LINEAGE
Cell Therapeutics

From promise to people.

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

CORPORATE PRESENTATION JANUARY 23, 2023
NYSE AMERICAN: LCTX
lineagecell.com

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Lineage Cell Therapeutics

#ReplaceAndRestore

Broad Capabilities

Cell manufacturing and transplant technology

5

Cell types in active development

>200

Cell types for future targeting

∞

Commercial scalability and cell line supply

Highly Differentiated

Allogeneic product candidates

3

Product candidates in active clinical trials

0

>50 patients treated with zero cases of rejection

>$1B

Addressing multi-billion dollar markets

Validated Technology

Global partnership for lead asset OpRegen®

$670M*

Partnership

Genentech
A Member of the Roche Group

5

Unprecedented cases of retinal regeneration

1

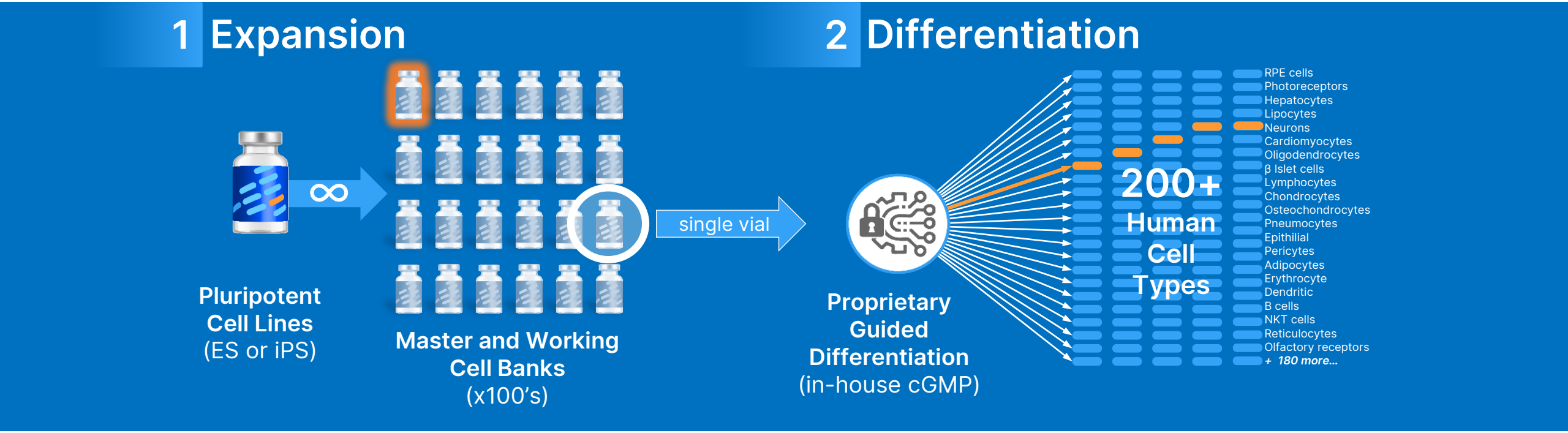
Single administration per patient

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

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			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

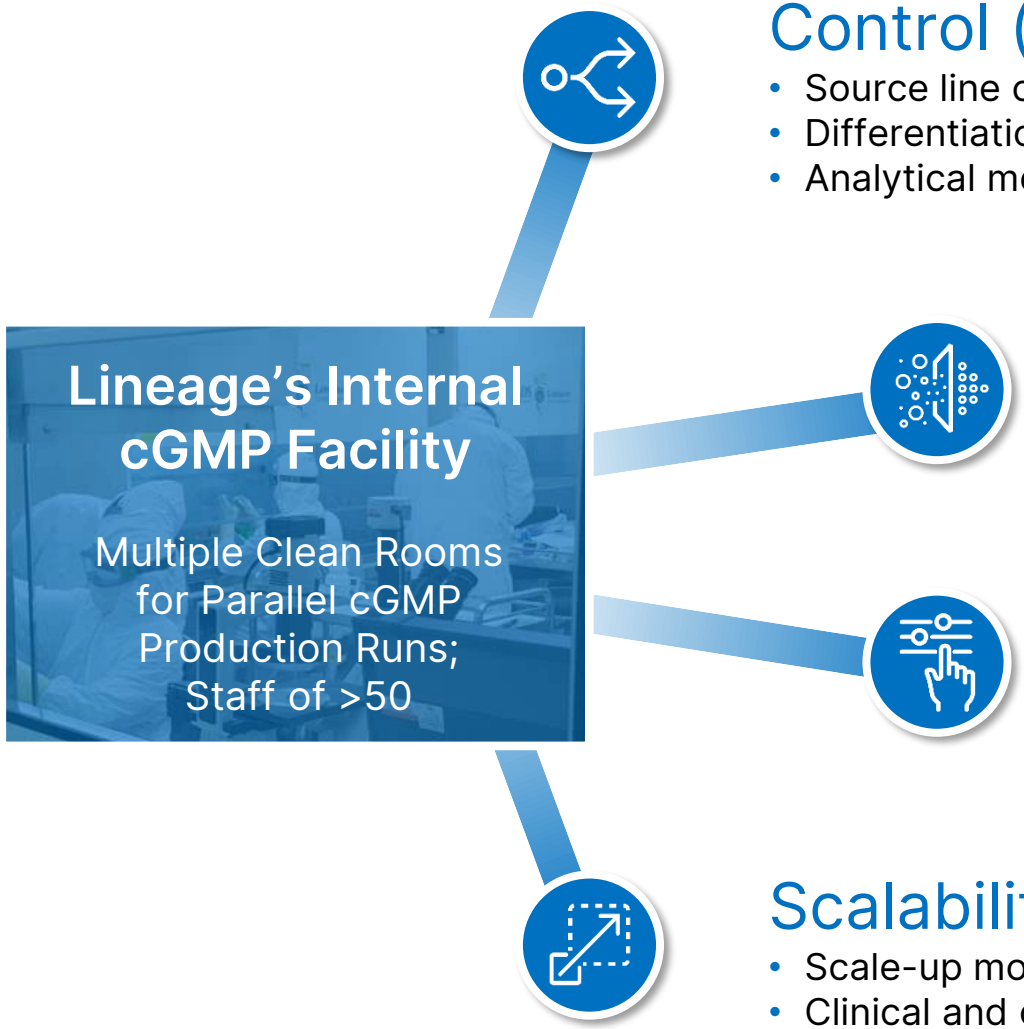
Lineage Technology: Two-Step Allogeneic Cell Production



- Pluripotent stem cell lines (PSCs) provide an *endless supply* of undifferentiated starting material for all programs
- PSCs can become each of the 200+ cell types of the human body
- No genetic editing is required

- The target cell has been validated by evolution
- Residual pluripotent cells are undetectable
- Generates IP (~500 issued and pending patents)
- Ready to inject formulation (no dose preparation delay)
- One-time treatment – cells integrate without rejection
- Scalable process for clinical and commercial

