

The future of cell therapy.



Raymond James 42nd Annual Institutional Investors Conference

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



Business Overview

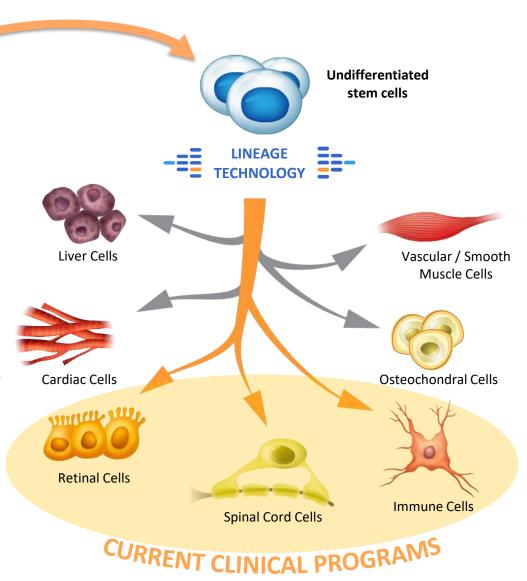
Lineage Cell Therapeutics – Investor's Overview

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 OPC1: Phase 1/2a in Cervical Spinal Cord Injury VAC2: Phase 1 in Non-small Cell Lung Cancer (oncology platform)
Differentiated Clinical Data	 First-ever report of retinal tissue <u>restoration</u> in a dry AMD patient One-third of spinal cord patients gained <u>2 levels</u> of motor function Potent <u>induction of immune responses</u> observed in cancer patients
Market Opportunity	- Billion-dollar commercial potential for each program
Near-Term Clinical Events	 - 3- and 6-month data from dry AMD program, expected Q1 and Q2 - Completion of enrollment in Phase 1 lung cancer trial, expected Q2
Financial Position	- Cash and marketable securities of \$38 million as of September 30, 2020
Market Capitalization	~\$264 million as of December 31, 2020



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





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



Backed by hundreds of cell therapy-related patents



Pipeline and Validating Partnerships

Clinical Programs	Financial Support Received	Phase 1	Phase 2a	Next Steps
OpRegen® (RPE Cells) Dry AMD with Geographic Atrophy (GA)	רשות החדשנות srael Innovation (בין Authority \$16M			Enrollment completed; data in Q1 and Q2
OPC1 (Oligodendrocytes) Spinal Cord Injury (SCI)	CIRM CALIFORNIAY / TEM CELL AGENCY \$14M			Data collected; planning for Phase 2b/3
VAC2 (Dendritic Cells) Non-Small Cell Lung Cancer (NSCLC)	CANCER RESEARCH UK			2 patients left to enroll









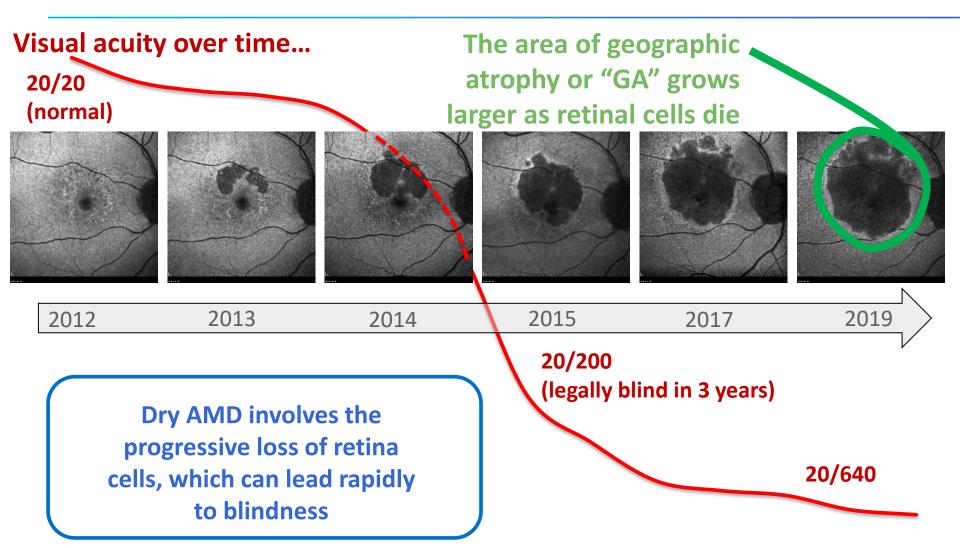
AMD is the **leading cause** of irreversible vision loss in the US



