



Commercialization of Cellular Therapies

Lonza

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EuroBIO 2009
September 25, 2009



What does “Commercial Scale” mean anyway?

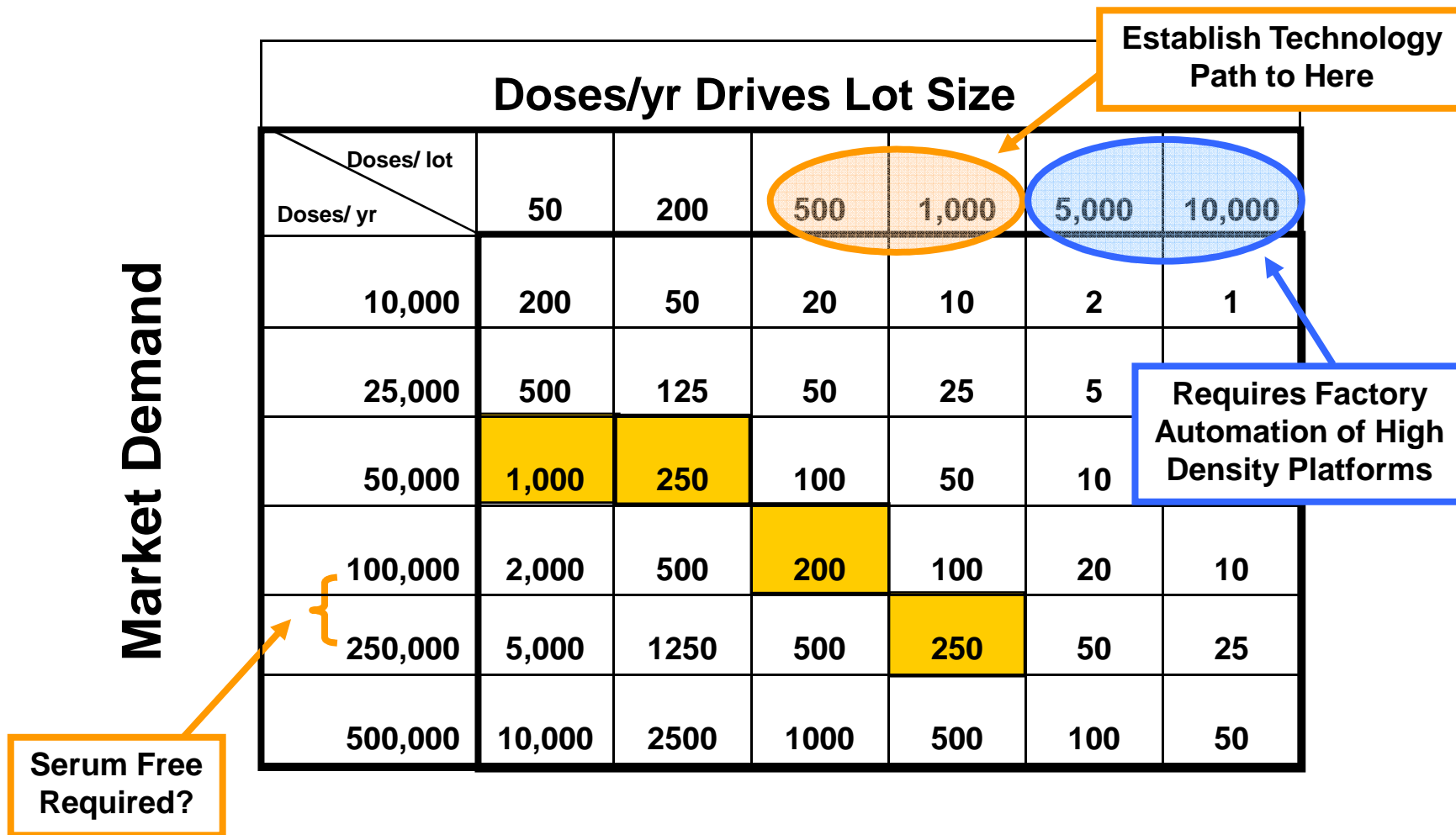
Start with the end in mind...

- How many patients?
- How many doses?
- How many cells per dose?
- What packaging?
- Process – Autologous or Allogeneic
 - Facilities
 - Labor
 - Materials management
 - Logistics and distribution (global)
 - Regulatory differences world-wide

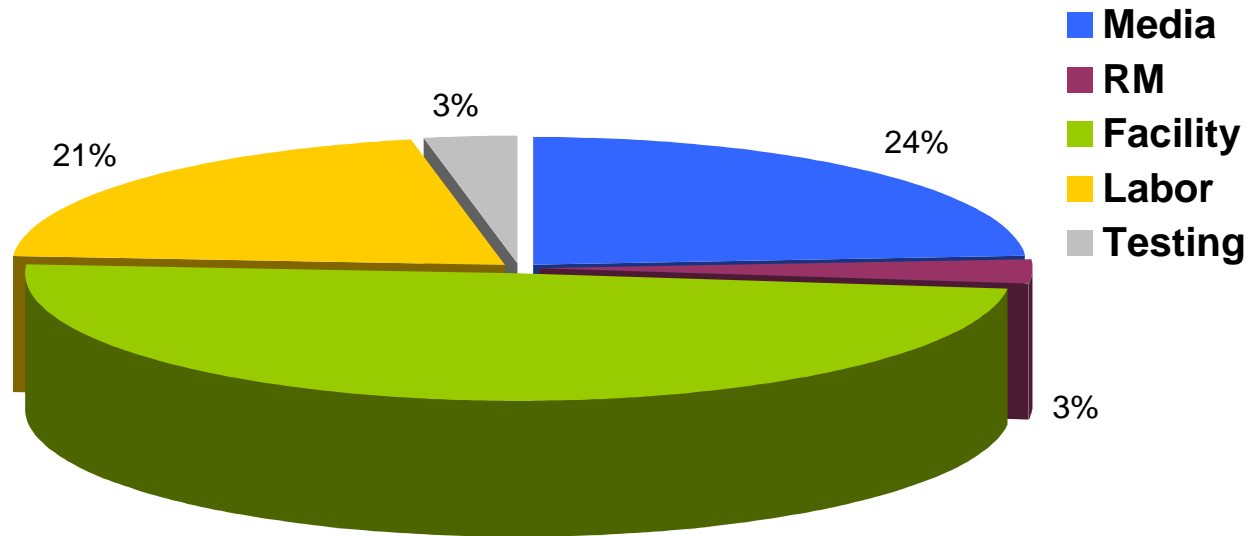


Where Do We Need to Go?

