



## Corporate Overview

# Forward-Looking Statements

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**“We aim to pioneer a new branch of medicine, based on transplanting specific cell types into the body”**

## **Business Overview**

# Company Overview

## Innovative Platform

Manufacturing and transplanting *specific cell types* from a single pluripotent cell line; scalable “off the shelf” cell transplants for multiple conditions

## Validating Partnerships

**Genentech**  
A Member of the Roche Group

**CIRM**  
CALIFORNIA / STEM CELL AGENCY

 **CANCER RESEARCH UK**

## Five Allogeneic Product Candidates in Development

**OpRegen:** Dry Age-Related Macular Degeneration (dry AMD)  
**OPC1:** Spinal Cord Injury  
**VAC2:** Oncology (NSCLC)  
**ANP1:** Hearing Loss (Auditory Neuropathy Disorders)  
**PNC1:** Various Forms of Blindness

## Differentiated Data

Outer retinal structure improvement observed in five dry AMD patients  
One-third of spinal cord injury patients gained at least 2 levels of motor function  
Potent induction of immune responses observed in advanced cancer patients

## Market Opportunity

Multiple billion-dollar commercial opportunities

## Financial Position

\$72 million in cash and cash equivalents as of June 30, 2022

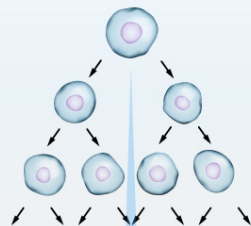
## Market Capitalization

~\$290 million\*

# Lineage Technology Platform – Allogeneic Cell Transplants

## Expansion

- Product development starts from a frozen vial of self-renewing stem cells
- These pluripotent cells can become any cell type in the body when provided with the correct instructions



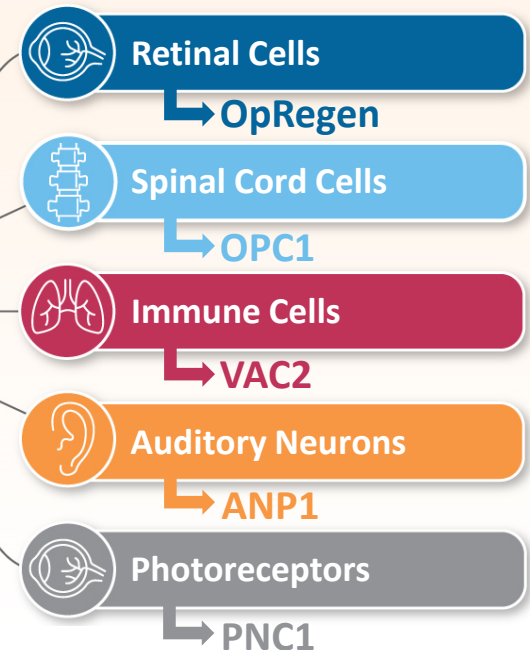
## Differentiation

- Lineage's proprietary process, honed from decades of institutional experience, creates only the cell type which is desired
- No alterations are made to the cell's DNA
- In-house cGMP manufacturing allows for commercial-scale production from a single vial of stem cells



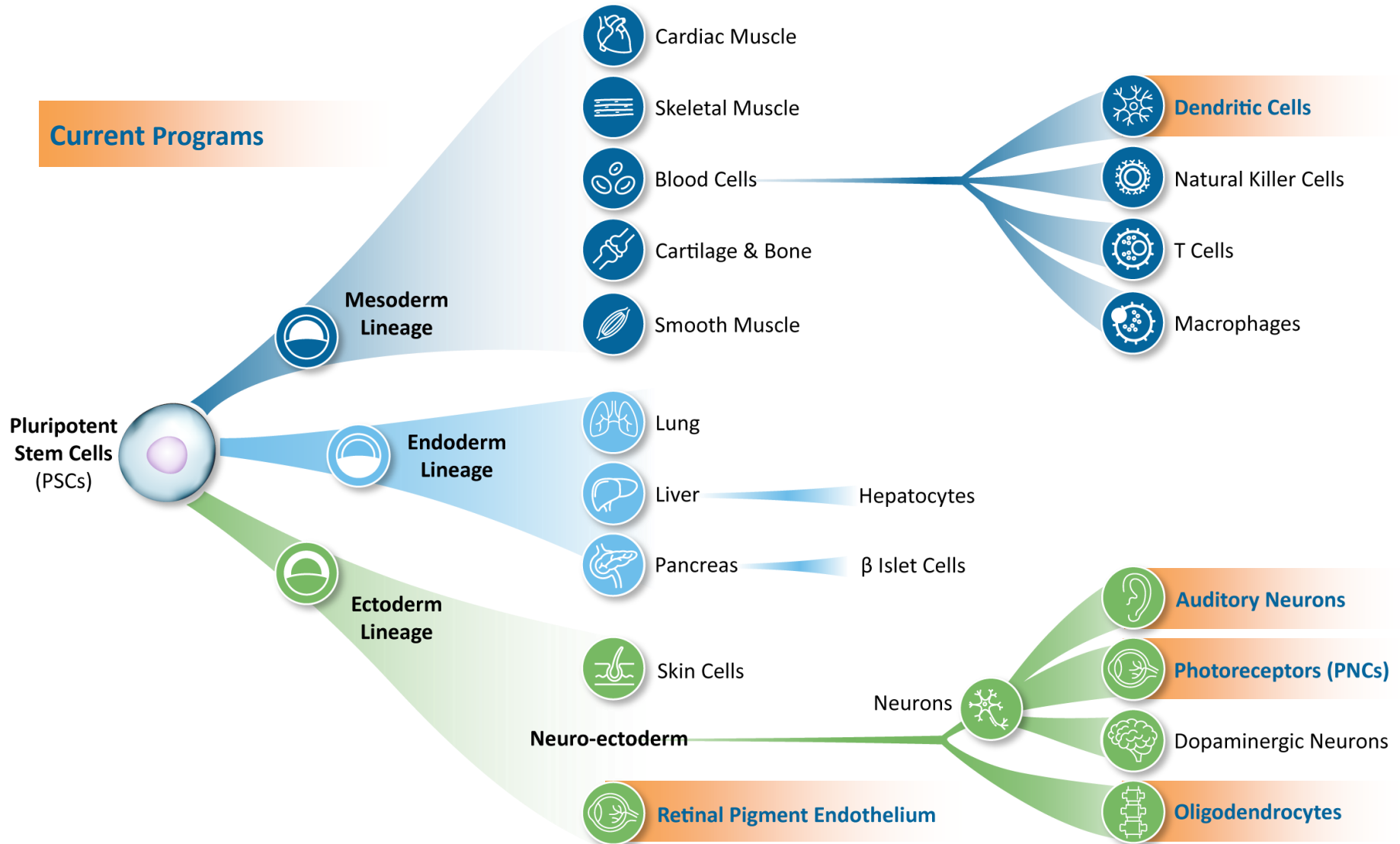
## Development

- Value is created by developing *clinically and commercially-viable* product attributes
- Expansion occurs via broadening indications or adding new cell types











# Many Potential Product Opportunities



# Cell Therapy Pipeline

LINEAGE	PROGRAM	PHASE 1	PHASE 2	PHASE 3	PARTNERS
 Ophthalmology	<b>OpRegen®</b> Dry AMD with Geographic Atrophy (GA)		24 patients treated		<b>Genentech</b> A Member of the Roche Group
 Demyelination	<b>OPC1</b> Spinal Cord Injury (SCI)		30 patients treated		<b>CIRM</b> CALIFORNIA STEM CELL AGENCY
 Immuno-oncology	<b>VAC2</b> Non-Small Cell Lung Cancer (NSCLC)	8 patients treated			 <b>CANCER RESEARCH UK</b>
 Neurology	<b>ANP1</b> Auditory Neuropathy (Hearing Loss)	Preclinical			Internally-Owned
 Ophthalmology	<b>PNC1</b> Various Forms of Blindness	Preclinical			Internally-Owned

# Competitive Advantage – Differentiation (Process Development)

**Lineage's competitive advantage is the *differentiation* of an *unlimited* supply of pluripotent stem cells into *specialized cell types***

## Capabilities

- Source cell characterization, banking and versatile expansion systems
- Differentiation process development; culture conditions, systems, optimization of differentiation cues (growth factor selection, timing, etc.)
- Analytical method development for process control and product release
- Scale-up modalities, substrates, harvesting protocols
- Enhancements; genetic modification (optional), various expression systems
- Clinically compatible post-production processing

