LINEAGE
CELL THERAPEUTICS

The future of cell therapy.



2020 Solebury Trout Virtual Investor Conference

Brian M. Culley, Chief Executive Officer

May 26, 2020

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Lineage Cell Therapeutics

Lineage is a clinical-stage cell therapy company which manufactures and transplants specific cell types to treat injuries and disease

OpRegen®

RPE cells

for Vision Loss
(dry AMD)

Phase 1/2a

VAC2

Dendritic cells

for Cancer
(solid tumors)

Phase 1

OPC1

Oligodendrocyte cells

for Motor Activity
(spinal cord injury)

Phase 1/2a

All product candidates are allogeneic ("off-the-shelf"), meaning the material is derived from cell lines, not from individual patients, facilitating large-scale production and lower production costs than patient-specific treatments

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Pipeline, Partnerships, and Progress

Programs	Phase 1	Phase 2a	Partnerships & External Funding
OpRegen® Dry AMD with Geographic Atrophy (GA)	4 patients to enroll in ongoing phase 1/2a		רשות החדשנות Israel Innovation Authority **$16M**
VAC2 Non-Small Cell Lung Cancer (NSCLC)	2 patients to enroll in ongoing phase 1		CANCER RESEARCH UK **>$10M in-kind**
OPC1 Spinal Cord Injury (SCI)	25 patients completed, planning phase 2b/3		CIRM CALIFORNIA'S STEM CELL AGENCY **>$14M**

Partners & Collaborators

Lineage technologies are covered by hundreds of ES and iPS cell therapy-related patents, providing many opportunities for additional collaborations

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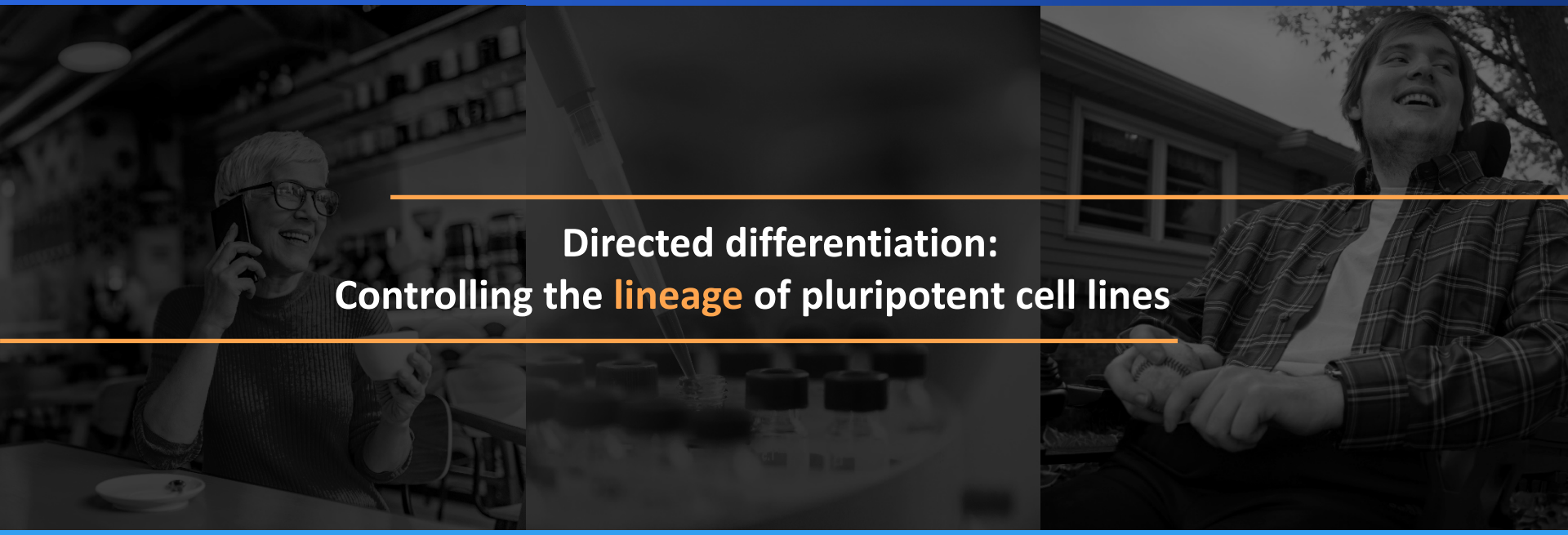
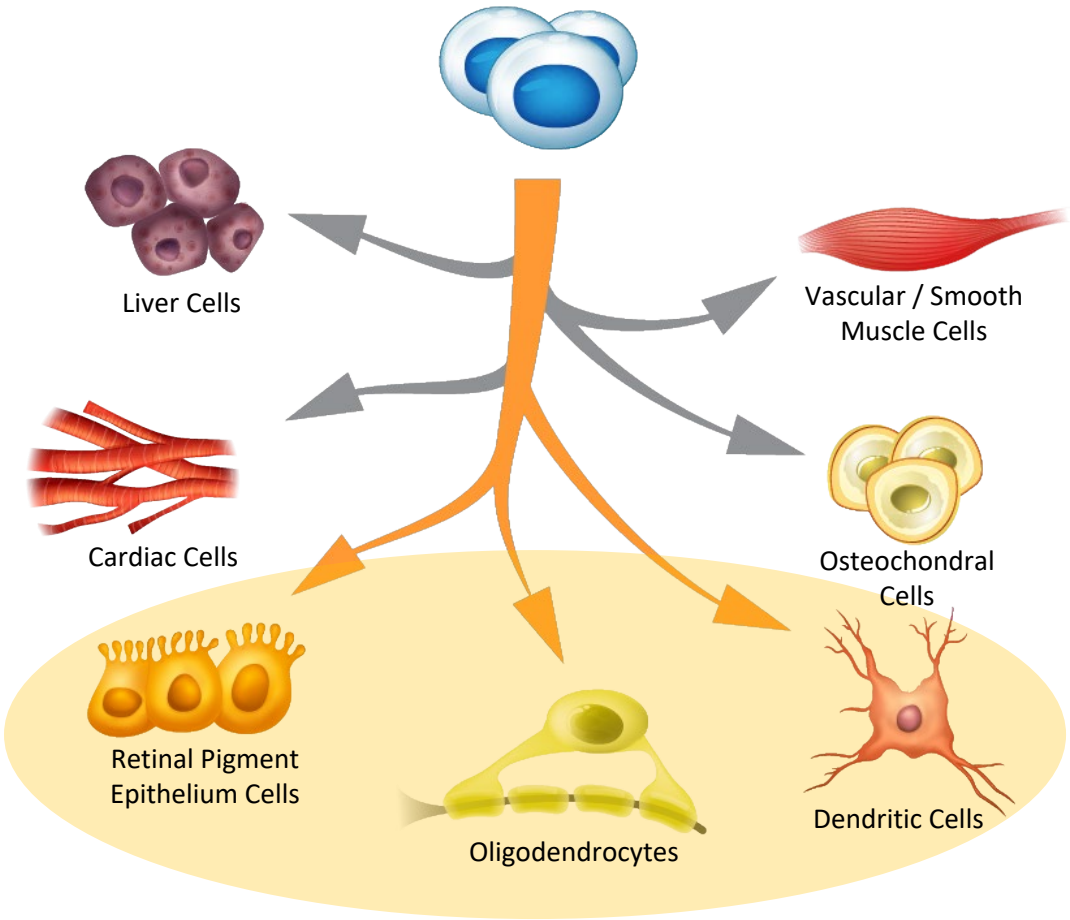


Directed differentiation:
Controlling the lineage of pluripotent cell lines

Lineage Technology Overview

Lineage Technology Platform

- **The Lineage Platform starts with *normal pluripotent cell lines***
- **Pluripotent cells have the capacity to become *any* human cell type**
- **A highly controlled process generates *only* the desired cell type**
- **No genomic manipulation or epigenetic memory risks**
- **Frozen cell banks enable commercial production and are not limited by donor availability**



CURRENT CLINICAL PROGRAMS

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In-House cGMP Production

Lineage has extensive experience directing the lineage of pluripotent cells into terminally differentiated, specialized cell types such as retinal or glial cells

- **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**

Cell therapy manufacturing facility
(Cell Cure Neurosciences subsidiary), Israel

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Commercial Scale cGMP Production

Current Capability with Retina Pigmented Epithelium (RPE) Cells

- **>99% pure RPE cells are manufactured from a pluripotent cell line**
  - NIH approved line was established >20 years ago
  - Extensive characterization and karyotyping completed
  - No genetic modifications are made to the cells

- **Immediate-use "thaw and inject" formulation**
  - No dose preparation means more eligible sites
  - From frozen cells to injection device in 5 minutes

- **Current production scale is 5 billion cells per 3-liter bioreactor**
  - Current production is >2,500 clinical doses/batch
  - Further scale-up can be performed in larger or additional (i.e. parallel) reactors

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

Source: aao.org

OpRegen®: A Cell Therapy Product Candidate for Dry AMD

Dry Age-Related Macular Degeneration

- **Dry AMD involves the loss of retina cells (RPE) in an area of geographic atrophy (GA), causing impaired vision and blindness**

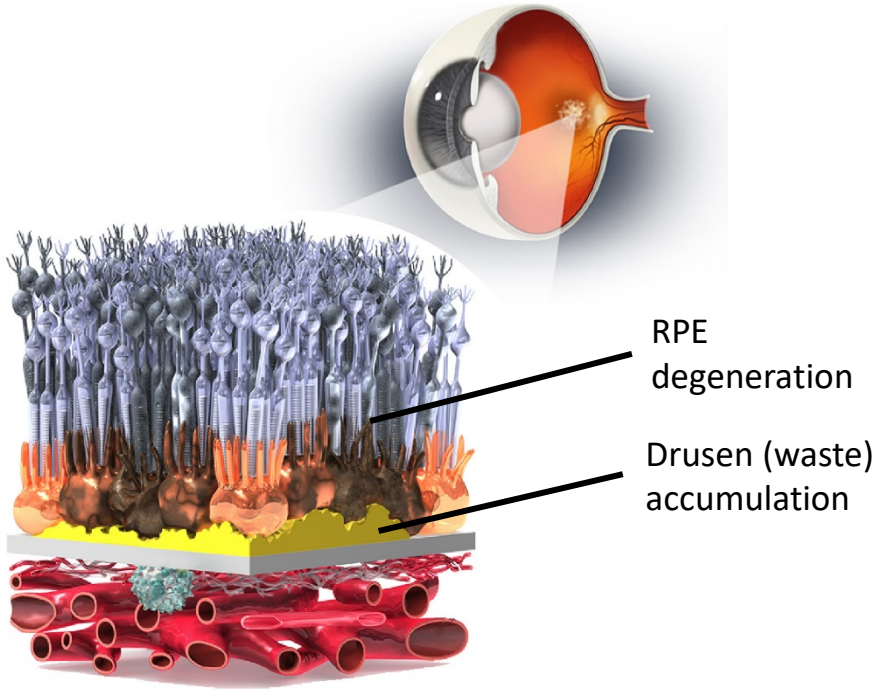

Image adapted from scienceofamd.org

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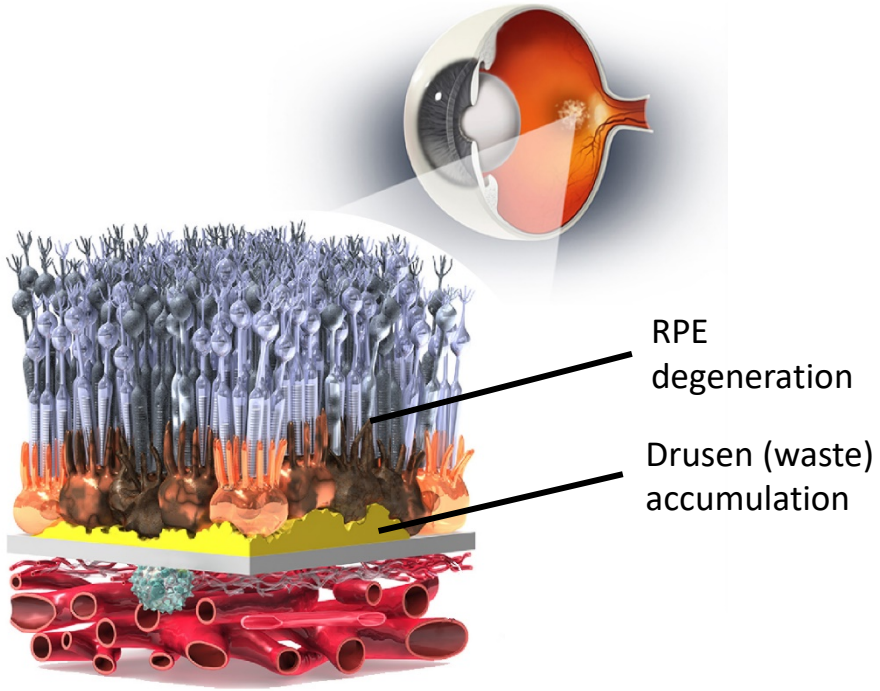

