PBS BIOTECH®

CELL GENE MEETING ON THE MESA

Enabling The Commercialization Of Allogeneic Cell Therapy Products

VERTICAL-WHEEL™ BIOREACTORS

The next generation of single-use bioreactors inspired by forward thinking

October 13, 2021

Carlsbad, CA

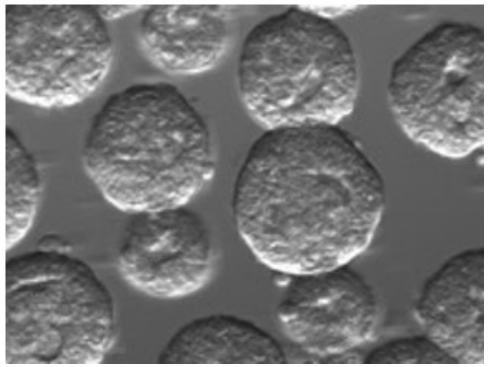
Company Mission

“PBS Biotech improves the lives of patients by enabling the development and manufacturing of cell therapy products”

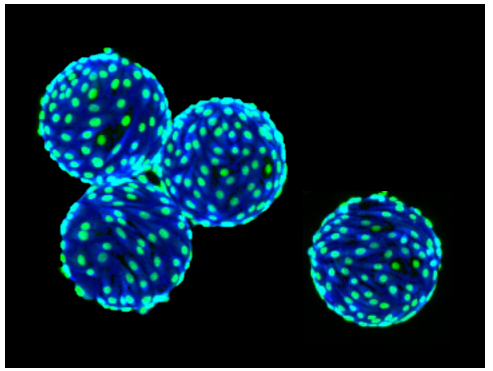
Our vision is to provide the industry-standard manufacturing platform along with unsurpassed technical expertise to unlock clinical and commercial manufacturing of allogeneic cell-based therapies.

Sources Of Allogeneic Cell Therapy Products

- **Pluripotent Stem Cells (PSC) – Induced (iPSC) & Embryonic (ESC)**
  - Expansion and differentiation as aggregates – uniform morphology is critical
  - Example: (i) iPSCs → β-islet cells to produce insulin for Type 1 diabetes
    (ii) iPSCs → Cardiomyocytes for heart disease
    (iii) iPSCs → NK or T-cells for immunotherapy
  - ~73 companies developing PSC-derived products; PBS working with 52



- **Human Primary Cells (HPC) – Mesenchymal Stem Cells (MSC), Exosomes, Chondrocytes**
  - Grown on the surface of microcarriers in suspension – shear sensitive
  - Example: (i) MSCs for heart disease treatment
    (ii) Chondrocytes for Osteoarthritis treatment
  - ~124 companies developing HPC-derived products; PBS working with 52

