LINEAGE
Cell Therapeutics

# From promise to people.

Our mission is to help pioneer a new branch of medicine based on the directed differentiation and transplant of allogeneic cells to patients

## 1st Annual Spinal Cord Injury Investor Symposium

Brian M. Culley, CEO

JUNE 29, 2023
NYSE AMERICAN: LCTX
lineagecell.com

# Forward-Looking Statements

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# OPC1

## Oligodendrocyte Progenitor Cell Transplants for Spinal Cord Injuries

# Lineage Corporate Profile

**Corporate Headquarters**
Carlsbad, California

**Research & Development**
Carlsbad, California

**Manufacturing**
Jerusalem BioPark, Israel

## Financial Position

**$46.8M**

Cash & equivalents at 3/31/23

## Market Capitalization

**~$240M***

## Employees

**~78**

(U.S. & Israel)

*Based on common shares outstanding and closing trading price as of 5/11/2023

# Lineage Cell Therapeutics

#ReplaceAndRestore

## Broad Capabilities

Cell manufacturing and transplant technology

**5**

Cell types in active development

Scalable pluripotent cell supply

## Highly Differentiated

Allogeneic product candidates

**3**

Product candidates in active clinical trials

**0**

>50 patients treated with zero cases of rejection

## Validated Technology

Global partnership for lead asset OpRegen®

**5**

Unprecedented cases of retinal regeneration

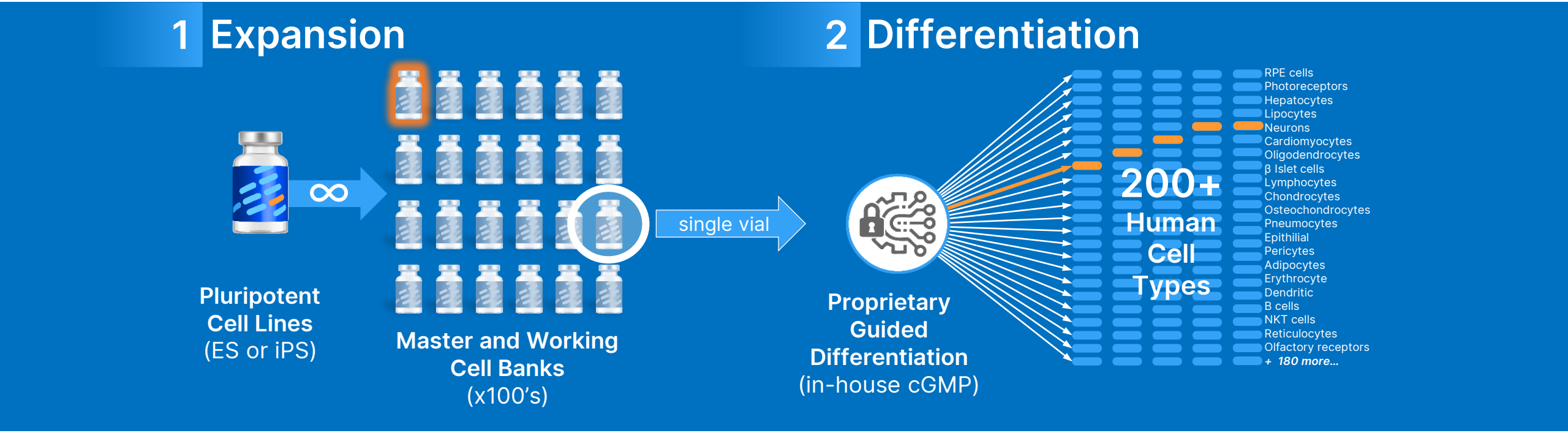
**$670M***

Partnership

Genentech
A Member of the Roche Group

** Includes $50M up front payment received Jan 2022, $620M of eligible milestones and double-digit royalties on sales*

# Lineage Technology: Two-Step Allogeneic Cell Production




- Pluripotent stem cell lines provide an *endless supply* of undifferentiated starting material for all programs
- No genetic editing is required

- No residual pluripotent cells are detectable
- Ready to inject formulations (no dose preparation delay)
- One-time treatment
- Scalable process for clinical and commercial use

# Cell Therapy Pipeline – 100% Allogeneic

| | FIELD | PROGRAM | PHASE 1 | PHASE 2 | PHASE 3 | PARTNERS |
|---|---|---|---|---|---|---|
| Neuroscience |  Ophthalmology | **OpRegen** Dry AMD with Geographic Atrophy (GA) | 24 patients treated | Enrolling | | Genentech A Member of the Roche Group |
| Neuroscience |  Demyelination | **OPC1** Spinal Cord Injury (SCI) | | 30 patients treated | | CIRM CALIFORNIA'S STEM CELL AGENCY |
| Neuroscience |  Neurotology | **ANP1** Auditory Neuropathy (Hearing Loss) | *Preclinical* | | | *Internally-owned* |
| Neuroscience |  Ophthalmology | **PNC1** Vision loss; Retinitis Pigmentosa | *Preclinical* | | | *Internally-owned* |
| Oncology |  Immuno-oncology | **VAC2** Non-Small Cell Lung Cancer (Oncology) | 8 patients treated | | | CANCER RESEARCH UK |

