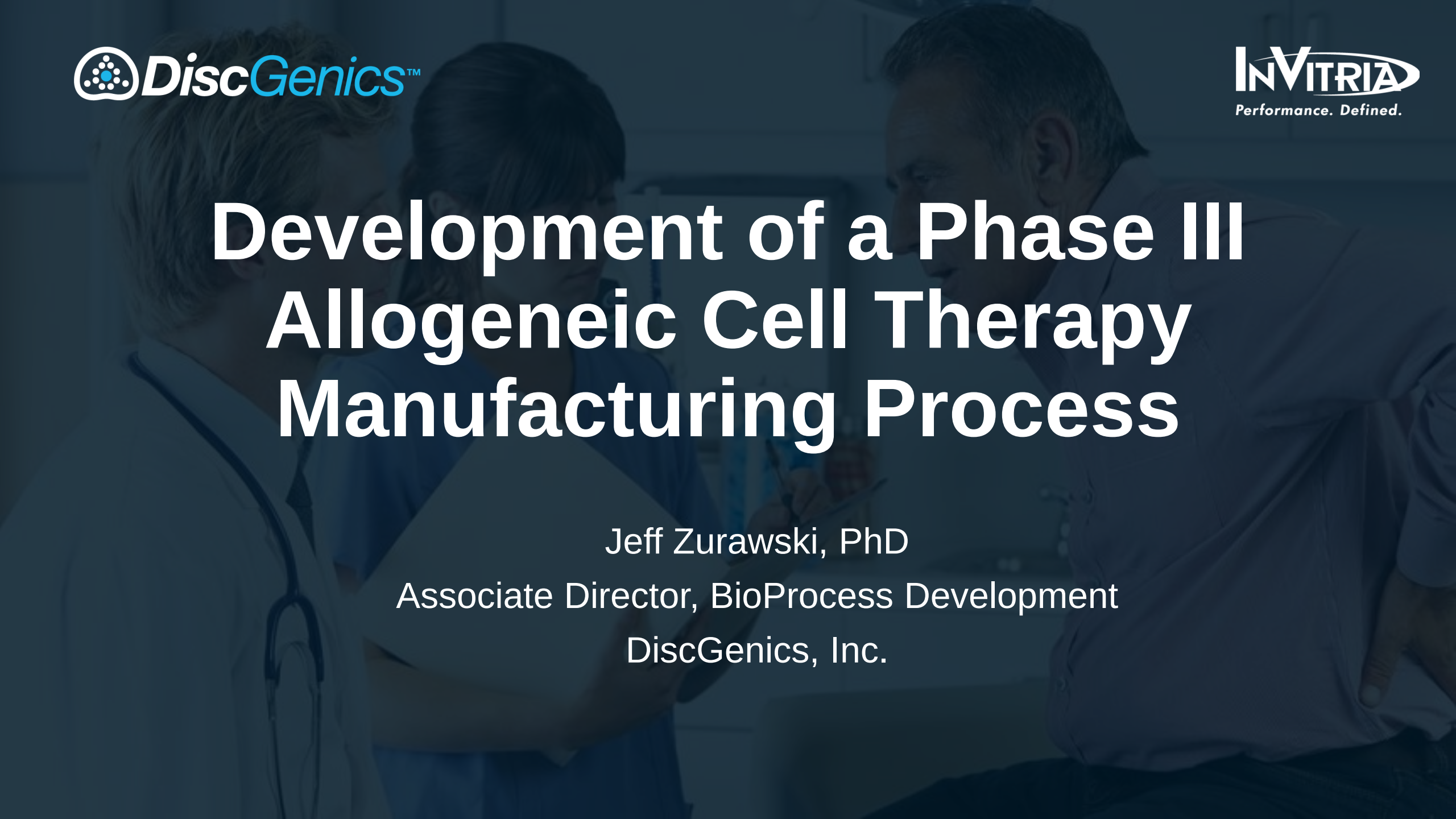


Development of a Phase III Allogeneic Cell Therapy Manufacturing Process

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DiscGenics™

REVOLUTIONIZING CARE FOR CHRONIC BACK PAIN

Lumbar Disc Degeneration



Affects more than 250 million individuals worldwide every year [1]



Is a leading cause of disability worldwide [2]



Costs more than $100B per year in the U.S. alone [3]



Is the primary reason for non-cancer opioid prescriptions [4]

The Problem

Lumbar disc degeneration is a serious medical condition with a profound lack of treatment options that can lead to missed work, lost wages and addiction to pain medication, including opioids.

