LINEAGE
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Solebury Trout
Therapeutic Area Expert Day
November 15, 2019

NYSE American: LCTX

Today's Agenda

Time	Topic	Presenters
11:00 – 11:10	Introduction	Brian M. Culley, CEO, Lineage Cell Therapeutics (LCTX)
11:10 – 11:30	Dry AMD; OpRegen	Allen C. Ho, M.D. FACS, Wills Eye Hospital Attending Surgeon and Director of Retina Research
11:30 – 11:40	Dry AMD Q&A	Allen C. Ho (cont.)
11:40 – 12:00	Spinal Cord Injury; OPC1	John Steeves, B.Sc., Ph.D., Emeritus Principal Investigator at ICORD, Professor, Department of Neuroscience, University of British Columbia
12:00 – 12:10	Spinal Cord Injury Q&A	John Steeves (cont.)
12:10 – 12:15	Concluding Remarks	Brian M. Culley

Forward Looking Statements

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Lineage Cell Therapeutics

Lineage is a cell therapy company which manufactures and transplants specific types of cells to treat injuries and disease

Three Clinical-Stage Programs

OpRegen®
for Dry Age-Related Macular Degeneration with GA (dry AMD)

Phase 1/2a

OPC1
for Spinal Cord Injury (SCI)

Phase 1/2

VAC2
for Oncology (Non-Small Cell Lung Cancer, NSCLC)

Phase 1

Hundreds of cell therapy-related patents and pending applications worldwide

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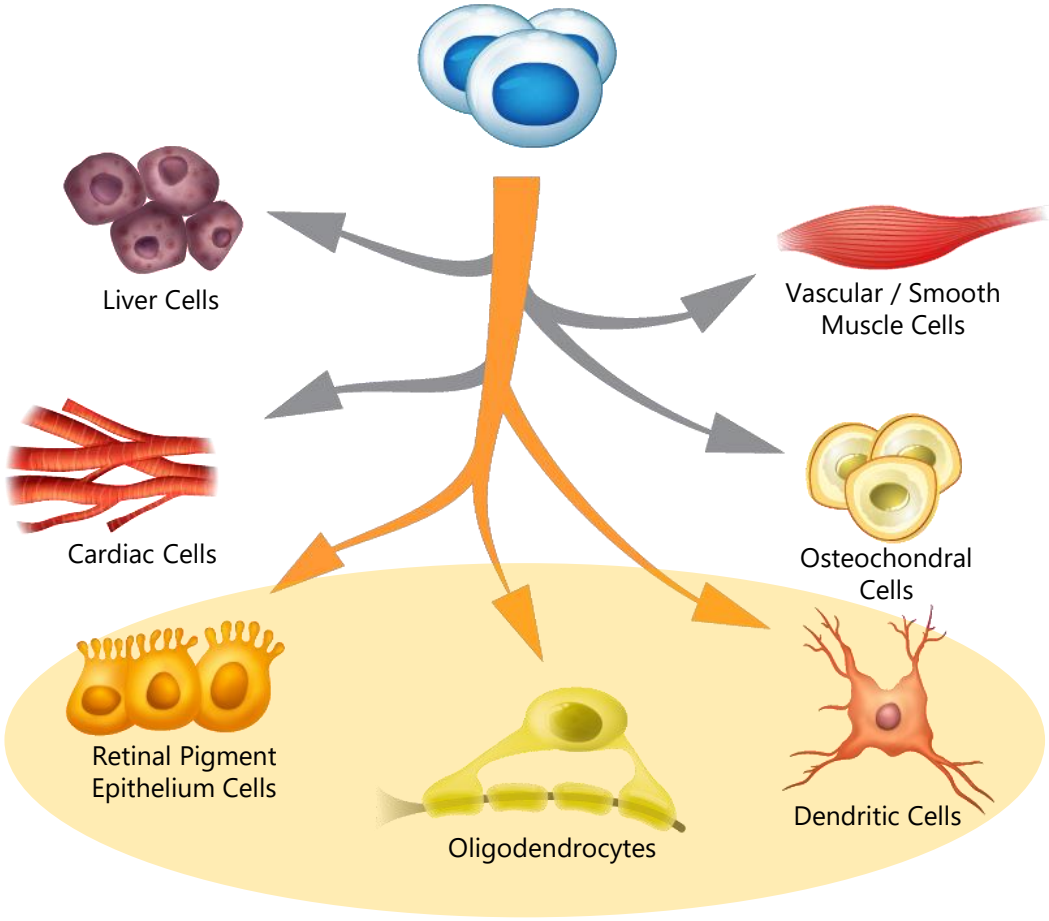
Lineage Platform Technology

- **The Lineage Platform starts with normal human cell lines, which avoids risks from genetic modifications**
- **These cells have the capacity to become any human cell type, offering many potential indications**
- **A cell's lineage is controlled to generate only the desired cell type**
- **The cells have high proliferative capacity and can produce abundant clinical material**



CURRENT CLINICAL PROGRAMS

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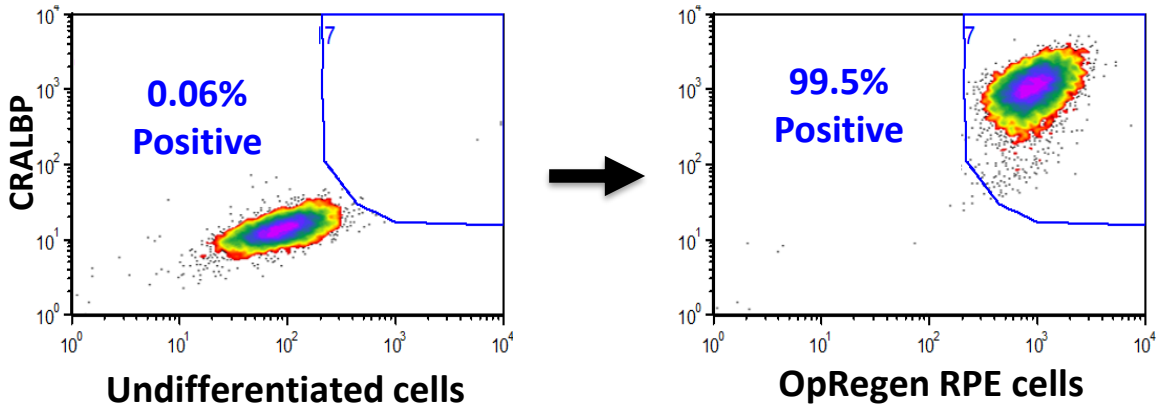
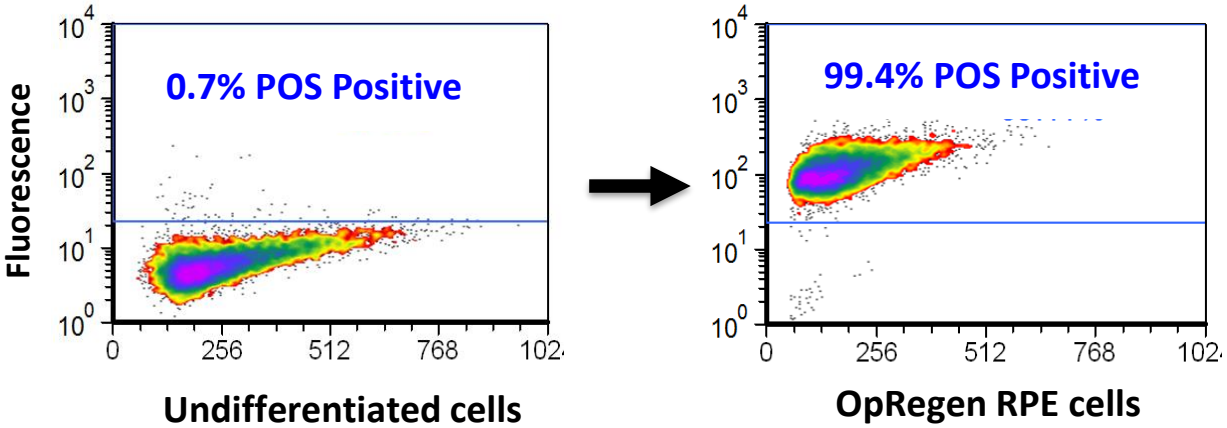
In-House cGMP Manufacturing