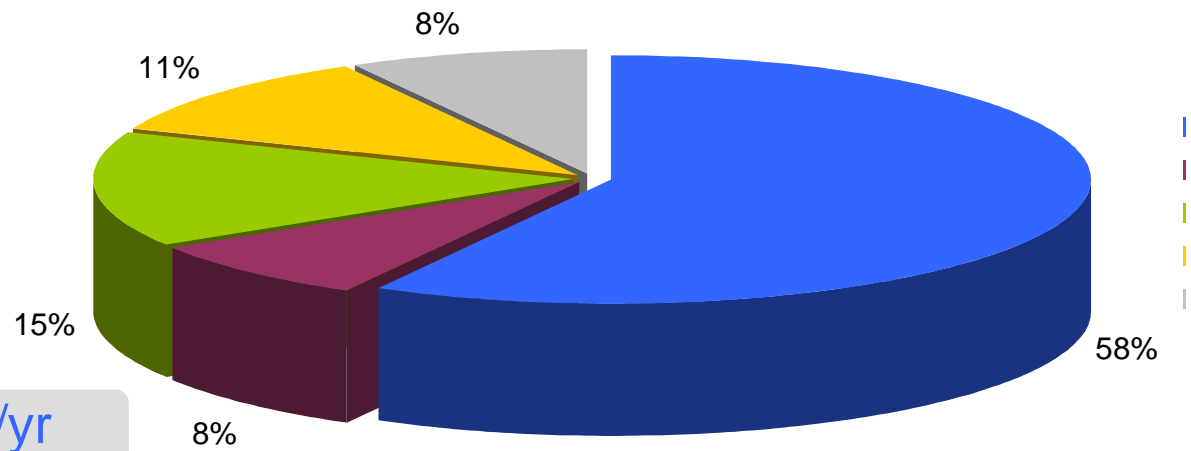
First, Establish Lot Size Requirements



CoGs Breakdown at Clinical and Commercial Scales (allogeneic product)

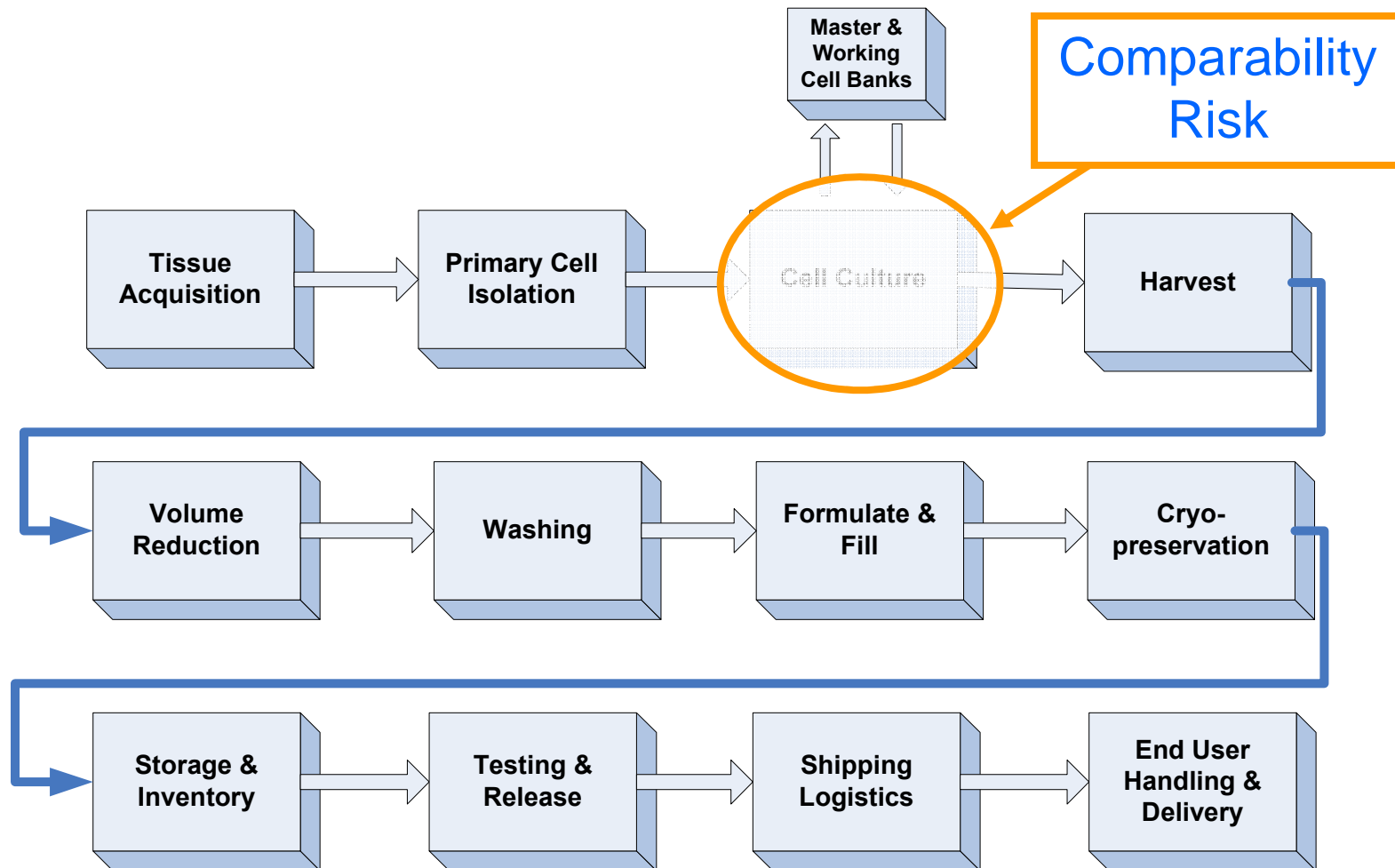


~1000 doses/yr



~ 100,000 doses/yr

Challenges for Scale Up



Scalable Cell Culture

Important to think ahead to commercial scale because each step up can be a major process change