The Solution

DiscGenics is the only company in the world to develop an allogeneic cell therapy that originates from intervertebral disc tissue to treat lumbar disc degeneration.

Allogeneic Disc Progenitor Cells Safely Increase Disc Volume and Improve Pain, Disability and Quality of Life in Patients with Lumbar Disc Degeneration

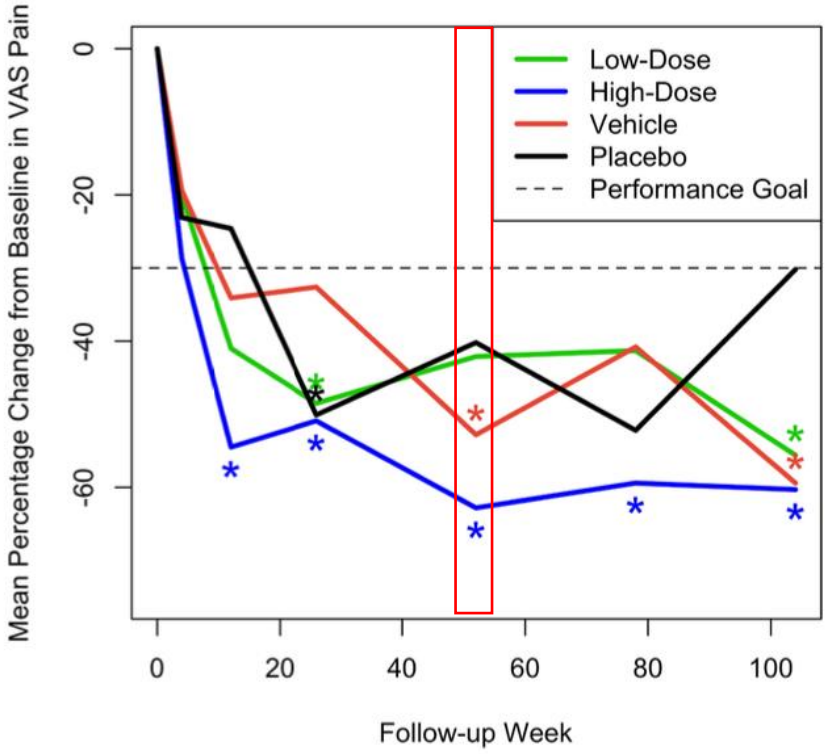


Figure 2. Mean percent change across time from baseline in visual analog scale (VAS) pain scores for the 4 treatment groups. Asterisks denote statistically significant improvement of greater than 30%.



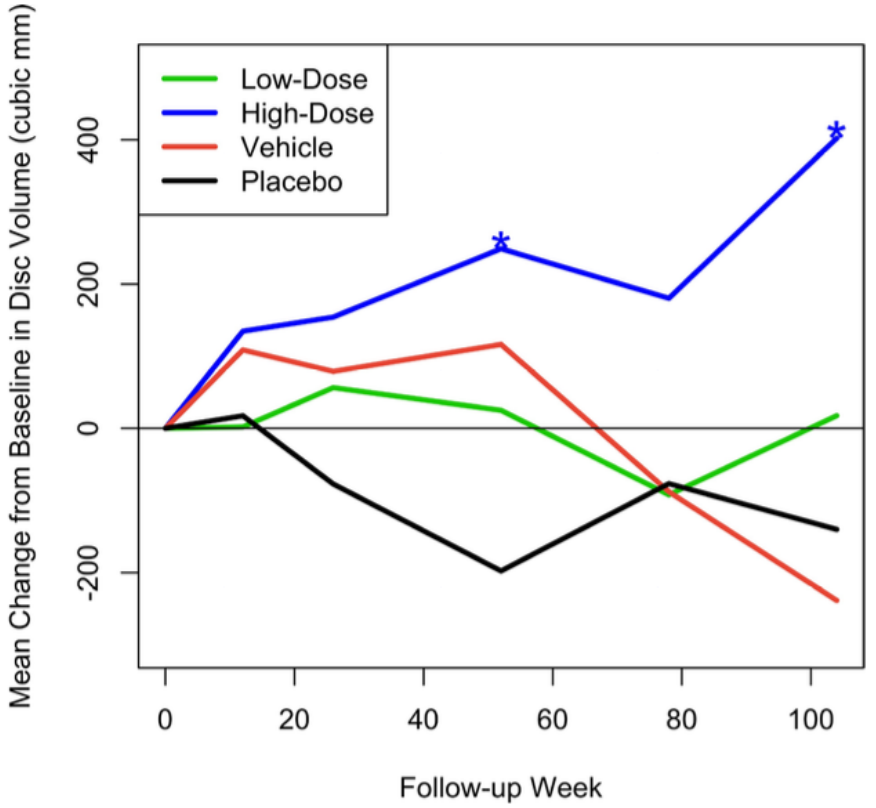


Figure 5. Mean change from baseline in disc volume (mm^3). Asterisks denote statistically significant change.