# OPC1 Development History

## Geron Corporation: 1999-2012

- IND cleared in 2009 – first ever ES-derived IND in the US
- Thoracic trial discontinued ("deprioritized") in 2011 (N=5)

## Asterias Biotherapeutics: 2013-2019

- Acquired SCI assets from Geron
- Completed a cervical SCI clinical trial (N=25)

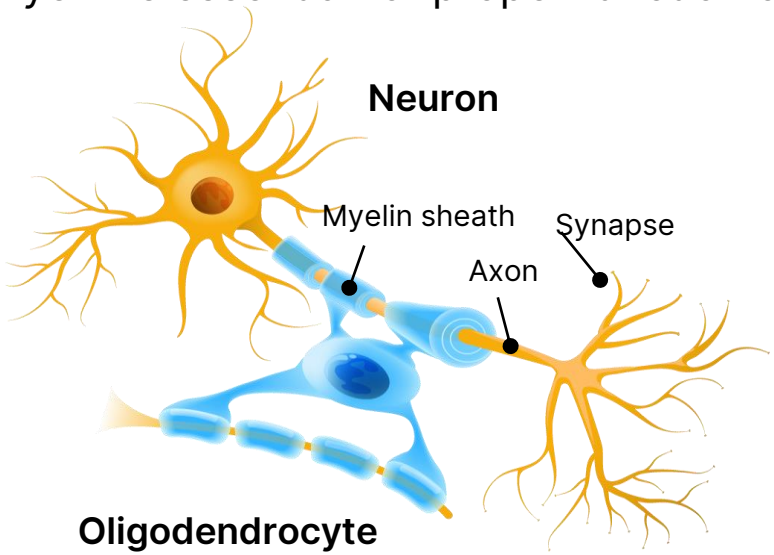
## **Lineage Cell Therapeutics (LCTX): 2019 – present**

- Acquired Asterias in 2019
- Focused on manufacturing and surgical procedure:
  - Significant improvements made to cell manufacturing
  - Clinical testing of a new delivery device planned
- Planning to conduct an efficacy trial after device and cells are cleared for use

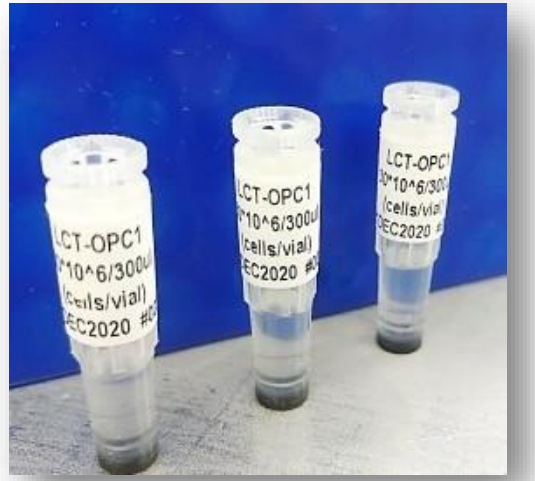
# Oligodendrocyte Progenitor Cells (OPC1) for SCI

## Transplanting neural cells may provide additional upper extremity function and improve quality of life

- Oligodendrocyte progenitor cells (OPCs) are precursors to the myelinating cells of the central nervous system
- Myelinating cells provide nerve axons with a myelin sheath
- Myelin is essential for proper function of neurons

