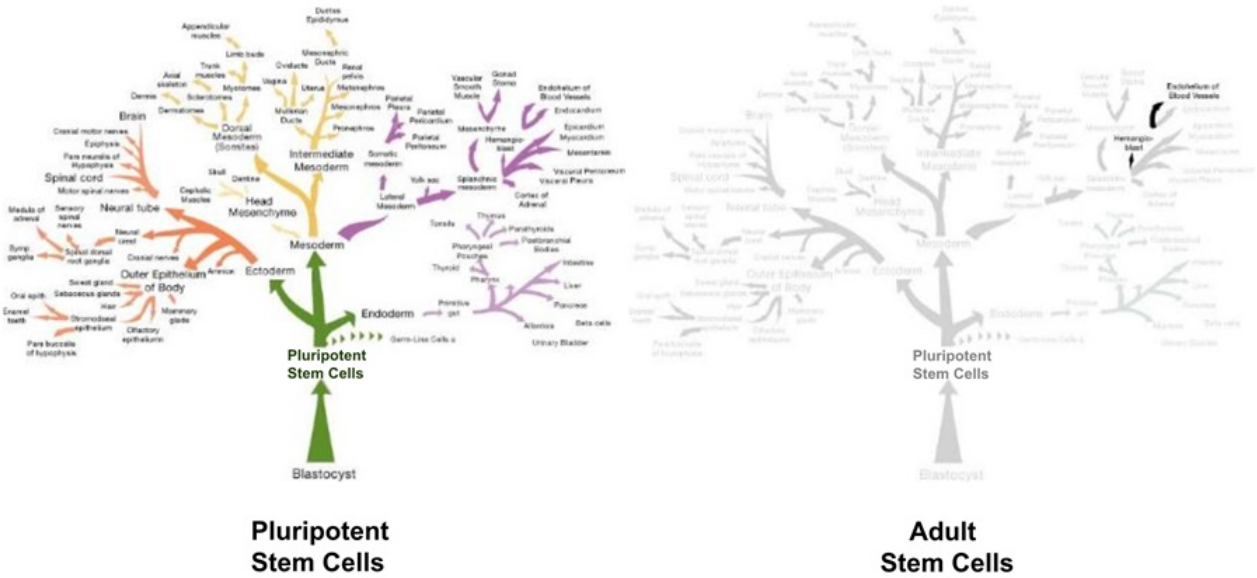
Indefinite  
Replicative  
Capacity

Scalable batch production

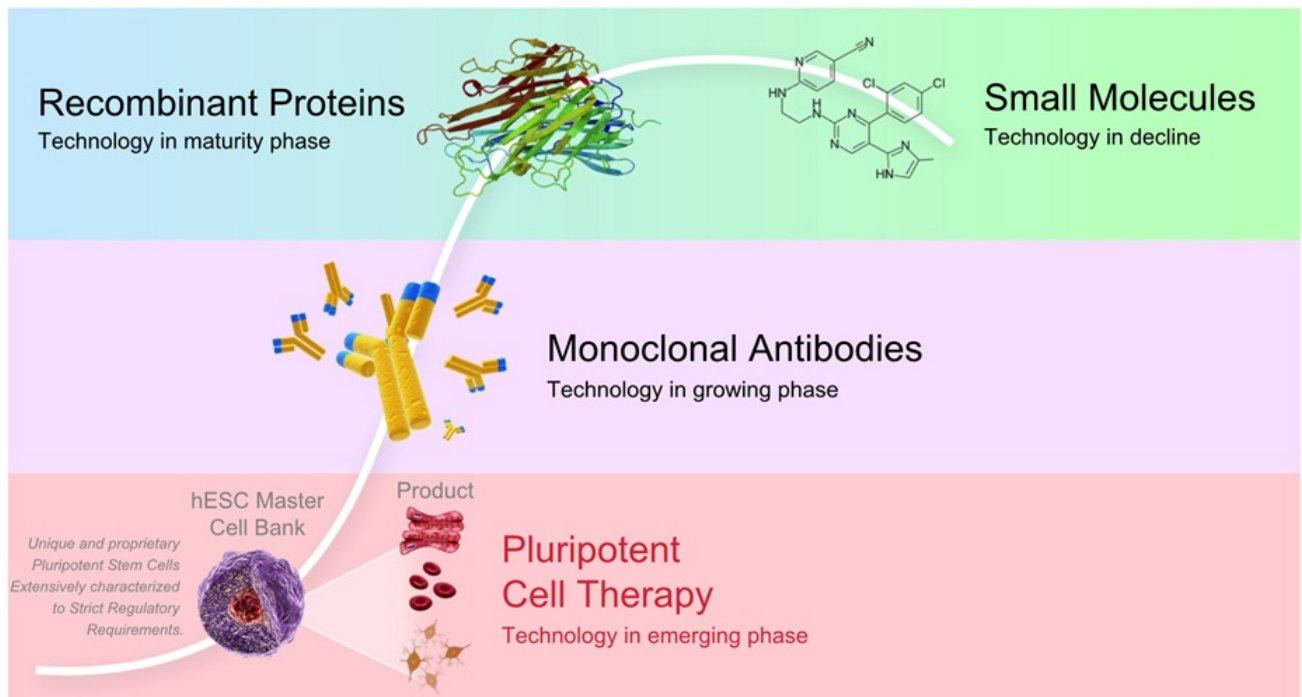
Not Possible With  
"Tissue Sourced"  
Stem Cells



Pluripotent stem cells allow for the first time in history the capacity of medicine to produce all human cell types



Cell therapy: In growth phase – potentially long lifespan due to lack of regulatory pathway for generics or biosimilars

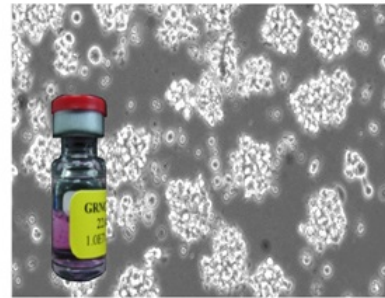




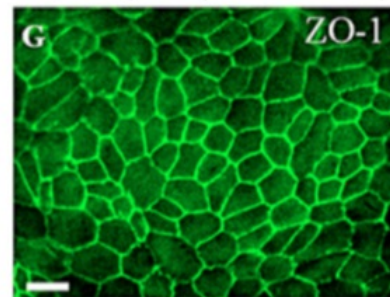
- Safe and feasible in world's first clinical trial of human embryonic stem cell-derived therapy
- FDA clearance for expansion of Phase I/IIa trial in cervical SCI
- Initiation of CIRM-funding of 3 yr \$14M grant
- Asterias listed NYSE MKT
- Follow-on opportunities in MS, Stroke, other neurodegenerative diseases

- Complete Process Development of *VAC2*
- CRUK to fund Phase I/II clinical trial in Lung CA

## *VAC2* (Dendritic Cells)



## *OpRegen* (RPE Cells)



- *OpRegen* IND Cleared for Phase I/IIa



## HyStem Matrices





LifeMap™  
DISCOVERY

MalaCards  
The Human Malady Compendium



## Integrated Biomedical Knowledgebase

- More than 14 Million page views from more than 3,000 institutions world-wide, including academia, research hospitals, patent offices, and leading biotech and pharma
- Premium services now being offered for a fee
- LifeMap Solutions developing mobile health applications

***OPC1*** – Spinal cord injury, oligodendrocytes

- \$20B annual economic impact of spinal cord injury in the U.S.
- Developed by Asterias Biotherapeutics (BioTime owns 70.6%)

***VAC2*** – Cancer, telomerase immunotherapy

- \$38B economic impact of non-small-cell lung cancer in the U.S
- Targeted by Asterias Biotherapeutics (BioTime owns 70.6%)

***OpRegen*** – Dry AMD, retinal pigment epithelial cells

- >\$5B annual spend on drug therapies for wet AMD
- Cell Cure Neurosciences (BioTime owns 62.5%)

***Renovia*** – HyStem, device for lipoatrophy

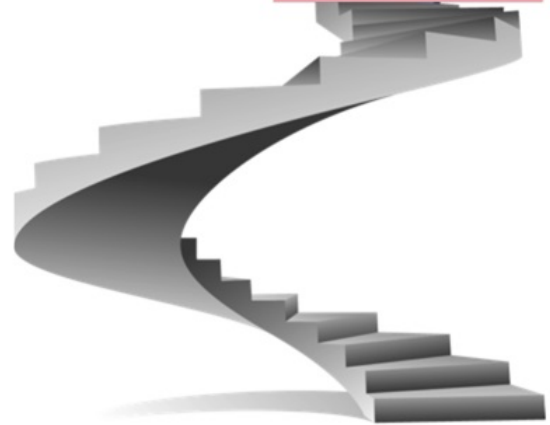
- >3M HIV+ patients with lipoatrophy
- *Renovia* developed by BioTime (owns 100%)

***PanC-Dx*** – Cancer diagnostic, breast, lung, bladder CA

- \$7B annual cost of mammography in the US
- Targeted by OncoCyte (BioTime owns 75.3%)

- Diversified, lower-cost, lower-risk strategy
- Not a bet on a single clinical program
- Multiple, growing revenue streams currently
- Seven clinical phase programs by Q4 2014
- Internal focus on low-cost, low-risk, near-term programs
- Partnering strategy for select high-cost potential blockbusters
- Subsidiaries often invite outside investors, corporate partners
- Capitalize on lack of generic or biosimilar pathways

Positioned as the technology leader in the coming regenerative medicine revolution



**Asterias Biotherapeutics**  
(NYSE MKT: AST)

*Leveraging Proprietary Regenerative Medicine Platforms to  
Address Significant Unmet Medical Needs*



## Forward Looking Statements

Statements pertaining to future financial and/or operating results, future growth in research, technology, clinical development, and potential opportunities for Asterias, along with other statements about the future expectations, beliefs, goals, plans, or prospects expressed by management constitute forward-looking statements. Any statements that are not historical fact (including, but not limited to statements that contain words such as “will,” “believes,” “plans,” “anticipates,” “expects,” “estimates”) should also be considered to be forward-looking statements. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. Actual results may differ materially from the results anticipated in these forward-looking statements and as such should be evaluated together with the many uncertainties that affect the businesses of Asterias, particularly those mentioned in the cautionary statements found in Asterias’ Registration Statement on Form S-1 and Prospectus filed with the Securities and Exchange Commission. Asterias disclaims any intent or obligation to update these forward-looking statements.



## Key Investment Highlights

- Two potential transformative platforms: 1) industry leading Pluripotent Stem Cells; 2) Allogeneic Dendritic Cell Immunotherapy
- Two products entering dose escalation clinical trials
- Partnerships with leading scientific institutions provide validation and access to significant, non-dilutive capital (~\$40 mil raised to date)
- Large potential target markets with significant unmet medical needs
- Significant potential milestones during next 24 months





## Additional Investment Considerations

- Regenerative medicine in emerging growth phase and approaching valuation inflection point
- Clinical development focus on de-risked, proof-of-concept initial product indications
- Deep, experienced management team with scientific and business expertise

## Recent Key Accomplishments

- Successfully completed stock and warrant distribution to GERN shareholders, became publicly traded and listed on NYSE MKT under ticker “AST”
- Received FDA clearance for Phase 1/2a dose escalation trial of AST-OPC1 in complete cervical spinal cord injury
- Launched partnership with California Institute of Regenerative Medicine (CIRM) to initiate AST-OPC1 Phase 1/2a clinical trial
- Partnered with Cancer Research UK (CRUK) to develop AST-VAC2 immunotherapy product candidate for lung cancer



# Asterias' Programs are Built on Potentially Transformative Technology Platforms

## Pluripotent Stem Cells

- Highly scalable platform enables production of essentially unlimited quantities of therapeutic cells in large, multi-dose production lots
- 12 years of research, significant R&D investment by Geron in hESC platform
- Broad IP estate with >400 issued and pending patents worldwide
- 3 years of data with clean safety profile from first in human study of hESC-derived product

- Major scientific validation by top scientists in multiple countries
- De-risked by extensive nonclinical data & long term clinical safety data

# Asterias' Programs are Built on Potentially Transformative Technology Platforms

## Allogeneic Dendritic Cell Immunotherapy

- Proof-of-concept data from autologous vaccine programs
- Potential for significant scalability, functionality and feasibility advantages from allogeneic (non-patient specific) product vs autologous (patient specific)
- Broad potential applications in oncology and infectious disease
- Mode of action synergistic with immune checkpoint inhibitors
- Initial antigen (telomerase) with external POC and expression in >90% of cancers

- Major scientific validation by top scientists in multiple countries
- De-risked by clinical data for first generation, autologous product

## AST-OPC1 for Neurodegenerative Diseases

### Lead indication: Spinal Cord Injury

- Devastating injury affecting 12,000 patients per year in US<sup>1</sup>
- No currently approved therapies
- Lifetime cost of care per patient of \$2-4 mil<sup>1</sup>
- Healthcare costs to system of \$14.5 bil per year in US alone, plus \$5.5 bil in lost productivity<sup>2</sup>

<sup>1</sup> National Spinal Cord Injury Statistical Center, Facts and Figures 2013

<sup>2</sup> Berkowitz et al, Spinal Cord Injury: An Analysis of Medical and Social Costs, 1998

## AST-VAC2 (Cancer Immunotherapy)

### Unique mode of action in emerging field of Immune Cancer Therapeutics

- Cancer Immunotherapy market projected to reach \$35 bil in annual revenues by 2024<sup>1</sup>
- Partial HLA mismatch from allogeneic vaccine may serve as an adjuvant to enhance efficacy as compared to autologous vaccines
- AST-VAC2 mechanism of action is likely synergistic with that of other immunotherapies such as immune checkpoint inhibitors
- Initial indication of lung cancer selected due to high level of unmet medical need, proof of concept for sensitivity to immunotherapy

<sup>1</sup> Kresge and Langreth, Bloomberg May 29, 2014

## First hESC-Derived Product in Clinic



- Phase 1 successfully completed
- Extensive data in animal studies demonstrates:
  - Engraftment over periods of at least 1 year
  - Extensive cavity filling and myelination
  - Improved locomotor function
  - No observed toxicity or immunogenicity
- FDA clearance for P1/P2a POC study in complete cervical SCI (target initial commercial indication)
- Clear path to market - Endpoint measurement established by independent SCOPE initiative (Spinal Cord Outcomes Partnership Endeavor)<sup>1</sup>
- Up to \$3 billion opportunity of peak annual US revenues for Asterias

## Feasible and Safe

- Five subjects received 2 mil AST-OPC1 cells, followed for 2-3 years
- Clean safety profile observed to date:
  - No serious adverse events related to surgery, AST-OPC1, or immunosuppression
  - No unexpected neurological changes to date
  - No adverse changes on MRI
  - Monitoring through one year shows no evidence of immune responses to AST-OPC1
- Potential evidence of biological activity:
  - MRI results in 4 of 5 subjects are consistent with prevention of lesion cavity formation





# AST-OPC1 Phase 1/2a Trial in Complete Cervical SCI

## Indication: Complete Cervical Spinal Cord Injury

- High level of unmet medical need – no approved therapies, high level of disability & lifetime cost of care
- Clear path to market – endpoint measurements established by SCOPE initiative

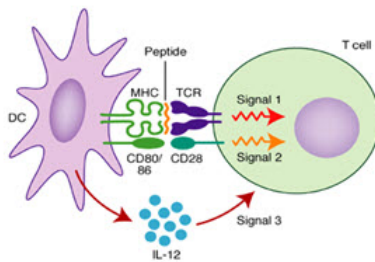
## Objectives: Safety and preliminary efficacy

- Establish safety of AST-OPC1 in cervical sensorimotor complete SCI
- Assess effects on upper extremity motor function
- Investigate effects on additional measures of neurological function

## Trial Design: Sequential cohort, dose escalation

- Dose three pts with two million AST-OPC1 cells
- After 30 days, dose five pts with 10 million AST-OPC1 cells
- After 30 days, dose five pts with 20 million AST-OPC1 cells
- First patient enrollment anticipated in second quarter of 2015

## A New Class of Cancer Immunotherapy



**Dendritic Cells: Potent Antigen Presenting Cells**

### Advantages of Human Embryonic Stem Cell-Derived Dendritic Cell (hESC-DC) Vaccine Platform:

- Existing proof-of-concept data for dendritic cell vaccines from first generation, autologous products
- Significant scalability, cost and feasibility advantages of hESC-derived allogeneic dendritic cell platform
- Potential for adjuvant effect from partial allogeneic mismatch
- hESC-derived cells have expected properties of mature dendritic cells
- Broad potential applications in a wide range of cancer indications
- Likely synergistic with immune checkpoint inhibitors

# Proof of concept for Dendritic Cell Telomerase Immunotherapy from First Generation AST-VAC1 Product

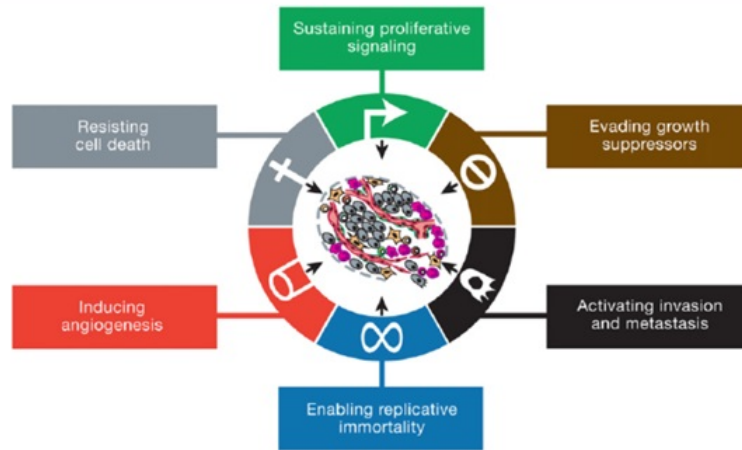
Two Clinical Trials of Autologous AST-VAC1 Product Show that Dendritic Cell Based Immunotherapies Targeting Telomerase Can Stimulate Immune Responses and Clinical Activity

Prostate Cancer	Acute Myelogenous Leukemia
Phase 1, Single center (Duke)	Phase 2, Multi-center
Investigator-sponsored	Industry-sponsored
20 patients	21 patients
95% Patients Develop Immune Responses to Telomerase	55% Patients Develop Immune Responses to Telomerase
<ul style="list-style-type: none"><li>• Highly Significant Increase in PSA Doubling Times</li><li>• Clearance of Circulating Immune Complexes</li></ul>	<ul style="list-style-type: none"><li>• Significant Increase in 12 Month DFS in High Risk Group (N=11) Compared to Published Historical Controls</li></ul>



J. Immunol 2005, 174: 3798  
Khoury, ASH 2010

## Rationale for Telomerase



Hanahan and Weinberg, "The Hallmarks of Cancer"

### Telomerase Antigen:

- Expressed in >90% of human cancers
- Rarely expressed in normal adult cells
- Plays critical role in conferring replicative immortality to cancer cells
- Evidence for immunogenicity from previous trials