The lineage of an established line of pluripotent cells can be controlled to create a population of substantially pure, fully-differentiated RPE cells

Identity Assay (purity)



Phagocytosis Assay (activity)



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Pipeline and Partners

Cell Therapy Programs	Phase I	Phase II	Partnerships & External Funding
OpRegen® Dry Age-Related Macular Degeneration with GA (Dry AMD)	→		רשות החדשנות Israel Innovation Authority **$16M**
OPC1 Spinal Cord Injury (SCI)	→		CIRM CALIFORNIA'S STEM CELL AGENCY **>$14M**
VAC2 Non-Small Cell Lung Cancer (NSCLC)	→		CANCER RESEARCH UK **>$10M in-kind**
RENEVIA Medical Aesthetics	**CE Mark Received September 2019**		

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The future of cell therapy.

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OpRegen®
Cell Therapy for Dry Age-Related Macular Degeneration

Dr. Allen Ho, Wills Eye

Allen C. Ho, M.D. FACS, Wills Eye Hospital Attending Surgeon and Director of Retina Research, Professor of Ophthalmology, Thomas Jefferson University

Dr. Ho maintains special interests in macular diseases, diabetic retinopathy, surgical retinal diseases and clinical trials investigating new treatments for vitreoretinal diseases including gene and cell therapies and new surgical drug delivery devices and techniques. His experience includes collaborative translational and clinical trial clinical research with expertise in study design, methodological testing, data analyses, surgical instrumentation and procedure development, execution and communication of these studies and their study results. He is the current President of The Retina Society and serves on its Executive Committee.

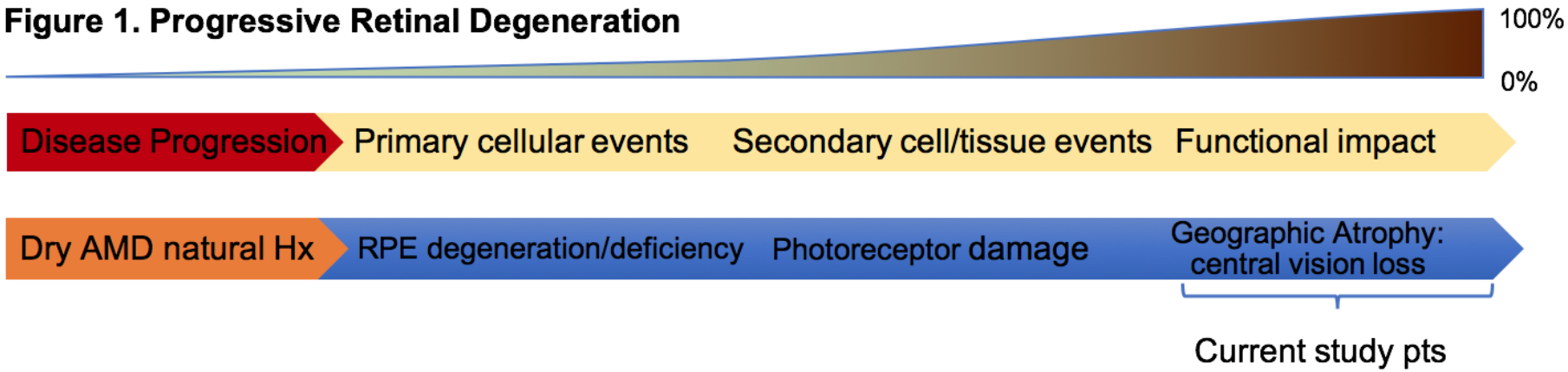
He has been Study Chair, Steering Committee Member or Principal Investigator of over 50 clinical trials. Dr. Ho has served on the US FDA Ophthalmic Device Panel, American Academy of Ophthalmology (AAO) Ophthalmic Retina Technology Assessment Committee, AAO Retina Measures Group, AAO IRIS Registry Committee and is past Chair of the AAO Retina Subspecialty Days and Vail Vitrectomy meetings. Through the Wills Eye Hospital Retina Fellowship he has mentored over 60 retina fellows and international research trainees. Dr. Ho has authored over 200 peer reviewed publications and several textbooks and is Editor-in-Chief of Current Opinion in Ophthalmology and Chief Medical Editor of Retina Today.

Overview of Age-Related Macular Degeneration Progression

Age-Related Macular Degeneration (AMD) is the leading cause of blindness in people > 50 years of age in the developed world

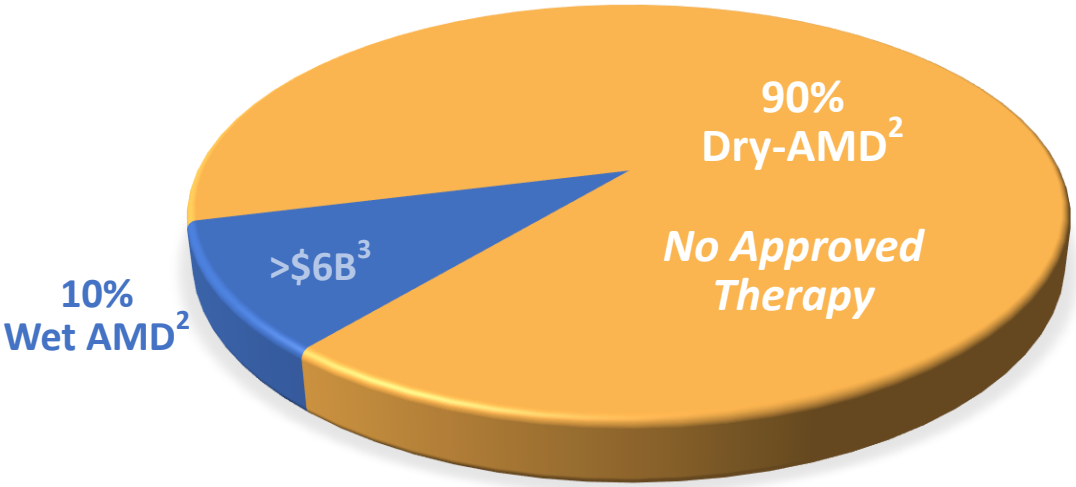
- Demographics will likely significantly increase the number of affected individuals

Figure 1. Progressive Retinal Degeneration



Significant Unmet Medical Need

- **AMD afflicts ~11 million people in the United States**
  - ~$6B in sales of approved wet AMD therapies: Lucentis® and Eylea®
  - But 90% of AMD patients have the dry form
  - Currently, there are no approved therapies for Dry-AMD aside from nutritional supplements[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) 2016 product sales summary based on publicly reported revenue figures for Lucentis and Eylea.