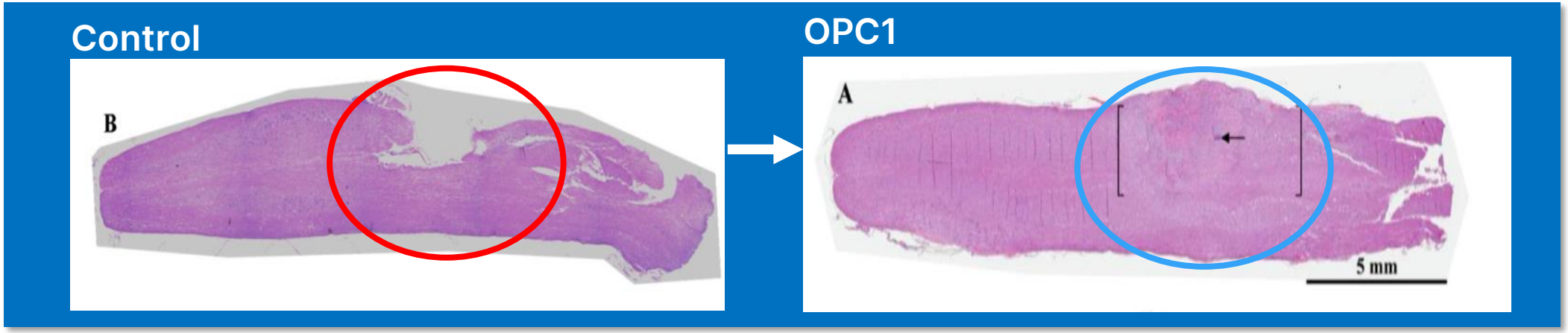



- OPC1 is generated from an NIH-registered cell line
- Cells are **allogeneic ("off the shelf")** and not taken from the patient
- **OPC1 is a one-time injection** into the spinal cord
- Dosing occurs 3-6 weeks post-injury, providing time for consent and transportation
- Immunosuppression is brief (60 days)