- **OpRegen is a suspension of RPE cells delivered to the sub-retinal space to restore activity and support photoreceptors**

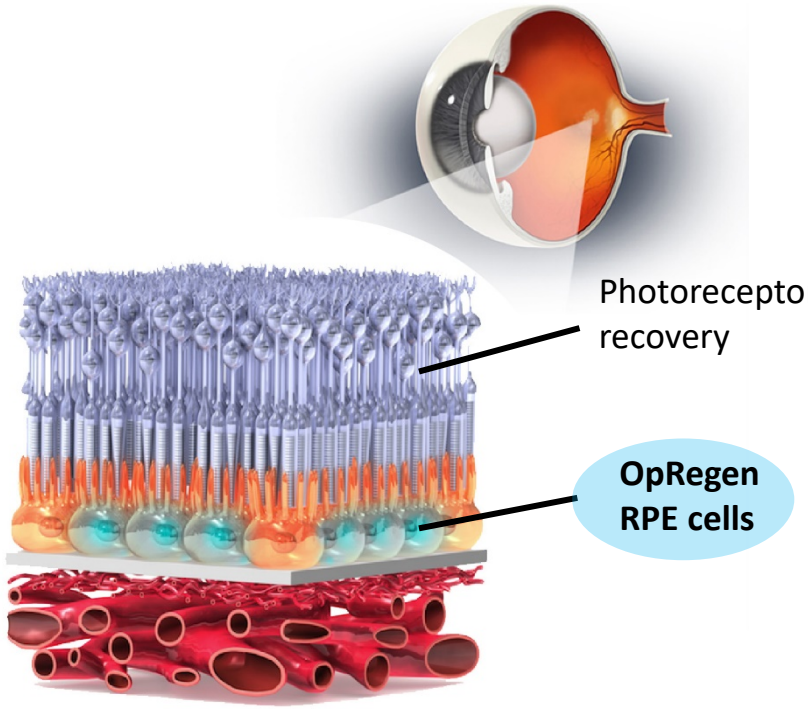

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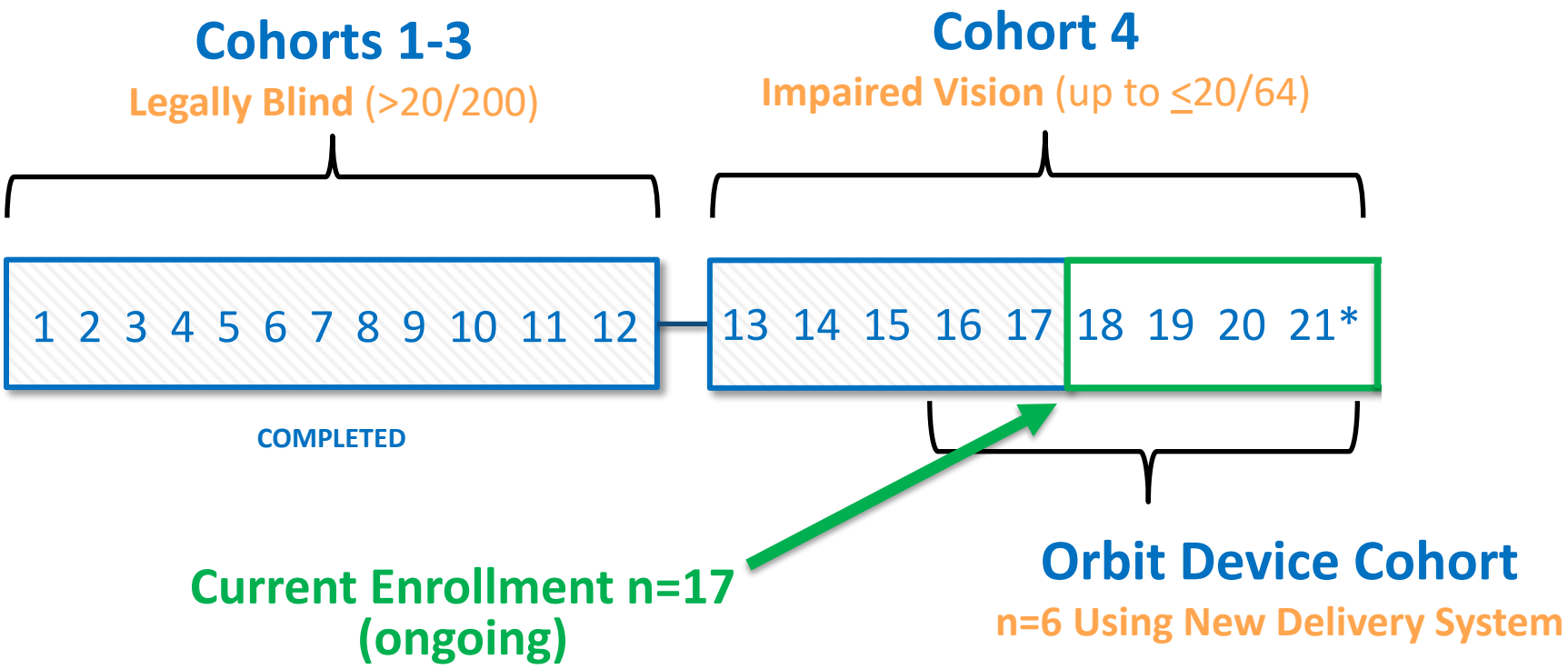
Image adapted from scienceofamd.org

Ongoing Phase 1/2a Clinical Trial in Dry AMD

Design: Open label, single-arm, multi-center (5 sites)



*** Protocol provides for up to 24 subjects**

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Key Patient Characteristic – Baseline Vision

Currently Enrolling Targeted Patient Population in Cohort 4

Parameter	Cohorts 1-3 (legally blind) n=12 (complete)	Cohort 4 (better baseline vision) n=9 (5 complete)
Subretinal Dose Route	3 dose levels n = 12 via traditional method	1 dose level n = 3 via traditional method n = 6 planned via Orbit device (2 completed)
Maximum Baseline Vision	20/200	20/65
Mean area of GA (mm^2)	12.7 mm^2	7.9 mm^2

Higher Baseline Vision and Smaller GA is expected to provide better outcomes (less advanced disease)

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Clinical Findings to Date

- **OpRegen RPE cells have been well-tolerated; no marked, sustained reductions to vision in any patients (n=17)**
- **Most Cohort 4 patients (4/5) have improved vision at the 1-year time point or at their last available visit**
- **Directionally-positive findings across separate assessments - multiple patients have exhibited evidence for:**
  - **Reduced growth of geographic atrophy**
  - **Improved visual acuity**
  - **Improved reading speed**
  - **Improved retina structure**
  - **Reductions in drusen waste material**
  - **Stable engraftment of cells**
- **No reports of acute or delayed inflammation or rejection of OpRegen cells**

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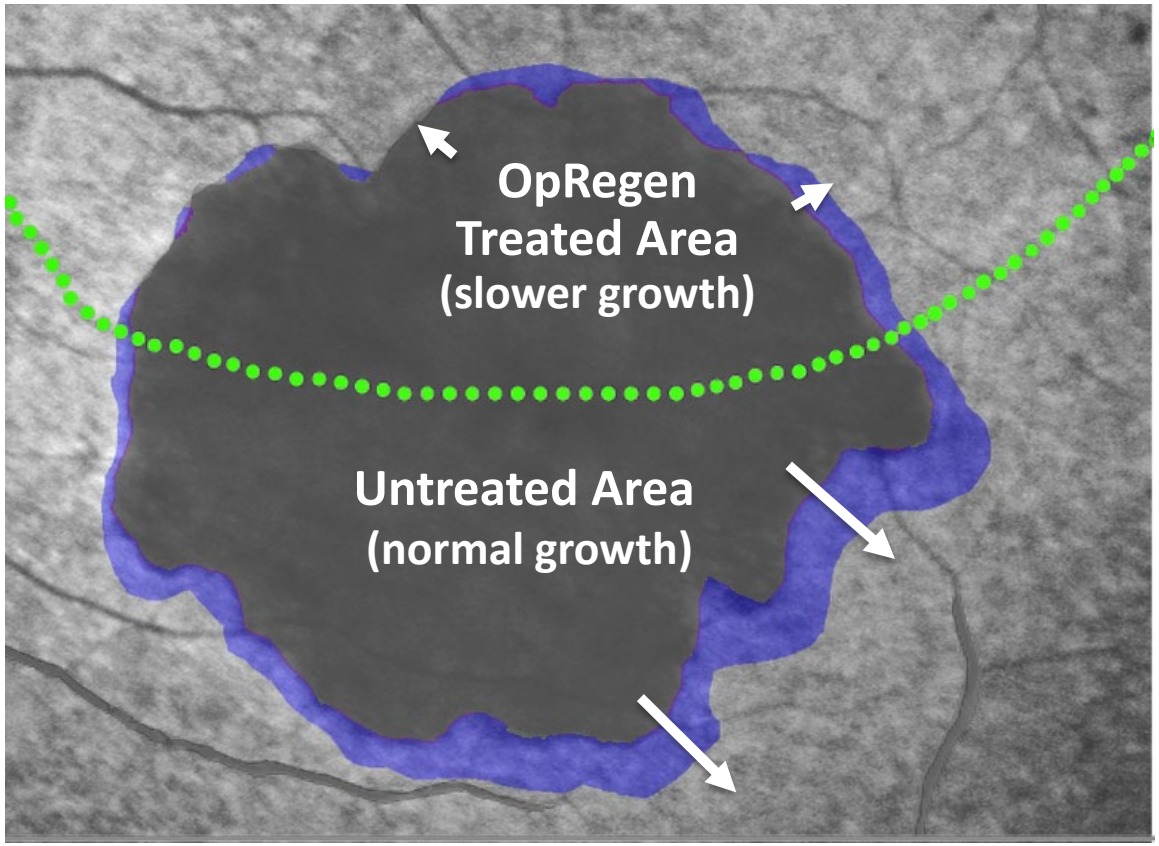
Data presented at 2020 ARVO Virtual Meeting

Evidence of Slower Growth of Area of Geographic Atrophy (GA)

- **Before and after comparison of the GA perimeter shows asymmetric growth**

Gray = pre-treatment **Purple = 12 months**



OpRegen cells were delivered above the green line

- **GA is a slow, unidirectional and degenerative process**
- **Asymmetrical growth of the GA evident at 12 months; slower growth in the OpRegen-treated area (above green line)**