10 Patients



100 Patients



1,000's
Patients

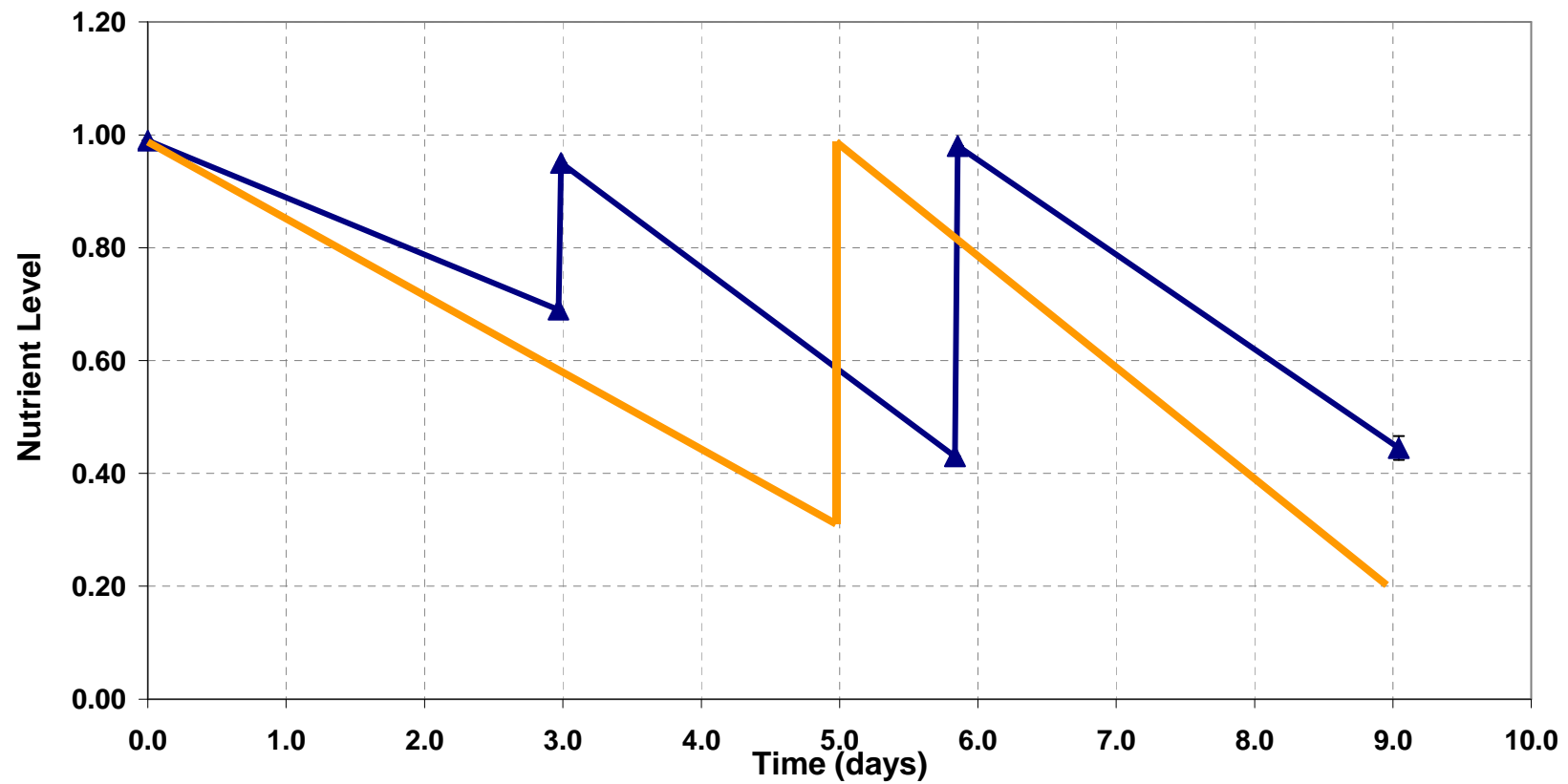


10,000's
Patients

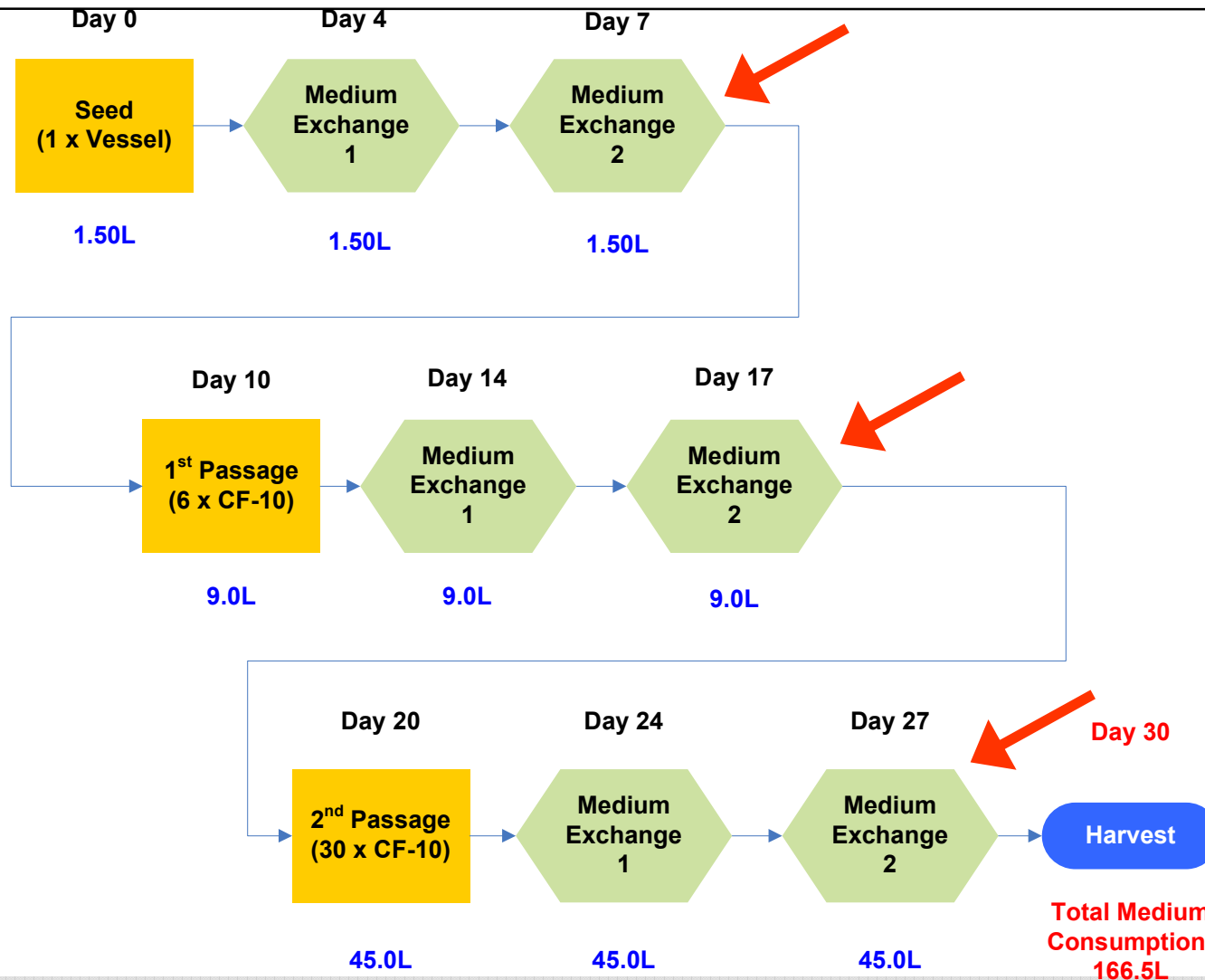


1,000,000's
Patients (?)