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

LINEAGE
Cell Therapeutics

OpRegen®

RPE Cell Transplants to Treat Dry AMD

Improving structure *and* function

Worldwide Collaboration for Dry AMD

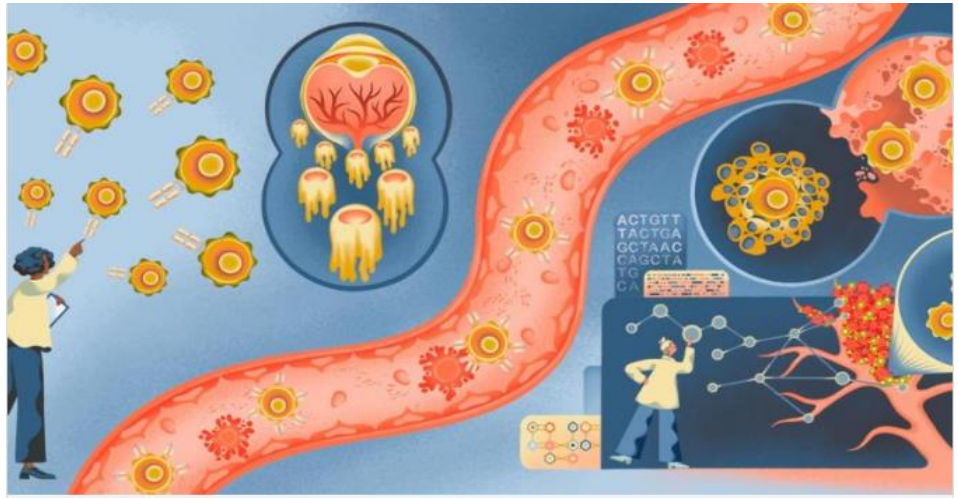
Genentech
A Member of the Roche Group

"Roche and Genentech embarked on an ambitious journey to revolutionise ophthalmology"

https://www.celebratelife.roche.com/explore/science/ophthalmology-restoration/

- Creating allogeneic retinal pigment epithelial (RPE) cells to either replace or support cells that are dysfunctional or absent due to degenerative disease
- Largest cell therapy license agreement outside of oncology at signing; funds development and commercialization of **RG6501 (OpRegen)** for all ocular disorders
- **$50M** up front received; eligible for additional **$620M of milestone payments** and double-digit royalties

James Sabry, Roche
"Cell therapy has the potential to change how we treat disease. At Roche and Genentech, our interest in cell therapy is directly tied to our commitment to inventing pioneering medicines with substantial patient benefit."



New Frontiers of Cell Therapy — January 5, 2023

Seppi Lin, Genentech
"This approach may allow for a robust supply of cells and the ability to have doses manufactured ahead of time, so they are readily available for patients."

https://www.gene.com/stories/cell-therapy

THE WALL STREET JOURNAL.

Brian Culley, Lineage CEO
"Being a global unmet need, it made a lot of sense for us to partner with Genentech, which bring the resources and capabilities to move quickly and globally."

Tom Zioncheck, Roche
"This deal and this collaboration represents what we believe could be the tip of the spear in our efforts in cell-based therapies."

December 20, 2021

Millions Suffer from Vision Loss due to Dry-AMD

- Age-related macular degeneration (AMD) presents in two forms, **wet** and **dry**
- **Wet** age-related macular degeneration (wet AMD) is usually caused by blood vessels that leak fluid or blood into the macula
- **Dry** age-related macular degeneration (dry AMD) involves the loss of retinal pigmented epithelium (RPE cells), creating an area of geographic atrophy (GA), causing impaired vision and blindness
- **Wet** AMD supports **>$10Bn**[2] in product sales, while **dry** AMD has ***no*** FDA-approved treatments, **yet is eight times more common**[1]

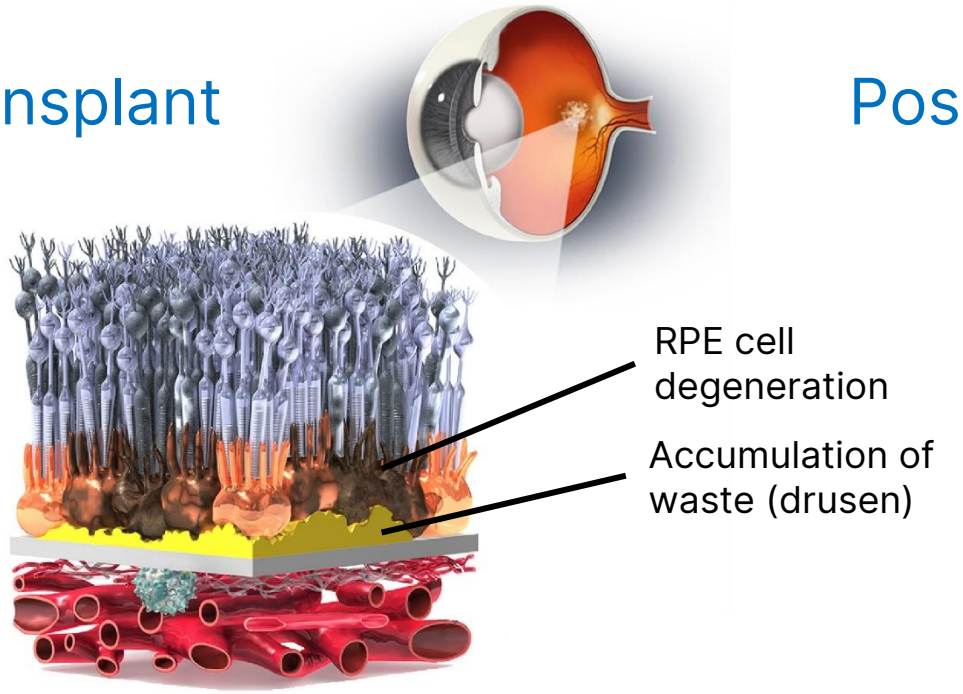
Image courtesy of Macular Society

(1) JM Seddon, Epidemiology of age-related macular degeneration. Retina, 3rd ed.;
(2) 2018 product sales summary based on publicly reported revenue figures for Lucentis and Eylea.

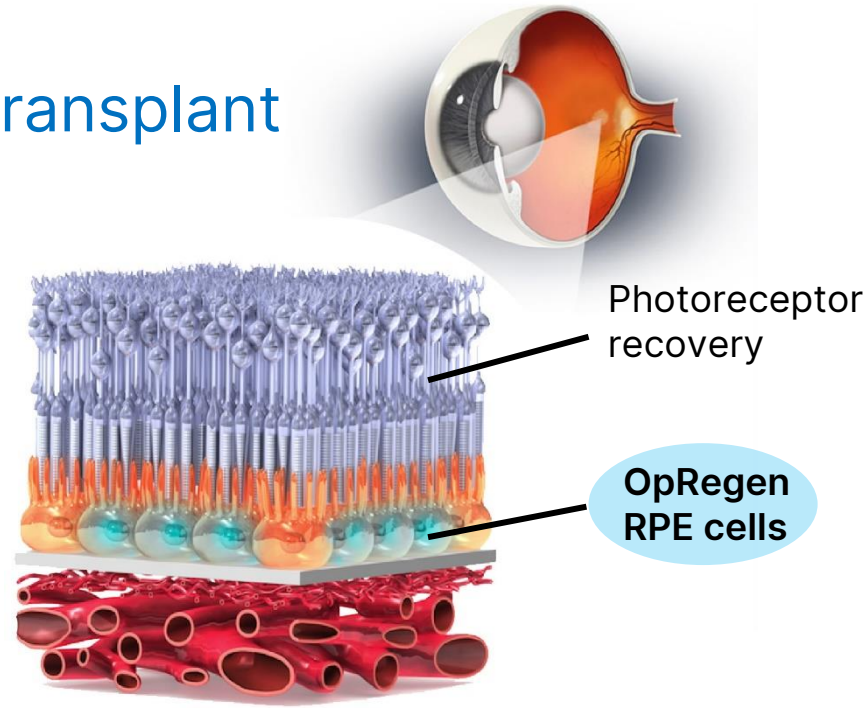
Lineage Approach - OpRegen, a “Complete” Approach

