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 12, 2022

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 **best manufacturing platform** and **unsurpassed technical expertise** to unlock clinical and commercial scale manufacturing of allogeneic cell-based therapies.

Clinical Milestones of PSC-Derived Cell Therapy

A Cure for Type 1 Diabetes? For One Man, It Seems to Have Worked.

A new treatment using stem cells that produce insulin has surprised experts and given them hope for the 1.5 million Americans living with the disease.

VERTEX

Brian Shelton may be the first person cured of Type 1 diabetes. "It's a whole new life," Mr. Shelton said. "It's like a miracle."

The New York Times Nov. 27, 2021

CRISPR Therapeutics and ViaCyte, Inc. Announce First Patient Dosed in Phase 1 Clinical Trial of Novel Gene-Edited Cell Replacement Therapy for Treatment of Type 1 Diabetes (T1D)

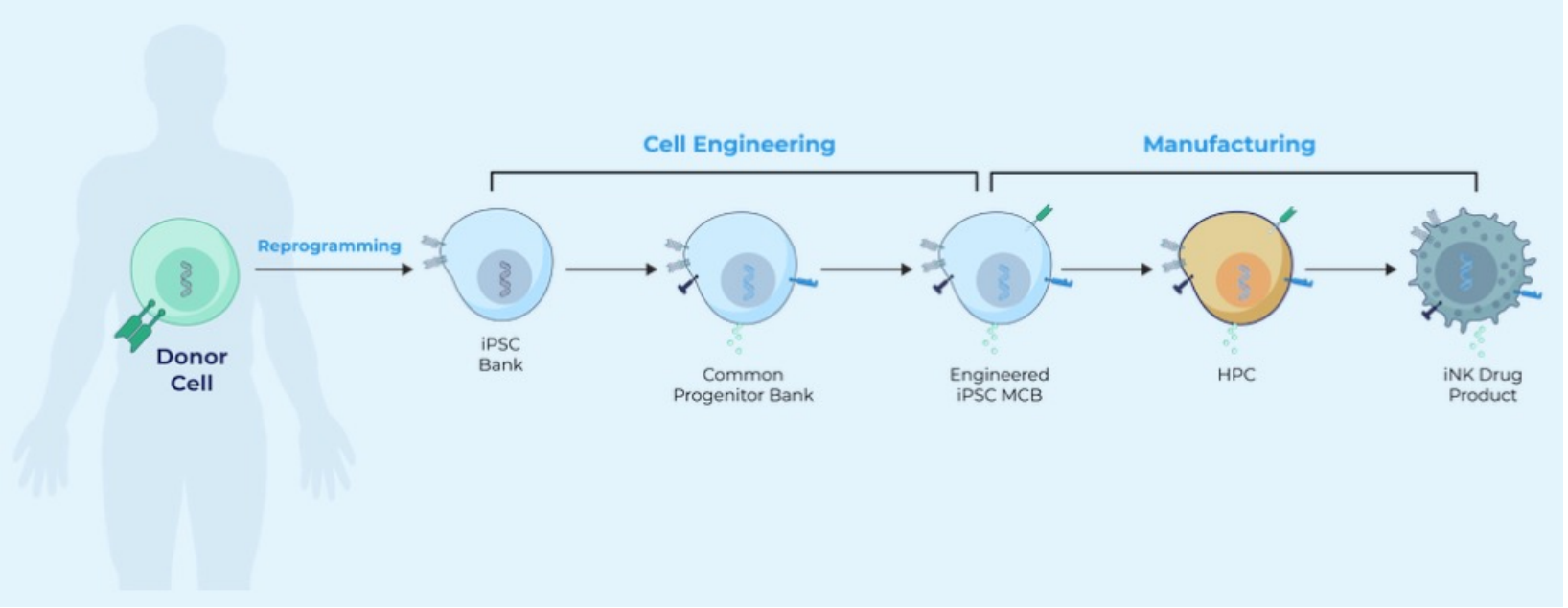
February 02, 2022 08:30 ET | Source: CRISPR Therapeutics AG