# AST-VAC2 Phase 1/2a Trial in Non-small Cell Lung Cancer (NSCLC)

## Indication: Non-small Cell Lung Cancer

- Immune blockade inhibitor trials demonstrate sensitivity of lung cancer to immunotherapy
- Proof of concept for telomerase antigen in lung cancer
- High level of unmet medical need with current therapeutic regime

## Objectives: Safety and preliminary efficacy

- Establish safety of AST-VAC2 in resected and advanced disease settings
- Assess generation of anti-telomerase and anti-VAC2 immune responses
- Investigate initial measures of clinical activity

## Trial Design:

- 5 pts w/ resected NSCLC: 6 vaccinations of 1 million AST-VAC2 cells
- 12 pts w/ resected NSCLC: 6 vaccinations of 10 million AST-VAC2 cells
- 12 pts w/ advanced NSCLC: 6 vaccinations of 10 million AST-VAC2 cells

## Partnerships Provide Validation and Non-dilutive Funding at Minimal Cost to AST Shareholders

### AST-OPC1



#### \$14.3 Million Grant

- Includes funding for:
  - Execution of Phase 1/2a study
  - Process and assay development activities to prepare for pivotal trials and commercialization
  - Facilities and indirect costs
- Potential follow-on grants to expand and accelerate trial

### AST-VAC2



#### Clinical Development Partnership

- Asterias performs scale-up and tech-transfer of AST-VAC2 manufacturing process
- CRUK provides personnel and funding for cGMP manufacturing, regulatory filing, Phase 1/2a trial
- Asterias has first option to reacquire program on preset, reasonable terms; majority revenue share on partner's development if does not choose to reacquire

**Estimated ~\$40 Million of Total Non-dilutive Funding Committed to Date**

# Asterias Milestones and Newsflow Next 24 Months

1H'15	2H'15	1H'16	2H'16
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✦ Initiate AST-OPC1 P1/2a Trial

✦ 30 day safety of 2M cell cohort;  
dose escalate to 10M cell cohort

6 mo efficacy data from  
AST-OPC1 10M cell cohort ✦

✦ Complete AST-VAC2 process transfer

✦ MHRA Clearance for AST-VAC2 P1/2a Trial

✦ Initiate AST-VAC2 P1/2a Trial

✓ Signature of NGA; disbursement of CIRM funds begins

✦ Warrant exercise - \$11.7M cash raised



## Significant Opportunities for Future Pipeline Expansion

### AST-OPC1

Broad potential applications in neurodegenerative disease:

- Multiple sclerosis
- Stroke
- Amyotrophic lateral sclerosis
- Leukodystrophies (e.g. Canavan disease)

### AST-VAC2

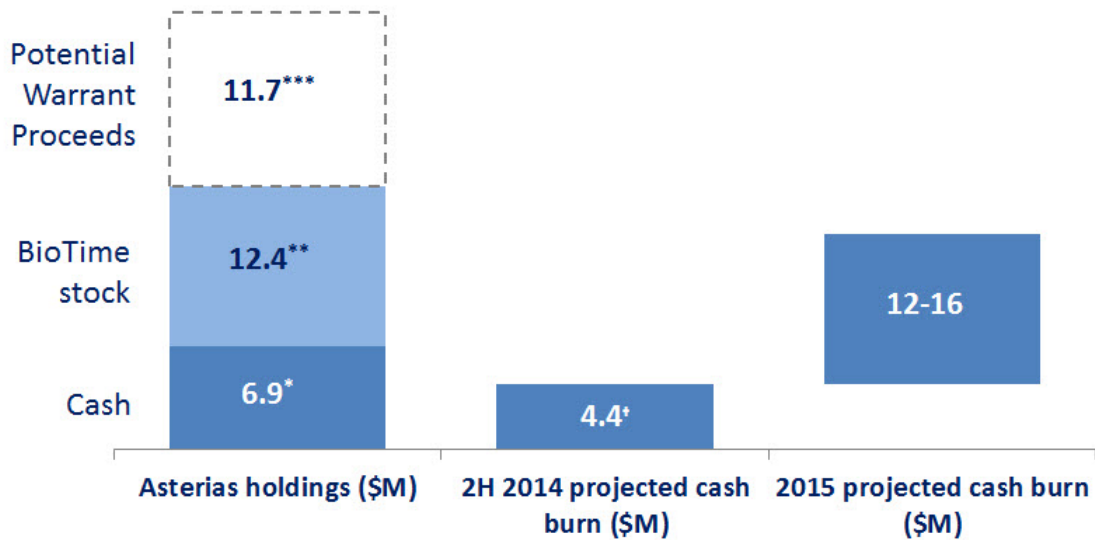
- Telomerase immunotherapy in additional cancer indications
- Use of hESC-DC platform with additional cancer antigens
- Non-cancer indications (e.g. hepatitis)

### Other Products

- Additional programs from existing Geron & BioTime portfolios (e.g. cardiovascular, orthopedics)
- Partnerships to leverage broad IP platform in additional therapeutic areas



# Asterias Has Sufficient Funds to Advance its Lead Programs in 2014 and 2015



- \$14.3 M in non-dilutive funding for AST-OPC1 project in 2014-2018 from CIRM
- Estimated \$20-30M cost avoidance from AST-VAC2 CRUK deal

\* As of 6/30/14, per Asterias Q2 10Q filing (\$12.9M cash - \$5.4 due to BioTime - \$0.5 M Accounts Payable and Accrued Liabilities)

\*\* 3.9 million shares at \$3.19 as of 10/9 market close

\*\*\* 5 million warrants at \$2.34/share, June 2015 term

† Expenses may increase by up to \$2 million depending on timing of CIRM funds release



## Capital Structure Profile

- Total 30.9 million outstanding shares valued at \$130 mil (\$4.20 per share) as of October 31, 2014
- Additional 5 million Warrants @ \$2.34/warrant expiry June 2015 – held by George Karfunkel Trust and Broadwood Partners, LLP
- Additional 3.5 million Warrants @ \$5.00/warrant expiry September 2016 – held by BioTime and Romulus
- Option pool of 4.5 million shares for management and employees



## Asterias Executive Team: Business Focused, with Best-in-Class Cell Therapy Product Development Experience

Name	Title	Summary of experience
Pedro Lichtinger	Chief Executive Officer	Former President & CEO, Optimer Pharmaceuticals. 25 year career at Pfizer including as President of Global Primary Care and Global Animal Health businesses
Jane Lebkowski, PhD	President of R&D	25 years experience in R&D of cell & gene therapies at Applied Immune Sciences, Rhone Poulenc Rorer, and Geron
Katy Spink, PhD	VP and Chief Operating Officer	Former SVP, Cell Therapy Program Operations at Geron. Experience in biotech strategy, BD & program management and operations at Geron and McKinsey
Ed Wirth, MD, PhD	Chief Translational Officer	25 years experience in translational research of cell therapies and medical devices at University of Chicago, Geron, and InVivo
Madelyn Marino	VP, Quality	30 years experience in QA/QC for small molecules, biologics, cell & gene therapy at Amgen and Onyx
Casey Case, PhD	SVP Research and Nonclinical Development	Former EVP Research at SanBio. Previous R&D leadership experience at Sangamo, Tularik, OSI

- **Broad expertise in pharma and biotech development throughout the product lifecycle**
- **Track record of establishing value creating alliances**
- **Unmatched expertise in development of cell therapies**





# Strong, Multilayer IP and Market Protection for Asterias' Products

## Example U.S. issued patents:

### Covering AST-OPC1:

**US 7,285,415:** "Method of Producing Oligodendrocytes from Human Embryonic Stem Cells for Drug Screening or Treatment of SCI"

**US 7,579,188:** "Oligodendrocytes Derived from Human Embryonic Stem Cells for Remyelination and Treatment of SCI"

**Exclusively licensed to Asterias from UC Irvine**

**US 8,252,585:** "Neural Progenitor Cell Populations"

**US 8,252,586:** "Neural Cell Populations from Primate Pluripotent Stem Cells"

**Asterias Owned**

**US 6,800,480:** "Methods and Materials for the Growth of Primate-Derived Primordial Stem Cells in Feeder Free Culture"

**US 8,097,458:** "Microcarrier Culture System for Rapid Expansion of Human Embryonic Stem Cells"

**Asterias Owned**

### Covering AST-VAC2:

**US 8,093,049:** "Differentiation of Primate Pluripotent Stem Cells to Hematopoietic Lineage Cells"

**Asterias owned**

**US 7,781,213:** Composition of Matter Claims to hESC-derived Dendritic Cells

**Exclusively licensed to Asterias from Isis Innovation, Ltd.**

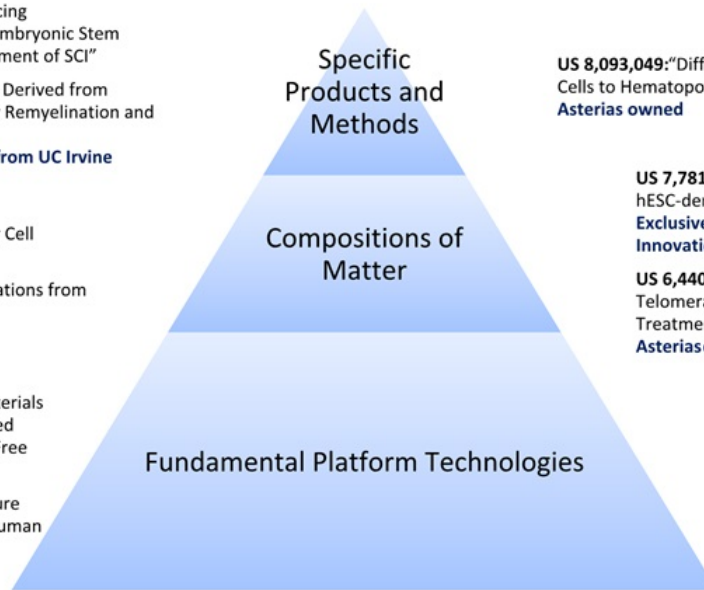
**US 6,440,735:** Dendritic Cell Vaccine Containing Telomerase Reverse Transcriptase for the Treatment of Cancer

**Asterias owned**

**US 6,800,480:** "Methods and Materials for the Growth of Primate-Derived Primordial Stem Cells in Feeder Free Culture"

**US 8,097,458:** "Microcarrier Culture System for Rapid Expansion of Human Embryonic Stem Cells"

**Asterias Owned**



### Additional market protection expected from:

- Lack of biosimilars pathway for cellular therapies
- Orphan designations (7 year market exclusivity) for OPC1 in SCI, VAC2 in certain cancer indications

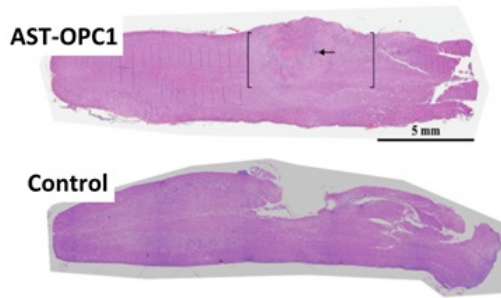


Confidential

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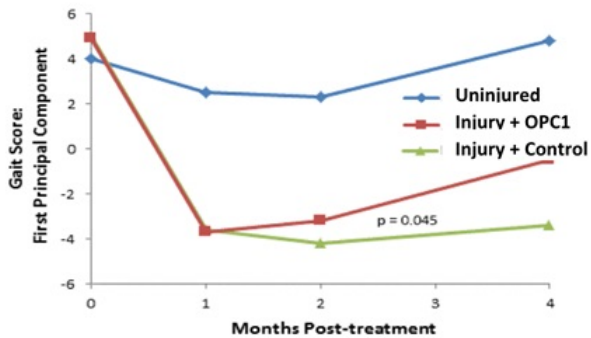


# AST-OPC1 Is Safe and Efficacious in Animal Models of SCI



## Four restorative functions observed:

- Secretes factors to stimulate nerve growth
- Increases myelination of axons
- Stimulates new blood vessels in injury site
- Reduces injury-related cavitation



**Improves locomotor function in rodent models of both thoracic and cervical SCI**

**28 Animal Studies; >3000 Rodents and Pigs**

- No evidence of clinically significant safety concerns
- Delivery of target doses is feasible

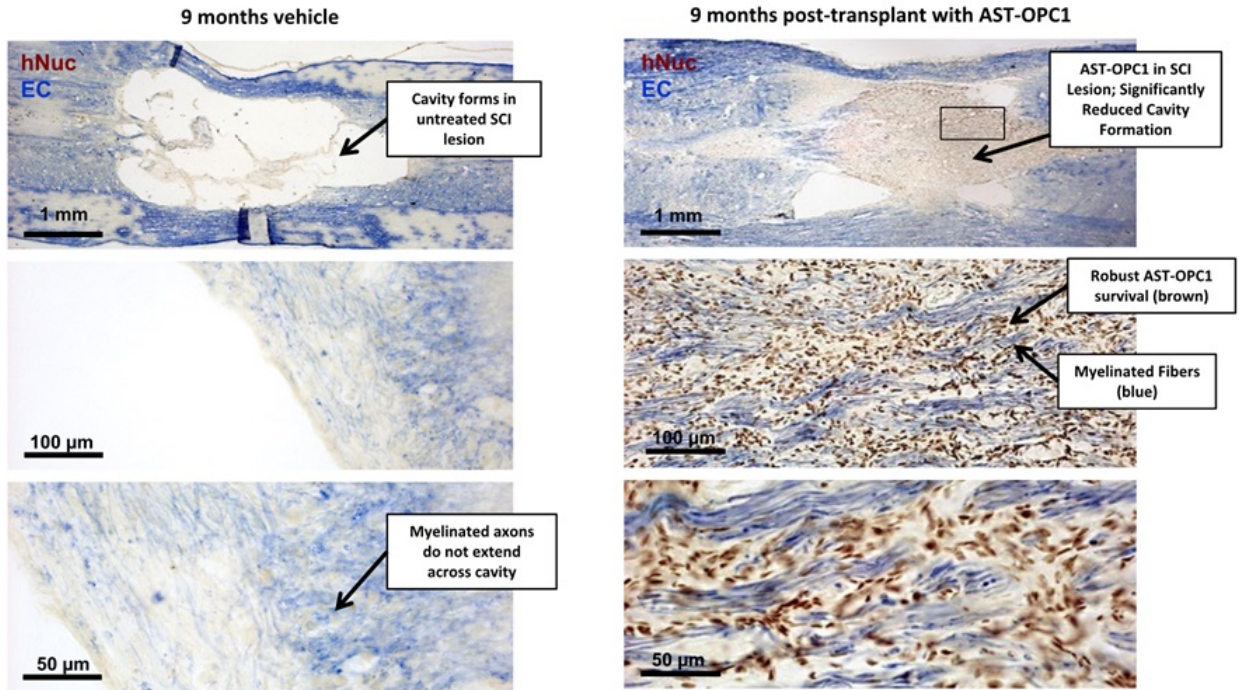


# Asterias Neurology Program

## AST-OPC1 Reduces Cavity Formation and Induces Persistent Myelination

### Myelinated Bundles of Nerve Fibers Traverse Injury

#### Rat Thoracic Spinal Cord Injury Model



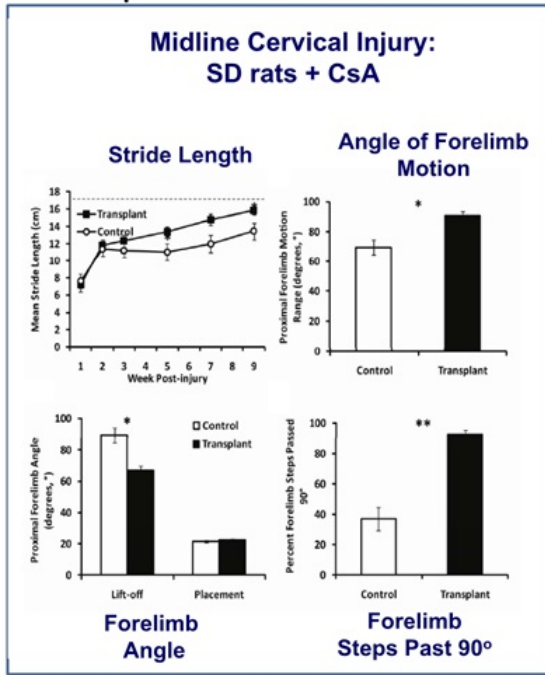
2.7

Brown: antibody to human nuclear antigen labels AST-OPC1; Blue: Eriochrome Cyanine stains myelin

Confidential

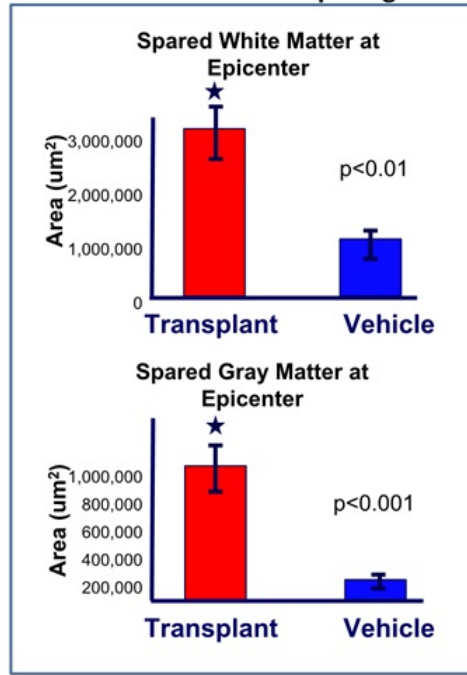
26

**Improves Locomotor Function**



Sharp et al., 2010

**Increases Tissue Sparing**



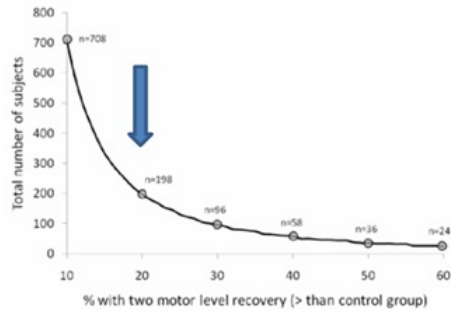
Sharp et al., 2010



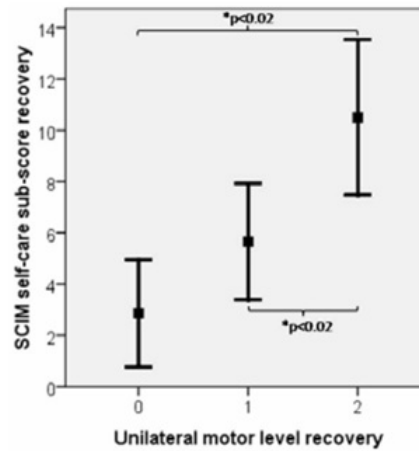
# Work of the SCOPE Consortium Has Defined Clinical Development Path in Complete Cervical Spinal Cord Injury