[5] Gornet et al., 2024

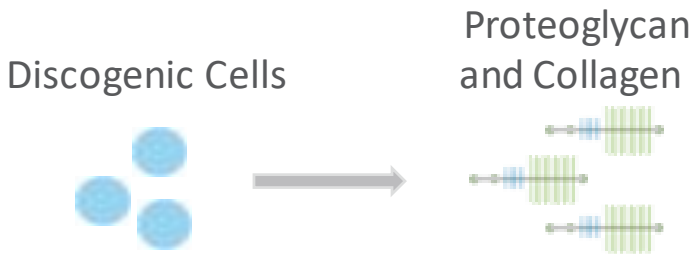
Overview

Drug Product Specifications
- Potency Attributes -> MOA

Manufacturing Process
- Scalability – Eliminate flask culture and viscous media
- Process Control
- Comparability to Phase I/II

Raw Materials
- Raw Material Control
- Human Derived and Proprietary Formulations
- Comparability to Phase I/II

Managing Donor Variability
- Small Scale Model Screening





Phase III – Drug Product Specification

Phase I/II Specifications:

- Appearance
- Cell Density and Viability
- Identity
- Purity
- Safety (Endotoxin, Mycoplasma, Sterility)

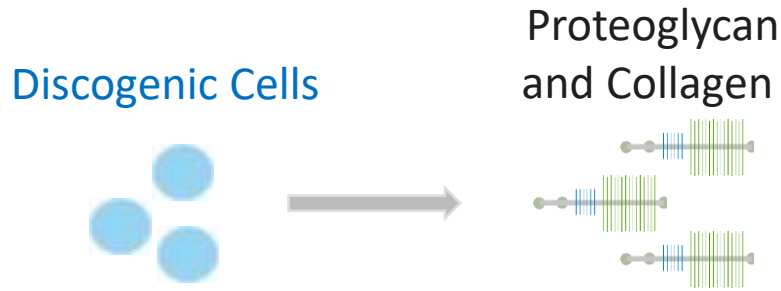
Anti-inflammatory



Phase III Specifications:

- Phase I/II +
- Potency
- Functional Excipients
- Residual Impurities
- Safety (viral)

Extracellular Matrix (ECM)