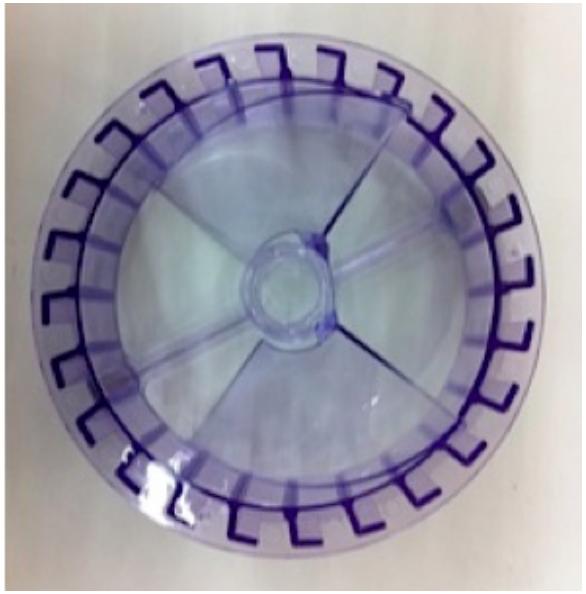


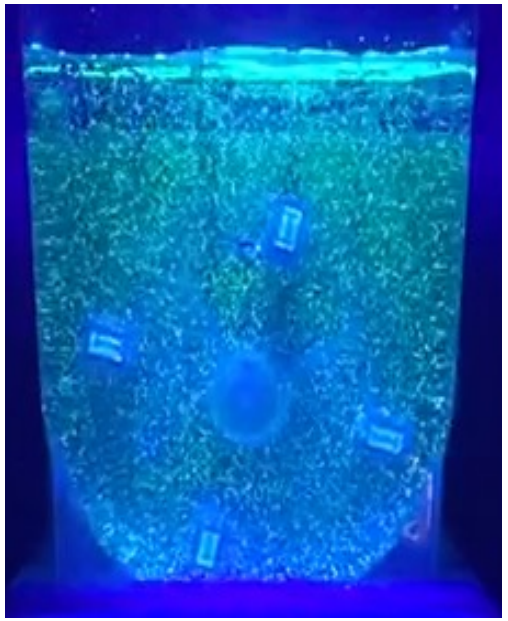
Challenges Of Manufacturing Allogeneic Cell Therapy Products

"Significantly different from biotech manufacturing experience"

- **Living cell** itself is the **product**
- 2D platforms commonly used at small scale but **cost prohibitive** to scale out – **3D needed** for **scale up**
- **Anchorage-dependent** cells grown in suspension on surface of **microcarriers** or as **aggregates**
- Suspension of these **large particles** in bioreactors requires **higher power inputs** (agitation rates)
- Anchorage-dependent cells are **sensitive** to a bioreactor's **hydrodynamic conditions**
- Inconsistent hydrodynamic conditions during **volumetric scale up of bioreactors** make it difficult to achieve desired **cell yields and quality** during cell culture processes

Vertical-Wheel™ Technology Provides The Solution





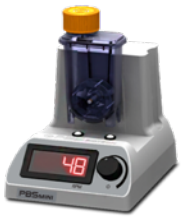
Combination of Vertical-Wheel (VW) impeller and U-shaped vessel offers unique benefits:

- Complete particle suspension with minimal power input and shear forces
- Uniform fluid mixing and distribution of turbulent energy dissipation
- Small scale hydrodynamic conditions consistently reproduced at larger volumetric scales

