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The future of cell therapy.



# Corporate Overview

August 12, 2021

# 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"

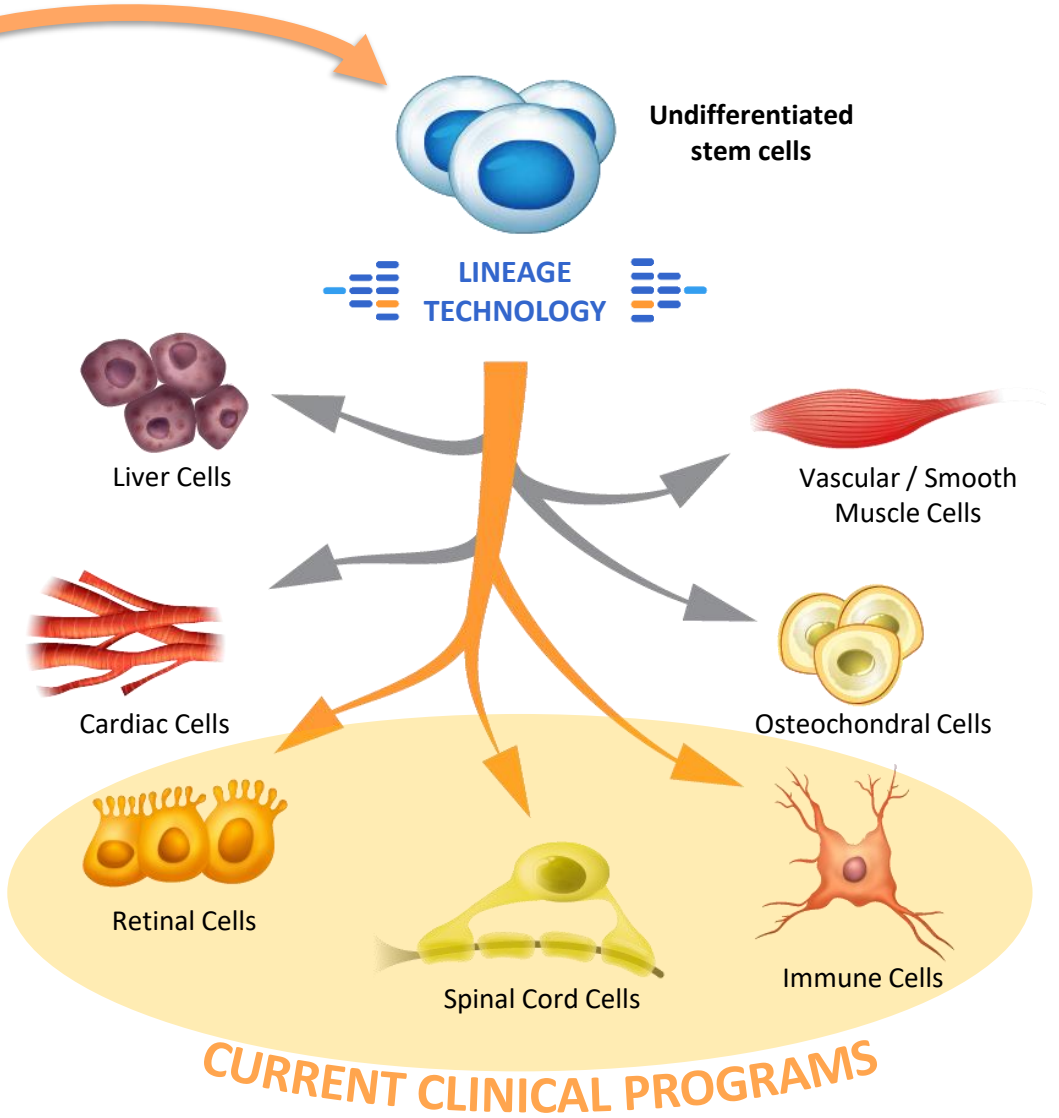
# Business Overview

# Lineage Cell Therapeutics – Investor's Overview

| | |
|---|---|
| Innovative Approach | - Transplanting "off the shelf" cells to treat serious medical conditions |
| Unique Advantage | - Can manufacture an unlimited supply of specialized cell types from established pluripotent cell lines |
| Three Clinical Programs | **- OpRegen**: Phase 1/2a in Dry Age-Related Macular Degeneration with GA<br>**- OPC1**: Phase 1/2a in Cervical Spinal Cord Injury<br>**- VAC2**: Phase 1 in Non-small Cell Lung Cancer (oncology platform) |
| Differentiated Clinical Data | - Three cases of retinal tissue *restoration* observed in dry AMD patients<br>- One-third of spinal cord patients gained *2 levels* of motor function<br>- Potent *induction of immune responses* observed in cancer patients |
| Market Opportunity | - Billion-dollar commercial potential for each program |
| Financial Position | - ~$68.7 million in cash and marketable securities as of June 30, 2021 |
| Market Capitalization | - ~$434 million as of August 12, 2021 |

# Lineage Technology Platform – Allogeneic Cell Transplants

- **The Lineage Platform starts with a frozen vial of *self-renewing stem cells***
- **These pluripotent cells can become *any* cell type in the body**
- **Lineage's proprietary processes create *only* the cell type which is desired**
- **No alterations are made to the cell's DNA**
- **Commercial-scale production occurs from a single vial of cells**

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# Competitive Advantage: In-House Manufacturing and Know-How

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

## Capabilities

- Cell banking and handling
- Process development
- Manufacture of clinical trial material
- Scale-up in multi-liter bioreactors
- Multiple clean rooms for parallel GMP production runs

## Facilities


**Cell Cure Neurosciences**
*(Subsidiary)*

**Backed by hundreds of cell therapy-related patents and patent applications**

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# Pipeline and Validating Partnerships

| Clinical Programs | Financial Support Received | Phase 1 | Phase 2a | Next Steps |
|---|---|---|---|---|
| **OpRegen® (RPE Cells)**<br>Dry AMD with Geographic Atrophy (GA) | רשות החדשנות Israel Innovation Authority<br>**$16M** | → | | Enrollment completed |
| **OPC1 (Oligodendrocytes)**<br>Spinal Cord Injury (SCI) | CIRM CALIFORNIA'S STEM CELL AGENCY<br>**$14M** | → | | Data collected; planning for Phase 2b/3 |
| **VAC2 (Dendritic Cells)**<br>Non-Small Cell Lung Cancer (NSCLC) | CANCER RESEARCH UK<br>**$10M** | → | | 1 patient left to enroll |

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

*Source: aao.org*

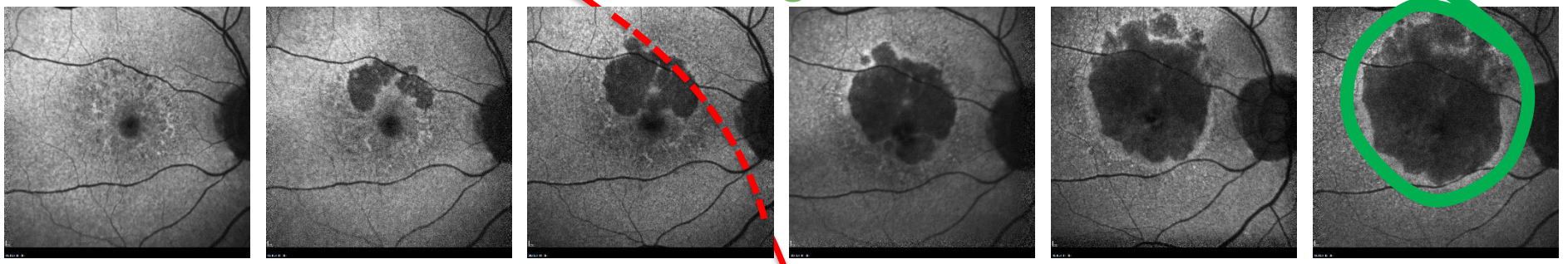
# OpRegen®: RPE Cell Transplants to Treat Dry AMD

# 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)**

**20/640**

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

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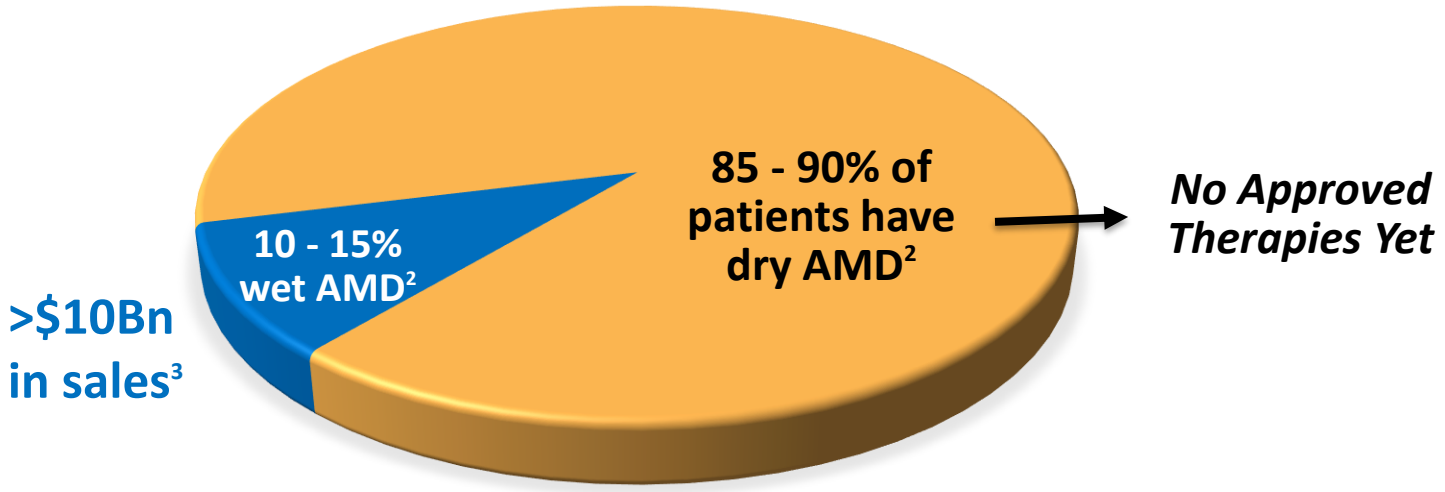
*Image courtesy of Jordi Monés, MD, PhD*

# Multi-Billion Dollar Market Opportunity in the U.S.

**Age-related Macular Degeneration (AMD) (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.*

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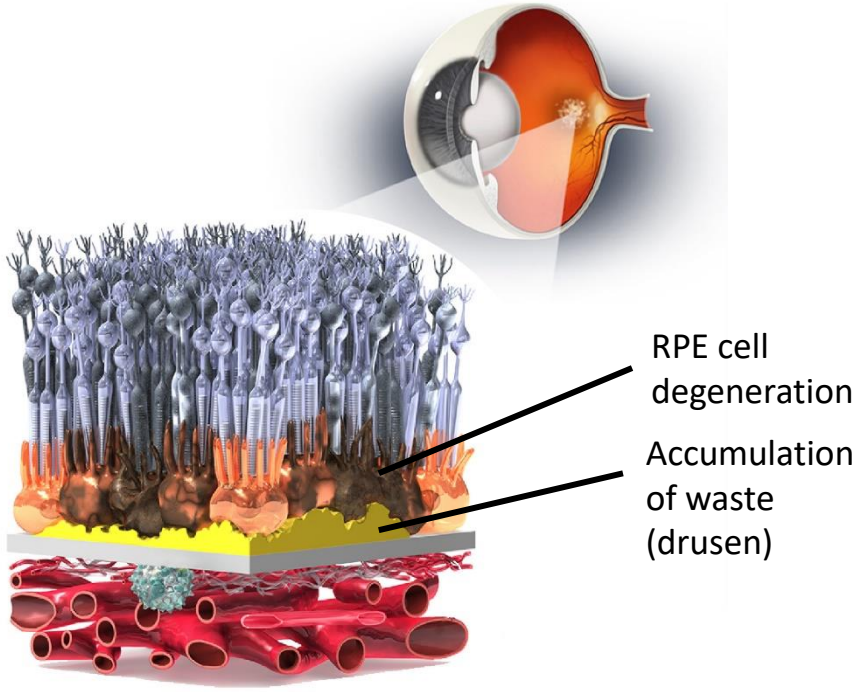
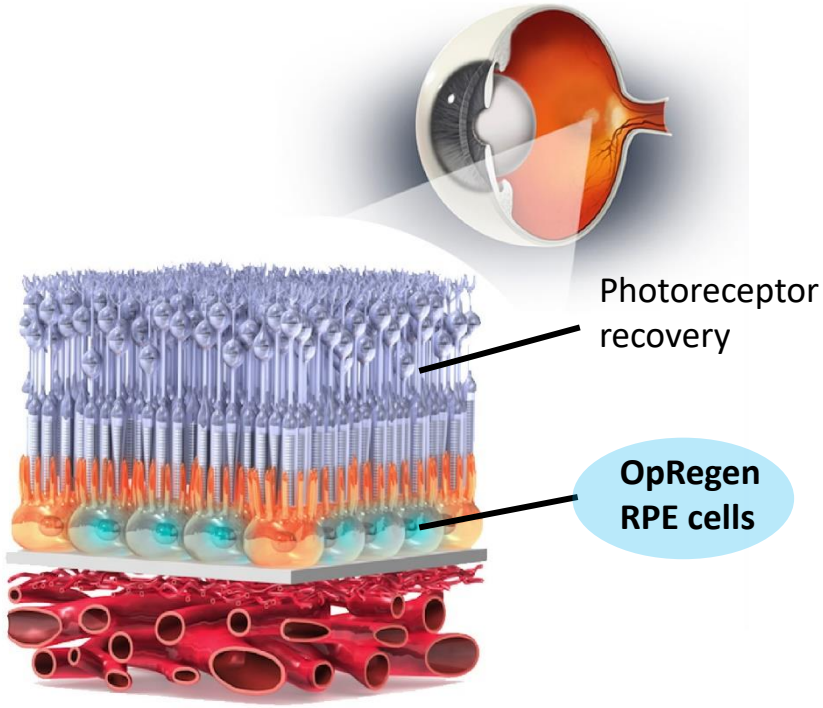
# Lineage Approach – OpRegen, an RPE Cell Transplant

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




Pre-Transplant

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




Post-Transplant

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*Image adapted from scienceofamd.org*

# Commercial-Scale Manufacturing Capabilities

- **OpRegen consists of >99% pure RPE cells**
  - Uses NIH-approved line was established >20 years ago
  - Extensive functional and identity characterization performed on each batch
  - No genetic modifications are made to the cells
  - No residual pluripotent cells detectable in clinical material

- **Immediate-use "thaw and inject" formulation**
  - No dose preparation is required
  - From frozen cells to injection device in 5 minutes

- **Current production scale is 5 billion cells per 3-liter bioreactor**
  - Equal to 2,500 clinical doses/batch
  - Further scale-up can be performed in larger or parallel reactors