Phase I/II Manufacturing Process

Bench Scale, Manual and Open

Flask Culture with Viscous Suspension Media

Proprietary and Human Derived Raw Materials









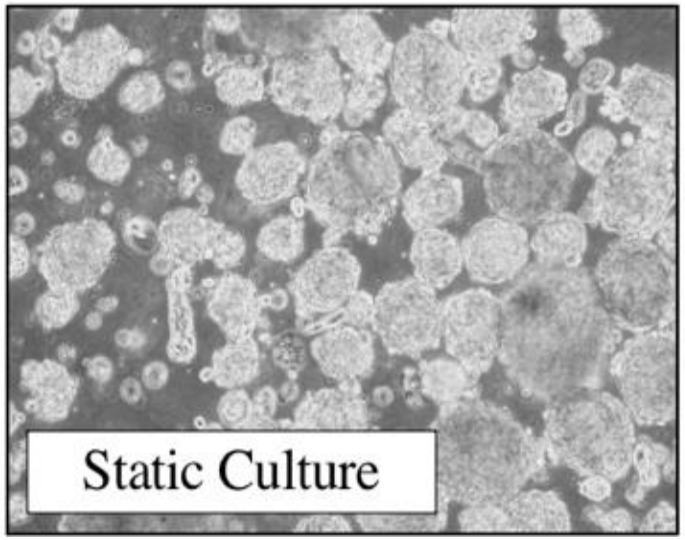


~100 doses

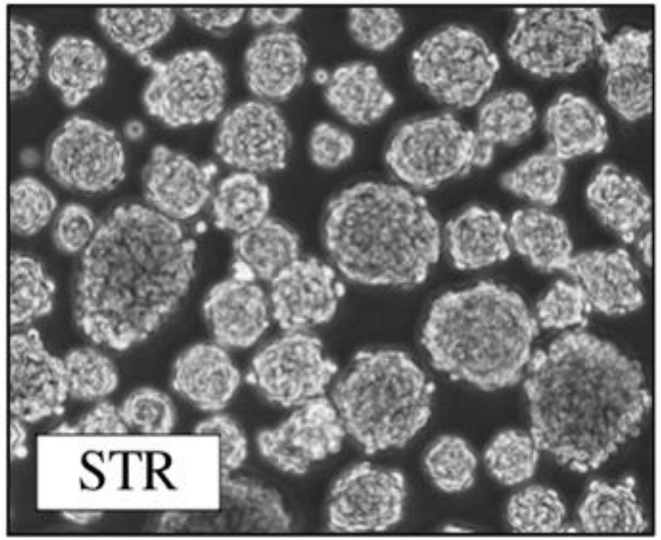
Scalable Suspension Culture System

- Assessed many modalities for dynamic culture
  - Vertical wheel, rocker bag, shaker flask, and stirred tank reactors
  - Selection of stirred tank bioreactors – 250 mL small scale model



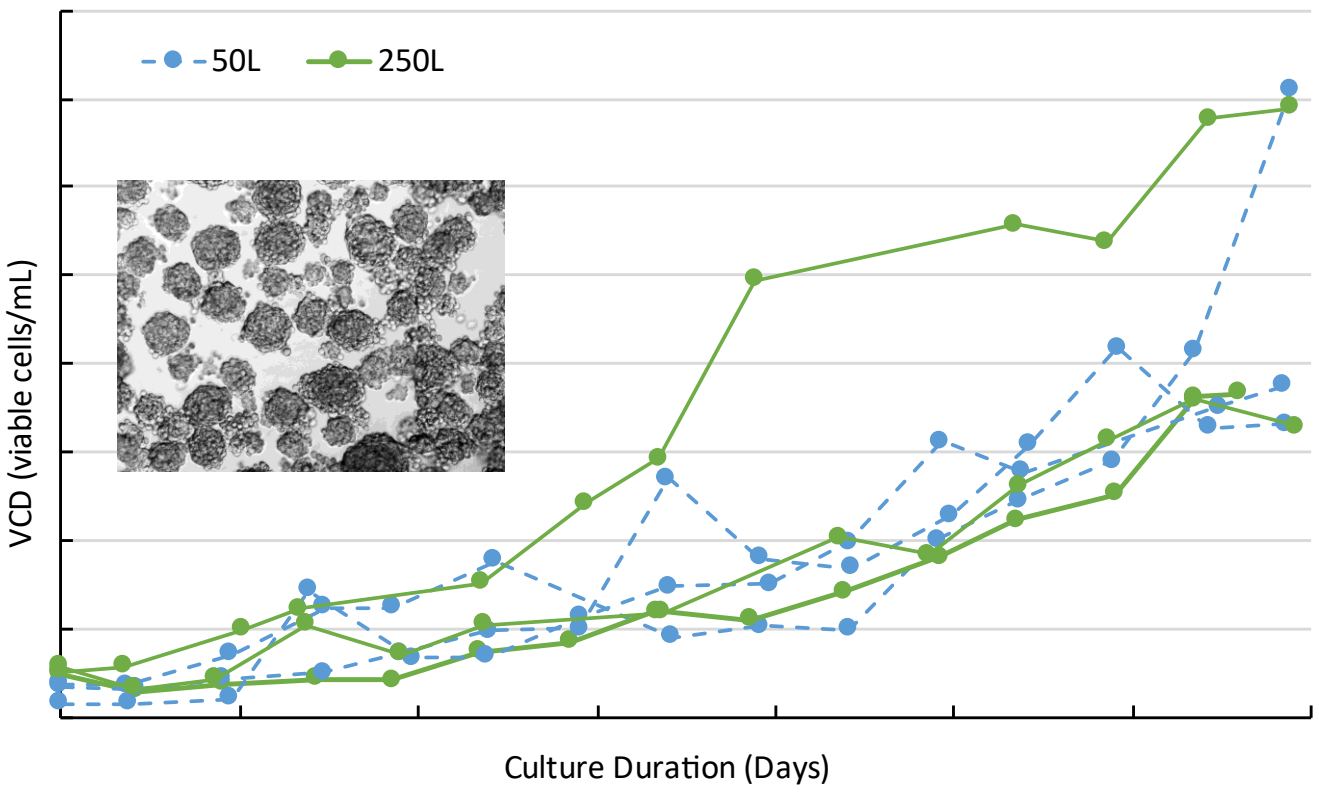


✓ Eliminate flask culture
✓ Eliminate viscous media
✓ Increased process control



Scaling Up to 50L Pilot and 250L Commercial Scales

- ✓Comparable between scales (donor variability)
- ✓Growth acceptable for commercial doses (250L)
- ✓Cells meet critical quality attributes (CQAs)