PBS Biotech Offers World-Class Equipment and R&D Services

Vertical-Wheel Single-Use Bioreactors

0.1 L



0.5 L

3 L

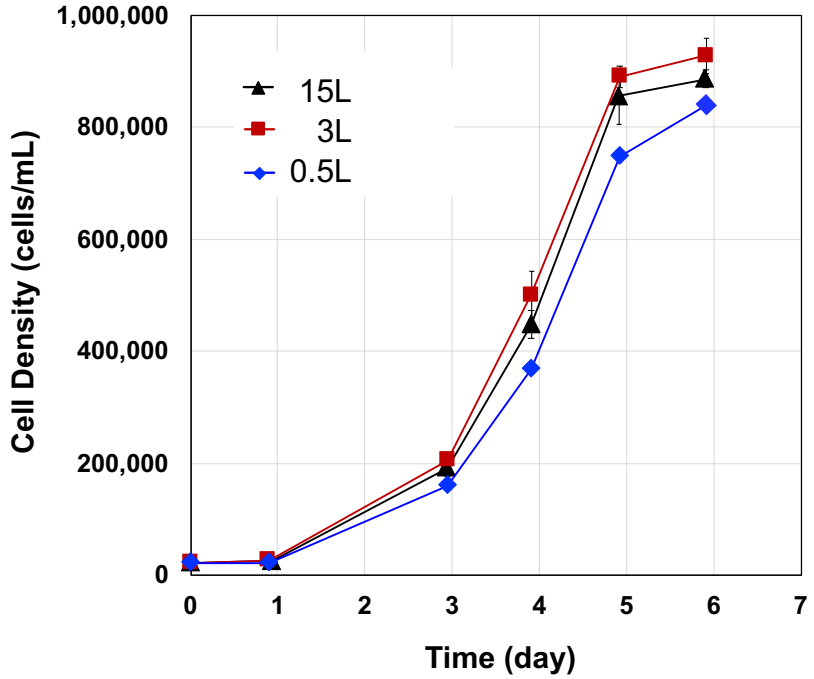
15 L

80 L

Contract Process Development

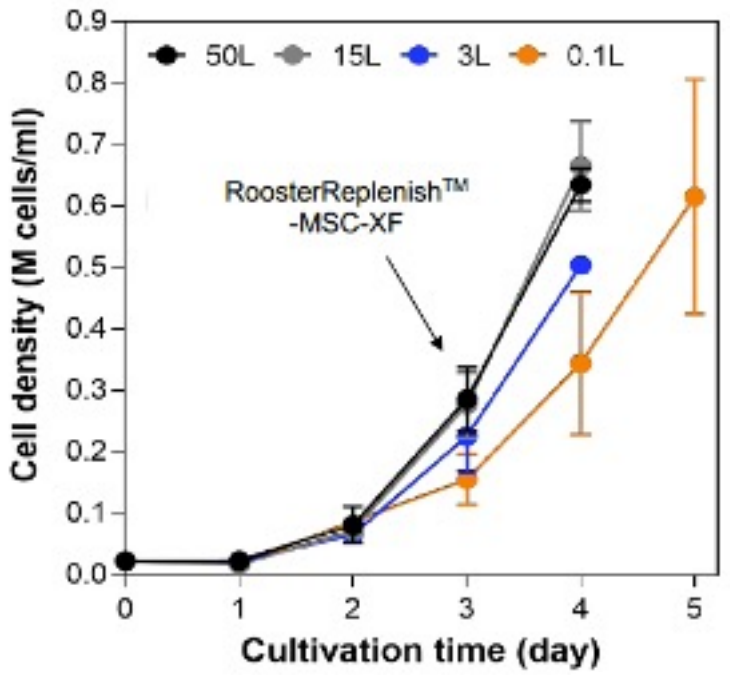
Scalable Expansion of MSCs in VW Bioreactors

SCM Lifescience



- Over 800,000 cells/mL achieved at 0.5, 3, and 15L

RoosterBio®
Radically Simplifying Use of MSCs



(n=3 for each size)

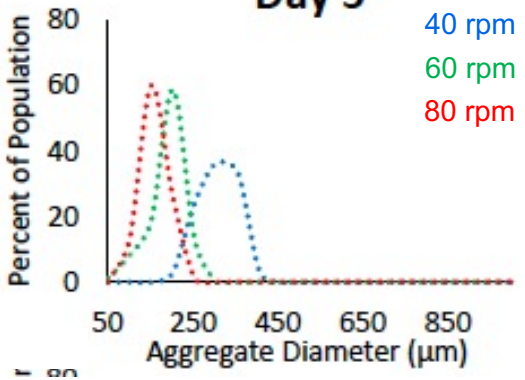
- Over 0.5 M cells/mL achieved repeatedly at 0.1 – 50L

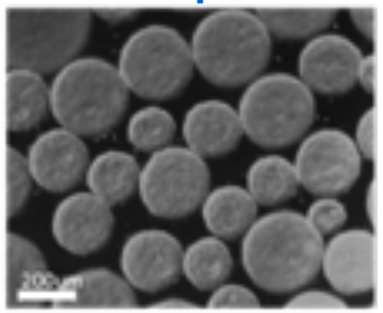
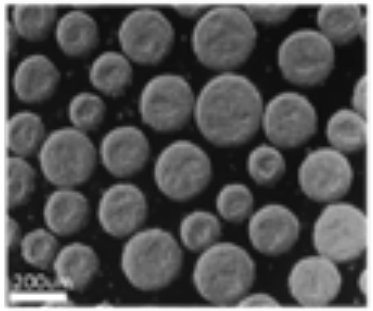
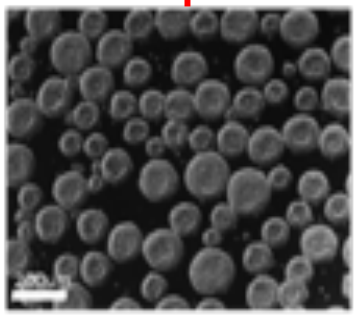
Superior iPSC Aggregate Formation in VW Bioreactors

- Uniform morphology of PSC aggregates critical for efficient expansion and differentiation processes, which allows even diffusion of nutrients / growth factors to avoid necrosis / heterogeneous differentiation