OpRegen is a one-time injection of fully-differentiated RPE cells intended to:
1) replace and restore retinal tissue (anatomy), and
2) preserve or improve vision (function)

Pre-Transplant



Post-Transplant



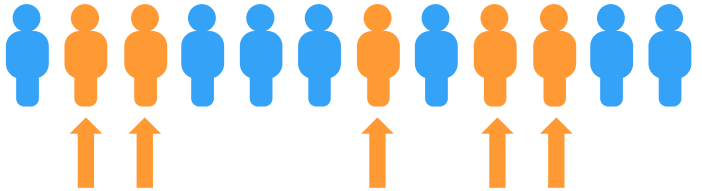
Retina cross-section images adapted from scienceofamd.org

Phase 1/2a Trial Complete, Long-Term Follow-Up Ongoing

Cohorts 1-3 (Dose and Safety)
12 Legally Blind Patients

Generally well-tolerated,
no reports of rejection

Cohort 4 (Initial Efficacy)
12 Impaired Vision Patients



Cells delivered across entire area of atrophy (n=5):

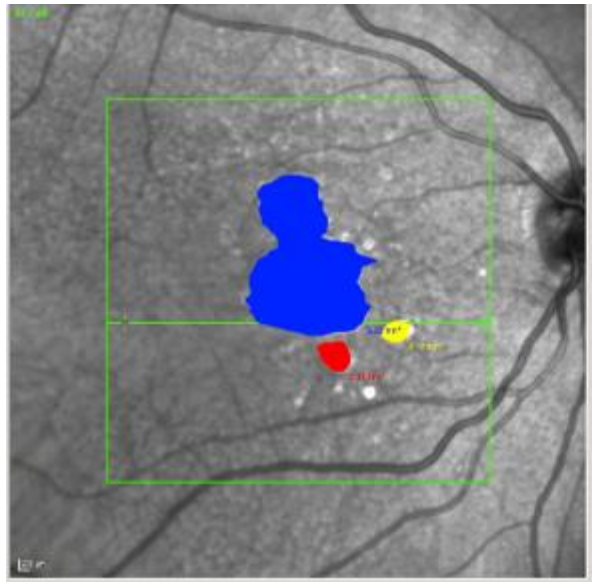
12-month gains in visual acuity averaged +12.8 letters

100% of patients who received OpRegen across their area of atrophy represent the only known clinical cases of outer retinal structure improvement in dry AMD

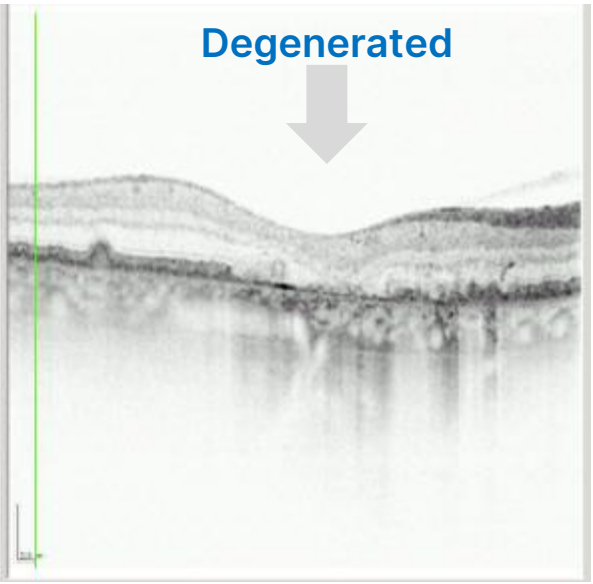
Improved Structure (Smaller GA) Detectable Within Three Months

OCT 2020

FAF Image

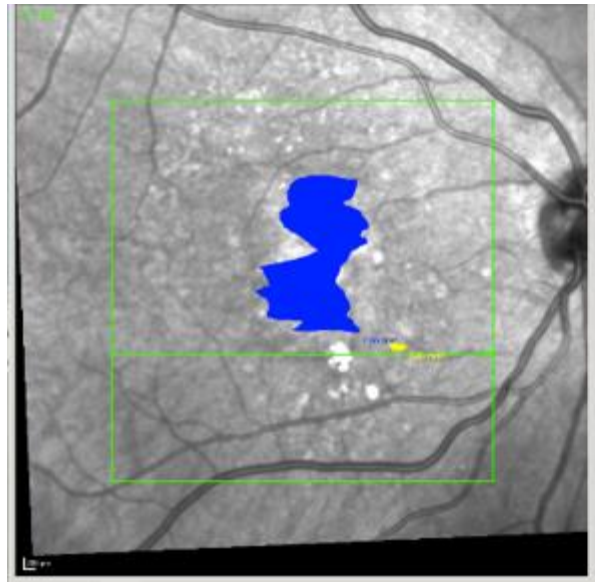


OCT Image

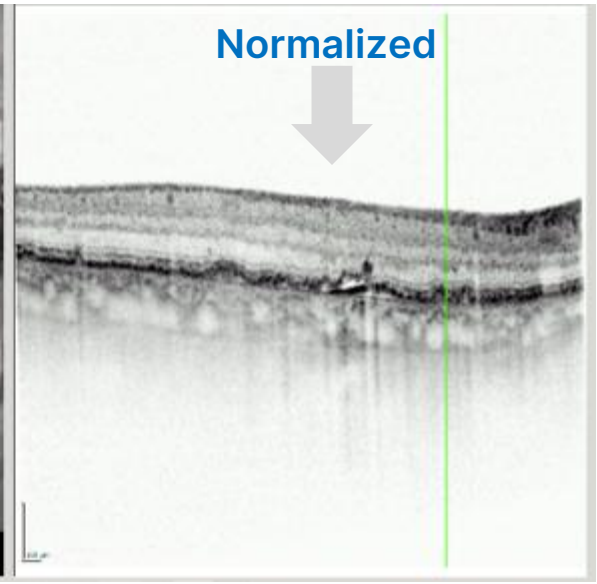


JAN 2021

FAF Image



OCT Image



GA AREA: 3.56 mm^2 → **GA AREA: 2.69 mm^2 = *negative* growth rate!**

Total area	3M GROWTH RATE:	– 0.87 mm^2	(ANNUAL RATE – 3.48 mm^2)
SQRT transformation	3M GROWTH RATE:	– 0.23 mm	(ANNUAL RATE – 0.92 mm)

