



LINEAGE
CELL THERAPEUTICS

The future of cell therapy.



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



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

Four cases of retinal tissue restoration in dry AMD patients
One-third of spinal injury patients gained at least 2 levels of motor function
Potent induction of immune responses observed in advanced cancer patients

Market Opportunity

Billion-dollar commercial opportunities with no or few treatment options

Financial Position

~\$83 million in cash and cash equivalents as of January 31, 2022

Market Capitalization

~\$240 million[°]

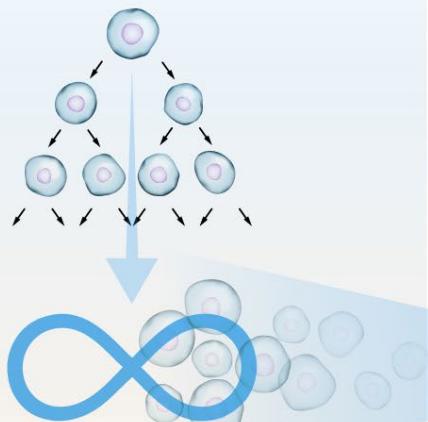
Cell Therapy Pipeline

LINEAGE	PROGRAM	PHASE 1	PHASE 2	PHASE 3	PARTNERS
 Ophthalmology	OpRegen®	 24 patients treated			Genentech <small>A Member of the Roche Group</small>
 Demyelination	OPC1	 30 patients treated			CIRM <small>CALIFORNIA'S STEM CELL AGENCY</small>
 Immuno-oncology	VAC2	 8 patients treated			 CANCER RESEARCH UK
 Neurotology	ANP1	<i>Preclinical</i>			<i>Internally-Owned</i>
 Ophthalmology	PNC1	<i>Preclinical</i>			<i>Internally-Owned</i>