Source: aao.org

OpRegen®: RPE Cell Transplants to Treat Dry AMD

Dry AMD Can Lead Rapidly to Blindness

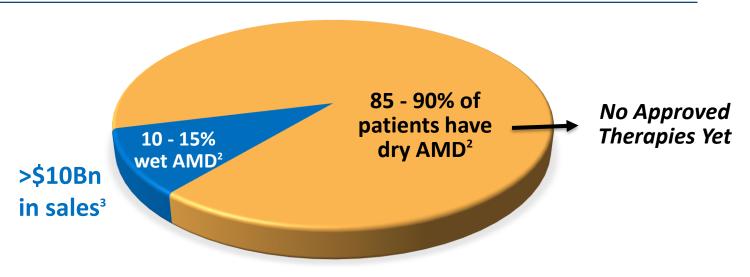




Multi-Billion Dollar Market Opportunity in the U.S.

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

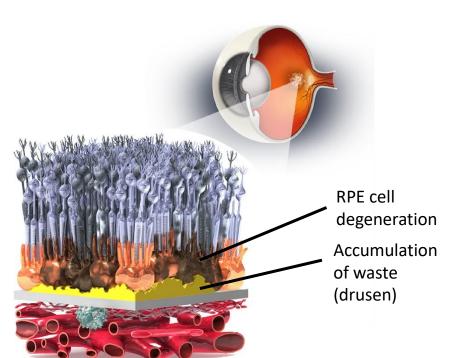




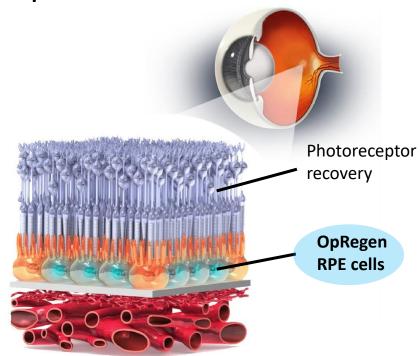
Sources: (1) Bright Focus Foundation. Macular Degeneration Facts & Statistics: Bright Focus Foundation. http://www.brightfocus.org/macular/about/understanding/facts.html; (2) JM Seddon, Epidemiology of age-related macular degeneration. (AP Schachat, S Ryan eds.) Retina, 3rd ed. St. Louis, MO: Mosby;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

Lineage Approach – OpRegen, an RPE Cell Transplant

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

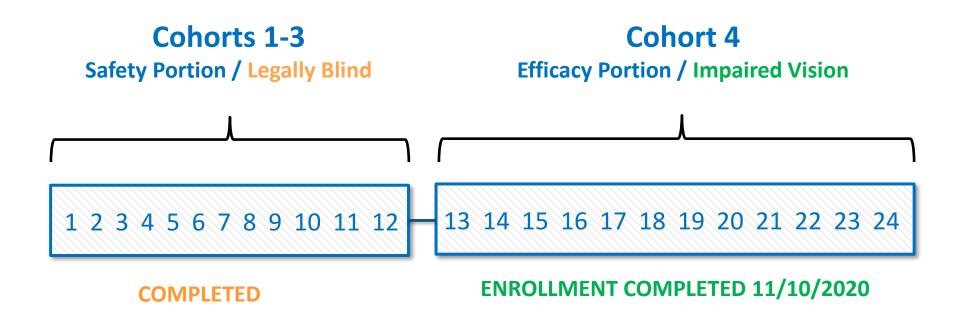


 OpRegen is an injection of RPE cells beneath the retina, to replace lost retinal cells, recover function, and preserve or improve vision





Ongoing Phase 1/2a Clinical Trial of OpRegen for Dry AMD



Purpose: To evaluate the safety and efficacy of transplanted RPE cells

in patients with dry AMD with geographic atrophy (GA)

Design: Open label, single arm and multi-center

Dose and Administration: One 50-100 ul dose of cells injected into the subretinal space



Promising Results

(As of AAO 2020 Update)