Nutrient & Metabolite Analysis Drives Media Design & Feed Strategy

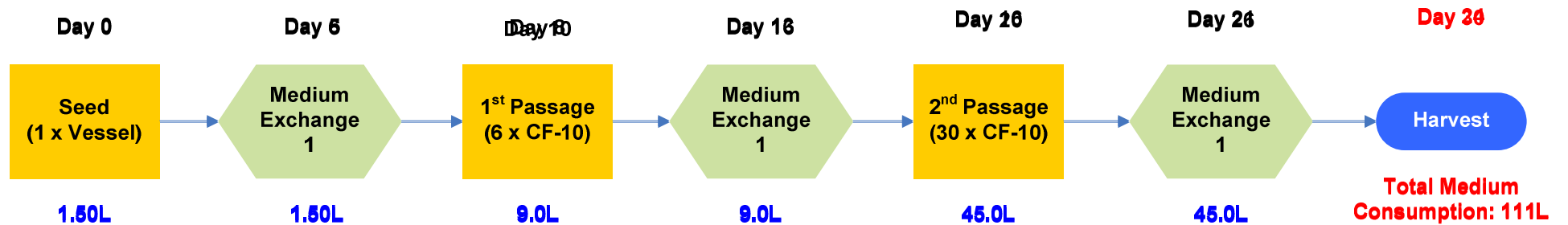


Optimized Medium Usage



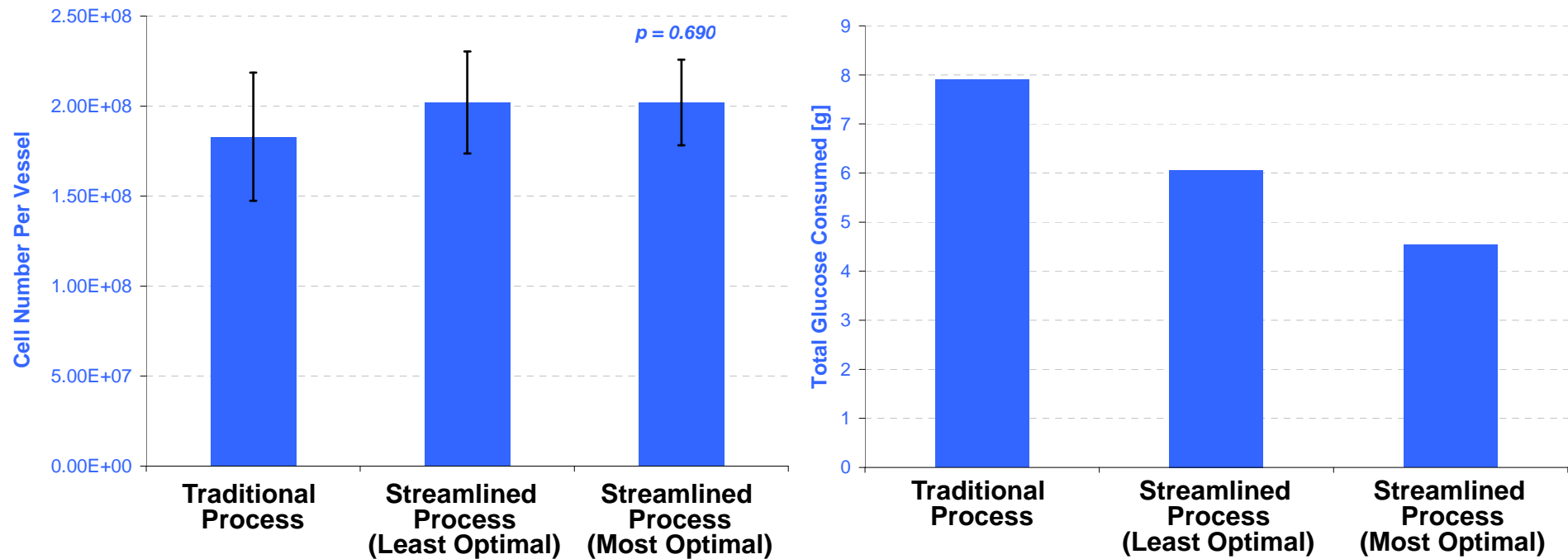
Optimized Medium Usage

Vol/Feed	# Feeds	Total Vessels	Doses	Total Media	Media \$/L	Total Cost	\$ /Dose
1.5	3	37	50	166.5	\$150	\$24,975	\$500