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



Retinal Cells

→ OpRegen



Spinal Cord Cells

→ OPC1



Immune Cells

→ VAC2



Auditory Neurons

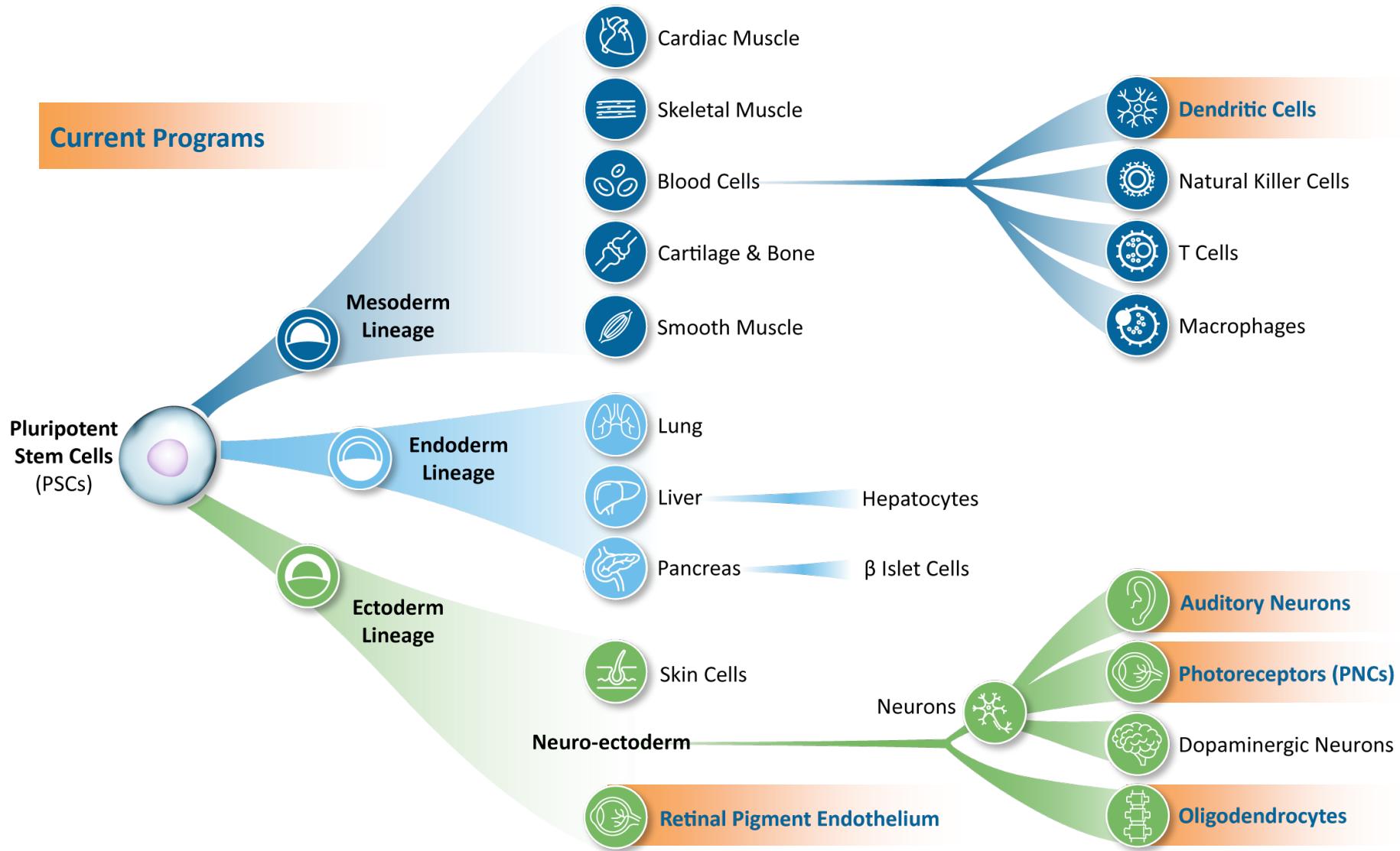
→ ANP1



Photoreceptors

→ PNC1

Many Potential Product Opportunities



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



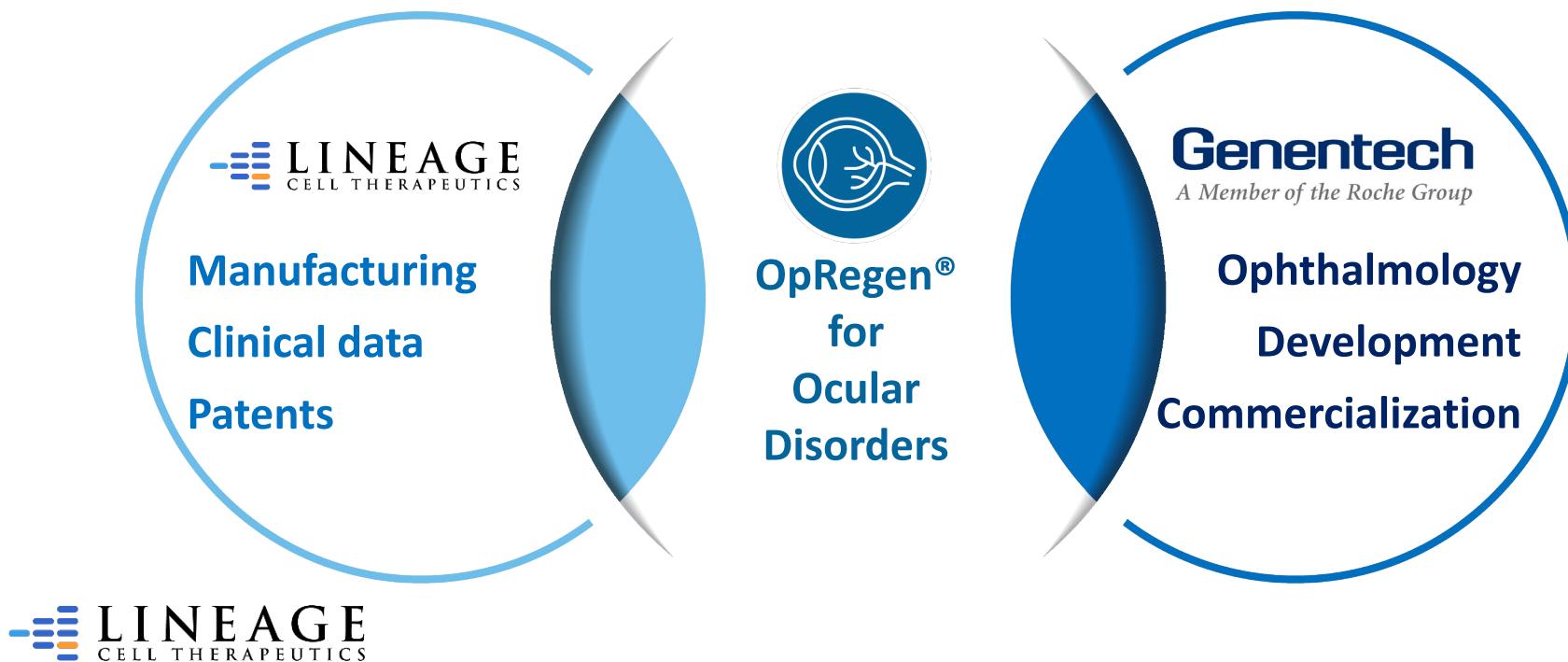
Source: aao.org

OpRegen® : RPE Cell Transplants to Treat Dry AMD

Worldwide Collaboration in Ocular Disorders

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

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

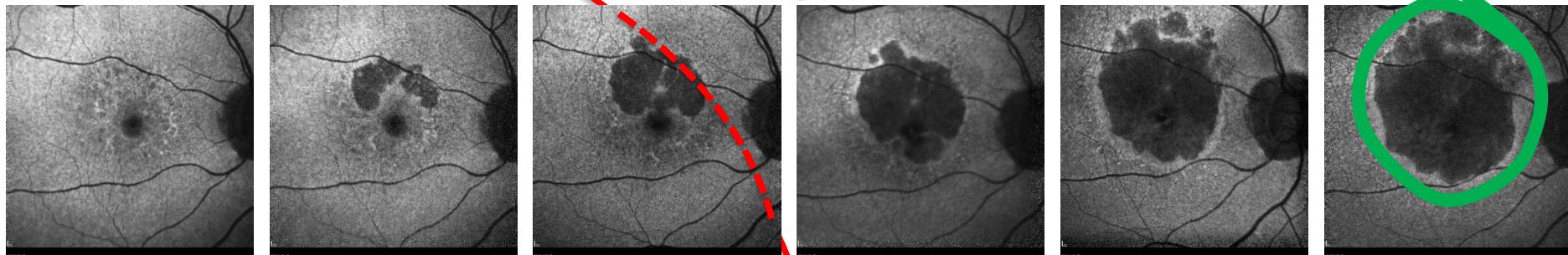


Dry AMD Can Lead Rapidly to Blindness

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

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

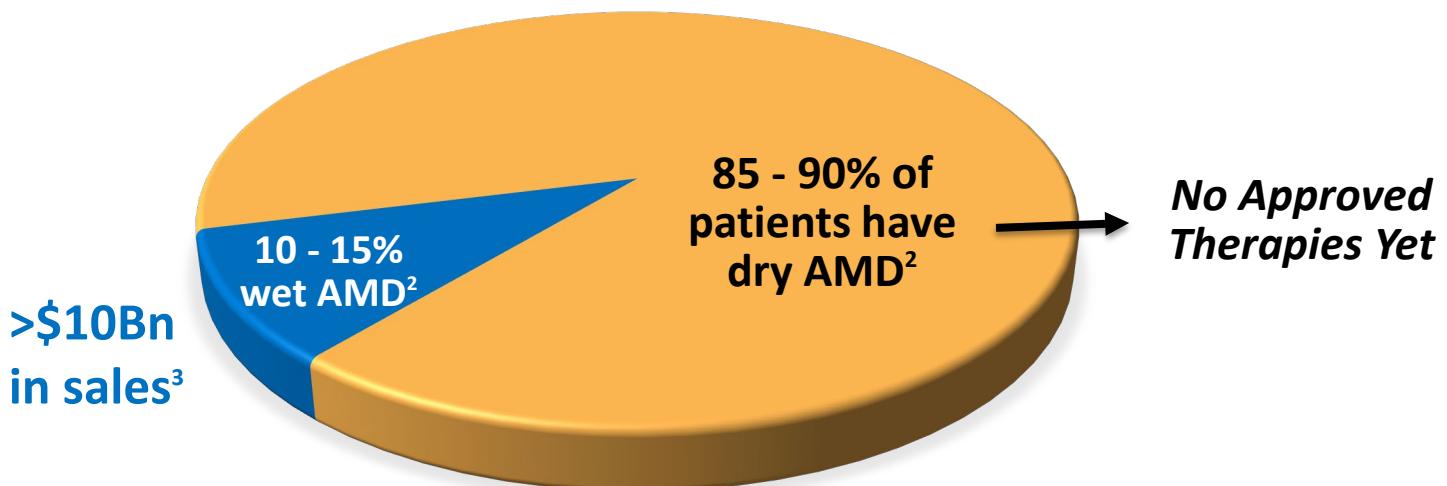
20/200
(legally blind in 3 years)

20/640

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**

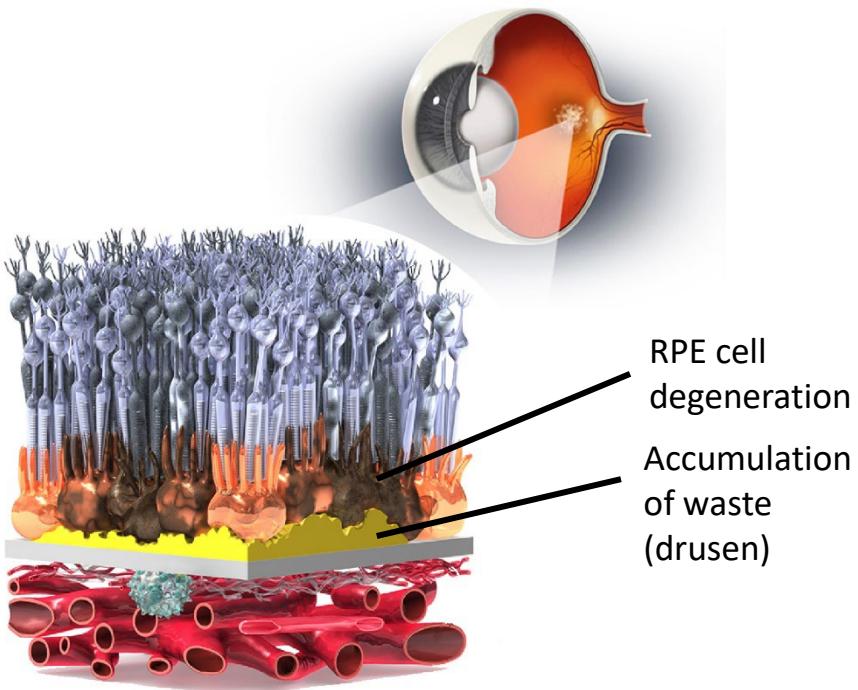
Type of AMD	% of AMD Cases	FDA Approved Therapies
Wet AMD	10 – 15%	Lucentis & Eylea (\$10 Billion in annual sales)
Dry AMD	85 – 90%	None



Sources: (1) Bright Focus Foundation. Macular Degeneration Facts & Statistics: Bright Focus Foundation. <http://www.brightfocus.org/macular/about/understanding/facts.html>; (2) JM Seddon, Epidemiology of age-related macular degeneration. (AP Schachat, S Ryan eds.) Retina, 3rd ed. St. Louis, MO: Mosby; 2001;1039-50; (3) 2018 product sales summary based on publicly reported revenue figures for Lucentis and Eylea.

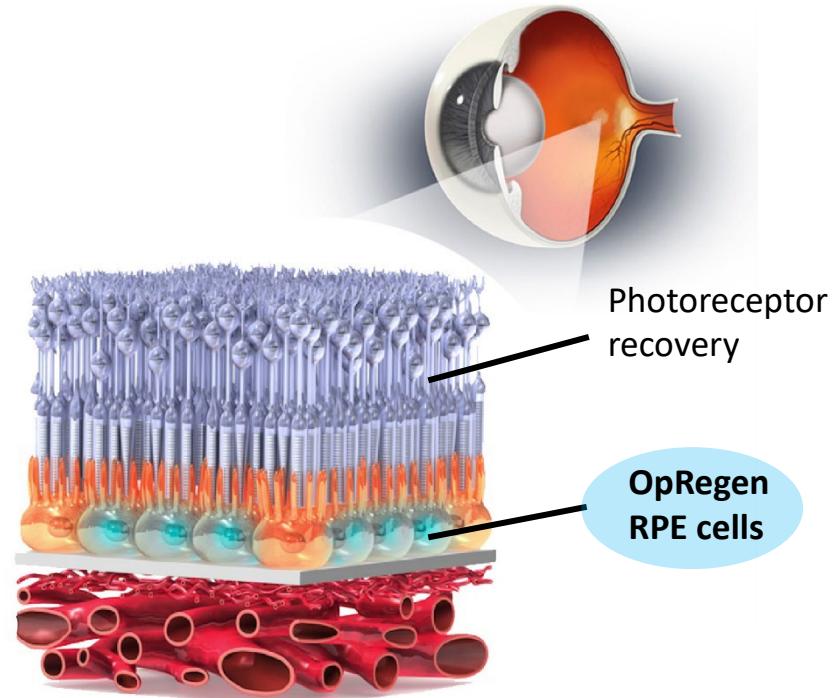
Lineage Approach – OpRegen, an RPE Cell Transplant

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

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

- Four cases of retinal restoration reported (only known clinical cases)
- Market opportunity is not limited by monogenic deficiencies (e.g. gene therapy)
- Treatment has been well-tolerated; meaningful improvements in clinically-relevant metrics such as visual acuity, GA growth, and reading speed
- Potential application in other retinal diseases (example: Stargardt's Disease)
- 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:

- Transplanting RPE cells may provide transformational benefits beyond the reach of traditional approaches



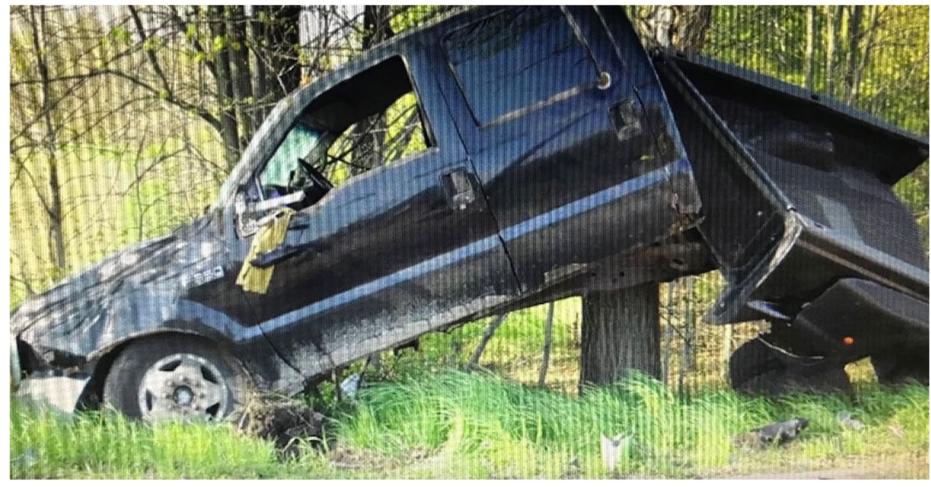
Lifetime care for an SCI
patient can cost nearly
\$5 million