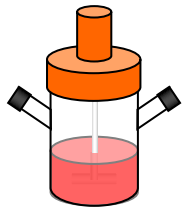
Vertical-Wheel

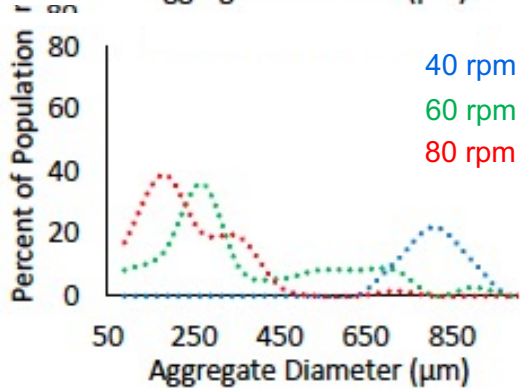
Both 0.1 L scale

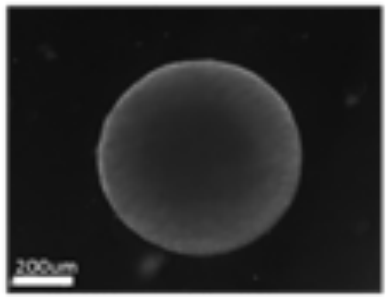
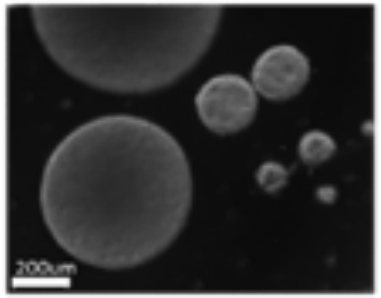
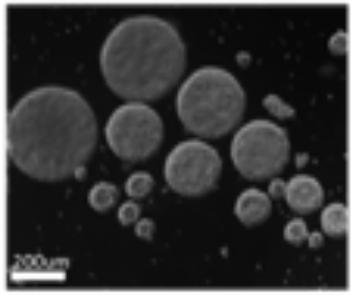


40 rpm	60 rpm	80 rpm
		
16.7 ± 1.1 cells/mL	11.2 ± 0.9 cells/mL	7.7 ± 0.5 cells/mL

Horizontal Impeller





		
4.9 ± 2.8 cells/mL	3.3 ± 0.3 cells/mL	6.3 ± 2.7 cells/mL

- VW produces spherical aggregates with narrow distributions of diameters; horizontal impeller has much more variation
- Control of optimal, average aggregate diameter through inverse correlation with agitation