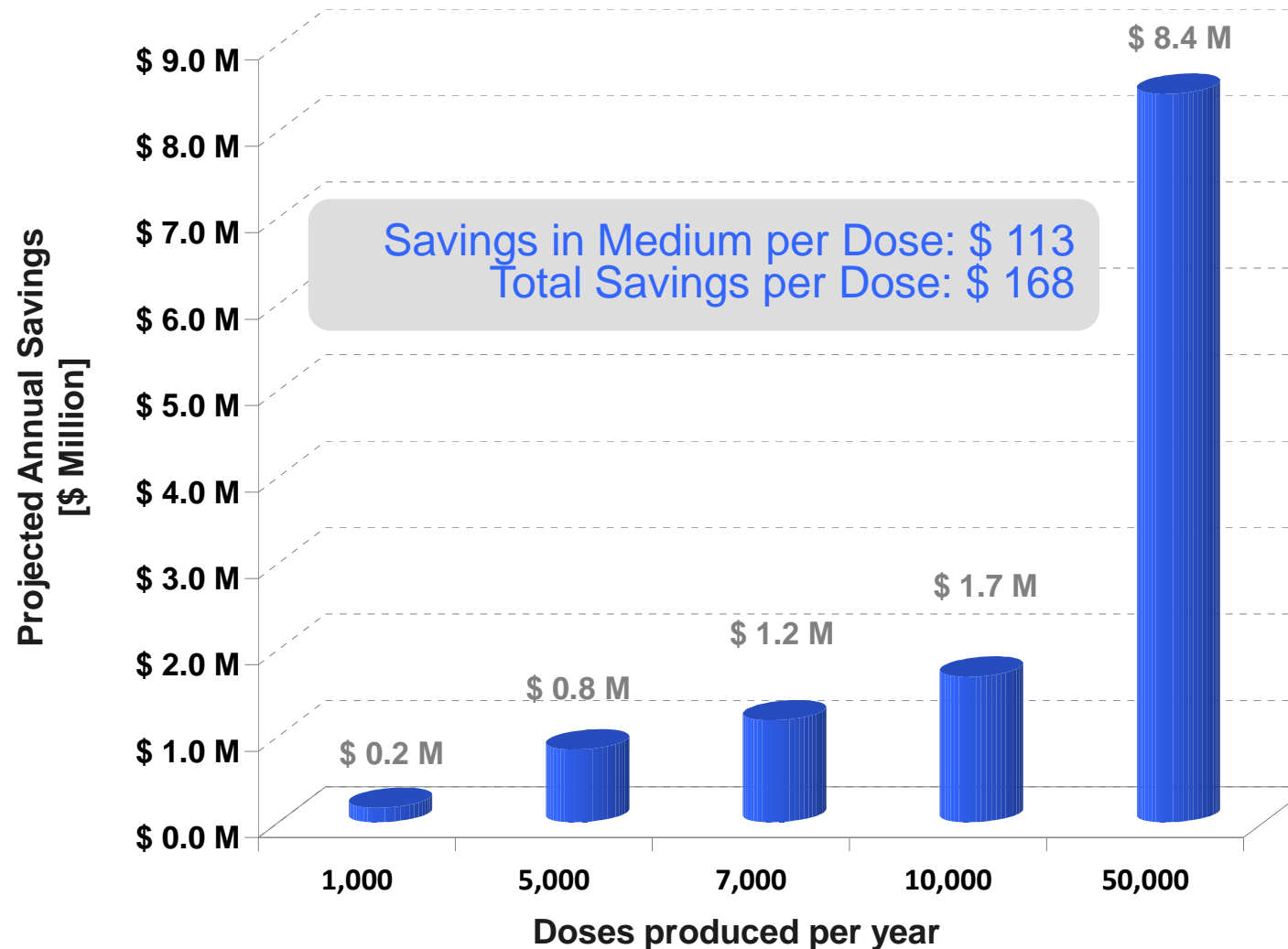


Streamlined process comparable in yields

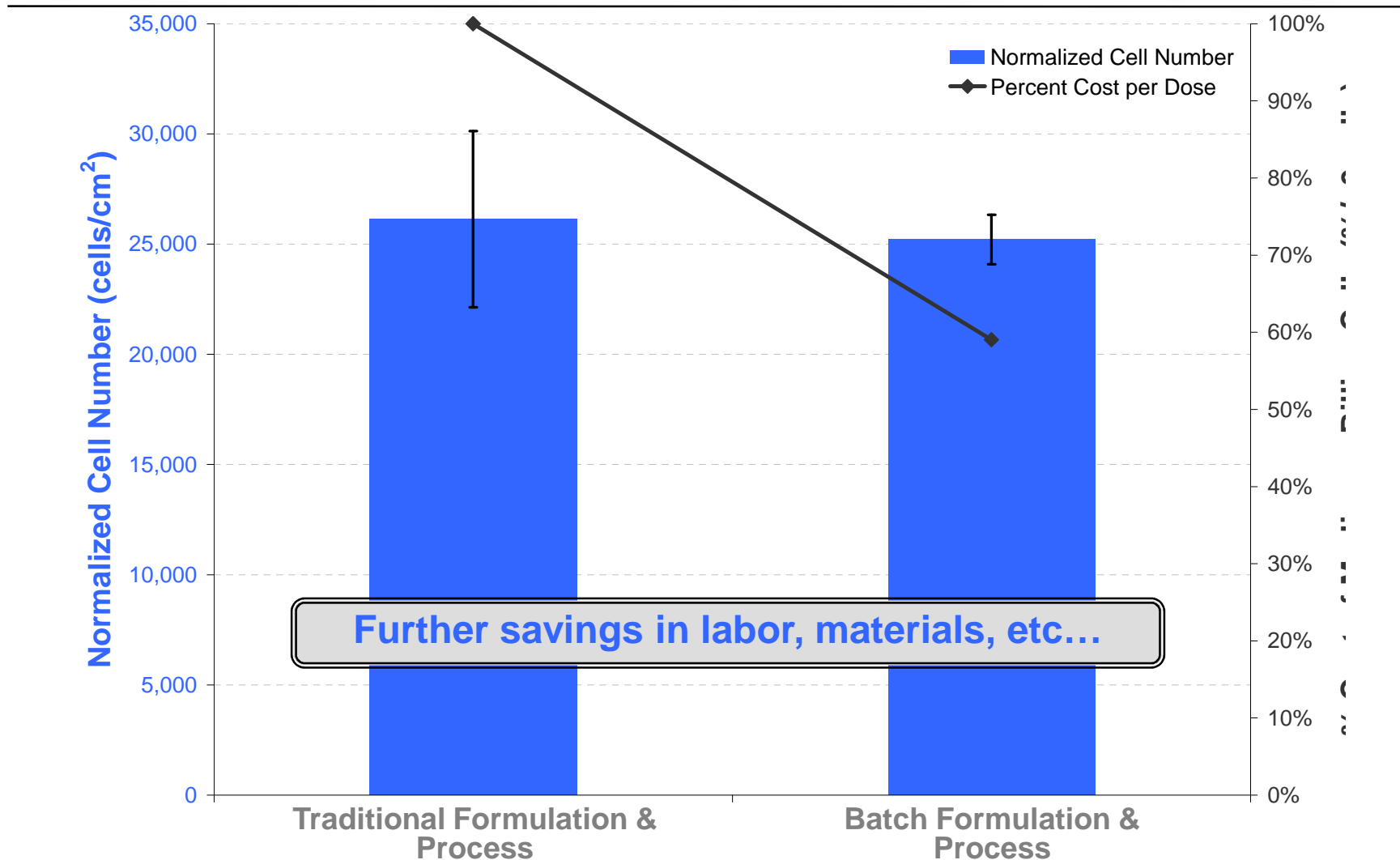