Source: christopherreeve.org



OPC1: Cell Therapy for Spinal Cord Injuries

Why Spinal Cord Injury (SCI) Matters

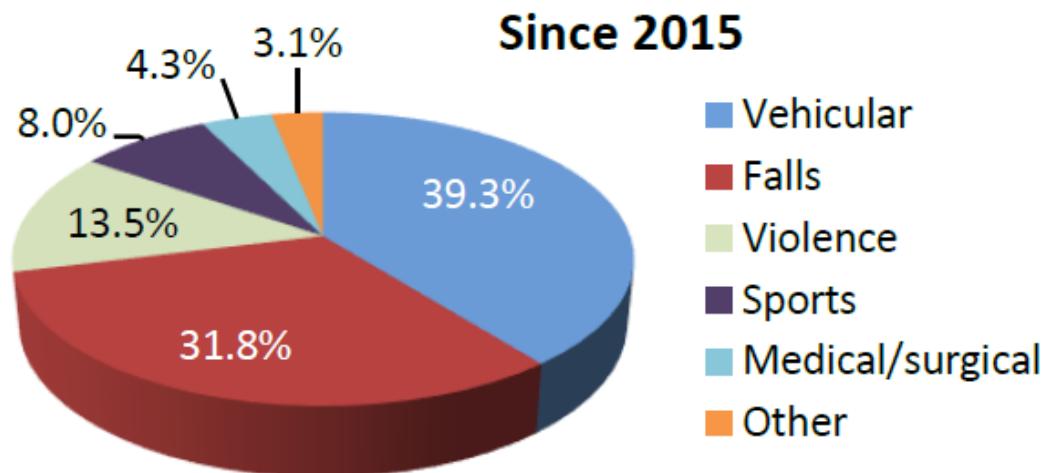


**Lucas Linder, an OPC1 clinical trial participant, was paralyzed from the neck down.
The next year, he threw out the first pitch at a Major League Baseball game.**

Spinal Cord Injury (SCI) Overview

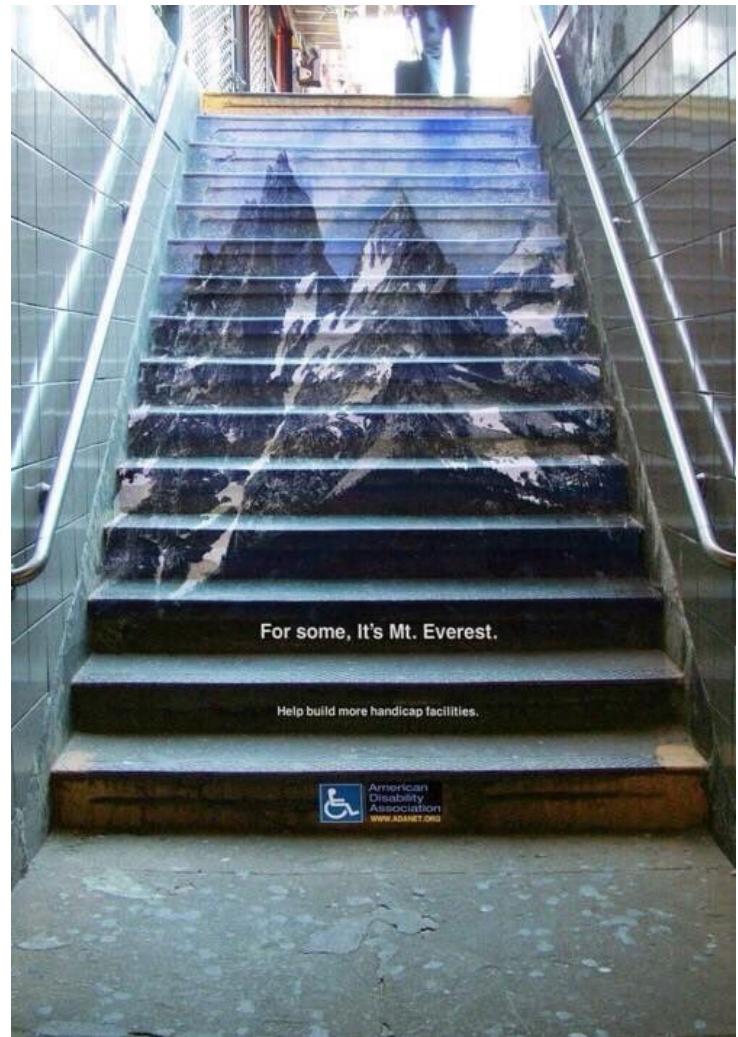
Lifetime care for an SCI patient can cost nearly \$5 million

- **Incidence**
 - Approximately 18,000 new cases in the U.S. each year
- **Prevalence**
 - Between 249,000 and 363,000 people in the US
- **Causes**



SCI Burden and Unmet Needs

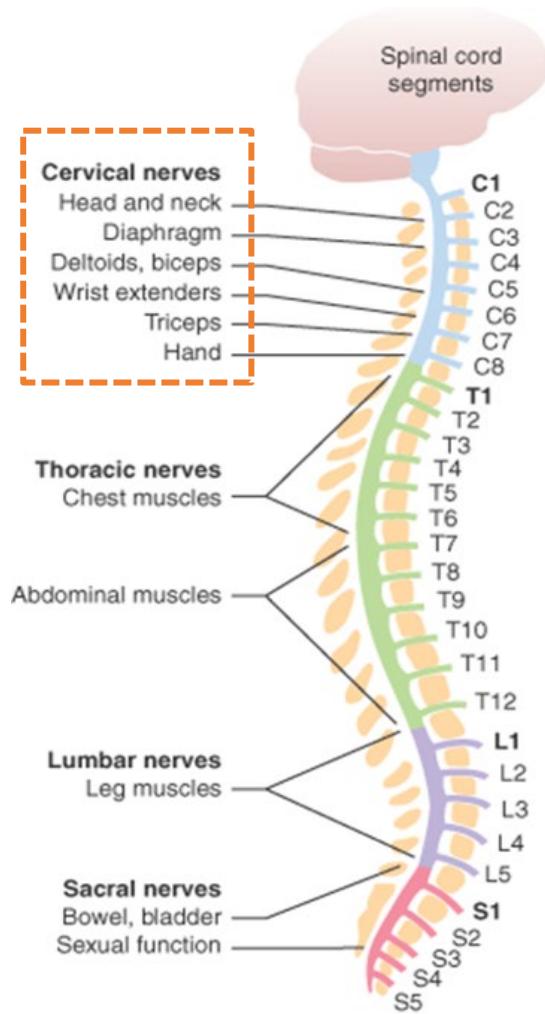
- **A significant burden for patients and caregivers***
 - 67% of patients are unemployed 10 years post-injury
 - Lifetime healthcare costs can reach \$5M for one patient
- **Potential lifelong impairments**
 - Mobility (wheelchair)
 - Pain
 - Re-hospitalizations
 - Infections
 - Ventilator dependency
 - Depression
 - Shortened life expectancy



SCI Treatment Objectives

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

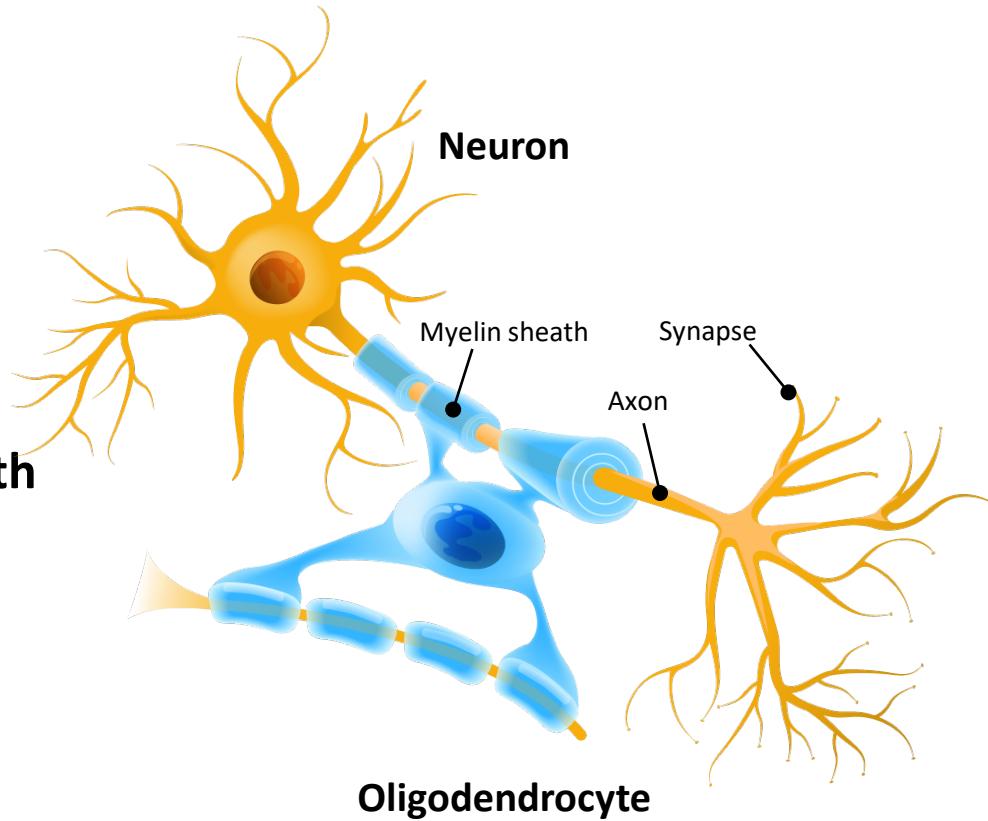
- **Higher-level injuries result in more extensive impairments**
- **Gains in motor function, particularly in the upper extremities, can provide significant benefits in self-care and lower costs of care**
- **The goal of Lineage's cell therapy is to provide additional arm, hand, and finger function,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