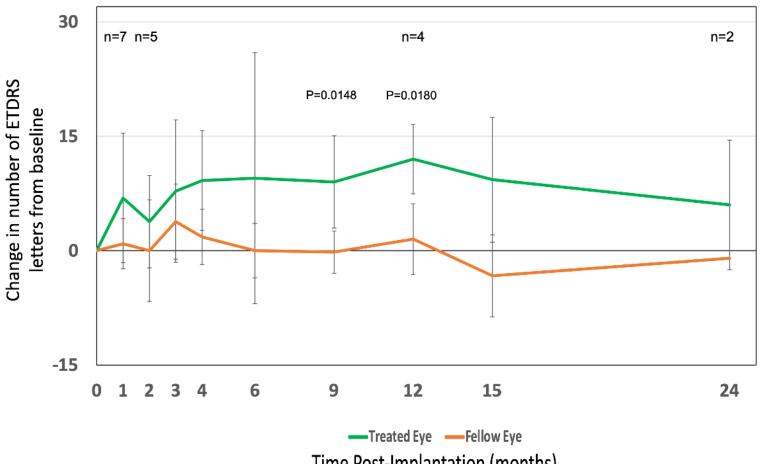
- Transplanted OpRegen cells have been well tolerated with no cases of rejection
- Cohort 4 patients (the intended commercial population) have better vision at 9 & 12 months, with improvements lasting >24 months in some patients
- A trend towards slower GA growth was observed in first 6 Cohort 4 patients, also maintained for as long as 24 months in some patients
- Encouraging findings across unrelated assessments; various patients have exhibited evidence for one or more of:
 - 1. Reduced growth of geographic atrophy
 - 2. Improved visual acuity
 - 3. Improved reading speed
 - 4. Improved retina structure
 - 5. Reductions in waste material
 - 6. Stable engraftment of cells (4+ years)
 - 7. Restoration of retinal tissue maintained to 23 months (continuing to monitor)





Improved Visual Acuity in Treated vs. Fellow Eye Statistical Significance at 9 & 12 Months

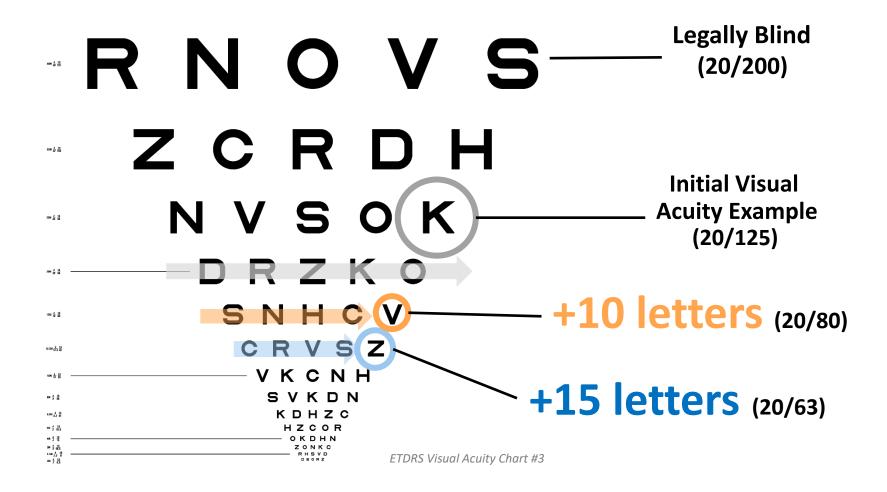
Mean Change in Cohort 4 BCVA – Treated & Fellow Eye



Time Post-Implantation (months)



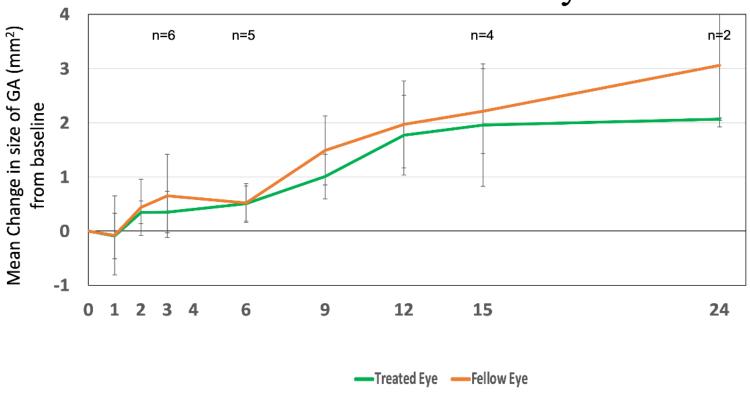
Real-World "Letters of Improvement"





Slower Growth of GA Observed in Pooled Cohort 4 Patients

Mean Change in Cohort 4 GA (mm²) – Treated and Fellow Eye

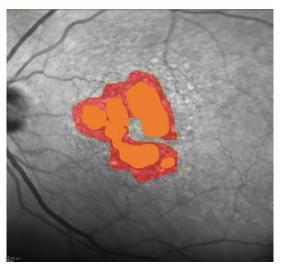


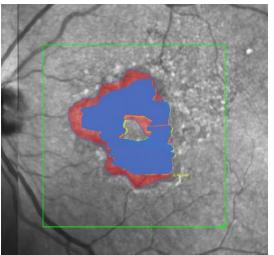
Time Post-Implantation (months)