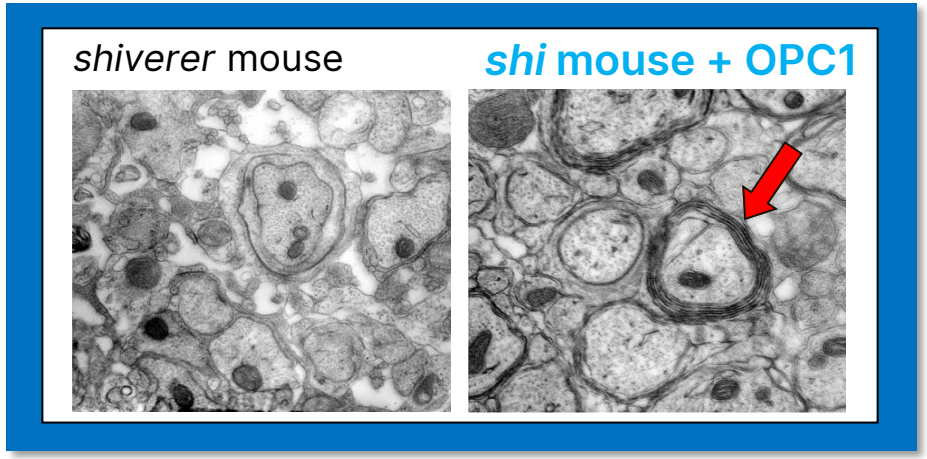


# OPC1 Three Potential Mechanisms of Action

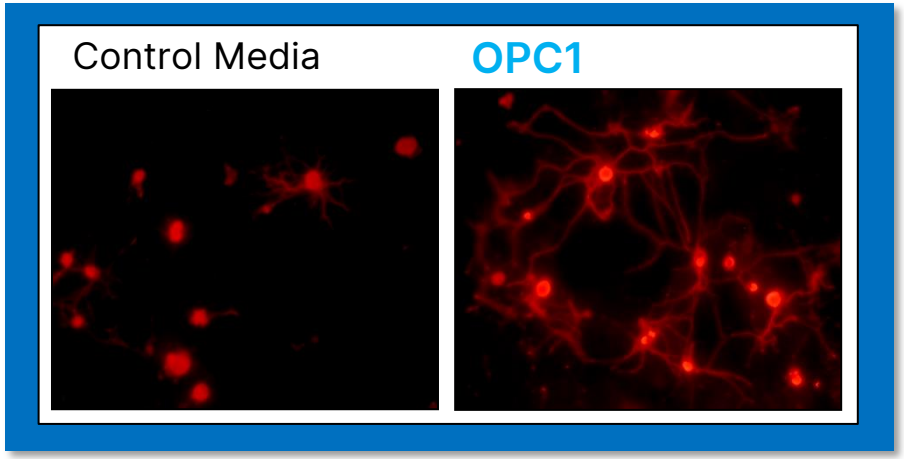
## Preventing Cavitation



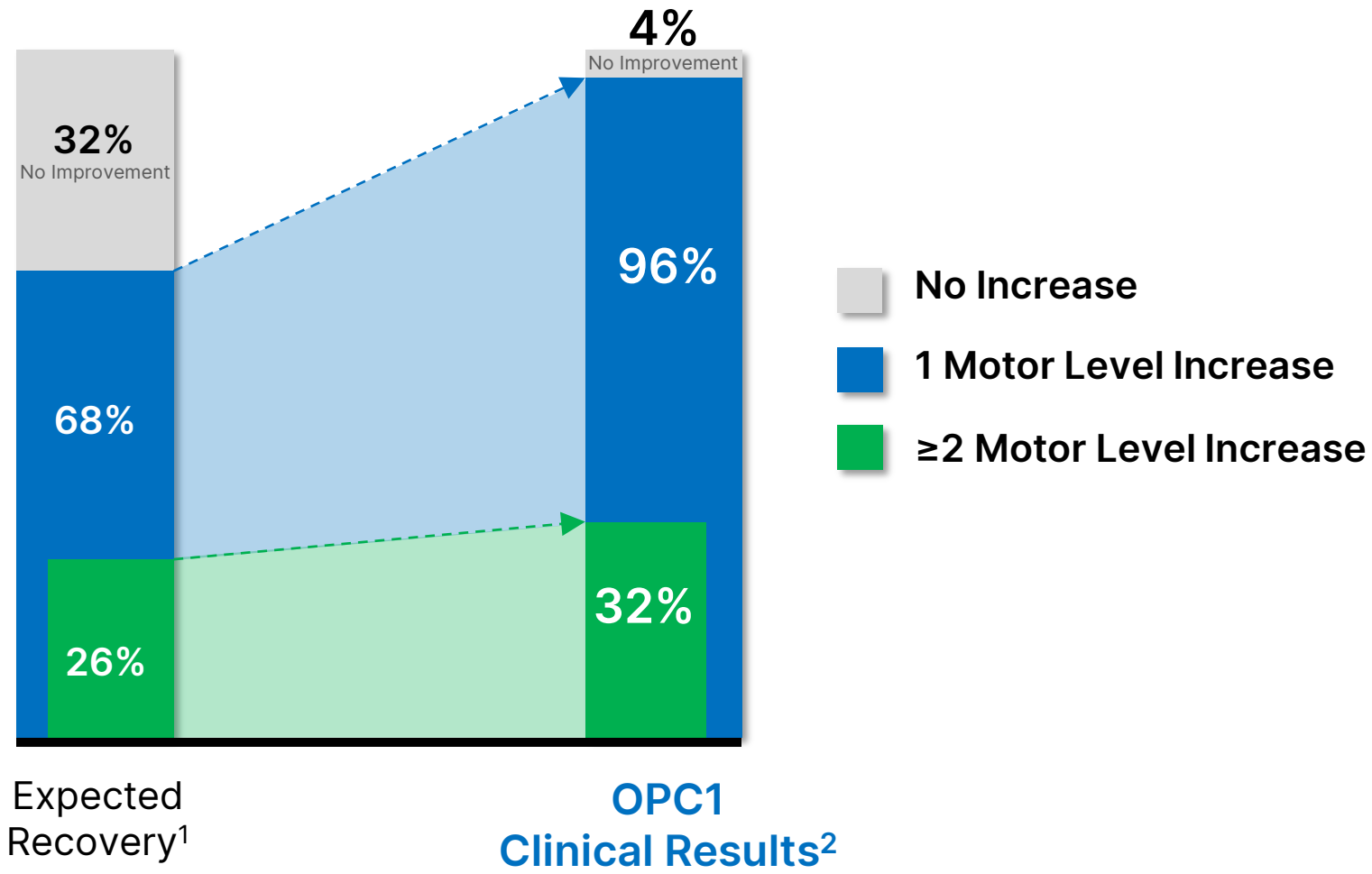

## Myelination of Axons




## Neurotrophic Factors



# Expected Recovery[1] vs OPC1: Motor Function Gains





1. Steeves JD, Lammertse DP, Kramer JL, Kleitman N, Kalsi-Ryan S, Jones L, Curt A, Blight AR, Anderson KD. Outcome Measures for Acute/Subacute Cervical Sensorimotor Complete (AIS-A) Spinal Cord Injury During a Phase 2 Clinical Trial. Top Spinal Cord Inj Rehabil. 2012 Winter;18(1):1-14. doi: 10.1310/sci1801-1. Epub 2012 Jan 31. PMID: 23239927; PMCID: PMC3519288.

2. Fessler, R. G., Ehsanian, R., Liu, C. Y., Steinberg, G. K., Jones, L., Lebkowski, J. S., Wirth, E. D., III, & McKenna, S. L. (2022). A phase 1/2a dose-escalation study of oligodendrocyte progenitor cells in individuals with subacute cervical spinal cord injury, Journal of Neurosurgery: Spine (published online ahead of print 2022). Retrieved Aug 19, 2022, from https://thejns.org/spine/view/journals/j-neurosurg-spine/aop/article-10.3171-2022.5.SPINE22167/article-10.3171-2022.5.SPINE22167.xml

# OPC1 Cervical Trial - Summary of Adverse Events

## Majority of adverse events were mild to moderate in severity

| All Treated Subjects (N=25) | AEs | SAEs |
|---|---|---|
| Total | 534 | 29 |
| Related to OPC1 | 1* | 0 |
| Related to Injection Procedure | 20 | 1 |
| Related to Tacrolimus | 11 | 1 |