Image courtesy of Jordi Monés, MD, PhD

Re-Thinking the Dry AMD Treatment Paradigm

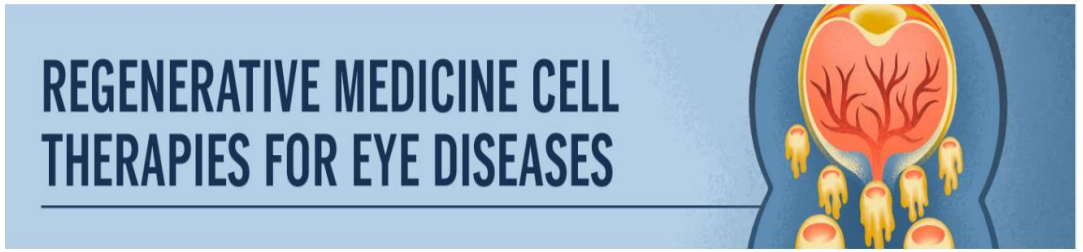
Roche

125 YEARS
Celebrate Life

"The moment our goal shifted from preservation to restoration"

"Our recent partnership with Lineage Cell Therapeutics…is one of the important routes we are pursuing….The hope is that this treatment could not only slow down progression of the dry form of AMD, **but also restore function to the retina**."

https://www.celebratelife.roche.com/explore/science/ophthalmology-restoration/



Cell therapy is a powerful approach for turning cells into living medicines

"Cell-based therapies provide the possibility to replace dying or damaged eye cells with new healthy ones. Our aim is to repair the underlying cellular structure of the retina – a thin layer of tissue that lines the back of the eye – **to preserve and even restore vision.**"

-Tom Zioncheck, Roche

https://www.gene.com/stories/cell-therapy

Ongoing Development: Phase 2a Trial

Genentech
A Member of the Roche Group

A multicenter, open-label, single arm clinical study in patients with geographic atrophy (GA), secondary to age-related macular degeneration

- Managed and funded by Genentech
- Seeks to optimize subretinal surgical delivery and evaluate safety/activity
- Approximately 30 (up to 60) patients
- Primary objectives:
  - Proportion of patients with subretinal surgical delivery to target regions under the retina, and
  - Safety of subretinal surgical delivery
- Secondary objective:
  - Proportion of patients with qualitative improvement in retinal structure, determined by SD-OCT

Currently enrolling – primary *and* secondary endpoints occur at 90 days

OpRegen - A Multi Billion-Dollar Opportunity

- The **only known reported clinical cases** of outer retinal structure improvement with improved vision observed in five dry AMD patients
- Market opportunity **not limited** by monogenic deficiencies (e.g., gene therapy)
- Well-tolerated; **no cases of rejection** (only 90d of peri-operative immunosuppression)
- Potential application in **additional retinal diseases** (example: Stargardt disease)
- **Issued** patents cover aspects of production, characterization, and formulation
- **Fast Track** designation from FDA
- Validating **development partnership** with global ophthalmology leader, **Genentech**
  - Phase 2a clinical study launched November 2022

Key Takeaway for the Lineage Approach

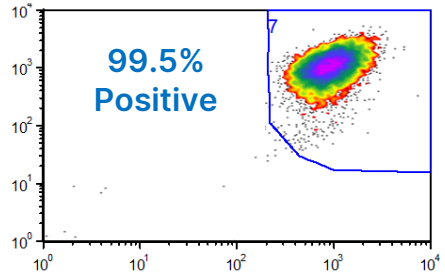
In certain settings, replacing whole cells may provide restorative benefits beyond the reach of traditional approaches

#replaceandrestore

Repeating Success – OpRegen as a Case Study and Guide

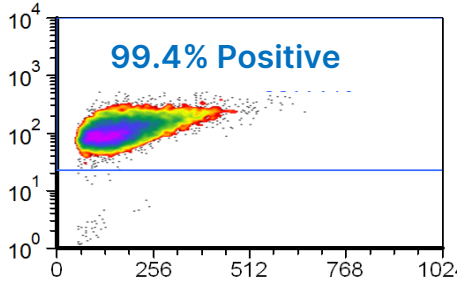
Control (Safety) & Reproducibility

- Multiple clinical batches generated and released
- Extensive comparability testing performed
- Single source, master bank cell line
- No reports of rejection



Purity/Identity

- Highly pure (>99%) RPE via flow cytometry
- Multiple identity markers utilized
- No residual PSCs detectable



Potency/Functionality

- Phagocytosis (>99%)
- Trans-epithelial resistance (polarization)
- Differential apical and basal growth factor secretion

Scalability

- Dynamic culturing system (3D, not 2D)
- Bioreactor and microcarriers for expansion and scale-up
- More than 2500 treatment courses per 3L batch

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Cell Therapeutics

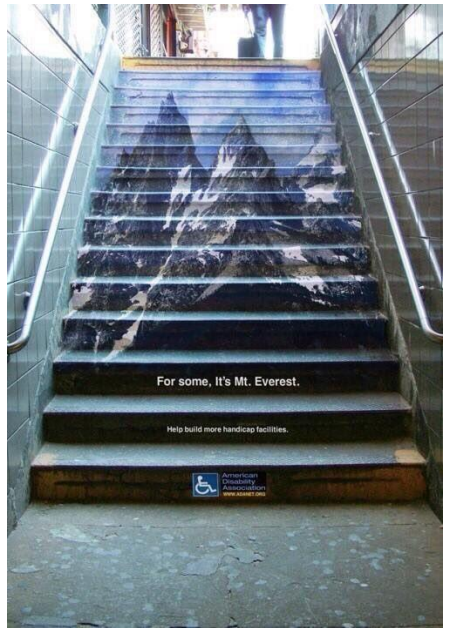
OPC1

Oligodendrocyte Cell Transplants for Spinal Cord Injuries

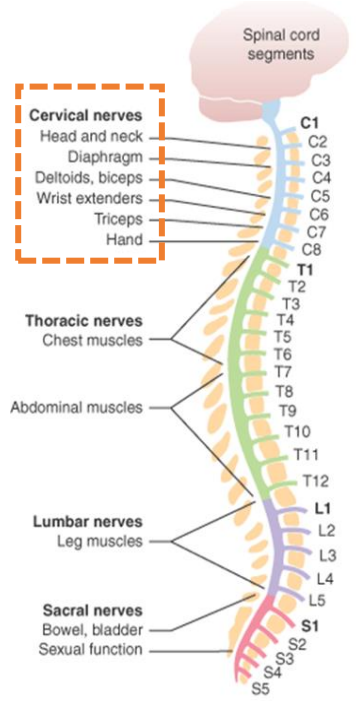
30 patients treated to date

Spinal Cord Injury (SCI) Burden & Unmet Needs

- Approx. 18,000 cases per year (US)[1]
- A significant burden for patients and caregivers[2]
  - 67% of patients are unemployed 10 years post-injury
  - Lifetime healthcare costs can reach $5M for one patient
- Lifelong impairment
  - Most common in ages 16-30



- Primary feature of a SCI is loss of mobility
- Goal of OPC1 therapy is to **restore arm, hand, and finger function**
- Greater mobility increases independence and quality of life
- **Gains in motor function**, particularly in the upper extremities, **can provide significant benefits in self-care and lower costs of care**