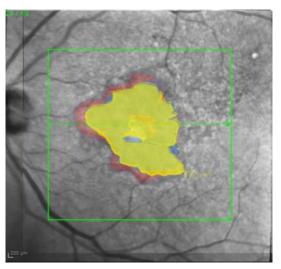


Retinal Restoration – *Smaller* Area of GA, Maintained for 2 Years

Date	Time in Study	Colored area on Figure below	Area mm² (SQRT)	Changes in rate of progression from previous	Changes in rate of progression from baseline
May 2017	Minus 1 year	Orange	4.21 mm² (2.05)	N/A	N/A
July 2018	Baseline	Red	7.90 mm² (2.8)	+ 0.64 mm sqrt/yr	N/A
April 2019	Month +9	Blue	5.74 mm² (2.39)	- 0.61 mm sqrt/yr	- 0.61 mm sqrt/yr
October 2019	Month +15	Green	6.48 mm² (2.54)	+ 0.30 mm sqrt/yr	- 0.20 mm sqrt/yr
June 2020	Month +23	Yellow	6.52 mm² (2.55)	+ 0.015 mm sqrt/yr	- 0.13 mm sqrt/yr









Dry AMD Competitive Landscape

Only cell and gene therapy offer infrequent dosing -andOnly Lineage has shown evidence of retinal restoration

Cell Therapy

- Lineage Cell (Ph1/2)
- Astellas (Ph1/2)*
- Regen. Patch (Ph1/2)
- jCyte (Preclinical)

*Via acquisition of Ocata Therapeutics for \$379M

Oxidative Stress Approaches

- Alkeus (Ph3), Vitamin A "dimers"
- Allegro (Ph2), integrins
- Stealth Bio (Ph2), mitochondria
- Boehringer (Ph1), inflammasome

LINEAGE CELL THERAPEUTICS

Complement Inhibitors

- Apellis (Ph3)
- Iveric (Ph3)
- Roche (Ph2)
- Annexon (Ph 2)
- NGM (Ph1)
- Biogen (Preclinical)

Gene Therapy

(also targeting complement)

- Gyroscope (Ph1/2)
- Hemera (Ph1)

Commercial-Scale Manufacturing Capabilities

- OpRegen consists of >99% pure RPE cells
 - Uses NIH-approved line was established >20 years ago
 - Extensive characterization and karyotyping performed on each batch
 - No genetic modifications are made to the cells
- 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





OpRegen – Positioned for Commercial Success

OpRegen has been designed 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)
- Treatment to date has been well-tolerated
- Some patients have exhibited clinically meaningful improvements in clinicallyrelevant metrics such as visual acuity and reading speed
- Potential for recurring revenues (with multiple treatments years apart)
- May have application in other retina diseases (ex: Stargardt's Disease)
- Issued patents cover aspects of production, characterization, and formulation
- Fast Track designation from FDA
- Exclusive option to evaluate new delivery device
- Opportunities for strategic partnerships for late-stage development









Source: christopherreeve.org



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

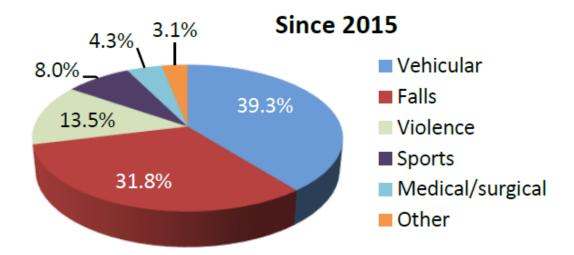
Incidence

Approximately 18,000 new cases 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

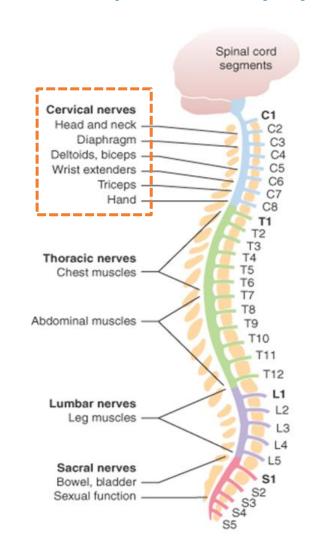




SCI Treatment Objectives

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





Lineage's OPC1 cells for Spinal Cord Injury

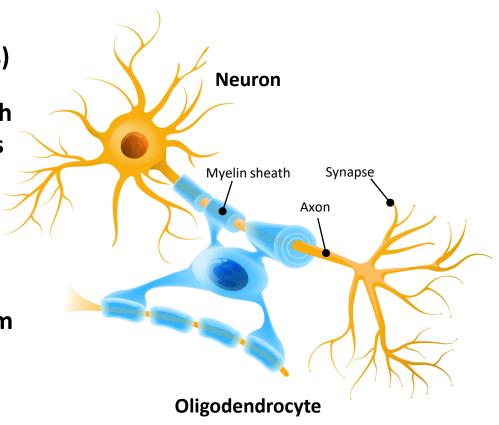
Replacing oligodendrocytes may provide additional upper limb and finger function and improve the quality of life for patients