## Target Product Profile for AST-OPC1 in Complete Cervical SCI:

- Increase of  $\geq 20\%$  in the percentage of patients regaining two or motor levels of function

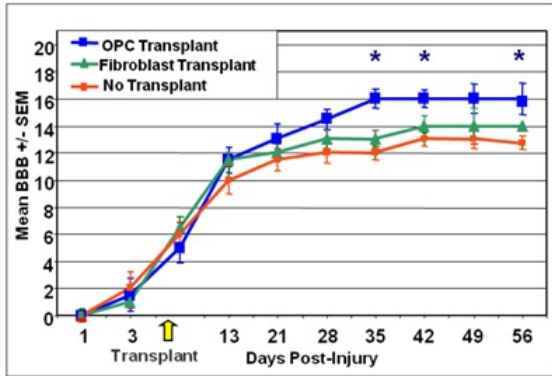


Enables powering of trial with only ~200 subjects

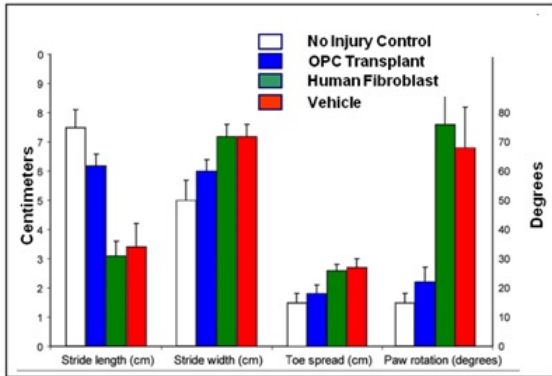


Translates into clinically significant improvements in ability to self-care

# AST-OPC1 Improves Locomotor Recovery in SCI Rats



- Increased Weight Bearing
- Improved HL-FL Coordination
- Improved Hind Paw Clearance
- Improved Trunk Stability
- Decreased Tail Drag



- Increased Stride Length
- Decreased Stride Width
- Decreased Paw Rotation
- Decreased Toe Spread

2.8

## Asterias has Rapidly Executed on Expanding Clinical Development of AST-OPC1 to Complete Cervical SCI

### Geron:

- Worked with FDA to define path to clinic for hESC-derived therapy
- Performed >20 nonclinical studies to enable first in man testing of AST-OPC1
- Resolved two clinical holds to satisfaction of FDA
- Enrolled five subjects in AST-OPC1 trial in complete, thoracic SCI
- Initiated nonclinical studies to support expansion to cervical SCI
- **2011:** Announced decision to divest stem cell assets to focus on two Phase 2 oncology programs

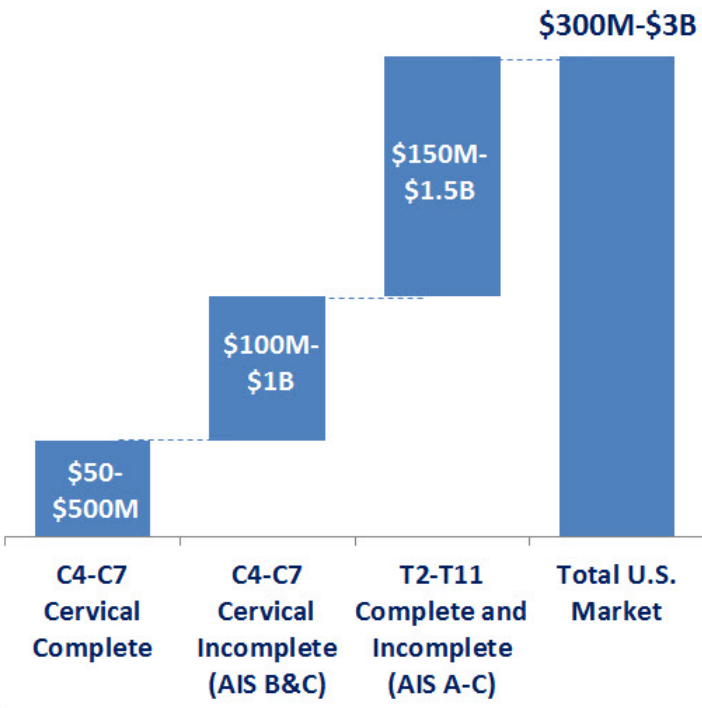
### Asterias:

**October 2013:** completed acquisition of Geron stem cell assets

- Completed analysis and study reports for nonclinical studies in cervical SCI
- Wrote clinical study report for thoracic SCI study
- Worked with KOLs to establish clinical development plan for AST-OPC1
- Held meeting with FDA to discuss proposed Phase 1/2a study
- Secured \$14.3M grant from CIRM to fund Ph 1/2a study in cervical SCI
- Submitted regulatory dossier seeking IND amendment for cervical study

**August 2014:** obtained FDA clearance for Phase 1/2a dose escalation POC study in complete cervical SCI

# Spinal Cord Injury Represents a Substantial Market Opportunity Due to A High Level of Unmet Need, Lack of Competing Therapies



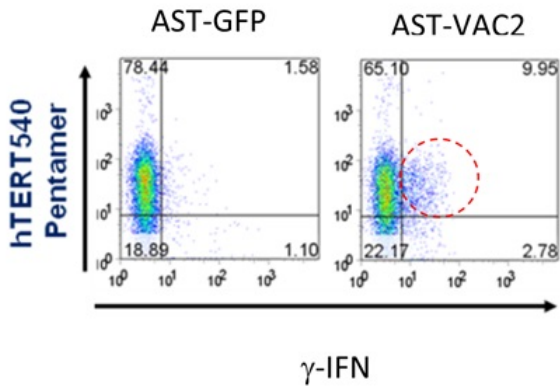
- **Estimated Market Opportunity of \$300M-\$3B in U.S. alone**
- **Driven by magnitude of impact on high lifetime costs of care for cervical (\$3-4M) and thoracic (\$2.3M) injury patients**
- **Defined clinical endpoints with potential to support approval from <300 patient trial**
- **Potential for breakthrough therapy and orphan designation**



Confidential

## AST-VAC2 Has Expected Properties of Mature Dendritic Cells

### AST-VAC2 Stimulates Telomerase Specific T-cells

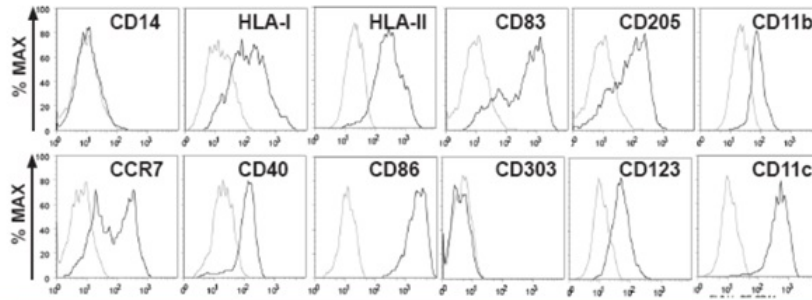


- Expresses Markers of Mature Dendritic Cells
- Activates T Cells
- Migrates in Response to Inflammation
- Can be Cryopreserved and Irradiated Without Loss of Function

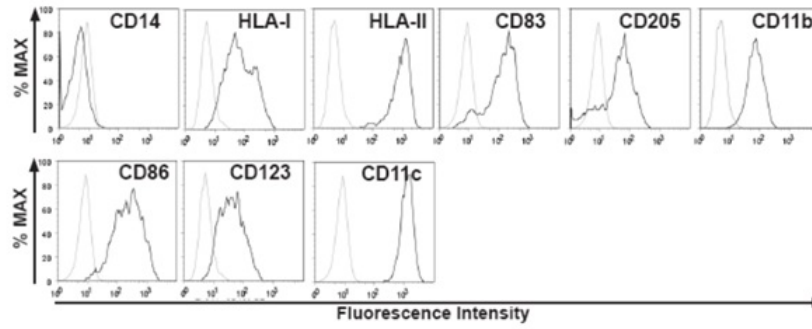
Confidential and Proprietary

## AST-VAC2 is Phenotypically Similar to PBM-Derived DC

hESC-derived  
Mature DC



PBM-derived  
Mature DC



AST-VAC2 and PBM-derived mature DC show similar DC marker expression profiles

4.2

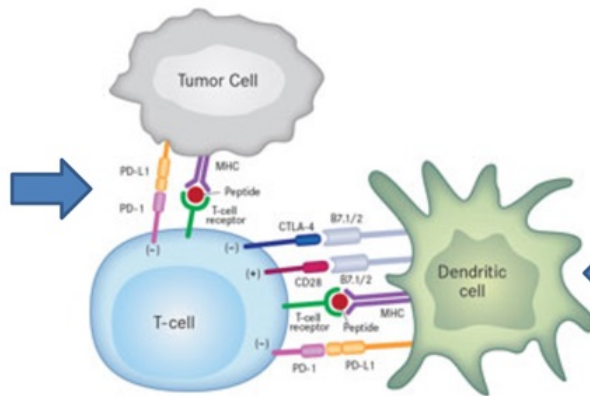
Tseng et al, Regen Med. 2009



Confidential

# hESC-DC Vaccines Are Likely to Be Synergistic With Immune Checkpoint Inhibitors

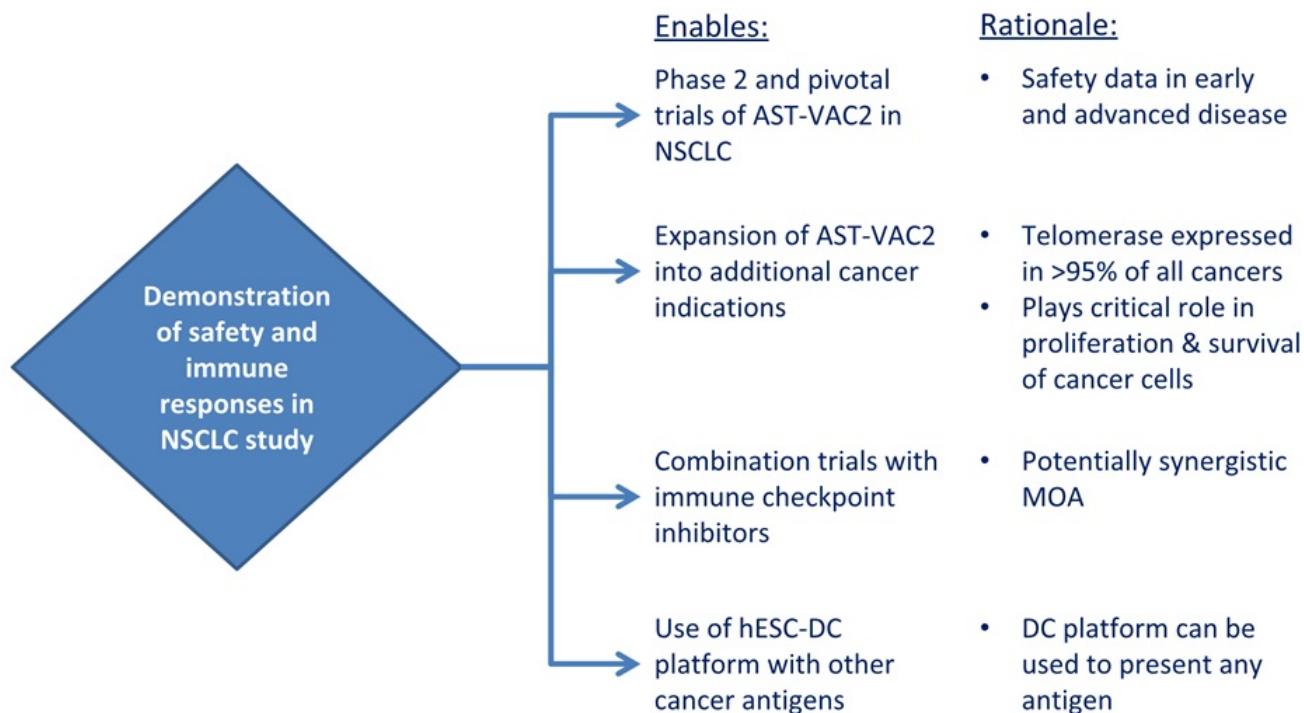
Immune Checkpoint Inhibitors Block Pathways that Tumors Use to Evade Immune Surveillance



**AST-VAC2 is the Only Allogeneic Dendritic Cell Cancer Immunotherapy That Educates the Immune System to Recognize Antigens on Tumor Cells**

- Off-the Shelf Product
- Available on Demand
- Stimulates Immune Responses to Tumors
- Can Complement Immune Checkpoint Inhibitors
- Potential for adjuvant effect from allogeneic cells

# POC Data from Phase 1/2a Study of AST-VAC2 in NSCLC Enables Broad Development of hESC-DC Platform







*Human embryonic stem cell –derived products  
for the treatment of retinal and neurodegenerative diseases*

## BIOTIME ANNUAL MEETING SHAREHOLDER UPDATE

Dr Charles Irving, CEO

04 Nov 2014

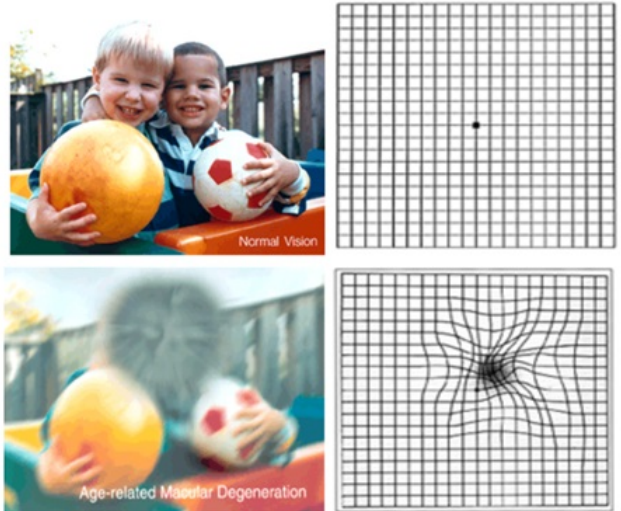
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# Safe Harbor Statement

The matters discussed in this presentation include forward looking statements which are subject to various risks, uncertainties, and other factors that could cause actual results to differ materially from the results anticipated. Such risks and uncertainties include but are not limited to the success of BioTime in developing new stem cell products and technologies; results of clinical trials of BioTime products; the ability of BioTime and its licensees to obtain additional FDA and foreign regulatory approval to market BioTime products; competition from products manufactured and sold or being developed by other companies; the price of and demand for BioTime products; and the ability of BioTime to raise the capital needed to finance its current and planned operations. Any statements that are not historical fact (including, but not limited to statements that contain words such as "will," "believes," "plans," "anticipates," "expects," "estimates") should also be considered to be forward-looking statements. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. As actual results may differ materially from the results anticipated in these forward-looking statements they should be evaluated together with the many uncertainties that affect the business of BioTime and its subsidiaries, particularly those mentioned in the cautionary statements found in BioTime's Securities and Exchange Commission filings. BioTime disclaims any intent or obligation to update these forward-looking statements.

# Dry AMD: A Major Incurable Disease of Aging

- Leading eye disease responsible for visual impairment of the elderly in the US, EU and Australia
- Loss of fine visual detail; Central vision blind spots; Mostly affects both eyes; 10% progress to wet AMD and legal blindness
- In the US:
  - 1.6 million new cases/yr of dry-AMD
  - 7.3 million with early stage dry-AMD
  - 1 million with geographic atrophy (GA), the advanced stage dry-AMD
  - Annual economic loss to GDP from -AMD: \$24.4 billion
- Est. WW market opportunity > \$5B



<http://www.blindness.org/content.asp?id=46>

***No FDA Approved Treatment for Dry AMD***

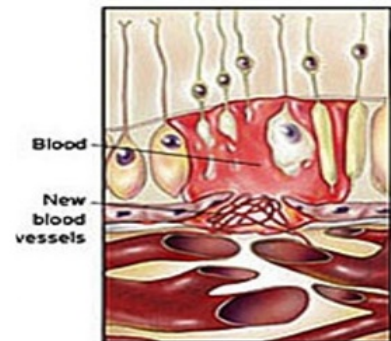
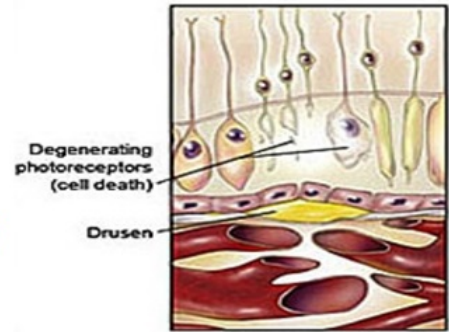
# Types of Age-Related Degeneration

- **Dry AMD** (non-neovascular) is characterized by drusen and RPE changes which lead to central atrophy of photoreceptors.
- **Geographic atrophy** (GA) is the severe form of dry-AMD.

**No FDA approved therapy.**

- **Wet AMD** (neovascular) can develop from dry-AMD. Pathological neovascularization leaks and/or bleeds in the macular area can occur rapidly and result in blindness.

