



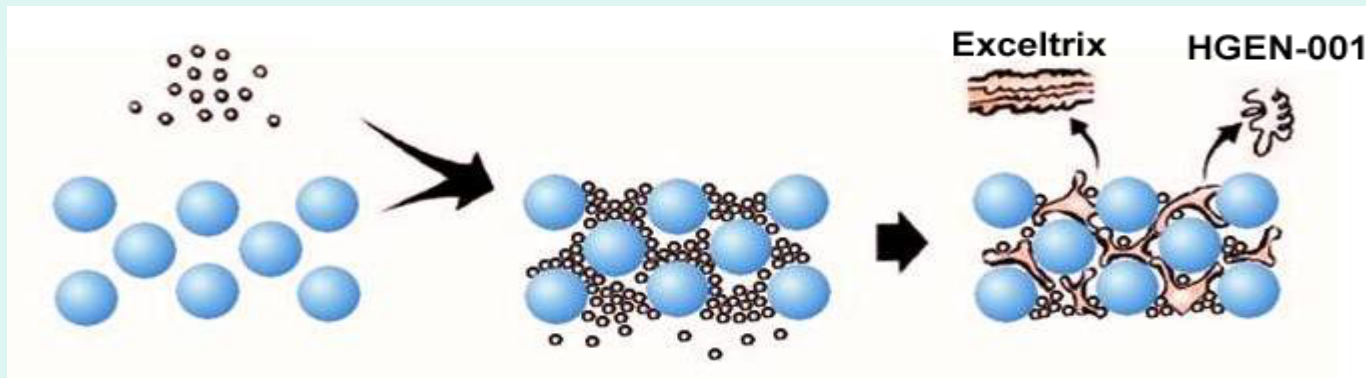
# Histogen

Redefining Regenerative Medicine

<http://www.histogeninc.com>

### Overview

- Regenerative medicine company based on naturally produced products from newborn fibroblasts grown in a bioreactor that mimics an embryonic environment characteristic for rapid growth /scarless healing
- Since the technology simulates an embryonic environment, it naturally produces embryonic proteins and growth factors to be extracted and utilized
- Embryonic stem cells or animal products are not used thus avoiding controversial issues and problems
- A rich product portfolio places the company in a unique position to enter a board range of underserved and growing markets



## Overview

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- The product pipeline
  - short-term products - no or little regulatory hurdles (2008-09)
  - medium term products - PMA and pilot/pivotal trials (2013)
  - longer term products – Biologics and clinical trials (2015)
- Short-term products allow the company to build solid financial foundation while the medium and longer term products are in research and development
- Hair regrowth product
  - longer term
  - substantiated by strong scientific data
  - huge market and “homerun” potential

### Why Now? Why Histogen?

Histogen scientists have developed regenerative medical technologies without the use of stem cells or animal serum

Through the company's core technology, Histogen is capable of manufacturing active wnt proteins, growth factors and human extracellular matrix products factors outside the body, offering significant benefits over competitive products.

### **Histogen has a foundation of proven products**

In vitro experiments have shown wnt proteins are capable of inducing cell proliferation and maturation of:

- keratinocytes
- intestinal epithelial cells
- respiratory epithelium
- bone marrow progenitors



### Pain / Solution

#### The Pain

- Controversial issues and problems due to use of embryonic stem cells and animal products
- Long time for commercialization of products
- Lack of Product Mix

#### The Solution

- Histogen does not use embryonic stem cells or animal products
- Model of short, medium and longer term products, revenue streams start within first 5 years.
- Rich product mix

## **Current Status**

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- Three patents filed in US and Europe
  - # 20060134074, *Compositions & Methods for Promoting Hair Growth*
  - # 20060115460, *Compositions & Methods Comprising WNT Proteins to Promote Repair of Damaged Tissue*
  - App # 61\024,854, *Extracellular Matrix Compositions including Embryonic Proteins*
- Financed from inception to 12/31/07 by Dr. Naughton; Series A opened 12/07/07
- Bioreactors are currently manufacturing two products (ECM and HGEN-001) for research

## **Current Status**

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- Two major research tool companies evaluating material for in vitro stem cell growth
- Final stage of negotiations for cosmeceutical product
- Discussions underway for Licensing Agreements for three of the five 510ks.
- Consultants for Accounting, Legal, and Regulatory in place
- Experienced Scientific Advisory Board / Board of Directors
- Executive Management in place with over 70 years of combined experience in bringing human fibroblast based regenerative medicine products from concept to market