 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





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

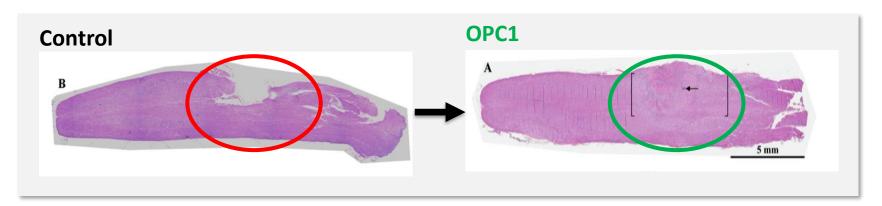


OPC1 Transplant Procedure



OPC1 Mechanisms of Action

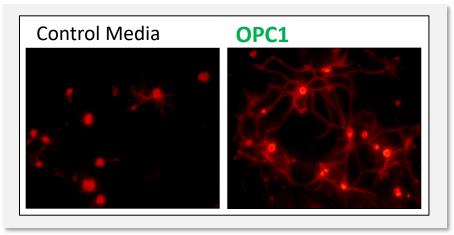
Prevention of Cavitation



Myelination of axons



Secretion of neurotrophic factors





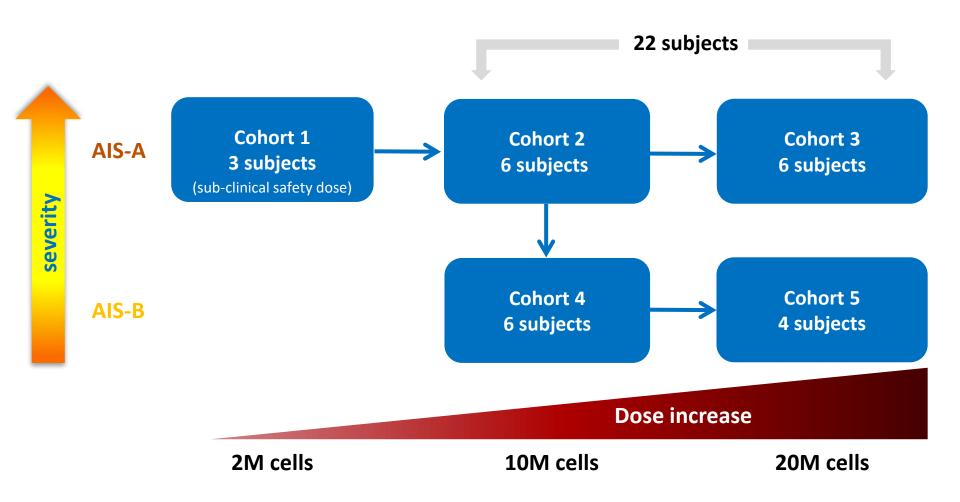
OPC1 for Spinal Cord Injury

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





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 cavitation
- 96% (24/25) of OPC1 patients had serial MRI scans that indicated <u>no</u> <u>sign</u> of a lesion cavity at 12 months (or 24 months for 22 scans available)