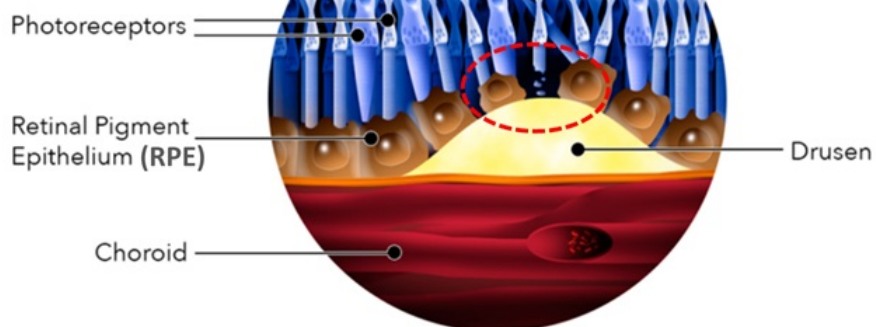
**Can be treated with VEGF inhibitors, whose current estimated annual worldwide sales are greater than \$7 billion**



# Role of Retinal Pigment Epithelium (RPE) Cells in Dry AMD

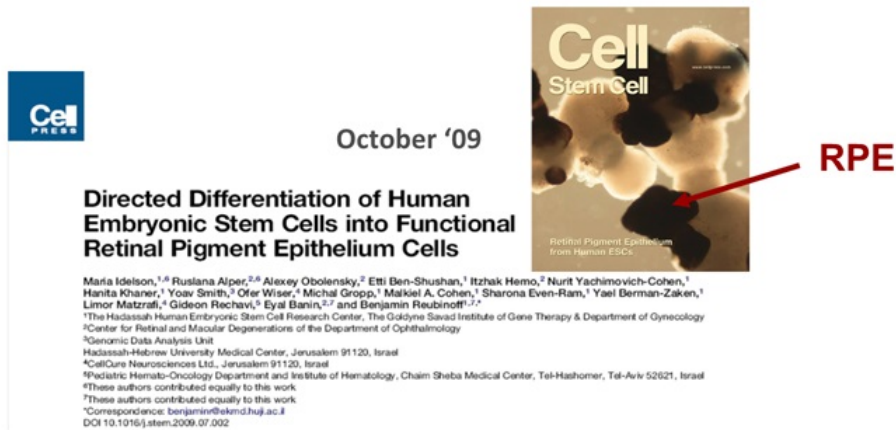
- Photoreceptors depend on RPE cells for nourishment, recycling of visual pigment and waste disposal
- When RPE cells die, the photoreceptors also die and central vision is lost

## Geographic Atrophy

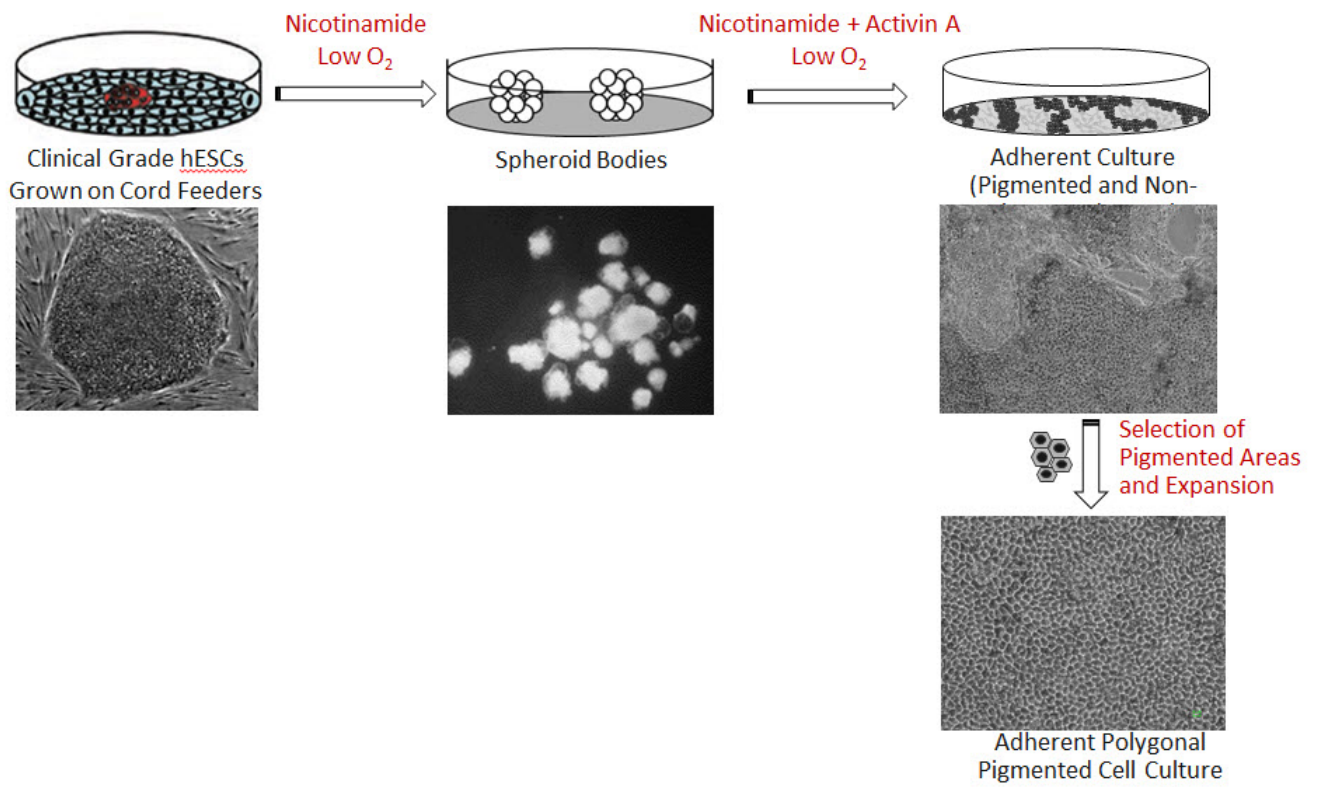


# RPE Transplantation Therapy: A Promising Approach That Lacked a Reliable Source of RPE Cells

- Healthy RPE cells can replace old, dysfunctional RPEs
- Human Embryonic Stem Cells (hESCs) could provide an unlimited supply of well-characterized RPE cells, if a method better than spontaneous differentiation was available
- Cell Cure's new directed differentiation method produces homogenous batches of large numbers of pure and robust RPE cells



# Production of RPE by Directed Differentiation of hESCs



# IP Status of Directed Differentiation Method

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- **Cell Cure has exclusive license from Hadasit Ltd.**
- **Publ. #: WO2008/129554; Publ. Date: 30-Oct-2008**
- **Granted**
  - Japan – 5,395,058; Australia – 2008242106; China -200880020748.0; Israel -201600
- **Allowed**
  - Europe
- **Pending**
  - USA, Canada, Hong Kong, India, various divisionals



# Cell Cure's In-licensed Patent Portfolio

## Some of Cell Cure's Patent Families

Title	PCT Publication #	Granted
METHODS OF SELECTING RETINAL PIGMENTED EPITHELIAL CELLS (Cell Cure & Hadasit)	WO2013114360	
Stem Cell Derived Retinal Pigmented Epithelium Cells (Hadasit)	WO2008129554	JP 5,395,058; AU 2008242106; CH 200880020748 IL 201600
Stem Cells Culture System (Hadasit)	WO2006070370	
Embryonic stem cells and neural progenitor cells derived therefrom (ESI)	WO0168815	AU 779694 US 7,011,828 US 7,504,257
Methods of controlling differentiation of embryonic stem cells by culturing in the presence of BMP2 pathway antagonists (ESI)	WO0198463	AU6570401 US 7,112,437
Implanting neural progenitor cells derived from human embryonic stem cells (ESI)		US 7,011,828
Generation of neural stem cells from undifferentiated hES (ESI)	WO03104444	GB 2407821 GB 2427616
Embryonic stem cells (ESI)	WO0027995	IL 142748

➤ **The BioTime family of companies has the world's largest patent estate in pluripotency with >600 patents and patent applications worldwide.**

➤ Examples of relevant IP:

- ✓ Feeder free culture of hES cells
- ✓ Directed differentiation methods
- ✓ Neuronal differentiation (NCAM positive lineages)
- ✓ License to WARF estate
- ✓ RPE-specific claims

# Open-Source, Clinical-Grade, NIH -Registered hESCs: A Source for Manufacturing Xeno-free RPE Cells

OPEN ACCESS Freely available online

PLoS one

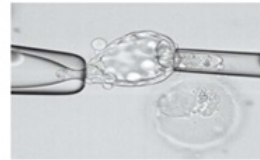
## Derivation of Xeno-Free and GMP-Grade Human Embryonic Stem Cells – Platforms for Future Clinical Applications

Shelly E. Tannenbaum<sup>1,3</sup>, Tikva Tako Turetsky<sup>1,3</sup>, Orna Singer<sup>1,3</sup>, Einat Aizenman<sup>2</sup>, Sophie Kirshberg<sup>1</sup>, Nili Ilouz<sup>1</sup>, Yaniv Gil<sup>1</sup>, Yael Berman-Zaken<sup>1</sup>, Temima Schnitzer Perlman<sup>1</sup>, Nitschia Geva<sup>2</sup>, Ora Levy<sup>2</sup>, Daniel Arbel<sup>1</sup>, Alex Simon<sup>2</sup>, Assaf Ben-Meir<sup>2</sup>, Yoel Shufaro<sup>1,2</sup>, Neri Laufer<sup>2</sup>, Benjamin E. Reubinoff<sup>1,2\*</sup>

<sup>1</sup> The Hadassah Human Embryonic Stem Cell Research Center, Goldyne Savad Institute of Gene Therapy, Hadassah Hebrew University Medical Center, Jerusalem, Israel, <sup>2</sup> Department of Obstetrics and Gynecology, Hadassah Hebrew University Medical Center, Jerusalem, Israel, <sup>3</sup> Department of Pediatric Surgery, Hadassah Hebrew University Medical Center, Jerusalem, Israel

### Abstract

Clinically compliant human embryonic stem cells (hESCs) should be developed in adherence to ethical standards, without risk of contamination by adventitious agents. Here we developed for the first time animal-component free and good manufacturing practice (GMP)-compliant hESCs. After vendor and raw material qualification, we derived xeno-free, GMP-grade feeders from umbilical cord tissue, and utilized them within a novel, xeno-free hESC culture system. We derived and characterized three hESC lines in adherence to regulations for embryo procurement, and good tissue, manufacturing and laboratory practices. To minimize freezing and thawing, we continuously expanded the lines from initial outgrowths and samples were cryopreserved as early stocks and banks. Batch release criteria included DNA-fingerprinting and HLA-typing for identity, characterization of pluripotency-associated marker expression, proliferation, karyotyping and differentiation in-vitro and in-vivo. These hESCs may be valuable for regenerative therapy. The ethical, scientific and regulatory methodology presented here may serve for development of additional clinical-grade hESCs.



NIH Human Embryonic Stem Cell Registry	
Cell Lines	HAD-C 100; HAD-C 102; HAD-C 106
NIH Registration Number	0123; 0124; 0125
NIH Approval Number	NIHhESC-11-0123; NIHhESC-11-0124; NIHhESC-11-0125
Available for Distribution	Yes
Provider Restrictions	Available for non-clinical research subject to an MTA that specifies the proposed research and includes a commitment to handle the stem cells ethically. Possible availability for clinical use subject to a review of the research proposal, ethical, and regulatory approvals.
NIH Restrictions	(No Additional Restrictions)
Submitting Organization	Hadassah Hebrew University Medical Center
Provider Name	Benjamin E. Reubinoff
Provider Phone	011-972-507-874569
Provider Email	benjaminr@ekmd.huji.ac.il
Provider URL	<a href="http://www.hadassah.org.il/English/Eng_SubNavBar/TheDoctors/ReubinoffBenjamin.htm">http://www.hadassah.org.il/English/Eng_SubNavBar/TheDoctors/ReubinoffBenjamin.htm</a>
Approval Date	06/16/2011

Research Using This Line is Eligible for NIH Funding

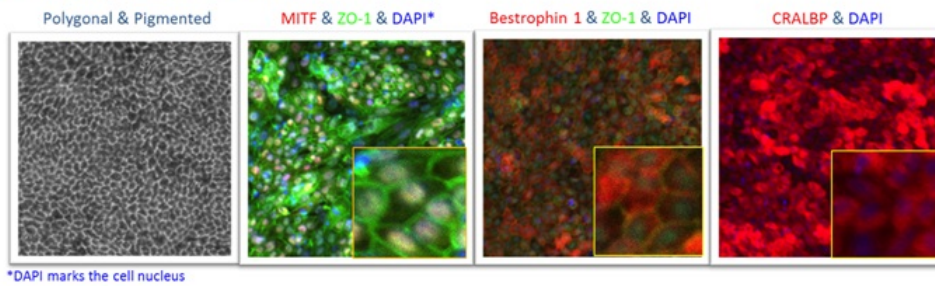
# Cell Cure's RPE Cell Product for Dry AMD: OpRegen®

- **OpRegen®**: Cell replacement therapy for the dry form of age-related macular degeneration (dry-AMD) utilizing a suspension of RPE cells produced from human embryonic stem cells (hESCs).
- **Cells**: Allogeneic human RPE cells produced under cGMP conditions from NIH approved HAD-C 102 hESC line, using cGMP, xeno-free cells and reagents
- **Indication**: Patients with geographic atrophy (GA), the severe dry-form AMD
- **Formulation**: Provided as cell suspension in BSS Plus; ready for injection
- **Delivery Route**: Subretinal injection
- **Mechanism of Action**: Integration into subretinal space and replacement of missing or diseased RPE cells
- **Planned Clinical Trial**: Phase I/IIa Study of OpRegen® in Progressive Dry-Form AMD with GA
- **Study Site**: Hadassah Univ Medical Center, Jerusalem
- **Stage of Development**: **FDA authorization received;** Israel Ministry of Health approval is in process



# CMC Characterization of OpRegen<sup>®</sup> (1)

- **Morphology:** Cells can form a monolayer of polygonal pigmented cells
- **Identity:** Cells express the RPE markers



- **Purity:** Total non-RPE cellular impurities <1.7% show using a new proprietary assay. No hESC impurity in neither the final product or even at early stage of production
- **Potency:**
  - Combined ability of cells to a) Generate a polarized monolayer with barrier function and b) Secrete PEDF and VEGF secretion in a polarized manner
  - Cells can phagocytose pHrodo E.Coli BioParticles and fluorescently labeled mouse Photoreceptor Outer Segments (POS); an assay with greater specificity is in development

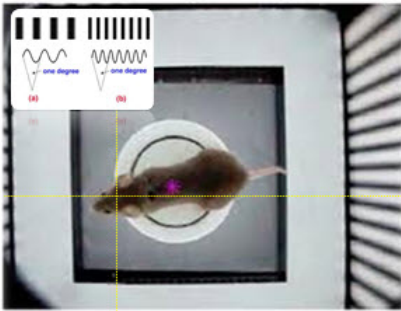
# OpRegen<sup>®</sup> Preclinical Studies Results

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- Three independent CRO studies conducted: **Safety/Biodistribution , Tumorigenicity and Spiking and Efficacy**
- No teratomas or human tumors found neither in 328 NOD/SCID mice nor in 180 RCS rats that received a maximal feasible dose of OpRegen<sup>®</sup>
- No teratomas found with OpRegen<sup>®</sup> spiked with up to 10% hESCs, which is 1000 -fold higher than the batch release criteria (< 0.01%)
- No product biodistribution from the contained subretinal treatment site
- No product-related mortality/morbidity and no product related ocular, clinical, body weight, macroscopic and microscopic adverse findings were found
- OpRegen<sup>®</sup> treated eyes rarely contained human proliferating cells (Ki67 immunostaining)
- OpRegen<sup>®</sup> cells survived over the lifetime of the NOD/SCID mouse (9 months)
- OpRegen<sup>®</sup> cells injected as a suspension organized into a monolayer within a few weeks
- OpRegen<sup>®</sup> cells rescued photoreceptors and mediated phagocytosis of RCS rat photoreceptor outer segments (POS)
- Optomotor functional studies in RCS rats demonstrated statistically significant, dose dependent functional rescue

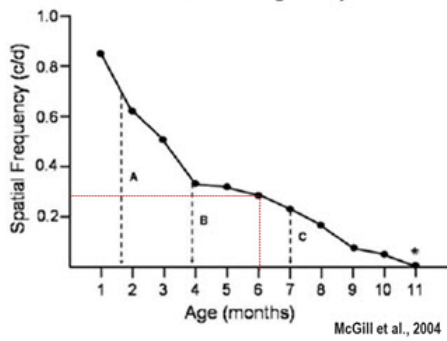
# Highlights of Preclinical Studies: Vision Rescue in RCS Rat

Optomotor response (motion)

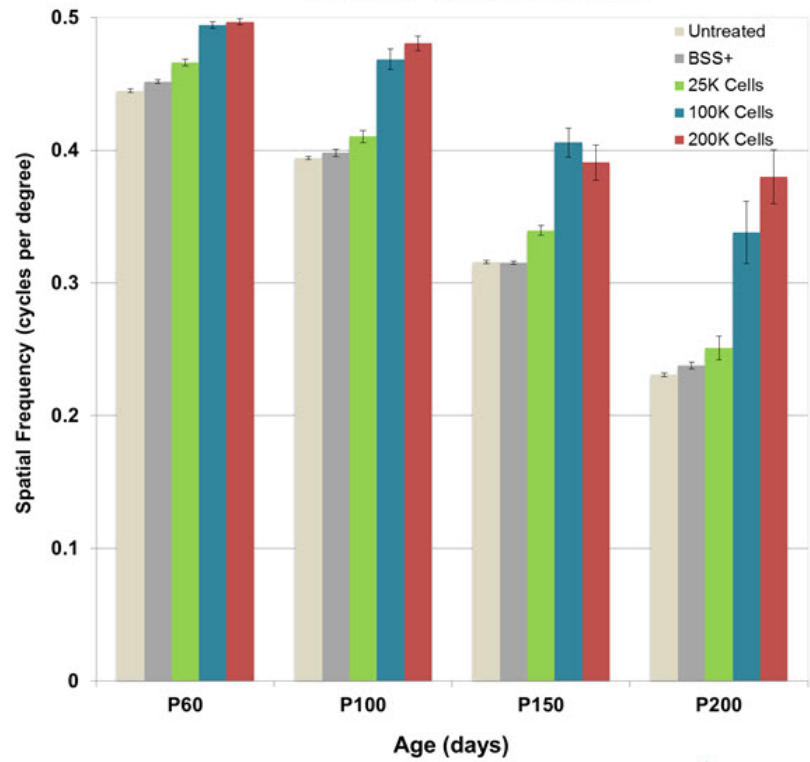


Historical Data:

RCS Rat Grating Acuity

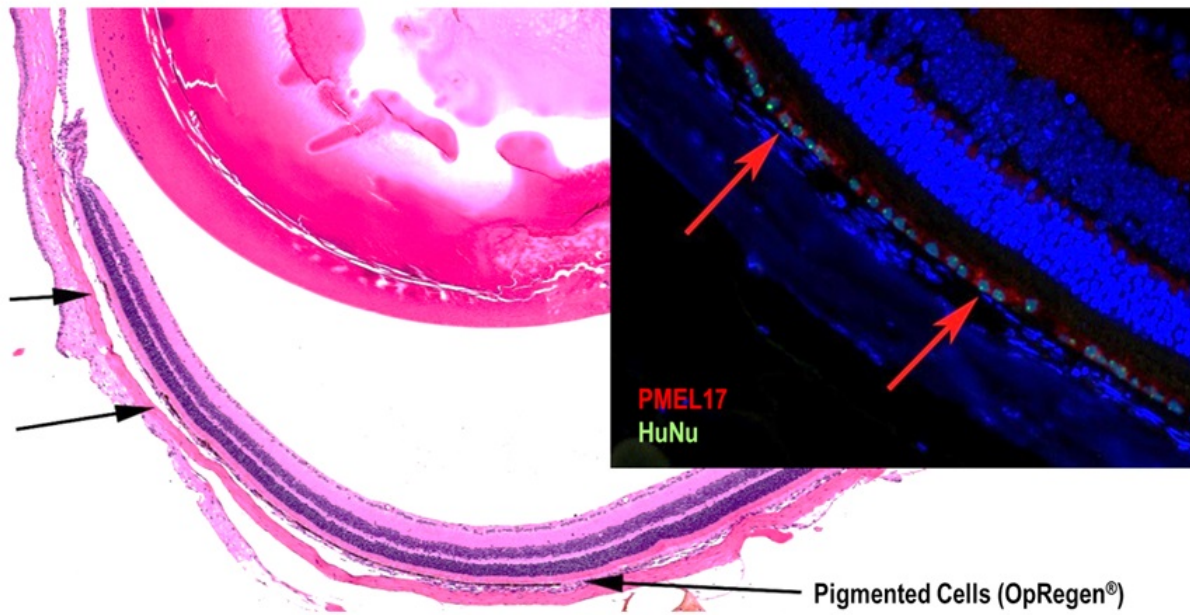


Optomotor Tracking Thresholds



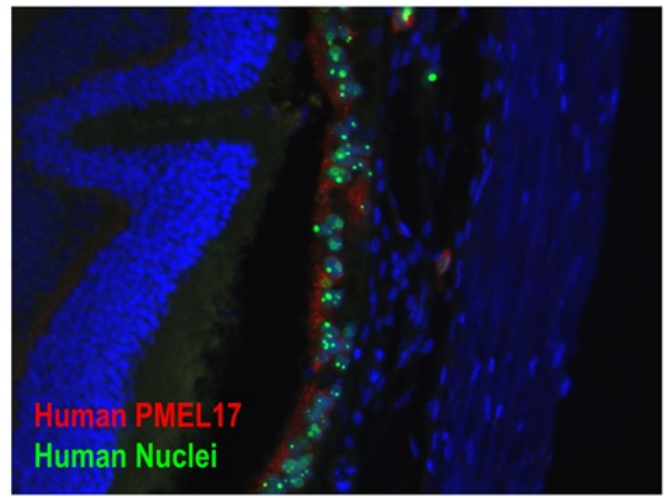
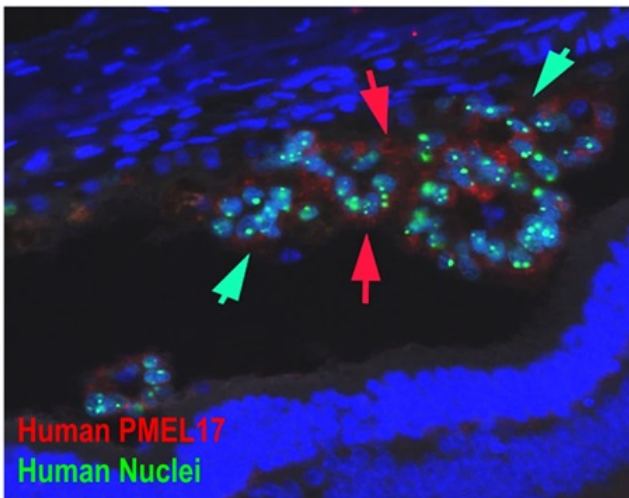
# Highlights of Preclinical Studies: Long Term Graft Survival

Long term (9 months –post transplant) engrafting of viable OpRegen® cells (pigmented cells stained positive for HuNu and PMEL17) in NOD/SCID subretinal space



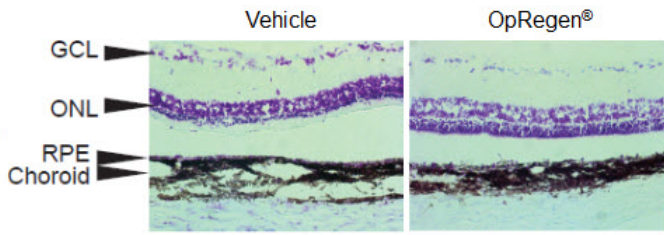
# Highlights of Preclinical Studies: Cells Form Monolayer

OpRegen® cells are clustered at the place that the bleb was formed and then organize themselves into the monolayer structure found in healthy animals

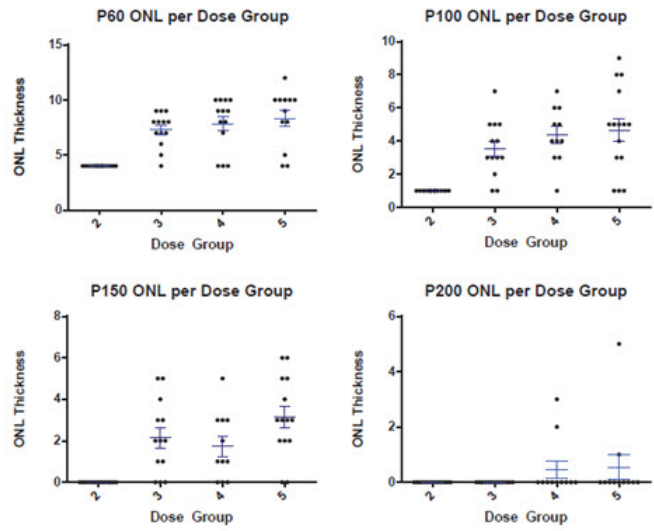
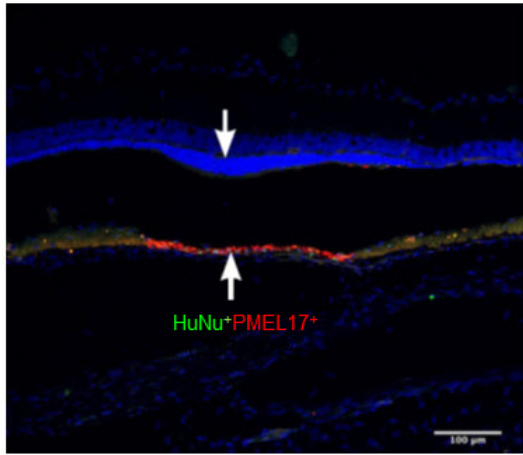




# OpRegen<sup>®</sup> -Mediated Rescue of Photoreceptors



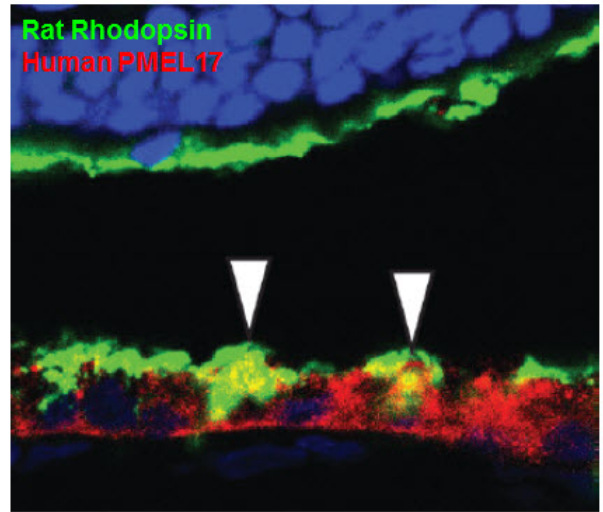
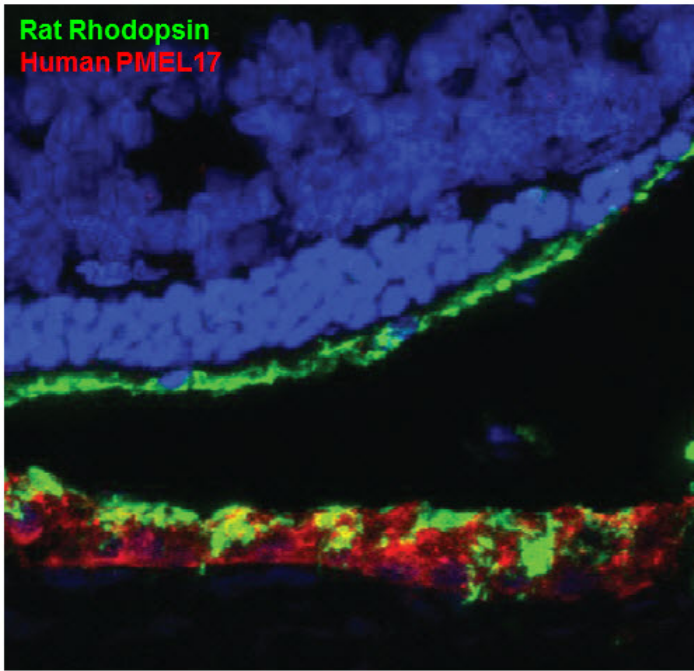
ONL Thickness (number of nuclei layers) in OpRegen<sup>®</sup> treated eyes is above vehicle control (group 2) at all time points



Group 2: Vehicle  
 Group 3: 25,000 OpRegen<sup>®</sup>  
 Group 4: 100,000 OpRegen<sup>®</sup>  
 Group 5: 200,000 OpRegen<sup>®</sup>

# OpRegen<sup>®</sup> Mediated Phagocytosis in Treated RCS Rats

Rat rhodopsin outer segments (green) rest along the grafted cells (human PMEL17, red) and rat rhodopsin within transplanted OpRegen<sup>®</sup> cells (yellow)



# Cell Cure Phase I/IIa Clinical Study (1)

---

- Phase I/IIa Dose Escalation Safety and Efficacy Study of OpRegen® Transplanted Subretinally in Patients with Advanced Dry-Form AMD (Geographic Atrophy)
- Open label, non-randomized, sequential, single center trial
- **Study Site:** Hadassah University Medical Center, Jerusalem, Israel
- **Dose and Administration:** Single injection of 50,000-500,000 viable cells in 100-150 µl BSS+ delivered via a cannula through a small retinotomy into the subretinal space in the macular area along the border between areas of GA and the better preserved extra-foveal retina and RPE layer.
- **Part 1**
  - Cohort 1:** 3 Patients, BCVA 20/200 or less (legally blind), 50,000 OpRegen® cells
  - Cohort 2:** 3 Patients, BCVA 20/200 or less, 200,000 OpRegen® cells
  - Cohort 3:** 3 Patients, BCVA 20/200 or less, 500,000 OpRegen® cells
- **Part 2**
  - Cohort 4:** 6 Patients, BCVA 20/100, 500,000 OpRegen® cells

## Phase I/IIa Clinical Study (2)

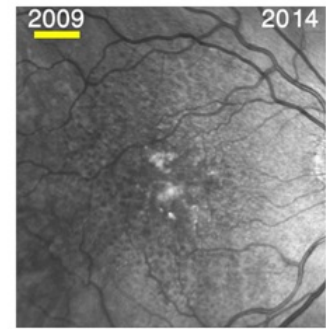
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- **Primary Objective:** Safety and tolerability of transplanted OpRegen®
- **Secondary Objective:** Initial exploration of the ability of transplanted OpRegen® to engraft, survive, and *moderate disease progression*
- **Duration and Follow Up:** Enrollment period plus 12 months post transplant follow-up; weekly during 1<sup>st</sup> month post-transplant, and then at 2, 3, 4, 6, 9, and 12 months post-transplant. Continued follow up at 15 months, 2, 3, 4, and 5 yrs post surgery.
- **Immunotherapy:**
  - Topical steroidal and antibiotic treatment
  - Systemic Tacrolimus to 6 weeks post surgery
  - Systemic Mycophenolate mofetil to 1 year post surgery.

# Phase I/IIa Clinical Study Efficacy Outcome Measures

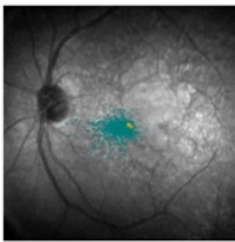
- Selection of outcome measures based on an ongoing “Cohort Study” that tracks disease progression in patients, who might be candidates for the Phase I/II Study

- **Visual Acuity**
  - **Rate of GA Progression over 6 and 12 months**
  - **Retinal sensitivity to light in the engrafted regions**
  - **Extent and depth of central stomata**
- 
- **A Cohort Study will provide quantitative assessments of disease progression patients prior to enrollment**

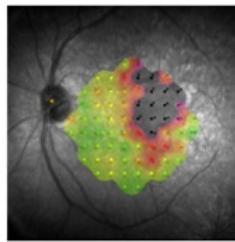


Infrared Imaging

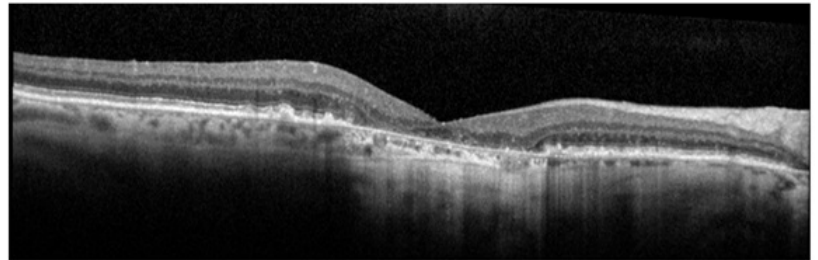
Fixation Map



Sensitivity Map



Microperimetry



OCT

# Company Overview

---

## ➤ Platform Technology

- Manufacturing of diverse cell products from xeno-free, GMP-grade human embryonic stem cells
- Lead product - **OpRegen®**, human Retinal Pigment Epithelium Cells

## ➤ History

- Founded in 2005 in Jerusalem, Israel
- Major investments by BioTime starting in 2010
- Present Shareholdings:
  - BioTime Inc (incl. ESI & Asterias) 62.5%
  - Hadasit BioHoldings Ltd 21.2%
  - Teva Pharmaceutical Industries Ltd 16.1%

## ➤ Management

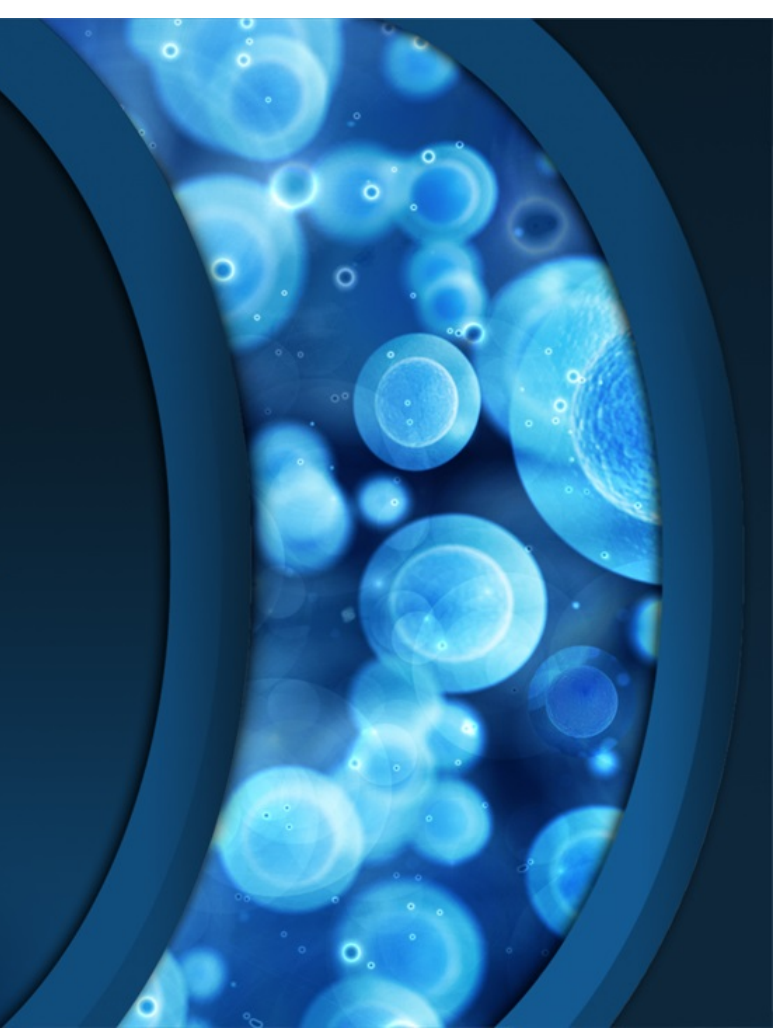
- Charles S. Irving – CEO
- Benjamin Reubinoff – CSO
- Moshe Hukaylo – CFO



**Joseph Wagner, Ph.D.**

Chief Executive Officer  
OncoCyte Corporation

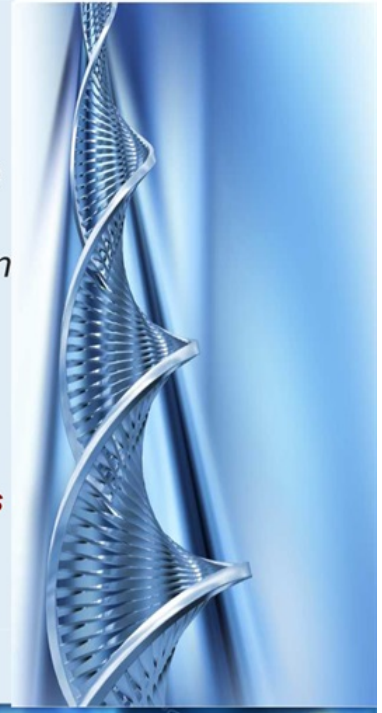
**Shareholder Update**  
**November 4, 2014**



Our mission is to develop novel products for the diagnosis and treatment of cancer in order to improve both the quality and length of life of cancer patients

- Internally developed cancer gene discovery platform
- Platform based on extensive microarray dataset
- Marker discovery principle based on similarity of gene expression in embryonic development and cancer
- Scores of potential targets identified and IP filed – *Pan-Dx™*
- Multiple product opportunities

***Goal: Develop and market low-cost molecular diagnostic tests for major cancers with rapid adoption by initial users followed by widespread use in large patient populations***



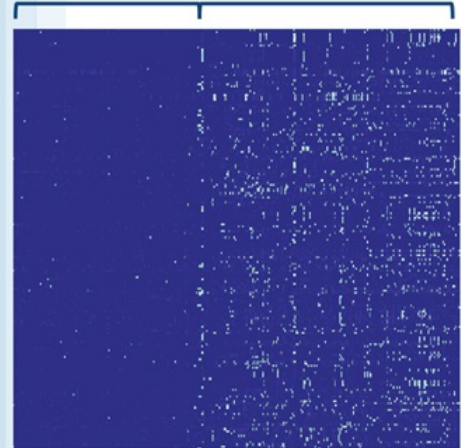


Many of the same genes that drive embryonic development drive tumor formation and growth

- A substantial proportion of the mammalian genome is exclusively activated during embryonic development
- These embryo-exclusive genes regulate:
  - Cell proliferation
  - Cell signaling
  - Organ formation
  - Angiogenesis
- Many of these genes are accessed/activated by cells after oncogenic mutation & transformation
- Many of these genes have not been previously associated with cancer

Adult  
Tissues

Developin  
g Tissue &  
Tumors



Translating proprietary cancer marker platform into near-term revenue opportunities in oncology markets

## **Cancer Marker Discovery (2011-):**

- Assembled >700 sample microarray dataset
- Bioinformatics generated >3000 candidate markers