N = 3 donors, 3 vessels per condition



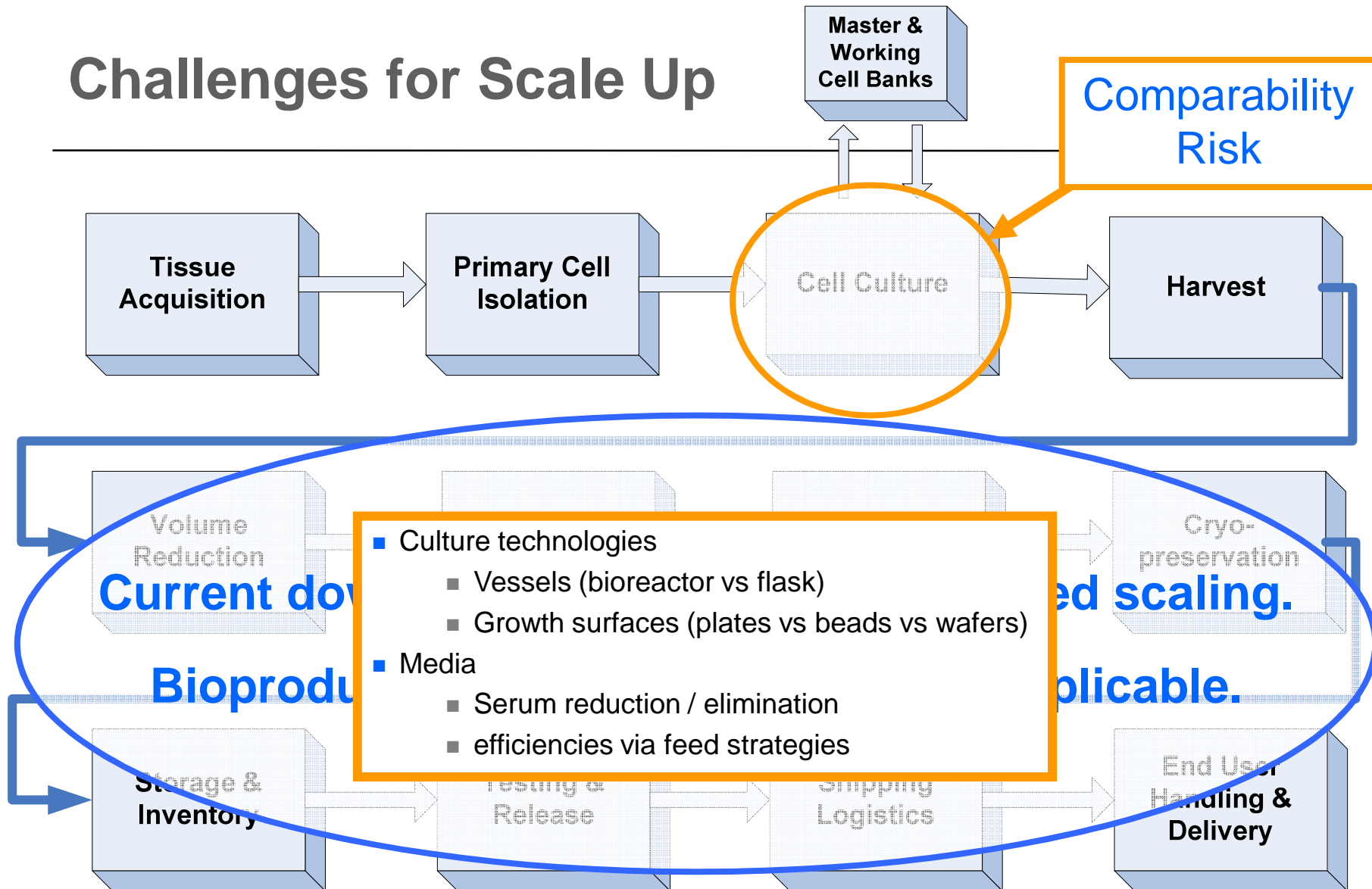
Cost savings become significant at early market scales