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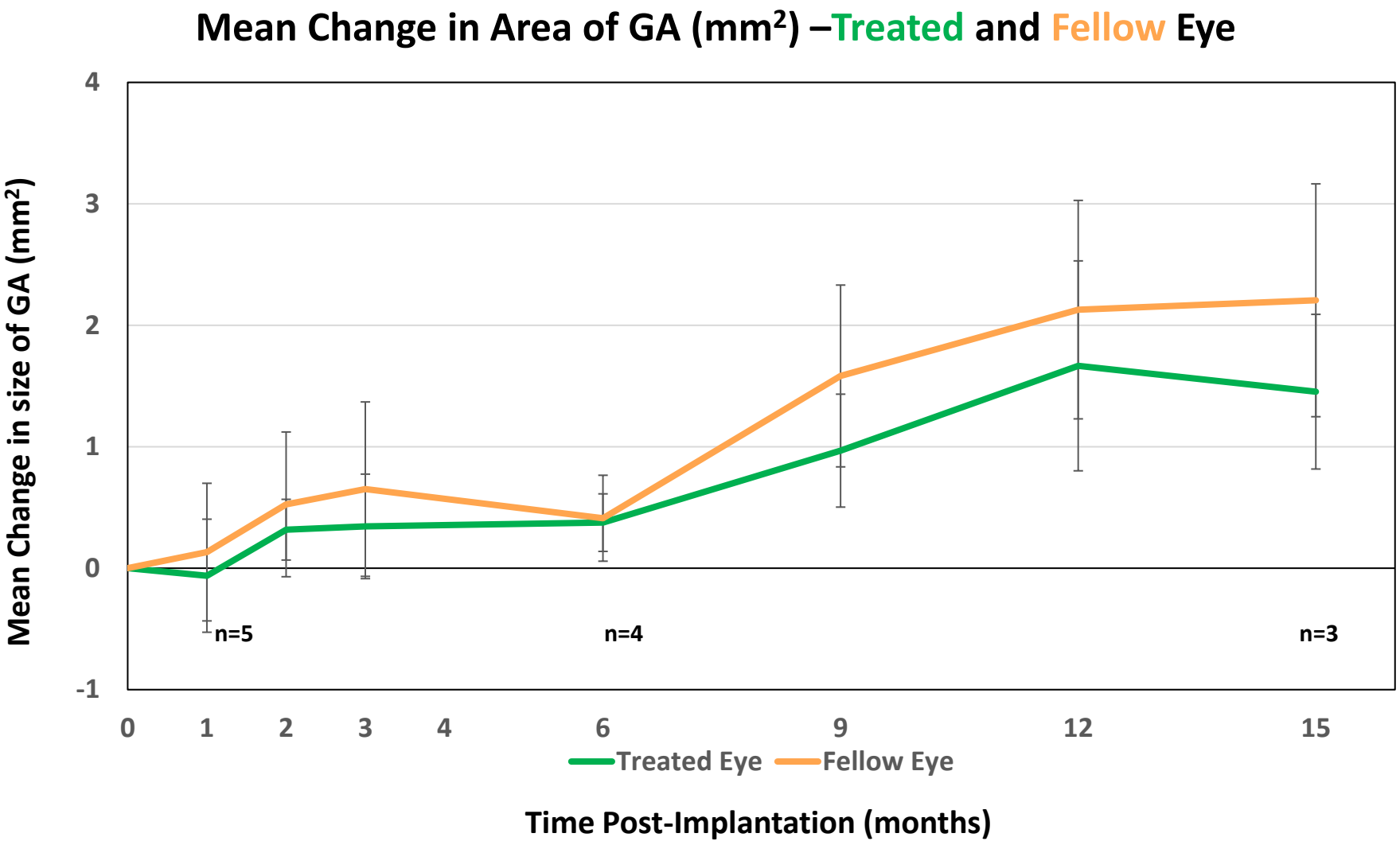
All Cohort 4 (Better Vision) Patients – Slower GA Growth



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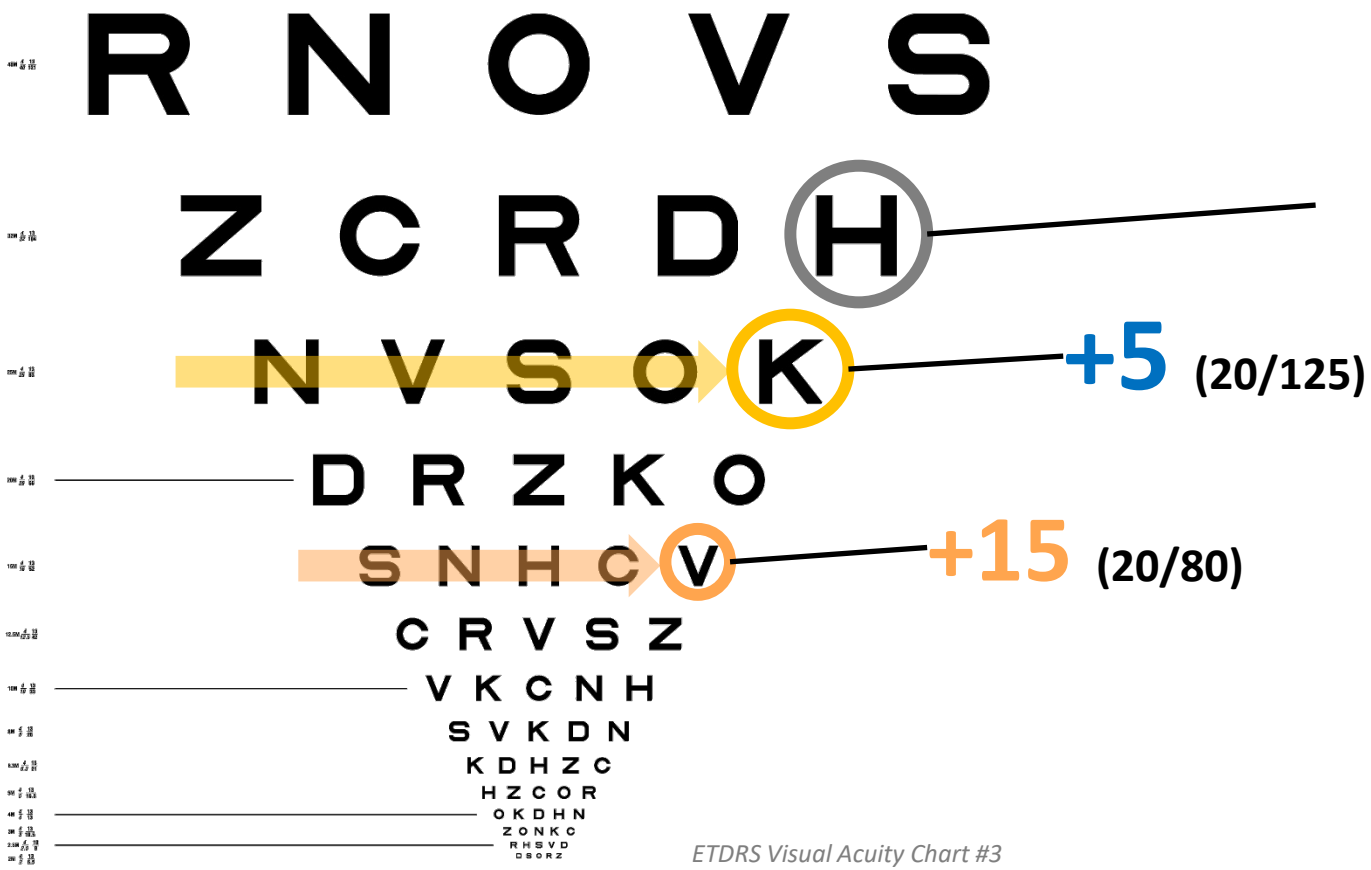
Visual Acuity Test “Letters of Improvement”



ETDRS Visual Acuity Chart #3

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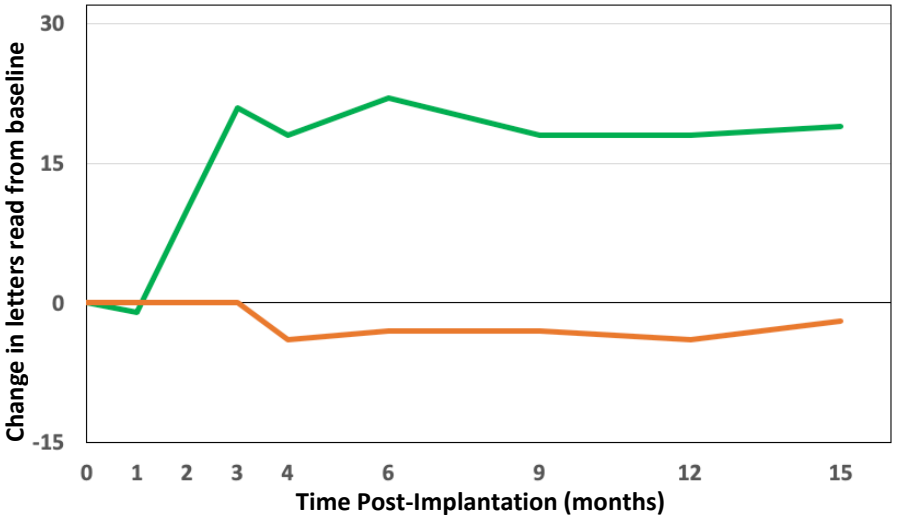
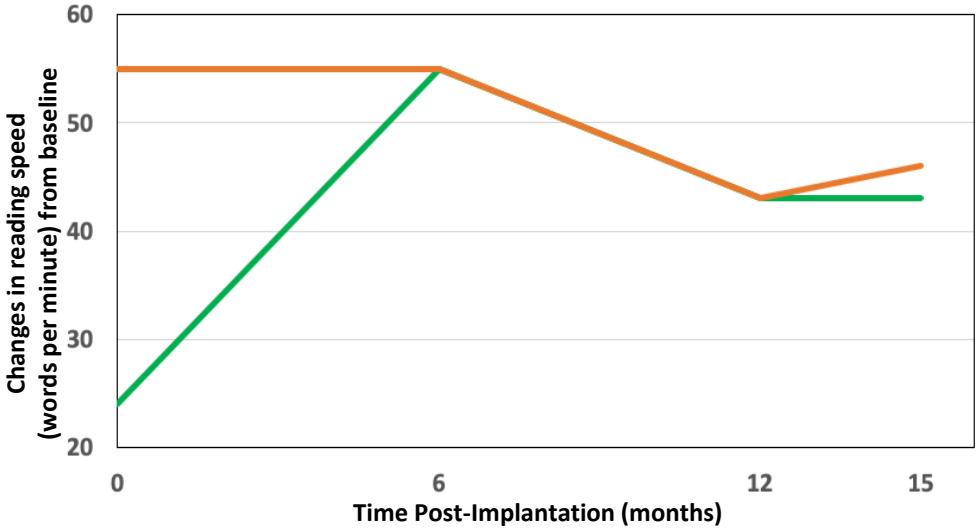
Case Study - 1st Cohort 4 ("Better Vision") Patient

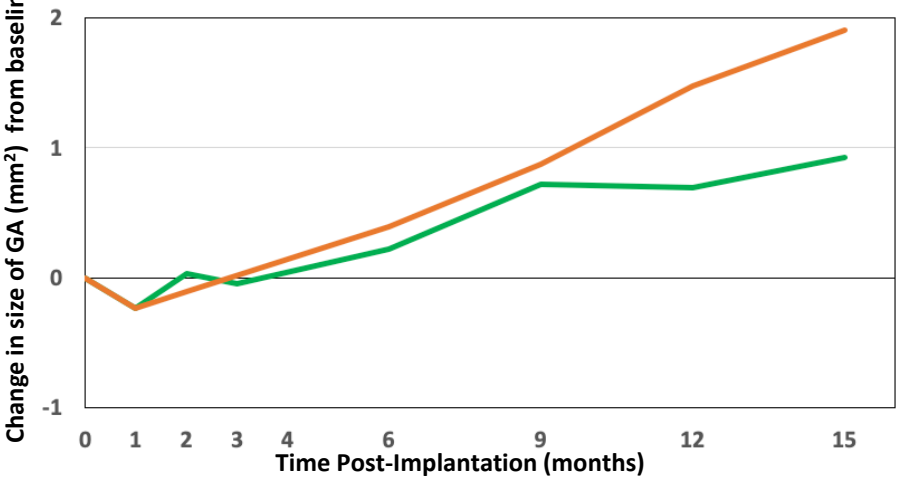
Individual BCVA Changes – Treated vs. Fellow Eye