## cGMP Facility



**Multiple Clean Rooms for Parallel  
cGMP Production Runs**

**Extensive IP portfolio covers  
processes, products, and methods  
of use**





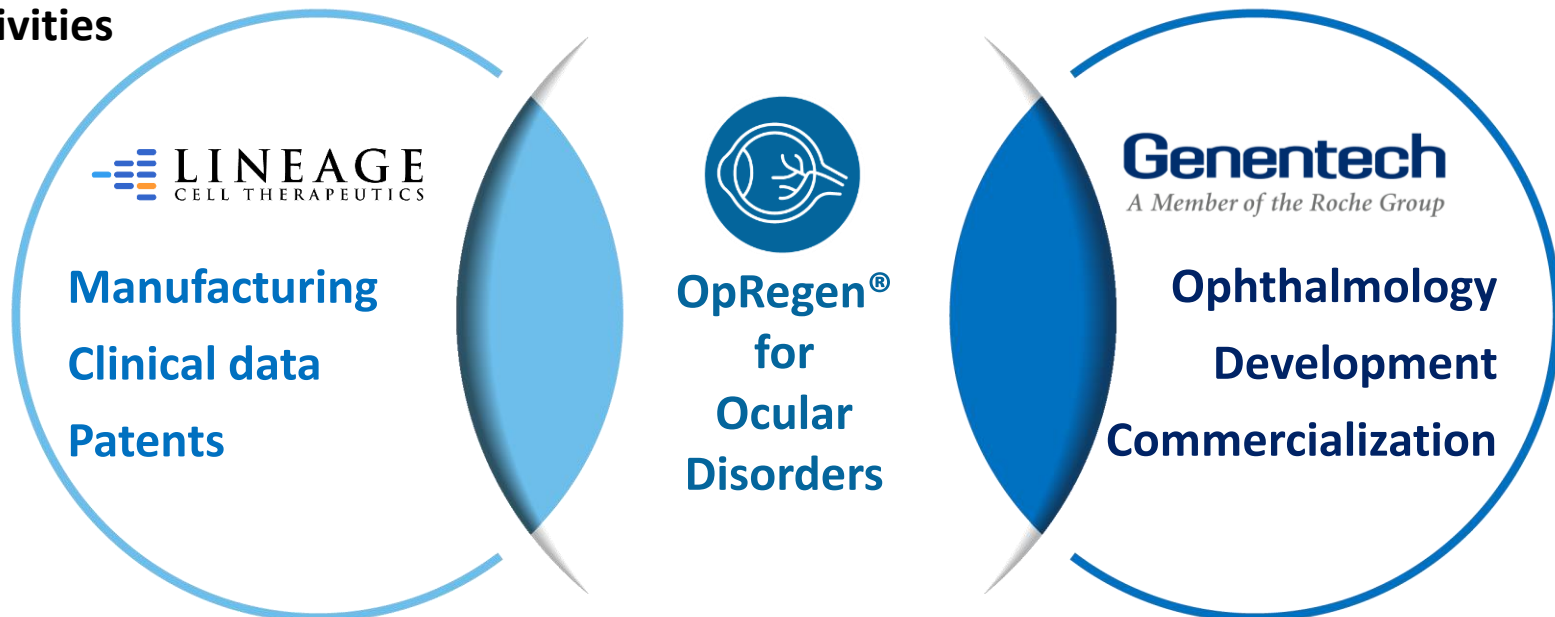
AMD is the **leading cause** of  
irreversible vision loss in the US

*Source: [aao.org](http://aao.org)*

OpRegen<sup>®</sup> : RPE Cell Transplants to Treat Dry AMD

## Exclusive collaboration for the development and commercialization of OpRegen for the treatment of ocular disorders

- \$50 million up front; \$620 million of potential milestone payments; double-digit tiered royalties
- Genentech responsible for clinical development and commercialization
- Lineage to complete ongoing study and continue certain development and manufacturing activities

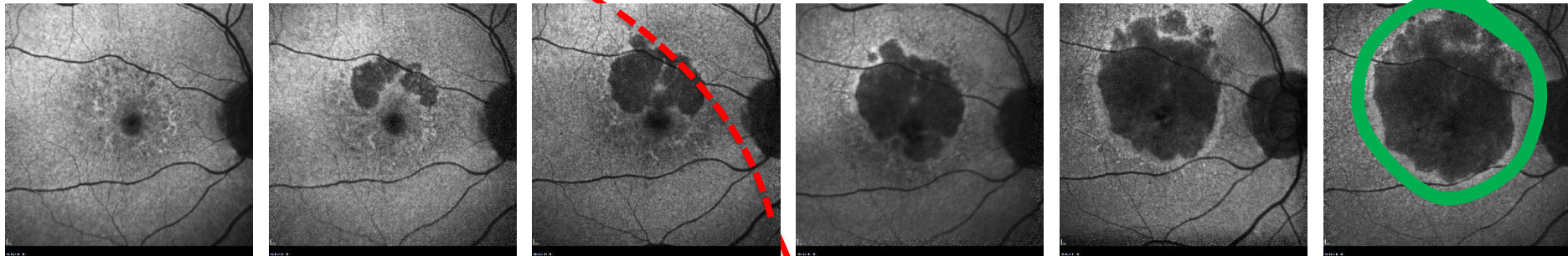


# Dry AMD Can Lead Rapidly to Blindness

## Visual acuity over time...

20/20  
(normal)

The area of geographic atrophy or “GA” grows larger as retinal cells die



2012

2013

2014

2015

2017

2019

20/200  
(legally blind in 3 years)

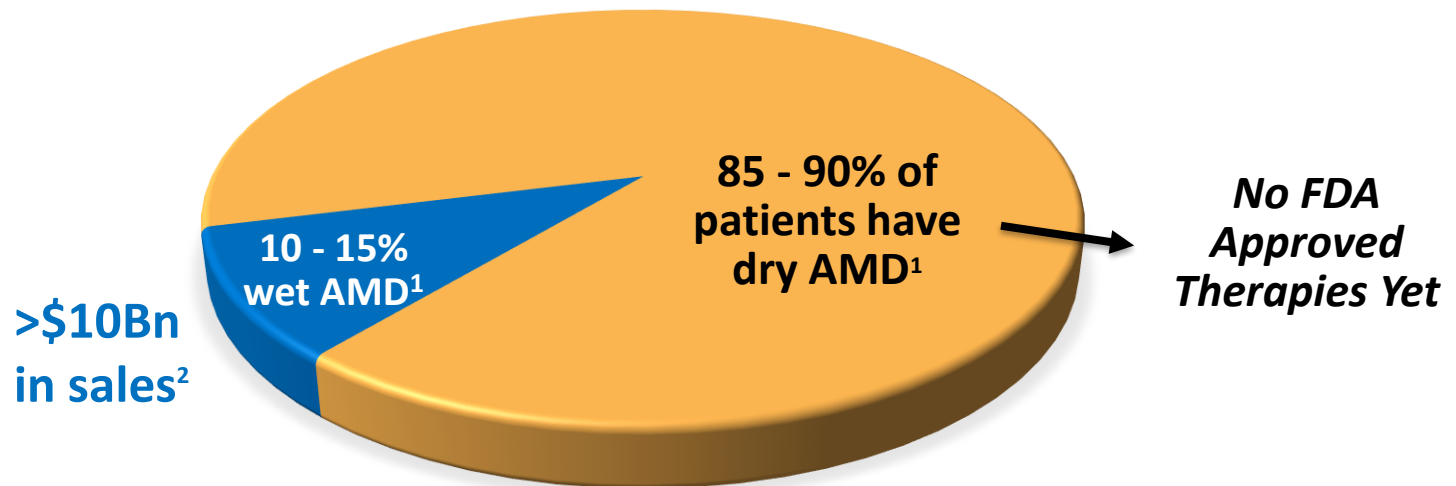
Dry AMD involves the  
progressive loss of retina  
cells, which can lead rapidly  
to blindness

20/640

# Dry AMD: A Multi-Billion Dollar Market Opportunity in the U.S.

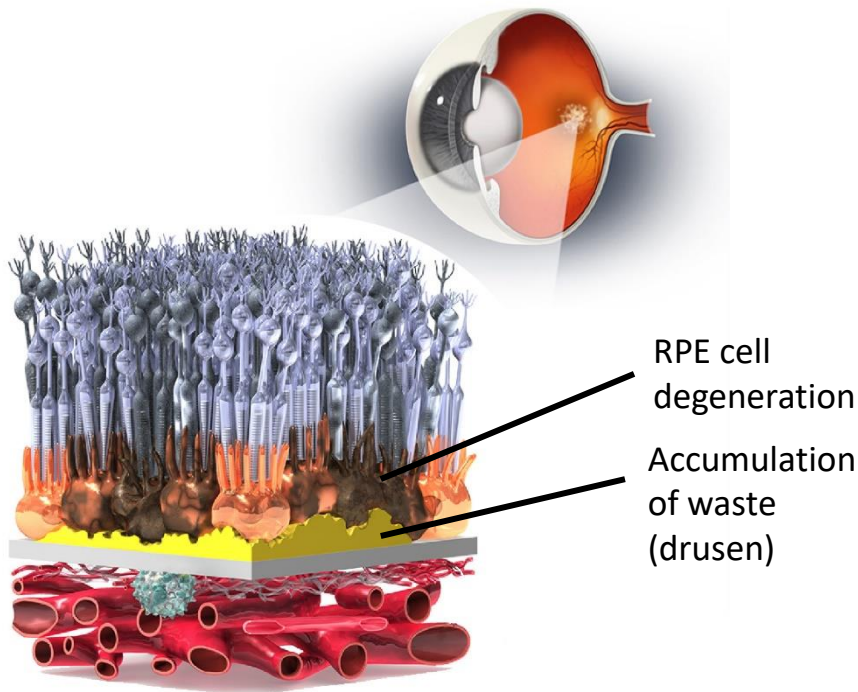
**Age-related Macular Degeneration (AMD) in all forms afflicts  
~11 million people in the United States**

Type of AMD	% of AMD Cases	FDA Approved Therapies
Wet AMD	10 – 15%	Lucentis & Eylea (\$10 billion in annual sales)
Dry AMD	85 – 90%	None