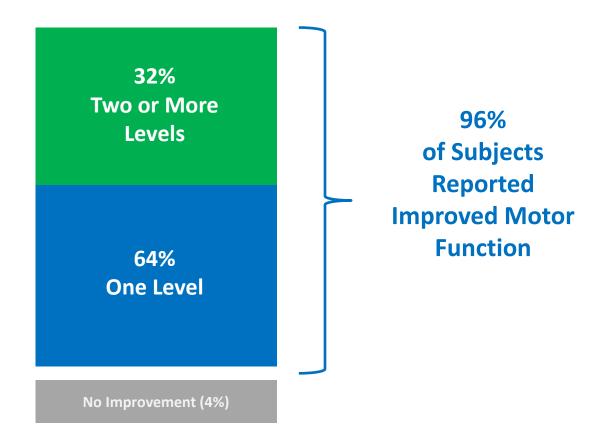


Weighted sagittal MRI



SCiStar Clinical Trial - Motor Function Gains

22 Patients at 12 months





INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

2. MOTOR

as on reverse



Patient Name_		Date/Time of Exam	

Most caudal level with any innervation

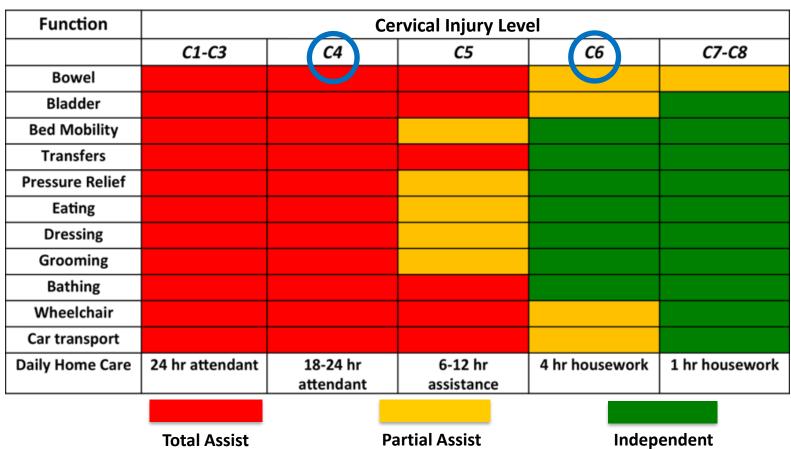
AMERICAN SPINAL INJURY ASSOCIATION	(ISNCSCI)	INTERNATIONAL SERVICE CONTRACTIONS	Examiner Name		Signature
RIGHT MOTO				SENSORY KEY SENSORY POINTS Light Touch (LT) Pin Prick (PP)	MOTOR LEFT
	C2 C3 C4	→			C2 C3 C4
UER Wrist extensors C6 (Upper Extremity Right) Elbow extensors C7 Finger flexors C8 Finger abductors (tittle finger) T1		(2)	C3 C3 C3 C5 C5 T5 C5 T5 T5 T6		C5 Elbow flexors C6 Wrist extensors UEL C7 Elbow extensors (Upper Extremity Left) C8 Finger flexors T1 Finger abductors (little finger)
Comments (Non-key Muscle? Reason for NT? Pain?):	T3 T4 T5 T6 T7 T8 T9 T10 T11 T12 L1	Cap	TIS		T3
Hip flexors L2 Knee extensors L3 Ankle dorsiflexors L4 Long toe extensors L5 Ankle plantar flexors S1 (VAC) Voluntary anal contraction (Yes/No)	\$2 \$3 \$4-5	1.5	Dorsum L4		L2 Hip flexors L3 Knee extensors L4 Ankle dorsiflexors (Lower Extremity Left) L5 Long toe extensors S1 Ankle plantar flexors S2 S3 S4-5 (DAP) Deep anal pressure (Yes/No)
MOTOR SUBSCORES UER + UEL = UEMS TOTAL MAX (25) (25)	(50) (56) (56) LER + LEL (25) (25)	= LEMS TOTAL (SENSORY SU RLT + LL (50) MAX (56)		LEFT TOTALS (50) (MAXIMUM) RPP + LPP = PP TOTAL (12) MAX (56) (56) (112)
NEUROLOGICAL LEVELS 1. SENSORY Steps 1-5 for classification 2. MOTOR	L 3. NEUROLOGIC LEVEL OF INJUI		4. COMPLETE OR INCO. Incomplete = Any sensory or motor fur 5. ASIA IMPAIRMENT SC	nction in S4-5	(In complete injuries only) ZONE OF PARTIAL PRESERVATION MOTOR

(NLI)

5. ASIA IMPAIRMENT SCALE (AIS)

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

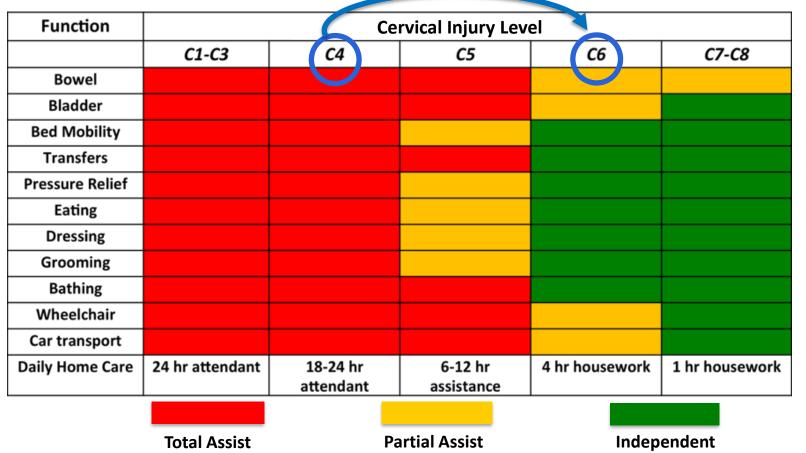




Real-World Benefit from a 2 Motor Level Improvement

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	В	5	20 M	62	37
2203	6	N	C6	Α	3	20 M	45	31
2105	6	N	C4	А	3	10 M	19	20
2004	5	N	C6	В	4	10 M	21	25
2007	4	N	C4	В	4	10 M	55	38
2307	4	Υ	C5	В	5	10 M	19	38
2303	3	Υ	C6	В	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