New media formulations enable batch-style culture of stem cells

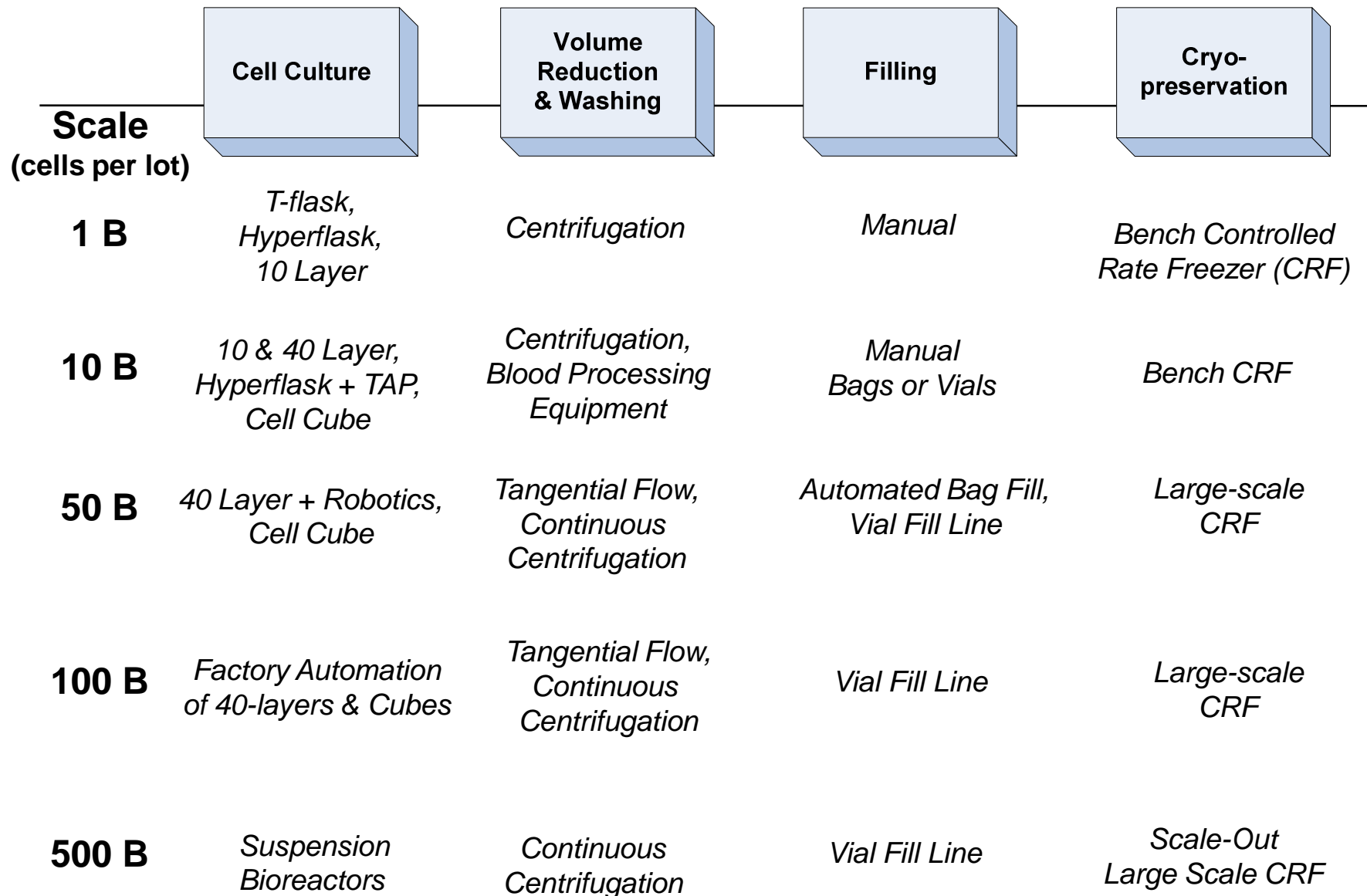


Challenges for Scale Up

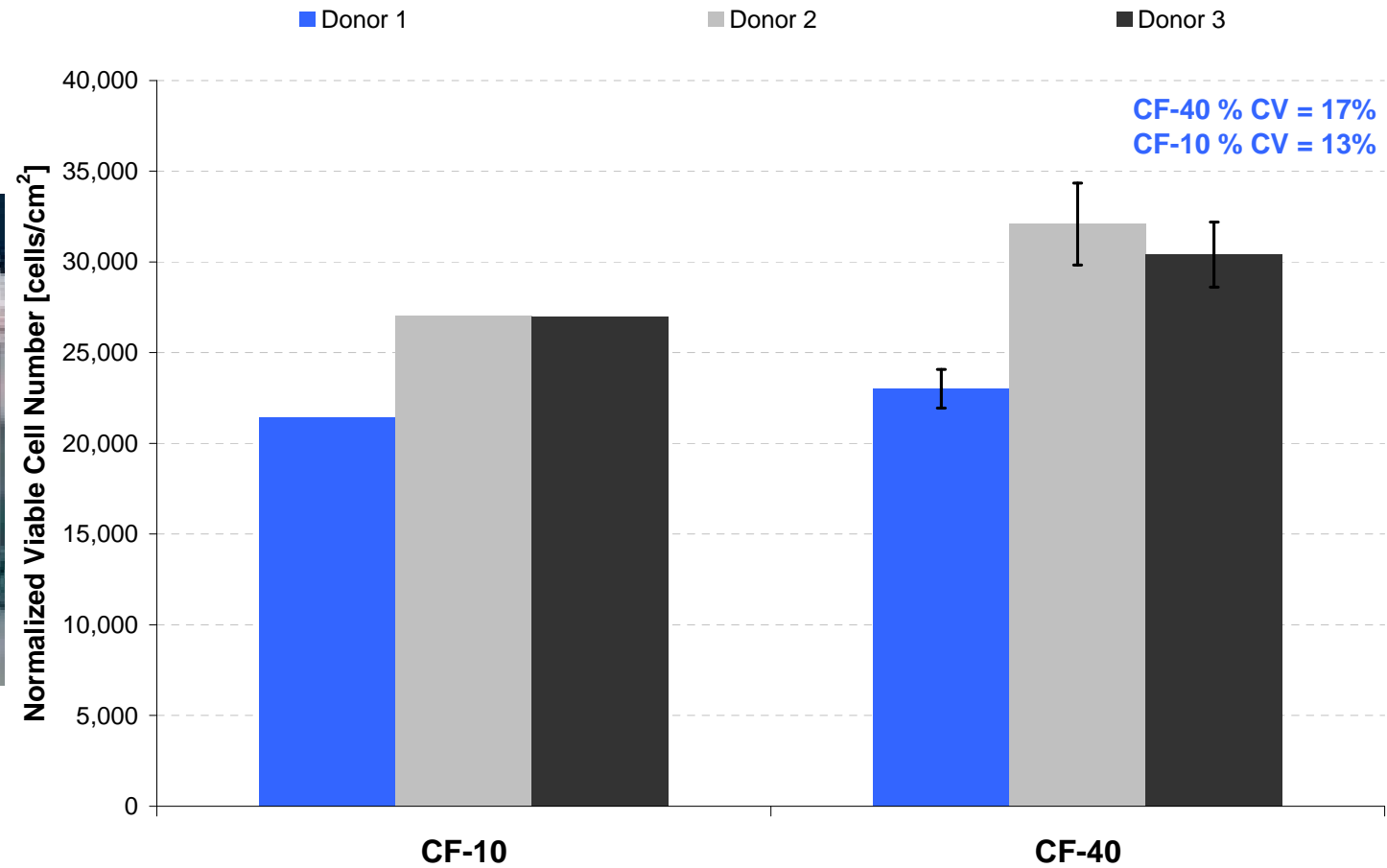


Technology Landscape for Scalable Manufacturing

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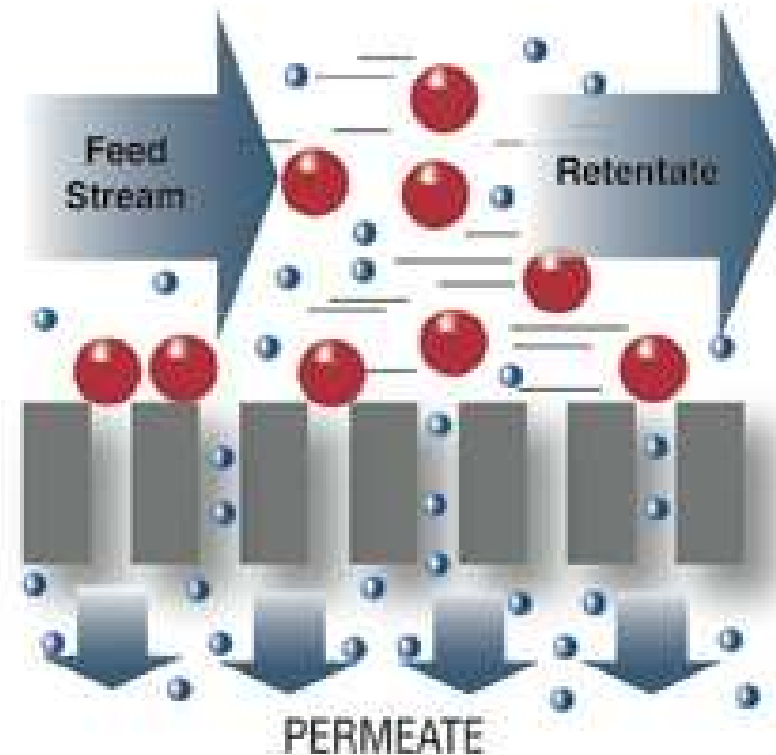
Comparable Yield between 10 & 40-Layers