## **Customers/Partners (targets)**

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- Short Term Products
  - Invitrogen (research products)
  - Becton Dickinson (research products)
  - Smith & Nephew (wound healing/orthopedics)
  - CR Bard (hernia/urological)
- Medium Term Products
  - Galderma / Isolagen / Allergan (facial filler)
  - Medtronic (ECM coating for cardiovascular devices)
  - J&J / Smith & Nephew (ECM paste for cartilage/bone)
- Longer Term Products
  - Hair growth: Initial conversations/interest from Aderans (Bosley Clinics) P&G and Allergan



## **Market**

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### **Tissue Growth Factors Market**

- Early stage of development
- Market and demand expected to grow
- Estimated to be growing at annual rate of 28.9%
- Revenues for 2008 expected to be \$324.7 million

(Frost and Sullivan Reports, *US Growth Factors Market: Tissue Growth Factors Market: Market Overview*. 12 February, 2002)

### **Stem Cell Research**

- Rapidly expanding
- By 2016 the stem cell market is estimated to be \$8.5 billion
- Stem cell therapies are applicable for over 2.5 million patients in the US and growing

(Market Analysis, Stem Cell Summit February 2007)

### **Histogen Products**

- applicable to above markets
- fall into other markets and submarkets due to variety of uses

### Common Bioreactor System



### ECM Products

Uses	Market (s)
Human matrix for cell culture coating	Stem cell research
Tissue regeneration patches	Urinary Incontinence Rotator Cuff Repair Dura Mater Repair Pelvic Floor Repair
Coatings for the improvement of tissue ingrowth	orthopedic implants cardiovascular implants urinary slings pelvic floor patches pacemaker leads
Injectables	soft tissue replacement (deep wrinkles/furrows) bulking agent for GERD, urinary incontinence

### HGEN Products

Uses	Market (s)
Additive to tissue culture media	Stem cell research
Injectable	hair growth
Topical spray	nasal/oral/esophageal lesions
Eye drops	Corneal repair
Respiratory Inhaler	premature infant lung development/ treatment of emphysema
Retentive enema	Ulcerative colitis, Crohn's disease

### ECM + HGEN Products

Uses	Market (s)
Research for stem cell growth	3D matrix for cell culture
Paste for repair/regeneration	Orthopedics: critical sized defects Spinal cord repair



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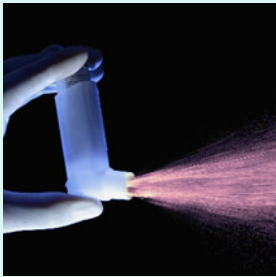
## **Technology & Products**

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- One Technology
  - Proprietary closed bioreactors
  - Mimics embryonic environment
  - Produces multiple products with applications for various markets/uses
- Products
  - Extracellular Matrix (ECM) – opaque jelly-like substance
  - HGEN-001 - liquid formula containing wnt proteins and growth factors
  - Combination product (ECM+HGEN-001)
    - Scaffold (3D Matrix)
    - Paste-like substance
- Product Introduction
  - Short term (2008-09) – revenue potential \$293 million first 5 years
  - Medium term (2013 - 2014) – revenue potential \$320 million 2013-14
  - Longer term (2015 - 2018) – revenue potential \$3 billion 2015-18
  - A 25% hair growth market share at 70% of gross leads to potential of \$49 billion

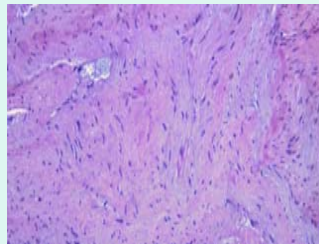
### Technology

Within Histogen's proprietary closed bioreactors, newborn fibroblasts are seeded onto beadlike structures, which are conditioned with a liquid media and grown under embryonic conditions. In this environment the fibroblasts produce a non soluble matrix material characteristic of young, rapidly developing tissue.



The conditioned fibroblasts also produce a variety of soluble factors. The liquid media is infused with these factors to create a proprietary liquid formula.

When the matrix and the liquid formula are combined, a paste like material is formed containing the same properties of the matrix and the formula.