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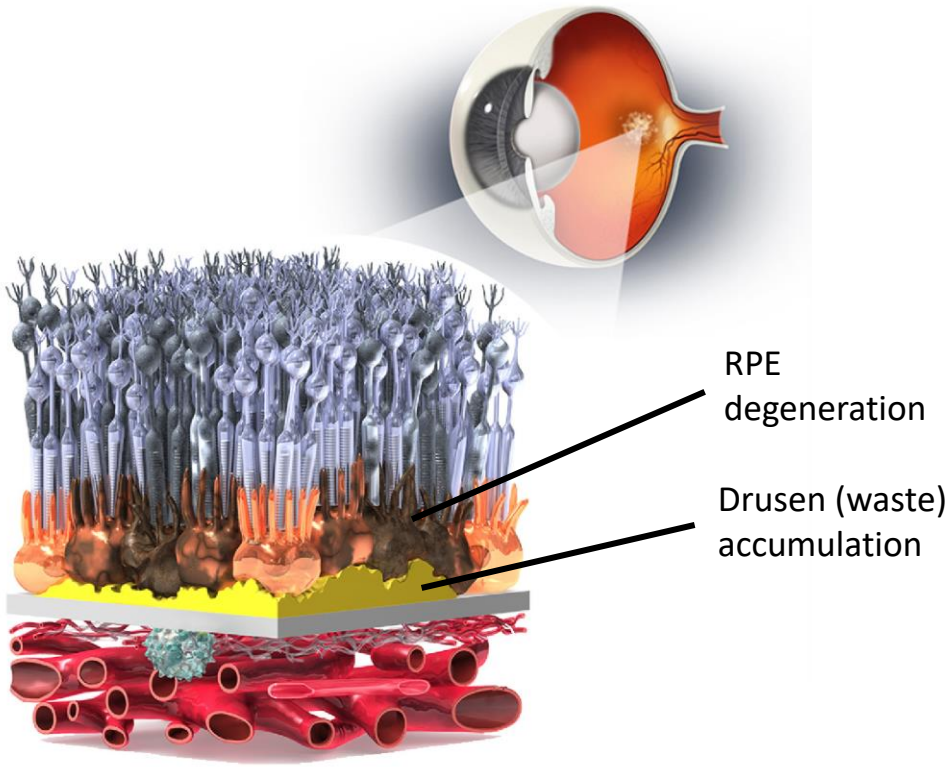
Dry AMD Pathogenesis

- **Neuronal retina (photoreceptors) produce metabolic waste**
- **With aging, retinal pigment epithelium (RPE) cells lose the ability to digest metabolic waste**
- **Accumulation of intra- and extracellular waste (drusen) leads to inflammation**
- **Bruch membrane and the RPE cells degenerate, leading to atrophy and progressive visual loss**
- **Risk factors include smoking, cholesterol, age, and area of retina affected**



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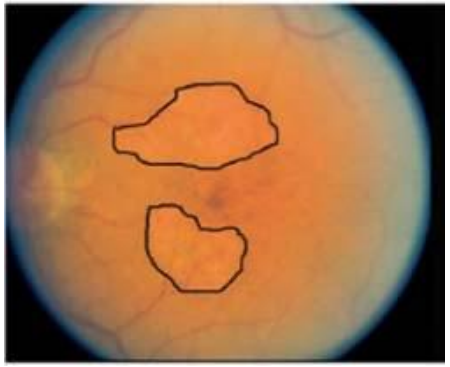
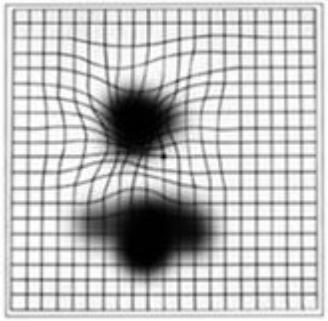
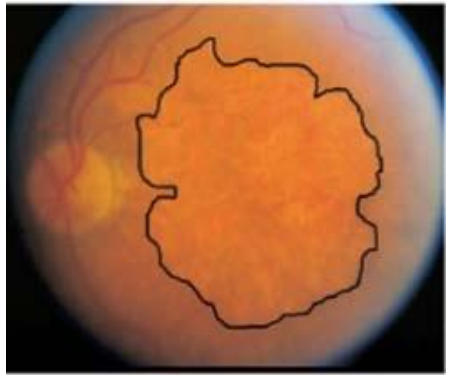
What Does The Patient Experience?

- **Extrafoveal GA**
  - Poor vision in dim light
  - Difficulty reading
  - Impaired Contrast
  - Reasonable central visual acuity
  - 50% lose 3+ lines vision within 2 years





- **Subfoveal GA**
  - Severe central vision loss
  - Eccentric fixation



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J.S. Sunness et al. Visual Function Abnormalities in Eyes with Age-related Geographic Atrophy of the Macula and Good Visual Acuity