Proposed iPSC Manufacturing Process Using VW Bioreactors

Cell Bank → **Seed Expansion Stage** → **Production Stage**

One PBS-80 Run

Yield: ~50 B cells

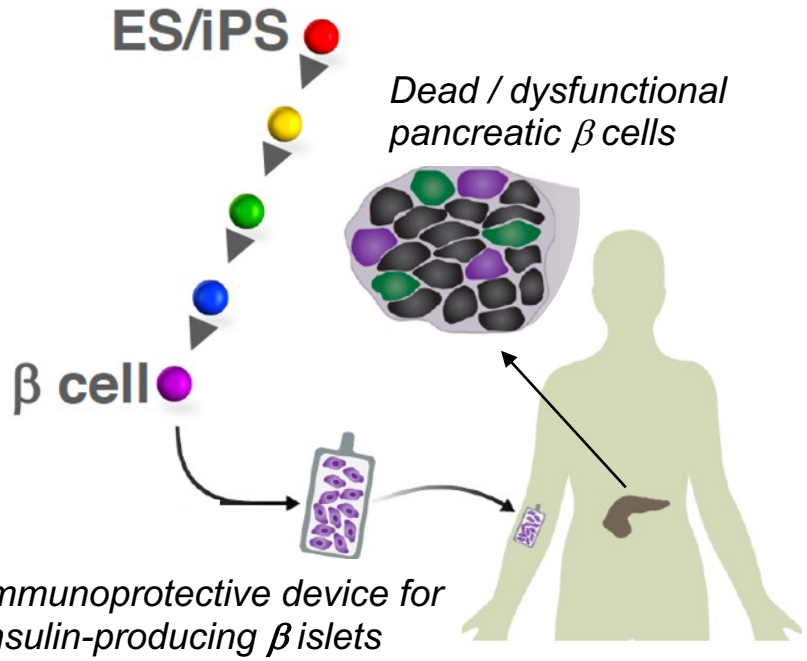
1.2 M cells

Differentiation or Downstream Processes

20 Days | **14-30 Days**

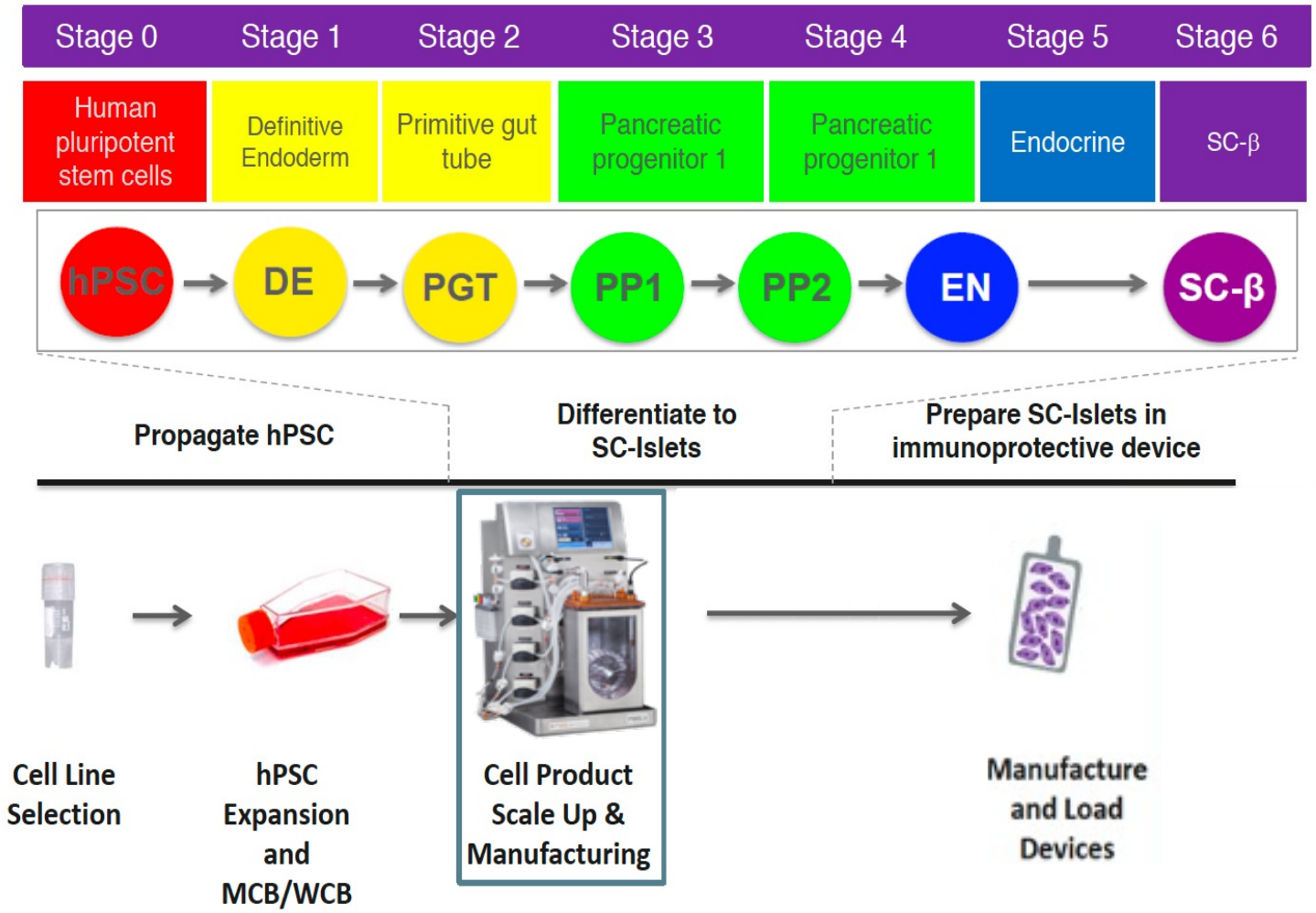
- Optimization of seed expansion and bioreactor processes (e.g., medium exchange, dissociation, & harvesting) significantly improves cell yield and quality

Stem Cell-Derived β Cell Transplantation For Type 1 Diabetes



- Type 1 patients in US: >1.25 M and growing
- Children majority of Type 1 patients

Complex, multi-step differentiation process



Potential Large Scale Autologous Cell Therapy Application

- Recellularize pig heart scaffolds with patient's iPSC-derived heart cells
- Eliminate need for immunosuppressants and matching of deceased donors