**To date, there have been no serious adverse events related to the OPC1 cells**

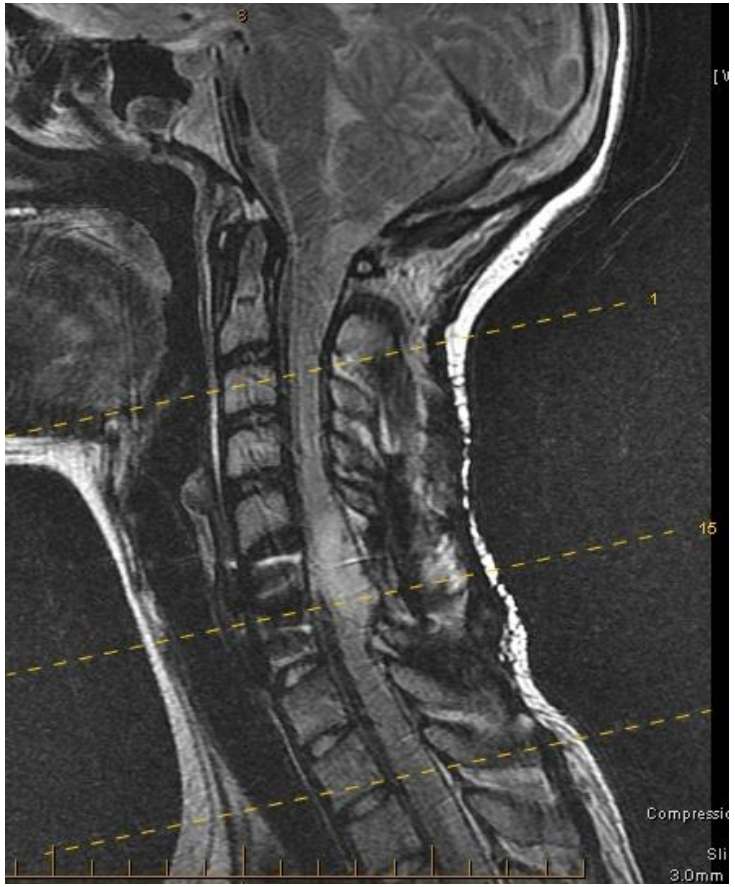
**Safety data is available for 2-5 years on all 25 patients**

**One AE possibly related to OPC1 was a Grade 2 dysesthesia that began 47 days post-injection but had resolved by the Year 2 follow-up visit*

# OPC1 Cervical Clinical Trial - Cell Engraftment

## 12- and 24-Month MRI Scans Indicate Durable Engraftment

- Cystic cavitation (syringomyelia) is a disorder which can damage nerve fibers and is expected to occur in ~80% of matched SCI cases
- MRIs show formation of a tissue matrix at the injury site, indicating OPC1 cells have durably engrafted to help prevent syringomyelia
- 96% (24/25) of OPC1 patients had serial MRI scans that indicated no sign of a lesion cavity at 24 months (for 22 available scans)



**Weighted sagittal MRI**

# OPC1 Thoracic & Cervical Clinical Trials Overview

- **Thoracic phase 1 clinical trial (N=5)**
  - All **subjects followed for at least 10 years** *(Journal of Neurosurgery Spine, Vol 37, Issue 3, 2022)*
  - **No unexpected serious adverse events attributable to the OPC1 transplant**:
    - No evidence of neurological decline
    - No enlarging masses
    - No further spinal cord damage
    - No syrinx formation

- **Cervical phase 1/2a clinical trial (N=25)**
  - All **subjects evaluated for at least 2 years** *(Journal of Neurosurgery Spine, Vol 37, Issue 6, 2022)*
  - **No unexpected serious adverse events related to the OPC1 transp**lant;
  - No enrolled patients had worsening of neurological function;
  - **Durable motor improvements**:
    - 4 of 6 subjects gained at least 2 motor levels of improvement on at least one side at 12 months (cohort 2)
    - 5 of 6 subjects gained at least 2 motor levels of improvement on at least one side at 24 months (cohort 2)
    - 1 subject achieved 3 motor levels of improvement on one side; maintained at 3 years (cohort 2)

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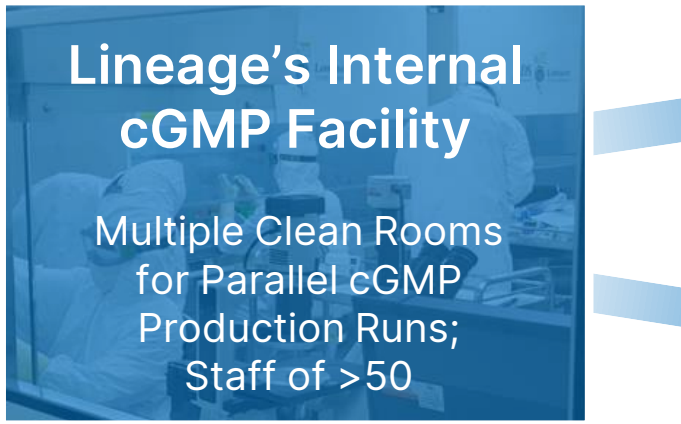
# Requirements for a Successful Cell Therapy