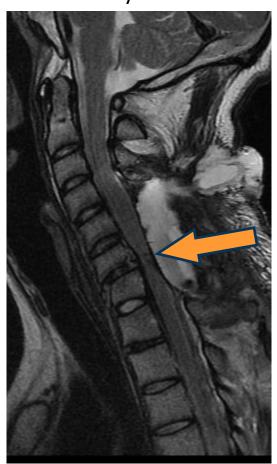


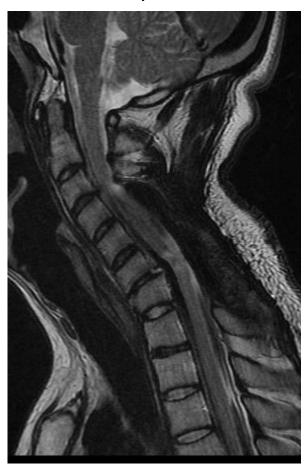
SCiStar Clinical Trial – Cord Compression

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

Baseline Day 30 Day 365









SCiStar Clinical Trial – 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



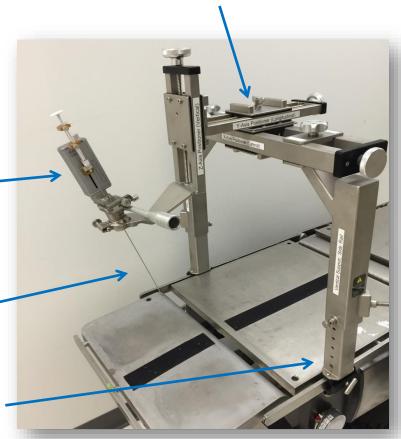
SCiStar Clinical Trial - Original Syringe Positioning Device





Outer cannula and needle

Tableattached support frame



Storage trays

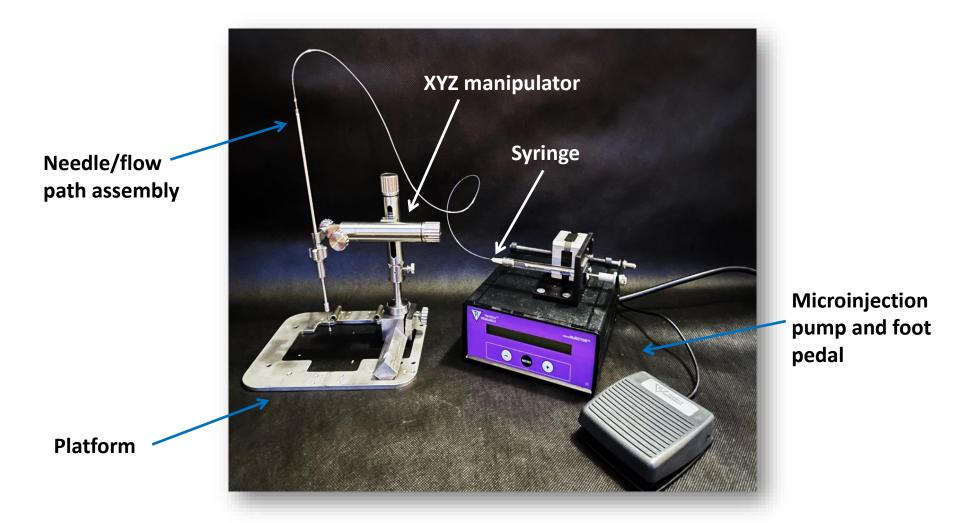


Supply Kits





Overview of Novel Parenchymal Delivery Injection (PDI) System





Benefits of New Parenchymal Delivery Injection (PDI) 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)

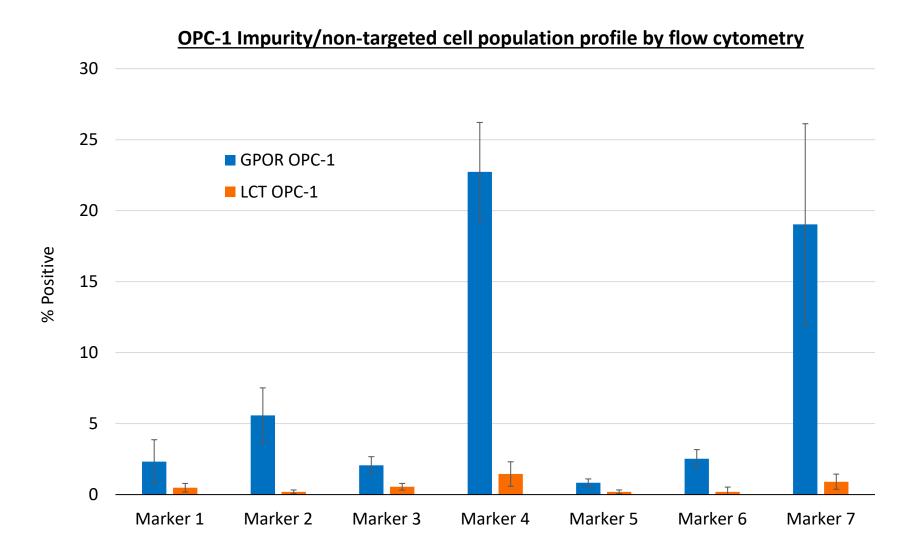
Lineage has made major improvements in production and quality of OPC1