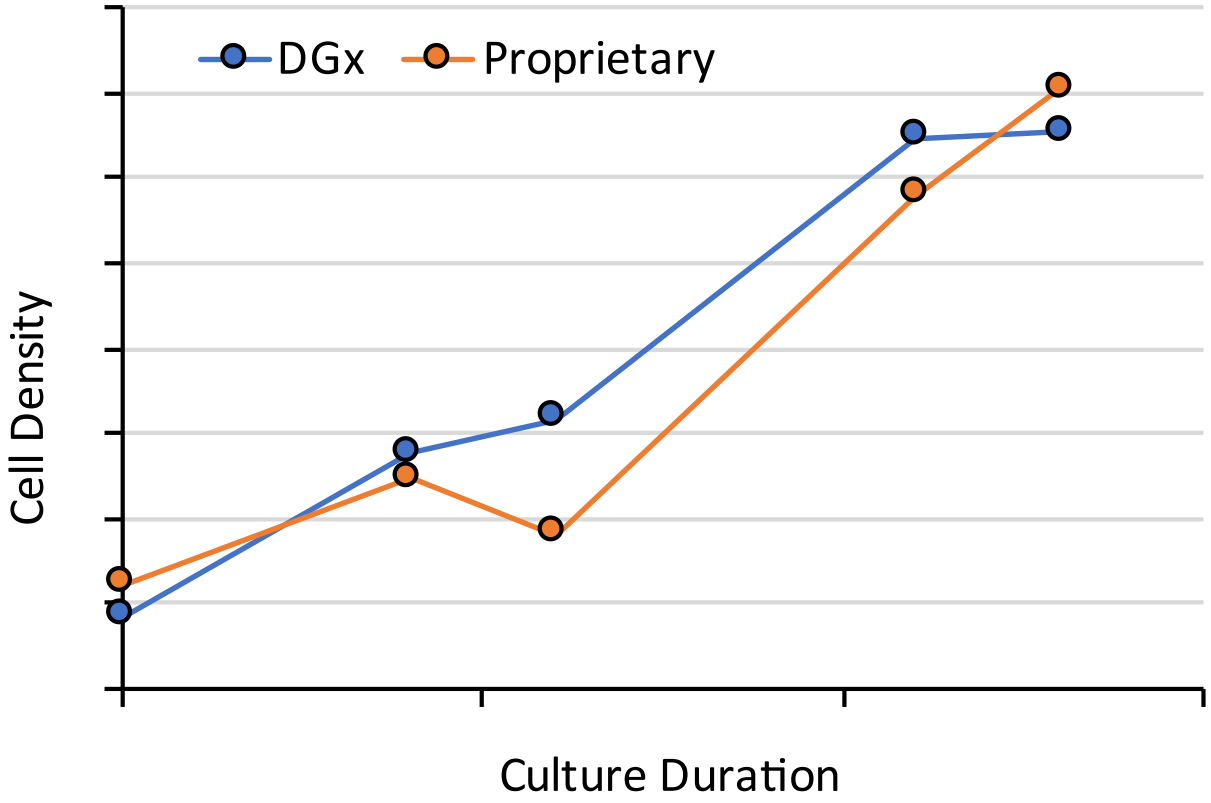
Cell Culture Supplement Development

Phase I/II Process:

- Proprietary cell culture supplement
- Human Derived Components
- FDA master file
- PMDA – requires control of all raw materials

Phase III/Commercial Process:

- Developed new cell culture supplement based on literature and laboratory experimentation
- Growth media with 20 additional bioactive components (albumin, transferrin, vitamins, hormones and fatty acids)





Cellastim

Recombinant HSA by InVitria, Inc.



Optiferrin

Recombinant Transferrin by InVitria, Inc.