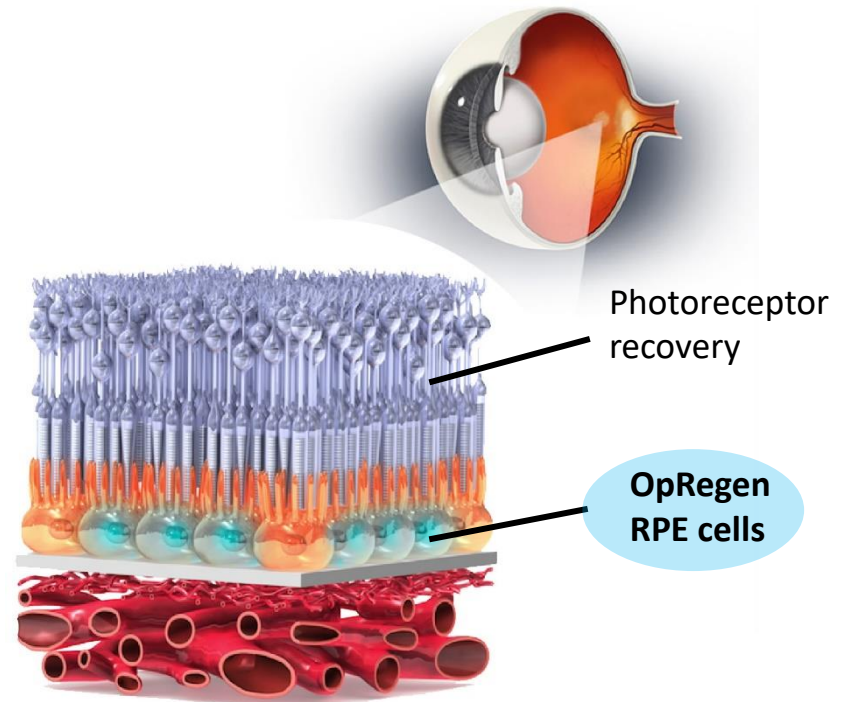
# Lineage Approach – OpRegen, an RPE Cell Transplant

## Pre-Transplant



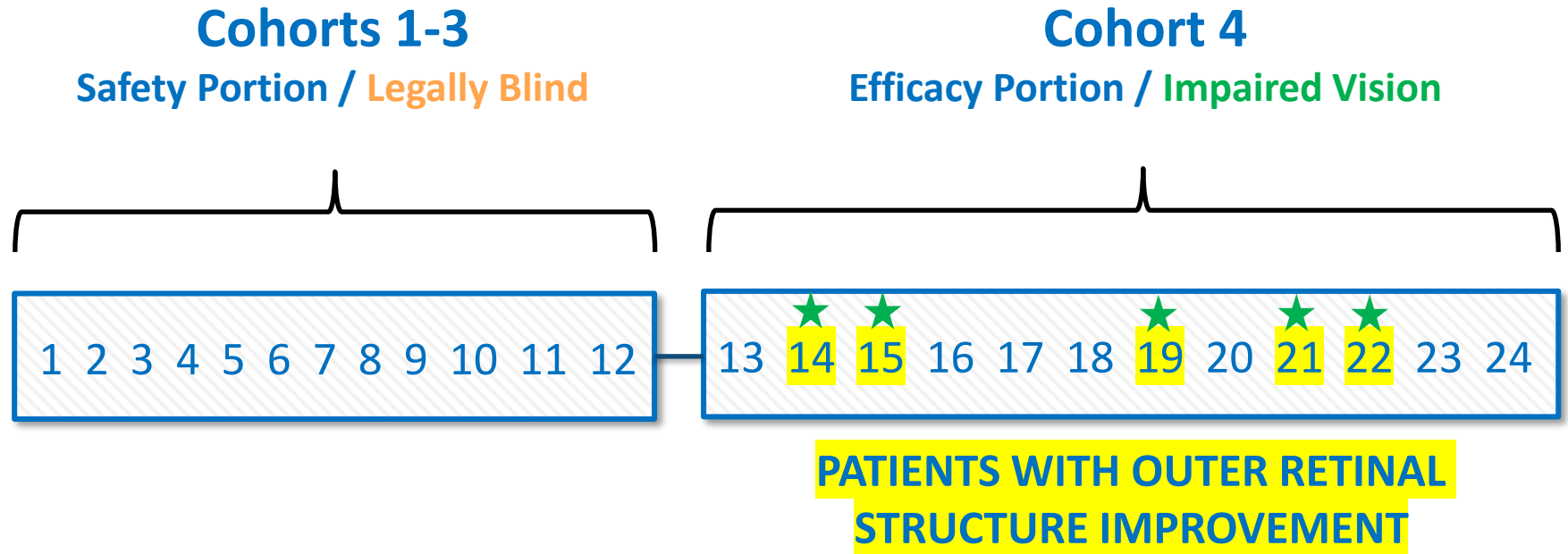
**Dry (atrophic) AMD involves the loss of retina cells, creating an area of geographic atrophy (GA), which causes impaired vision and blindness**

## Post-Transplant



**OpRegen is an injection of RPE cells beneath the retina, to potentially replace and restore lost retinal cells, and preserve or improve vision**

# Phase 1/2a Clinical Trial of OpRegen – Enrollment Complete, Long-Term Follow-Up Ongoing



## Purpose:

To evaluate the safety and efficacy of transplanted RPE cells in patients with dry AMD with geographic atrophy

## Design:

Open label, single arm, international, multi-center

## Dose and Administration:

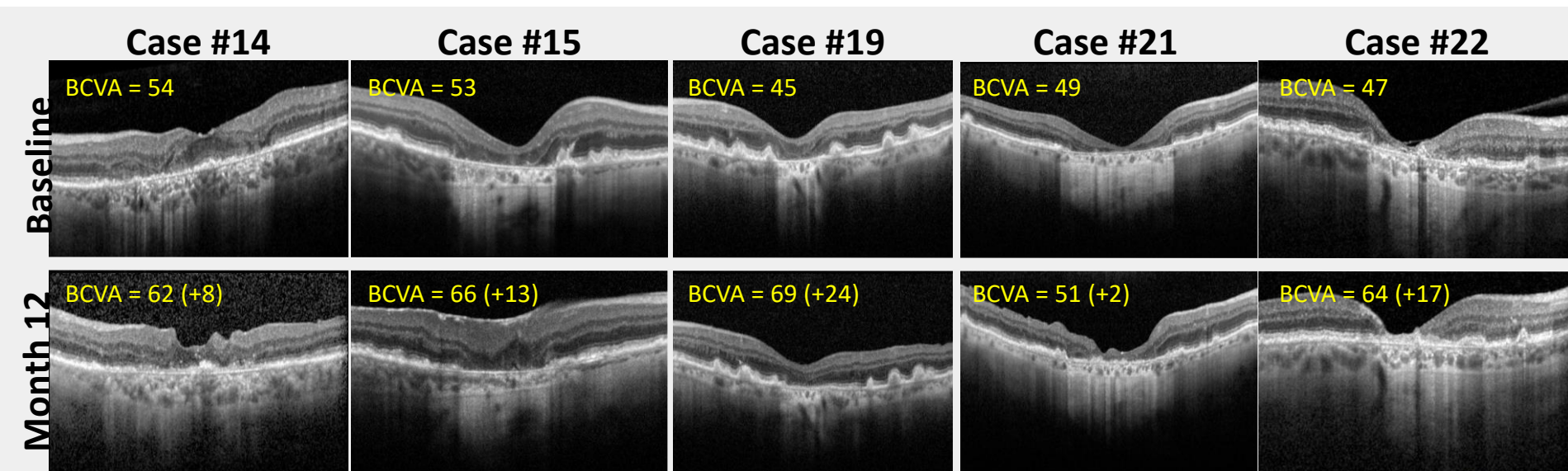
One 50-100 ul dose of cells injected into the subretinal space



# Phase 1/2a Clinical Trial - Subretinal Delivery of OpRegen to GA Area and Fovea

## Greater Visual Function Gains With Areas of Outer Retinal Structure Improvement

- Five patients in Cohort 4 had OpRegen delivered to most or all of the GA area, including the fovea
  - These 5 patients had greater gains in visual function (average 12.8 letter gain), with evidence for regions of apparent improvement of outer retinal structure as assessed by SD-OCT