## Control (Safety) & Reproducibility

- Source line characterization, cell banking, versatile expansion systems
- Differentiation process development; culture conditions, optimization
- Analytical methods, in-process controls, release criteria

## Purity / Identity

- Clinically compatible post-production processing
- Analytical method development for process control and product release

## Potency

- Functionality and performance testing
- Enhancements; genetic modification (optional), various expression systems

## Scalability

- Scale-up modalities, substrates, harvesting protocols
- Clinical and commercial throughputs
- Reduced cost of goods

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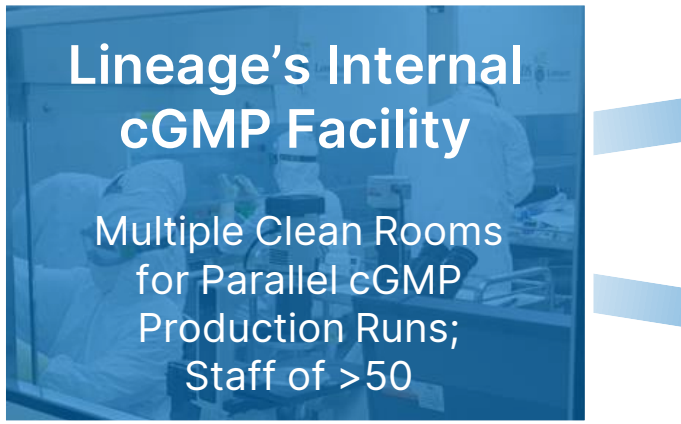


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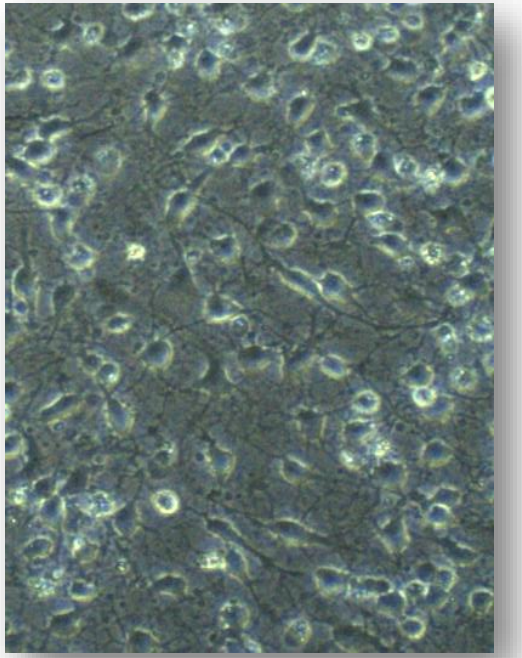
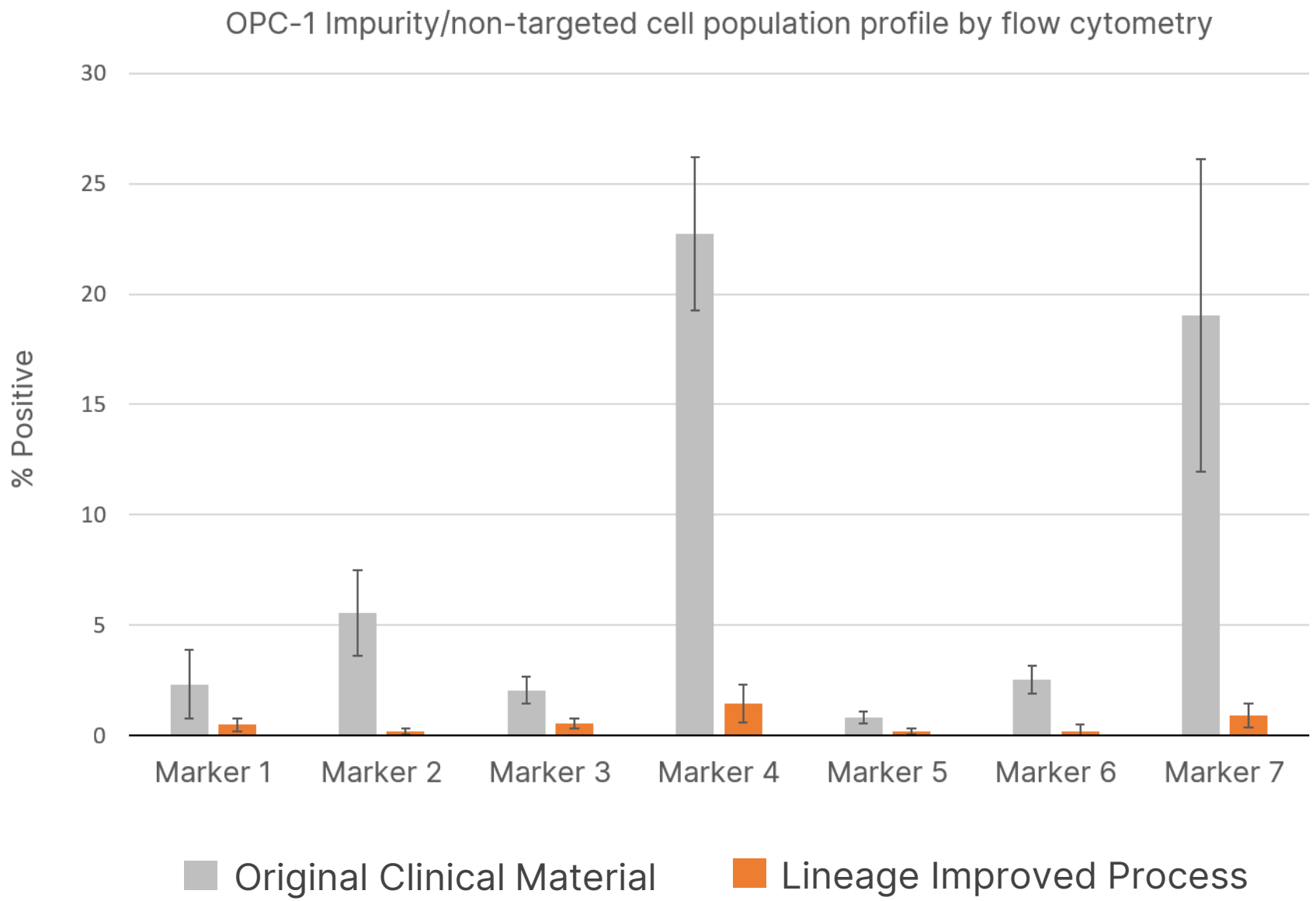
# Manufacturing Improvements Completed Since Acquisition