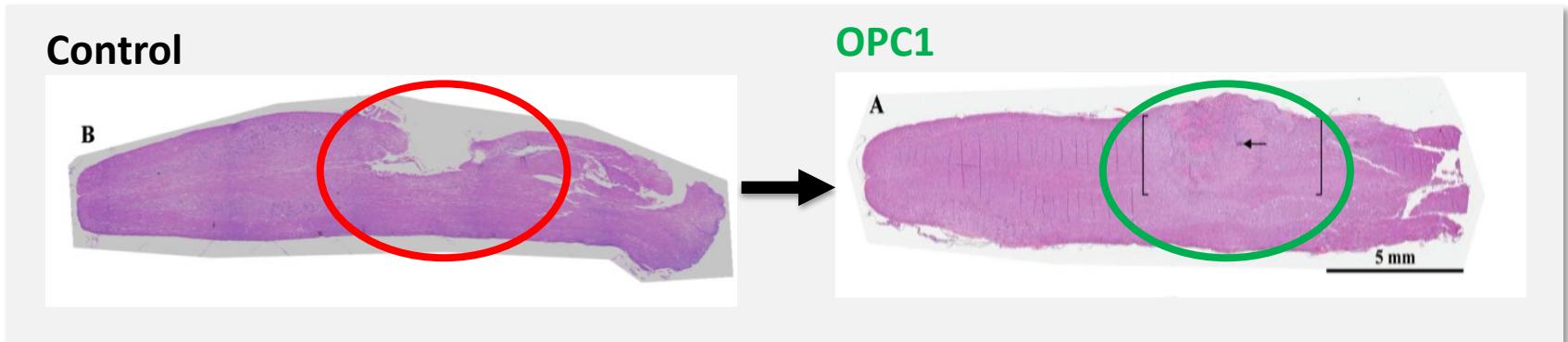
- OPC1 utilizes targeted cell replacement (similar approach as OpRegen)
- OPC1 is covered by multiple issued patents
- OPC1 has RMAT Designation
- OPC1 has Orphan Drug Designation
- OPC1 has received >\$14M in support from CIRM (California Institute for Regenerative Medicine)
- OPC1 has application to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



OPC1 Transplant Procedure

OPC1 Mechanisms of Action

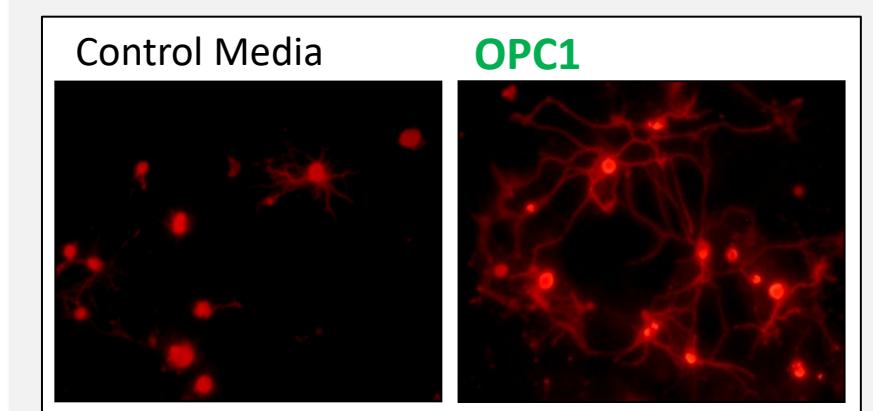
Suppression of Cavitation



Myelination of axons



Secretion of neurotrophic factors



OPC1 for Spinal Cord Injury

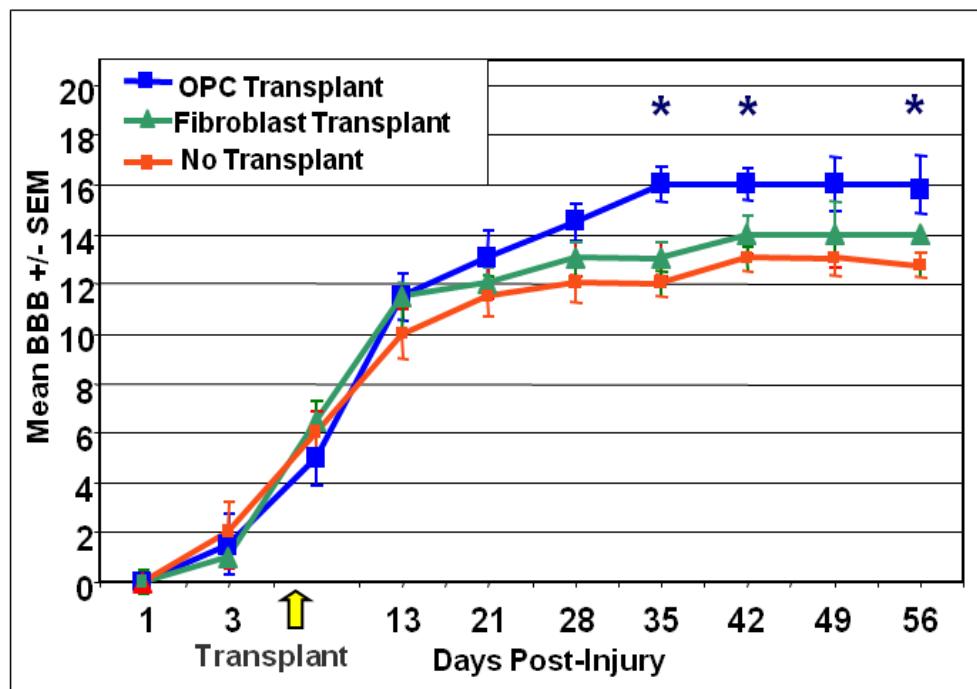
- Lineage's OPCs are derived from an NIH-registered cell line
- The OPCs are allogeneic ("off the shelf"), and not taken from the patient
- Treatment of SCI occurs 3-6 weeks post-injury and includes short-course (60-day) immunosuppression
- The OPCs are "ready to use" in a cryopreserved thaw-and-inject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



OPC1 Improved Motor Function in Preclinical Animal Models

Locomotor Improvement in Thoracic SCI

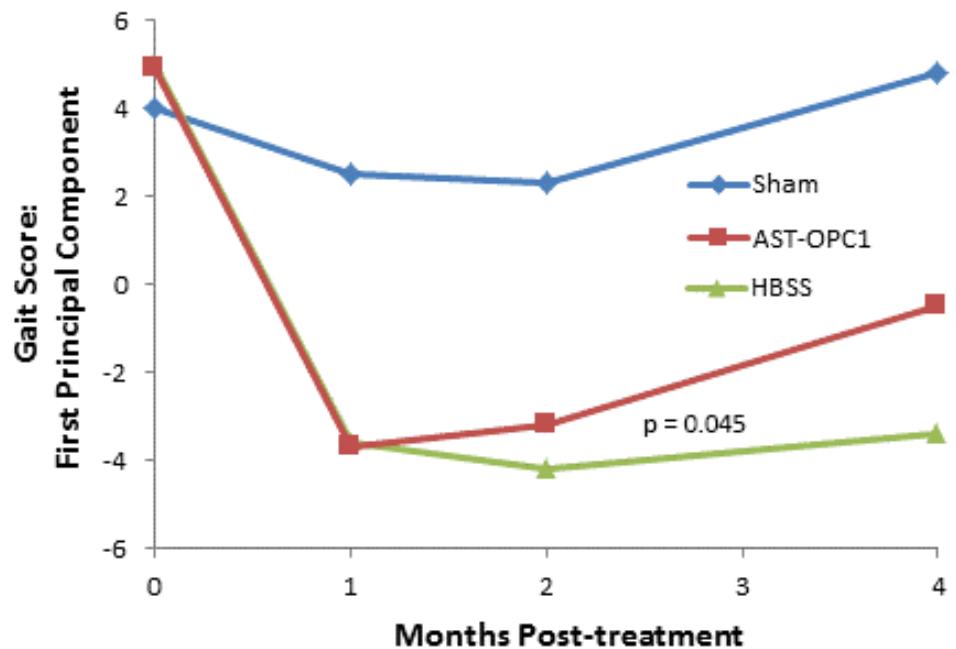
- Increased weight bearing
- Improved hindlimb-forelimb coordination
- Improved hind paw clearance
- Improved trunk stability
- Decreased tail drag



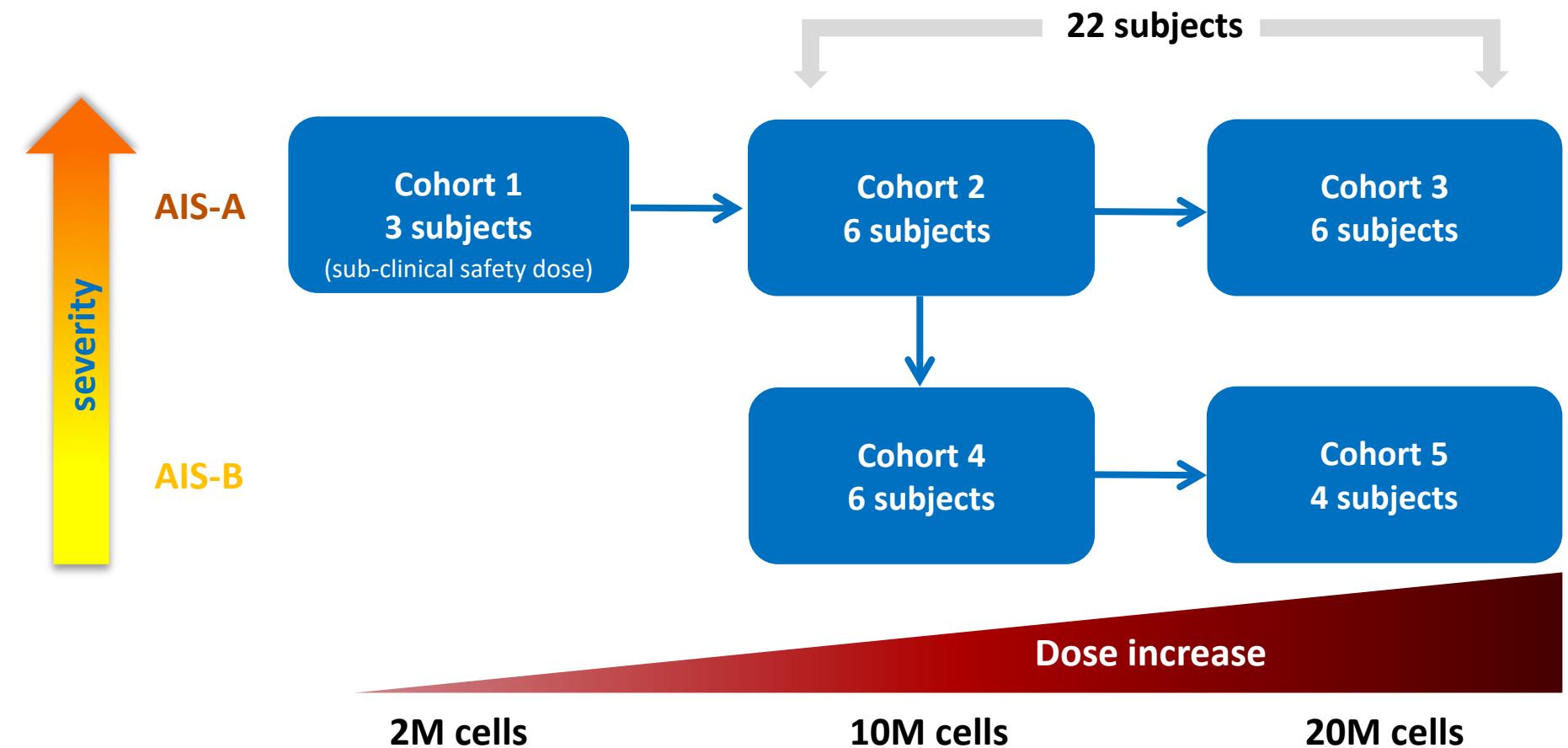
OPC1 Improved Motor Function in Preclinical Animal Models