A 3-d scaffold is derived from freeze drying the matrix and conditioning it with the liquid formula. ECM beads can also be manufactured for the improved growth of human embryonic and adult cells in culture



## Products

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### Short Term

- Research Tools
  - Require no regulatory approval
  - Applicable for all products
    - **ECM**
    - **HGEN-001**
    - **Combination Products**
    - **Uses include coatings and additives**
  - Launch Q1 of 2009
  - Revenue potential upwards of \$120 million first 5 years
- 510k's
  - Approval process 180 days following FDA submission
  - ECM for tissue regeneration patches
    - **Wound care**
    - **Hernia repair**
    - **Urological surgery**
  - Product Approval / License Q4 of 2008
  - Revenue potential upwards of \$173 million first 5 years

### Market Opportunity for Short-term products

#### Research tools - *Potential Revenues Upwards of \$120 million for first 5 years*

<b>Cell Culture</b> <i>Coating and Additives</i>	<ul style="list-style-type: none"> <li>✦ The market was estimated to be \$714.5 million in 2005</li> <li>⚡ Forecasted to grow to \$1.2 billion by 2012*</li> <li>✦ Trend towards serum-free media for cell culture as purity is critical</li> </ul>
<b>Cosmeceuticals</b> <i>Medical Retail Market</i>	<ul style="list-style-type: none"> <li>✦ U.S sales estimated at \$870 million in 2006</li> <li>✦ In 2005 estimated sales were \$1.8 billion Worldwide</li> </ul>

#### 510Ks - *Potential Revenues Upwards of \$173 million for first 5 years*

<b>Tissue Engineering Market</b> Tissue Regeneration patches <ul style="list-style-type: none"> <li>- Urinary Incontinence</li> <li>- Rotator Cuff Repair</li> <li>- Dura mater Repair</li> <li>- Pelvic Floor Repair</li> </ul>	<ul style="list-style-type: none"> <li>⚡ UI market expected to exceed \$11 billion by 2008</li> <li>✦ \$16-\$20 billion is spent every year on UI-related products</li> <li>✦ Over 200 million people are affected worldwide with UI</li> <li>✦ Over 230,000 rotator cuff repairs take place annually</li> <li>✦ The Dura Mater worldwide market is estimated at \$230 million</li> </ul>
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## **Products**

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### **Medium Term**

- PMA's
  - Pilot and pivotal trials required
  - ECM product and combination product (paste)
  - Uses include soft tissue replacement
  - Launch Q1 2013 and Q1 2014 respectively
  - Potential revenue upwards of \$320 million for 2013-2014

### **Longer Term**

- Biologics
  - Phase I, II, and III clinical trials required
  - HGEN-001 product and combination product (paste)
  - Uses include Hair Growth (HGEN-001) and Spinal Cord Repair (paste)
  - Launch Q4 2015 and Q1 2018 respectively
  - Potential revenues upwards of \$3 billion for 2015-2018



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## **Hair Growth Product**

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- Hair loss affects 35 million men and 21 million women in the United States
- Hair growth product (HGEN-001) has an estimated revenue of \$2.8 billion (represents 1% of the market)
- Suggested price for treatment is \$5k versus \$4-12k (2 procedures)
- Strong scientific data suggests potential homerun product
- Potential to capture 25% of market (revenue of \$70 billion = 56 million x .25 x \$5,000)
- Net Potential Revenue is \$49 billion (70% of gross)
- Strategy: secure global corporate partner after Phase I data is available





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## **Hair Growth Product**

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### **Competition**

- Surgical
  - Hair Transplant
    - Surgical procedure in which hair follicles are transplanted
  - Costs \$4k-12k per procedure – usually 2 procedures
    - Can leave an unnatural looking hairline
  - Scalp Reductions
  - Flap Surgery
- Drugs
  - Rogain
  - Propecia – helps but overtime effect decreases, possible side effects
- Hair Pieces