## **Protection of Intellectual Property (2011-):**

- Aggressive filings protecting all markers and all uses

## **Cancer Marker Validation (2012-):**

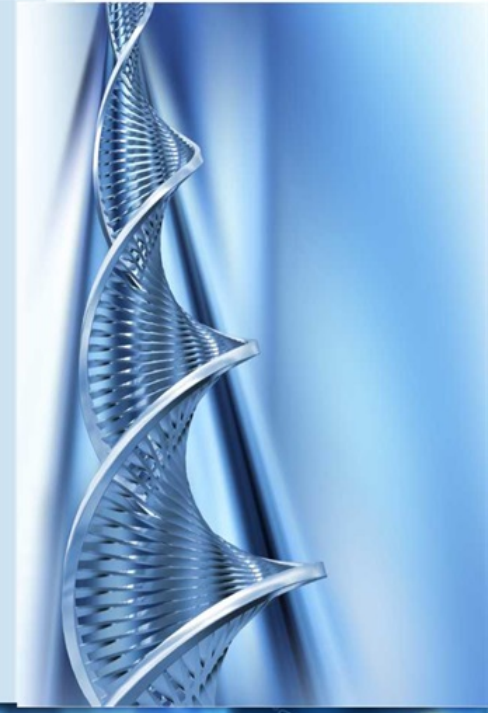
- Verify gene expression using alternate methodologies
- Verify protein expression in tumor tissue

## **Proof of Concept in Patient Samples (2013-):**

- Verify gene/protein expression in retrospective clinical sample banks
- Build candidate multiplex panels for large scale testing

## **Large Prospective Clinical Studies (2014-):**

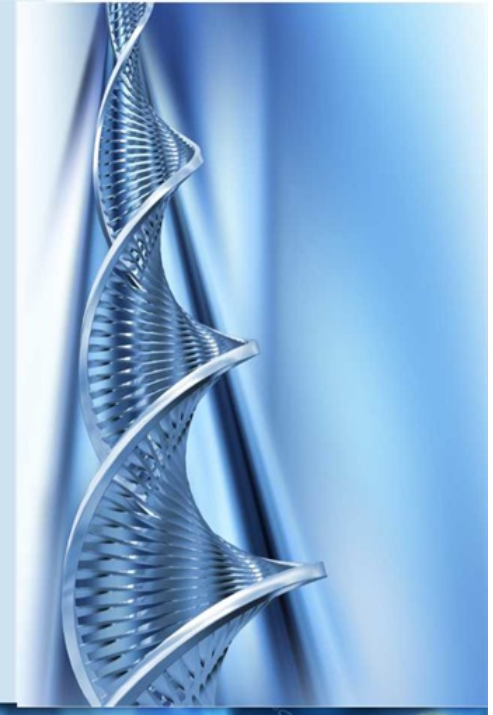
- Initiate larger studies in target patient populations
- Test performance of multiplex panels using platform-neutral proprietary test kits



# OncoCyte's Business Formula

Designed to translate proprietary cancer marker platform into near-term revenue opportunities

- **“Listen to Your Technology”**
- **“Listen to Your Customers”**
- **Create Scalable Business Model**
- **Early Revenues Fund Larger Trials**



# “Listen to Your Technology”

Technology platform defines product opportunities in subsectors of cancer diagnostics

## Potential products based on dataset structure:

- Screening diagnostics
- Recurrence diagnostics

## Potential products based on markers:

- Breast cancer
- Colorectal/GI cancers
- Bladder/urothelial cancers
- Thyroid cancer
- Lung cancer

## Potential products with low cost and ease of use:

- Blood-based tests
- Urine-based tests



Physician adoption is the key barrier to entry for cancer screening diagnostics

## User Will Adopt Tests That:

- Key Opinion Leaders support
- Resolve diagnostic dilemmas
- Justify the need for procedures
- Eliminate unnecessary procedures
- Have reasonable cost/reimbursement

## User Will Not Adopt Tests That:

- Create diagnostic ambiguity
- Replace procedures
- Create unnecessary costs

***Technology alone does not drive user adoption***



How does OncoCyte identify and prioritize its products?



**Strategically develop diagnostic products that will be rapidly adopted and have short- and long-term revenue potential**

**Focus on developing products that:**

- Fit with proprietary technology
- Are simple to perform and interpret
- Are relatively low cost and easy to use
- Appeal to an immediate user base
- Have long-term large market potential
- Are based on protectable/enforceable IP



Create a scalable business model beginning with an immediate market with early adopters, successively expanding into larger opportunities



### Initial Use & Market:

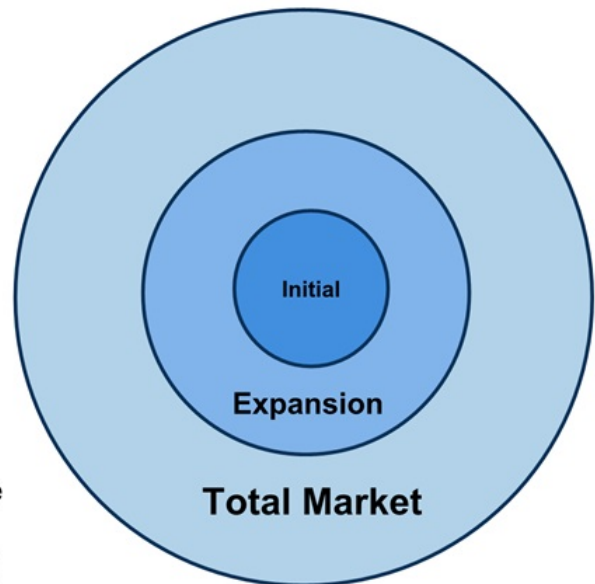
- Early adopters with immediate needs
- Can be addressed rapidly with relatively low cost
- Comparable approach: Veracyte (VCYT)

### Expanded Use & Market:

- Larger markets and user bases
- Requires additional clinical validation

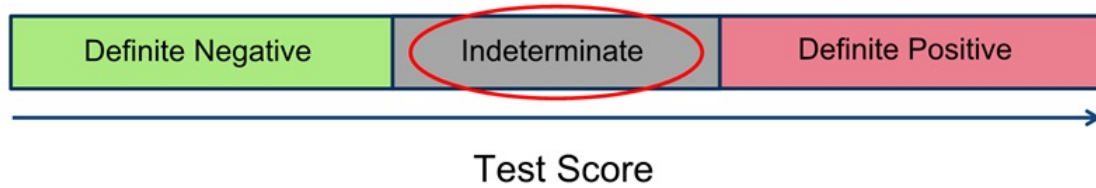
### Final Target Use & Market:

- Addresses very large markets and tens of thousands of users
- Requires partnerships to meet ultimate revenue goals
- Comparable approach: Exact Sciences (EXAS)



# Key Driver: Limitations of Current Tests

Initial users/use will be to clarify diagnostic dilemmas due to uncertainties in imaging and other traditional tests



## Current Tests With Significant Limitations Include:

- Mammography for breast cancer
- Urine cytology for bladder cancer recurrence surveillance
- Low-dose CT for lung cancer screening



Simple, low cost cancer screens that address current unmet user needs in large patient markets

## **Breast Cancer Diagnostic (BR-001):**

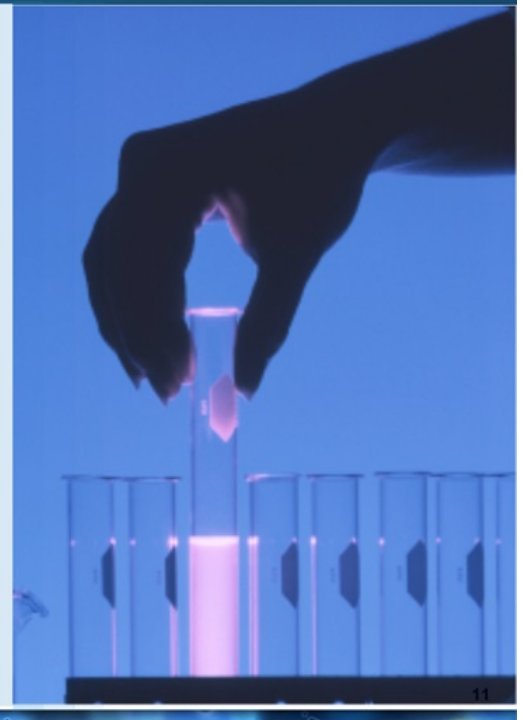
- Blood-based screening diagnostic
- Panel of protein markers

## **Bladder Cancer Diagnostic (BL-002):**

- Urine-based screening diagnostic for recurrence
- Panel of RNA markers

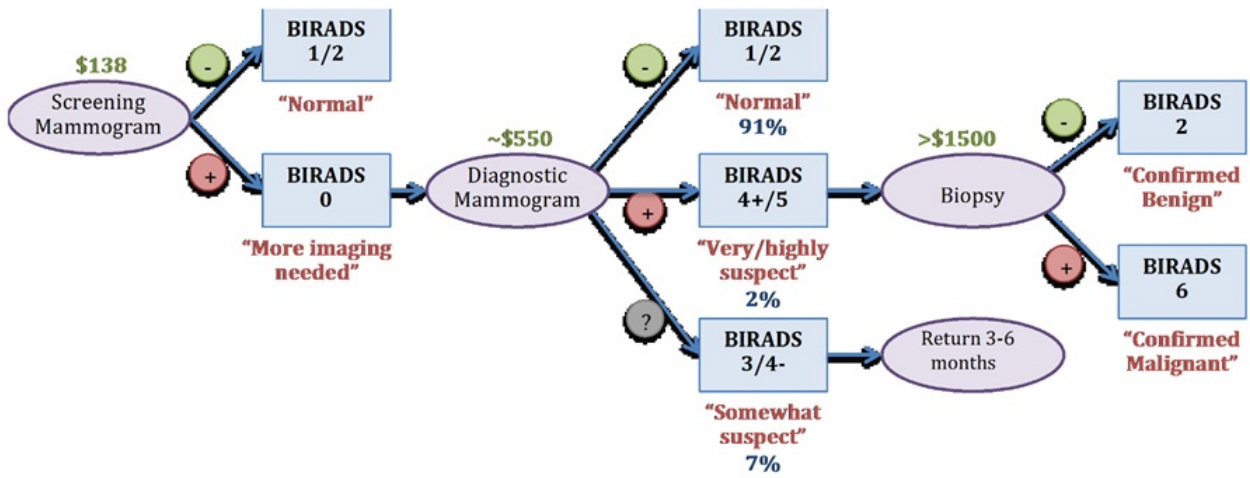
## **Lung Cancer Diagnostic (LN-003):**

- Blood-based screening diagnostic for high-risk patients
- Panel of RNA markers



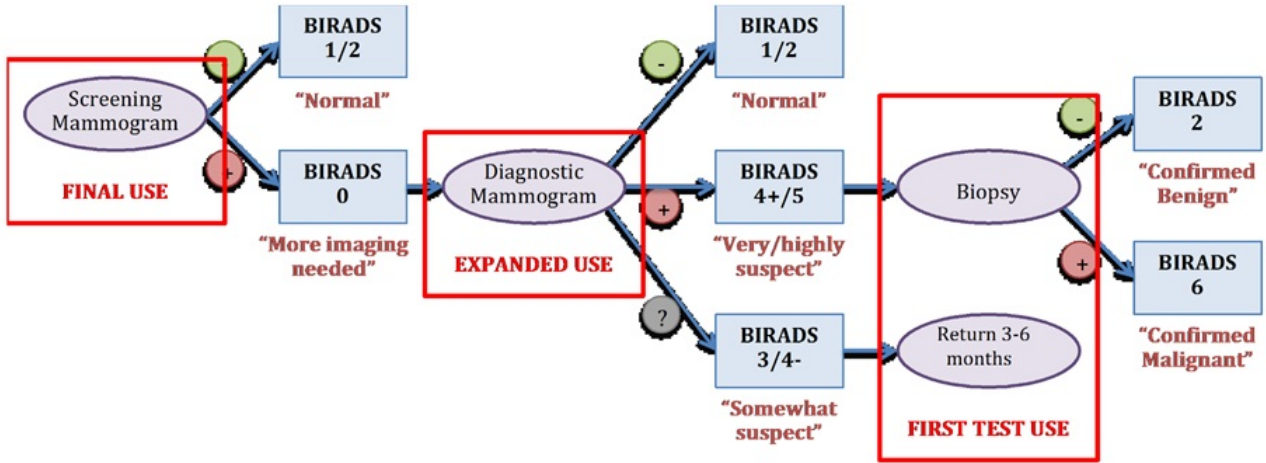
# ONC-BR-001: Breast Cancer Product

Initial test use late in diagnostic tree with progressive data driving test use earlier and earlier



# ONC-BR-001: Breast Cancer Product

Initial test use late in diagnostic tree with progressive data driving test use earlier and earlier



Blood-based screening diagnostic measures sera protein biomarkers using ELISA

### Initial Use & Market:

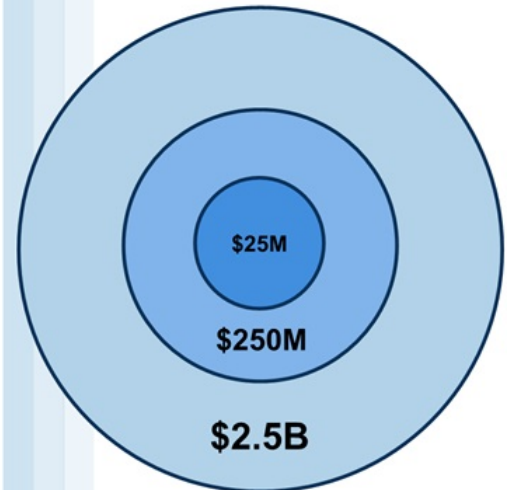
- Radiologist: Management of BIRADS 3-4 patients
- 350K tests/year in US

### Expanded Use & Market:

- Radiologist: In conjunction with all diagnostic mammography
- Oncologist: Recurrence surveillance
- 3M tests/year in US

### Final Target Use & Market:

- PCP/Radiologists: In conjunction with or surrogate for screening mammography
- >30M tests/year in US



Prospective, multisite study in diagnostic mammography patients

**Subjects:**

- N = 600
- At time of diagnostic mammography

**Endpoints:**

- Primary: Correlation with BIRADS score
- Secondary: Correlation of biomarker with pathology

**Sites:**

- Up to 6 total
- Currently enrolling: Ron Korn, SMIL, Scottsdale, AZ
- Abcodia providing additional samples

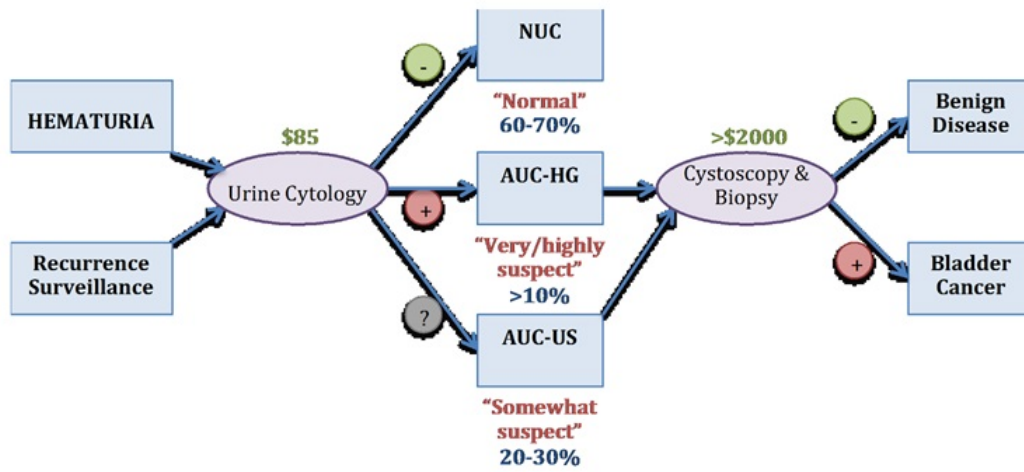
**Timing:**

- First subject enrolled early Jan 2014
- Complete study by end of 2014
- Data presentation at ACR & ASCO in May, 2015



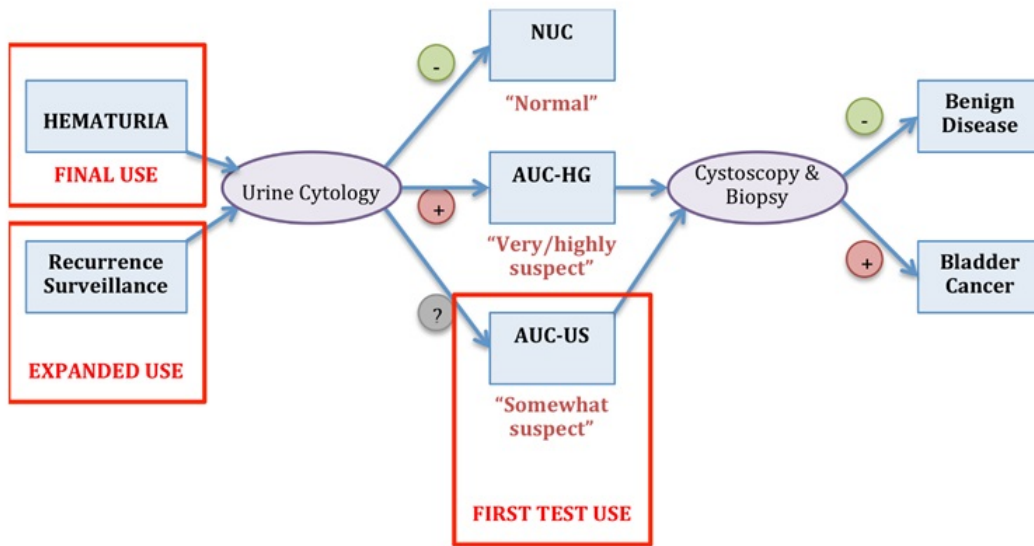
# ONC-BL-002: Bladder Cancer Product

Initial test use late in diagnostic tree with progressive data driving test use earlier and earlier



# ONC-BL-002: Bladder Cancer Product

Initial test use late in diagnostic tree with progressive data driving test use earlier and earlier



### Initial Use & Market:

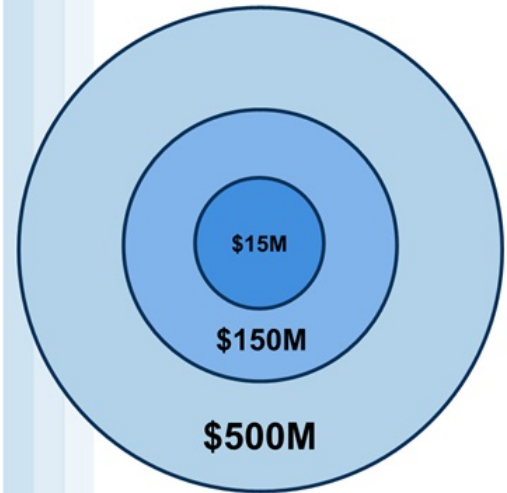
- Pathologist: Resolution of indeterminate cytology during recurrence surveillance
- 500K tests/year in US

### Expanded Use & Market:

- Urologist: All recurrence surveillance
- 1.5M test/year in US

### Final Target Use & Market:

- Urologist: Management of hematuria
- >5M tests/year in US





## Multisite clinical studies in setting of surveillance cytology testing or cystoscopy

### Subjects:

- N = 100/1200
- At time of surveillance cytology/cystoscopy

### Endpoints:

- Correlation of markers to cytology/cystoscopy results

### Sites:

- Cytopathology: Johns Hopkins
- Cystoscopy: Four large urology clinics in Texas, Ohio, Indiana and South Carolina