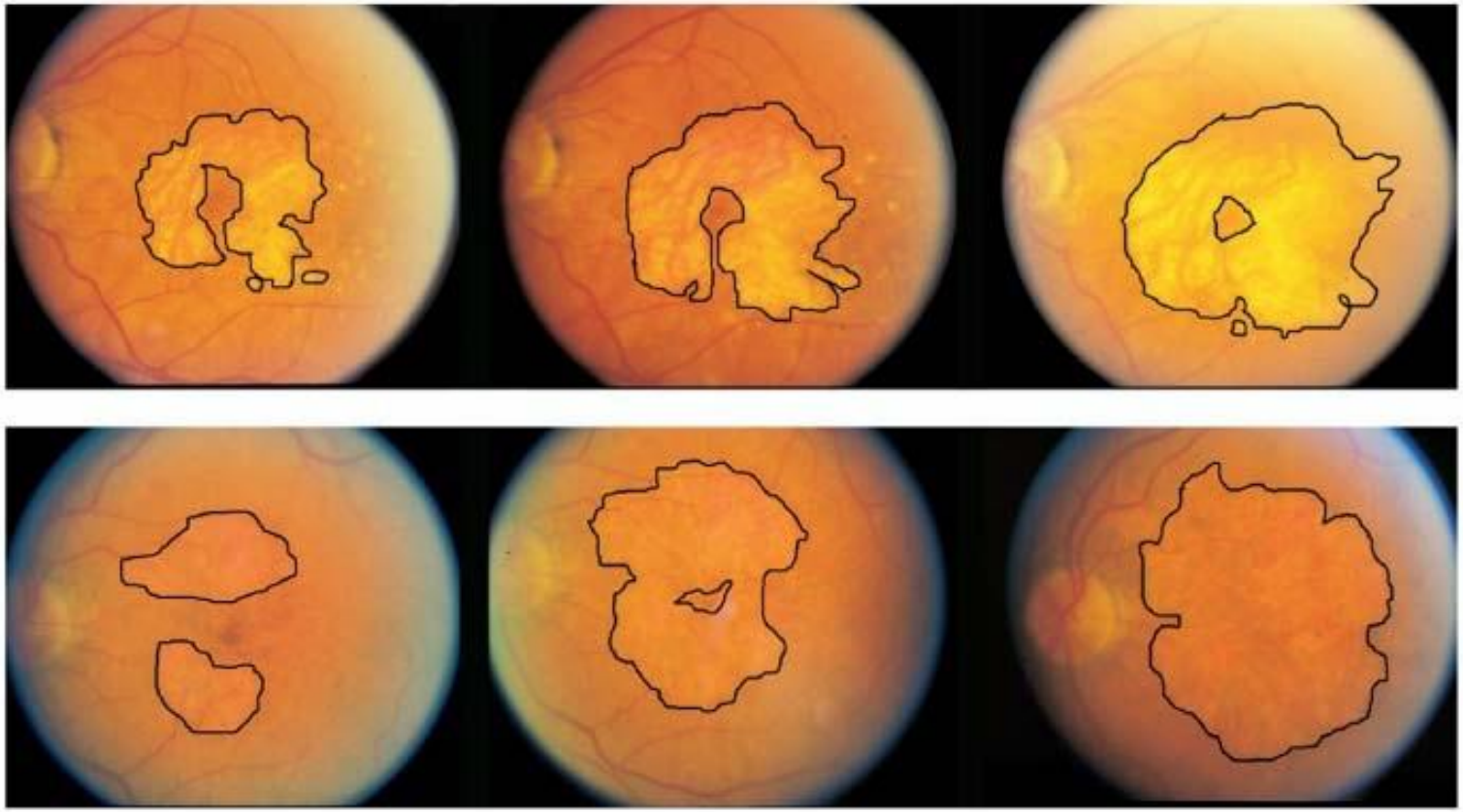
Diagnosis and Management

- **Clinical & Investigations**
  - Diagnosis usually made clinically
  - Atrophy in the presence of drusen/RPE change with the exclusion of other mimicking disorders
- **Current standard of care**
  - No proven intervention halts the progression of geographic atrophy (GA)
  - Smoking cessation
  - AREDS vitamins may slow progression to wet AMD

Natural History of Geographic Atrophy (GA)

#1

#2



Atrophy expands at median 2.1mm^2/year – confirmed with lampalizumab pivotal studies

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J.S. Sunness et al. Long-term Natural History of Geographic Atrophy from Age-Related Macular Degeneration

Standard Endpoints in Dry AMD Studies

- **Growth rate of geographic atrophy (GA)**
- **Best corrected visual acuity (BCVA)**
- **Low luminance visual acuity**
- **Reading speed**
  - Maximal reading speed
  - Critical print size
  - Lesion position may affect reading speed – limitations for validated languages
  - Reproducibility
- **Microperimetry**
- **Dark adaptation**
- **Contrast sensitivity**
- **Quality of life questionnaires**

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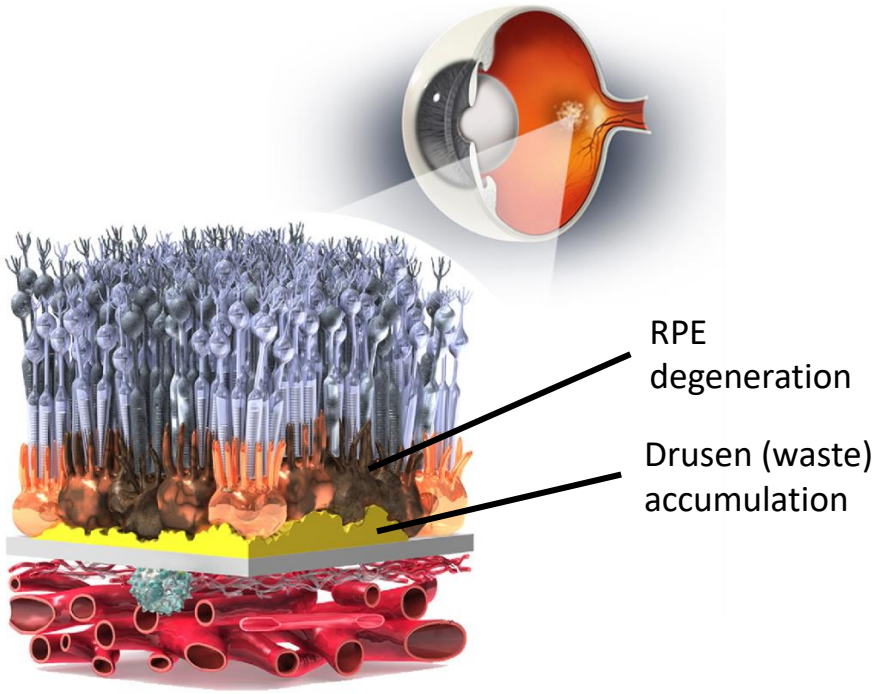
Potential Therapeutic Approaches

- **Protect remaining cells from damaging stimuli or environmental influences**
- **Reduce or stop stimuli of continuing damage (anti-inflammatory processes)**
- **Gene therapy (e.g. anti-inflammatory processes)**
- **Repair, replace or regenerate damaged cells (e.g. OpRegen cell therapy)**

OpRegen for Dry AMD

- **Dry AMD involves the loss of specialized retina cells (RPE)**
- **OpRegen is a <u>suspension of RPE cells</u>, manufactured from a cell line and injected into the sub-retinal space**