CRISPR THERAPEUTICS®

VIACYTE

Development of PSC-derived Allogeneic Immunotherapies

CENTURY THERAPEUTICS



editas MEDICINE

Allogeneic *Ex Vivo* Gene Edited Cell Medicines Including NK and T Cells

INNOVATIVE BIOPROCESS SOLUTIONS

Large Scale Autologous Cell Therapy By Tissue Engineering

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

Patient-derived Stem Cells

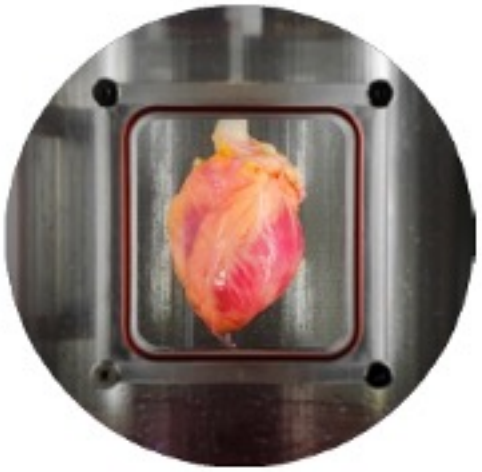
+

Large Scale Expansion and Differentiation into Cardiovascular and Parenchymal Cells

+

Healthy Mammalian ECM (Ghost Heart)

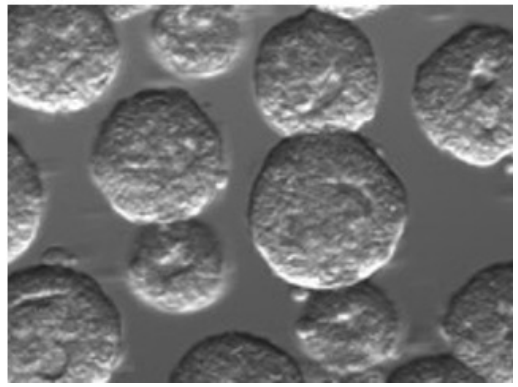
=



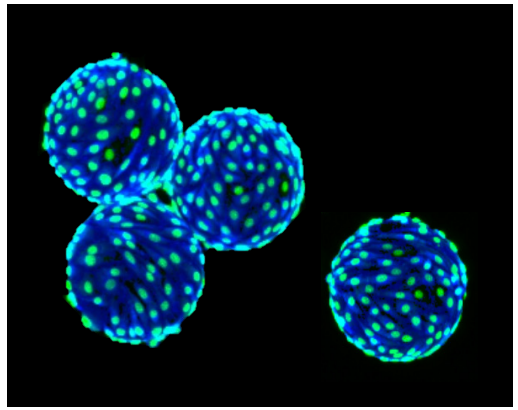
Bioengineered Autologous Heart

Human Cell Types Of Allogeneic Cell Therapy Products

- **Pluripotent Stem Cells (PSC) – Induced (iPSC) & Embryonic (ESC)**
  - Expansion and differentiation as aggregates in suspension
  - ~120 companies developing PSC-derived products
  - PBS working with 78



- **Human Primary Cells (HPC) – MSC, Exosomes, Chondrocytes**
  - Grown on the surface of microcarriers in suspension
  - ~120 companies developing HPC-derived products
  - PBS working with 69



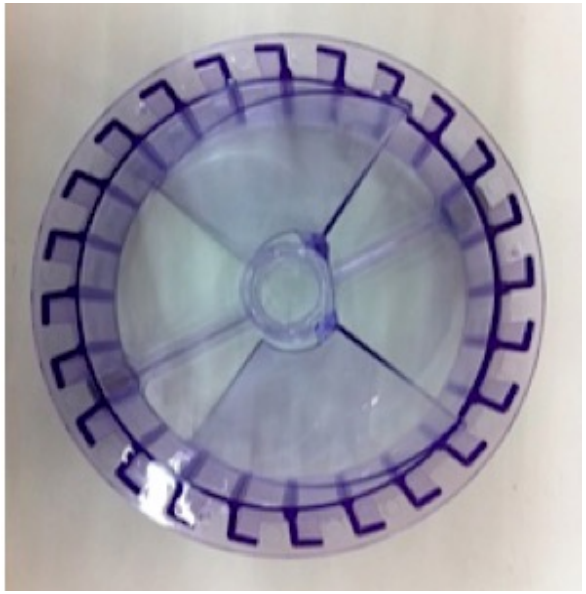
- 2D platforms commonly used are neither scalable nor cost effective: **3D needed** for **scale up**