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# Dry AMD Competitive Landscape

## Cell Therapy

**OpRegen** (Ph1/2, Lineage Cell Therapeutics)
**CPCB-RPE1** (Ph1/2, Regenerative Patch Tech.)
**ASP7317** (Ph1, Astellas) (Enrollment Paused)
**jCell** (Preclinical, jCyte)

## Visual cycle modulation

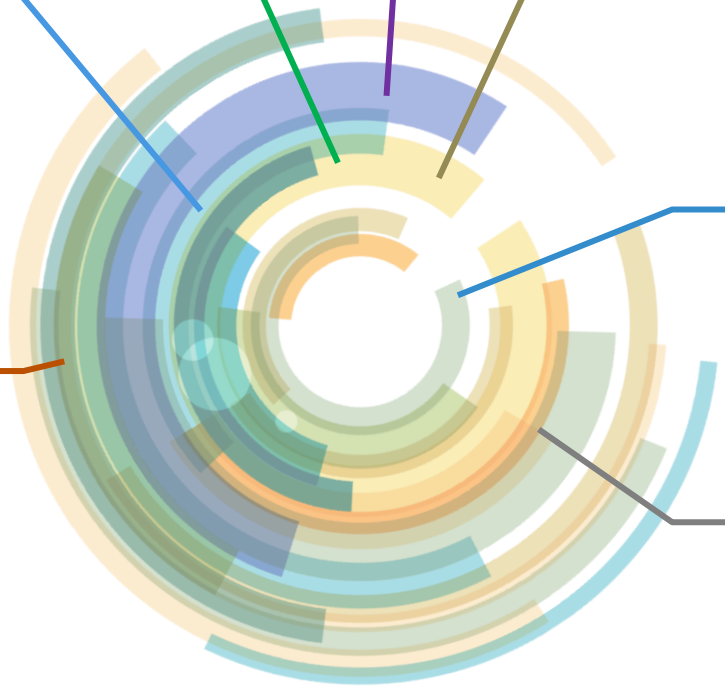
**ALK-001** (Ph. 3, Alkeus)
**FAILED**
*fenretinide (Sytera)*
*emixustat (Acucela)*
*OT-551 (Othera)*

## Anti-inflammatory

*Complement inhibition location and molecule:*
**ANX007** (Ph2, Annexon)
**APL-2** (Ph3, Apellis)
**CB2782** (Preclinical, Catalyst)
**Zimura** (Ph3, Iveric bio)
**ALXN1720** (Ph1, Alexion)
**HMR59** (Ph2, Hemera)
**danicopan** (Ph1, AstraZeneca RD)
**Ionis-FB-LRX** (Ph2, Ionis)
**NGM621** (Ph2, NGM Bio)
**FAILED**
*eculizumab (Alexion)*
*tesidolumab (Novartis)*
*lampalizumab (Genentech/Roche)*
*CLG561 (Novartis)*

## Toxic by-product reduction

*Prevent Amyloid Aß oligomer assembly:*
**GAL-101** (Ph1, Galimedix)
**ALZ-801** (Preclinical, Alzheon)
*Reduce DHA peroxidation:*
**RT011** (Preclinical, Retrotope)
**FAILED**
*Glatiramer acetate (Teva)*
*RN6G (Pfizer)*
*GSK933776 (GSK)*



## Gene Therapy

Gyroscope (Ph1/2)
Hemera/Janssen (Ph1)
Novartis (Preclinical)

## Neuroprotection

*Repair mitochondrial dysfunction/oxidative stress:*
**elamipretide** (Ph2, Stealth)
**risuteganib** (Ph2, Allegro)
**photobiomodulation** (Ph N/A, LumiThera)
**brimonidine tartrate** (Ph2, Allergan)
**FAILED**
*NT-501 (Neurotech)*
*tandospirone (Alcon)*
*OT-551 (Othera)*

## Other approaches

*Inflammasome Inhibition:*
**kamuvudine** (Ph1, Inflammasome Therapeutics)
**Xiflam** (Preclinical, OcuNexus)
*Matrix Modulation:*
**doxycycline** (Ph2/3, Oracea)
*HtrA1 inhibitor:*
**FHTR2163** (Ph2, Genentech/Roche)

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*Adapted from https://retinatoday.com/resource/therapeutic-pipeline-for-amd (Accessed August 12, 2021)*

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# OpRegen Phase 1/2a Clinical Trial Interim Results

## Replace and Restore

# Phase 1/2a OpRegen Clinical Trial - Promising Interim Results Continue

## STRUCTURE:

- **3 OpRegen treated patients have shown evidence of retinal tissue restoration**
  - Earlier and first-known clinical report of restoration has been maintained for 3 years
  - Reductions in drusen waste material observed in some patients

## FUNCTION:

- **83% of all Cohort 4 patients continued to exhibit stable or improved BCVA** (6mo to ~3y post-treatment)
  - Visual acuity continued to decline in the majority (83%) of untreated eyes
- **Encouraging interim data collected on patient-reported visual function, reading speed, and microperimetry**

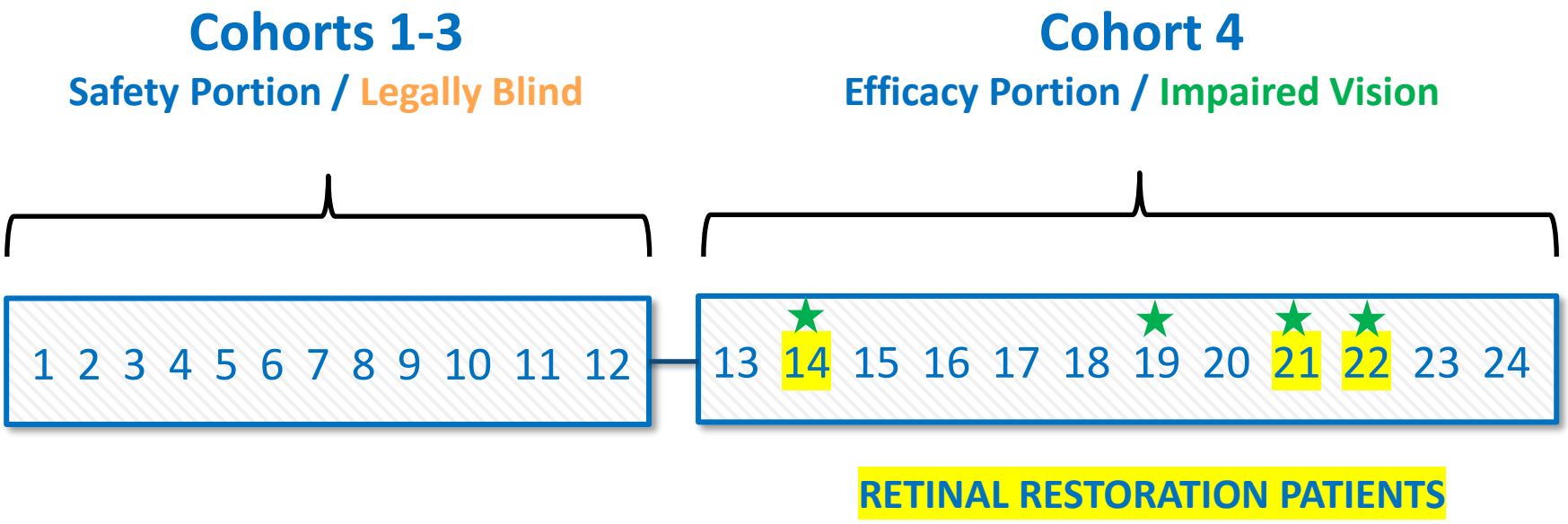
## SAFETY and TOLERABILITY:

- **OpRegen transplants have been well tolerated with no unexpected AEs or SAEs**

## DURABILITY:

- **Earliest grafts have persisted for more than 5 years; no cases of rejection (N=24)**

# Phase 1/2a Clinical Trial of OpRegen – Enrollment Complete




| | |
|---|---|
| **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** |

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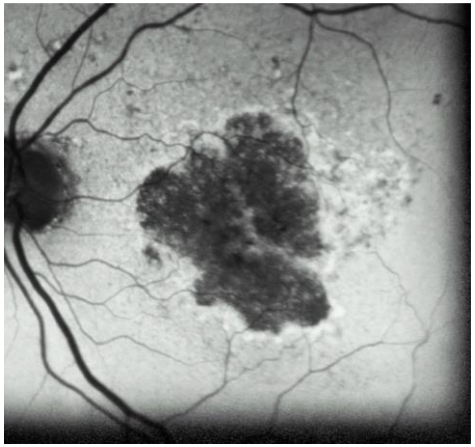
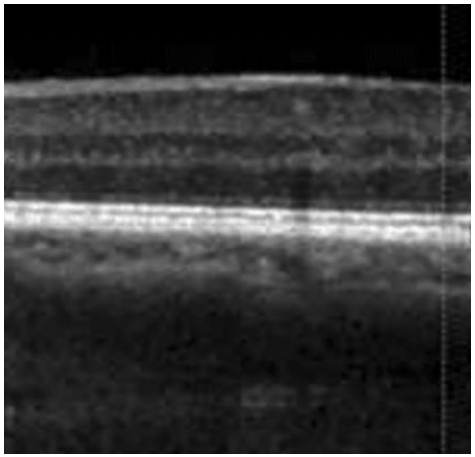
★ = OpRegen placed across area of atrophy

# Imaging the Retina - Fundus Autofluorescence (FAF) and Optical Coherence Tomography (OCT)

## FAF



## OCT



- **A flash of light causes cells to fluoresce, which is recorded in a single plane and with minimal structural resolution**
- **OpRegen cells lack lipofuscin, the material which fluoresces, so OpRegen cells appear as atrophic areas**

- **Differences in light returned to a detector creates a 3D images of all retinal layers**
- **The AAO considers OCT the "gold standard" for imaging the retina**
- **Offers much greater detail of anatomical structures**

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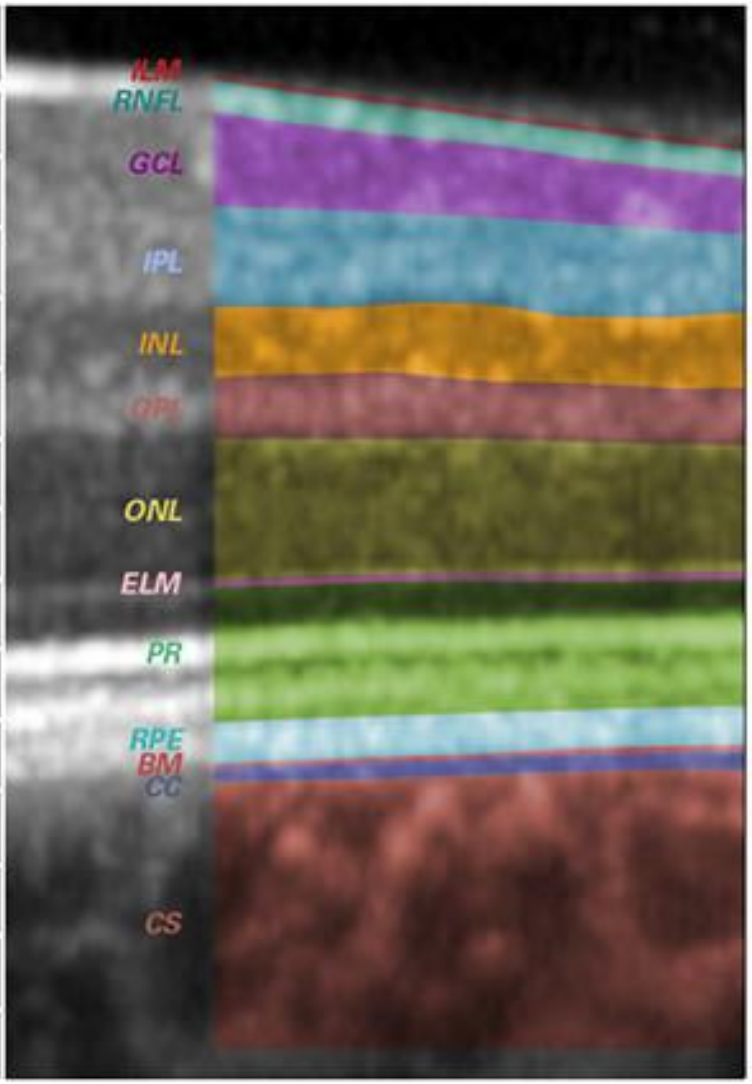
# High Resolution OCT Provides Resolution Close to Histology

| Retinal Layers | |
|---|---|
| **Abbr.** | **Name** |
| ILM | Internal Limiting Membrane |
| RNFL | Retinal Nerve Fibre Layer |
| GCL | Ganglion Cell Layer |
| IPL | Inner Plexiform Layer |
| INL | Inner Nuclear Layer |
| OPL | Outer Plexiform Layer |
| ONL | Outer Nuclear Layer |
| ELM | External Limiting Membrane |
| PR | Photoreceptor Layers |
| RPE | Retinal Pigment Epithelium |
| BM | Bruch's Membrane |
| CC | Choriocapillaris |
| CS | Choroidal Stroma |