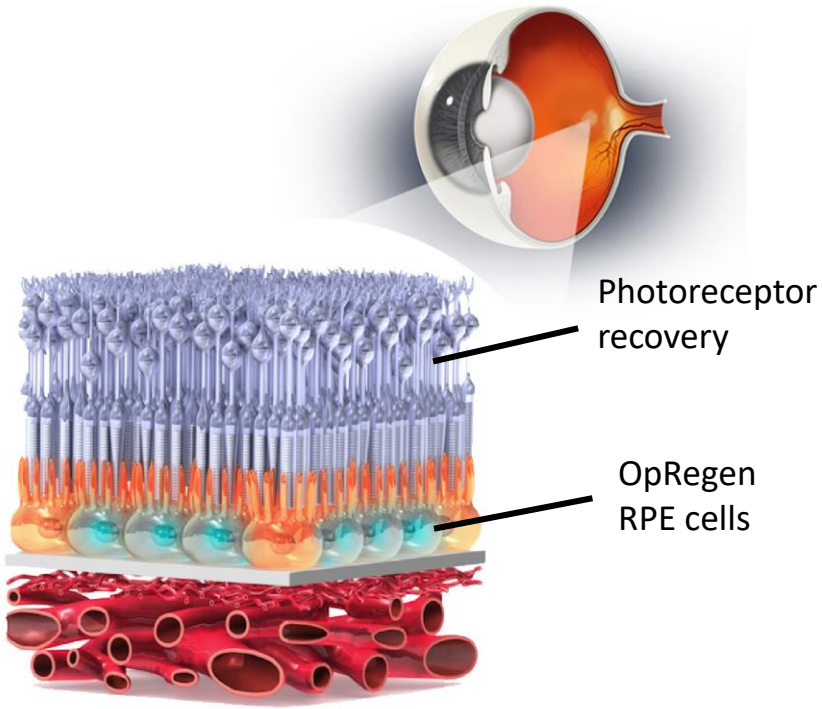


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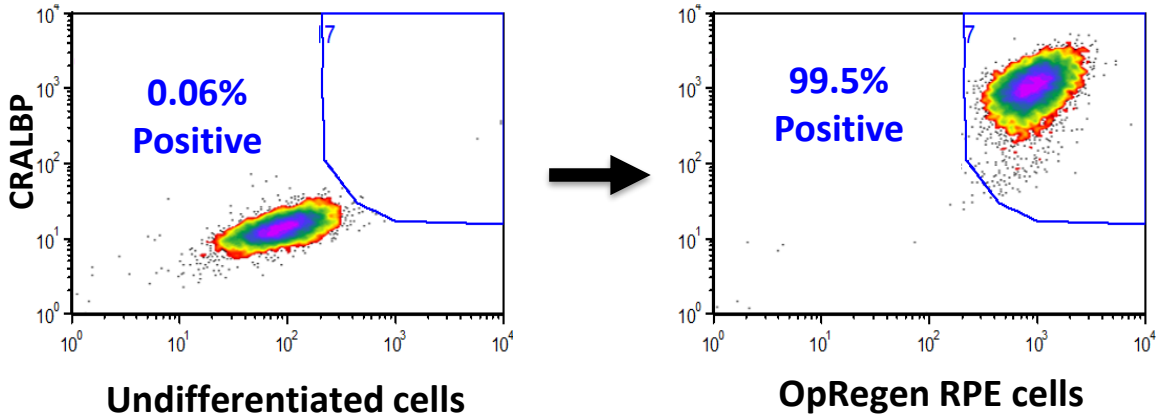
Image adapted from scienceofamd.org

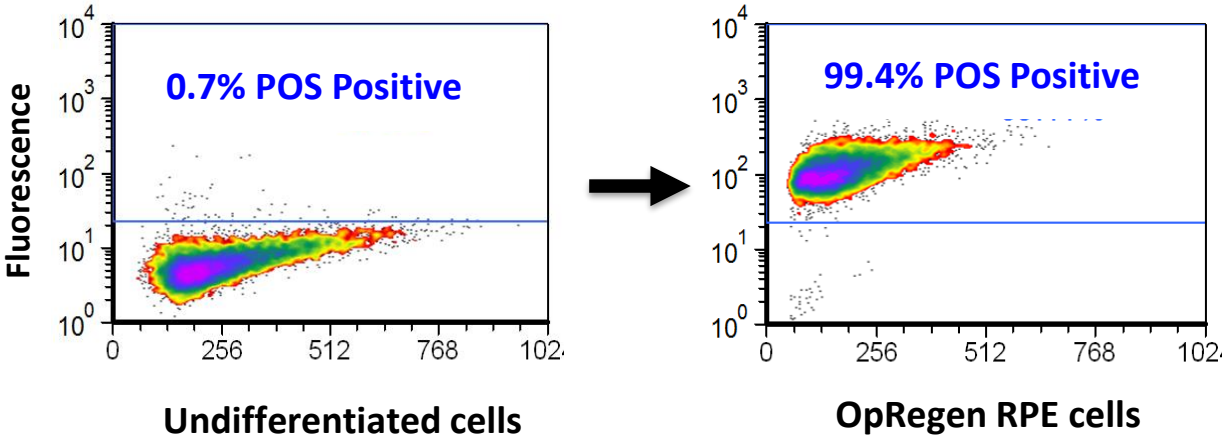
In-House cGMP Manufacturing of RPE Cells

The lineage of an established pluripotent cell line can be controlled to create a population of nearly 100% RPE cells

Identity Assay (purity)



Functional Assay (phagocytosis)



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OpRegen Clinical Study

Phase I/IIa Dose Escalation Safety and Efficacy Study of Human Embryonic Stem Cell-Derived Retinal Pigment Epithelium Cells Transplanted Subretinally in Patients with Advanced Dry-Form Age-Related Macular Degeneration (Geographic Atrophy)

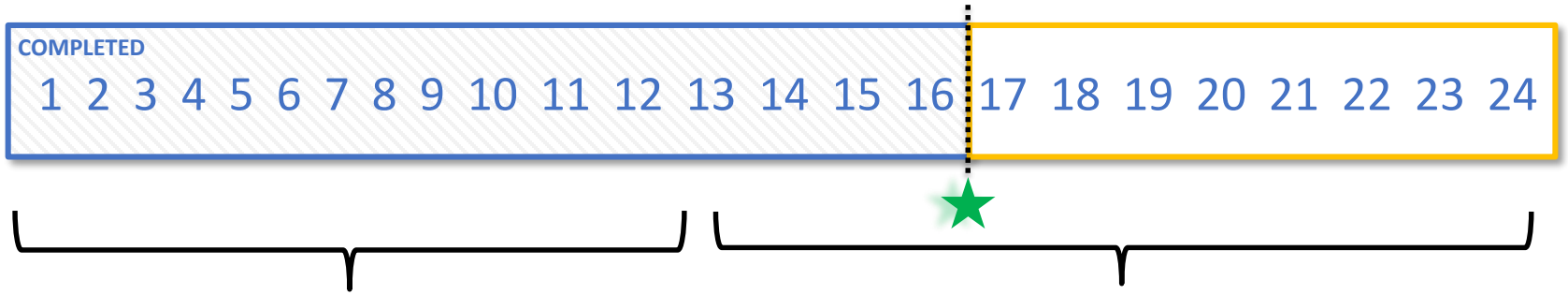
Ongoing Phase I/IIa OpRegen Clinical Study

Purpose: To evaluate the safety and efficacy of subretinally transplanted RPE cells in patients with advanced dry AMD with geographic atrophy (GA)

Design: Open label, single-arm, and multi-center trial

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

Enrollment:



Part I

Safety and Anatomical Changes

Legally Blind (>20/200)

Part II

Safety and Visual Acuity

Impaired Vision (20/65 to 20/250)

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Study Objectives

Primary Objective:

To evaluate the safety and tolerability of human embryonic stem cell-derived retinal pigment epithelium cells (OpRegen), transplanted subretinally to subjects with advanced dry age-related macular degeneration (AMD) with geographic atrophy (GA)

Secondary Objective:

To evaluate survival and possible effects of OpRegen treatment by assessing changes in retinal structure and function

Exploratory Objective:

Evaluate safety in cohort 4 participants who receive a subretinal injection of OpRegen “thaw and inject” preparation using the Orbit Subretinal Delivery System (Orbit SDS)