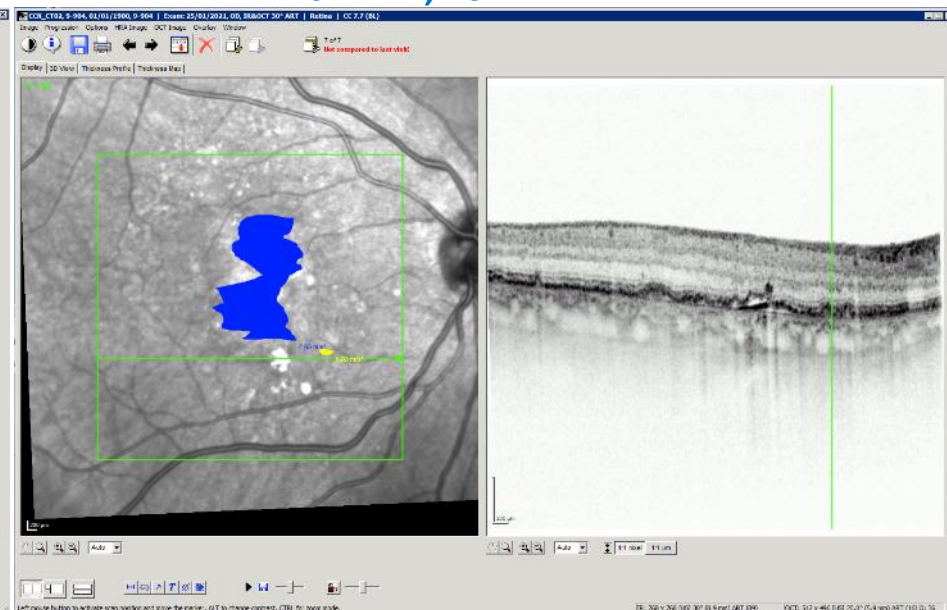
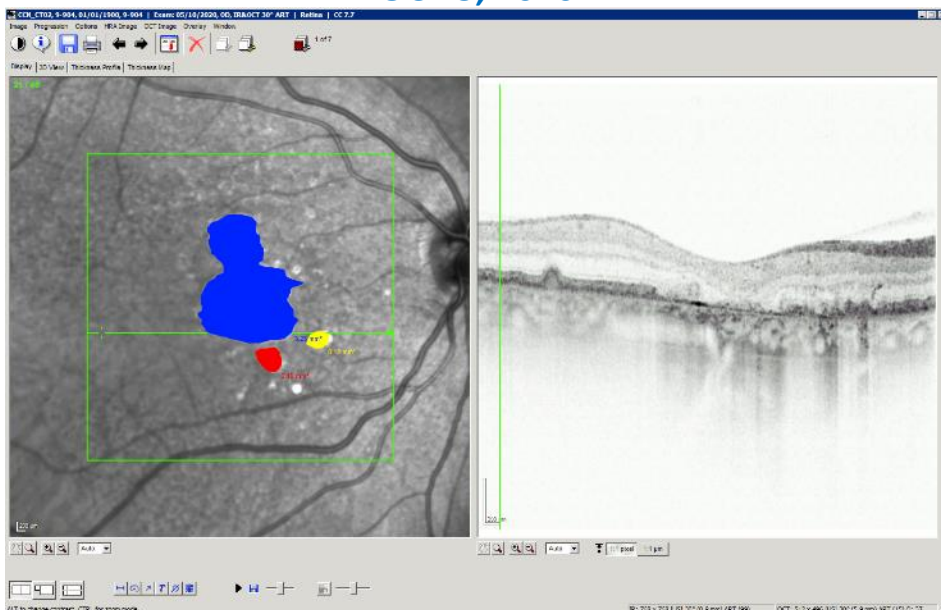
SD-OCT, spectral domain optical coherence tomography. BCVA measured by ETDRS letter score.

# Third Case of Retinal Restoration – Evident at 3 Months

## ELM-based Area of Atrophy (Baseline to 3 Months)

OCT 5, 2020

JAN 21, 2021



TOTAL AREA: 3.56 mm<sup>2</sup>

TOTAL AREA: 2.69 mm<sup>2</sup>

Total area

3M GROWTH RATE:

– 0.87 mm<sup>2</sup>

(ANNUAL RATE – 3.48 mm<sup>2</sup>)

SQRT transformation

3M GROWTH RATE:

– 0.23 mm

(ANNUAL RATE – 0.92 mm)

# Commercially-Suitable Manufacturing Process

- **OpRegen consists of pure RPE cells >99%**
  - Starts from an NIH-approved cell line established >20 years ago
  - Extensive functional and identity characterization is employed for product release
  - No genetic modifications are made to the cells
  - No residual pluripotent cells detectable in clinical material
- **Clinic-ready, immediate-use “thaw and inject” formulation**
  - No dose preparation required
  - From frozen cells to delivery device in 5 minutes
- **Current production scale is 5 billion RPE cells per 3-liter bioreactor**
  - Equal to 2,500 clinical doses/batch
  - Further scale-up can be performed in larger or parallel reactors



# OpRegen - A Multi Billion-Dollar Commercial Opportunity

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- **Outer retinal structure improvement was observed in five dry AMD patients (the only known clinical cases)**
- **Market opportunity is not limited by monogenic deficiencies (e.g. gene therapy)**
- **Treatment has been well-tolerated; no cases of rejection (90d immunosuppression)**
- **Potential application in other retinal diseases**
- **Issued patents cover aspects of production, characterization, and formulation**
- **Fast Track designation from FDA**
- **Validating development partnership with global ophthalmology leader, Genentech**

## Key Takeaway for the Lineage Approach:

- **In certain settings, replacing whole cells may provide restorative benefits beyond the reach of traditional approaches; #replaceandrestore**



Lifetime care for an SCI  
patient can cost nearly  
**\$5 million**



*Source: [christopherreeve.org](http://christopherreeve.org)*

**OPC1: Cell Therapy for Spinal Cord Injuries**



# Why Spinal Cord Injury (SCI) Matters

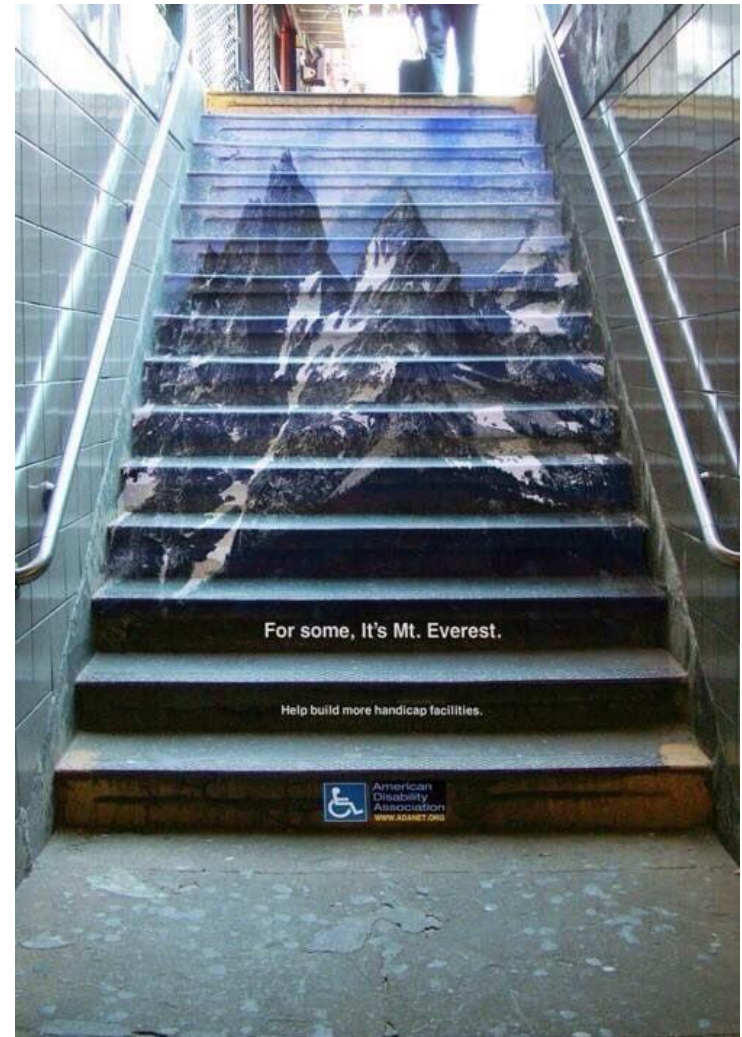


Lucas Linder, an OPC1 clinical trial participant, was paralyzed from the neck down.  
The next year, he threw out the first pitch at a Major League Baseball game.



# SCI Burden and Unmet Needs

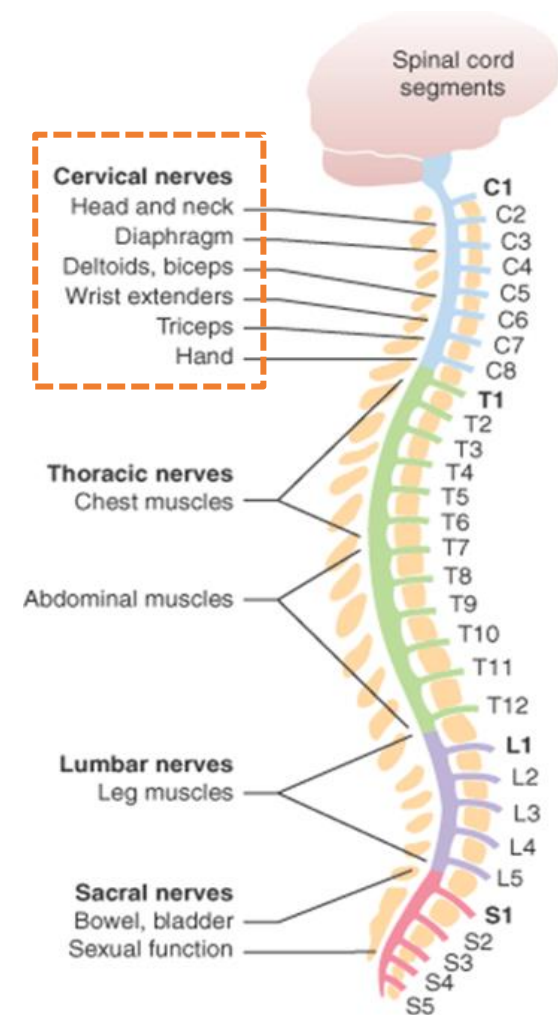
- **Approx. 18,000 cases per year (US)<sup>1</sup>**
- **A significant burden for patients and caregivers<sup>2</sup>**
  - 67% of patients are unemployed 10 years post-injury
  - Lifetime healthcare costs can reach \$5M for one patient
- **Potential lifelong impairments**
  - Mobility (wheelchair)
  - Pain
  - Re-hospitalizations
  - Infections
  - Ventilator dependency
  - Depression
  - Shortened life expectancy