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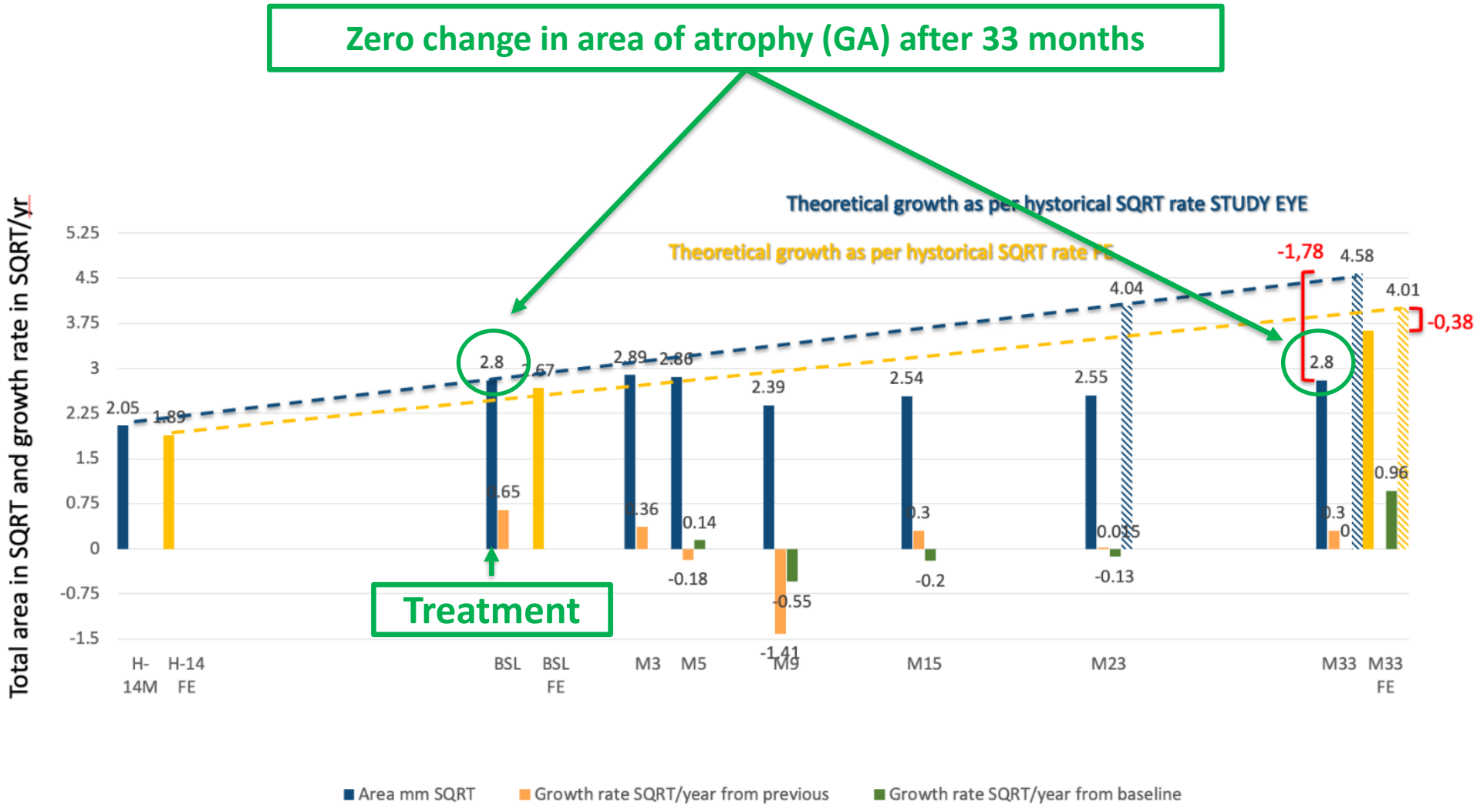
Source: https://www.heidelbergengineering.com/int/news/know-your-retinal-layers-33401465/

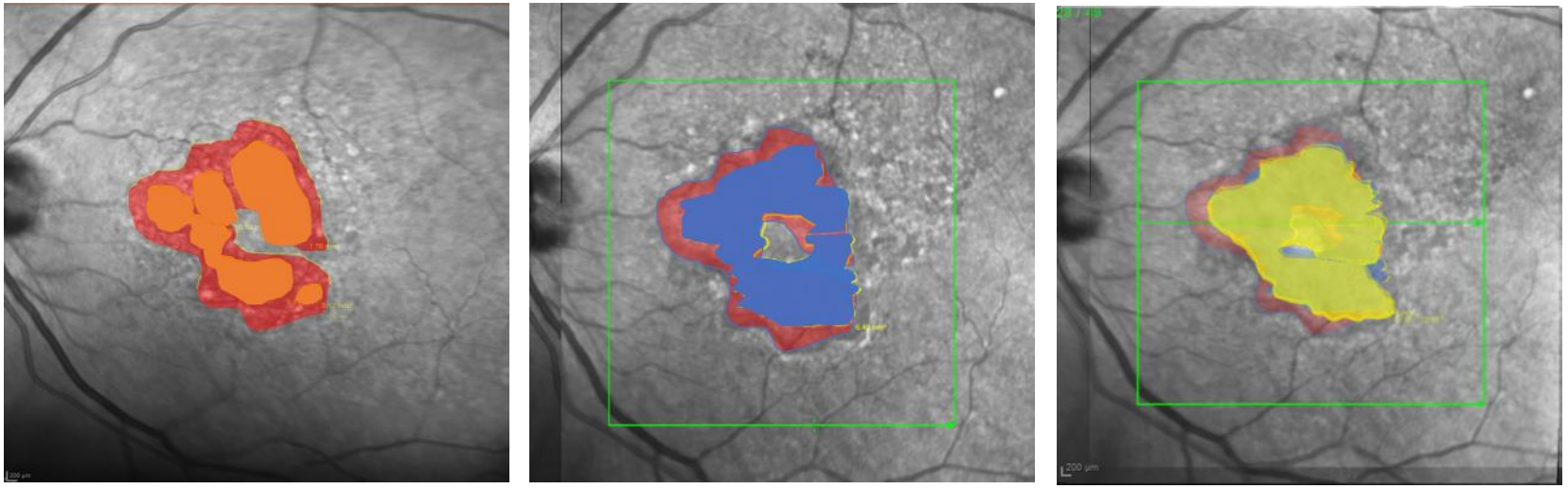
# First Case of Retinal Restoration – Assessing GA Progression Using FAF Alone or OCT and Multimodality Imaging




*Note: Theoretical growth is based on the rate of change (squared root, SQRT) between the historical (H) image 14 Months prior to the Baseline (BSL) assessment. That rate of change is applied over the duration of the patient's follow-up (the dashed lines) at the various time points indicated.* ***(FE = Fellow Eye)***

# First Case of Retinal Restoration – *Smaller* Area of GA, Maintained for ~3 Years

| Date | Time in Study | Colored area on Figure below | Area $mm^2$ (SQRT) | Changes in rate of progression from previous | Changes in rate of progression from baseline |
|---|---|---|---|---|---|
| May 2017 | Minus 1 year | Orange | 4.21 $mm^2$ (2.05) | N/A | N/A |
| July 2018 | Baseline | Red | 7.90 $mm^2$ (2.8) | + 0.64 mm sqrt/yr | N/A |
| April 2019 | Month +9 | Blue | 5.74 $mm^2$ (2.39) | - 0.61 mm sqrt/yr | - 0.61 mm sqrt/yr |
| October 2019 | Month +15 | Green | 6.48 $mm^2$ (2.54) | + 0.30 mm sqrt/yr | - 0.20 mm sqrt/yr |
| June 2020 | Month +23 | Yellow | 6.52 $mm^2$ (2.55) | + 0.015 mm sqrt/yr | - 0.13 mm sqrt/yr |



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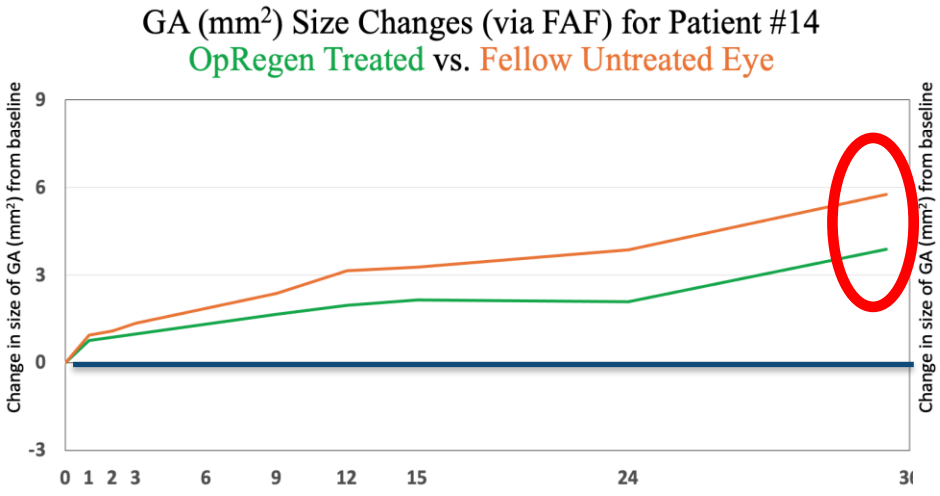
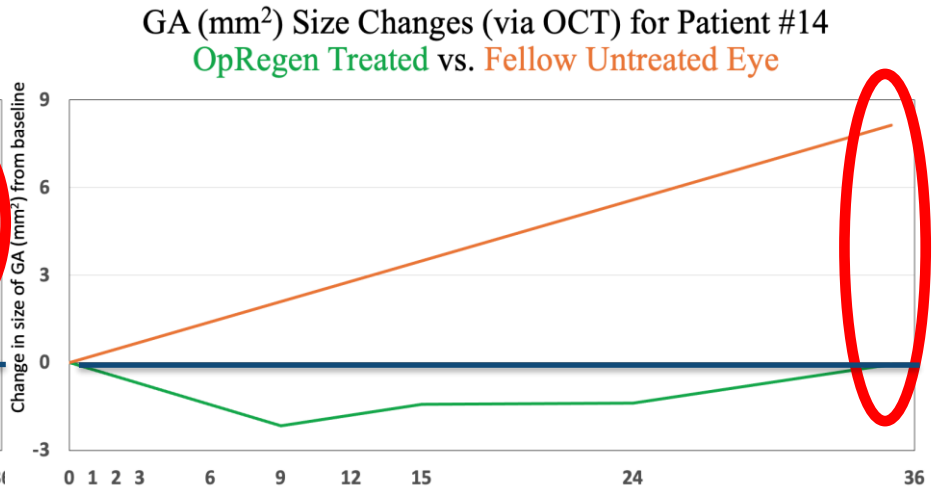
*Data presented at 2020 AAO Virtual Meeting*

# First Case of Retinal Restoration - Utilizing OCT to Collect GA Measurements

**FAF**




**OCT**




Treated Fellow

Time Post-Implantation (months)

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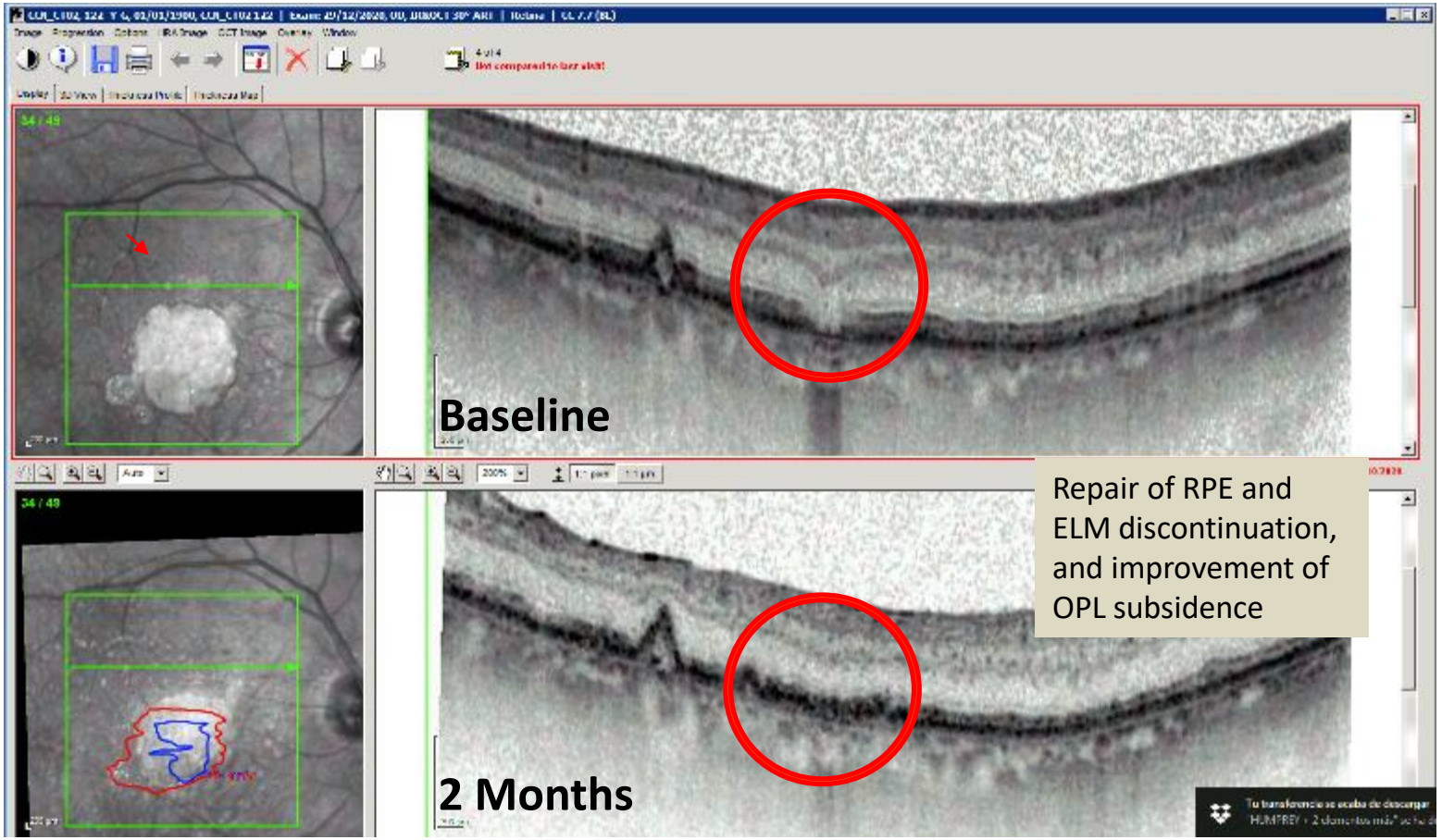
# Second Case of Retinal Restoration – Evident at 2 Months

Evidence of outer retinal regeneration and *complete resolution* of iRORA lesion




**iRORA = Incomplete Retinal Pigment Epithelial and Outer Retinal Atrophy**

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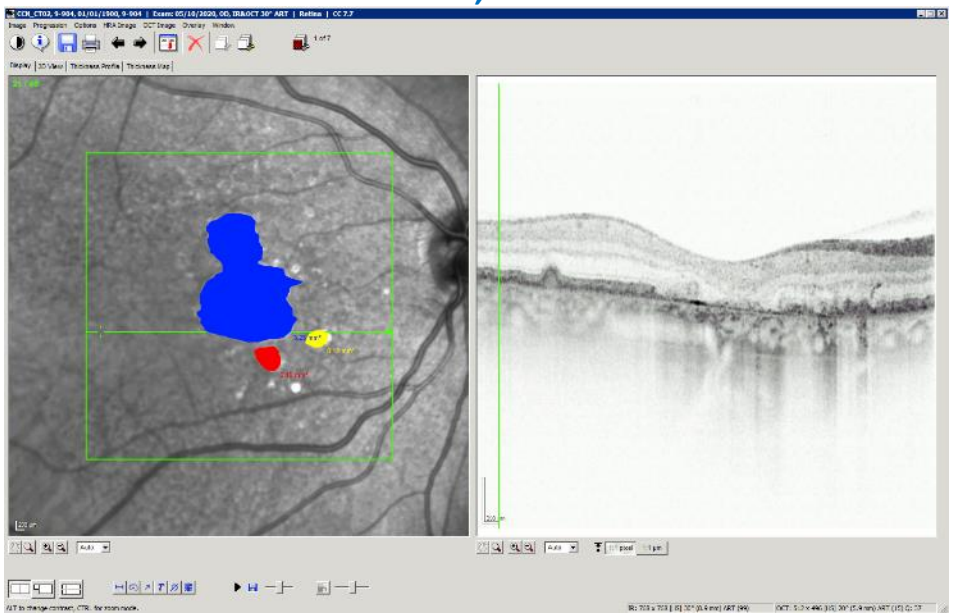
*Image courtesy of Jordi Monés, MD, PhD*