✓ Raw Material Control

Human Derived Components

Excipient Cryopreservation Formulation

Phase I/II Process:

- Proprietary Cryopreservation Media
- Human Derived Components
- Sodium Hyaluronate mixed at Clinic

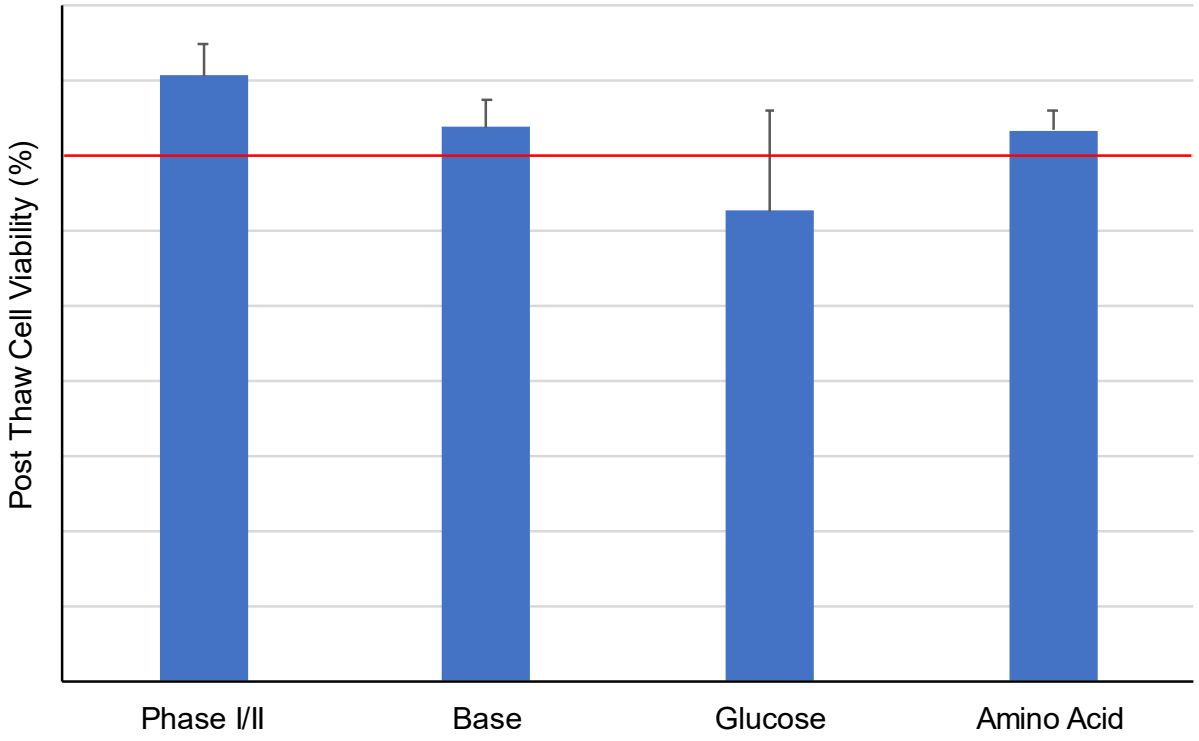
Phase III/Commercial Process:

- ✓ Remove Proprietary Formulations
- ✓ Remove Human Derived Components
- ✓ Incorporate Sodium Hyaluronate
- ✓ Maintain comparability to Phase I/II drug product formulation