Individual Reading Speed Changes – Treated vs. Fellow Eye



Individual GA Changes – Treated vs. Fellow Eye



The first better vision patient treated exhibited durable improvements in visual acuity (BCVA), slower progression of GA, and doubling of reading speed in the treated eye compared with the untreated eye

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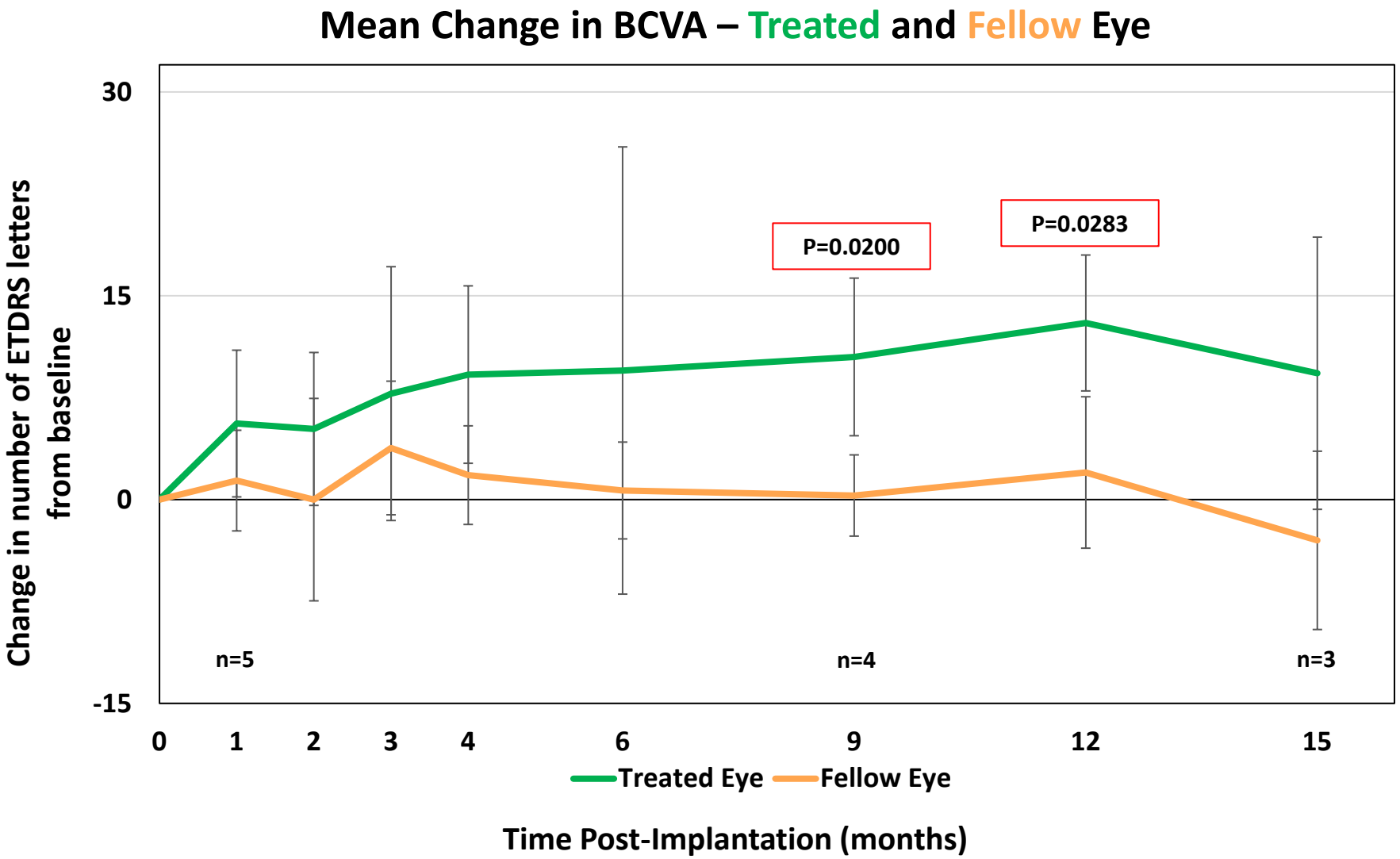
Data presented at 2020 ARVO Virtual Meeting

All Cohort 4 Patients - Best Corrected Visual Acuity



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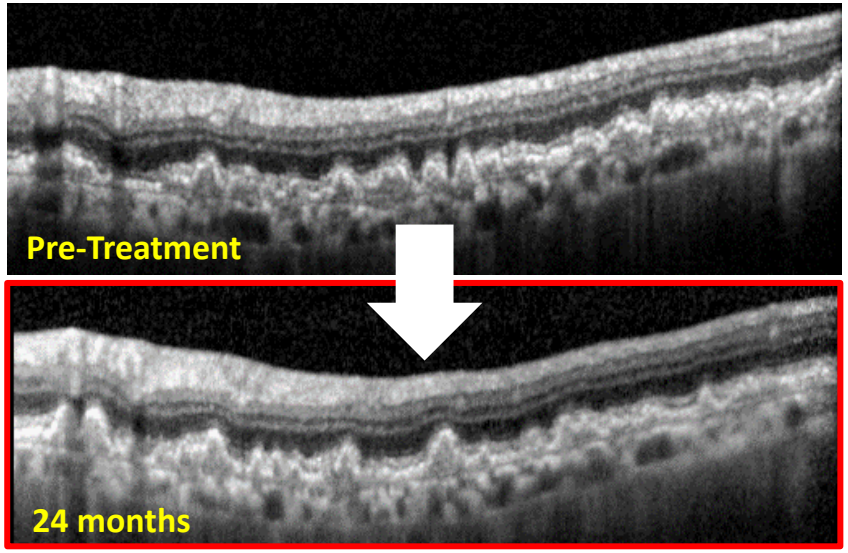
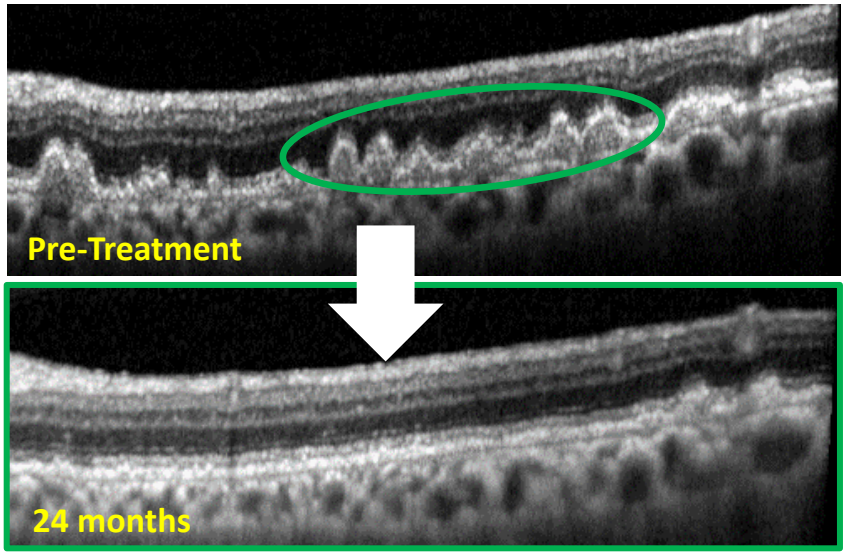
Evidence of Reductions of Drusen

- **Drusen are deposits of waste material associated with dry AMD**
- **Reductions or changes to drusen has been observed through 24 months in some patients (wrinkled white line becomes flat)**

Untreated



Treated



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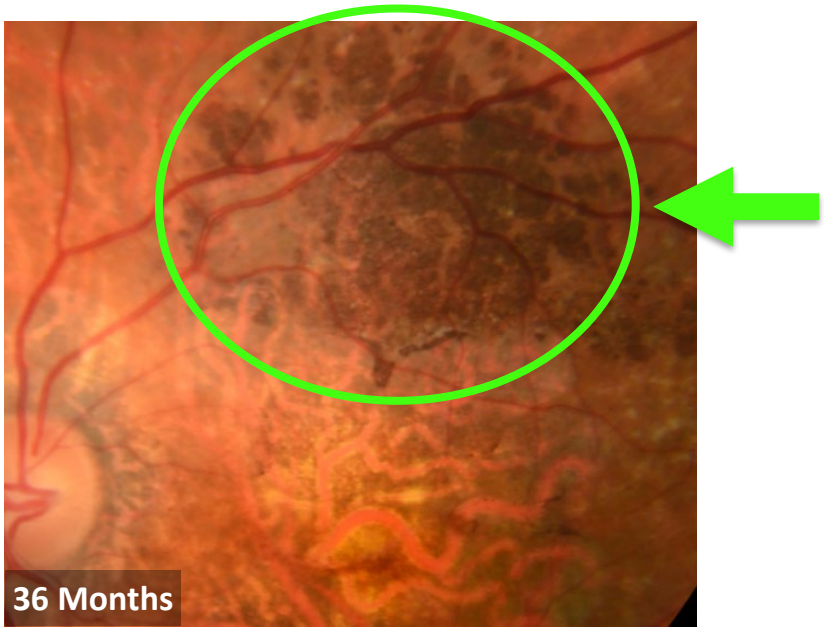
Evidence of Stable Engraftment of Transplanted RPE Cells

- **OpRegen may be amenable to infrequent or even one-time treatment**



Punctate shaded areas are indicative of stable engraftment of pigmented cells for more than 36 months

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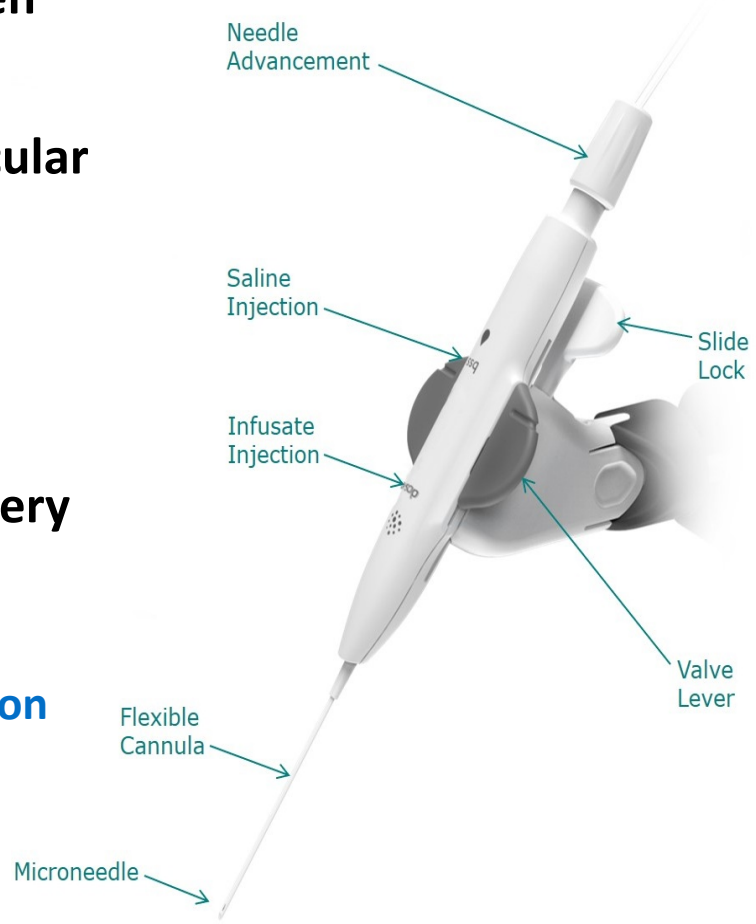
Images obtained through Color Fundus Photography