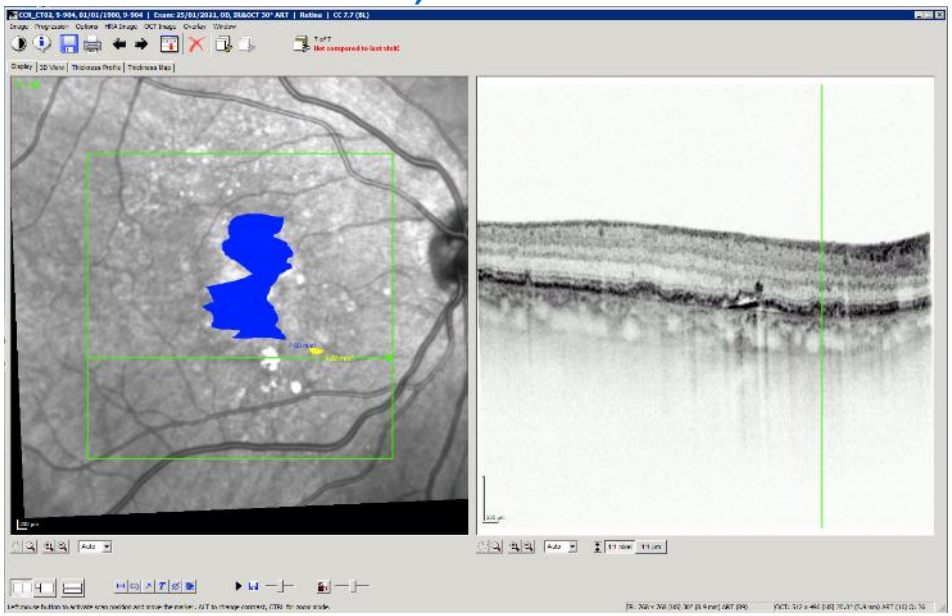
# Third Case of Retinal Restoration – Evident at 3 Months

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

**OCT 5, 2020**



**JAN 21, 2021**



**TOTAL AREA: 3.56 mm²**

**TOTAL AREA: 2.69 mm²**

| | | | |
|---|---|---|---|
| **Total area** | **3M GROWTH RATE:** | **– 0.87 mm²** | **(ANNUAL RATE – 3.48 mm²)** |
| **SQRT transformation** | **3M GROWTH RATE:** | **– 0.23 mm** | **(ANNUAL RATE – 0.92 mm)** |

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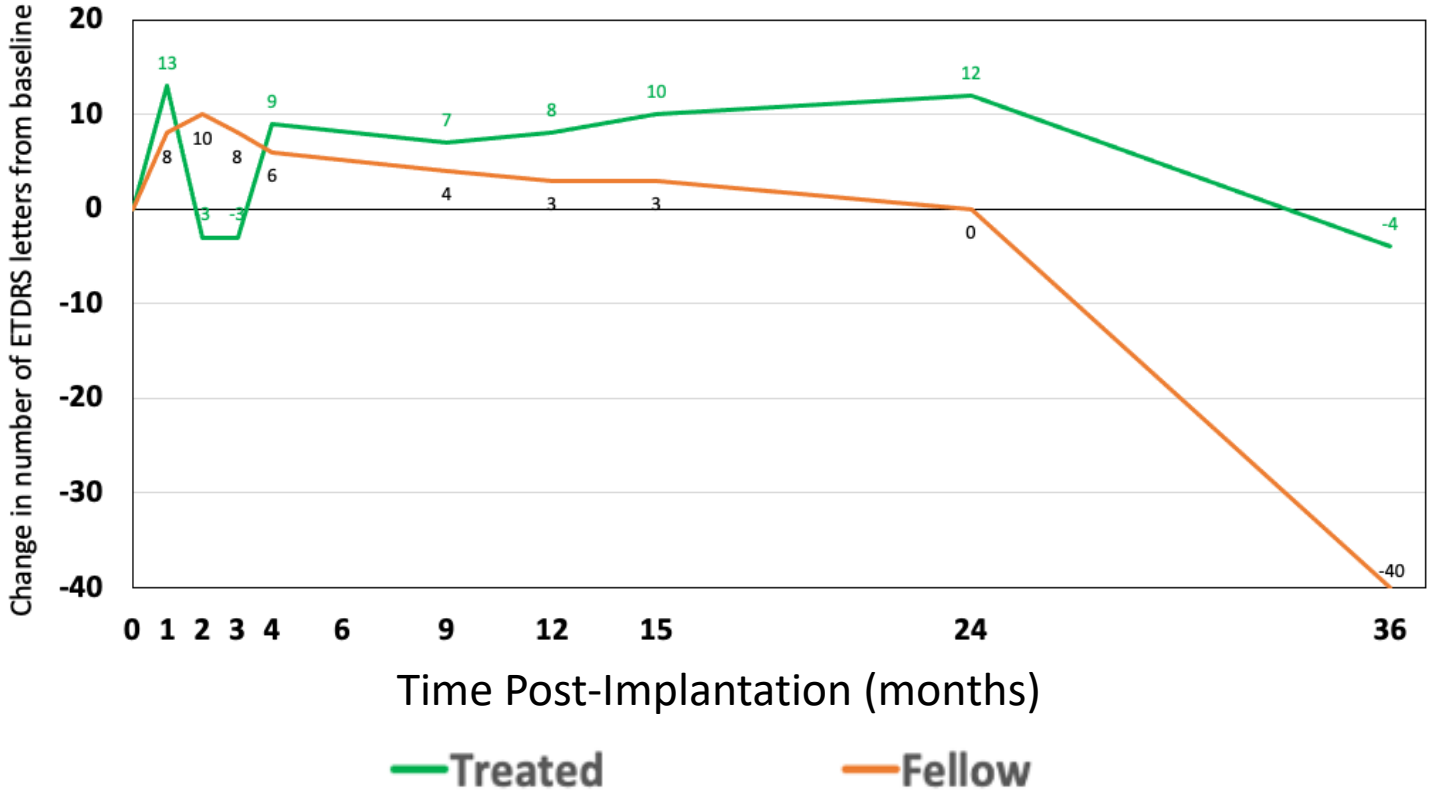
*Image courtesy of Jordi Monés, MD, PhD*

# First Case of Retinal Restoration - Durable Improvements

## BCVA Changes for Patient #14 – Treated vs. Fellow Eye




| Time point | Fellow (OD) | Treated (OS) |
|---|---|---|
| Baseline | 61 letters read (20/63) | 54 letters read (20/80) |
| 3 years post-op | 21 letters read (20/400) | 50 letters read (20/100) |

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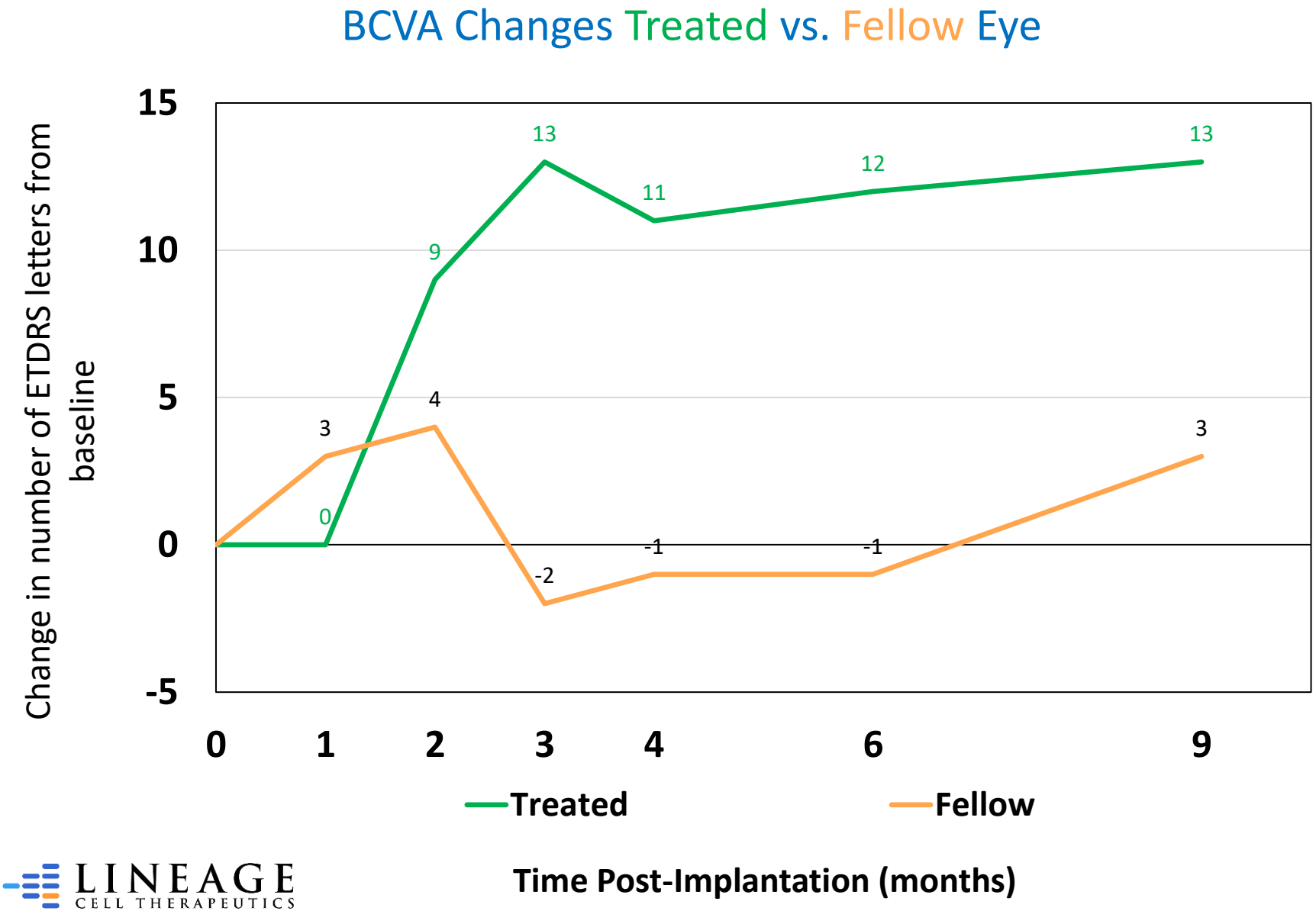
# Third Case of Retinal Restoration - Vision in Treated Eye Dramatically Improved

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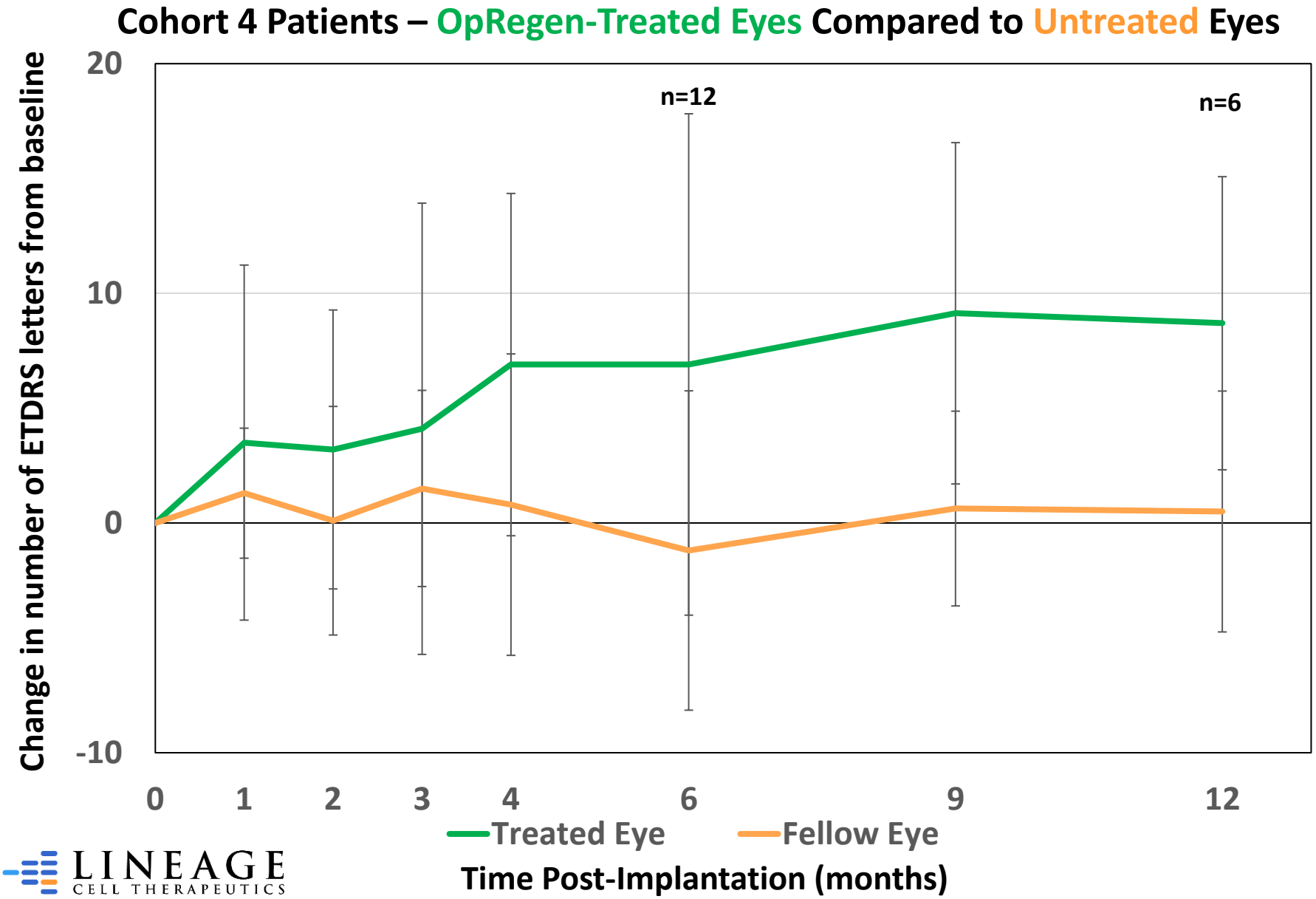
# Improvements in Visual Acuity Observed with OpRegen RPE Transplant