# SCI Treatment Objectives

## Loss of movement is the primary feature of a spinal cord injury

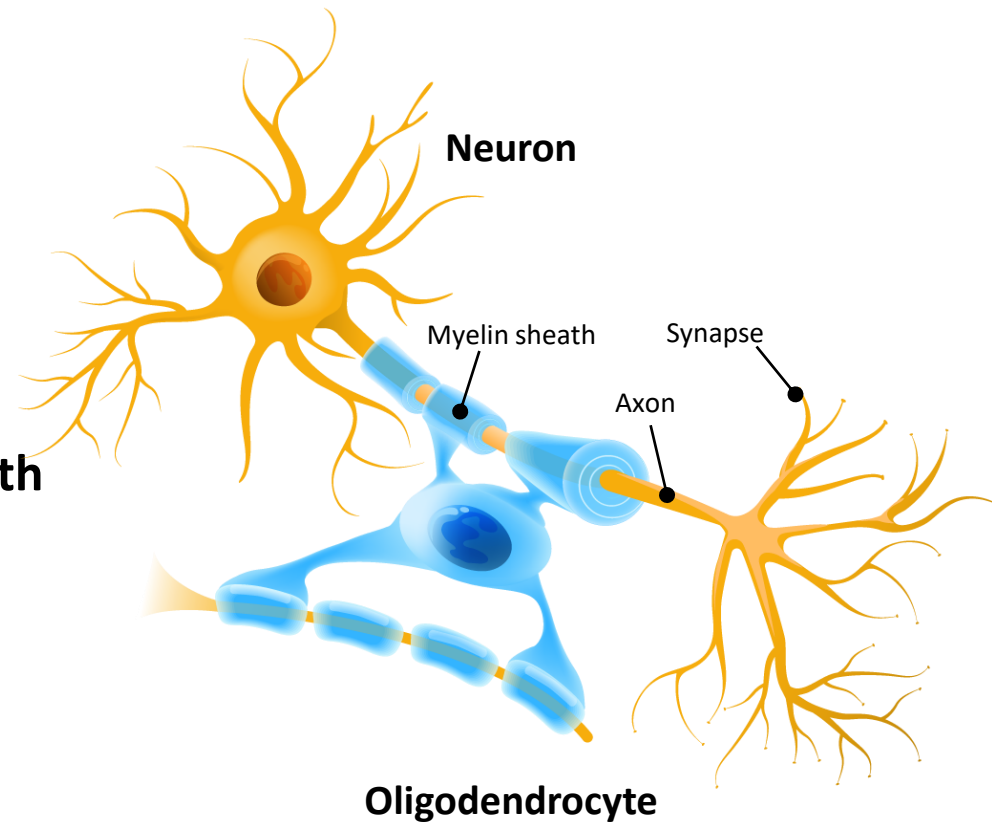
- **Higher-level injuries result in more extensive impairments**
- **Gains in motor function, particularly in the upper extremities, can provide significant benefits in self-care and lower costs of care**
- **The goal of Lineage's cell therapy is to provide additional arm, hand, and finger function, increasing independence and quality of life**



# OPC1 cells for Spinal Cord Injury

**Transplanting oligodendrocytes may provide additional upper extremities function (arms and fingers) and improve quality of life**

- **OPC1 is comprised of OPCs (oligodendrocyte progenitor cells)**
- **OPCs are precursors to oligodendrocytes, the myelinating cells of the central nervous system which provide insulation to nerve axons in the form of a myelin sheath**
- **Myelin is essential for proper function of neurons**
- **OPC1 cells are implanted into the spinal cord at the injury site**



# OPC1 Asset Overview

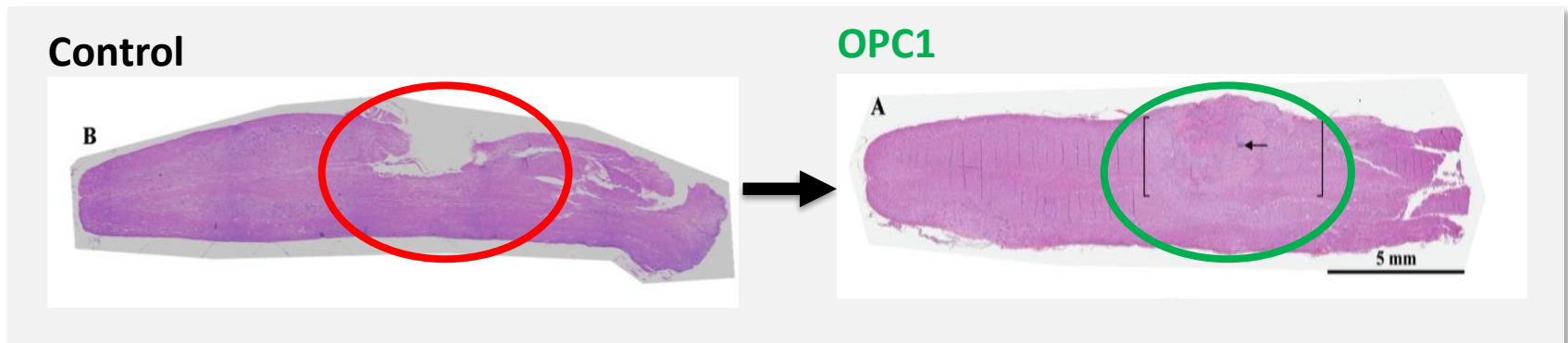
- **OPC1 utilizes targeted cell replacement (similar approach as OpRegen)**
- **OPC1 is covered by multiple issued patents**
- **OPC1 has RMAT Designation**
- **OPC1 has Orphan Drug Designation**
- **OPC1 has received >\$14M in support from CIRM (California Institute for Regenerative Medicine)**
- **OPC1 may have application to other demyelinating conditions**



**OPC1 Transplant Procedure**

# OPC1 Mechanisms of Action

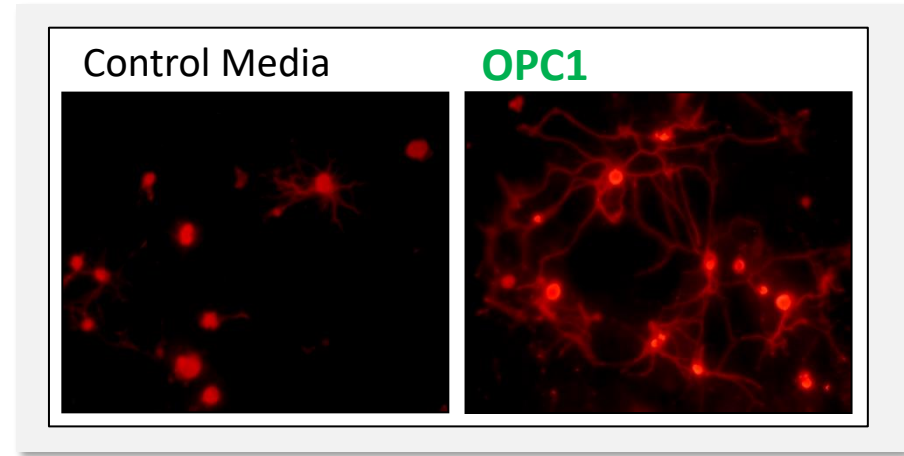
## Suppression of Cavitation



## Myelination of axons



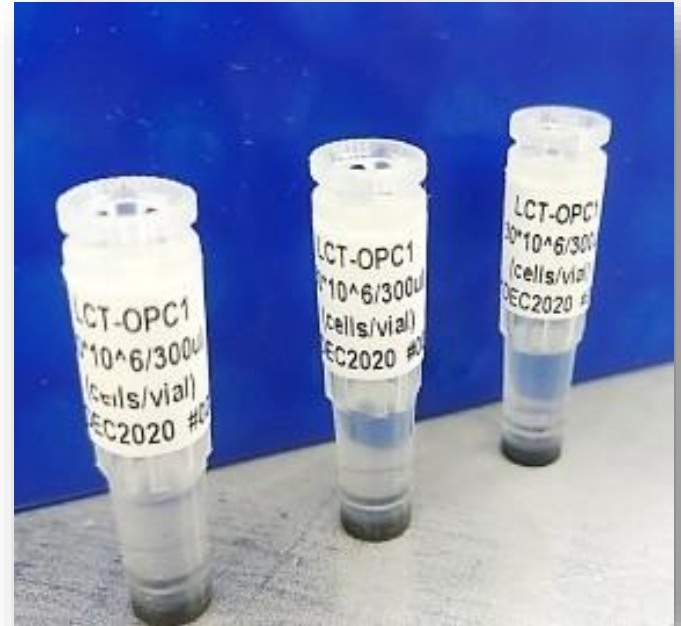
## Secretion of neurotrophic factors





# OPC1 for Spinal Cord Injury

- Lineage's OPCs are derived from an NIH-registered cell line
- The OPCs are allogeneic ("off the shelf"), and not taken from the patient
- Treatment of SCI occurs 3-6 weeks post-injury and includes short-course (60-day) immunosuppression
- The OPCs are "ready to use" in a cryopreserved thaw-and-inject formulation