Phase I/IIa OpRegen Clinical Study
Patient Characteristics

Parameter	Part 1 - Cohorts 1-3 (legally blind)	Part 2 - Cohort 4 (better visual acuity)
Patients	12	12 (4 completed)
Baseline BCVA	≥20/200	≤20/64 to ≥20/250
ETDRS BCVA: mean (SD/min-max)	23.7 (± 11.7/0-39) letters [23 letters≈20/400]	55 (± 13.5/42-59) letters [55 letters≈20/80]
GA area: mean (SD/min-max)	12.7 (± 7/6-30) mm^2	7.1 (± 1.4/5.5-8.3) mm^2

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Data presented at 2019 American Academy of Ophthalmology Annual Meeting

Primary Endpoints: Systemic and Ocular Safety and Tolerability

Most reported AEs were eye-related (n=121 events); most frequent were:

AE Term	PPV Treated (n=15)
Conjunctival Hemorrhage	13/15
Eye Irritation	1/15
Subretinal Fluid, persisting >24 hrs	4/15; all resorbed within 72 hours
Subretinal Pigmentation	10/15 (potentially a positive sign)
CNV	1/15 (> 2 years post-procedure)
Lamellar hole	2/15 (associated with ERM)
Retinoschisis	1/15 (associated with ERM)
ERM (new/worsened)	13/15 (most mild – moderate)

Ocular SAEs	PPV treated (n=15)
ERM	1/15, severe ERM requiring surgical peel; BCVA improving to a few letters above baseline and restoration of retinal structure post-op
Retinal Detachment	1/15 (2 weeks post-procedure; causality unknown)

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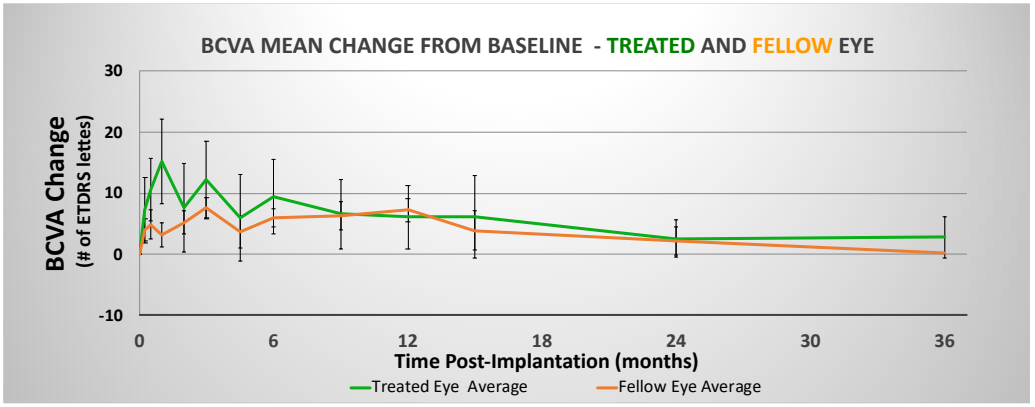
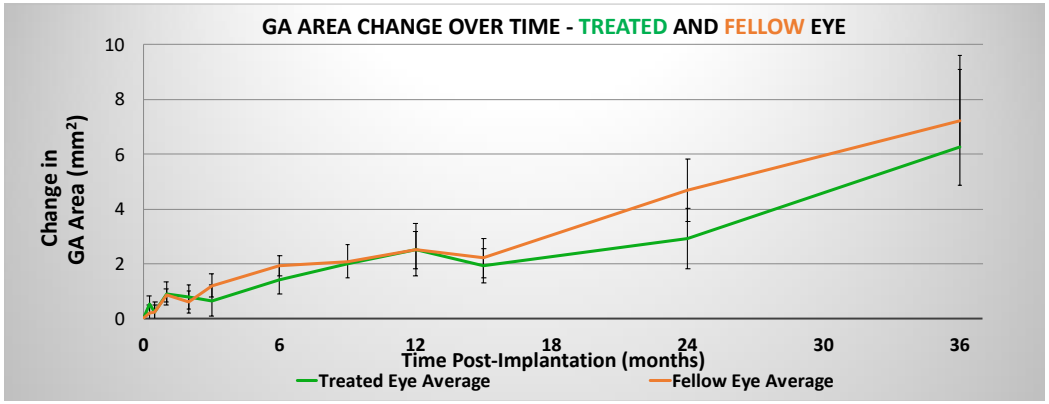
Phase I/IIa OpRegen Clinical Study Results

BCVA & GA change from baseline (Cohort 1-3, legally blind at baseline, n=12)

BCVA



GA



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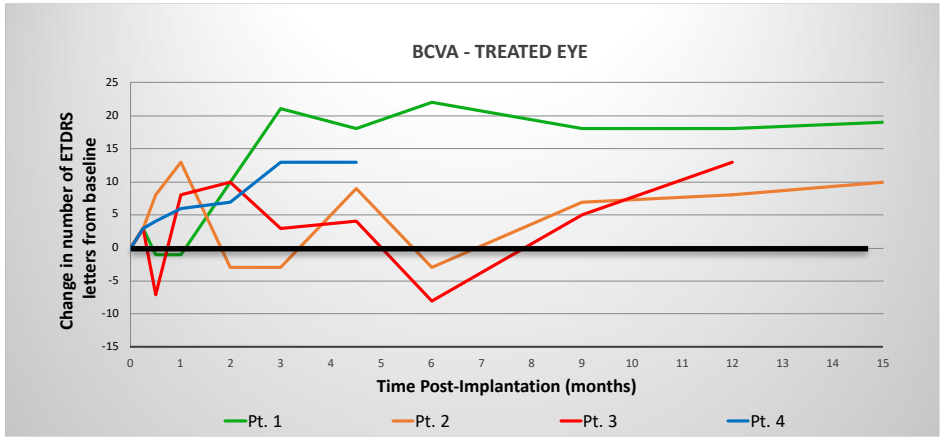
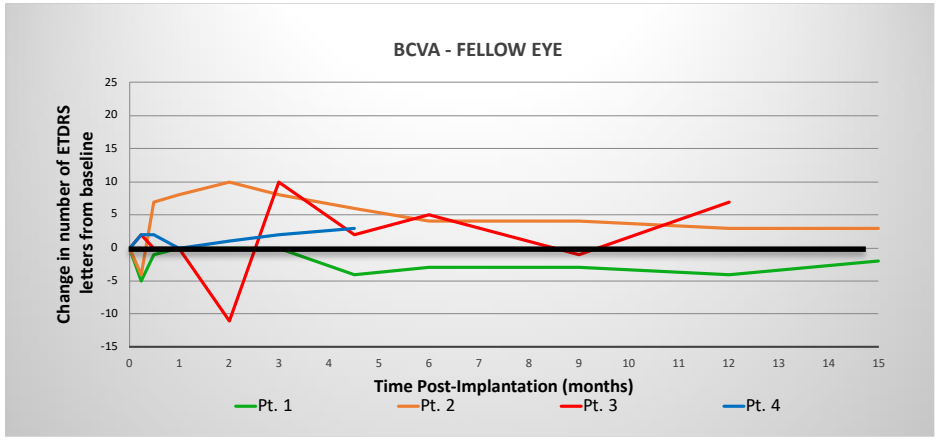
Phase I/IIa OpRegen Clinical Study Results: Cohort 4