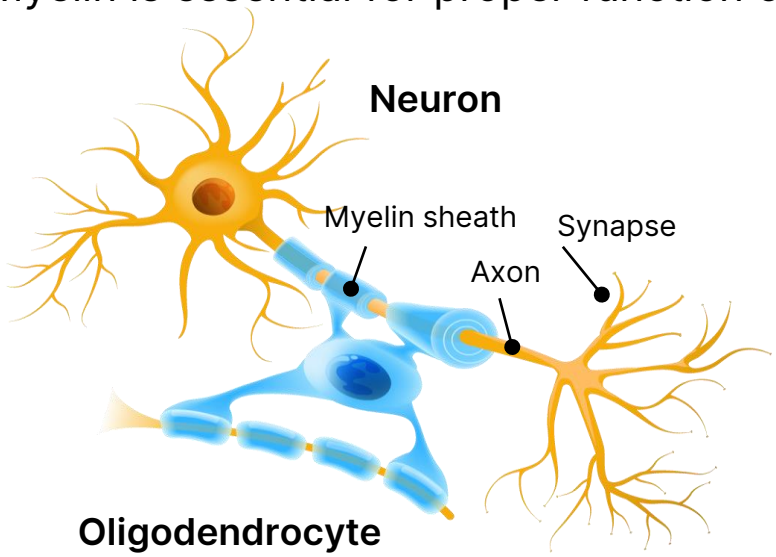


(1) National Spinal Cord Injury Statistical Center
(2) National SCI Statistical Center, 2019 SCI Data Sheet

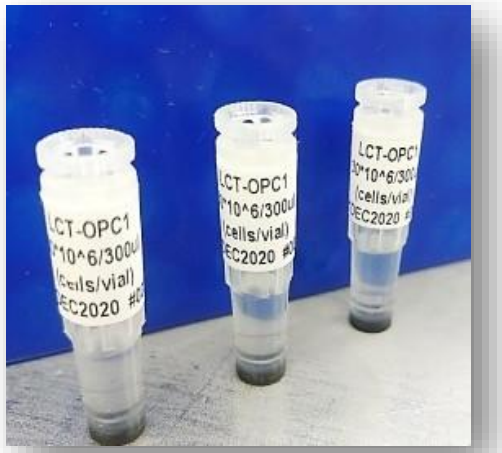
Oligodendrocyte Cells as a Solution – OPC1 for SCI

Transplanting oligodendrocytes may provide additional upper extremity function and improve quality of life

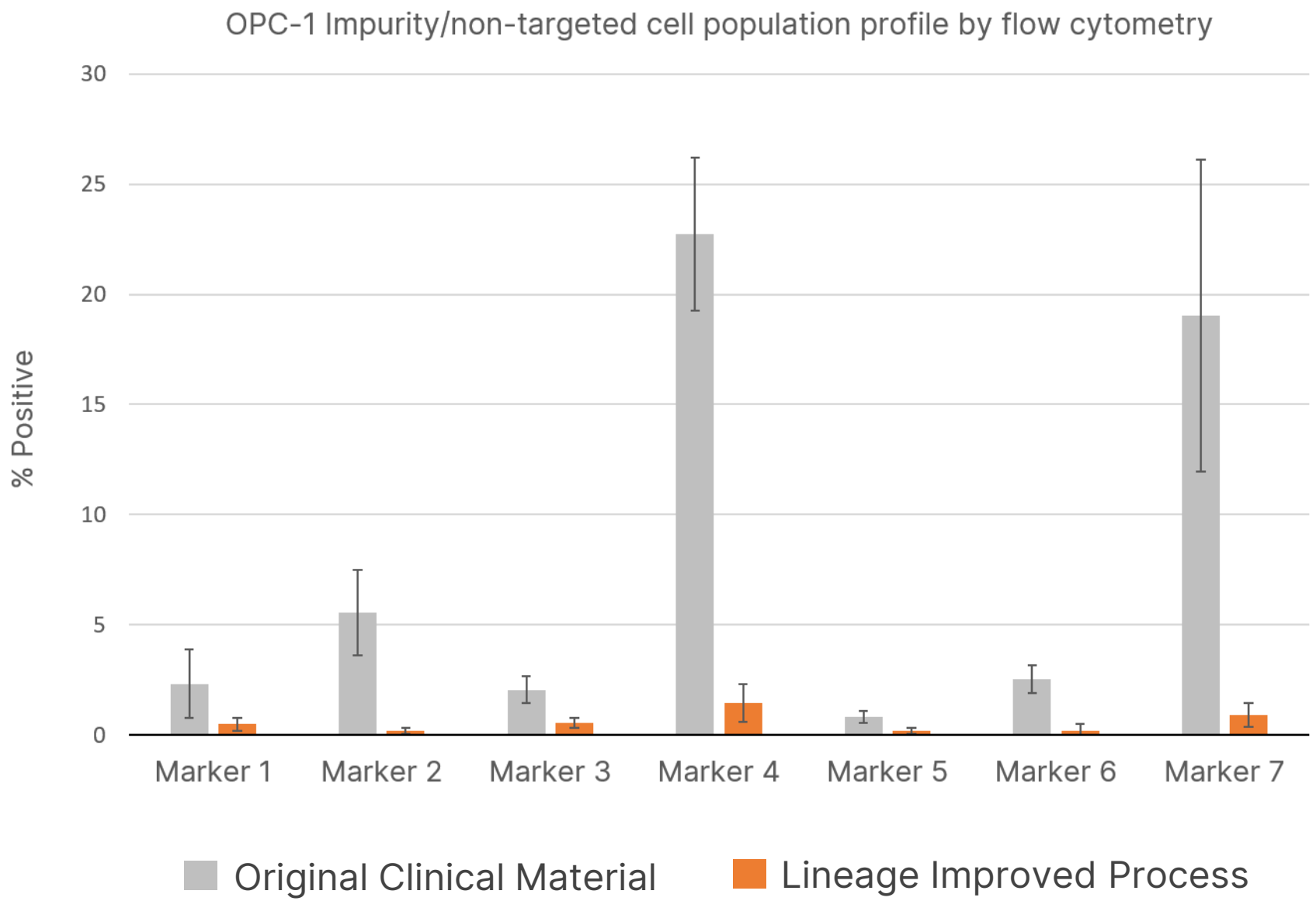
- Oligodendrocyte progenitor cells (OPCs) are precursors to the myelinating cells of the central nervous system
- Myelinating cells provide insulation to nerve axons in the form of a myelin sheath
- Myelin is essential for proper function of neurons



- 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)
- Cells are cryo-preserved in a ready to use, **thaw-and-inject formulation**