Safety Considerations

Turning an Adverse Event Finding Into a Competitive Advantage

- **Treatment with OpRegen RPE cells has been well-tolerated**
- **The most common adverse event was macular fibrosis (ERM)**
  - **An ERM was observed in 13 of 15 patients:**
  - **ERMs are attributable to puncture hole (retinotomy) formed during surgery**
- **Solution: Gyroscope Orbit Subretinal Delivery System ("Orbit SDS")**
  - **Eliminates need to cut a hole in the retina**
  - **0 of 2 patients formed or had an exacerbation of an ERM after using new Orbit device**



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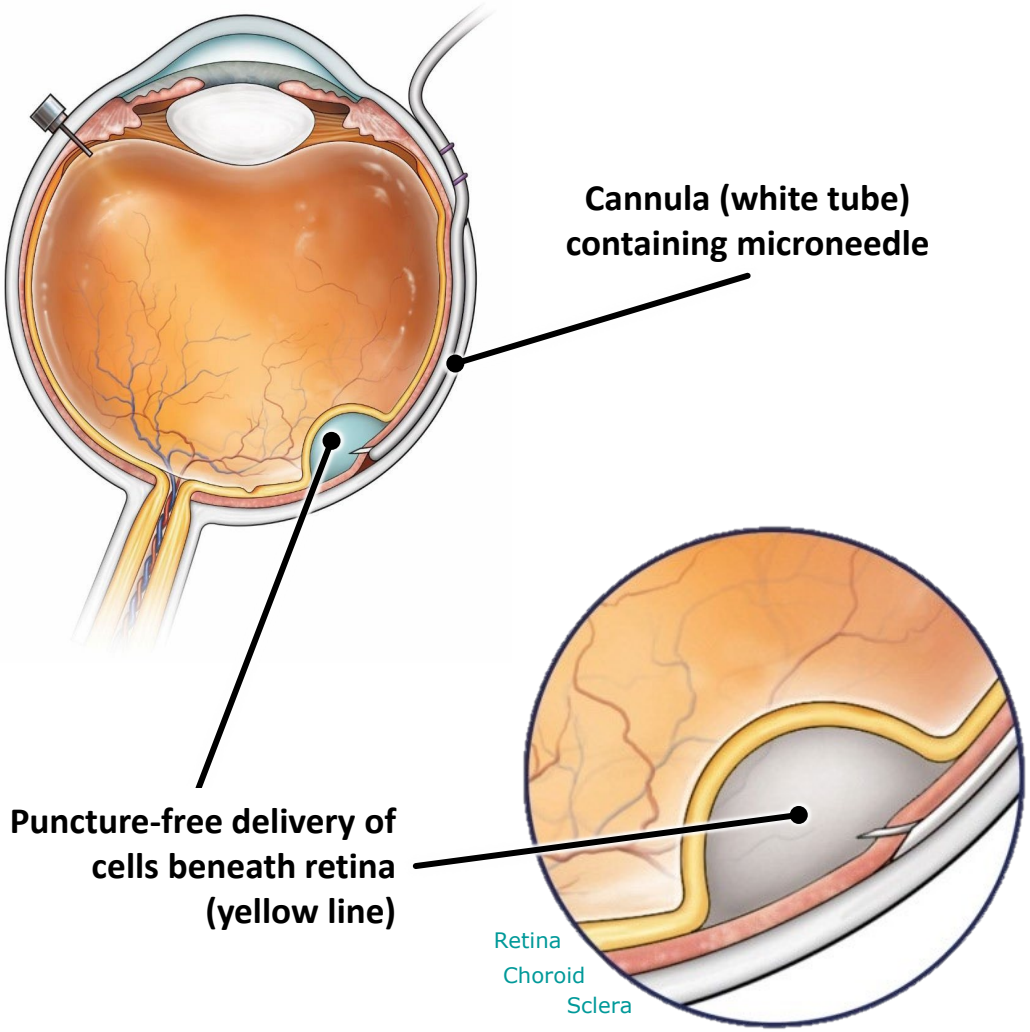
Orbit Subretinal Delivery Device



- **The Orbit device creates a stable bleb of cells beneath the retina with a self-sealing hole**
- **Key advantages include:**
  - **Greater dose control,**
  - **Less variability, and**
  - **Fewer adverse events from leakage of cells out of injection site into vitreous space**
- **Lineage has an exclusive option on the use of Orbit to deliver cells for dry AMD**

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Image used with permission from Gyroscope Therapeutics Ltd.

Building Confidence in a Treatment Effect

Increasing evidence supports the expectation of a clinically-meaningful treatment effect from the transplant of RPE cells in patients with dry AMD with GA

Key Attribute	Any Evidence?	Setting
Engraftment as a Monolayer	Yes	Multiple Species
Long-Term Survival *in vivo*	Yes	Multiple Species
Treatment Effect	Yes	Rodent
Durable Engraftment	Yes	Rodent // Human
Structural Improvement	Yes	Human
Drusen Reduction	Yes	Human
Improved BCVA	Yes	Human
Slower GA Growth	Yes	Human

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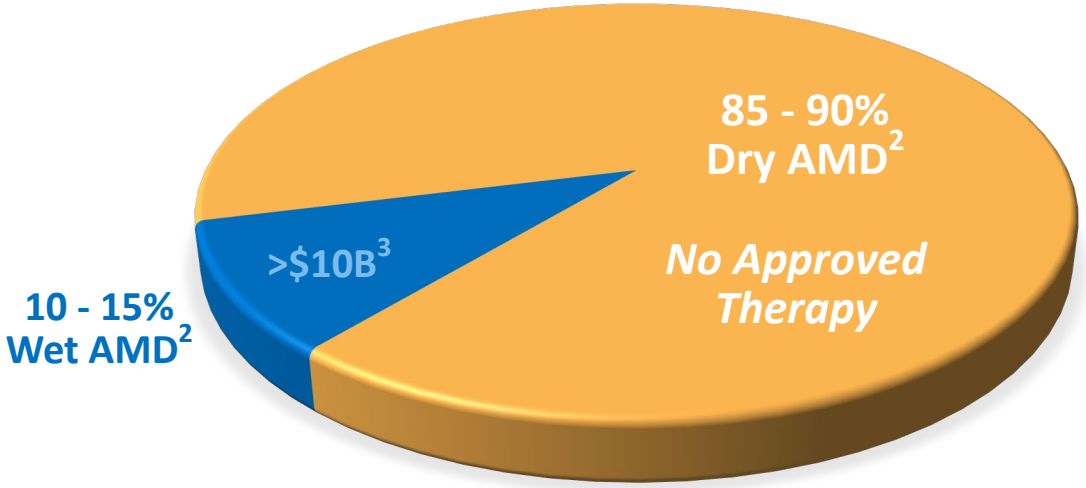
OpRegen is an experimental product candidate currently in a Phase I/IIa clinical study. Determinations of safety or efficacy can only be made by an authorized regulatory body such as the US FDA.

U.S. Market Opportunity

- **AMD afflicts ~11 million people in the United States**

Type of AMD	% of AMD Cases	Approved Therapies
Wet AMD	10 – 15%	Lucentis & Eylea ($10 Billion in annual sales)
Dry AMD	85 – 90%	None[1]



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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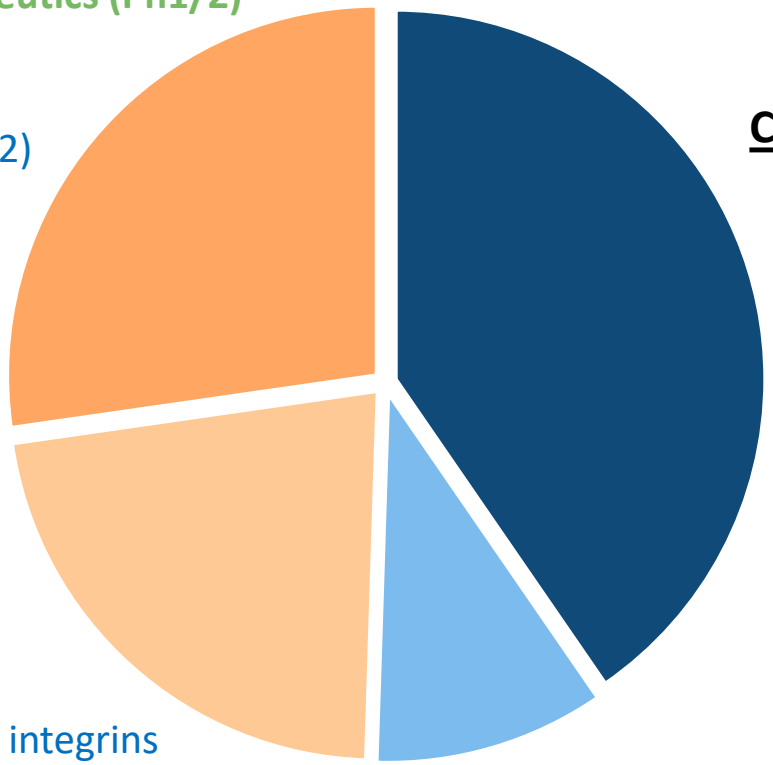
Dry AMD Competitive Landscape
Four Clinical-Stage Modalities

Cell Therapy

- Lineage Cell Therapeutics (Ph1/2)
- Astellas (Ph1/2)
- Regenerative Patch Technologies (Ph1/2)

Cell therapy has the potential for both disease REVERSAL and one-time treatment



Complement

- Genentech (Ph3 fail)
- Apellis (Ph3 ongoing)
- Alcon (Ph2) mAb
- Iveric (Ph2)
- NGM (Ph1) mAb

Oxidative Stress

- Allegro (Ph2) - integrins
- Stealth Bio (Ph2) - mitochondria

Gene Therapy

(also targets complement)

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

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Product Positioning

- **OpRegen RPE is well-positioned to capture a multi-billion dry AMD commercial opportunity**
  - **Transplanting RPE cells may provide benefits which complement inhibitors or oxidative stress approaches cannot**
  - **Market opportunity is not limited to monogenic patients (gene therapy)**
  - **Treatment has been well-tolerated with some patients exhibiting changes consistent with a treatment effect**
  - **Patents cover production, characterization, and formulation**
  - **Exclusive rights to unique delivery device**

OpRegen: Delivering the best cells, the best way, for the best outcomes.

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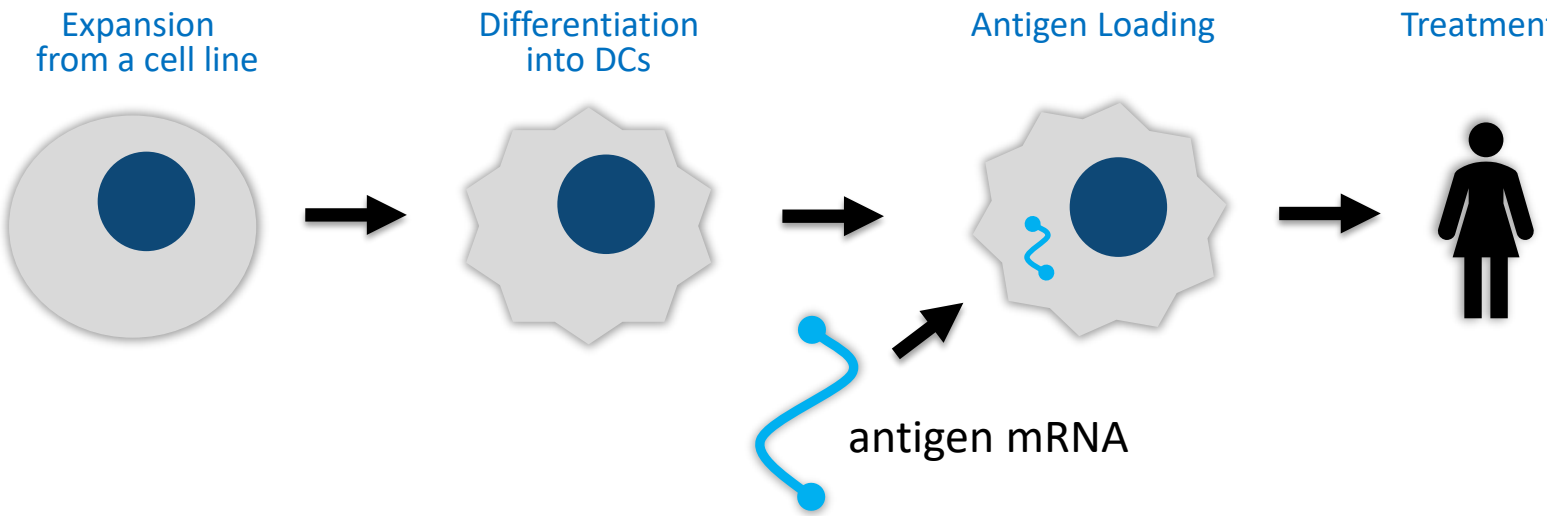
Immunotherapy is "poised to revolutionize treatment for all types of cancer"