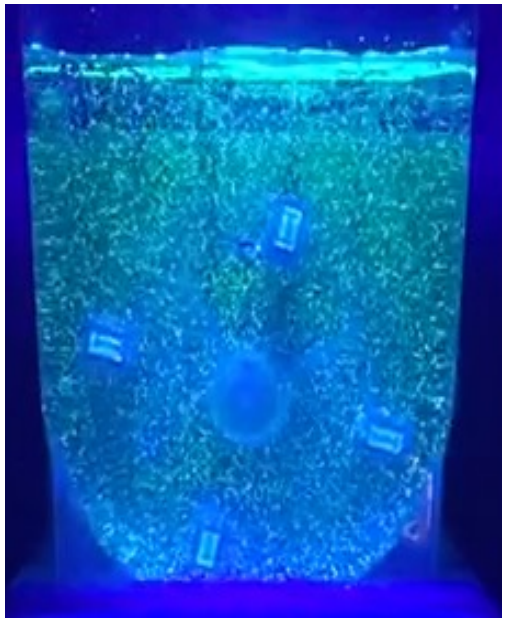
Manufacturing Challenges Of Allogeneic Cell Therapy Products

"Cell culture conditions are significantly different from biotech manufacturing experience"

- **Living cell** itself is the **product**
- **Anchorage-dependent** cells grown in suspension on surface of **microcarriers** or as **aggregates**
- These **large size particles** require **higher power inputs** (agitation) in conventional reactors
- Anchorage-dependent cells are **sensitive** to a bioreactor's **hydrodynamic conditions**
- Heterogeneous fluid mixing conditions during **volumetric scale up of conventional bioreactors** result in **inconsistent cell yields and quality** for human 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