Locomotor Improvement in Cervical SCI

- Increased running speed
- Increased right forelimb stride length
- Increased right forelimb maximal longitudinal deviation
- Increased right rear stride frequency



SCIStar Clinical Trial Study Design



SCiStar Clinical Trial - Summary of Adverse Events

Majority of adverse events were mild to moderate in severity

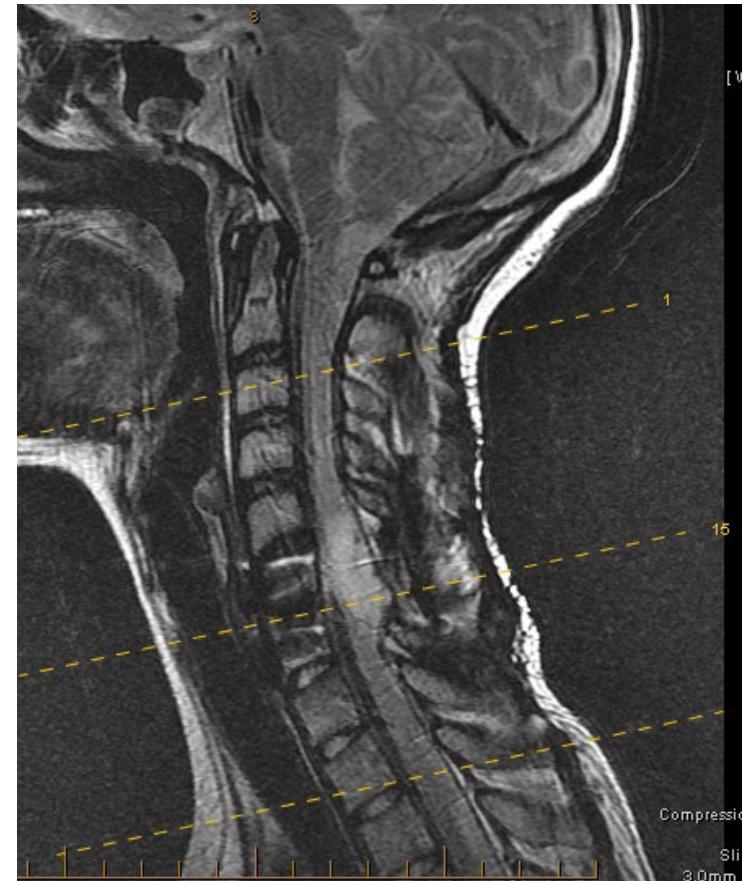
All Treated Subjects (n=25)	AEs	SAEs
Total	534	29
Related to OPC1	1*	0
Related to Injection Procedure	20	1
Related to Tacrolimus	11	1

**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**

SCIStar Clinical Trial - Cell Engraftment

12- and 24-Month MRI Scans Indicate Durable Engraftment

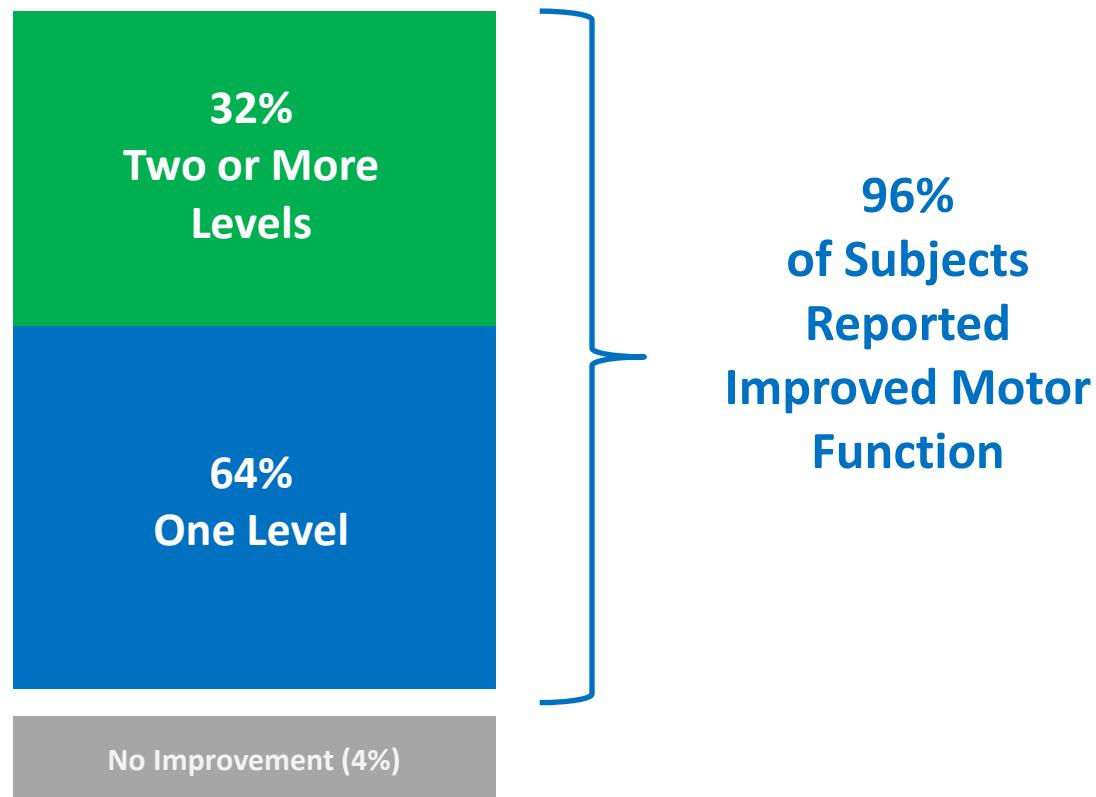
- Cystic cavitation (syringomyelia) occurs in ~80% of SCI cases
- MRI results suggest formation of a tissue matrix at the injury site, indicating that OPC1 cells have durably engrafted and helped prevent syringomyelia
- 96% (24/25) of OPC1 patients had serial MRI scans that indicated no sign of a lesion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



Weighted sagittal MRI

SCiStar Clinical Trial - Motor Function Gains

22 Patients at 12 months



Patient Name _____

Date/Time of Exam _____

Examiner Name _____

Signature _____

RIGHT

MOTOR
KEY MUSCLES

SENSORY
KEY SENSORY POINTS
Light Touch (LTR) Pin Prick (PPL)

C2	
C3	
C4	

UER
(Upper Extremity Right)

Elbow flexors

Wrist extensors

Elbow extensors

Finger flexors

Finger abductors (little finger)

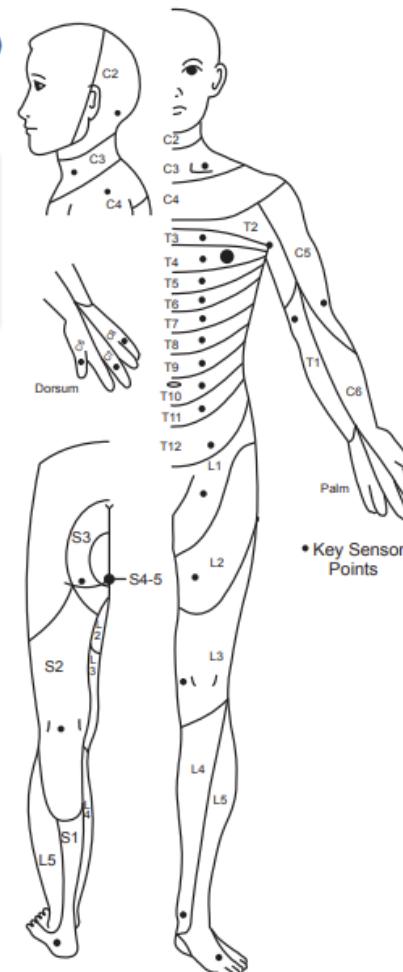
C5

C6

C7

C8

T1



LEFT

MOTOR
KEY MUSCLES

SENSORY
KEY SENSORY POINTS
Light Touch (LTL) Pin Prick (PPL)

C5 Elbow flexors
C6 Wrist extensors
C7 Elbow extensors
C8 Finger flexors
T1 Finger abductors (little finger)

UEL
(Upper Extremity Left)

MOTOR
(SCORING ON REVERSE SIDE)