Patient-derived Stem Cells

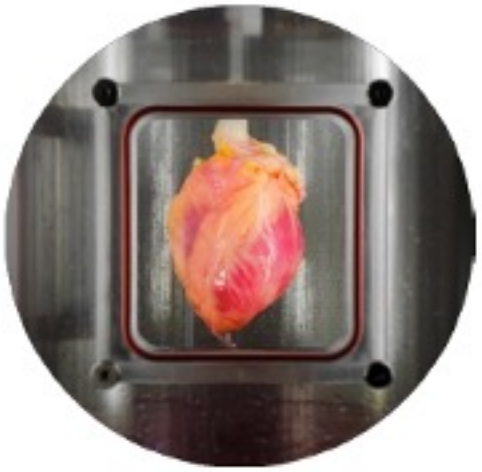
+

Large Scale Expansion and Differentiation into Cardiovascular and Parenchymal Cells

+

Healthy Mammalian ECM (Ghost Heart)

=



Bioengineered Autologous Heart

Recent Scientific Journal Publications

- **Overcoming bioprocess bottlenecks in the large-scale expansion of high-quality hiPSC aggregates in vertical-wheel stirred suspension bioreactors**. Borys, B. *et al*. *Stem Cell Research & Therapy*. 2021;12:55-74. doi: 10.1186/s13287-020-02109-4
- **Transcriptome profiling of human pluripotent stem cell-derived cerebellar organoids reveals faster commitment under dynamic conditions**. Silva, T.P. *et al*. *Biotechnol Bioeng*. 2021;118:2781–2803. doi: 10.1002/bit.27797
- **Computational fluid dynamic characterization of vertical-wheel bioreactors used for effective scale-up of human induced pluripotent stem cell aggregate culture**. Dang, T. *et al*. *Can J Chem Eng*. 2021;1-18. doi: 10.1002/cjce.24253
- **Bioreactor parameters for microcarrier-based human MSC expansion under xeno-free conditions in a vertical-wheel system**. Lembong, J. *et al*. *Bioengineering*. 2020;7(73). doi: 10.3390/bioengineering7030073
- **Scalable generation of mature cerebellar organoids from human pluripotent stem cells and characterization by immunostaining**. Silva, T.P. *et al*. *J. Vis. Exp*. 2020;160. doi: 10.3791/61143
- **Challenges and Solutions for Commercial Scale Manufacturing of Allogeneic Pluripotent Stem Cell Products**. Lee, B. *et al*. *Bioengineering*. 2020;7(31). doi: 10.3390/bioengineering7020031

Customers and Collaborators

PSCs:

semma THERAPEUTICS

VIACYTE Regenerating Health™

Cellular Dynamics international a FUJIFILM company

CRISPR THERAPEUTICS

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RoosterBio

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SCM Lifescience

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Goals to Meet Customer's Clinical and Commercial Development

- **Provide Robust and Reliable Products with GMP Qualification**
  - GMP-qualified products for different stages of regulatory requirements
  - 7 customers currently in clinical trials or entering soon; earliest commercial is anticipated by 2024
- **Improve Internal Operations**
  - **Supply Chain:** Ensure security of materials and components for on-time delivery
  - **Manufacturing:** Maintain consistency and efficiency
  - **Quality:** Maintain highest standards for products and internal procedures
- **Expand Products and IP Portfolios**
  - Develop new products that can solve the pain points of large-scale cell therapy manufacturing
  - Currently 7 granted U.S. patents and 12+ pending provisionals (U.S. & international)

New Facility and Increased Operational Capacity

4721 Calle Carga, Camarillo, California

- 63,800 sq.ft. on 4.5 acres
- Move completed in October 2020

Cleanroom for single-use product assembly

Biolab for bioprocess scale up development

Executive Team

Brian Lee, Ph.D

CEO

Co-founder with over 25 years of biotech R&D and management experience, including **Amgen** and **Merck & Co**.

Nelson Bermudez

COO

Over 25 years of executive management experience for biotech Operations and Manufacturing at **Amgen**

Mark Schneider

VP of Finance

Over 25 years of executive experience in financial, accounting, and business development in public companies, including **Amgen** and **Kythera**

Joe Petrosky

VP of Global Sales

Over 20 years of executive sales experience in biotech products, including **Millipore** and **Charter Medical**

Thank You For Attending

Q&A

"We look forward to serving you for your biomanufacturing needs!"