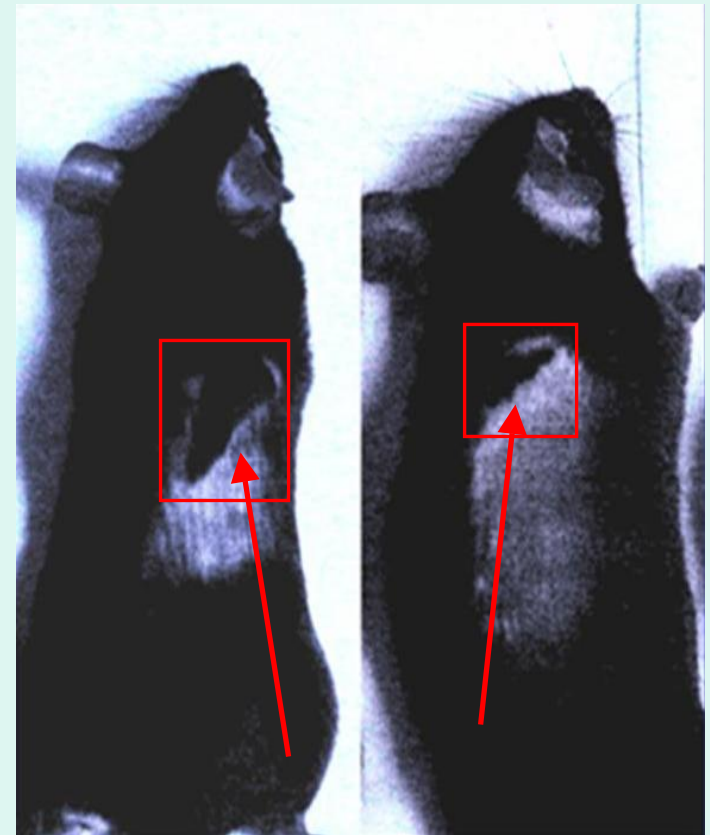
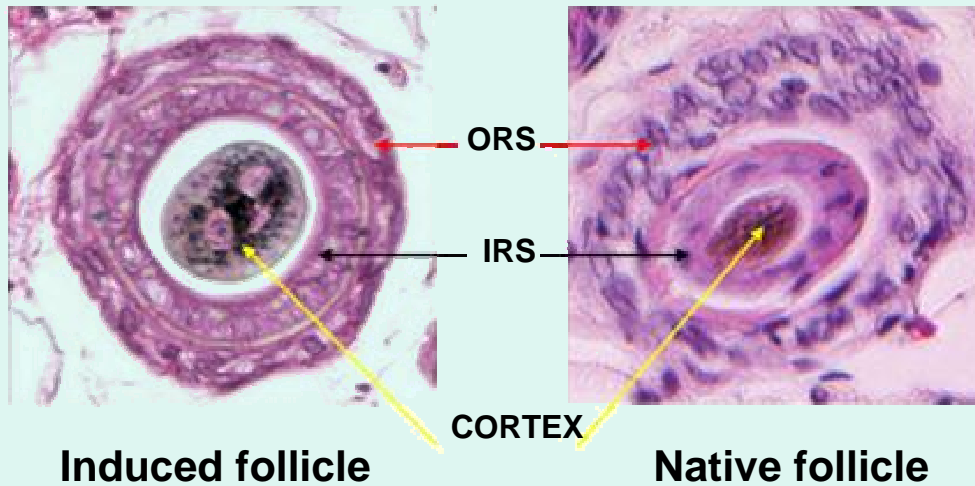


## **Hair Growth Data**

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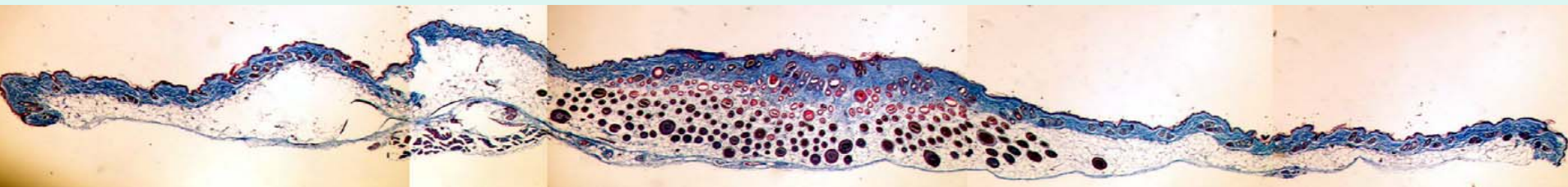
- HGEN-001 has demonstrated a significant increase in new hair follicle creation and hair growth in preclinical trials
- Preclinical toxicology studies are underway and Histogen plans to file an IND in Q1 2008, with phase 1 clinical trials commencing in Q3 2008
- In May 2007, Dr. Naughton's previous findings were substantiated in an article by George Cotsarelis - offered evidence that growth factors and wnt proteins lead to increase in creation of new hair follicles