Volume Reduction and Washing

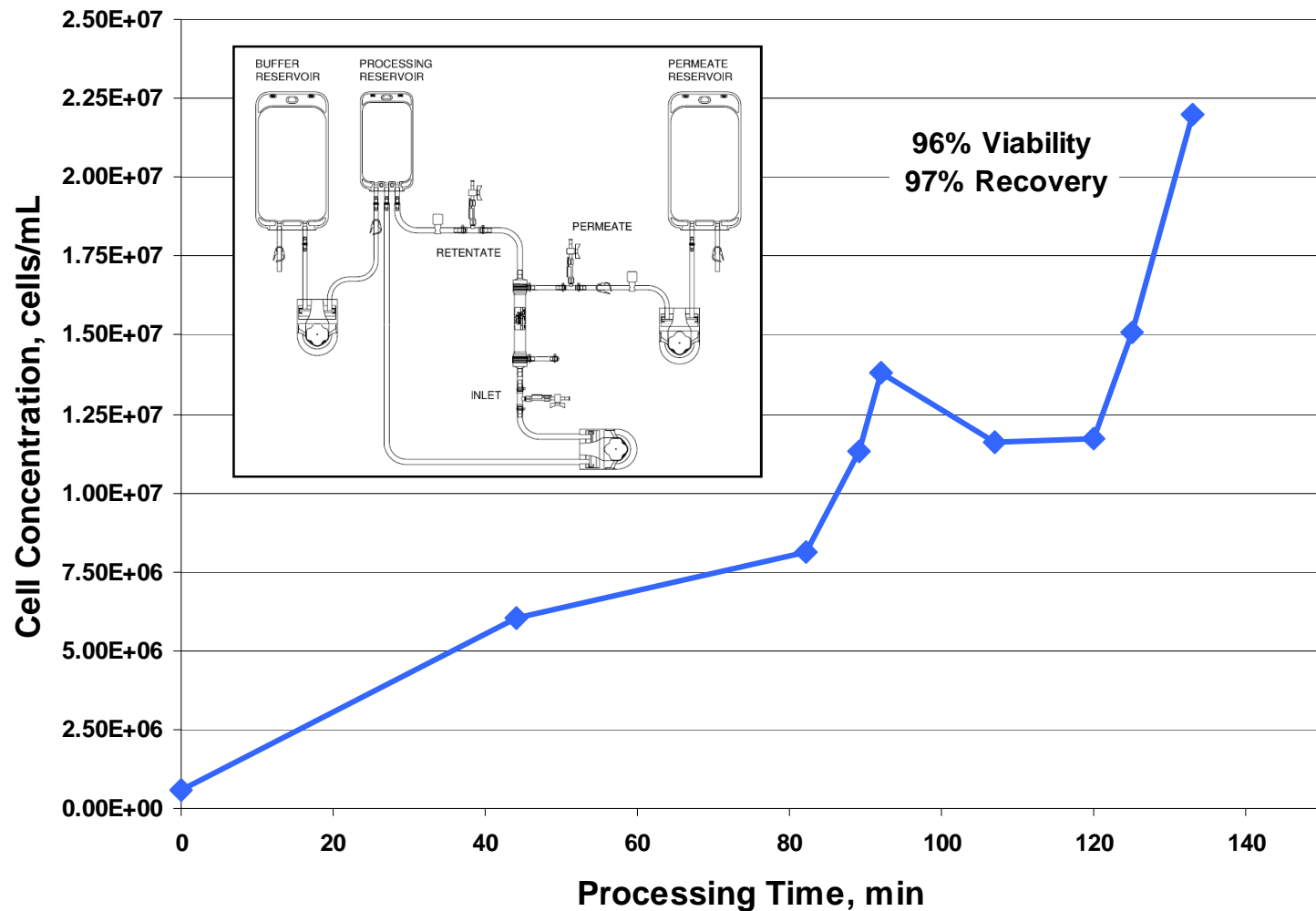
Scalable bioprocessing technologies must be adopted

- TFF
- Continuous centrifugation
- Next-gen technologies designed specifically for Cell Therapy

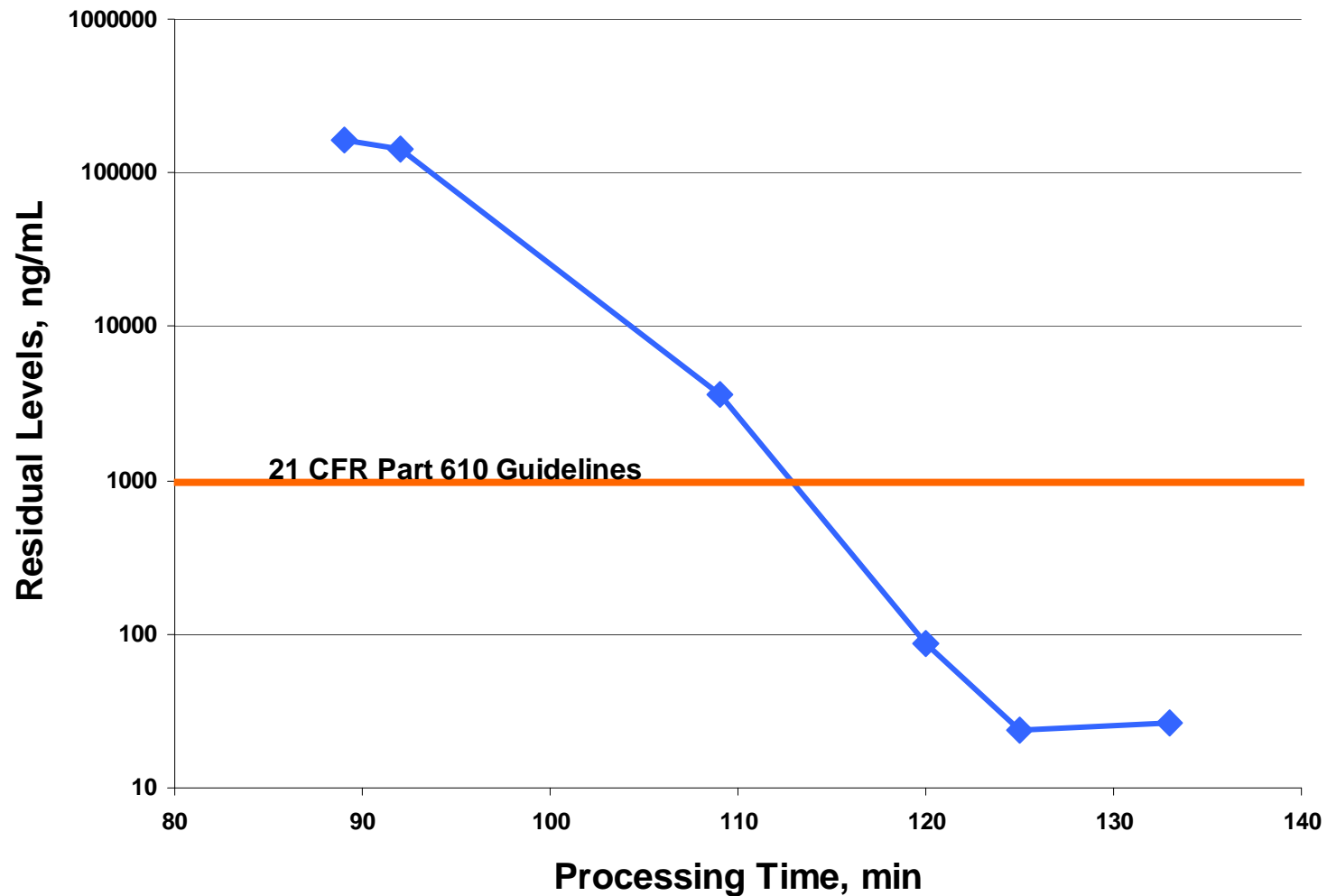


Tangential (Cross) Flow Filtration
(high permeate rate)

Single-use set-up for TFF-based volume reduction and wash of 25L harvest



Fluid exchange decreases residuals quickly



5 Steps to a Successful CMO Relationship

1. Plan for success

- Start process development early especially around media formulation (e.g. NAO, CD) and optimize media usage
- Understand your true costs and targeted cost of goods
- Map out contingency plans

2. Set realistic timelines

- Be realistic about patient enrollment

3. Understand scaling issues in **your process**

- Close the system as you scale up
- Are your cells well characterized?
 - Robust potency and purity assays
 - When to validate?
- Dosing requirements including packaging
 - Bags versus vials
 - Storage requirements

5 Steps to a Successful CMO Relationship (continued)

4. Plan to spend a lot of time with your CMO friends

- Attend regularly scheduled meetings
- Share information freely and communicate clearly
- Make your team available for discussions

5. Seek advice from those who have been there, done that

Thank you!

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