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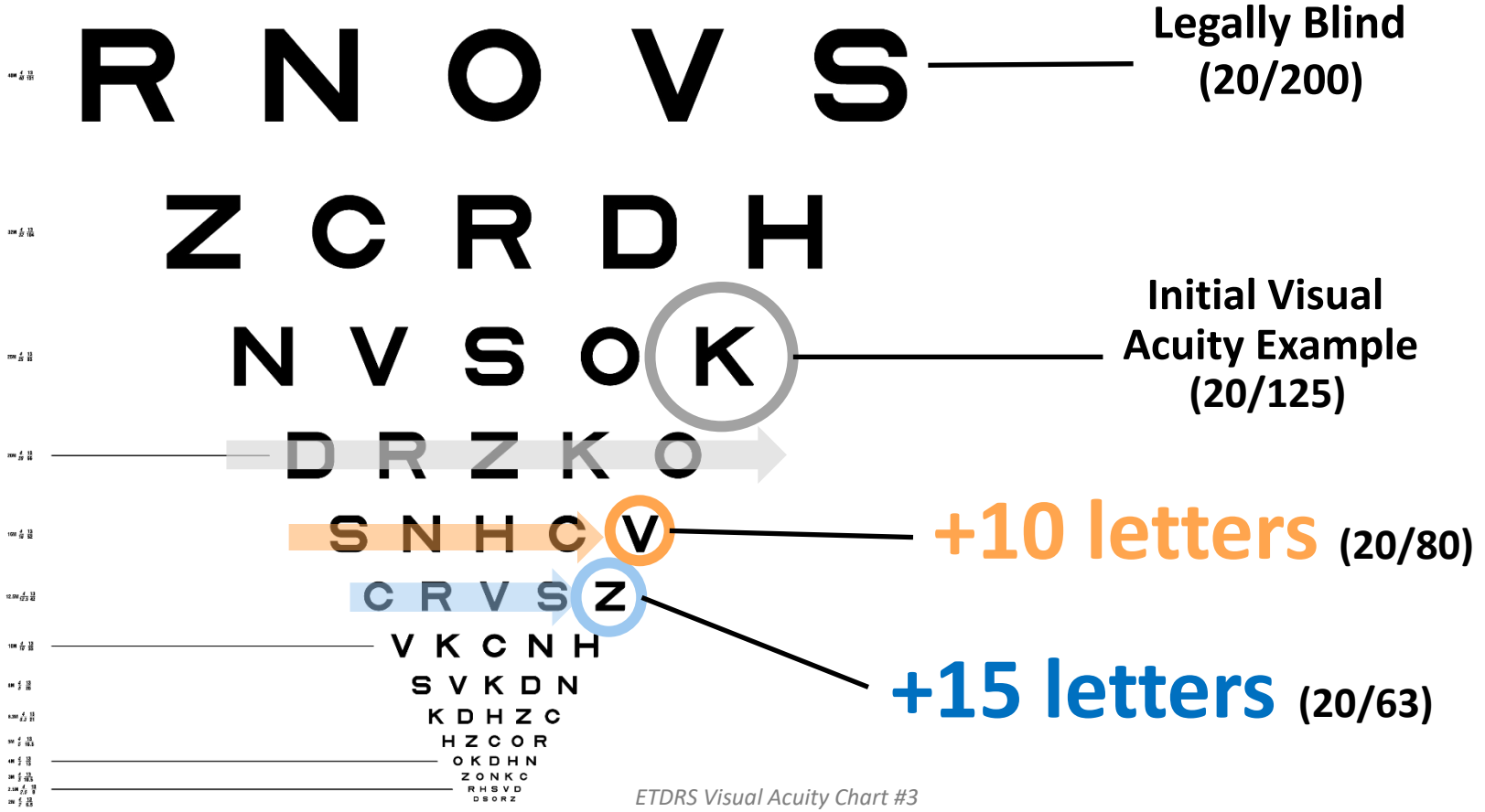
# Real-World “Letters of Improvement”




*ETDRS Visual Acuity Chart #3*

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# Positive Patient-Reported Outcomes (Quality of Life Questionnaire)

- **National Eye Institute (NEI) Visual Function Questionnaire (VFQ-25)**
- **25 vision-related questions reported across 11 constructs**
- **Improvement occurred in 9 of 11 categories and remained unchanged in one category in Cohort 4 patients**

| | Category | N (%) Change from Screening to Year 1 (n=5 available to date) |
|---|---|---|
| 1. | General Vision | 4/5 (80%) patients reported improvement |
| 2. | Ocular Pain | 2/5 (40%) patients reported improvement |
| 3. | Near Activities | 5/5 (100%) patients reported improvement |
| 4. | Distance Activities | 3/5 (60%) patients reported improvement |
| 5. | Vision Specific: Social Functioning | 3/5 (60%) patients reported improvement |
| 6. | Vision Specific: Mental Health | 5/5 (100%) patients reported improvement |
| 7. | Vision Specific: Role Difficulties | 4/5 (80%) patients reported improvement |
| 8. | Vision Specific: Dependency | 3/5 (60%) patients reported improvement |
| 9. | Driving | 0/5 (0%) patients reported improvement (only 2 subjects were driving at screening) |
| 10. | Color Vision | 0/5 (0%) no change from screening (all patients previously reported highest possible score, no improvement possible) |
| 11. | Peripheral Vision | 2/5 (40%) patients reported improvement |

# OpRegen – Positioned for Commercial Success

## OpRegen has the potential to capture a multi billion-dollar opportunity

- **Transplanting RPE cells may provide benefits other approaches cannot**
- **Market opportunity is not limited to monogenic deficiencies (e.g. gene therapy)**
- **Three clinical cases of retinal restoration reported**
- **Treatment to date has been well-tolerated**
  - Some patients have exhibited clinically meaningful improvements in clinically-relevant metrics such as visual acuity, GA growth, and reading speed
- **Potential for recurring revenues, but with multiple treatments years apart**
- **May have application in other retinal diseases (example: Stargardt's Disease)**
- **Issued patents cover aspects of production, characterization, and formulation**
- **Fast Track designation from FDA**
- **Opportunities for strategic partnerships for late-stage development**

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

*Source: christopherreeve.org*

# OPC1: A 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.**

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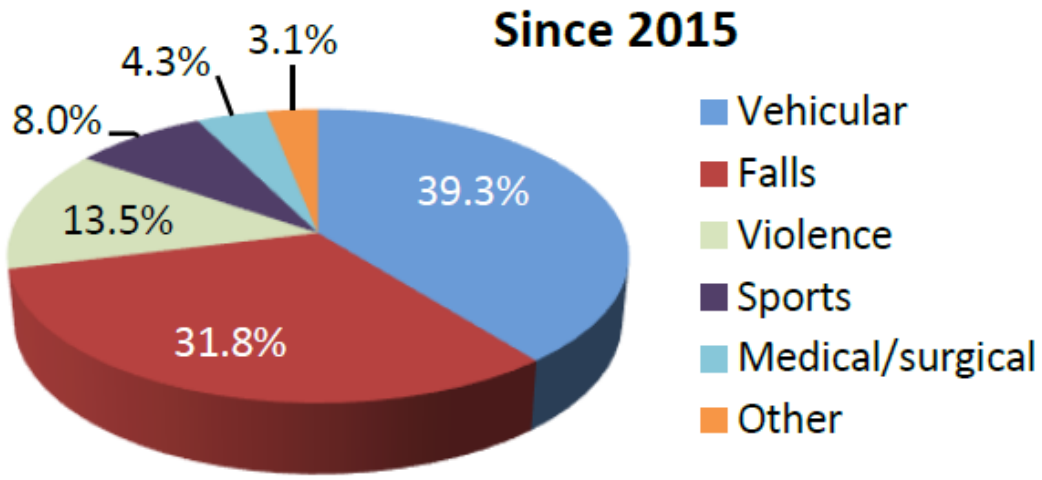
# Spinal Cord Injury (SCI) Overview

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

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

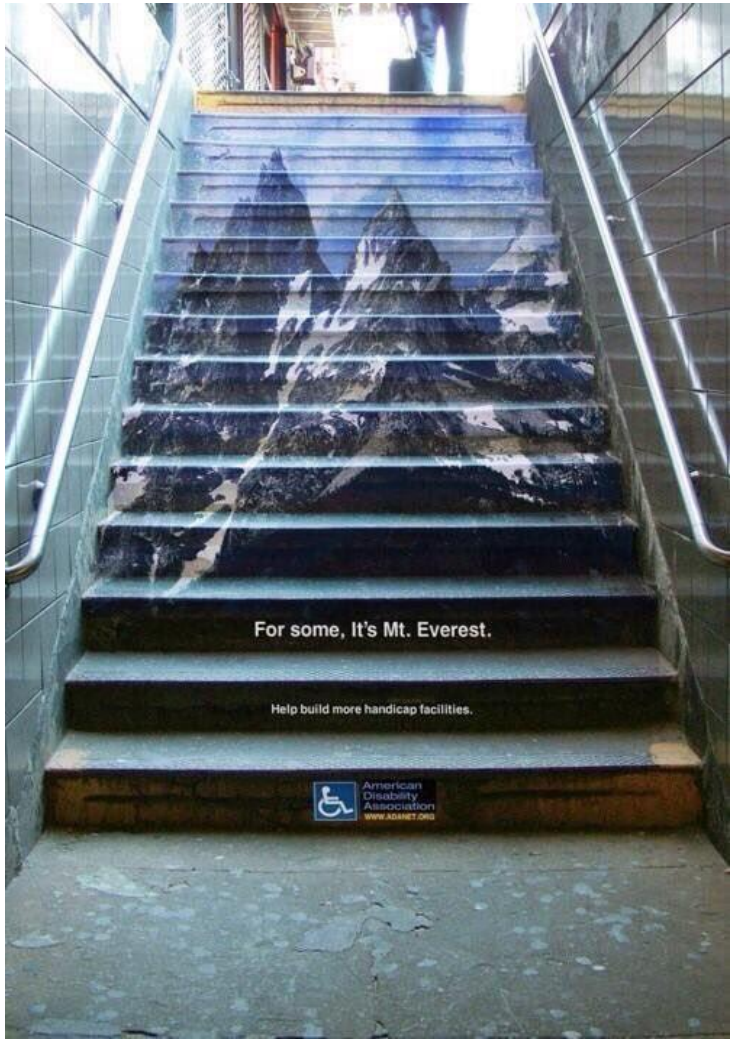



LINEAGE CELL THERAPEUTICS

*Source: National Spinal Cord Injury Statistical Center*

# 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



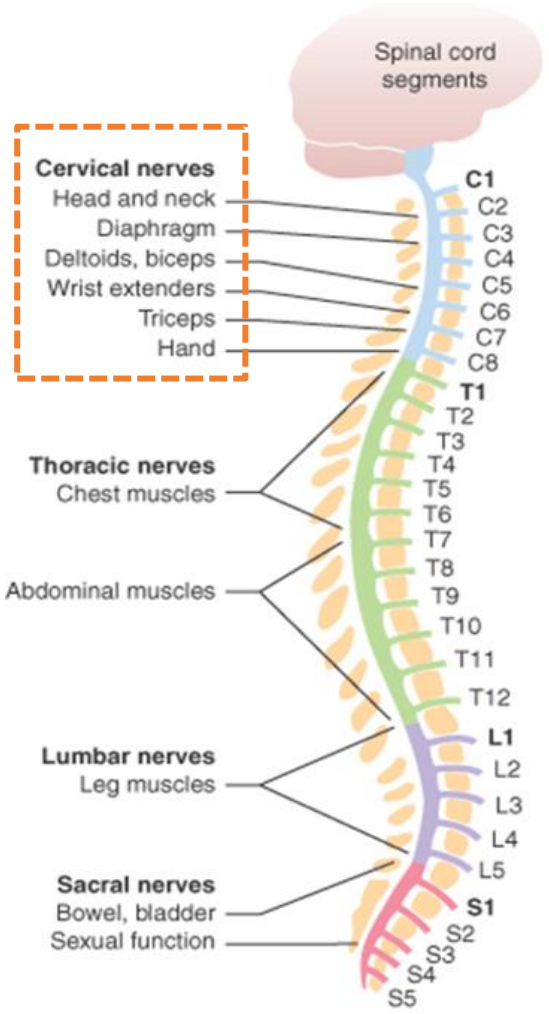

LINEAGE CELL THERAPEUTICS

*(*) National SCI Statistical Center, 2019 SCI Data Sheet.*

# 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**

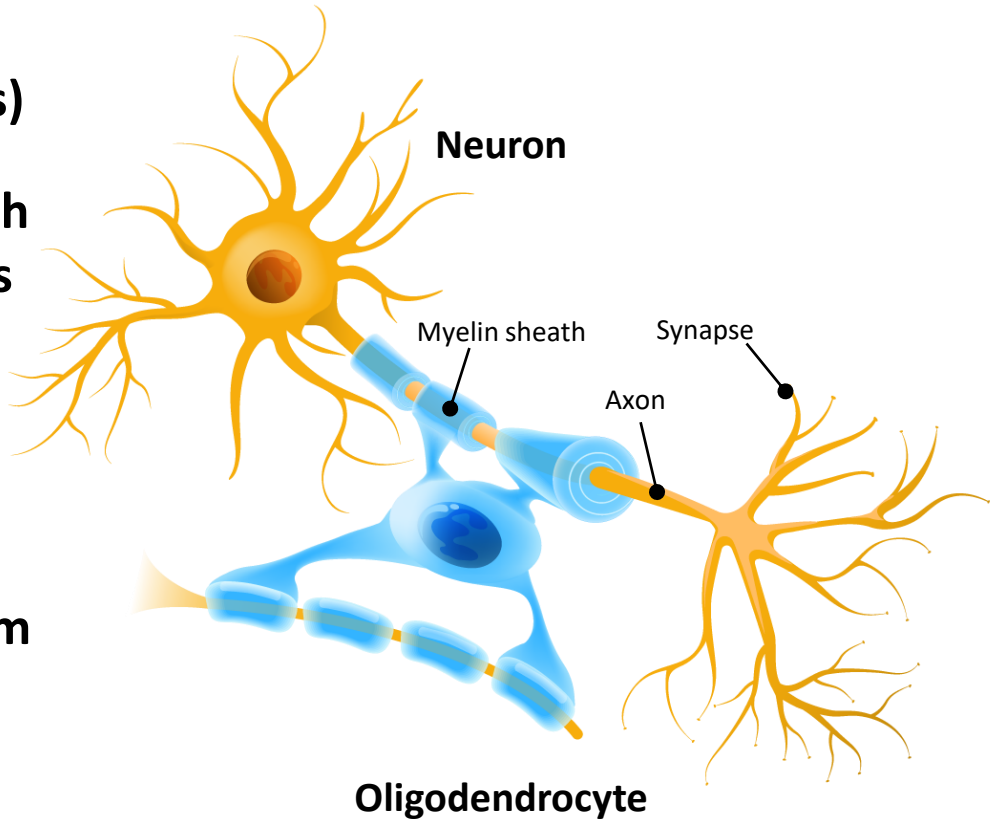



(*) National SCI Statistical Center, 2019 SCI Data Sheet.