Source: cancerresearch.org

VAC: A Cell Therapy Platform for Cancer (Immuno-Oncology) and Infectious Disease

VAC Platform

- **The VAC platform consists of *in vitro* production of mature dendritic cells (DC)**
- **DCs are manufactured and loaded to express either a tumor antigen (for cancer) or a viral antigen (for infectious diseases)**
- **Antigen presentation to the patient's T cells directs and increases the immune response, leading to tumor cell destruction or clearance of virus**



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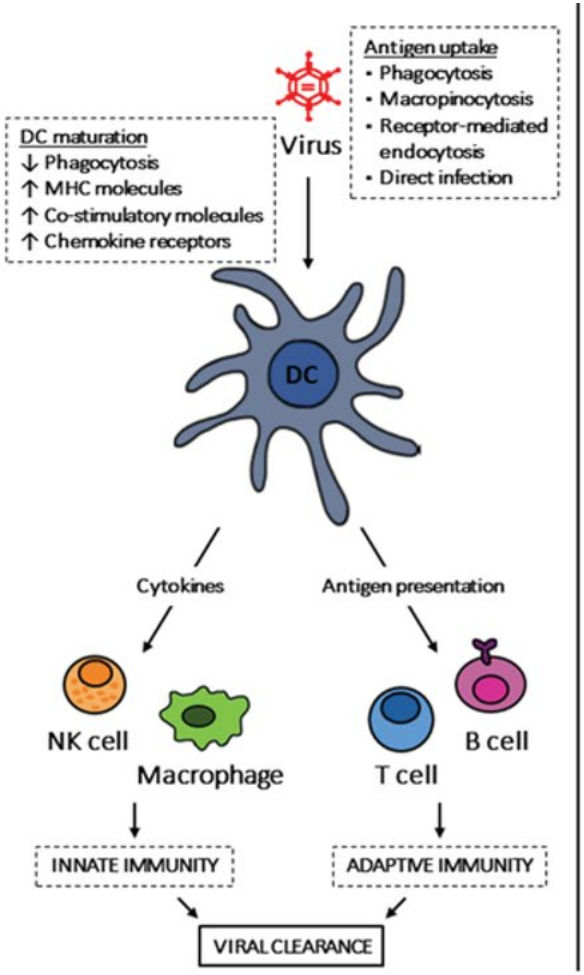
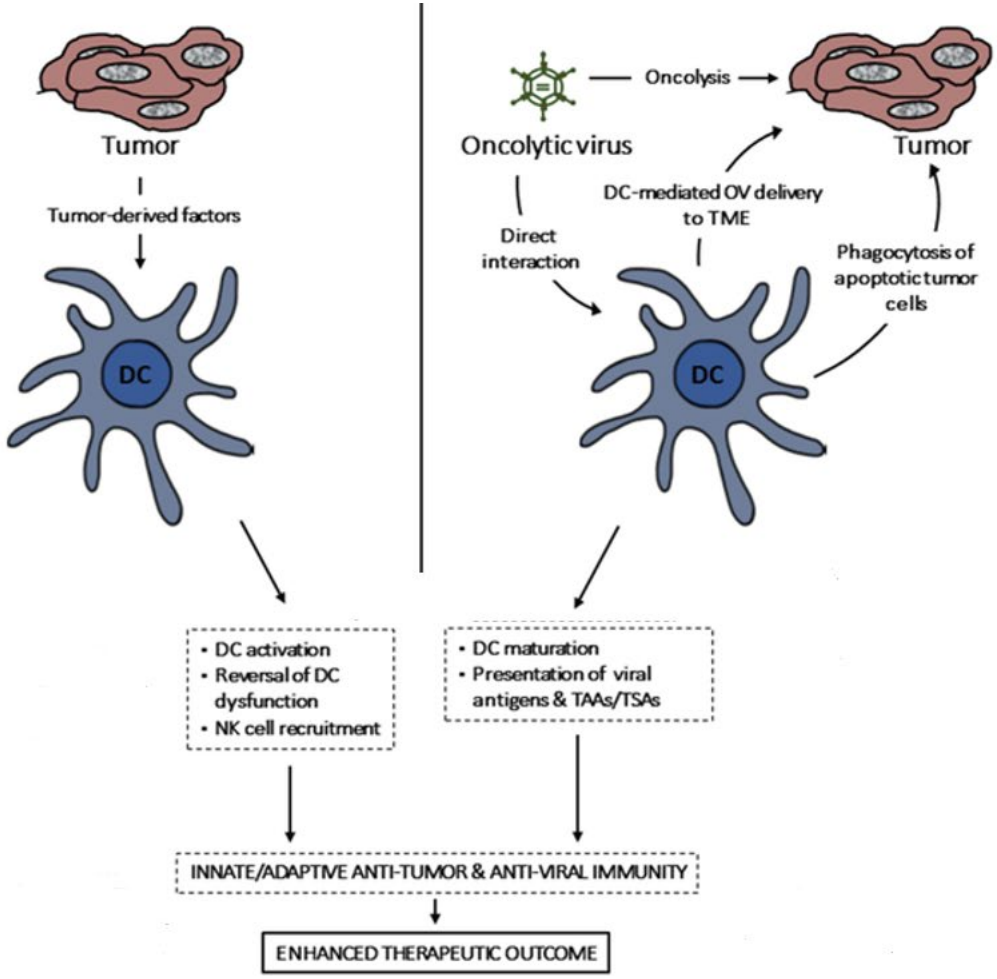
VAC Platform – Easily Adapted to Multiple Settings

Viral Infections



Cancer (including tumorviruses)



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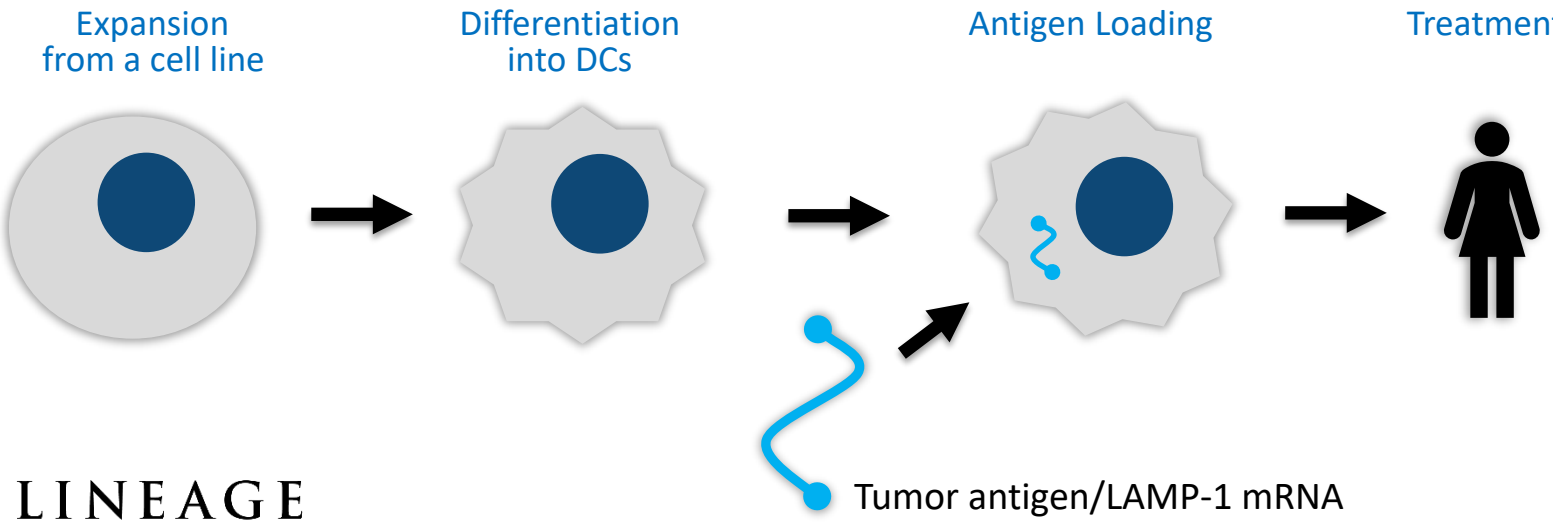
VAC for Immuno-Oncology

- **DCs are loaded with an antigen present in >85% of all cancers but absent from normal cells**
- **High levels of VAC antigen-specific T cells (above 3% at peak) have been observed in multiple clinical trials**
- **A strong clinical response reported with an earlier, autologous version of VAC (VAC1)**
- **Ongoing phase 1 data (VAC2) supports mechanism-based immunogenicity**
- **Plan is to evaluate combination of VAC2 with checkpoint inhibitors or chemo in phase 2**



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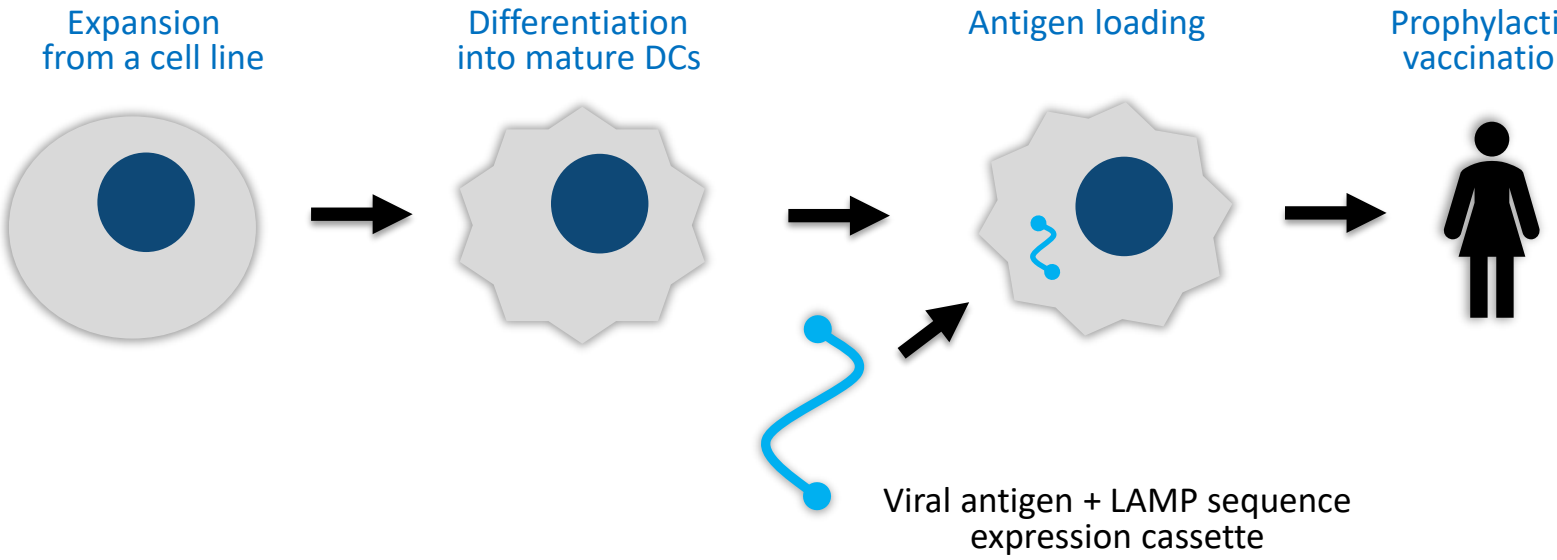
Potential Advantages of the VAC Approach for Immuno-Oncology