### Hair Growth Data



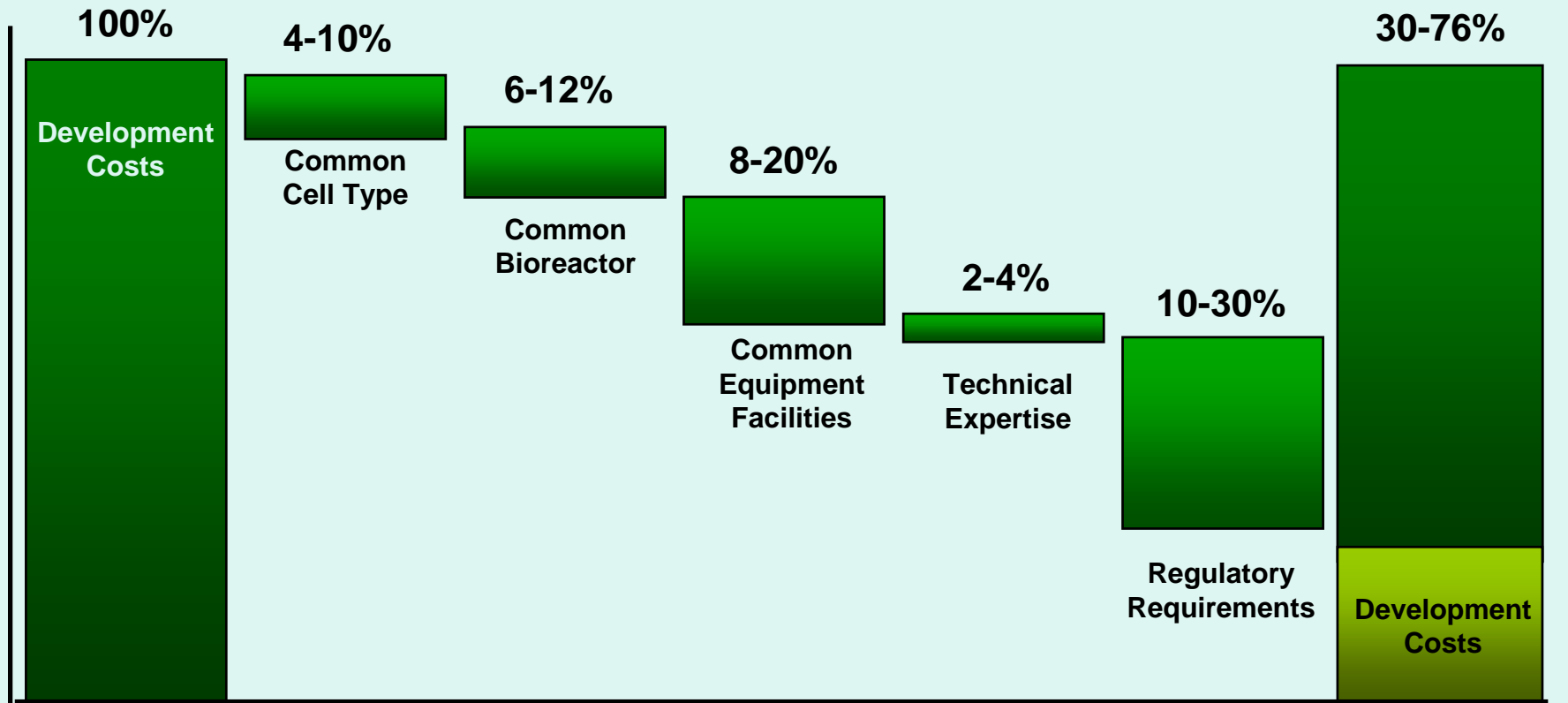
Above: Examples of hair growth at injection sites after 14 days

Below: Depicts site specificity



### Financials

#### Potential Impact of Value Creation Model on Product Development Costs



Range of potential cost savings for development of tissue-engineered product for new indications from concept to final process validation