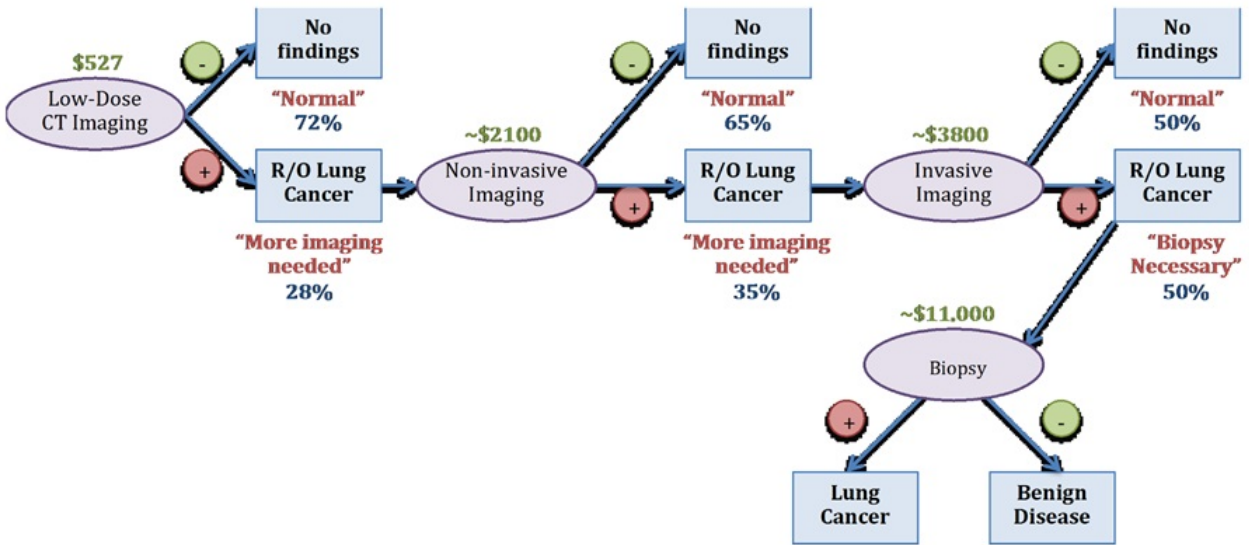
### Timing:

- Cytopathology: Complete late 2014
- Cystoscopy: July 2015
- Data presentation at AUA & ASCO in May, 2015



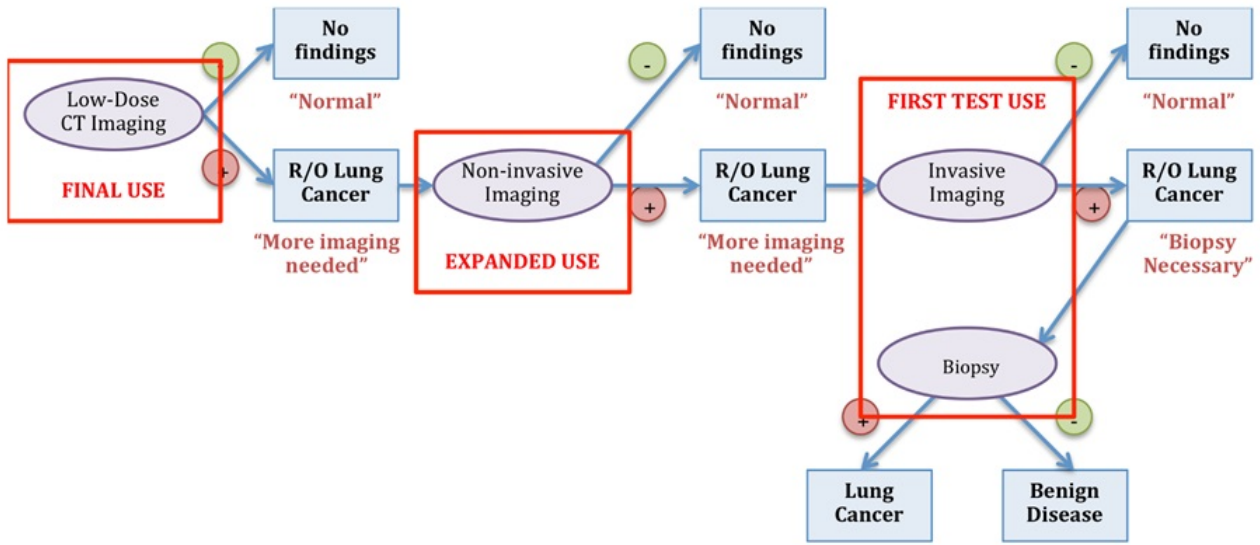
# ONC-LN-003: Lung Cancer Product

Initial test use late in diagnostic tree with progressive data driving test use earlier and earlier



# ONC-LN-003: Lung Cancer Product

Initial test use late in diagnostic tree with progressive data driving test use earlier and earlier



Blood-based lung cancer screen for high-risk population



### Initial Use & Market:

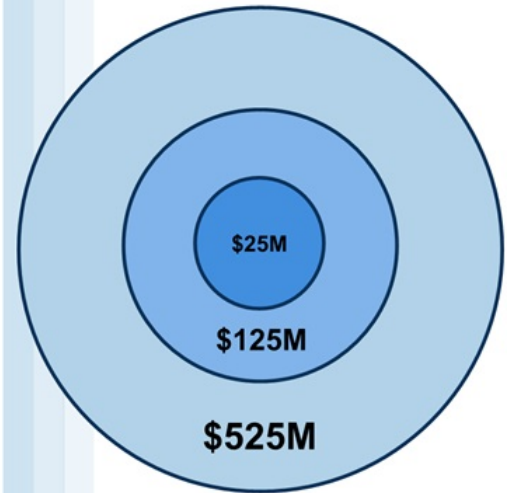
- Radiologists/thoracic surgeons: Management of need-to-biopsy decision
- 350K tests/year in US

### Expanded Use & Market:

- Radiologists/thoracic surgeons: Management of all LDCT+ patients
- 1.75M tests/year in US

### Final Target Use & Market:

- Radiologists/thoracic surgeons: Used in conjunction with/surrogate for LDCT in all high-risk patients
- >7M tests/year in US



Ongoing study in target population initiated by collaborators at the Wistar Institute

**Subjects:**

- N = 600
- All high-risk, includes cancer-free, benign nodules, confirmed cancer patients

**Endpoints:**

- Primary: Correlation with diagnosis
- Secondary: Correlation with tumor origin, stage, grade

**Sites:**

- 6 total including NYU, Temple, Penn, Christiana

**Timing:**

- Study completed enrollment May 2014
- Sample analysis completed October 2014
- Initial data publication late 2014
- Study data presentations at ATS & ASCO 2015



Superior product at lower cost to drive rapid adoption in initial markets, followed by widespread adoption

- **KOL endorsements**

- Drive adoption within KOLs' own practices as well as among other physicians
- Can lead to medical society recommendations

- **Strong Clinical Trial Data**

- Supports positive health economics and patient outcomes

- **Cost effectiveness of tests**

- Drives user willingness to acquire additional data
- As test volume increases, adoption point becomes earlier as test accuracy gains credibility



# Upcoming Development Milestones

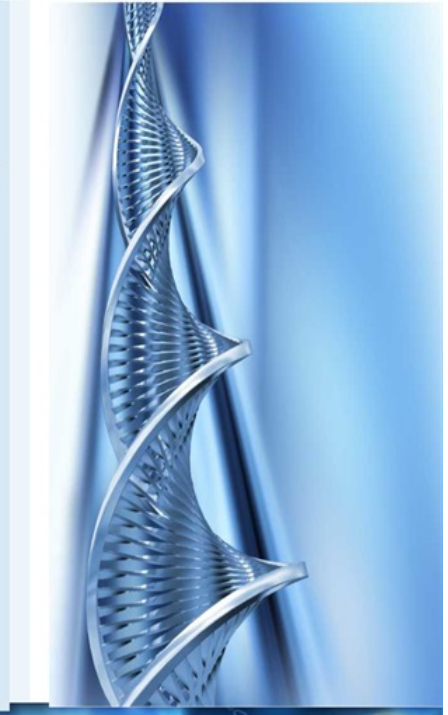
Positive clinical trial results will drive commercialization efforts with first test launch in late 2015

- **Q4 2014:**
  - Completion of breast, bladder and lung clinical trial enrollment and data analysis
  - Publication of lung trial results; submission of clinical study data for presentation at major oncology meetings
  - Expansion of executive management team
- **Q1 2015:**
  - Initiation of CLIA lab testing certification
- **Q2 2015:**
  - Presentation of breast, bladder and lung clinical trial at major oncology meetings
  - Publication of breast and bladder clinical trial data in peer-reviewed journals
- **Q3 2015:**
  - Assay validation completed for lead test
  - California CLIA certification obtained
- **Q4 2015:**
  - Commercial launch of first diagnostic test to be announced at major oncology meeting

# OncoCyte: Investment Highlights

Beginning with an immediate market with early adopters,  
expanding into large opportunities

- **Broad platform of cancer markers**
- **Cost-effective tests using standard methods**
- **Potential for rapid initial adoption and broad eventual adoption**
- **Scalable business model:**
  - **Significant revenue in initial markets**
  - **Early revenues fund studies necessary for broader use**
  - **Very large long-term potential revenue opportunity**







# *HyStem*<sup>®</sup> Product Development

November 4, 2014

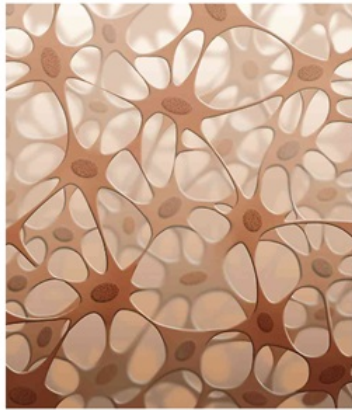
Thomas I. Zarembinski, PhD MBA  
Senior Director,  
New Product Development



The matters discussed in this presentation include forward looking statements which are subject to various risks, uncertainties, and other factors that could cause actual results to differ materially from the results anticipated. Such risks and uncertainties include but are not limited to the success of BioTime in developing new stem cell products and technologies; results of clinical trials of BioTime products; the ability of BioTime and its licensees to obtain additional FDA and foreign regulatory approval to market BioTime products; competition from products manufactured and sold or being developed by other companies; the price of and demand for BioTime products; and the ability of BioTime to raise the capital needed to finance its current and planned operations. Any statements that are not historical fact (including, but not limited to statements that contain words such as "will," "believes," "plans," "anticipates," "expects," "estimates") should also be considered to be forward-looking statements. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. As actual results may differ materially from the results anticipated in these forward-looking statements they should be evaluated together with the many uncertainties that affect the business of BioTime and its subsidiaries, particularly those mentioned in the cautionary statements found in BioTime's Securities and Exchange Commission filings. BioTime disclaims any intent or obligation to update these forward-looking statements.

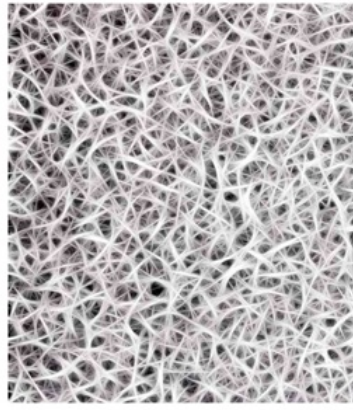
- **Background on the need for *HyStem***
- **Competitive Landscape**
- **Strategy**
- **Markets**
- **Product Pipeline & Development Status**

- Cells need a matrix for attachment or they often die
- An injectable matrix capable of polymerizing *in vivo* into 3-D tissue could revolutionize medicine



Cells

+



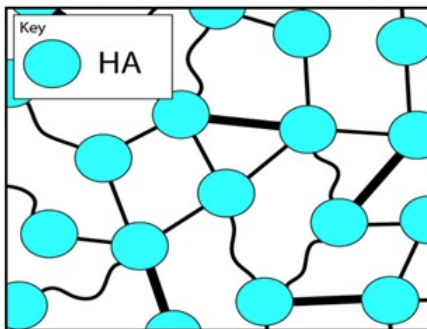
Matrix

=

Unprecedented  
Opportunities in  
Regenerative  
Medicine

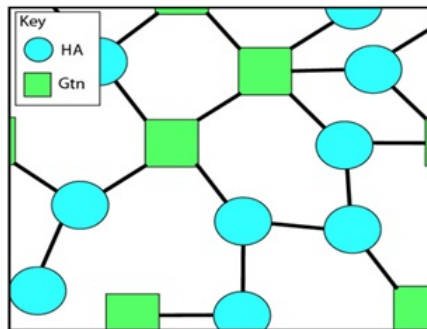
## The Elegance of Defined Minimal ECM

One Component



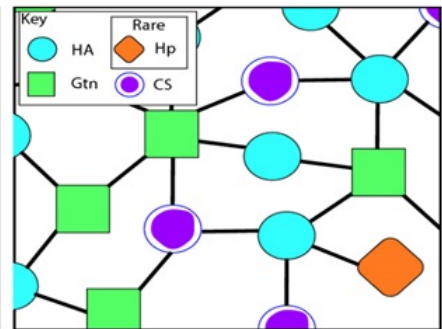
- *ReGlyde* - Adhesion prevention
- Potential applications in arthritis

Two Components



- *Renevia* – Cell transplants
- *Premvia* – Wound management

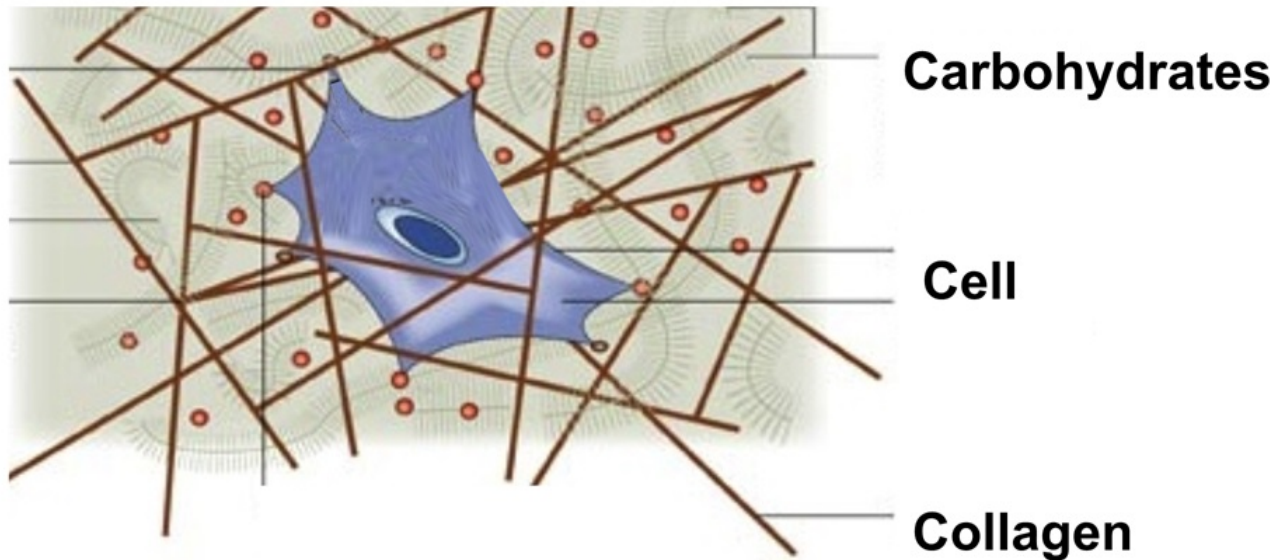
Multi-Component



- Controlled growth factor release
  - Stroke
  - Cancer

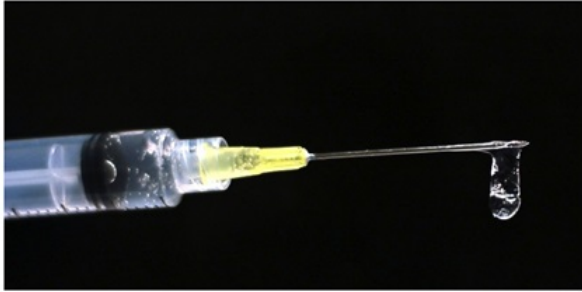
Prestwich, *J. Cell. Biochem.* **101**, 1370 (2007)  
Courtesy of Dr. Glenn D. Prestwich

- ✓ Biocompatible & Biodegradable



(Griffith and Schwartz, 2006) 5

**Safely polymerizes to make 3-D tissue with cells in the body**



→  
20  
min



**Addition of Bioactives  
(Growth factors, Cells)**

- ✓ **Strong IP – composition of matter & uses**  
2 U.S. patents issued with applications pending in the EU, Canada, Japan, and Australia
  - ✓ **Ease of manufacture**  
Modest capital investment - large gross margins (65% - 90%)
  - ✓ **Multiple products in rapidly emerging fields**  
Stem cell applications, tissue engineering, regenerative medicine, and cell-based therapies
  - ✓ **Simple – yet elegant technology**  
Nearly 200 scientific publications demonstrating applications
- 
-





Animal-derived  
Hydrogels for  
Research

Solid matrices



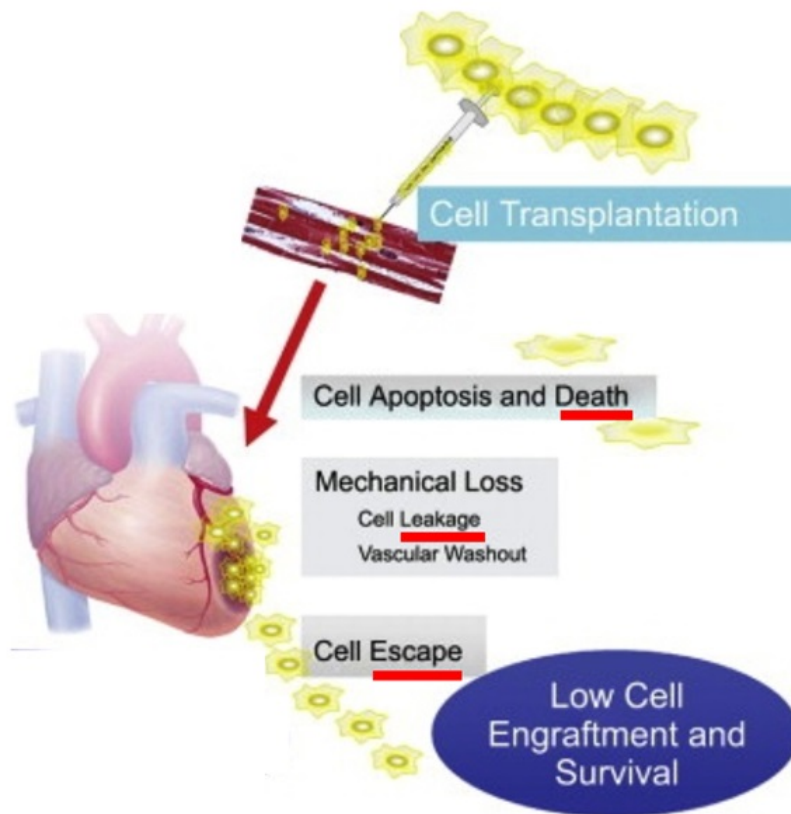


**Dermal Fillers**

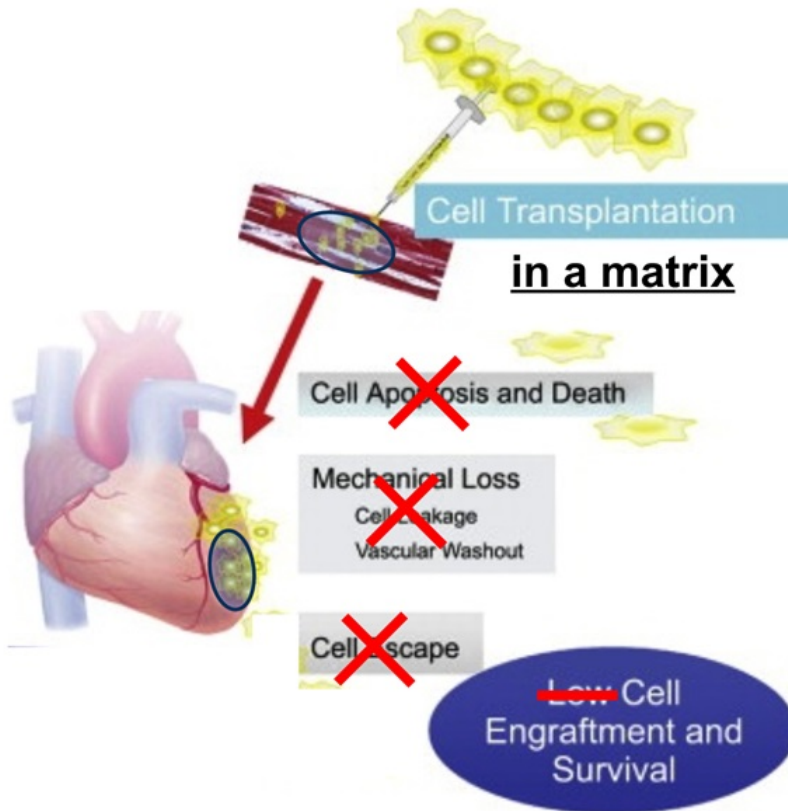
## Viscosupplementation



- ✓ pre-gelled dermal fillers can't be mixed with cells and often don't have the requisite attachment sites for cells.