- 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





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
- Next steps include collecting data to support FDA discussion of comparability plan (for new process and new delivery) and the regulatory path for a comparative trial
- New opportunities for regional and/or global partnership opportunities
- New opportunities for additional settings of demyelination







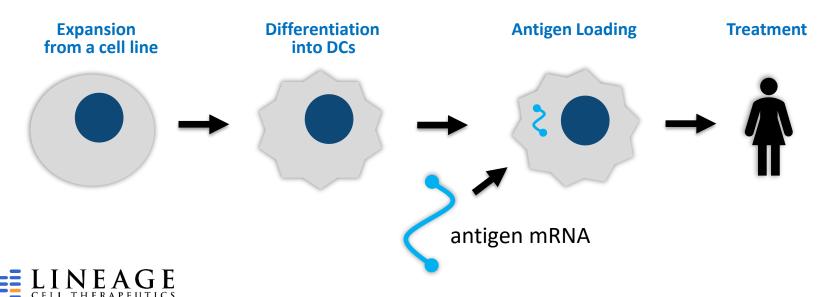
Immunotherapy is "poised to revolutionize treatment for all types of cancer"

Source: cancerresearch.org

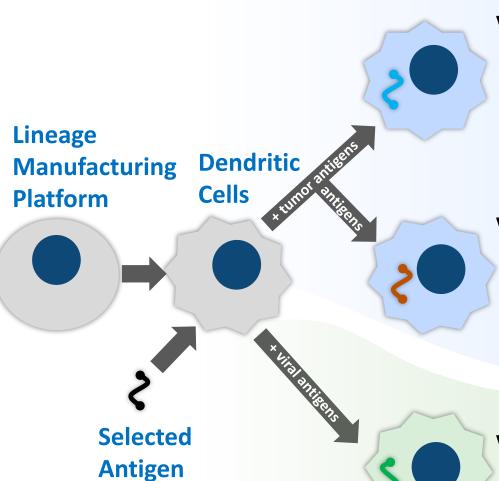
VAC: A Cell Therapy Platform for Cancer and Infectious
Diseases

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



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



VAC Platform Next Steps

Upcoming Events and Key Considerations:

- Complete dosing in ongoing clinical trial (2 patients remain)
- Evaluate options for VAC2 clinical development
- 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



Upcoming Milestones

PROGRAM	TIMING	INITIATIVES
OpRegen	Q1 2021	Present interim OpRegen data (3-month Cohort 4 update)
	Q2 2021	Present interim OpRegen data (6-month Cohort 4 update, ARVO)
	2H 2021	Planning discussions with the FDA on future clinical development
	Ongoing	Evaluate OpRegen partnership opportunities
OPC1	Q1-Q3 2021	Conduct preclinical studies with OPC1 and Neurgain PDI system
	Q2 2021	FDA RMAT meeting (Neurgain Device)
	Q1-Q3 2021	Complete process development to support late-stage clinical trial
	Q4 2021	FDA RMAT meeting (manufacturing)
	Q4 2021	FDA RMAT meeting (clinical)
	Ongoing	Consider regional and/or global partnership opportunities
VAC	Q2 2021	Complete dosing in ongoing clinical trial in NSCLC (2 pts. remain)
_	Q3 2021	Introduce manufacturing process improvements
	Q4 2021	Report Phase 1 NSCLC data
	Ongoing	Evaluate new product candidates with additional tumor antigens/neoantigens with and without partners



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

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







World class
in-house
process
development
and GMP
manufacturing



One of the largest patent portfolios in cell therapy



Funded well into 2022 with cost-efficient business model



Leader in the emerging field of regenerative medicine



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

OPC1 SCiStar Study Participants





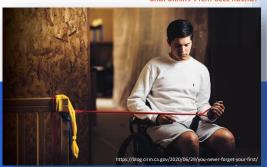
Lucas Lindner

"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