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## **2008 Peer-Reviewed Presentations / Publications**

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**MD & M Jan 31, 2008**

*Embryonic extracellular matrix contains unique composition of proteins for rapid cell proliferation and healing without scars:*

**Frost & Sullivan 2<sup>nd</sup> Annual Venture Connections Symposium Mar 12, 2008**

Company presentation

**12th Annual Hilton Head Workshop, Regenerative Medicine Mar 12-16, 2008**

*Hypoxic Fibroblasts Demonstrate Unique ECM Production and Growth Factor Expression*

*Production of Naturally-Soluble WNT Activity for Regenerative Medicine Applications*

**MDMI – Scheduled for May 2008**

*Human Extracellular Matrix for Medical Devices and Therapeutics*

**European Stem Cells & Regen Med Congress, London May 13-15, 2008**

*Challenges of commercializing stem cell therapies and creating a successful business model*



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## **2008 Peer-Reviewed Presentations / Publications**

**The International Investigative Dermatology, Kyoto, Japan May 14-17, 2008**

*Commercial-scale production of wnts for inducing hair follicle growth and neogenesis as a treatment for alopecias*

*Tissue-engineered human embryonic extracellular matrix (ECM) for therapeutic applications*

**Regenerative Medicine Journal May 2008**

*Company Profile*

**ASAIO June 19 - 20, 2008**

*Tissue-Engineered Human Embryonic Extracellular Matrix for Therapeutic Device Applications*

*A Unique Business Model – Regenerative Medicine Redefined*

**ISACB 11th Biennial Meeting - Sep 17-20, 2008 - Bordeaux, France**

*Tissue-Engineered Human Embryonic Extracellular Matrix for Cardiovascular Applications*



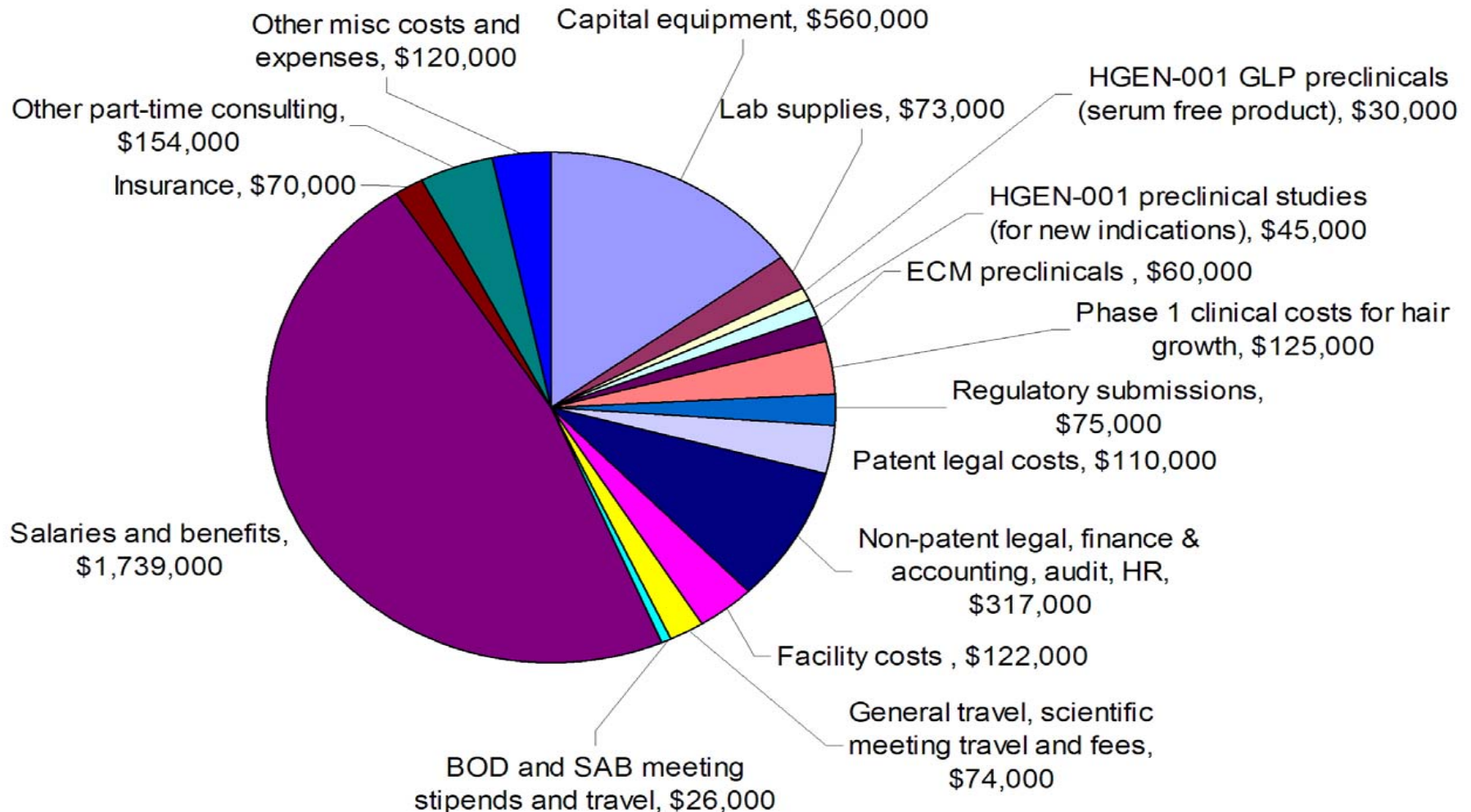
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## **Funding Sought**