# Lineage's **OPC1 cells** for Spinal Cord Injury

## Replacing oligodendrocytes may provide additional upper limb and finger function and improve the quality of life for patients

- **OPC1 is comprised of OPCs (oligodendrocyte progenitor cells)**
- **OPCs are precursors to cells which provide insulation to nerve axons in the form of a myelin sheath**
- **Myelin is necessary for proper function of neurons**
- **OPC1 cells are manufactured from a cell line and injected into the spinal cord at the injury site**




LINEAGE CELL THERAPEUTICS

*(*) National SCI Statistical Center, 2019 SCI Data Sheet.*

# OPC1 Asset Overview

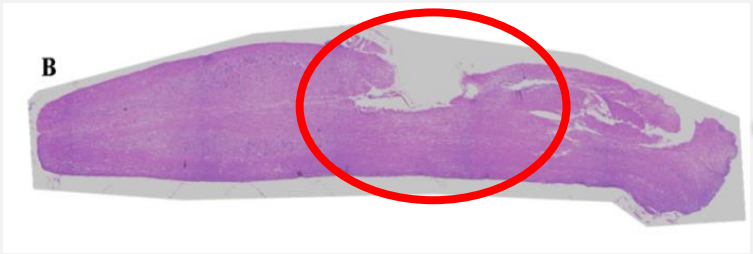
- **OPC1 is covered by multiple issued patents**
- **OPC1 has RMAT Designation**
- **OPC1 has Orphan Drug Designation**
- **OPC1 has received >$14M in support from CIRM (California Institute for Regenerative Medicine)**
- **OPC1 could have application to other demyelinating conditions**

**OPC1 Transplant Procedure**

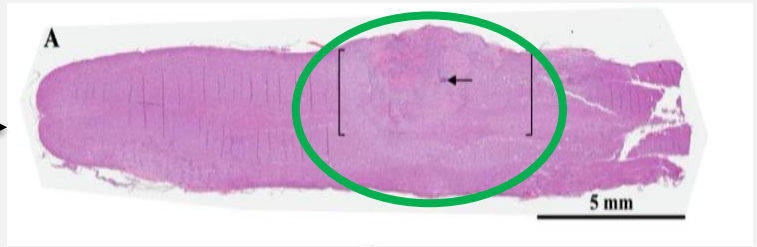
# OPC1 Mechanisms of Action

## Prevention of Cavitation

**Control**

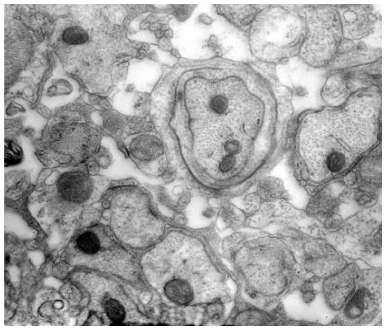



**OPC1**

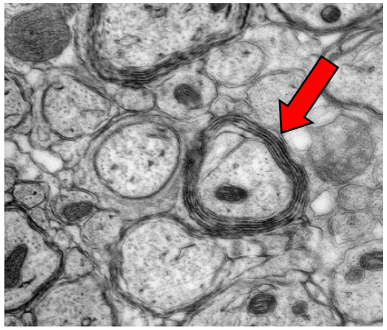



## Myelination of axons

*shiverer* mouse

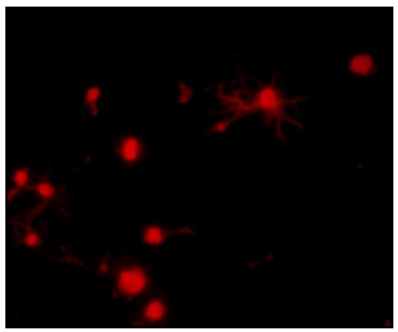


***shi* mouse + OPC1**

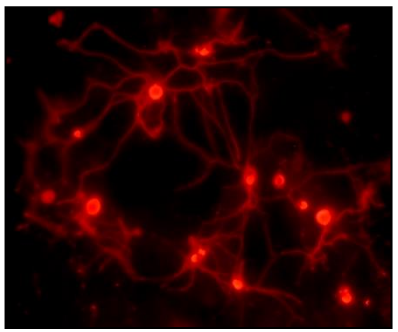


## Secretion of neurotrophic factors

Control Media



**OPC1**



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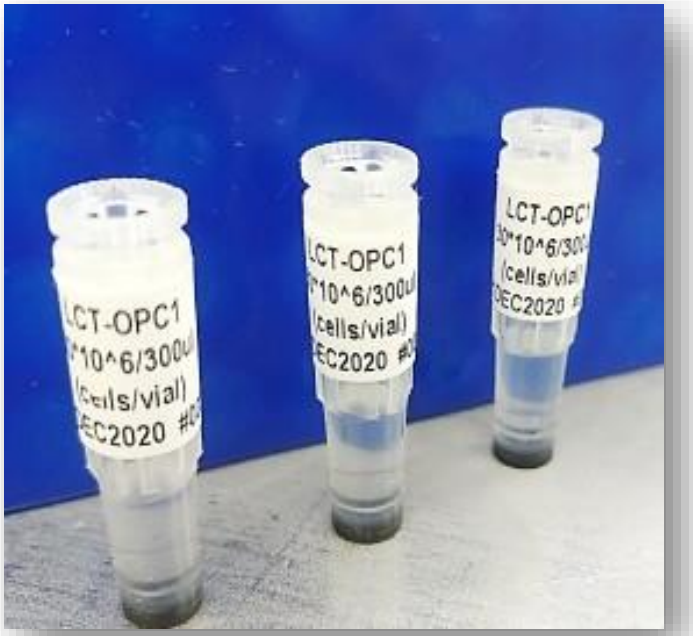
# OPC1 for Spinal Cord Injury

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

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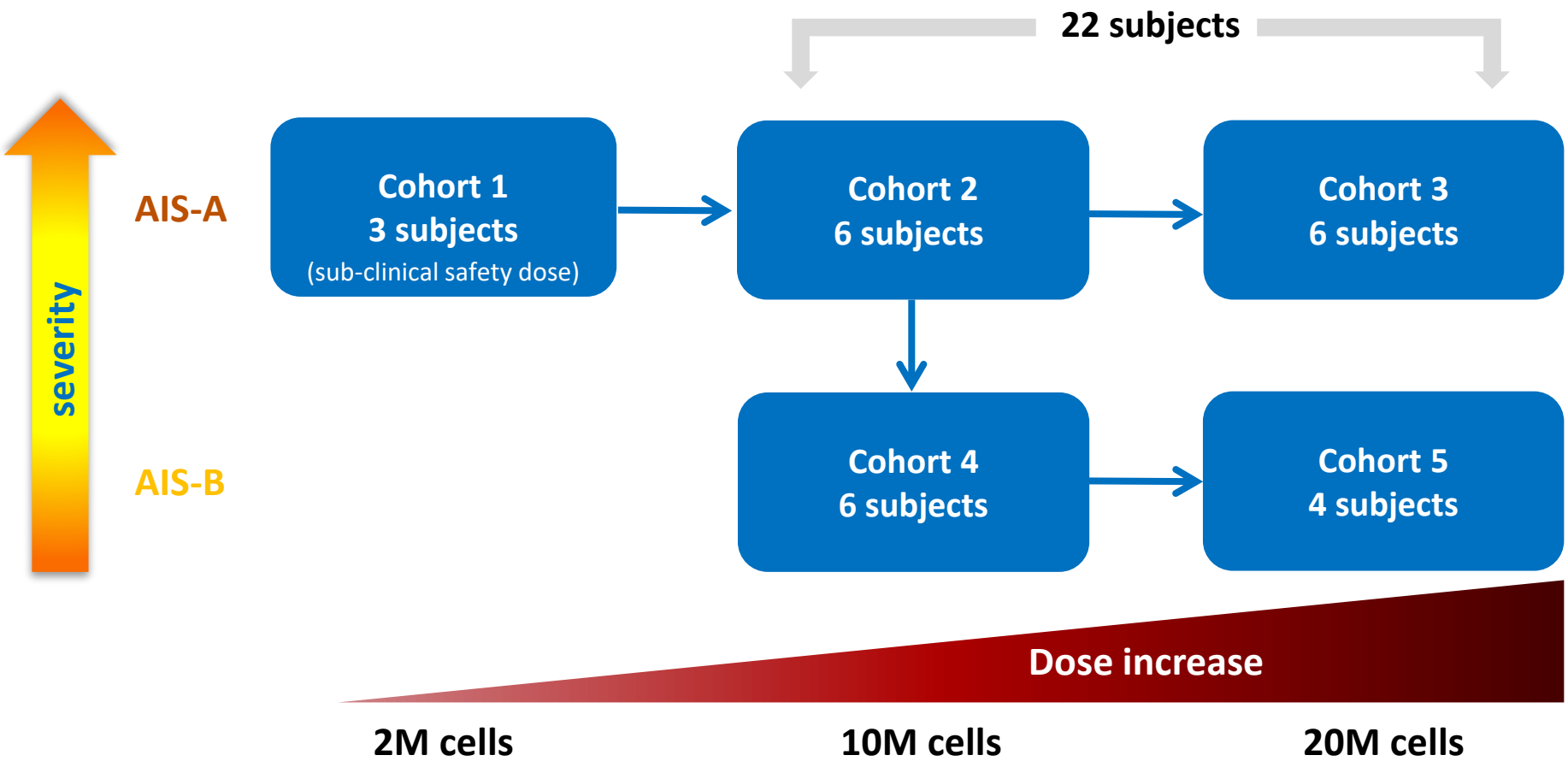
# SCiStar Clinical Trial Study Design

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# 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**

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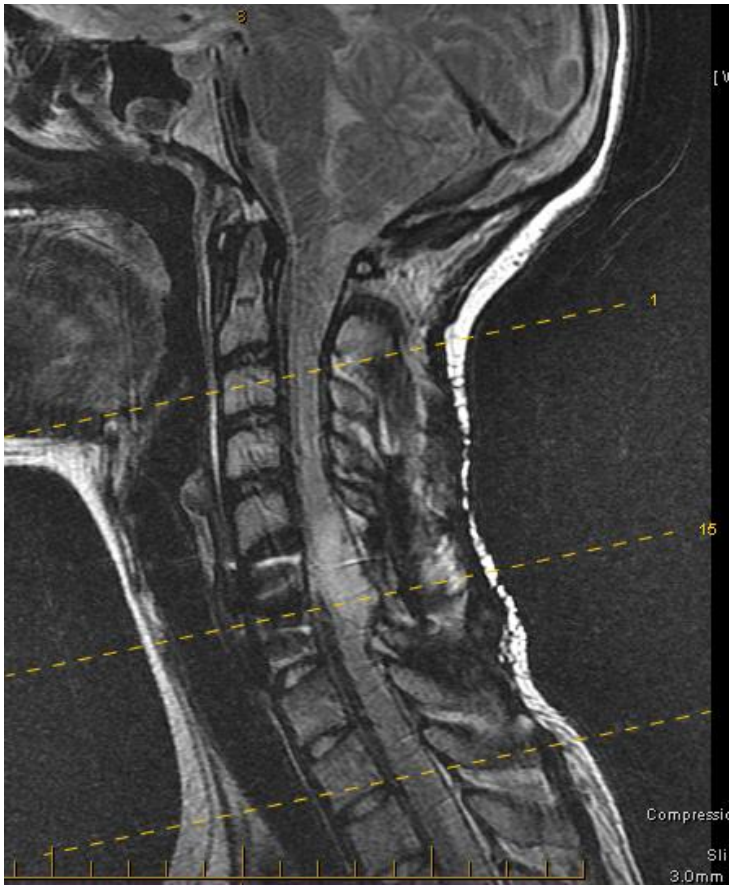
**One AE possibly related to OPC1 was a Grade 2 dysesthesia that began 47 days post-injection but had resolved by the Year 2 follow-up visit*

# 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 cavitation**
- **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**

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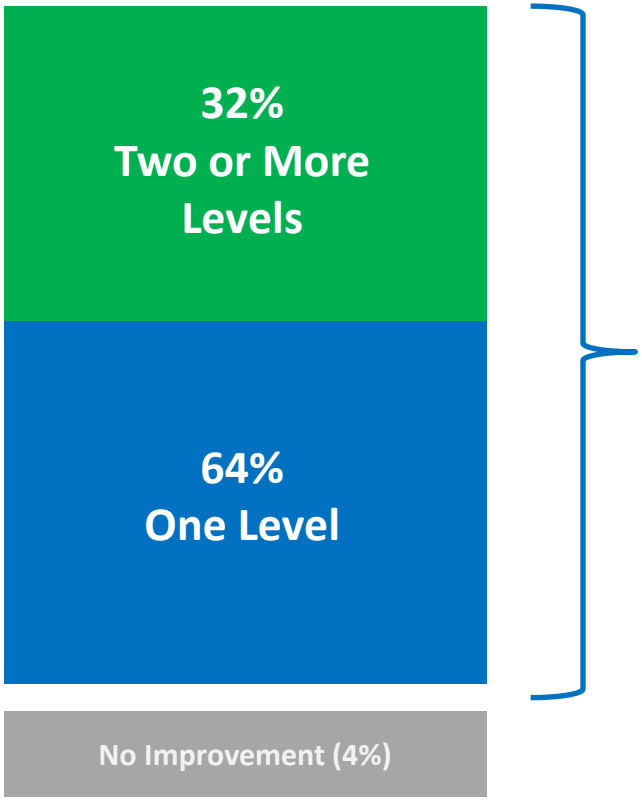
# SCiStar Clinical Trial - Motor Function Gains

## 22 Patients at 12 months




**96% of Subjects Reported Improved Motor Function**

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*N=22 because 3 patients from Cohort 1 received a sub-clinical "safety" dose of only 2M cells (the clinical dose is 10-20M cells)*

# INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY (ISNCSCI)

ASIA American Spinal Injury Association — ISCOS International Spinal Cord Society

Patient Name _____ Date/Time of Exam _____

Examiner Name _____ Signature _____

## RIGHT

## LEFT

| | MOTOR KEY MUSCLES | SENSORY KEY SENSORY POINTS Light Touch (LT) | SENSORY KEY SENSORY POINTS Pin Prick (PP) | MOTOR KEY MUSCLES |
|---|---|---|---|---|
| C2 | | | | |
| C3 | | | | |
| C4 | | | | |
| C5 | Elbow flexors C5 | | | C5 Elbow flexors |
| C6 | Wrist extensors C6 | | | C6 Wrist extensors |
| C7 | Elbow extensors C7 | | | C7 Elbow extensors |
| C8 | Finger flexors C8 | | | C8 Finger flexors |
| T1 | Finger abductors (little finger) T1 | | | T1 Finger abductors (little finger) |
| T2 | | | | |
| T3 | | | | |
| T4 | | | | |
| T5 | | | | |
| T6 | | | | |
| T7 | | | | |
| T8 | | | | |
| T9 | | | | |
| T10 | | | | |
| T11 | | | | |
| T12 | | | | |
| L1 | | | | |
| L2 | Hip flexors L2 | | | L2 Hip flexors |
| L3 | Knee extensors L3 | | | L3 Knee extensors |
| L4 | Ankle dorsiflexors L4 | | | L4 Ankle dorsiflexors |
| L5 | Long toe extensors L5 | | | L5 Long toe extensors |
| S1 | Ankle plantar flexors S1 | | | S1 Ankle plantar flexors |
| S2 | | | | |
| S3 | | | | |
| S4-5 | | | | |
| | RIGHT TOTALS | | | LEFT TOTALS |
| | (MAXIMUM) | (50) | (56) | (56) |