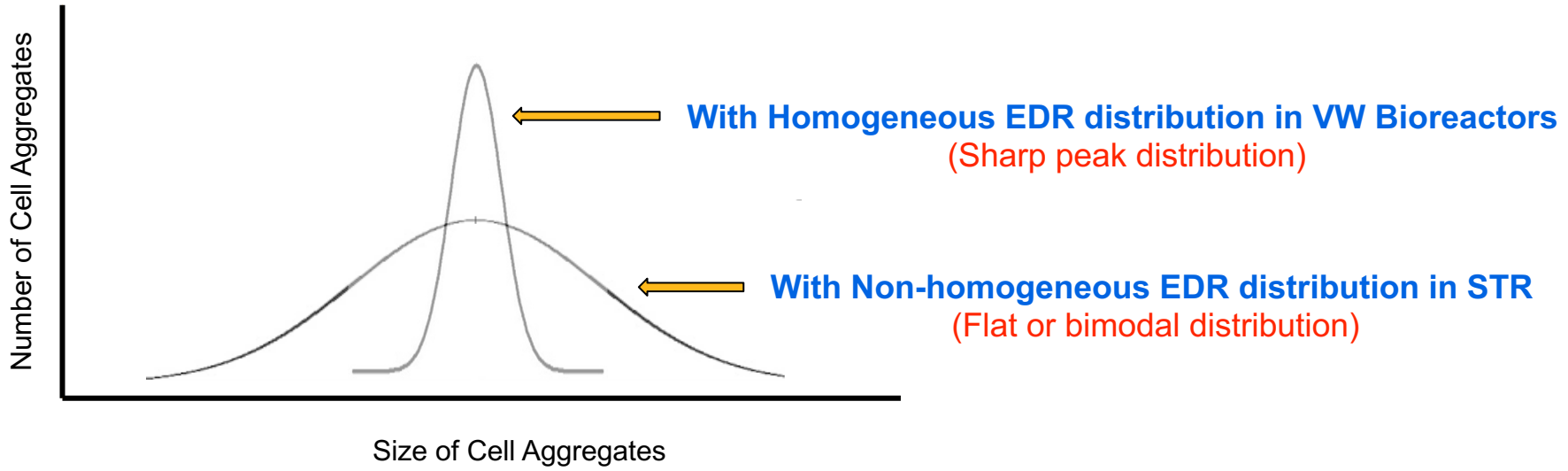
80 L

Contract Process Development

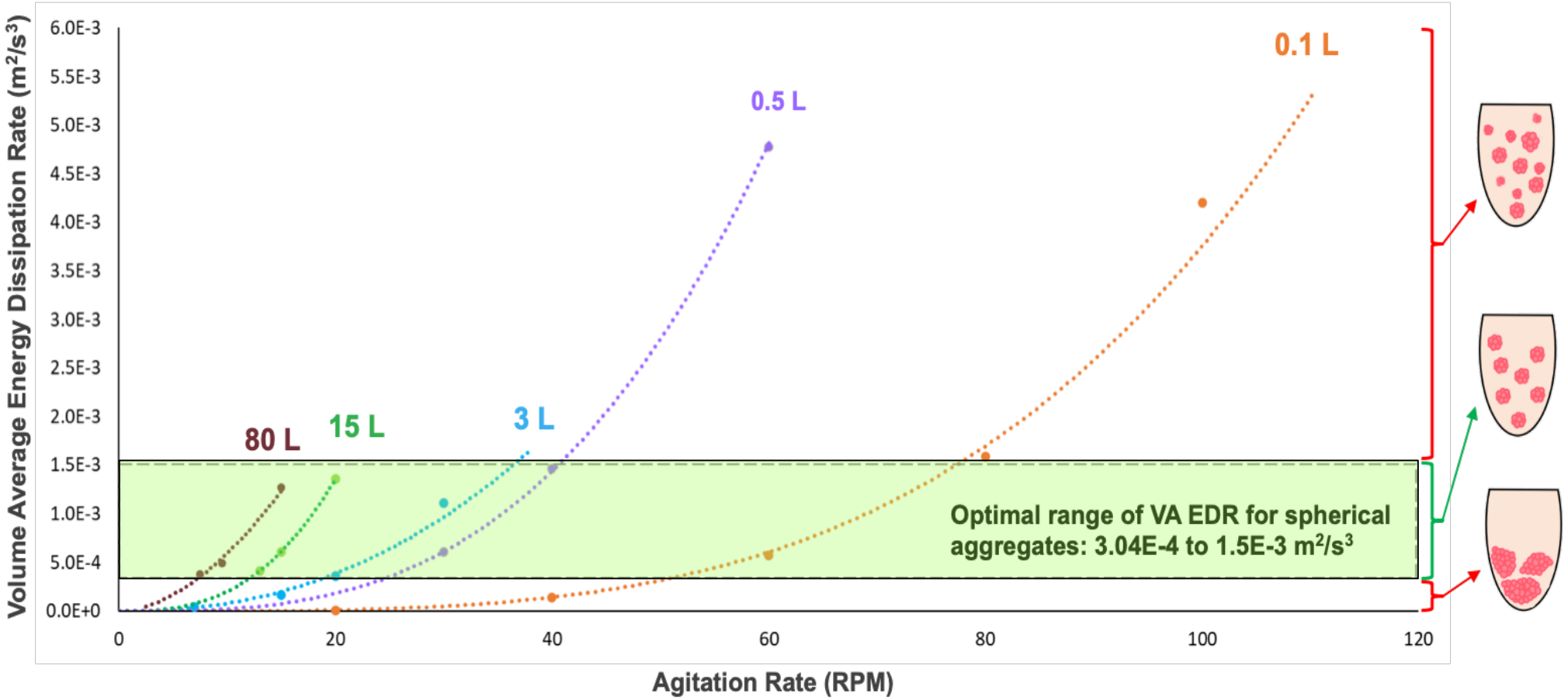
Uniformity of Aggregate Sizes and Morphology Is Critical for PSC Differentiation