Attribute	VAC2
Single master cell bank for scalability and consistency	✓
Available ‘off-the-shelf’, on demand	✓
No known significant off-target effects	✓
Low AE-related cost of treatment	✓
Lower anticipated COGS than CAR-T	✓
Use in combination with chemotherapy	✓
Use in combination with immune checkpoint inhibitors	✓

VAC2 is designed to overcome limitations of first-generation dendritic cell therapies, providing cost and safety advantages over autologous approaches and use in combination with chemotherapy or immune checkpoint inhibitors

VAC for Infectious Disease

- **Dendritic cells can also be loaded with a specific *viral* antigen**
- **A LAMP sequence facilitates MHC Class II presentation to CD4+ cells**
- **Goal is to stimulate both CD8+ and CD4+ T cell responses to drive long-term protection**
  - **Very high (1-3%) CD8+ antigen-specific peak responses observed in earlier VAC clinical studies**
  - **19 out of 20 (95%) of patients had detectable antigen-specific CD8+ T cells in prior studies**
- **Prior development work in oncology facilitates deployment to infectious diseases**



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VAC for COVID-19 - Vaccination

The goal of vaccination is to safely confer broad, durable protection through the induction of adaptive immunity

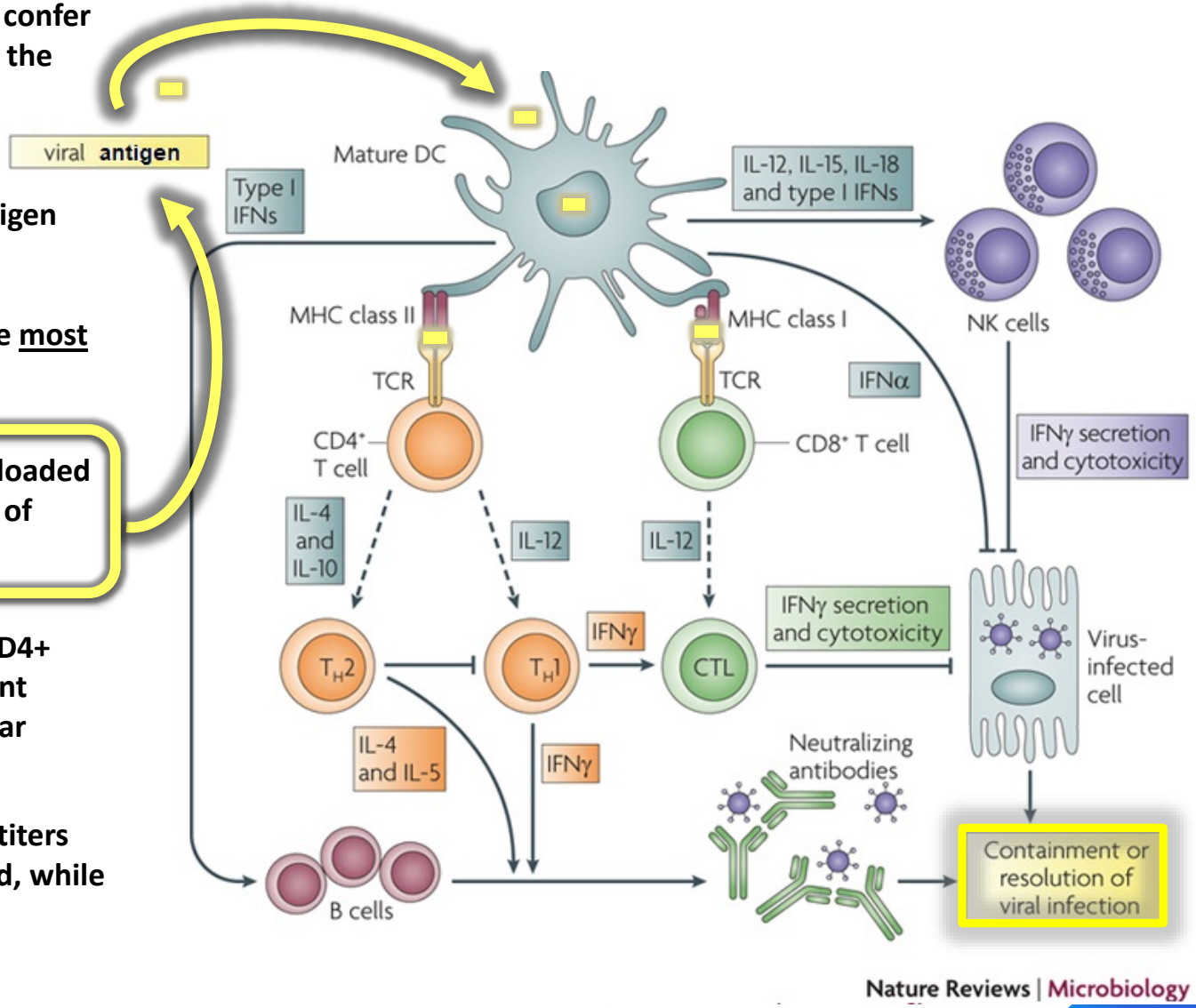
All vaccine modalities require information to be delivered by antigen presenting cells (APCs)

Dendritic cells (DCs, center) are the <u>most potent</u> antigen presenting cells

Mature allogeneic DCs can be pre-loaded with any antigen, ensuring fidelity of message (VAC Technology)

DCs can drive ~~a~~ robust CD8+ and CD4+ responses, leading to tissue resident memory cells (TRMs) and multi-year protection

SARS-CoV-1 neutralizing antibody titers and B cell responses are short-lived, while CD8+ T cells persisted 6+ years



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

Source: christopherreeve.org

OPC1: A Cell Therapy Product Candidate for Spinal Cord Injury

OPC1 Overview

- **OPC1 consists of manufactured oligodendrocyte progenitor cells (OPCs)**
- **OPCs become the cells which provide electrical insulation for nerve axons in the form of a myelin sheath**
- **RMAT Designation**
- **Orphan Drug Designation**
- **$14M of support from CIRM**

OPC1 Injection Procedure

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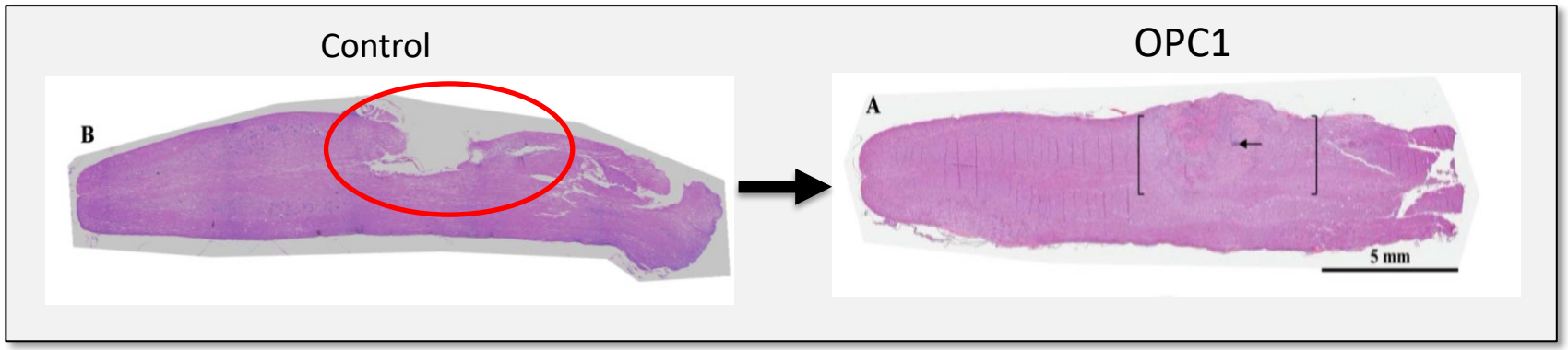
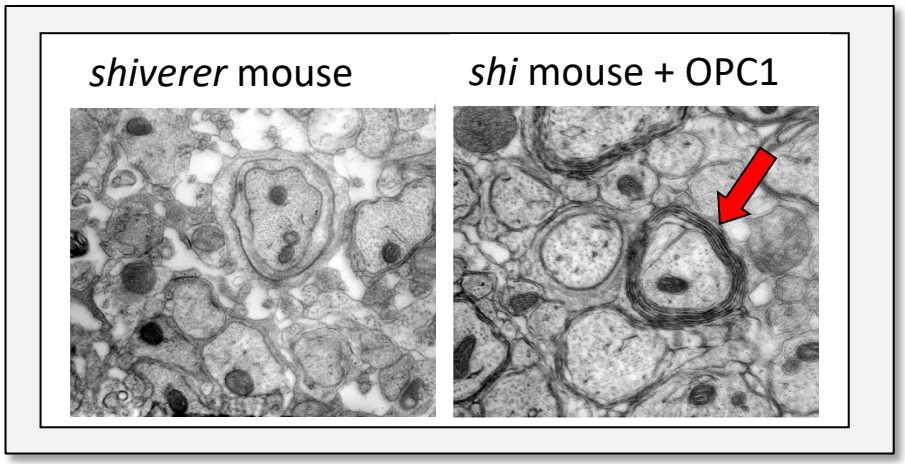
OPC1 Mechanisms of Action

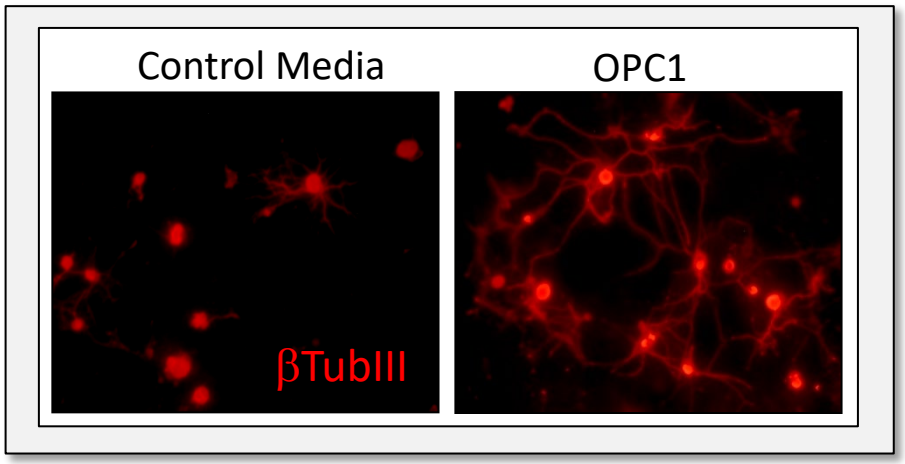
1. Prevention of Cavitation



2. Myelination of axons



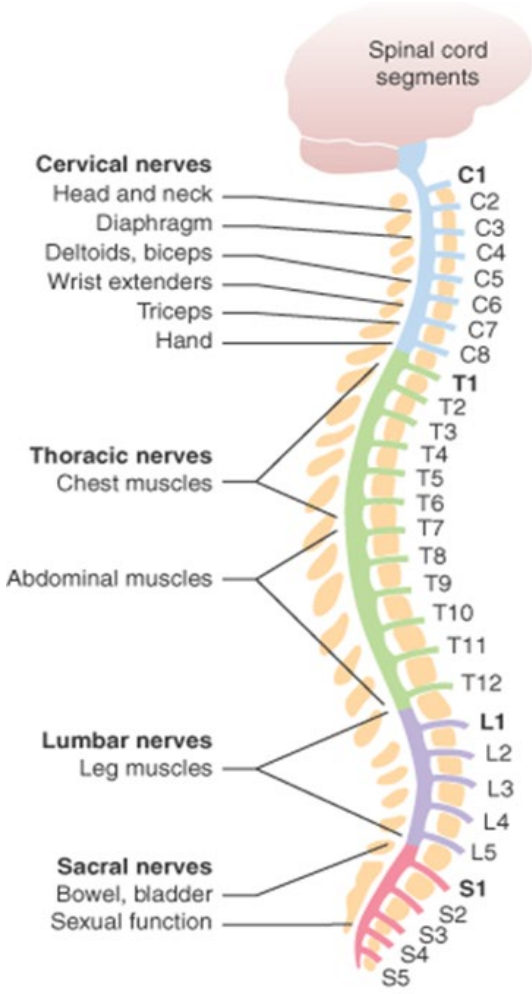
3. Secretion of neurotrophic factors



LINEAGE CELL THERAPEUTICS

Spinal Cord Injury (SCI) Unmet Need

- **Loss of motor activity is the primary feature of a spinal cord injury**
- **Motor level gains translate into clinically meaningful improvements in self-care and reductions in cost of care**
- **The therapeutic goal of OPC1 is to provide additional upper extremity (arm, hand, finger) function, increasing independence and quality of life**