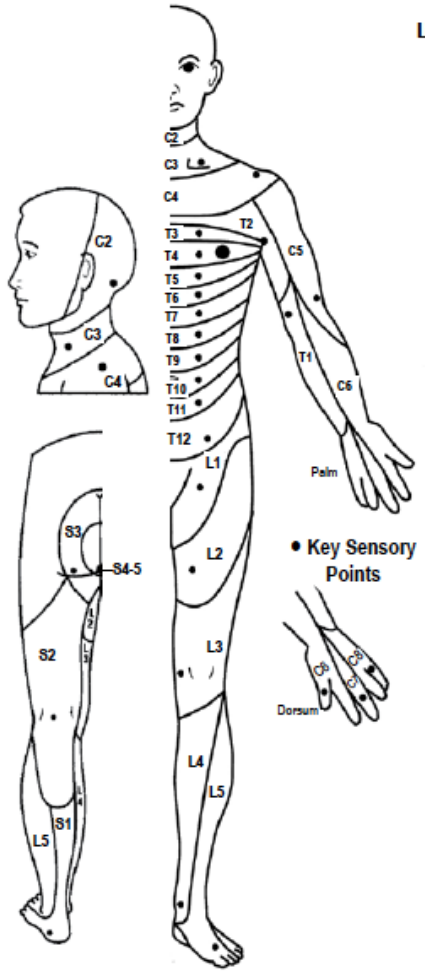
**UER** (Upper Extremity Right)

**UEL** (Upper Extremity Left)

**LER** (Lower Extremity Right)

**LEL** (Lower Extremity Left)

*Comments (Non-key Muscle? Reason for NT? Pain?):*




**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
5* = normal corrected for pain/disuse
NT = not testable

**SENSORY (SCORING ON REVERSE SIDE)**

0 = absent 2 = normal
1= altered NT = not testable

(VAC) Voluntary anal contraction (Yes/No) ☐

(DAP) Deep anal pressure (Yes/No) ☐

### MOTOR SUBSCORES

UER ☐ + UEL ☐ = UEMS TOTAL ☐ (MAX (25) (25) (50))

LER ☐ + LEL ☐ = LEMS TOTAL ☐ (MAX (25) (25) (50))

### SENSORY SUBSCORES

RLT ☐ + LLT ☐ = LT TOTAL ☐ (MAX (56) (56) (112))

RPP ☐ + LPP ☐ = PP TOTAL ☐ (MAX (56) (56) (112))

**NEUROLOGICAL LEVELS** Steps 1-5 for classification as on reverse

| | R | L |
|---|---|---|
| 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 complete injuries only) ZONE OF PARTIAL PRESERVATION Most caudal level with any innervation

| | R | L |
|---|---|---|
| SENSORY | | |
| MOTOR | | |



REV 02/13

# 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**

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

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# 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**

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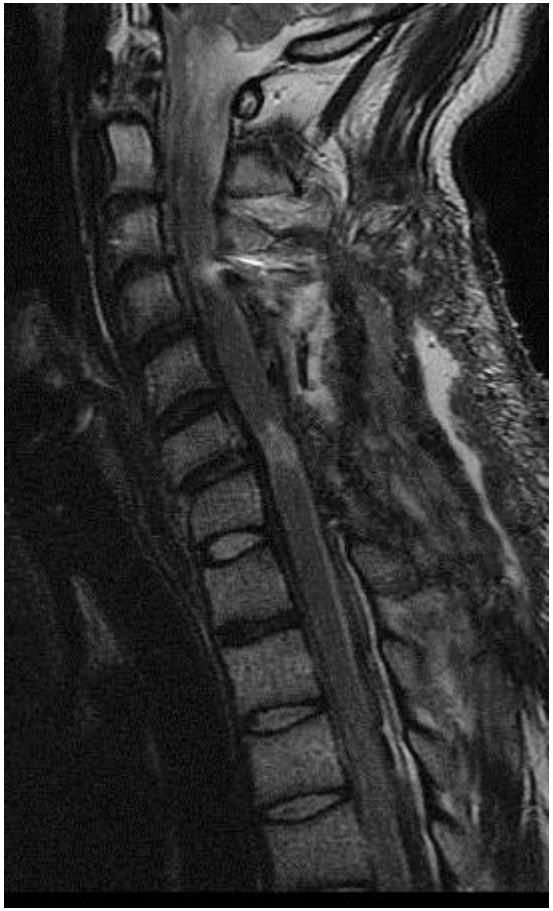
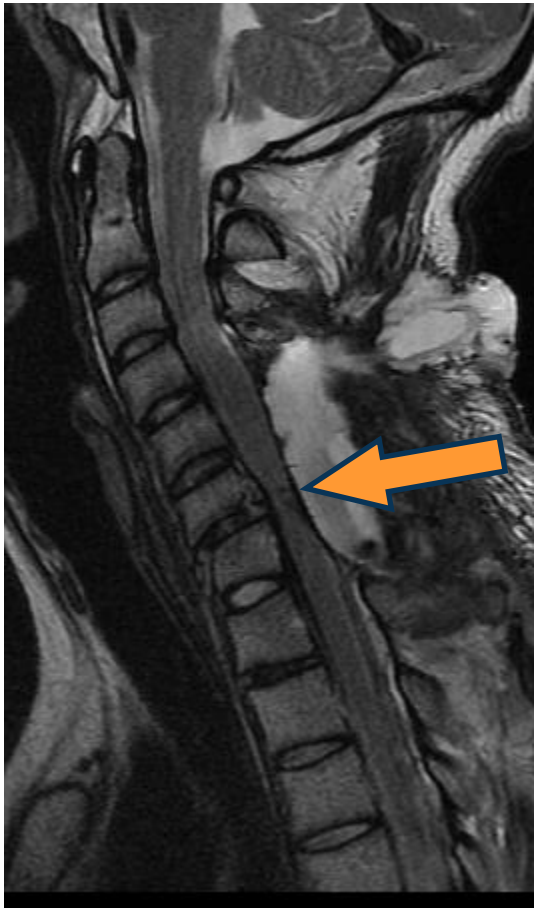
# SCiStar Clinical Trial – Cord Compression

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

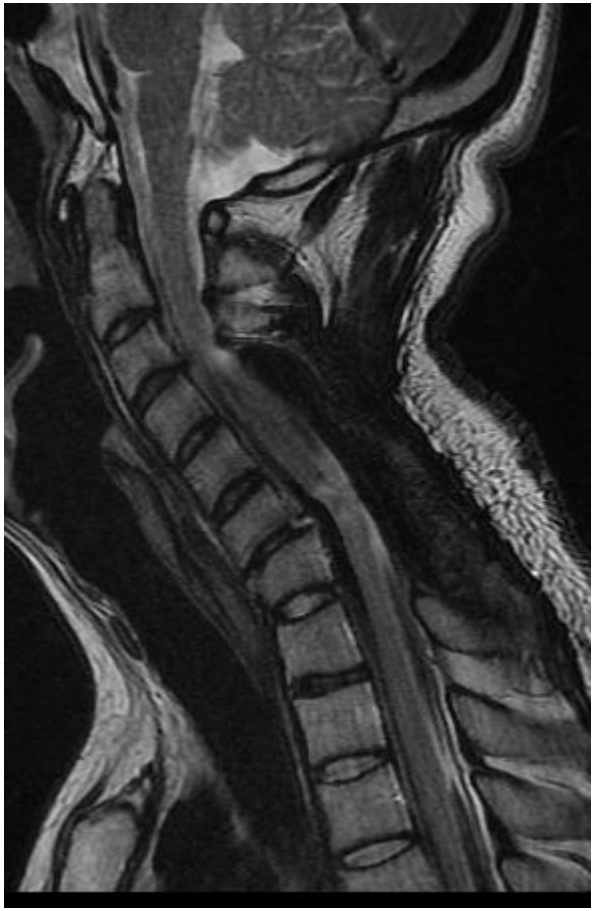
Baseline



Day 30



Day 365



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# SCiStar Clinical Trial – Takeaways

- **Excellent overall safety profile**
- **96% durable engraftment confirmed via MRI**
- **MRI scans through 24 months show no evidence of adverse changes**
- **No subjects had a decline in motor function from Year 1 to Year 2**
- **95% of patients exhibited motor recovery in the upper extremities at 12 months (requires at least 1 motor level gain on at least 1 side)**
- **Significant motor improvements achieved in five of six Cohort 2 subjects**
- **The two worst performing subjects had spinal cord compression (can be addressed in next trial)**
- **Results support further testing in a randomized, controlled clinical trial**

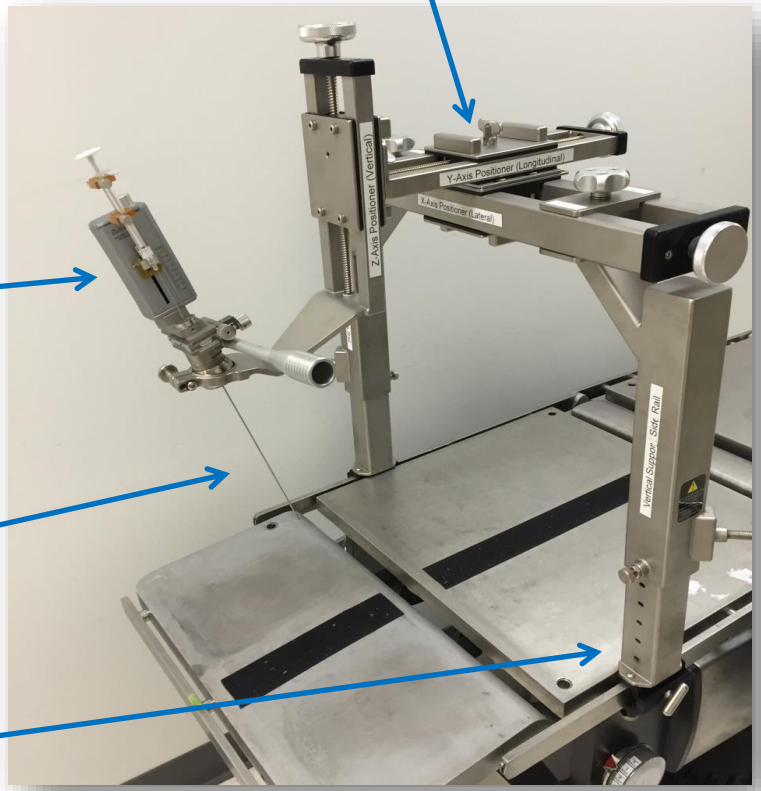
# SCiStar Clinical Trial - Original Syringe Positioning Device

**XYZ manipulator**

**Syringe & Microdrive assembly**

**Outer cannula and needle**

**Table-attached support frame**




**Storage trays**

**Supply Kits**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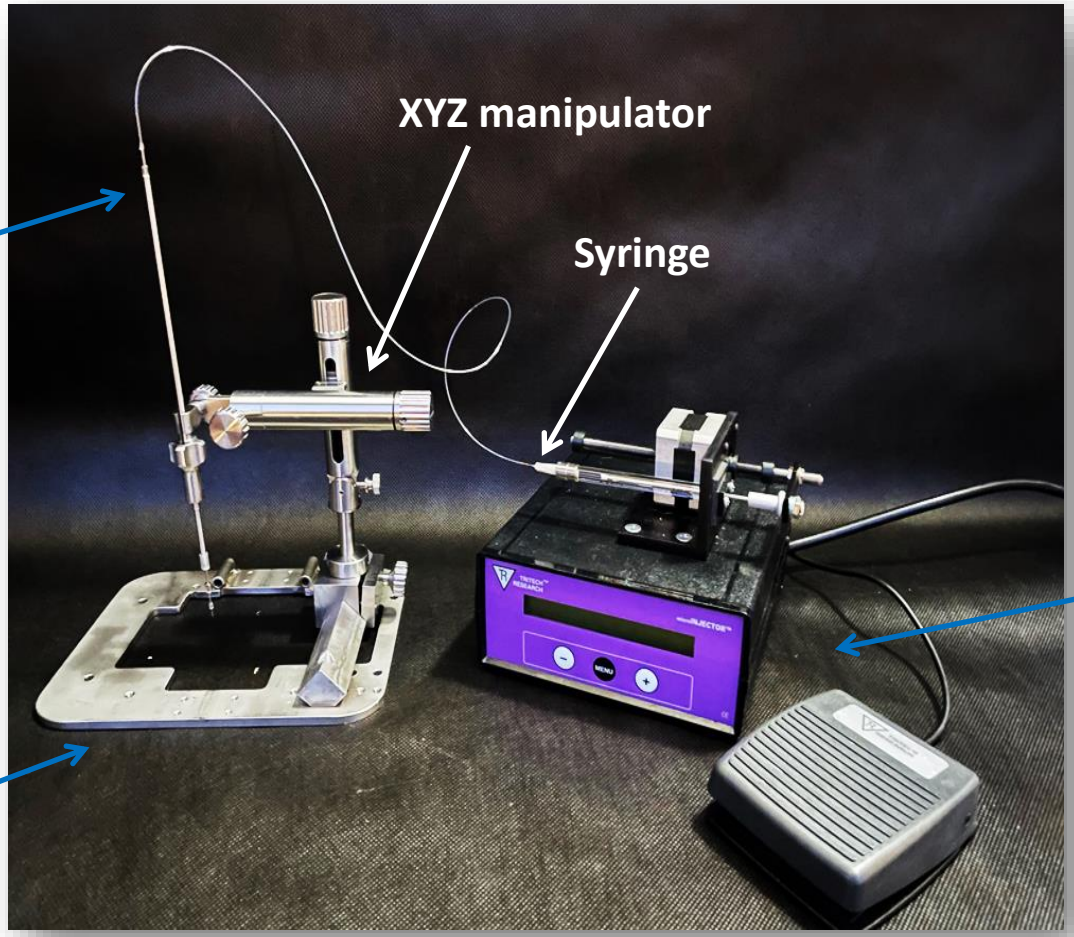
# Overview of Novel Parenchymal Spinal Delivery (PSD) System