- **Cell aggregate size varies inversely with local hydrodynamic conditions (Energy Dissipation Rates)**
  - Grown in High EDR condition → SMALLER size aggregates
  - Grown in Low EDR condition → LARGER size aggregates

- **Typical Size Distribution of Cell Aggregates Grown in Different Type of Bioreactors**



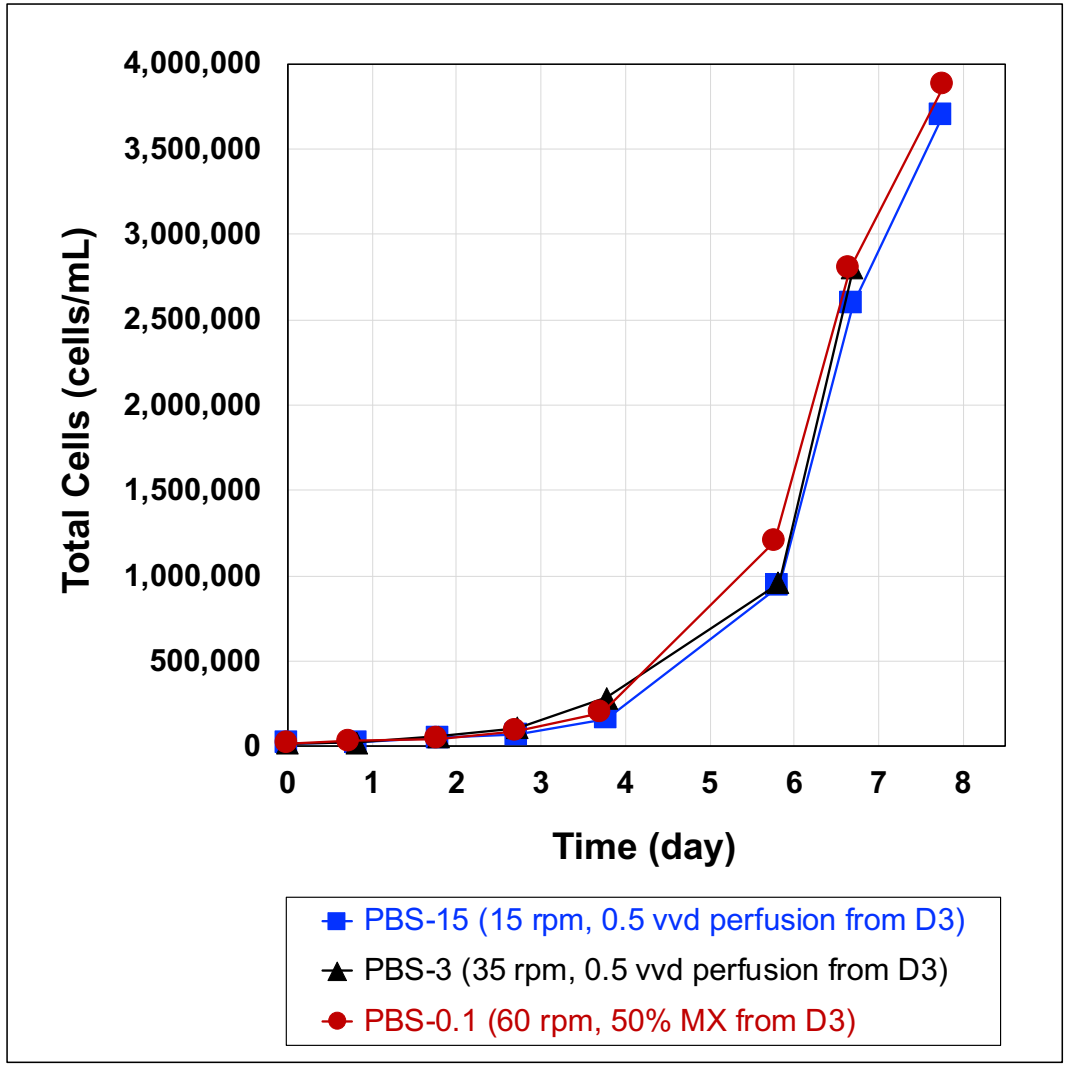
Scale-Up Correlations Using CFD Generated Hydrodynamic Variables