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- \$3-5 million from Angel Investment / Early Stage Money
- Few Investors who are willing to make high investment before April 15, 2008
- Value Proposition – Low Dilution
- 5% Warrant Bonus
- \$1 dollar for 1 share
- Preferred Convertible Series A Stock

### Use of Proceeds: 2007-2009







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### **Budget Breakdown**

Capital Equipment for manufacturing upscaling	\$560,000
Lab supplies: media, cells, beads, reagents	\$73,000
HGEN-001 GLP preclinicals with serum free product	\$30,000
HGEN-001 preclinical studies (for new indications)	\$45,000
ECM preclinicals to support market launch of 510K products	\$60,000
Regulatory submissions:	\$75,000
Patent costs	\$110,000
Non-patent legal costs	\$317,000
Phase 1 clinical costs for hair growth	\$125,000
Facility Costs	\$122,000
General travel, scientific meeting travel and fees	\$74,000
BOD and SAB meeting stipends and travel	\$26,000
Salaries & benefits	\$1,739,000
Insurance (property, liability, D&O)	\$70,000
Other Part-time consulting	\$154,000
Other	\$120,000
<b><u>Total</u></b>	<b>\$3,700,000</b>

## **Budget Narrative**

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### Key Points

- Salaries and Benefits
  - Top talent is needed in order to execute plan and accomplish science and business goals
  - Naughton as acting CEO for first 2-3 years (until phase II hair data)
- Capital Equipment
  - 100 liter bioreactors and control systems
  - Mini-mate cell feeders
  - Roller racks/large deli-style incubators
- Preclinicals/Clinical study
  - Biocompatibility study for ECM 510K submissions
  - Hair preclinicals with serum-free material
  - Hair toxicology studies
  - Phase I study for hair growth
  - Preclinicals for Crohn's disease, lung repair, wound healing

## **Value Propositions**

- Low Dilution
- Early Stage Investment
- Experienced Scientific Team & Advisory Board
- Experienced Management Team / Board of Directors
- Homerun Product with Huge Revenue Potential
- IPO or M&A in 5-7 years



## **Management Team**

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### **Dr. Gail Naughton**

- Dean, College of Business Administration, SDSU
- Co-founded Advanced Tissue Sciences, where she spent more than 15 years extensively researching the tissue engineering process and co-invented the company's core technology
- Raised \$350 million for Advanced Tissue Sciences from the public market and corporate partnerships
- Oversaw the design and development of the world's first upscale manufacturing facility for tissue engineered products
- Brought four human cell-based products from concept through FDA approval and market launch
- Established partnerships with companies including Smith & Nephew, St Jude Medical, Gibco (Invitrogen), Kirin, Medtronic and Inamed
- Inventor on over 90 patents in the field



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## **Management Team**

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### **James R Goode, Acting CFO**

- 30 years of consulting and senior management experience in helping organizations achieve their financial and operational goals, obtain funding, pursue acquisitions, expand their global business,
- Successfully participated in raising over \$100 mil for clients and the companies he worked for