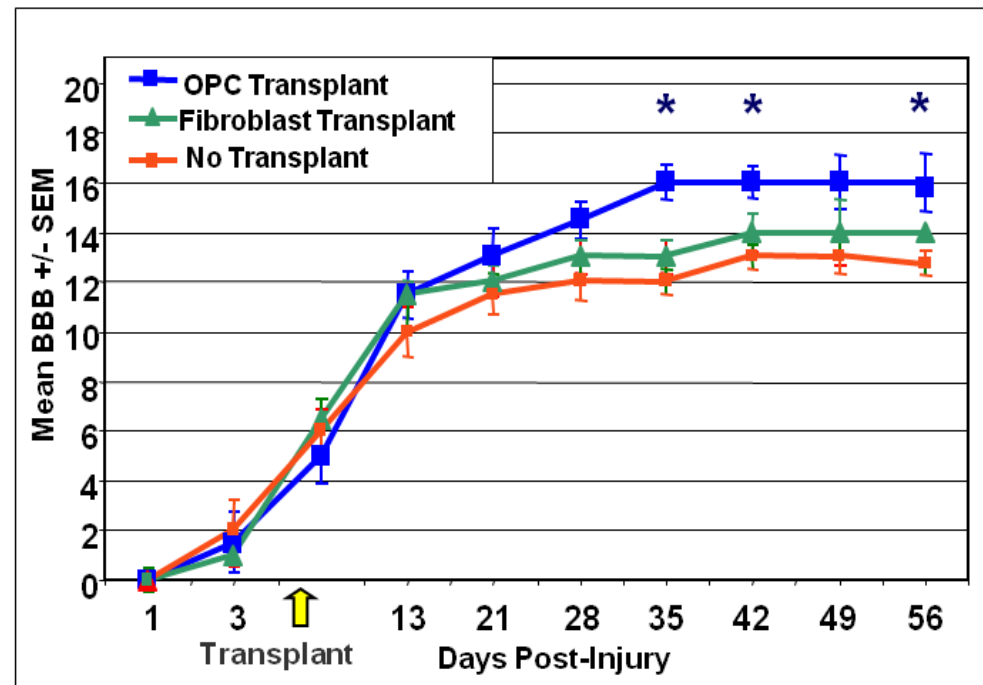




# OPC1 Improved Motor Function in Preclinical Animal Models

## Locomotor Improvement in Thoracic SCI

- Increased weight bearing
- Improved hindlimb-forelimb coordination
- Improved hind paw clearance
- Improved trunk stability
- Decreased tail drag



# OPC1 Cervical Clinical Trial - Summary of Adverse Events

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

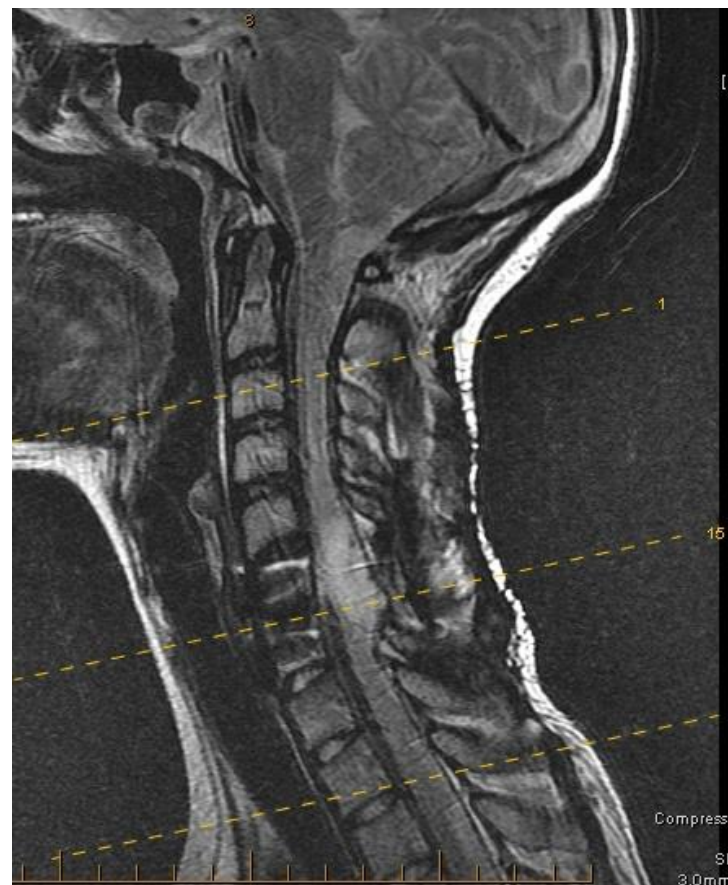
All Treated Subjects (n=25)	AEs	SAEs
Total	534	29
Related to OPC1	1*	0
Related to Injection Procedure	20	1
Related to Tacrolimus	11	1

**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**

# OPC1 Cervical Clinical Trial - Cell Engraftment

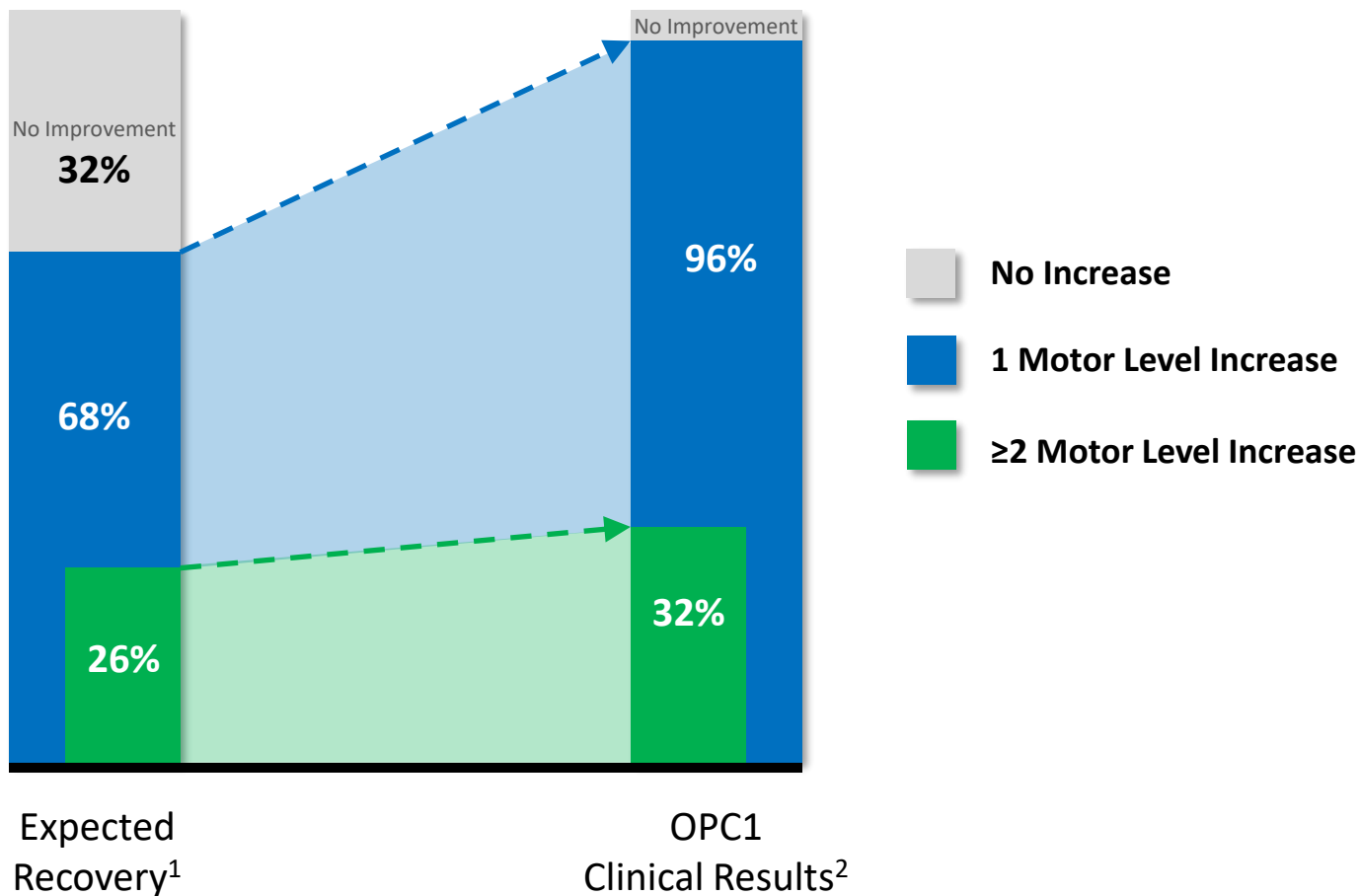
## 12- and 24-Month MRI Scans Indicate Durable Engraftment

- Cystic cavitation (syringomyelia) occurs in ~80% of SCI cases
- MRI results suggest formation of a tissue matrix at the injury site, indicating that OPC1 cells have durably engrafted and helped prevent syringomyelia
- 96% (24/25) of OPC1 patients had serial MRI scans that indicated no sign of a lesion cavity at 12 months (or 24 months for 22 scans available)



Weighted sagittal MRI

# Motor Function Gains – Expected Recovery<sup>1</sup> vs OPC1-Treated (Cervical Clinical Trial)




# Real-World Benefit from a 2 Motor Level Improvement


Motor level gains translate into clinically meaningful improvements in self-care and reductions in cost of care

32% had +2 Level Improvement


Function	Cervical Injury Level				
	C1-C3	C4	C5	C6	C7-C8
Bowel					
Bladder					
Bed Mobility					
Transfers					
Pressure Relief					
Eating					
Dressing					
Grooming					
Bathing					
Wheelchair					
Car transport					
Daily Home Care	24 hr attendant	18-24 hr attendant	6-12 hr assistance	4 hr housework	1 hr housework