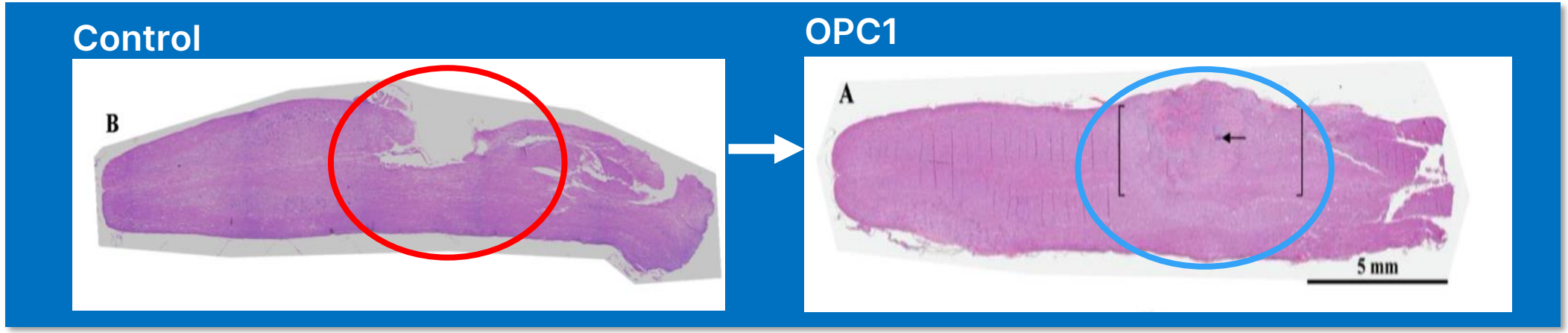


OPC1 Manufacturing Improvements: Lower Impurities

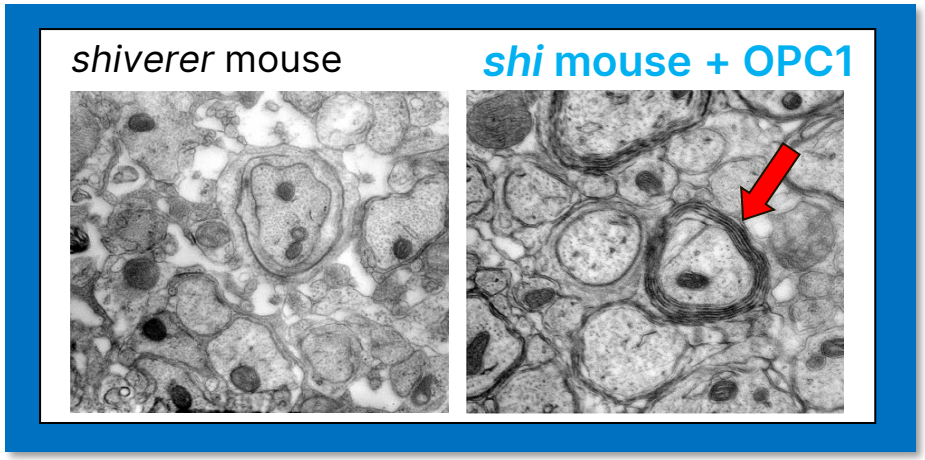


OPC1 Triple Mechanisms of Action

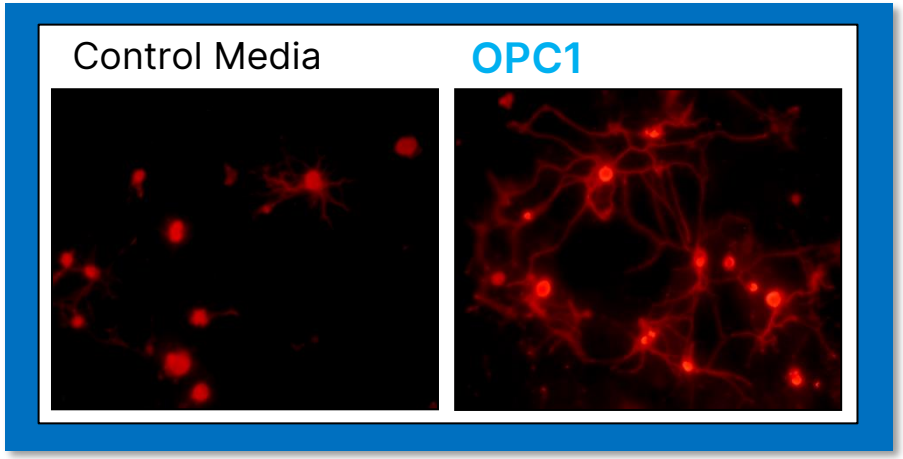
Preventing Cavitation



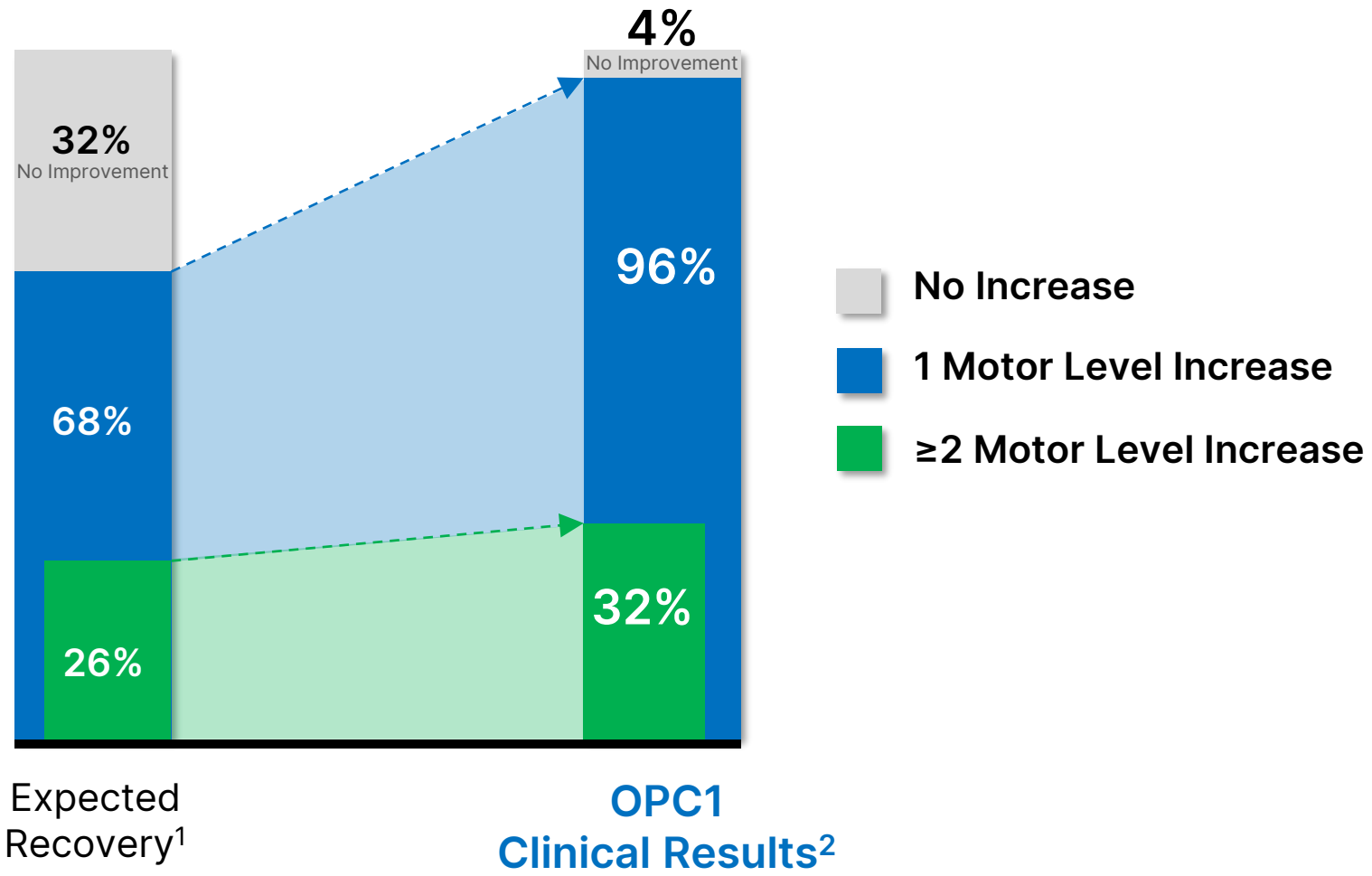
Myelination of Axons



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

Real-World Impacts from Motor Level Improvements

Motor level gains translate into meaningful improvements in self-care and large reductions in costs of care