- 0 = Total paralysis
- 1 = Palpable or visible contraction
- 2 = Active movement, gravity eliminated
- 3 = Active movement, against gravity
- 4 = Active movement, against some resistance
- 5 = Active movement, against full resistance
- NT = Not testable
- 0*, 1*, 2*, 3*, 4*, NT* = Non-SCI condition present

SENSORY
(SCORING ON REVERSE SIDE)

- 0 = Absent NT = Not testable
- 1 = Altered 0*, 1*, NT* = Non-SCI condition present
- 2 = Normal

LER

(Lower Extremity Right)

Hip flexors

Knee extensors

Ankle dorsiflexors

Long toe extensors

Ankle plantar flexors

L2

L3

L4

L5

S1

S2

S3

S4-5

RIGHT TOTALS

(MAXIMUM)

(50)

(56)

(56)

LEL

(Lower Extremity Left)

L2 Hip flexors

L3 Knee extensors

L4 Ankle dorsiflexors

L5 Long toe extensors

S1 Ankle plantar flexors

S2

S3

S4-5

(DAP) Deep Anal Pressure

(Yes/No)

LEFT TOTALS

(MAXIMUM)

(50)

(56)

(56)

MOTOR SUBSCORES

$$\text{UER } \boxed{\quad} + \text{UEL } \boxed{\quad} = \text{UEMS TOTAL } \boxed{\quad}$$

MAX (25)

(25)

$$\text{LER } \boxed{\quad} + \text{LEL } \boxed{\quad} = \text{LEMS TOTAL } \boxed{\quad}$$

MAX (25)

(25)

SENSORY SUBSCORES

$$\text{LTR } \boxed{\quad} + \text{LTL } \boxed{\quad} = \text{LT TOTAL } \boxed{\quad}$$

MAX (56)

(56)

(112)

$$\text{PPR } \boxed{\quad} + \text{PPL } \boxed{\quad} = \text{PP TOTAL } \boxed{\quad}$$

MAX (56)

(56)

(112)

NEUROLOGICAL LEVELS
Steps 1-6 for classification as on reverse

1. SENSORY
2. MOTOR

3. NEUROLOGICAL LEVEL OF INJURY (NLI)

4. COMPLETE OR INCOMPLETE?
Incomplete = Any sensory or motor function in S4-5
5. ASIA IMPAIRMENT SCALE (AIS)

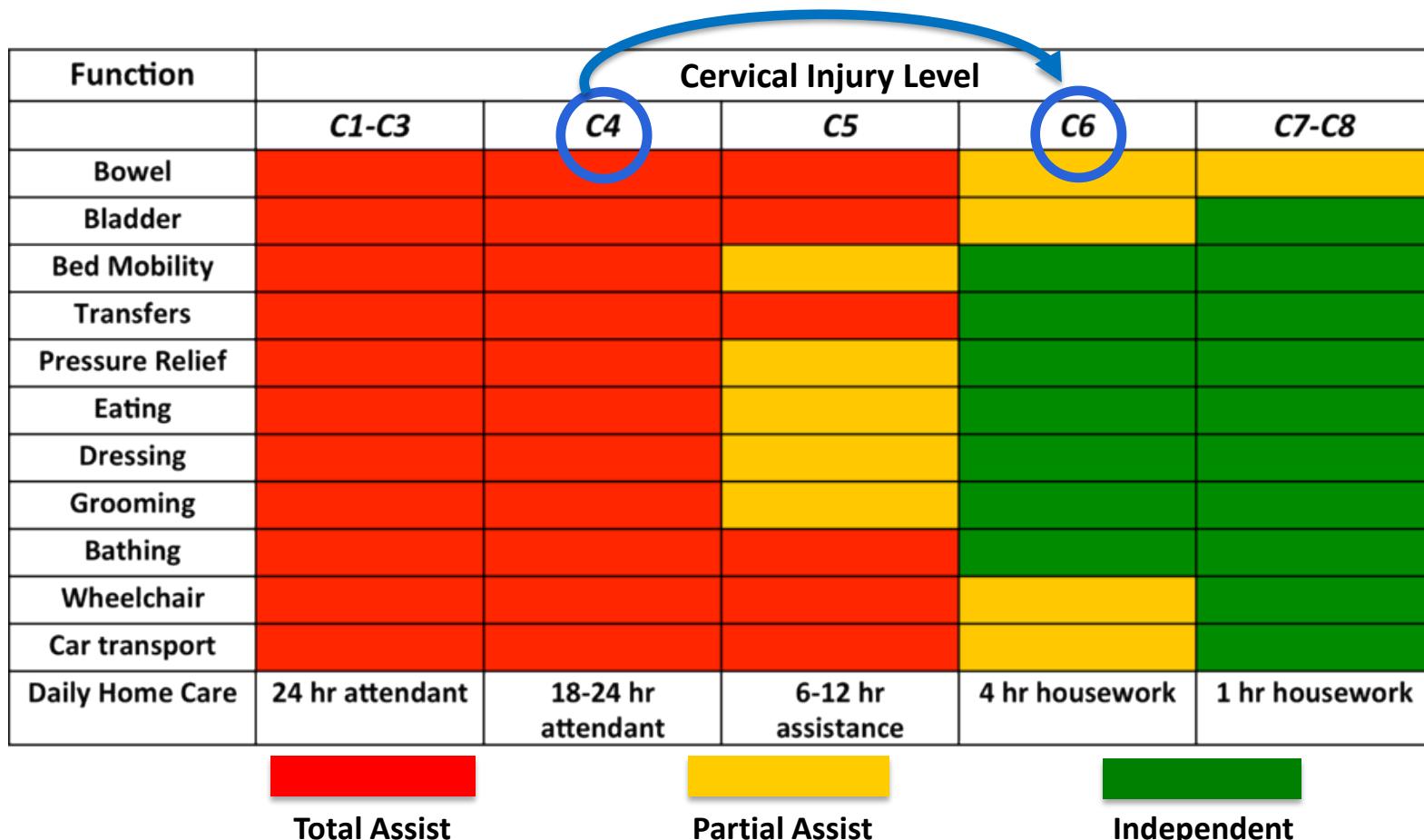
(In injuries with absent motor OR sensory function in S4-5 only)
6. ZONE OF PARTIAL PRESERVATION
Most caudal levels with any innervation

R L
SENSORY
MOTOR

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



SCiStar Clinical Trial - Analysis of Patients with Least UEMS Recovery

C4 or cord compressions occurred in 5 of the 7 worst patient outcomes and both issues can be addressed in the next trial

Subject	UEMS Change at 12 mo.	Cord Compression After OPC1 Injection?	NLI Baseline	Baseline AIS	Cohort	Dose	Age	Injection Days Post Injury
2207	7	N	C4	B	5	20 M	62	37
2203	6	N	C6	A	3	20 M	45	31
2105	6	N	C4	A	3	10 M	19	20
2004	5	N	C6	B	4	10 M	21	25
2007	4	N	C4	B	4	10 M	55	38
2307	4	Y	C5	B	5	10 M	19	38
2303	3	Y	C6	B	4	10 M	22	35

- Two patients had cord compression after OPC1 injection (2303 and 2307 at Day 30 and Day 7)
- Patients 2105, 2207, 2007 had a C4 (highest/most severe) injury level at baseline
- Patient 2105 also had a hematoma in the spinal cord at baseline & a failed graft

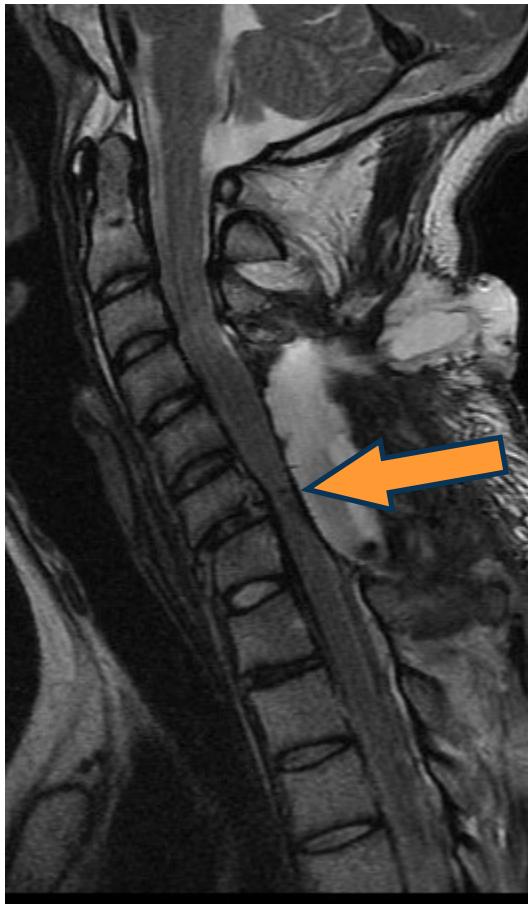
SCIStar Clinical Trial – Cord Compression