## Lineage has made major improvements to production and quality of OPC1

- Developed a cryopreserved “ready-to-inject” formulation
- Eliminated dose preparation (plating, washing, counting)
- Increased production scale 10- to 20-fold
- Significantly reduced impurities
- Maintained *in vivo* functional activity
- Developed 12 new analytical and functional methods
- Eliminated all animal-based production reagents
- Filed new intellectual property with expiration dates ranging from 2036 to 2040



# Manufacturing Improvements: Lower Impurities



# Delivery Improvements - Original Syringe Positioning Device

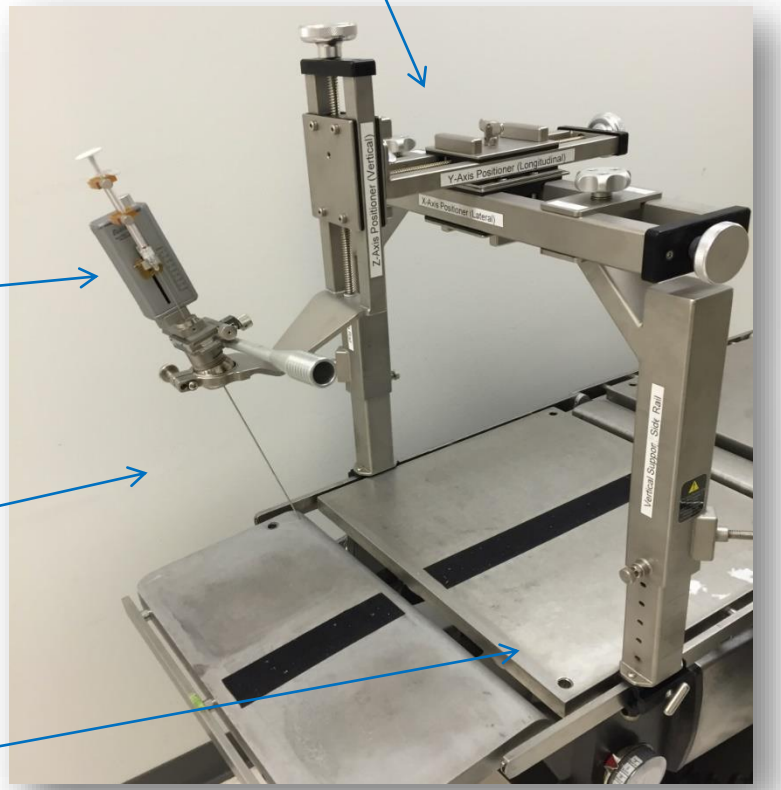
XYZ manipulator

Storage trays

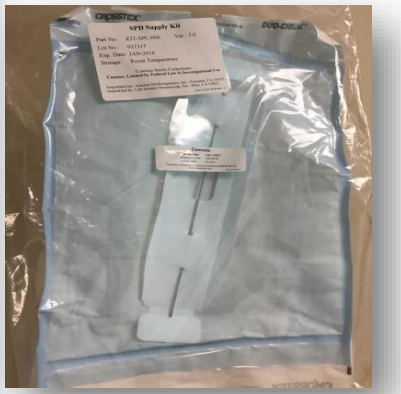
Syringe & Microdrive assembly

Outer cannula and needle

Table-attached support frame

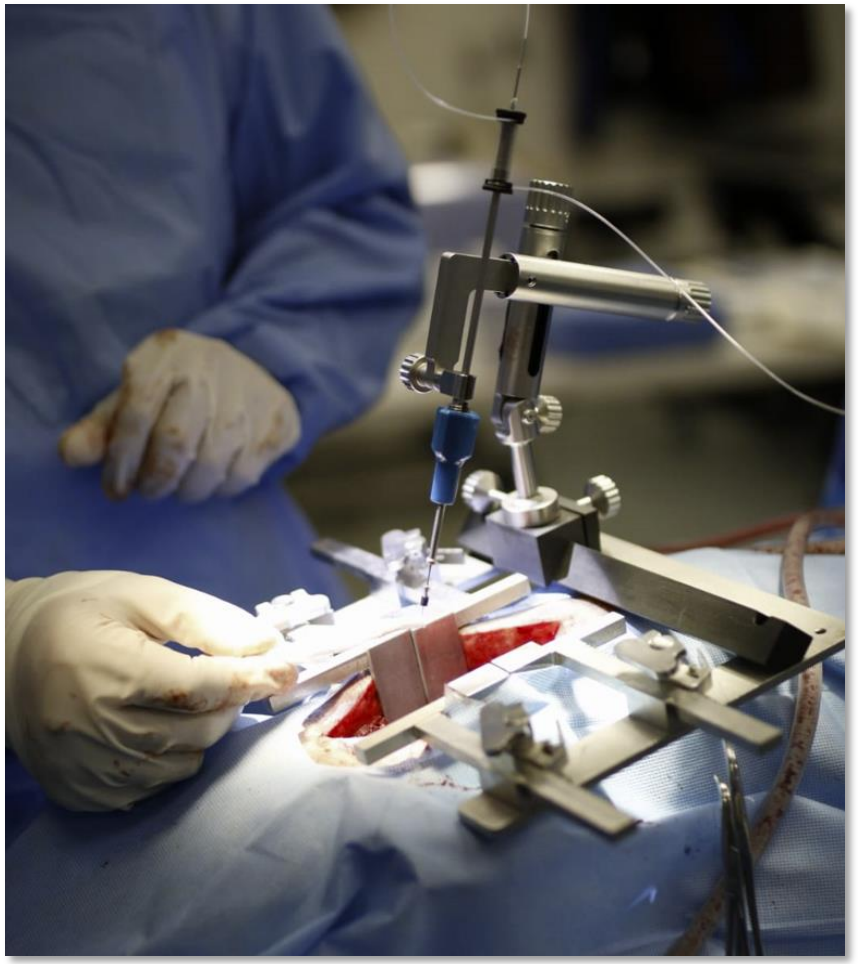



Supply Kits



# New Delivery System (Neurgain Agreement)

- **Better stability and control**
  - Eliminates motion between platform/XYZ manipulator/needle
- **Enhanced usability and safety: no cessation of ventilation**
  - Attaches directly to patient, compatible with breathing motion
  - Allows slower delivery of cells
- **Improved user experience**
  - Smaller and fewer components
  - Single hand operation
- **Verification, validation, and preclinical testing complete: data submitted to FDA**
- **Clinical trial planned in sub-acute and chronic patients (6-10 patients)**



# OPC1 Program Summary

## Key Takeaways

- **Experience** - one of the longest running trials in the field and first of its kind
- **Excellent overall safety profile**
  - 5 years follow up in cervical SCI
  - 10 years follow up in thoracic SCI
- **Indication of efficacy** compared to comparably matched historical control
- **Lessons** can be applied to next trial
  - Inadequate decompression was associated with the two worst outcomes

## Next Steps

- **Clinical testing of a new delivery system**
  - 3-5 subacute and for the first time, 3-5 chronic injury patients
- **Introduction of improved cell manufacturing process**
  - Improved scale, control, purity
- **Preparations underway for larger, controlled clinical trial**
  - Engaging with relevant expert and organizations
  - Assessing clinically-meaningful endpoints
- **Eligible/Apply for grants** from the California Institute of Regenerative Medicine (CIRM)

# Key Takeaway for the Lineage Approach:

In certain settings, replacing whole cells may provide restorative benefits beyond the reach of traditional approaches

**#replaceandrestore**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# Our Inspiration.

View their stories at
lineagecell.com/media