T. Dang et al. / Can J Chem Eng. 24253 (2021) 1-18

Patent Pending

Consistent PSC Growth As Aggregates In Various Scale VW Bioreactors



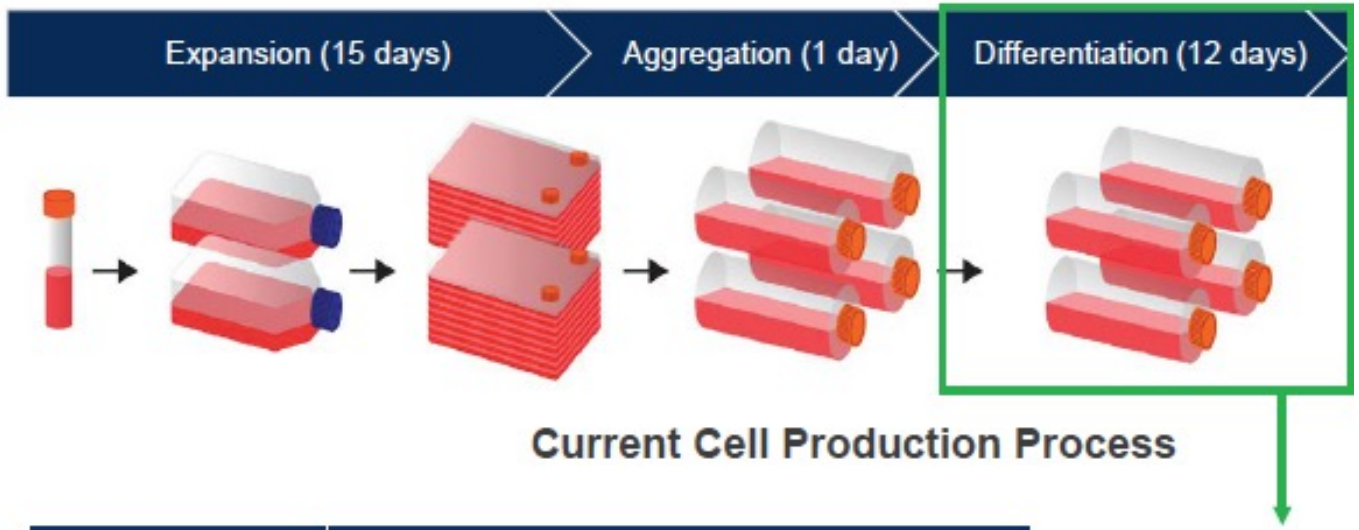
"Perfusion process improved cell yield and quality by achieving uniform cell aggregate sizes and shapes"