Subject 2303 (Cohort 4): Cord Compression at Day 30

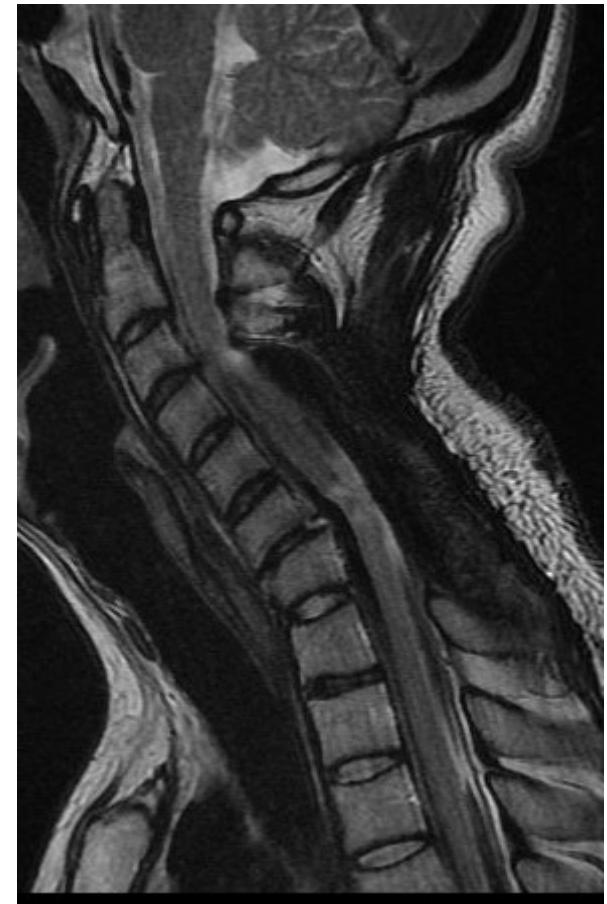
Baseline



Day 30



Day 365

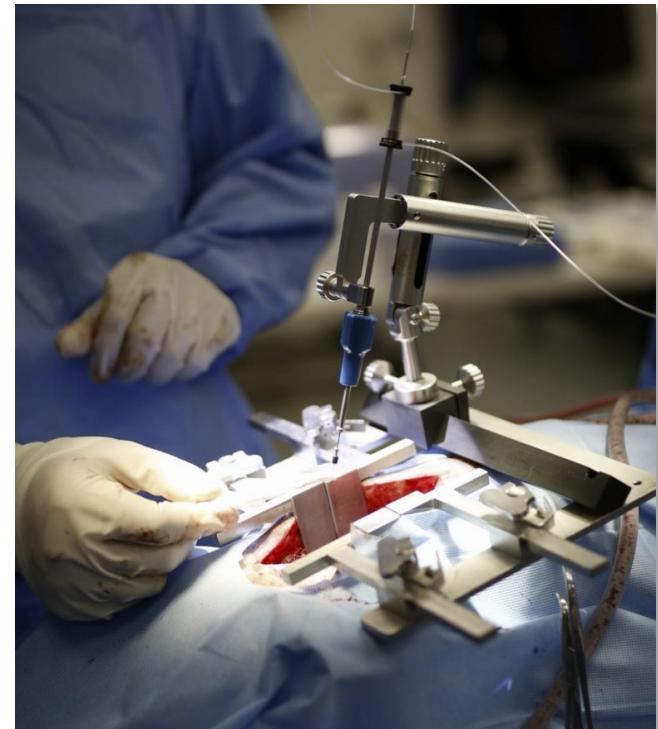


SCiStar Clinical Trial – 2 Year Results

- **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 in 2022

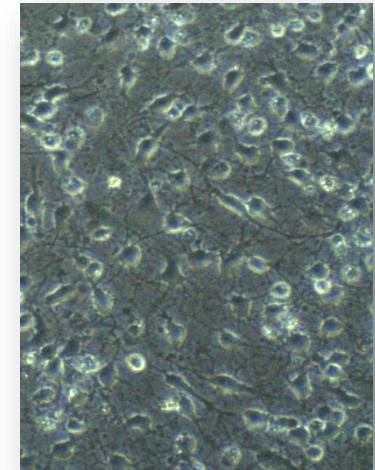
- **Better stability and control**
 - Eliminates motion between platform/XYZ manipulator/needle
- **Enhanced usability and safety: no cessation of ventilation**
 - Attaches directly to the patient, compatible with breathing motion
- **Improved user experience**
 - Smaller and fewer components
 - Single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



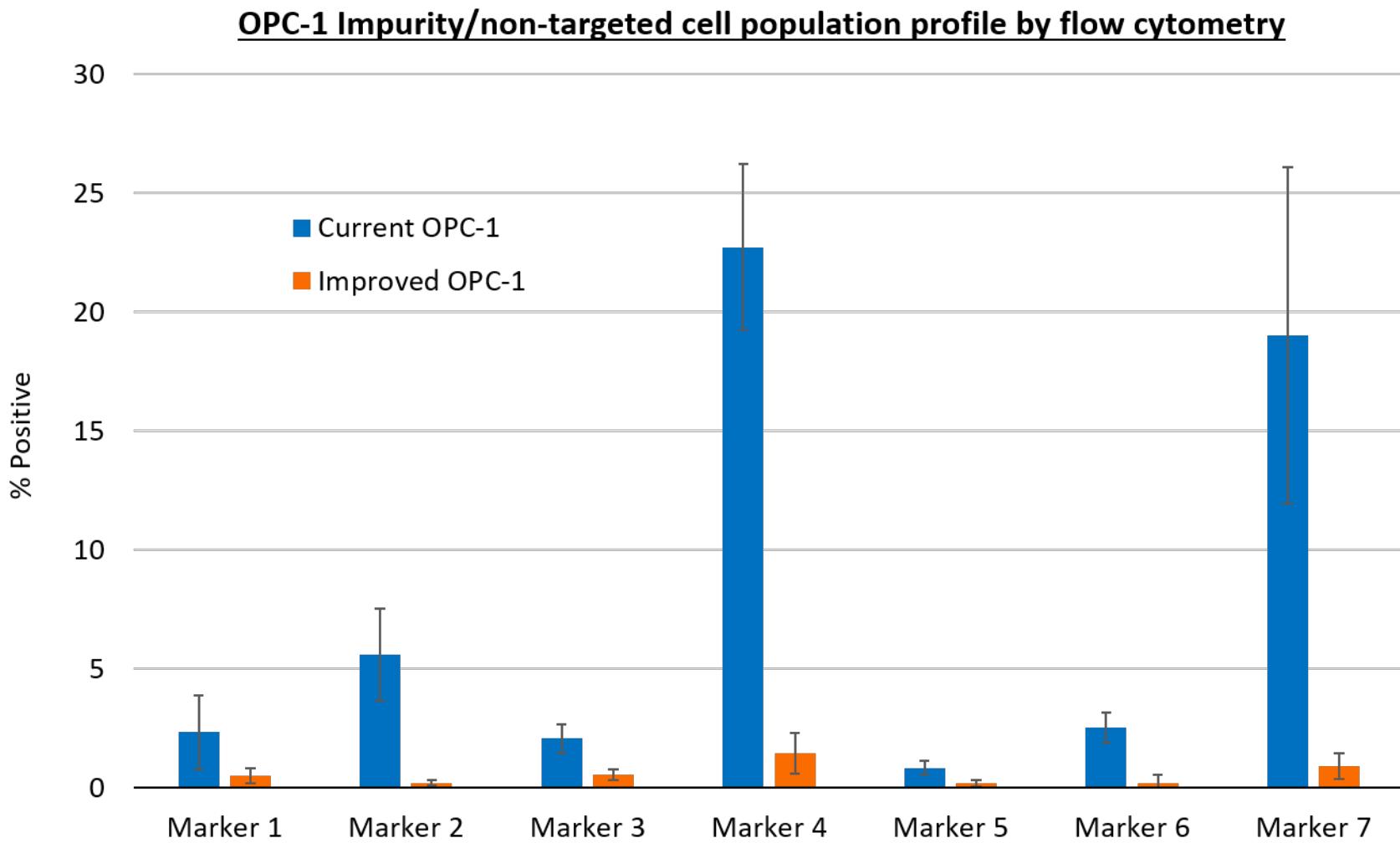
OPC1 Manufacturing Improvements Following FIM Study

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

- **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 and continues)**
- **Can enrich for better-performing patients in next trial**
- **Greatly improved purity and production scale of clinical material**
- **Superior delivery device entering clinical testing in 2022**
- **Planning underway for a randomized, controlled clinical trial**