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

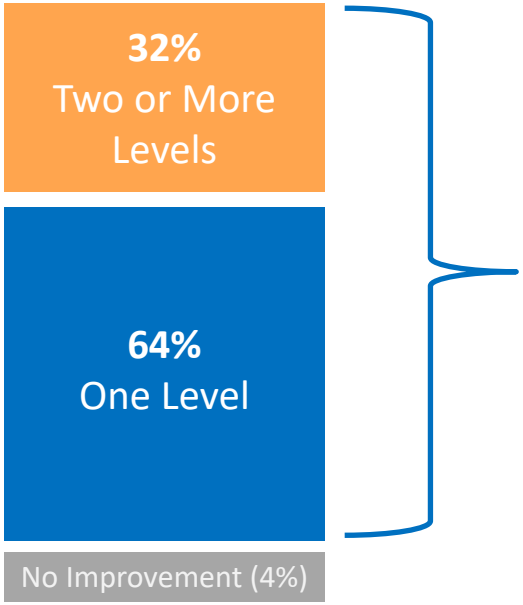
Safety and Efficacy from OPC1 Phase 1/2a Study

Cell Engraftment

(cohorts 2-5 at 12 months, n=22*)

Motor Function Gain

(cohorts 2-5 at 12 months, n=22*)

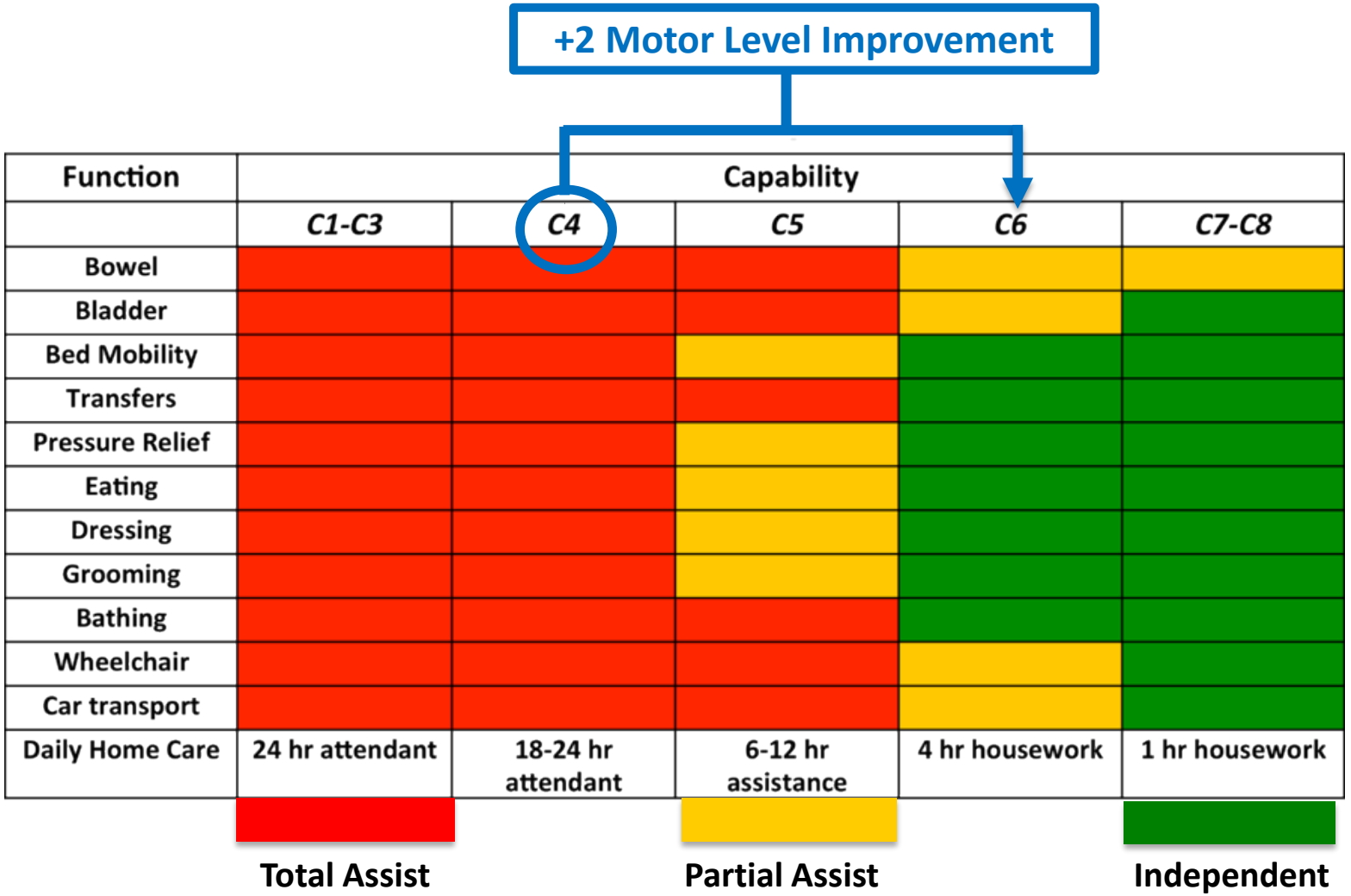


To date, there have been no serious adverse events related to the OPC1 cells

LINEAGE CELL THERAPEUTICS

*** Cohort 1 (n=3), not included, received a sub-clinical safety dose of 2M cells (clinical dose is 10-20M cells)**

Real-World Benefit of Motor Level Gains



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

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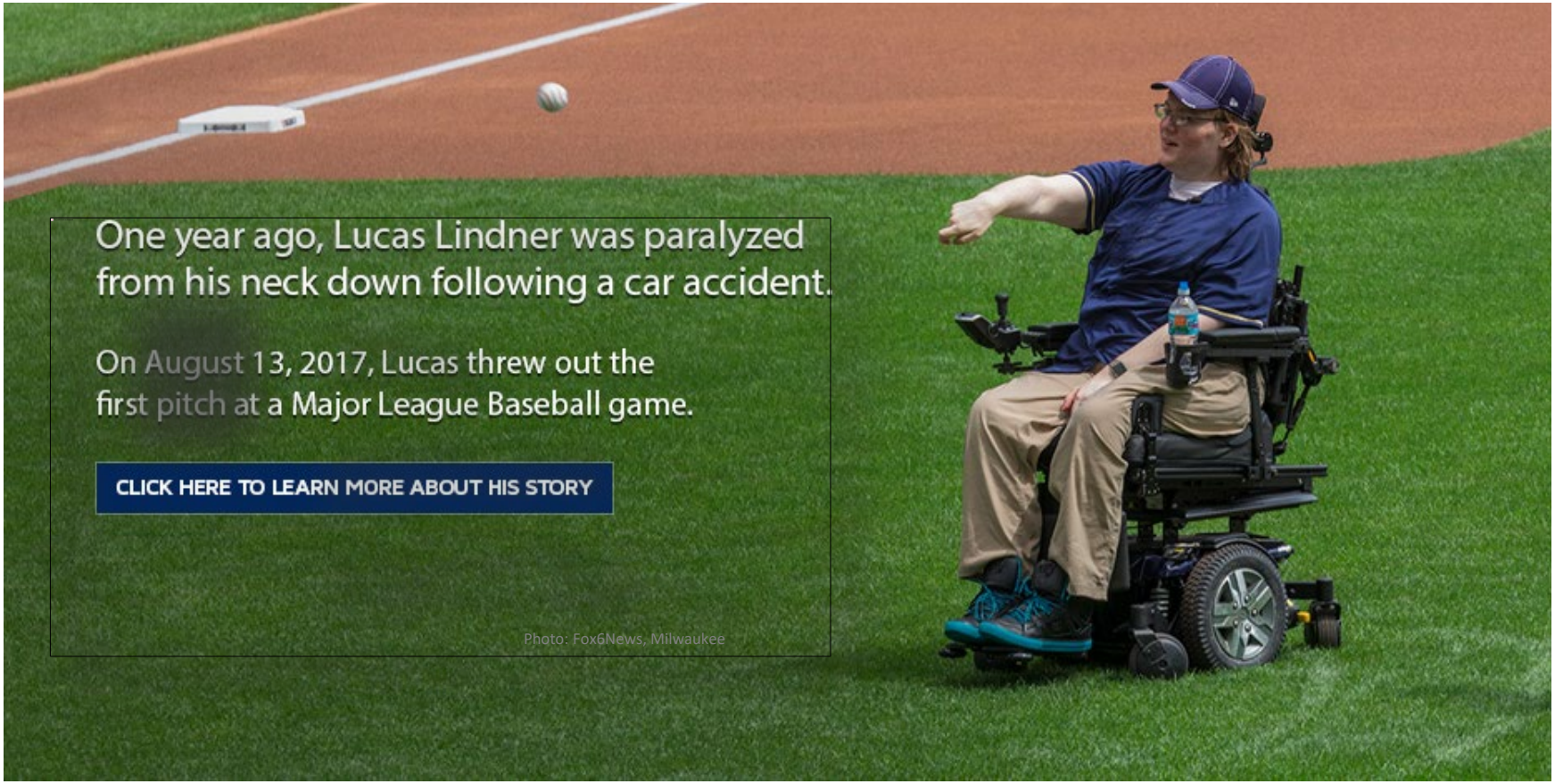
Lucas' Story



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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Upcoming Events and Milestones

- **Complete enrollment of final 4 patients in phase 1/2a study of OpRegen for dry AMD**
- **Report updated OpRegen dry AMD data at AAO (November)**
- **Explore US and ex-US opportunities for OpRegen program partnerships**
- **Discuss OpRegen dry AMD phase 2b/3 comparative study design with FDA**
- **Apply for grant support for VAC-COVID program**
- **Complete enrollment of VAC2 phase 1 trial (performed by CRUK)**
- **Announce VAC2 phase 1 trial data (performed by CRUK)**
- **Complete process development improvements for OPC1 for spinal cord injuries**
- **Evaluate novel injection device for OPC1 for spinal cord injuries**
- **Explore US and ex-US opportunities for OPC1 program partnerships**

Financial Overview

Cash, Cash Equivalents and Marketable Securities (As of 3/31/2020)	**~$25.8 mm**
Convertible Note Receivable from Juvenescence (At maturity date: 8/30/2020)	**~$24.6 mm**
Debt	**None**
Market Capitalization (As of 5/20/2020)	**~$136 mm**
Employees (As of 5/20/2020)	**54**

A new management team and prioritization of clinical cell therapy programs have resulted in a more efficient and cost-effective business model

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Why Invest in Lineage?

Lineage is well-positioned for near-term growth and long-term value

3 clinical-stage programs with billion dollar potential

World class in-house GMP manufacturing

One of the largest patent portfolios in cell therapy

Funded well into 2021* with cost-efficient business model

Leader in the emerging field of regenerative medicine

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** Assumes payment of $24.6M note receivable from Juvenescence due August 30, 2020.*

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The future of cell therapy.

Thank You

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