Total Assist



Partial Assist



Independent

# OPC1 Cervical Clinical Trial – 2 Year Results

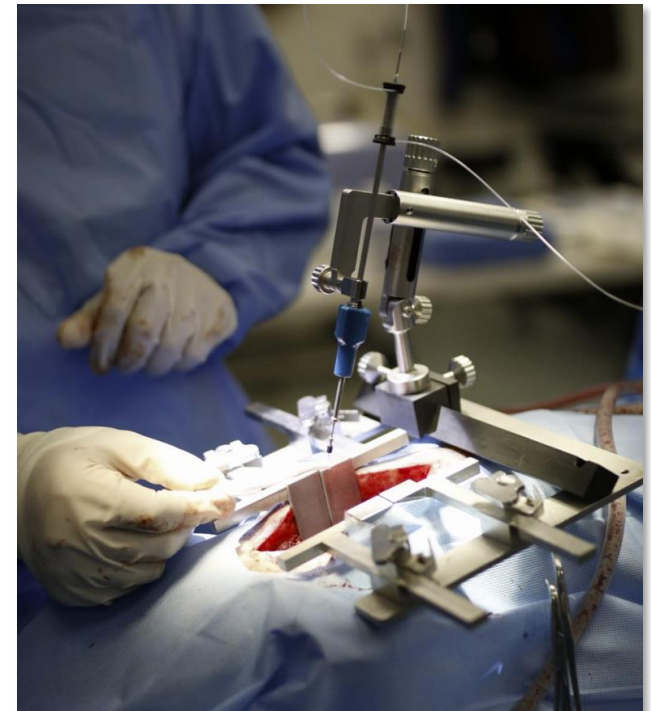
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- **Overall safety profile of OPC1 continued to be excellent**
  - All 25 subjects evaluated for at least 2 years
  - MRI scans showed no evidence of adverse changes
  - No unexpected serious adverse events related to the OPC1 cells
  - No study subjects had worsening of neurological function
- **Motor Level Improvements Have Been Durable; One Patient Improved Further**
  - Cohort 1 subjects continued to be stable 2-4 years after treatment
  - 5 subjects in cohort 2 achieved at least 2 motor levels of improvement over baseline on at least one side (previously 4 of 6 at 12 months)
  - 1 subject in cohort 2 achieved 3 motor levels of improvement on one side; maintained at 3 years



# New Spinal Cord Delivery System – Clinical Testing Planned

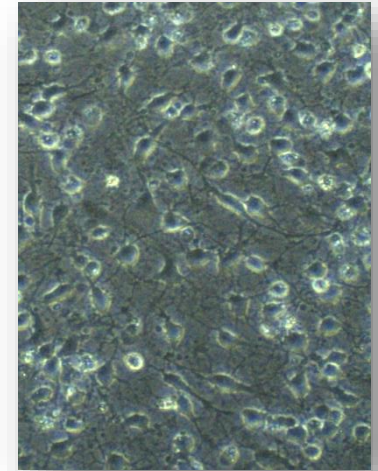
- **Better stability and control**
  - Eliminates motion between platform/XYZ manipulator/needle
- **Enhanced usability and safety: no cessation of ventilation**
  - Attaches directly to the patient, compatible with breathing motion
- **Improved user experience**
  - Smaller and fewer components
  - Single hand operation
- **Majority of verification and validation activities and preclinical testing completed**
- **Device clinical trial in sub-acute and chronic patients planned**



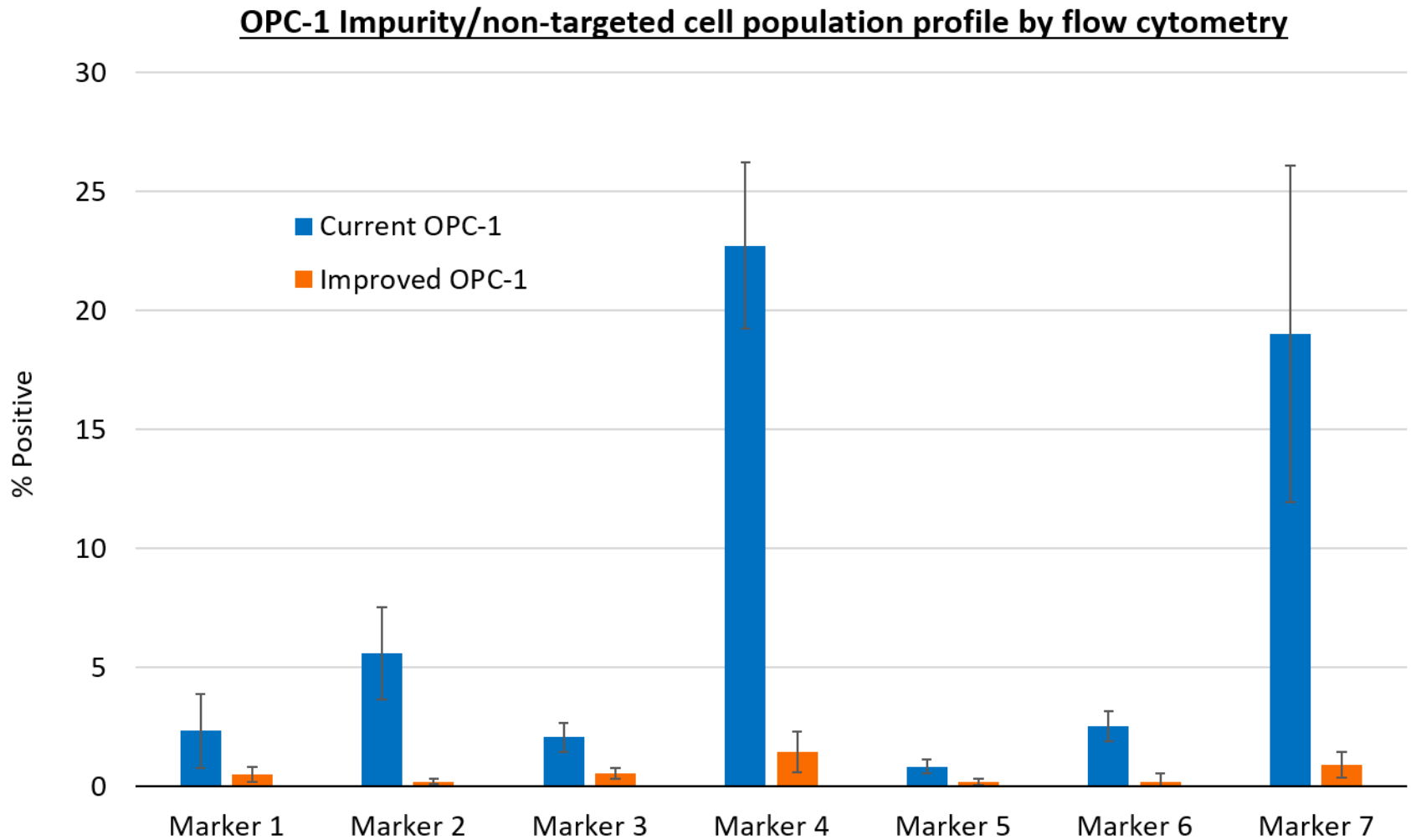
# OPC1 Manufacturing Improvements Following FIM Study

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

- A new ready-to-inject formulation was developed
- Elimination of dose preparation achieved
- 10- to 20-fold increase in production scale
- Significant reduction in impurities
- No reduction in functional activity
- 12 new analytical and functional methods developed
- Elimination of all animal-based production reagents
- Estimated expiration dates of pending patent applications range from 2036 to 2040



# OPC1 Manufacturing Improvements: Lower Impurities



## OPC1 Program – Key Clinical Trial Takeaways & Next Steps

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- **95% of patients exhibited UE motor recovery at 12 months (at least 1 motor level on 1 side)**
- **Syringomyelia events reduced to 4% (~80% expected)**
- **96% durable engraftment confirmed via MRI**
- **Excellent overall safety profile (5 years in cervical SCI and 10 years in thoracic SCI and continues)**
- **Can enrich for better-performing patients in next trial**
- **Improved purity and production scale of clinical material**
- **Superior delivery device to enter clinical testing**
- **Planning underway for a randomized, controlled clinical trial**
- **Engagement with California Institute of Regenerative Medicine (CIRM), various patient advocacy organizations and patient advocates, is underway**



Hearing loss currently **afflicts over 5% of the world's population**, and by 2050, it is estimated that over 700 million people will have disabling hearing loss

*Source: WHO*



**ANP1: Auditory Neuronal Progenitors for Hearing Loss**

# ANP1 (Auditory Neuronal Progenitors) for Hearing Loss

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- **Lineage's first internally-developed development program**
  - Auditory neuronal transplants with an initial focus on the treatment of auditory neuropathy spectrum disorders
  - Replacing auditory neurons or augmenting existing but damaged auditory neuron population may provide a benefit beyond the reach of alternate approaches
- **Can leverage knowhow and capabilities in neuronal lineage differentiation in an indication with a large and growing unmet need**
  - Hearing loss currently afflicts 430 million people
- **Filed new patent application covering the composition and methods for generating Auditory Neuronal Progenitors (ANPs)**
  - Filed IP includes methods of treatment that employ these cells for the treatment of auditory neuropathy





Globally, at least **2.2 billion people** have a  
near or distance vision impairment