Cervical Injury Level	Daily Home Care
C1-3	24 Hour Attendant
C4	18-24 Hour Attendant
C5	6-12 Hours of Assistance
C6	4 Hours Housework
C7-8	1 Hour Housework

32% of OPC1 Recipients had +2 Level Improvement

Activities of Daily Living across different levels of motor function after cervical complete SCI. Modified from Whiteneck et al. 1999)

OPC1 Cervical Clinical 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

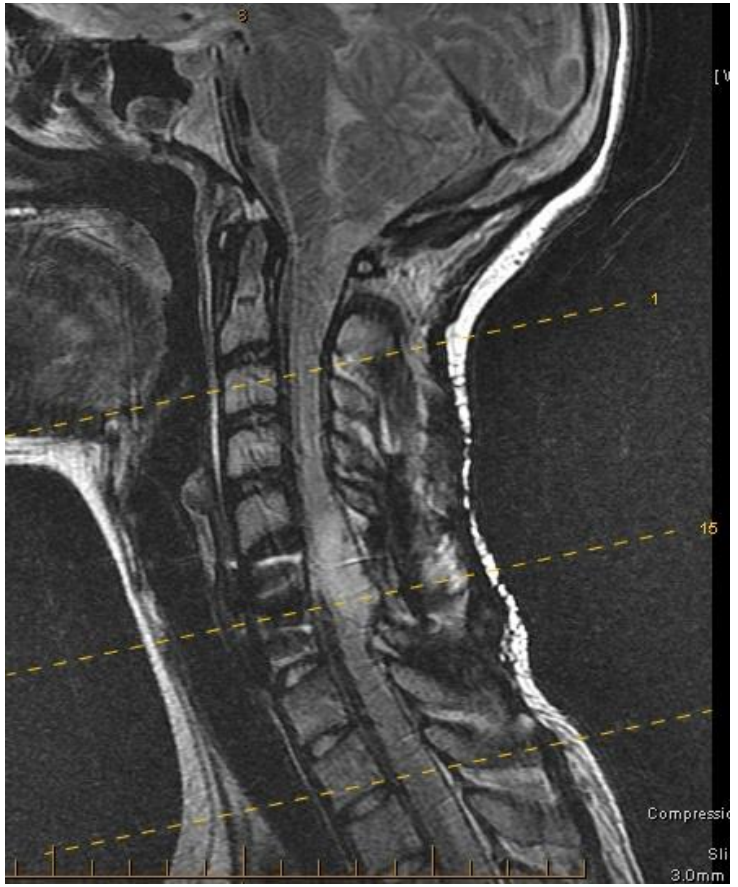
Safety data is available for 2 to 5 years on all 25 patients

**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)

OPC1 Program Summary

Key Takeaways

- **Unmatched experience** - one of the longest running trials in the field and first of its kind
- **Indication of efficacy** compared to best available matched control (32% two-level gain)
- **Excellent overall safety profile**
  - 5 years follow up in cervical SCI
  - 10 years follow up in thoracic SCI
- **Higher purity and production scale** has been achieved
- Learnings can be applied to next trial
  - Inadequate decompression was associated with the two worst outcomes

Next Steps

- **Clinical safety testing of new delivery system, starting in 2023**
  - 3-5 subacute and for the first time, 3-5 chronic injury patients
- **Preparations underway for larger, controlled clinical trial**
  - Engaging with patients and patient advocacy organizations
  - Assessing clinically-meaningful endpoints (no FDA precedent)
- **Eligible for grants** from the California Institute of Regenerative Medicine (CIRM)

OPC1 Asset Overview

- OPC1 utilizes targeted cell replacement (similar to OpRegen for dry AMD)
- OPC1 has RMAT & Orphan Drug Designations
- OPC1 has received >$14M in grant support from CIRM
- OPC1 may have application in other demyelinating conditions

"There's no reason to not look forward in the same way now that I had before all of this happened. I'm looking forward to driving again... it's a bright future."

- Lucas Lindner, OPC1 Patient

"I couldn't drink, couldn't feed myself, couldn't text or pretty much do anything, I was basically just existing. I wasn't living my life, I was existing."

- Kris Boesen, OPC1 Patient

"My recovery from the point of the trial until now has been immense. A lot more than I would have expected. So, if I had the chance to go back and do it again, I 100% would."

- Jake Javier, OPC1 Patient

"My AIS score improved from an AIS-A over to an AIS-B, because I've got a lot of feeling under my injury level that I didn't have right when I broke my neck. And I would attribute those directly to spinal cord injury cells."

- Chris Block, OPC1 Patient

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ANP1 and PNC1

Looking Ahead: Preclinical Programs

Preclinical Cell Transplant Programs

ANP1
Auditory neuron progenitor cells

- Intended to treat auditory neuropathy spectrum disorders (hearing loss)
  - Hearing loss afflicts >400 million people worldwide
- IP filed covering composition and methods of generating ANPs
- Preclinical studies: initiated Q1 2023
- Progressed from product concept to pre-clinical testing in <12 months and less than $1M
- Preparing for pre-IND meeting

PNC1
Photoreceptor cells (rods and cones)

- Intended to treat conditions of photoreceptor loss or dysfunction (vision loss; Retinitis Pigmentosa)
  - Leverages knowhow and capabilities in ophthalmology
- IP filed covering composition and methods of generating PRs
- Preclinical studies: ongoing
  - *In vivo* data shows PNC1 may connect to surrounding functional layers
  - Dynamic culturing offers path to industrial-scale production

Traditional Drug Discovery Pathway vs Lineage Technology

Traditional Discovery Process[1]
(e.g., small molecule)

$$$$$
4-5 years[1]

High Attrition
+ Target Validation Risk

Lineage PSC Technology
(e.g., ANP1)

$
<1 year

Differentiation Protocol ("Recipe")

No Target Validation Risk ⟶ target cell has confirmed role in the body
100% Probability of Success ⟶ PSCs by definition can become the target cell

1. Paul, S., Mytelka, D., Dunwiddie, C. et al. How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nat Rev Drug Discov 9, 203–214 (2010). https://doi.org/10.1038/nrd3078