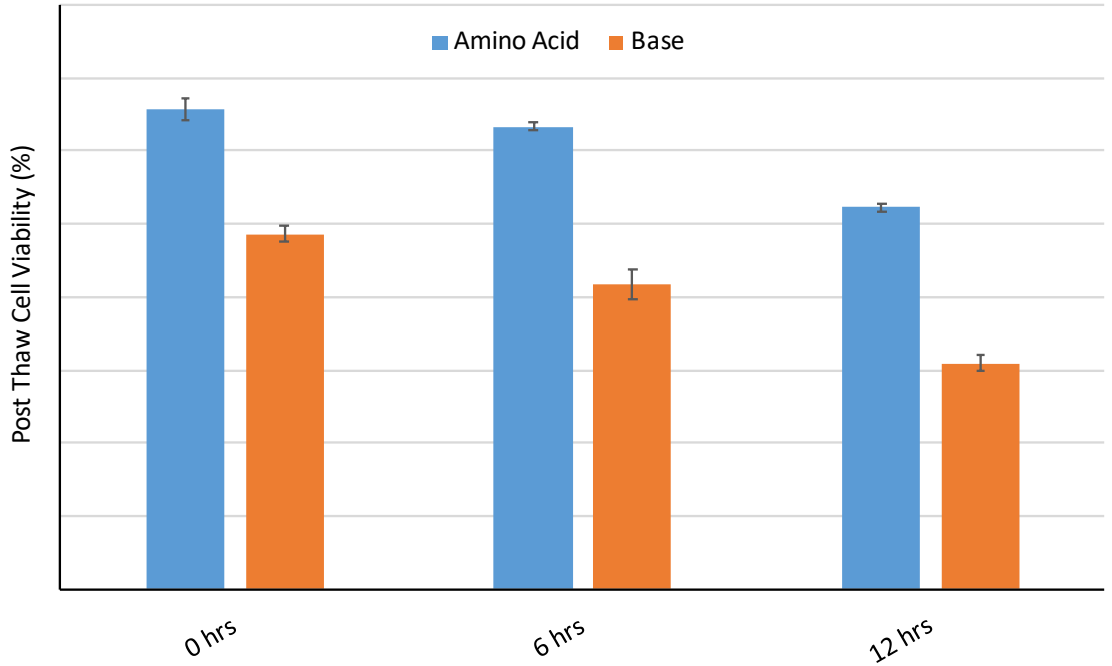
Exbumin

Recombinant human serum albumin, rHSA, excipient from InVitria, Inc.