*Source: WHO*



## PNC1: Photoreceptor Neural Cell Transplants for Diseases of Blindness

# PNC1 - Photoreceptor Neural Cells

## For Diseases Which May Lead to Blindness

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- **Lineage's second internally-developed development program**
  - Photoreceptor neural cell (PNC) transplants for the treatment of vision loss due to photoreceptor dysfunction or damage
  - Both types of photoreceptors; rods and cones
  - Dynamic culturing process offers path to clinical- and industrial-scale production
  - *In vivo* data demonstrated that these cells may be capable of forming reconstructed retina with high survivability and neural connectivity to surrounding functional layers
  - Leverages Lineage's knowhow and capabilities in neuronal lineage differentiation in an indication with a large unmet need
- **Filed new patent application covering the composition and methods for generating PNC transplants**



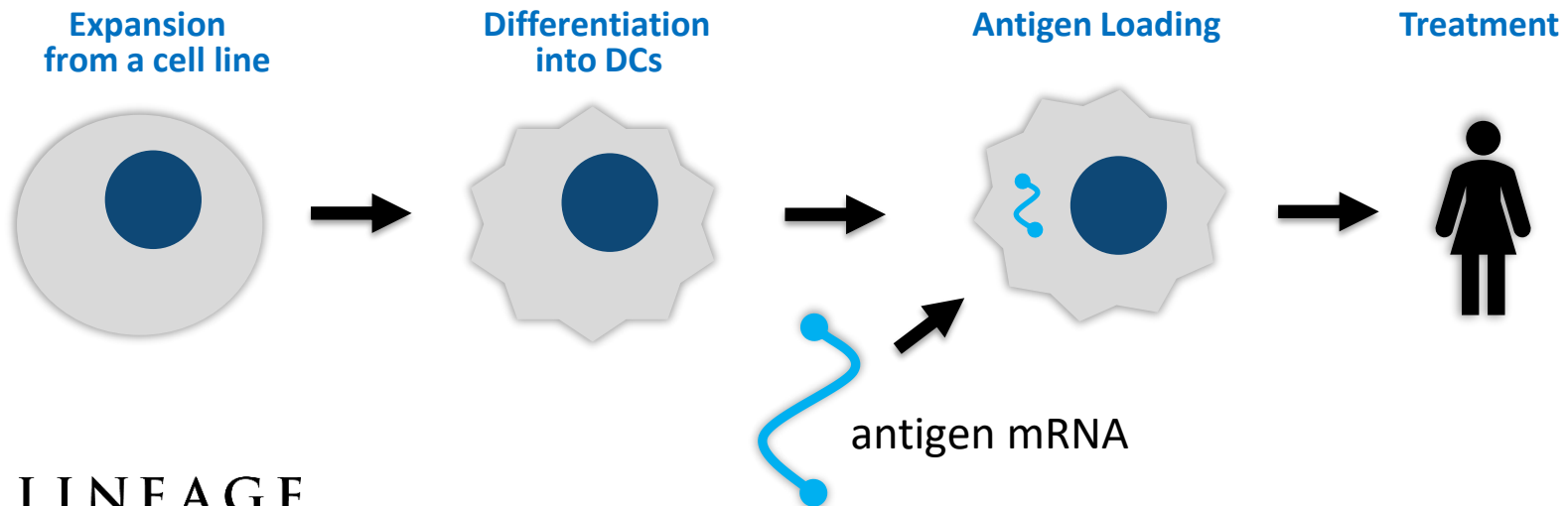
Immunotherapy is "poised to  
**revolutionize treatment** for all  
types of cancer"

*Source: [cancerresearch.org](http://cancerresearch.org)*

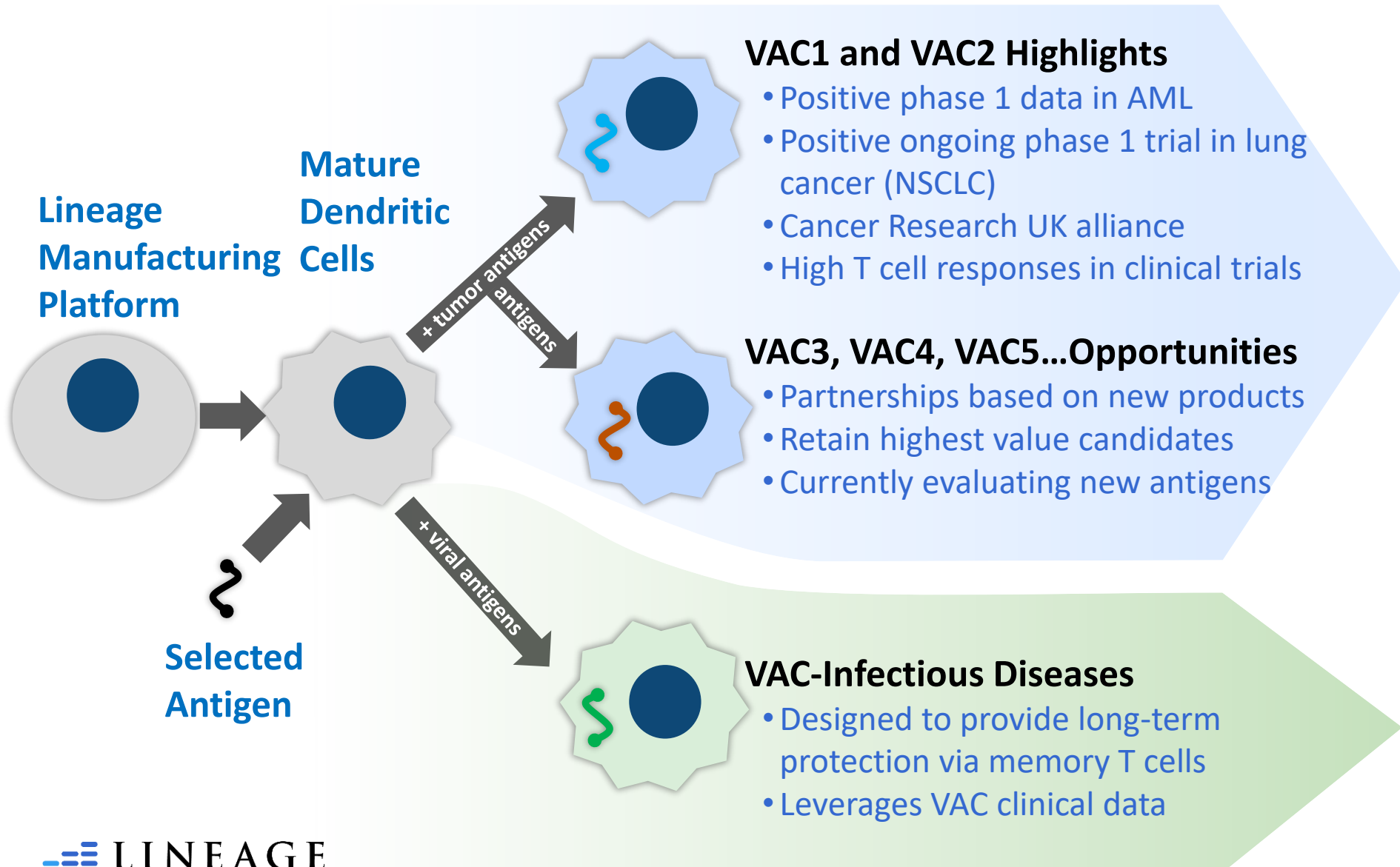
**VAC: A Cell Therapy Platform for Cancer and Infectious Diseases**

# The VAC Platform: On demand cell therapy for cancer

- The VAC platform consists of large-scale, allogeneic (“off the shelf”) production of mature dendritic cells (DCs). No production delay between diagnosis and treatment, as with autologous or patient-specific therapies.
- DCs are manufactured and loaded with either a **tumor antigen** (to treat cancer) or a **viral antigen** (as a vaccine for infectious diseases)
- Antigen presentation to the patient’s T cells creates a *targeted* and robust immune response (up to 3%), aiding tumor cell destruction or pathogen clearance



# VAC Development – A Platform for Multiple Product Candidates



# Our Goal is to Provide Life-Changing Cell Therapies to Patients

## Lineage Cell Therapeutics: Bringing the Promises of Cell Therapy into Clinical Reality



**Clinical-stage programs with billion-dollar potential and partnership opportunities**



**World class in-house process development and GMP manufacturing**



**One of the largest patent portfolios in cell therapy**



**Multiple validating corporate partnerships**



**Leader in the field of regenerative medicine**



# The Patients Are Our Inspiration.

View their stories at [lineagecell.com/media/#patients](https://lineagecell.com/media/#patients)

## OPC1 SCiStar Study Participants

**CIRM**  
CALIFORNIA STEM CELL AGENCY



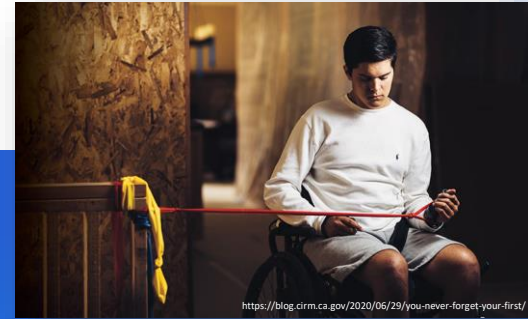
**Lucas Lindner**

“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.”



**Kris Boesen**

“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.”



**Jake Javier**

“Even though it’s a completely different perspective, I can still lead that way. I can just try to be the best I can and to persevere the best I can.”

*Diablo Magazine, Feb. 16, 2017*

## The Millions Worldwide Suffering from Dry AMD Vision Loss

“Macular degeneration is a very frustrating condition which can greatly affect your day-to-day life.”

- Macular Society



Courtesy of CIRM, American Macular Degeneration Foundation, and Macular Society