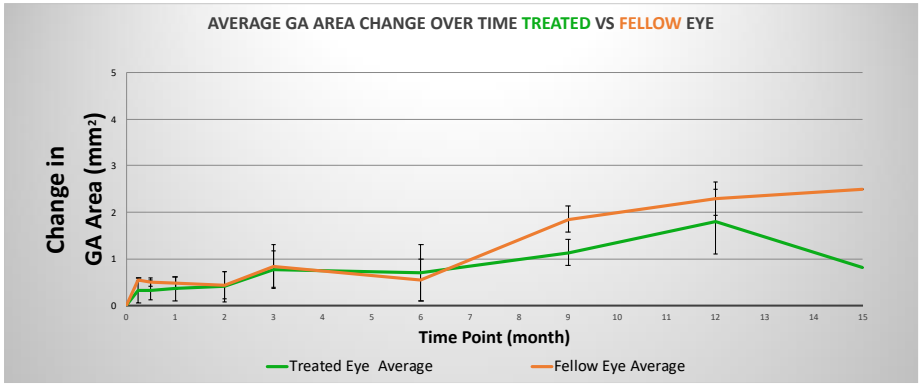
BCVA & GA Change from Baseline Over Time (n = 4)

BCVA





GA



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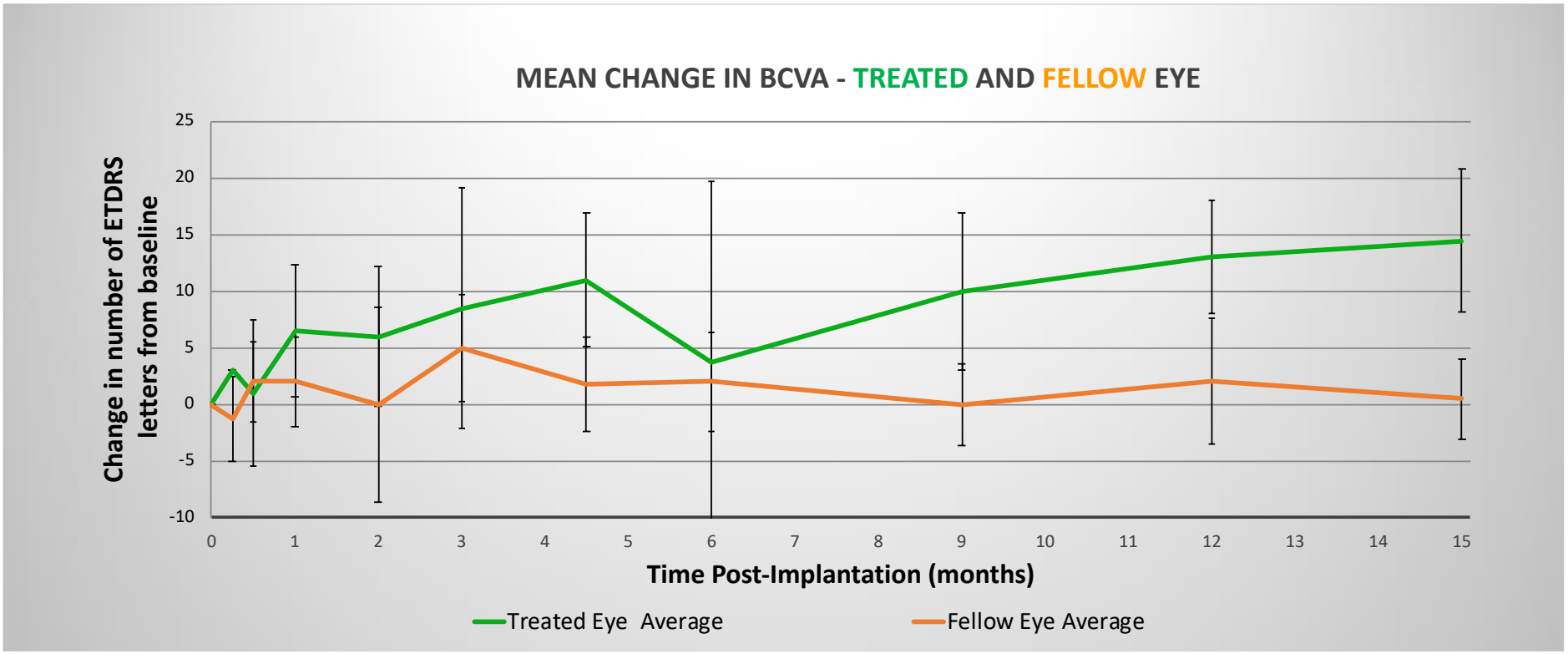
Data presented at 2019 American Academy of Ophthalmology Annual Meeting

Phase I/IIa OpRegen Clinical Study Results: Cohort 4

Mean Best Corrected Visual Acuity (BCVA) of 20/65 to 20/250 Patients via Early Treatment Diabetic Retinopathy Study (ETDRS)



(n=4)

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Phase I/IIa OpRegen Clinical Study Individual Results: Cohort 4

Individual Changes in Best Corrected Visual Acuity at Last Observation

Subject #	Change to Treated Eye	Last Timepoint*	Treatment Route
16	+ 13 letters	Month 4.5	Orbit SDS
15	+ 13 letters	Month 12	PPV/retinotomy
14	+ 10 letters	Month 15	PPV/retinotomy
13	+ 19 letters	Month 15	PPV/retinotomy

Gap in timepoints attributable to acquisition and validation of Orbit SDS following 510k approval in December 2018