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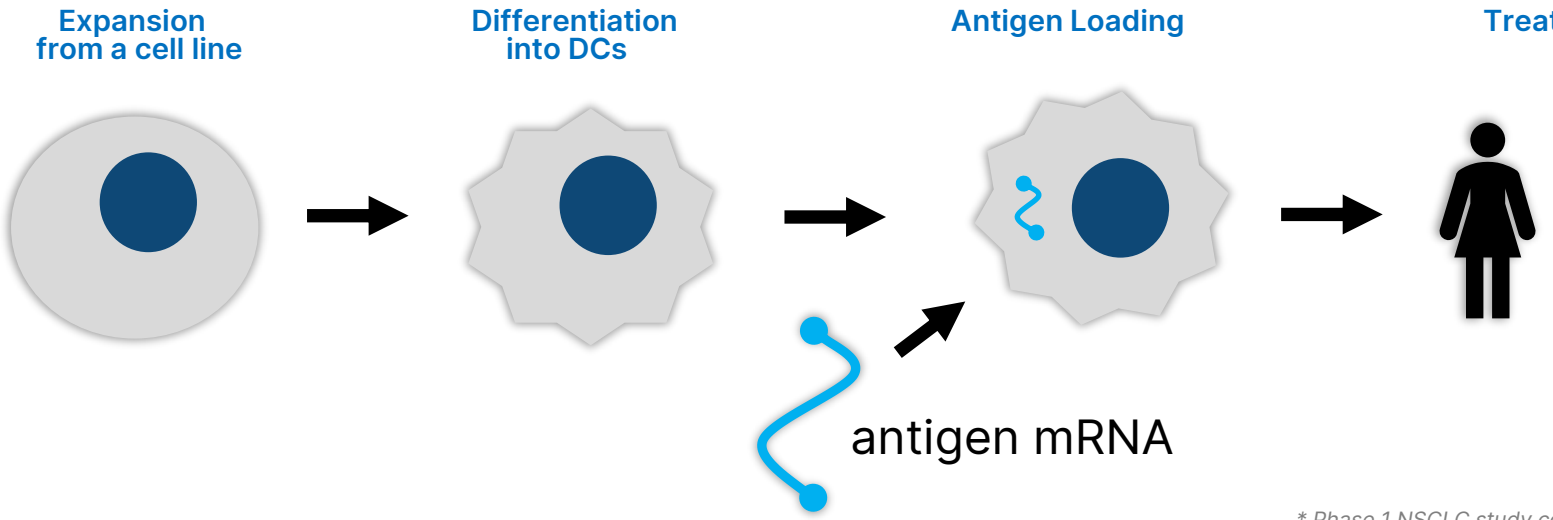
VAC

An Antigen-Presentation Platform for Cancer and Infectious Diseases

8 lung cancer patients treated to date

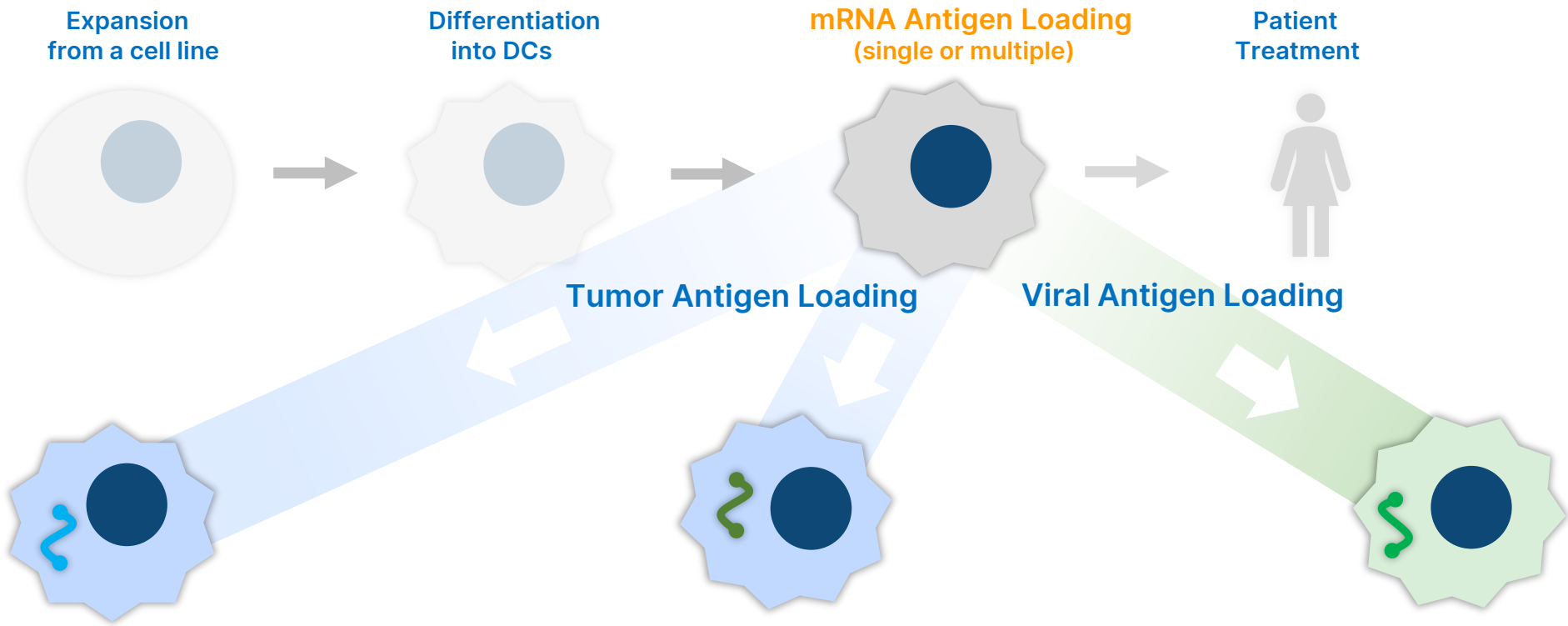
The VAC Platform: On Demand Cell Therapy Vaccine

- VAC consists of allogeneic (“off the shelf”) dendritic cells (DCs)
- No production lag between diagnosis and treatment, as required for autologous or patient-specific therapies
- DCs are manufactured and loaded with either a **tumor antigen** (as a cancer vaccine) or a **viral antigen** (as a vaccine for infectious diseases)
- Antigen presentation creates a *large, targeted* T cell response (can be >3%), responsible for tumor cell destruction or pathogen clearance*



** Phase 1 NSCLC study conducted by CRUK, ongoing (NCT03371485)*

VAC – A Platform for Many Product Candidates



VAC1 and VAC2 Immuno-Oncology

- Positive phase 1 data in AML
- Completed phase 1 in NSCLC, analyses ongoing

CANCER RESEARCH UK

Other Immuno-oncology Programs

- Partnerships based on new antigens
- Diversifies pipeline and shares cost

IMMUNOMIC Therapeutics, Inc.

VAC-Infectious Diseases

- Long-term protection via memory T cells
- Leverages clinical data from VAC oncology programs

Lineage Corporate Profile

Corporate Headquarters
Carlsbad, California

Research & Development
Carlsbad, California

Manufacturing
Jerusalem BioPark, Israel

Strong Financial Position

$66.4M

Cash & equivalents at 9/30/22

Market Capitalization

~$260M*

Employees

77

(U.S. & Israel)

*Based on common shares outstanding as of 11/4/2022 and closing trading price as of 1/17/2023

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The Patients Are Our Inspiration.

View their stories at lineagecell.com/media