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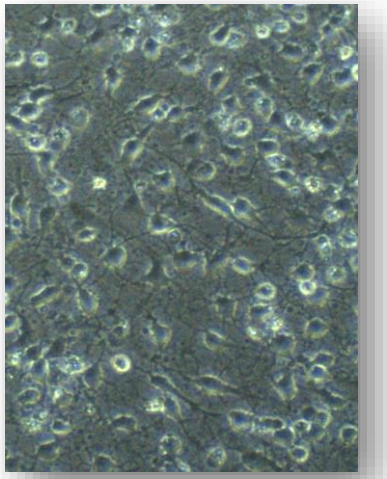
# Benefits of New Parenchymal Spinal Delivery (PSD) System

- **Device offers stability and control**
  - Eliminates motion between platform/XYZ manipulator/injection needle
  - Pump and syringe not in sterile field: programmed accurate dose rate
- **Device requires no cessation of ventilation**
  - Attaches directly to the patient, syncs with patient breathing motion
  - Magnetic needle provides stabilization from micromotion due to heartbeats
- **Device is easier to use in clinical setting**
  - Smaller and uses fewer components
  - Easily assembled prior to surgery
  - Single hand operation for XYZ positioning
  - Accurate needle depth insertion
  - Straightforward cleaning and sterilization
  - Compatible with OPC1 TAI formulation; eliminates prior-day dose prep
- **Device manufacturing and testing compatibility with OPC1 is ongoing**

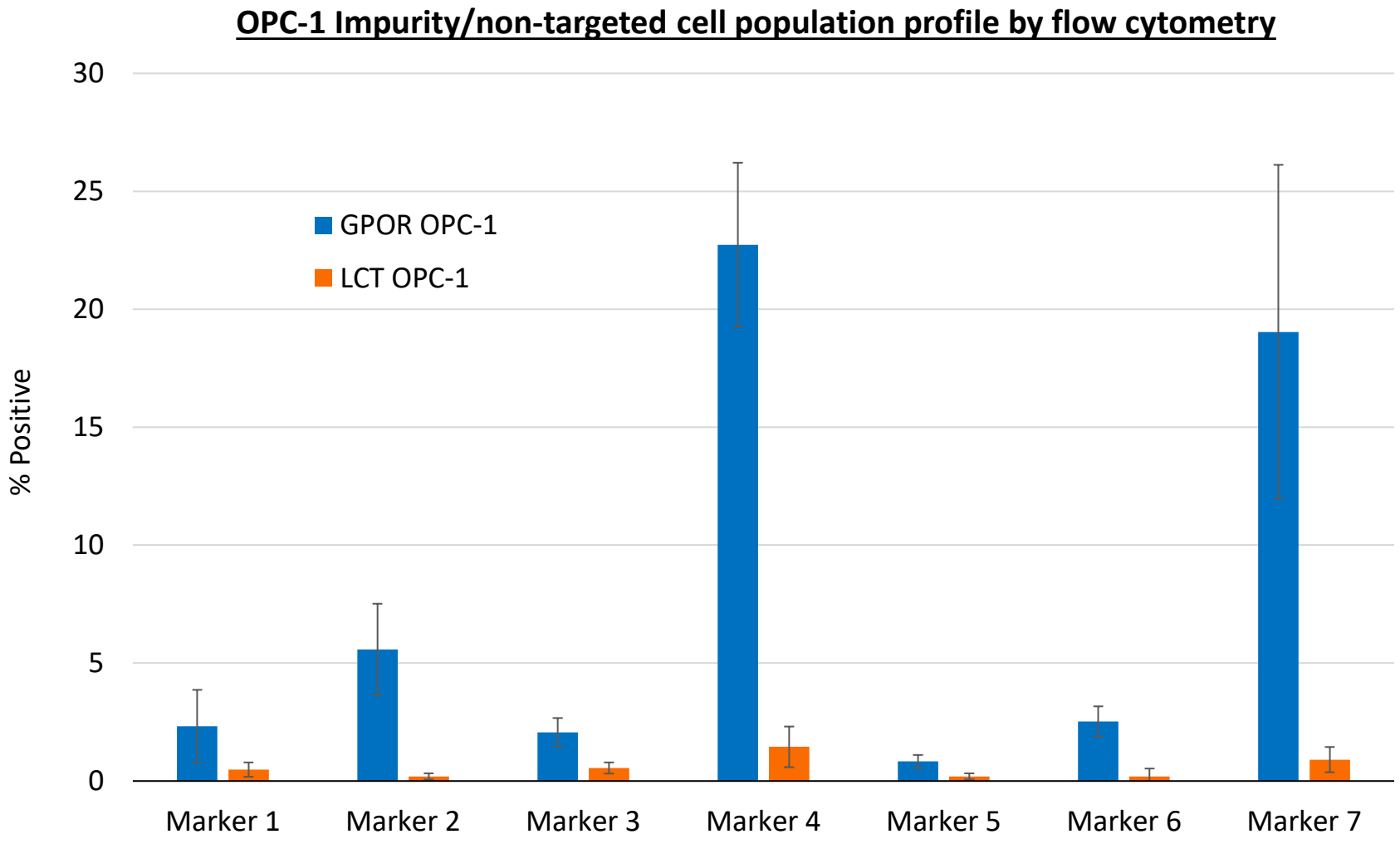
# OPC1 Manufacturing (December 2020 Update)

## 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 product impurities**
- **Improvements in functional activity**
- **12 new analytical and functional methods developed**
- **Elimination of all animal-based production reagents**
- **Patent applications recently filed on the process and product which if allowed, will have expiration dates of 2039 and 2040**



# OPC1 Manufacturing Improvements: Lower Impurities

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# OPC1 Program Key Considerations

- **OPC1 offers a compelling opportunity to deploy next-generation cell transplant technology against a high unmet need with low competition**
  - Clinical data supports moving to later-stage clinical development
  - Manufacturing issues: being addressed by Lineage in-house
  - Delivery issues: being addressed by Lineage through device alliance
- **Phase 1 clinical study to evaluate the Neurgain PSD will include treatment of chronic SCI patients, intended to validate the delivery system for use in a late-stage clinical study**
- **New opportunities for additional settings of demyelination**

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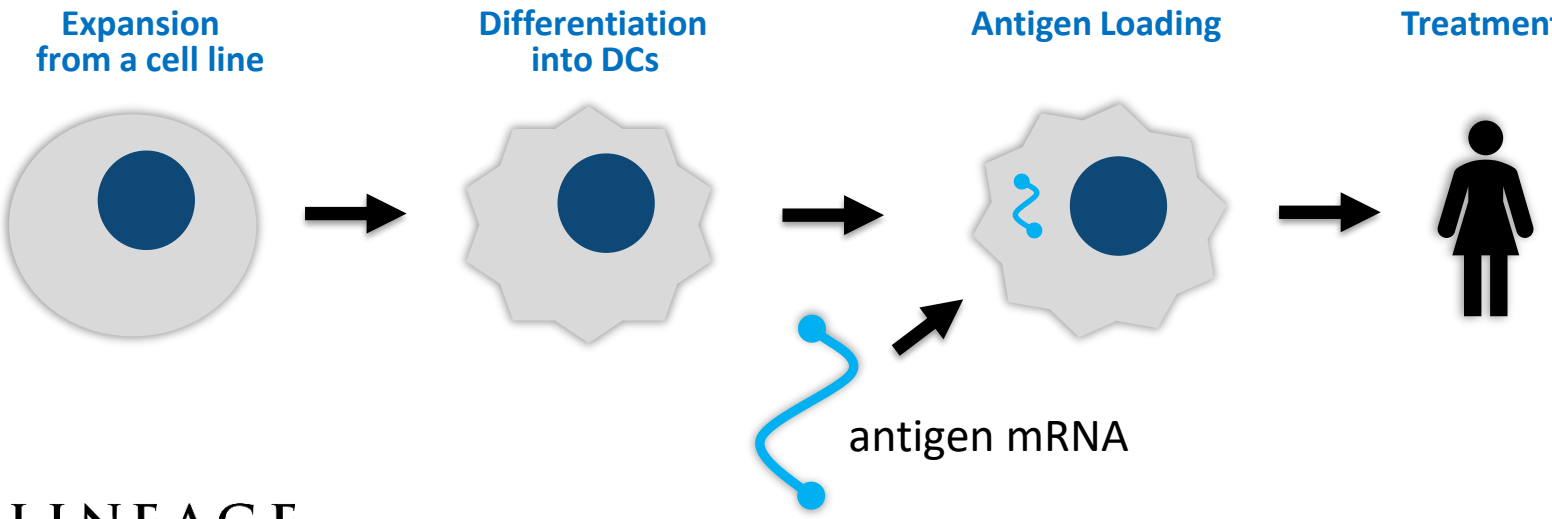
Immunotherapy is "poised to revolutionize treatment for all types of cancer"

*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 "off the shelf" production of mature immune cells called dendritic cells (DCs). No lead time or undue lead time between diagnosis and administration**
- **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 viral clearance**

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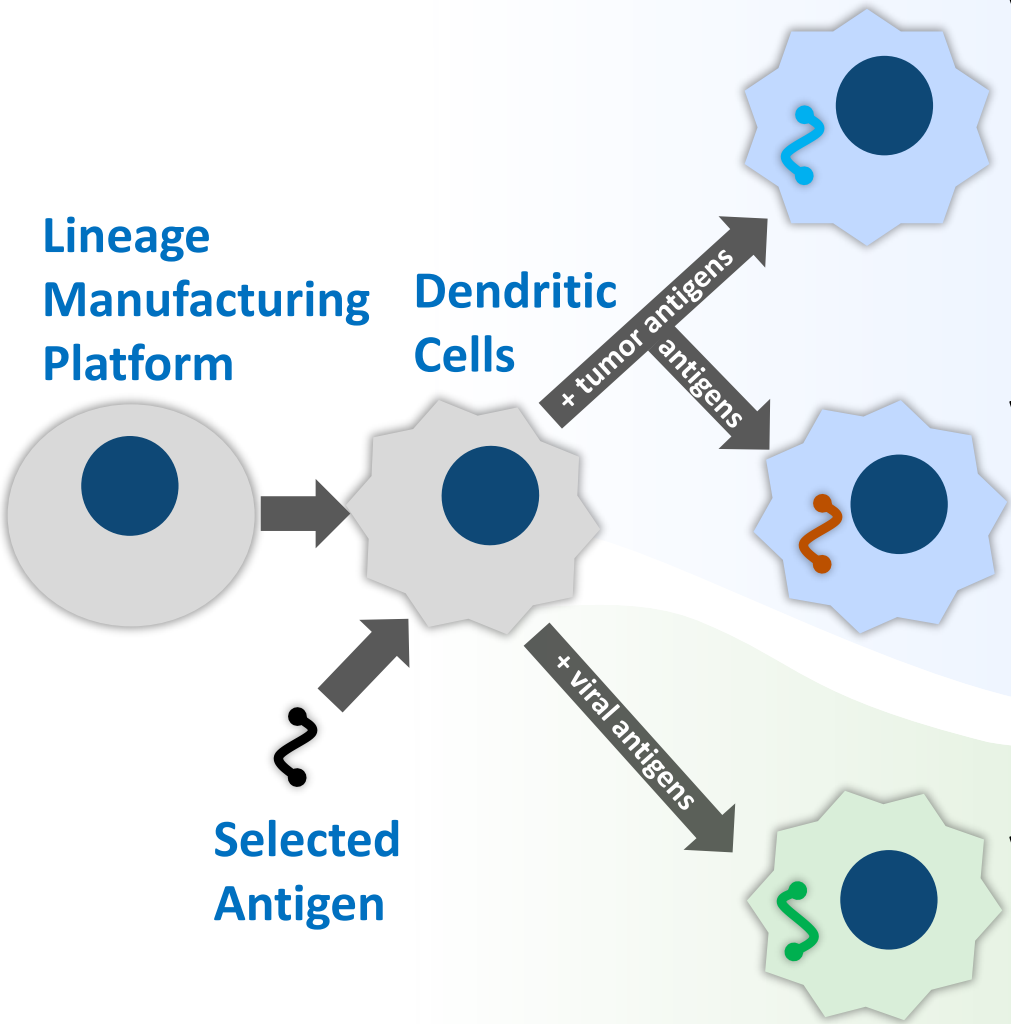
# VAC Development – A Platform for Multiple Product Candidates




## 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 seen

## VAC3, VAC4, VAC5…Opportunities

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

## VAC-Infectious Diseases

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

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# VAC Platform Next Steps

## Upcoming Events and Key Considerations:

- **Complete dosing in ongoing clinical trial (1 patient remaining)**
- **Design new products (i.e. VAC3, 4, 5, 6…) with newly discovered antigens**
- **Introduce improvements to the manufacturing process**
- **Identify potential partnership and grant opportunities for more rapid expansion of the VAC platform**
  - First strategic alliance (with Immunomic Therapeutics) announced April 2021

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

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

**3 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**

**Funded well into 2023 with cost-efficient business model**

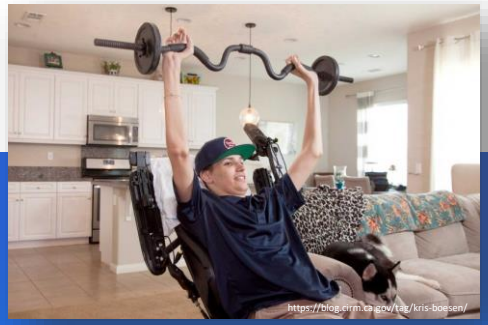
**Leader in the emerging field of regenerative medicine**

LINEAGE CELL THERAPEUTICS

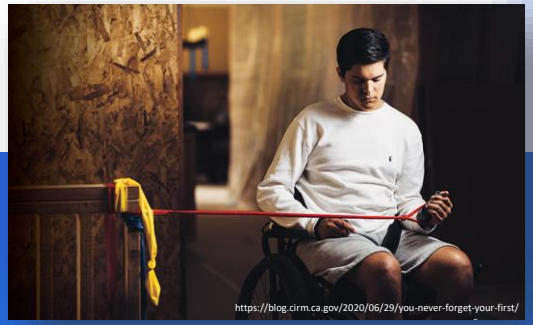
# The Patients Are Our Inspiration.
View their stories at **lineagecell.com/media/#patients**

## OPC1 SCiStar Study Participants


### 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."



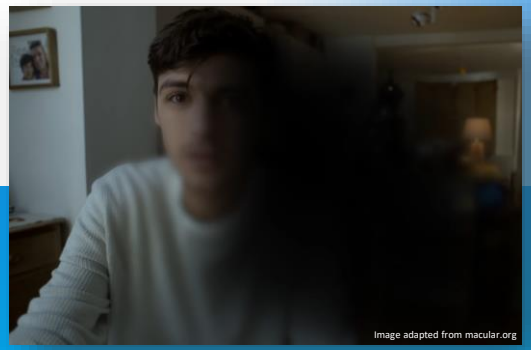

### Kris Boesen
"I couldn't drink, couldn't feed myself, couldn't text or pretty much do anything, I was basically just existing. I wasn't living my life, I was existing."




### 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***