### **Rob Kellar, Ph.D. VP of R&D**

- Previous Co-Owner & President of Development Engineering Sciences and previous positions with W.L Gore & Associates and ATS
- Involved with Commercial worldwide management of research and product development

### **Frank Zeigler, GM In-Vitro Business Unit**

- More than 18 years experience in research and product development and previous Senior Scientist positions at Genentech, ATS, Stem Cells
- 8 peer reviewed research publications and 3 patents



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## **Management Team**

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### **Mark Hubka, D.C, F.A.C.O., M.B.A., Director of Clinical Affairs**

- More than 25 years experience in orthopedics and sports medicine
- Administrator for orthopedic surgery center creates natural transition clinical trials

### **Mark Baumgartner, Director of Engineering**

- More than 20 years experience in product and process development for regulated biologic products
- Previous Director of Process Development for Smith-Nephew Wound Management and for ATS

### **Beverly Dunlap, M.S., Director of Business Development**

- More than 15 years of experience in various aspects of the health industry
- Private, Government and Non-profit sectors lends to a well rounded perspective to program and business development

### **Eileen Naughton, Director of Corporate Communications**

- More than 5 years of experience in communications and public relations
- Positions with Moore Media Relations and SDSU Entrepreneurial Management Center

## **BOD / SAB Chair**

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### **Stephen Francis Badylak, D.V.M., M.D., Ph.D.**

- Professor Dept. of Surgery and Director of the Center for Preclinical Testing at the McGowan Institute for Regenerative Medicine (Univ of Pittsburgh)
- Served as Director of the Hillenbrand Biomedical Engineering Center at Purdue
- Holds over 40 US patents and 200 patents worldwide
- Authored more than 170 scientific publications and 12 book chapters
- Served as the Chair of the Purdue University Tissue Engineering Advisory Board and as chair of several Study Sections for NIH
- Associate Editor for Tissue Engineering and for the journal Cells, Tissues, Organs
- Recipient of the Carnegie Science Center Award for Excellence in 2005
- PI on \$25M DARPA grant

## **BOD**

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### **Leonard Lavin**

- Founder, Chairman Emeritus and Director of Alberto-Culver Company
- Company operated Sally Beauty Company and Beauty Systems Group until Nov 2006 when it separated into two public companies
- Active in many professional and philanthropic organizations
- Lifetime Trustee of
  - University of Chicago Cancer Research Center
  - Northwestern Memorial Hospital
- Author of *Winners Make it Happen: Reflections of a Self-Made Man*



## **BOD**

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### **Dr. Stephen Chang**

- CEO of Multicell Technologies
- President of MCT Rhode Island Corp. and Xenogenics Corporation
- President of CURES and on the Board of BIOCOM
- Previous Chief Science Officer and Vice President of Canji Inc./Schering Plough Research Institute
- Holds over 20 patents and has initiated over fifteen IND's

## **SAB**

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### **Dale P. Devore, Ph.D.**

- leading expert in collagen research and the development, evaluation, and commercialization of natural polymer-based medical implants
- authored/coauthored more than 55 patent applications, 36 of which have been issued
- more than 55 technical publications
- Held VP R&D/CSO positions at Collagen Corp and Collagenesis
- served on the Editorial Review Board of the Journal of Long-term Effects of Medical Implants

## **SAB**

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### **Lawrence Rheins, Ph.D.**

- Vice President of Science and Technology at Floratech International
- Founded DermTech International; Company executive through 2004
- Co-inventor of DermTech's proprietary Epidermal Genetic Information Retrieval technology
- Previous Executive Director at Advanced Tissue Sciences
- Holds several patents
- Authored over 50 articles and book chapters on immunology, toxicology, dermatology and in vitro alternatives



## **Summary**

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- Histogen offers a unique opportunity to investors to make an early-stage investment in products and technology that have passed the “proof of principle stage”, thus reducing risk and at the same time accelerating timelines to commercialization
- Short term products will help build solid financial foundation while R&D is being conducted for medium and longer term products
- Funding will be used for start up costs, launching of short term products, completion of animal toxicology studies for the IND submission for hair growth and multiple 510K submissions
- Hair Growth is the most lucrative and easiest market to penetrate
- Other products will utilize global marketing partners under exclusive license



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## **Contact Info**

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