Wu et al Ann Thorac Surg 2011



Wu et al Ann Thorac Surg 2011

✓ **In the US - a medical device:**

*HyStem<sup>®</sup> alone – CDRH as a Class II (510K) or Class III (PMA).*

*HyStem<sup>®</sup> + drug – CDER as a combination new therapy.*

*HyStem<sup>®</sup> + cells – CBER as a combination new therapy.*

✓ **In the EU - a medical device:**

*HyStem<sup>®</sup> alone – Notified Body as a Class III.*

*HyStem<sup>®</sup> + patient's own "mm" cells – Notified Body as Class III*

*HyStem<sup>®</sup> + cultured donor cells – European Medicines Agency*

- ✓ Required for Regulatory Approval

**bsi.**



## Certificate of Registration

QUALITY MANAGEMENT SYSTEM - ISO 13485:2003

This is to certify that:

BioTime, Inc.  
1301 Harbor Bay Parkway, Ste. 100  
Alameda  
California  
94502  
USA

Holds Certificate No:

**FM 578945**

and operates a Quality Management System which complies with the requirements of ISO 13485:2003 for the following scope:

The design, development, manufacture, and distribution of hydrogels for cell delivery applications.

## Therapeutics in Development

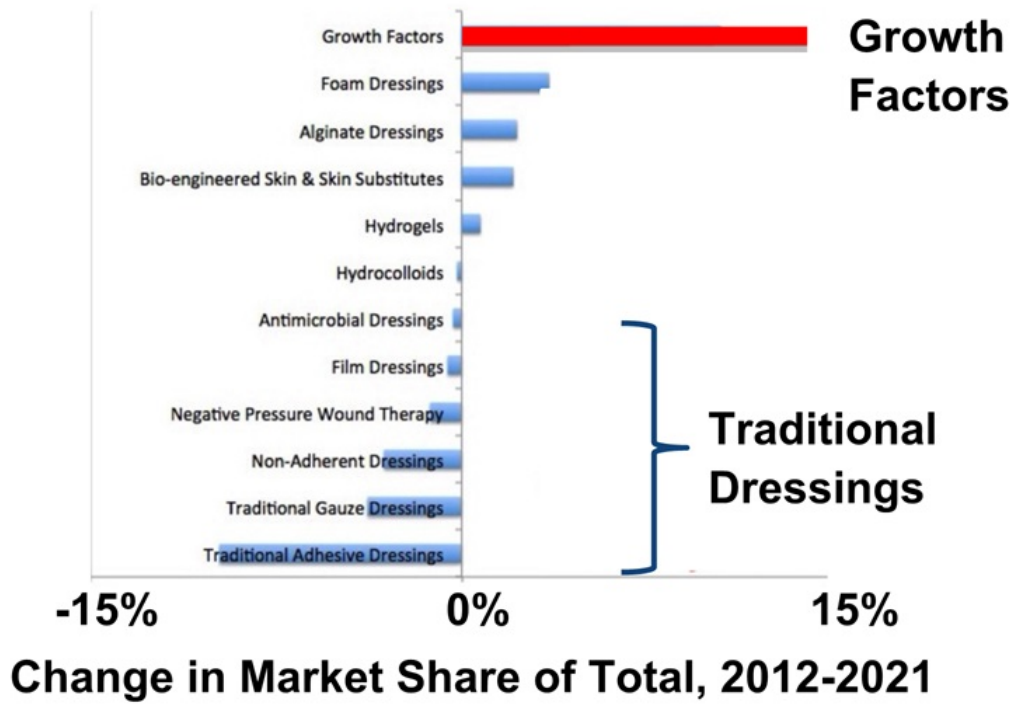
Platform	Early Pre-Clinical	Formulation Development / IND-Enabling Studies	Clinical development				Regulatory Pathway
			Safety	Efficacy	Pivotal	Marketed	
<b>HyStem<sup>®</sup></b>	University Collaborations						
<b>In-House R&amp;D</b>	New formulations and formats – films, sponges						Medical device in US & EU
<b>ReGlyde<sup>™</sup></b>	Management of tendon healing post surgery.		N/A	N/A	N/A		Medical device in US Class II 510(k)
<b>Premvia<sup>™</sup></b>	Wound management – partial & full thickness, ulcers, and burns.					510(k) Cleared	Medical device in US Class II 510(k)
<b>Renevia<sup>™</sup></b>	Cell delivery matrix for treating subcutaneous lipoatrophies.						CE Mark as Class III medical device in EU

**Premvia™** - an FDA-cleared device to treat dermal wounds and burns.

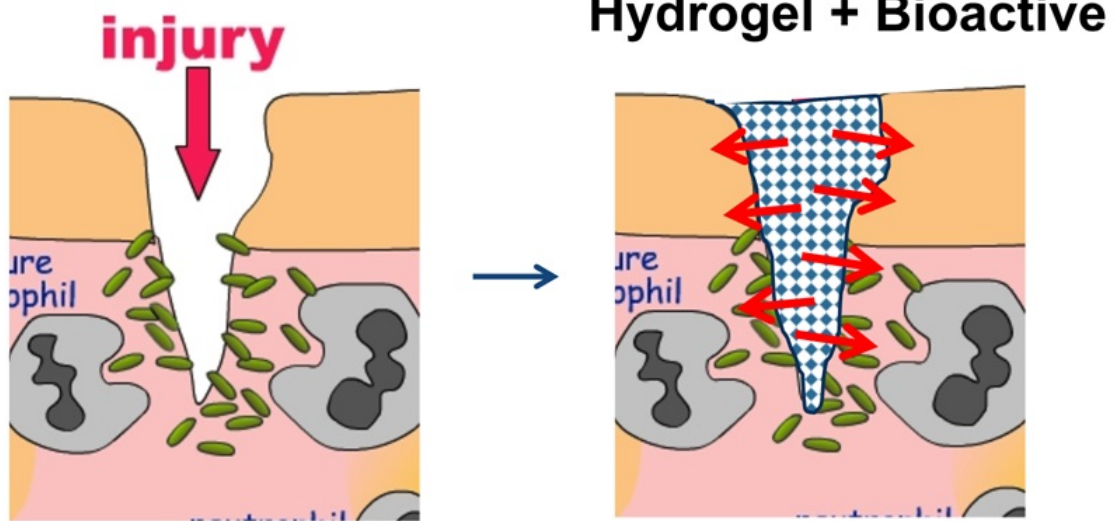





## Change in Segment Share of Global Wound Mgt Market, 2012-2021



MedMarket Diligence, LLC



	<b>DEPARTMENT OF HEALTH &amp; HUMAN SERVICES</b>	Public Health Service
		Food and Drug Administration 10903 New Hampshire Avenue Document Control Center - W066-G-609 Silver Spring, MD 20993-0002
		August 7, 2014
<p>BioTime Incorporated Mr. David C. Furr Principal Consultant 8708 Capehart Cove Austin, Texas 78733</p>		
<p>Re: K134037 Trade/Device Name: BioTime Premvia Regulatory Class: Unclassified Product Code: KGN Dated: July 7, 2014 Received: July 8, 2014</p>		
<p>Dear Mr. Furr:</p>		
<p>We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA).</p>		
<p><b>You may, therefore, market the device, subject to the general controls provisions of the Act. general controls provisions of the Act include requirements for annual registration, listing of manufacturers. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.</b></p>		

- *Renevia*<sup>TM</sup> is expected to have numerous applications in multiple tissue types.
- BioTime initially is seeking a CE mark for use in HIV-associated lipoatrophy in combination with autologous fat cells.
- An estimated 33M people worldwide have HIV. Number on HIV treatment has tripled in five years – now ~10M, target of 15M by the end of 2015<sup>1</sup>.
- An estimated 35-50% of patients on ARV therapy have lipoatrophy<sup>2</sup>.
- A greater number of people in the US have age-related lipoatrophy.



Age-Related Lipoatrophy

<sup>1</sup> GLOBAL UPDATE ON HIV TREATMENT 2013 RESULTS, IMPACT AND OPPORTUNITIES, WHO report in partnership with UNICEF and UNAIDS JUNE 2013  
<sup>2</sup> Source: AIDS Care Vol. 21, No. 5, May 2009, 664-671, VHA DIRECTIVE 2008003, Veterans Health Administration, January 22, 2008

*Indication: Renovia<sup>TM</sup> is a resorbable matrix to be used for the delivery of autologous adipose derived cells for the treatment of HIV-related facial lipoatrophy. Renovia<sup>TM</sup> serves as a temporary 3-dimensional matrix in which the implanted cells can attach, proliferate and differentiate into adipocytes.*

- **Multicenter, randomized, controlled, single blind, trial**
- **Treated vs. delayed treatment control, 25 - 92 subjects in each group with treatment effect measured a 1, 3, and 6 months**
- **Primary endpoint:**
  - Increase in skin thickness as measured by ultrasound at 6 months**
- **Secondary endpoint:**
  - Mid-face volume deficit score, Global Aesthetic Improvement Score**
- **Two sites in Palma de Mallorca, Spain**
- **Patients enrollment has begun**

.....The Stem Center, Palma de Mallorca, Spain  
Ramon Llull, MD, PhD - Medical Director



- **Obtained ISO-13485 Certificate of Quality Systems**
- **Premvia™ (Wound Management): Received 510(k) clearance**
- **Renevia™ (Repair of Contour Defects): Pivotal Trial starting soon.**



**Thank You!**

Thomas I. Zarembinski, PhD MBA  
Sr. Director, New Product Development  
[tzarembinski@biotimemail.com](mailto:tzarembinski@biotimemail.com)  
510-521-3390



# LifeMap Solutions

mHealth Industry Overview

BioTime Shareholder Update

November 4, 2014



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[lifemap-solutions.com](http://lifemap-solutions.com)

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# Safe harbor statement

The matters discussed in this presentation include forward looking statements which are subject to various risks, uncertainties, and other factors that could cause actual results to differ materially from the results anticipated. Such risks and uncertainties include but are not limited to the success of BioTime in developing new stem cell products and technologies; results of clinical trials of BioTime products; the ability of BioTime and its licensees to obtain additional FDA and foreign regulatory approval to market BioTime products; competition from products manufactured and sold or being developed by other companies; the price of and demand for BioTime products; and the ability of BioTime to raise the capital needed to finance its current and planned operations. Any statements that are not historical fact (including, but not limited to statements that contain words such as "will," "believes," "plans," "anticipates," "expects," "estimates") should also be considered to be forward-looking statements. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. As actual results may differ materially from the results anticipated in these forward-looking statements they should be evaluated together with the many uncertainties that affect the business of BioTime and its subsidiaries, particularly those mentioned in the cautionary statements found in BioTime's Securities and Exchange Commission filings. BioTime disclaims any intent or obligation to update these forward-looking statements.



# LifeMap Solutions: mission

Working in partnership with the Icahn School of Medicine at Mount Sinai, LifeMap Solutions seeks to develop an mHealth platform that integrates disparate sources of information to generate an increasingly accurate picture of an individual's health.



# Key partner: Mount Sinai

- Top-20 hospital
- Top-20 research medical school
- 36,000 employees, including 6,200 physicians
- 170,000 admissions yearly
- 2.6M non-ER outpatient visits yearly
- 490,000 ER visits yearly
- Direct partner is Icahn Institute for Genomics and Multiscale Biology, run by Eric Schadt, Ph.D., founding director



Source: [US News and World Reports](http://health.usnews.com/health-news/best-hospitals/articles/2014/07/15/best-hospitals-2014-15-overview-and-honor-roll) (<http://health.usnews.com/health-news/best-hospitals/articles/2014/07/15/best-hospitals-2014-15-overview-and-honor-roll>), [NIH Funding](http://www.brimr.org/NIH_Awards/2013/SchoolOfMedicine_2013.xls) ([http://www.brimr.org/NIH\\_Awards/2013/SchoolOfMedicine\\_2013.xls](http://www.brimr.org/NIH_Awards/2013/SchoolOfMedicine_2013.xls))

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# Experienced team



CAMERON - PACE



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# mHealth overview

Today: mostly consumer apps and “wearables”



# Major new entrants signal 2nd phase



Google Fit



Microsoft®  
HealthVault™

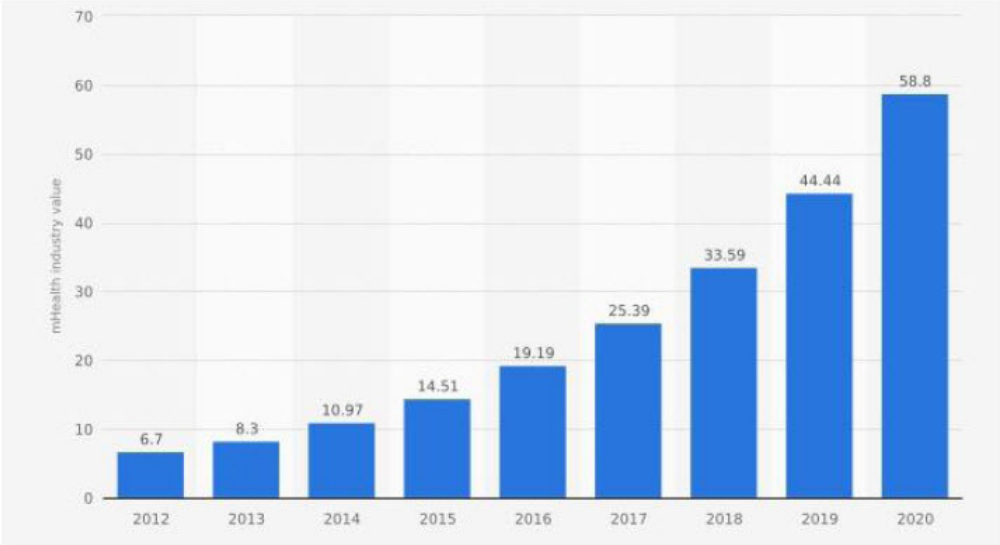


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# Market growth is accelerating

Predicted Global mHealth Market Size (Billions USD)



Source: [Allied Market Research](http://www.alliedmarketresearch.com/mobile-health-market) (<http://www.alliedmarketresearch.com/mobile-health-market>)

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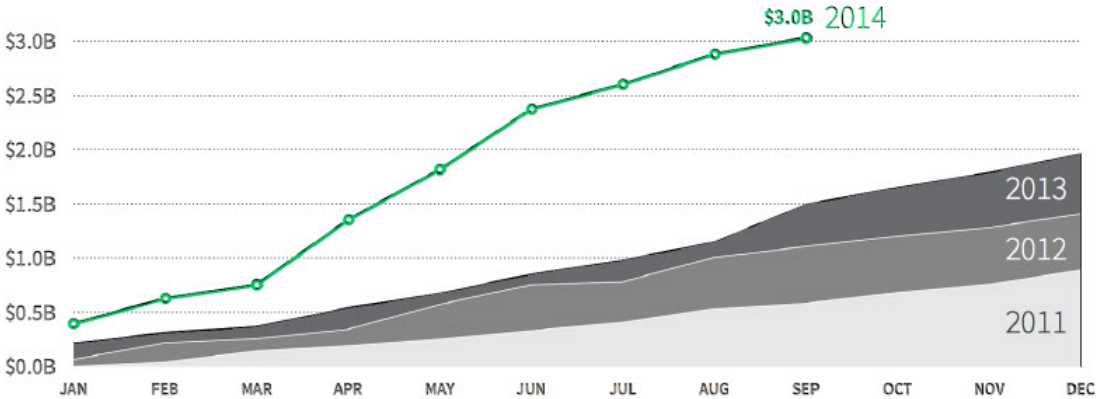
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# Investment is accelerating

Venture Funding of Digital Health Companies (2011 - Q3 2014)



Source: Rock Health funding database  
Note: Only includes deals >\$2M

Source: [RockHealth Q3 2014 Update](http://rockhealth.com/2014/10/q3-funding-update-digital-health-rakes-3b/) (<http://rockhealth.com/2014/10/q3-funding-update-digital-health-rakes-3b/>)

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# Why now?

- **Culture**

- Ubiquity of smartphones
- “Quantified Self” movement
- Expectation of accelerating tech

- **Technology**

- Powerful processors
- High bandwidth
- High-quality sensors
- Big data analytics and management tools



# Beneficiaries of mHealth



Consumers

Care Teams

Direct Researchers

Indirect Researchers

*All enabled by **big data***



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