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

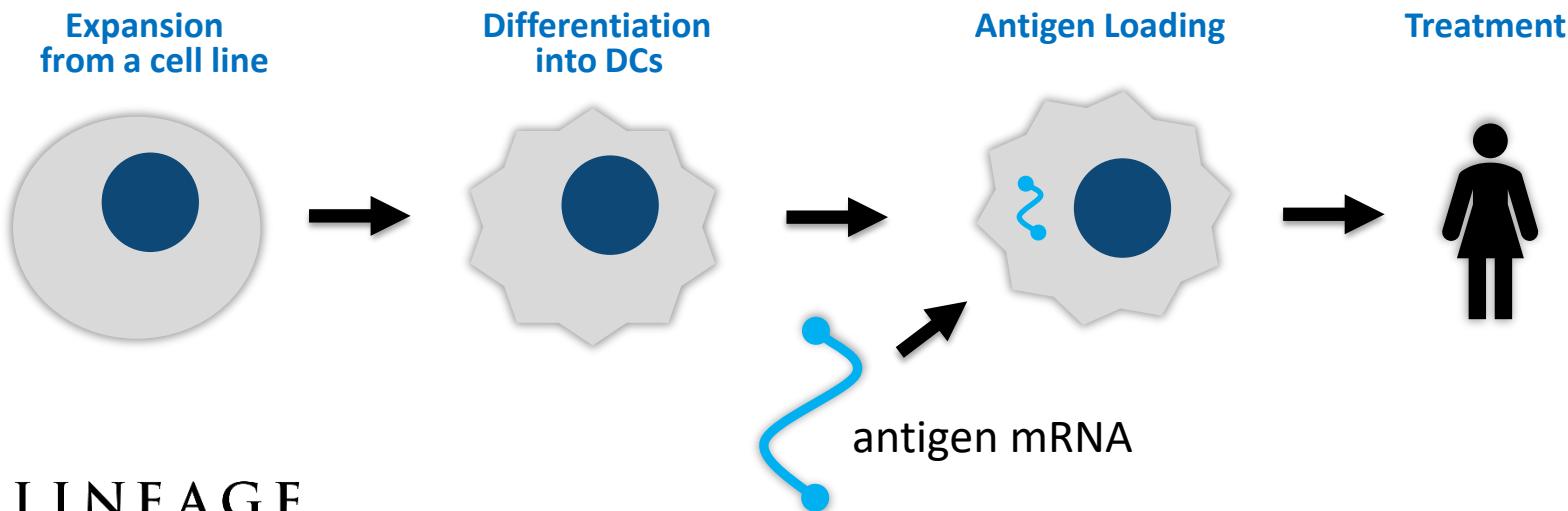


Source: cancerresearch.org

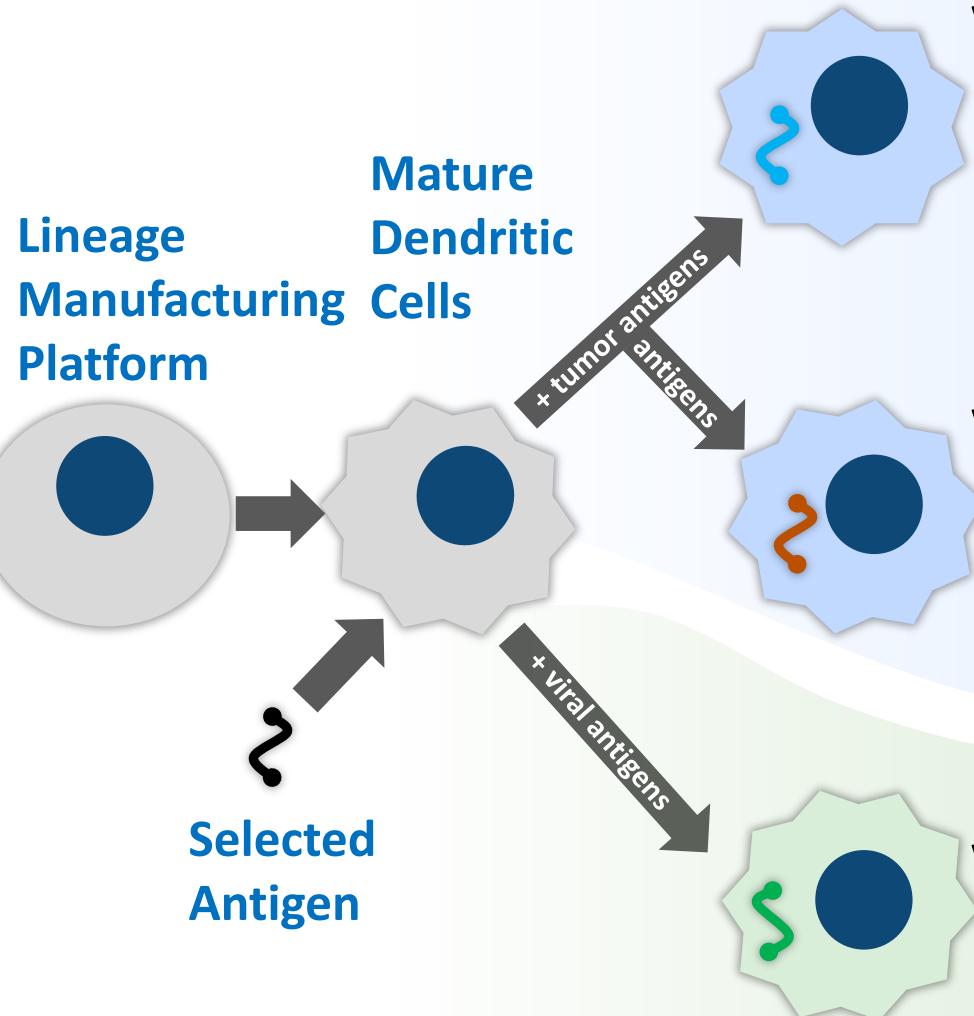
VAC: A Cell Therapy Platform for Cancer and Infectious Diseases

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



VAC1 and VAC2 Highlights

- Positive phase 1 data in AML
- Positive ongoing phase 1 trial in lung cancer (NSCLC)
- Cancer Research UK alliance
- High T cell responses in clinical trials

VAC3, VAC4, VAC5...Opportunities

- Partnerships based on new products
- Retain highest value candidates
- Currently evaluating new antigens

VAC-Infectious Diseases

- Designed to provide long-term protection via memory T cells
- Leverages VAC clinical data

VAC2 - Phase 1 Clinical Trial

Study is Ongoing, Being Conducted by Cancer Research UK

- VAC2 has been well tolerated in all patients; no treatment delays due to adverse events attributable to VAC2
- Encouraging Phase 1 data
 - Induction of durable, antigen-specific linked T cell help
 - T cell induction 40-400 times higher than with DNA/RNA vaccines
 - Well-tolerated: Injection site reactions, flu-like symptoms (all grade 1 or 2)
 - Adverse events suggest induction of an adaptive immune response
- Safety and mechanistic (immunogenicity) data from CRUK-led trial supports advancing VAC2 internally
- Planning to submit U.S. IND for next trial upon completion of ongoing CRUK study



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

Hearing Loss

- Hearing loss currently afflicts 430 million people
- Hearing depends on complex steps which change sound waves into electrical signals which are then carried by the auditory nerve to the brain
- **Auditory neuropathy**
 - Inner ear successfully detects sound but has a problem with sending signals from the ear to the brain
 - Caused by damage to auditory neurons inner hair cells, or auditory nerves or genetic mutations
 - Researchers seeking effective treatments

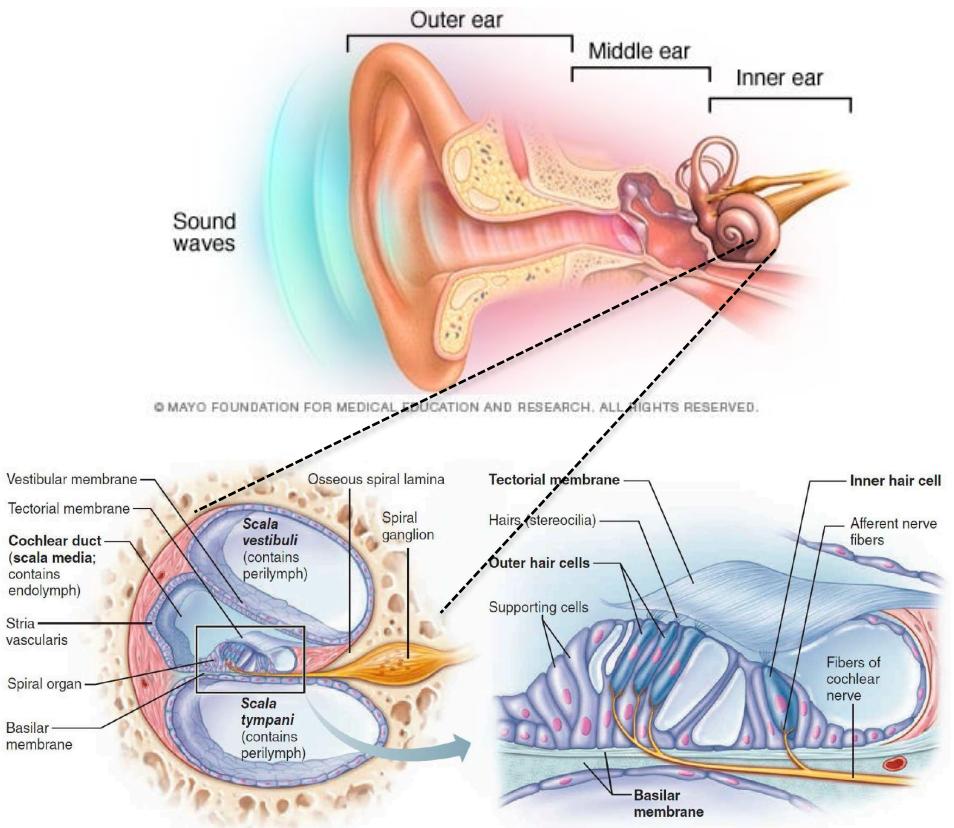


Figure 1. Cross-section of the cochlea with enlarged organ of Corti [40].
From Russo et al Computers 2019, 8, 5

ANP1 (Auditory Neuronal Progenitors) for Hearing Loss

- **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
 - Unique opportunity to leverage Lineage's knowhow and capabilities in neuronal lineage differentiation in indication with a large and growing unmet need
- **IP filed covering the composition and methods for generating Auditory Neuronal Progenitors (ANPs)**
 - ANPs are capable of functioning as sensory neurons and the connecting neuronal ganglion cells of the ear
 - Filed IP includes methods of treatment that employ these cells for the treatment of auditory neuropathy

Select 2022 Milestones

- Completion of GMP production of OPC1 via an improved and larger-scale manufacturing process and a new thaw-and-inject formulation
- FDA interaction to discuss recent manufacturing improvements made to OPC1
- Initiation of clinical performance and safety testing of a novel delivery system for OPC1, with an anticipated Investigational New Drug (“IND”) amendment submission
- Updates from the ongoing VAC2 Phase 1 non-small cell lung cancer study
- An anticipated IND submission for VAC2
- Continued development of a VAC cell-based therapeutic for glioblastoma with our strategic partner, Immunomic Therapeutics
- Preclinical development activities for ANP1 program
- Preclinical development activities for PNC1 program
- Evaluation of opportunities for new VAC product candidates based on internally identified or partnered tumor antigens
- Evaluation of partnership opportunities and expansion of existing collaborations

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

OPC1 SCiStar Study Participants



<https://blog.cirm.ca.gov/2018/01/24/how-a-stem-cell-transplant-may-help-transform-lucas-lindners-life/>

Lucas Lindner

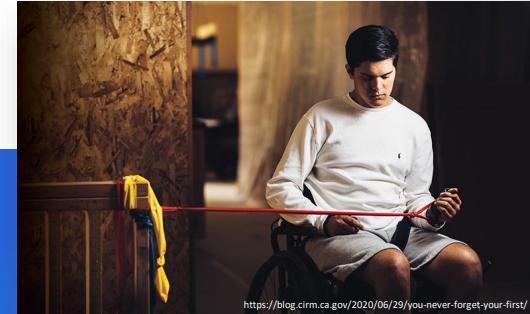
"There's no reason to not look forward in the same way now that I had before all of this happened. I'm looking forward to driving again... it's a bright future."



<https://blog.cirm.ca.gov/tag/kris-boesen/>

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."



<https://blog.cirm.ca.gov/2020/06/29/you-never-forget-your-first->

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



Image adapted from macular.org



Image adapted from macular.org

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