Base: rAlbumin (rHSA), DMSO, Sodium Hyaluronate, Buffer

Excipient Cryopreservation Formulation



Base: rAlbumin (rHSA), DMSO, Sodium Hyaluronate, Buffer

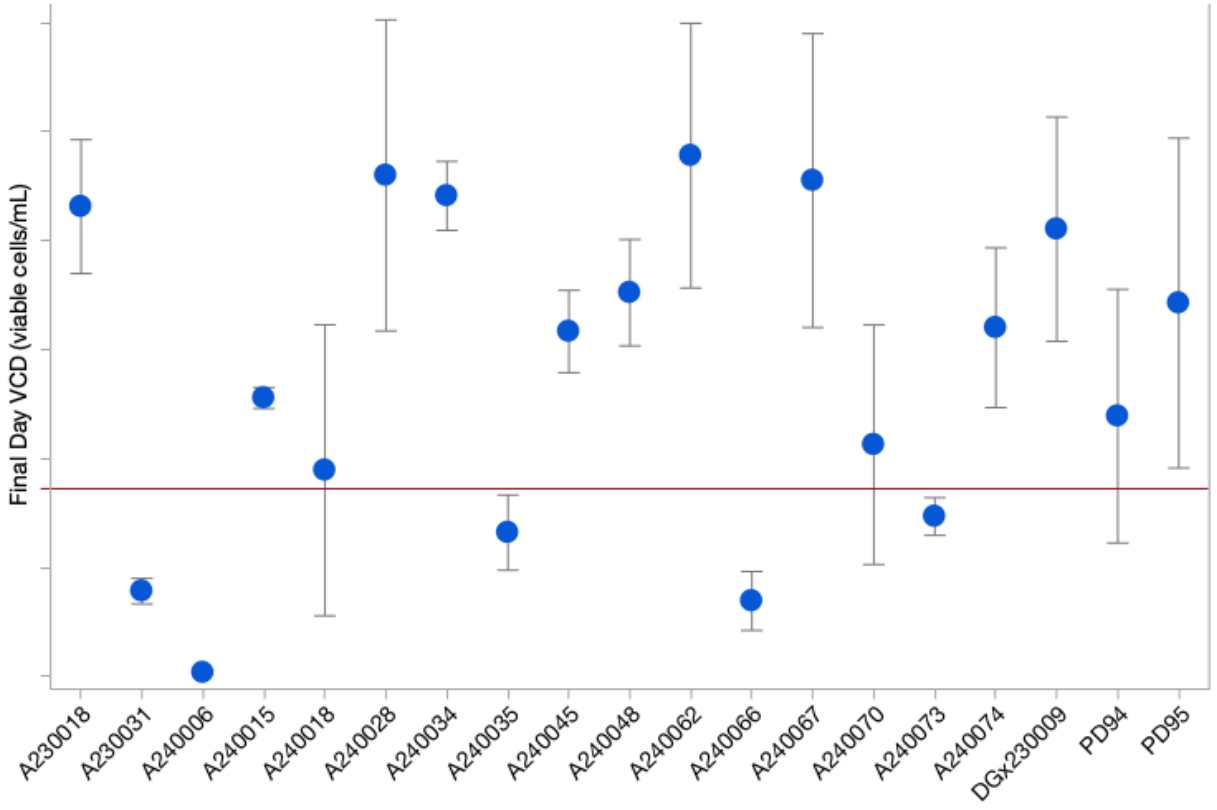


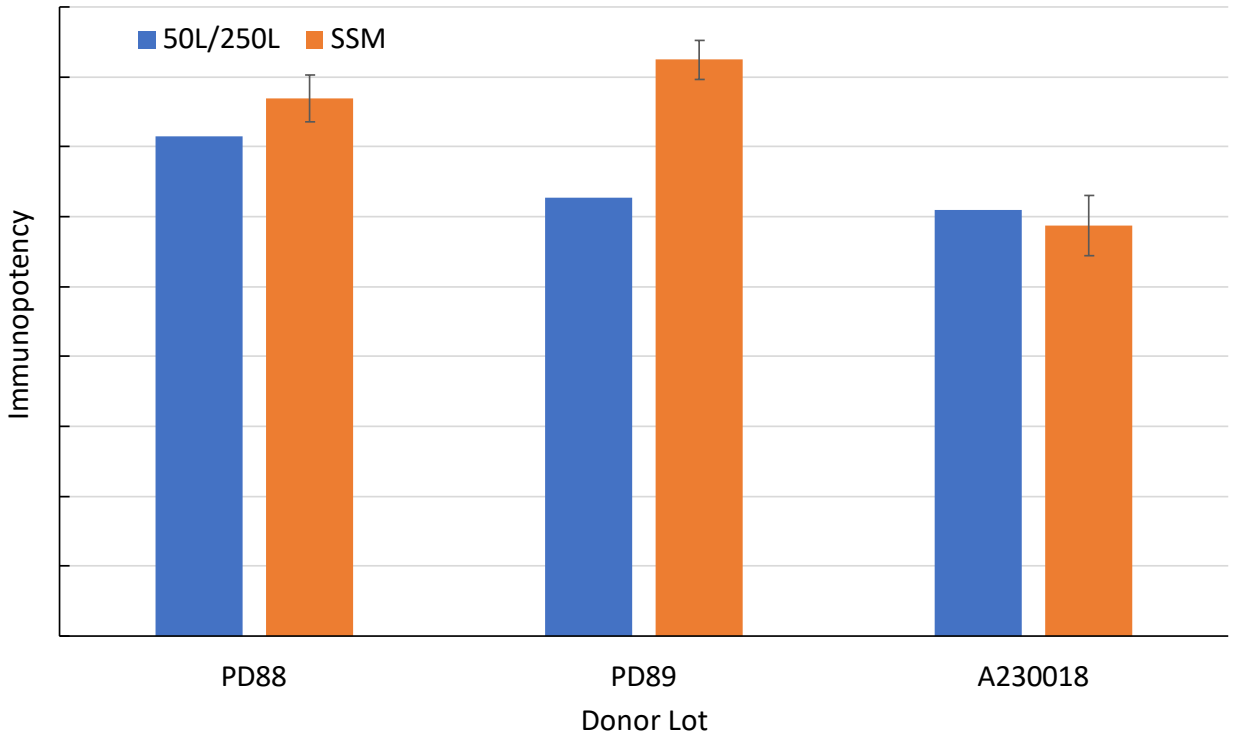
Exbumin

Recombinant human serum albumin, rHSA, excipient from InVitria, Inc.

SSM and Donor Raw Material Screening

Donor variability is greatest source of variability in IDCT manufacturing Process.
SSM used to screen donor lots to meet growth and potency acceptance for Phase III





Process Data -> Simplified commercial screening program

DiscGenics™

Questions?



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References

1. Ravindra et al, “Degenerative Lumbar Spine Disease: Estimating Global Incidence and Worldwide Volume.” Global Spine Journal 2018; 8(8):784-794.
2. Hoy D, et al. “The global burden of low back pain.” Ann. Rheum Dis 2014;73:968-974.
3. AD Davis, et al. “Where the United States Spends Its Spine Dollars.” Spine. 2012;37(19):1693-701.
4. Ringwalt et al, “Differential prescribing of opioid analgesics according to physician specialty for Medicaid patients with chronic noncancer pain diagnoses.” Pain Res Manag. 2014;19(4):179-185.
5. Gornet et al. “Allogeneic Disc Progenitor Cells Safely Increase Disc Volume and Improve Pain, Disability, and Quality of Life in Patients With Lumbar Disc Degeneration––Results of an FDA-Approved Biologic Therapy Randomized Clinical Trial.” *Int J Spine Surg* 2019; https://doi.org/10.14444/8609