Development of Scalable Manufacturing Processes for Human Embryonic Stem Cell Derived Cell Therapies

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Human Embryonic Stem Cells

- Renewable Source for Cell Based Therapies
- Cultured & Differentiated Efficiently
- Produce Functional Cells
- Efficacious and Safe Upon Transplantation
- Cells Can Be Produced at Scales and COGS for Widespread Commercialization
hESC-Derived Therapeutics Manufacturing

Blastocyst

Human Embryonic Stem Cells

Neural Cells

Spinal Cord Injury

Cardiomyocytes

Neural Cells

Cardiomyocytes

Islets

Diabetes

Tolerance Induction Cancer Immunotherapy

Chondrocytes

Arthritis

Osteoblasts

Osteoporosis And Bone Fractures

Hepatocytes

Drug Discovery Liver Failure

Therapeutic Cells
hESC-Derived Therapeutics Manufacturing

*hESCs Enable a Product-Based Business Model*

Classical Biologics

- Centralized Production Facility
- Distributed Inventory
- Point Of Care

hESC-Derived Biologics

- Centralized Production Facility
- Distributed Frozen Inventory
- Point Of Care

ENABLING:
- Multidose Production Lots
- Low COGS
- Biological Product Margins
Self-Renewal of hESC Enables Scalable Manufacturing

Classical Biologics Manufacturing Paradigm

Application of Tried and Tested Biologics Manufacturing Strategies to hESC Therapeutics
hESC Derived Therapeutics Manufacturing

Application of Biologics Manufacturing Strategies

Biologics Manufacturing Process

- Upstream Cell Culture & Scale-up
  - Thaw WCB
  - Maintain cell culture
  - Expand cell culture to required scale

- Protein Production
  - Initiate production
  - Harvest, Formulation, Fill & Finish

hESC Derived Cell Therapy Manufacturing Process

- Stage I: uhESC expansion
  - Thaw WCB
  - Maintain cell culture
  - Expand cell culture to required scale

- Stage II: Differentiation
  - Initiate Differentiation

- Stage III: Harvest, Formulation, Fill & Finish
  - Harvest Product
  - Formulation Fill and Finish
  - Drug Product

Harvest, Isolation, Purification, Formulation, Fill & Finish
Scalable Manufacturing Processes for hESC Derived Cell Therapies

*Anticipated Scalability of hESC Derived Cell Therapies*

**Estimated hESC derived cellular therapy annual production capacity based on production phase**

- **Phase 1**: 1.00E+11
- **Phase 2**: 1.00E+12
- **Phase 3**: 1.00E+13
- **Commercial**: 1.00E+15

**Needed:**
- Scalable manufacturing processes
- Improved raw materials (process variability, compliance, cost of goods)
- Product development infrastructure to support development/manufacturing
Improved Raw Materials for hESC-Derived Therapeutics

Corning Life Sciences – Geron Collaboration
Development of Synthetic Surfaces for hESC Growth and Differentiation

- Collaboration and Licensing agreement initiated in 2006
- Goal: Develop synthetic, surfaces suitable for scalable, cGMP manufacturing of hESCs and hESC derived, differentiated cells
- Approach: Acrylate based surface chemistry conjugated with bio-active peptides

Corning® Synthemax™ Surface
Scalable Manufacturing Processes for hESC Derived Cell Therapies

Undifferentiated hESC Cells Can Be Grown on Microcarriers in Static Culture

H7 hESC Attach to Extracellular Matrix (ECM) Coated Microcarriers

Microcarriers: UNCOATED ECM COATED

Calcein-AM stain

Microcarriers cultured in Ultra Low Attachment (ULA) polystyrene cell culture vessels
H7 Cells Maintain Undifferentiated Phenotype in Long-Term Microcarrier Culture

OCT4 Marker Expression

Time (Months)

OCT4 Positive Cells (%)