PBS-0.1

PBS-3

PBS 15

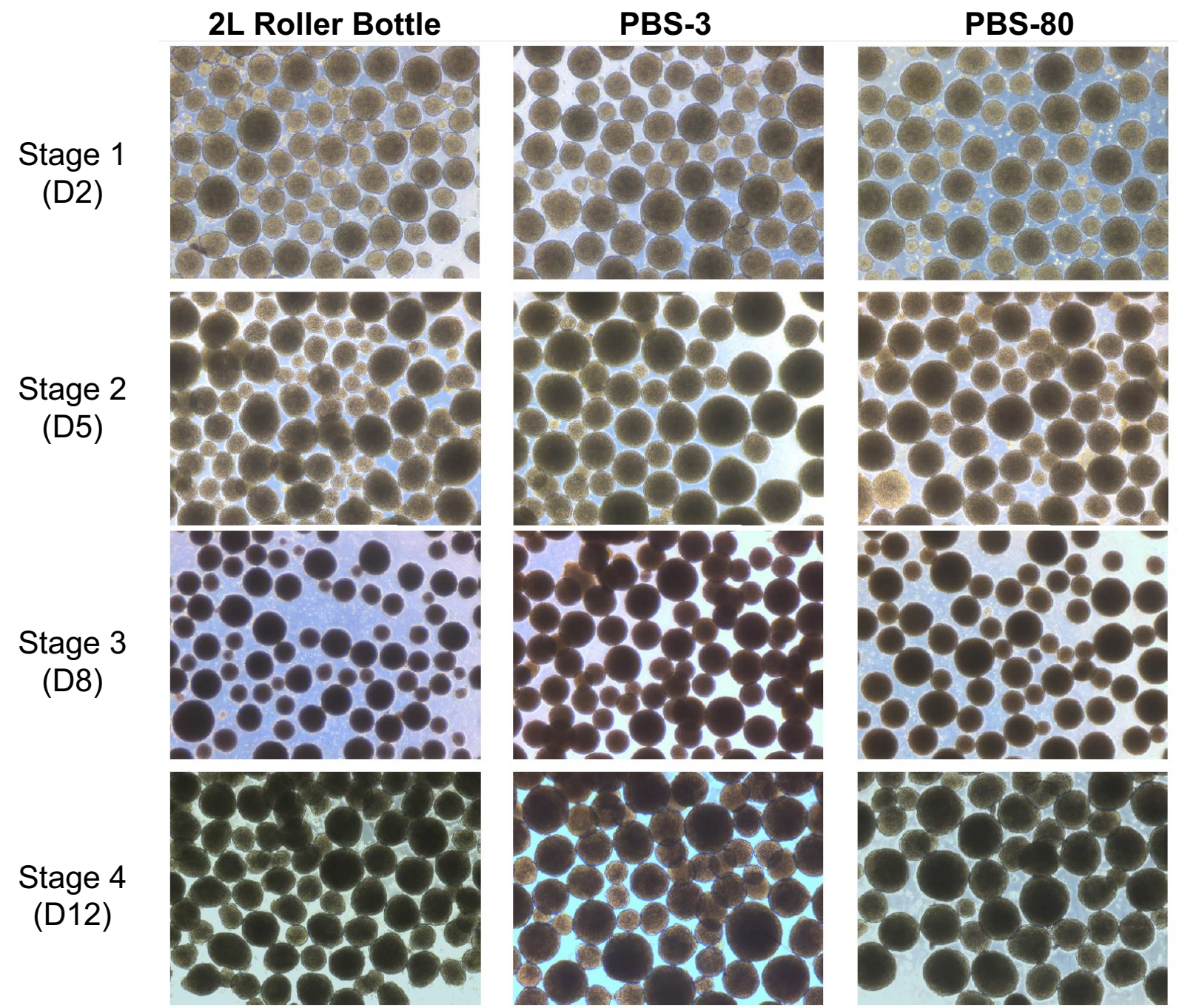
Successful Scale Up of Endocrine Cell Differentiation In PBS-80 Bioreactor



Current Cell Production Process

PEC-01 Production Scale	Vessels Required	
	QTY 2L RB	QTY 80L
1x (current)	53	0.5
2x	106	1
4x	212	2
10x	530	5

Scale Up of PSC Differentiation into Endocrine Cells in PBS-80 Bioreactor



VIACYTE Regenerating Health™

Customers and Collaborators

Partnership with Stem Cell Technologies

- PBS-Mini Product Launch by Stem Cell Technologies
- Recommendation to Scale from 2 mL to 500 mL Suspension Culture
- Ongoing Collaborations to Increase Scale and Capacity

6-well plate on orbital shaker

2 mL/well; 70 RPM

Nalgene™ Rapid-Flow™ Sterile Filter Storage Bottles on orbital shaker (ThermoFisher 455-0250)

PBS MINI Bioreactors
Base Unit: IA-UNI-B-501
Vessels: IA-0.1-D-001; IA-0.5-D-001

Thank You For Attending

Q & A

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