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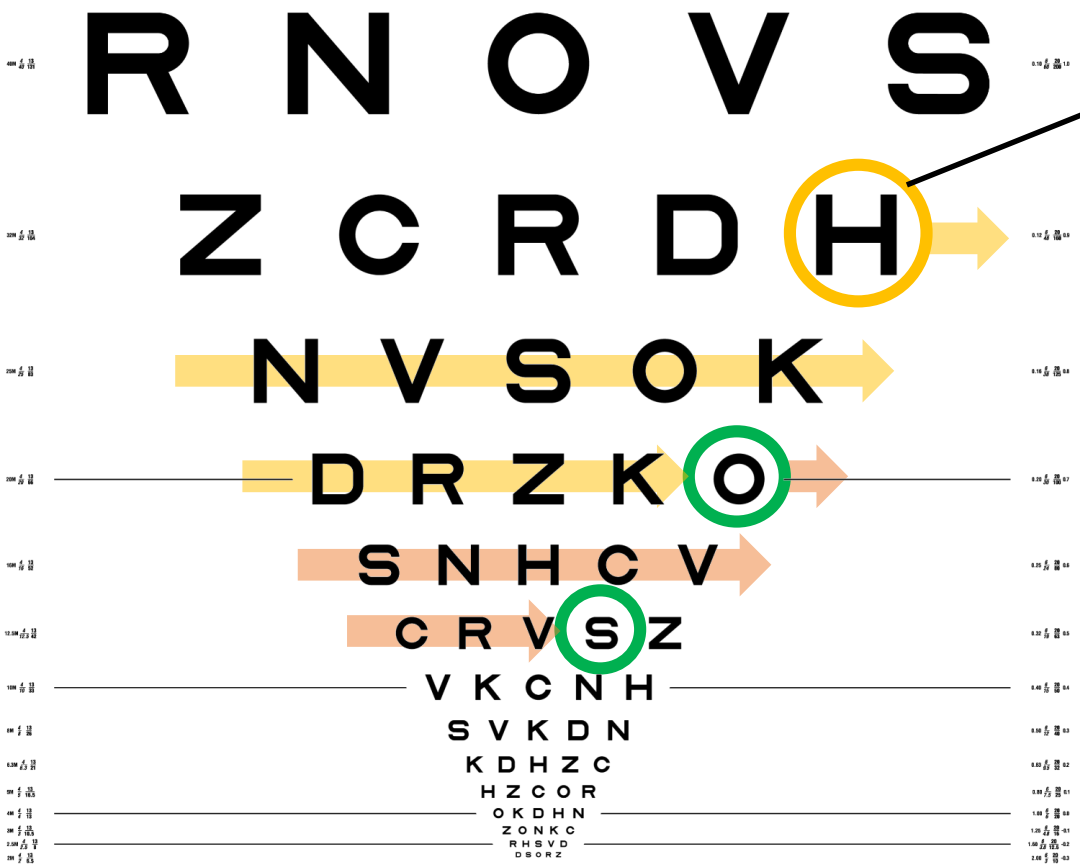
Visual Acuity Test "Letter Improvement"



ETDRS Visual Acuity Chart #3

Initial Visual Acuity Score
(20/160)

10
Letter Improvement
(20/100)

19
Letter Improvement
(20/63)

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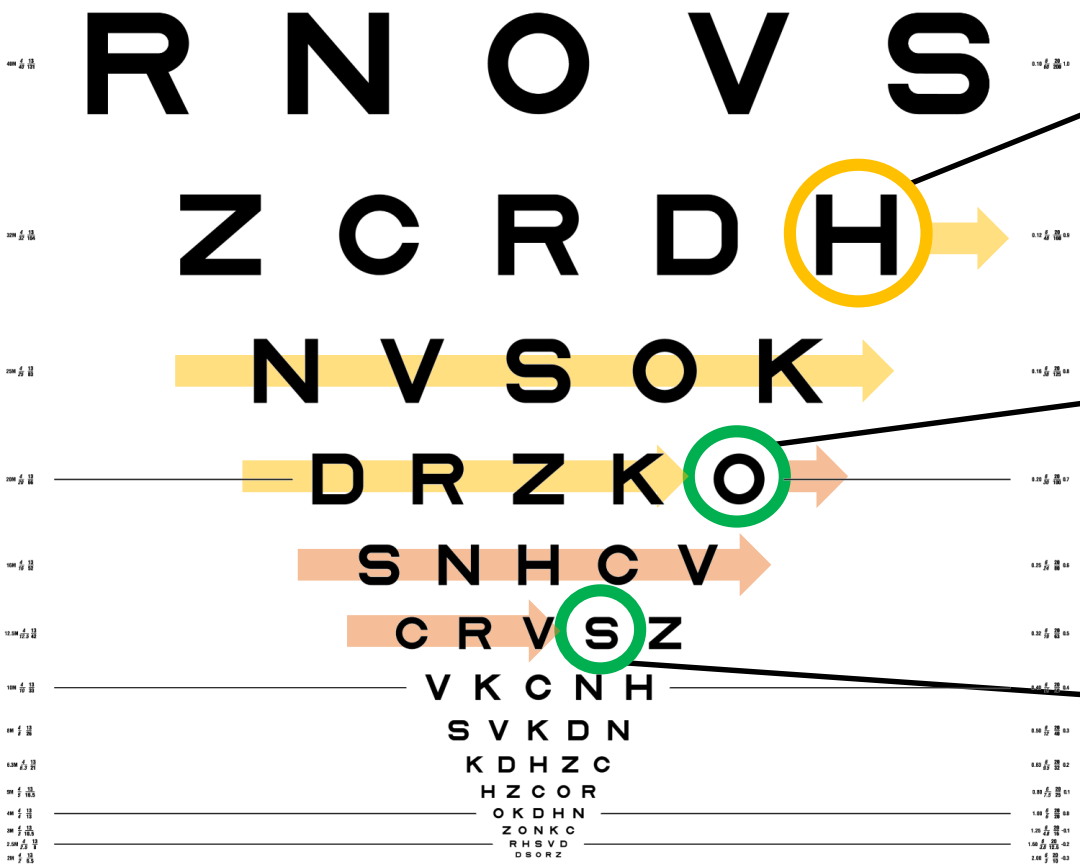
Visual Acuity Test "Letter Improvement"



Initial Visual Acuity Score
(20/160)

10
Letter Improvement
(20/100)

19
Letter Improvement
(20/63)

ETDRS Visual Acuity Chart #3

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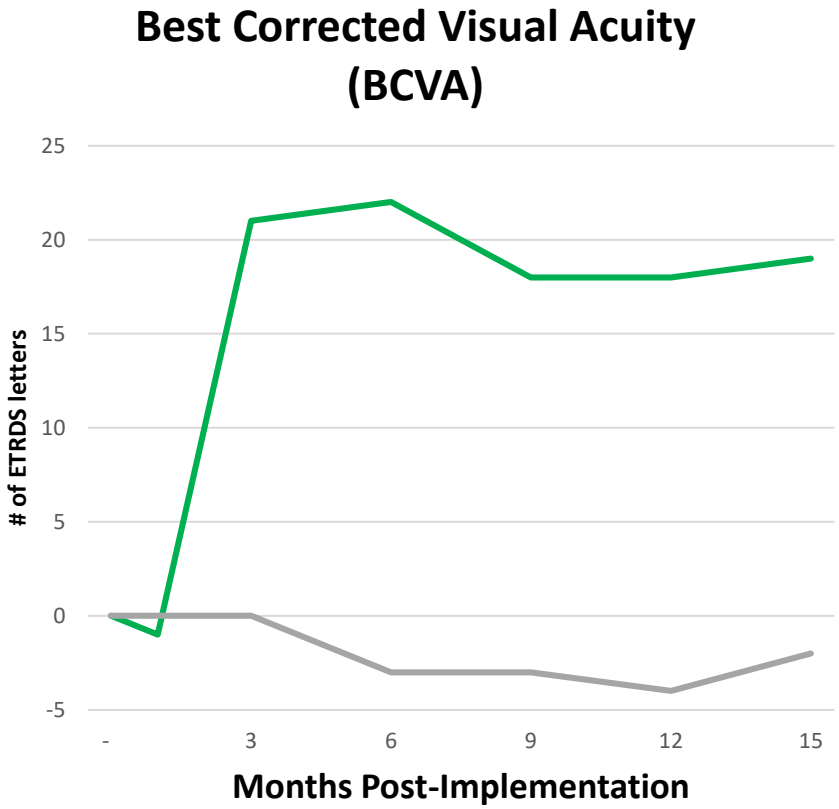
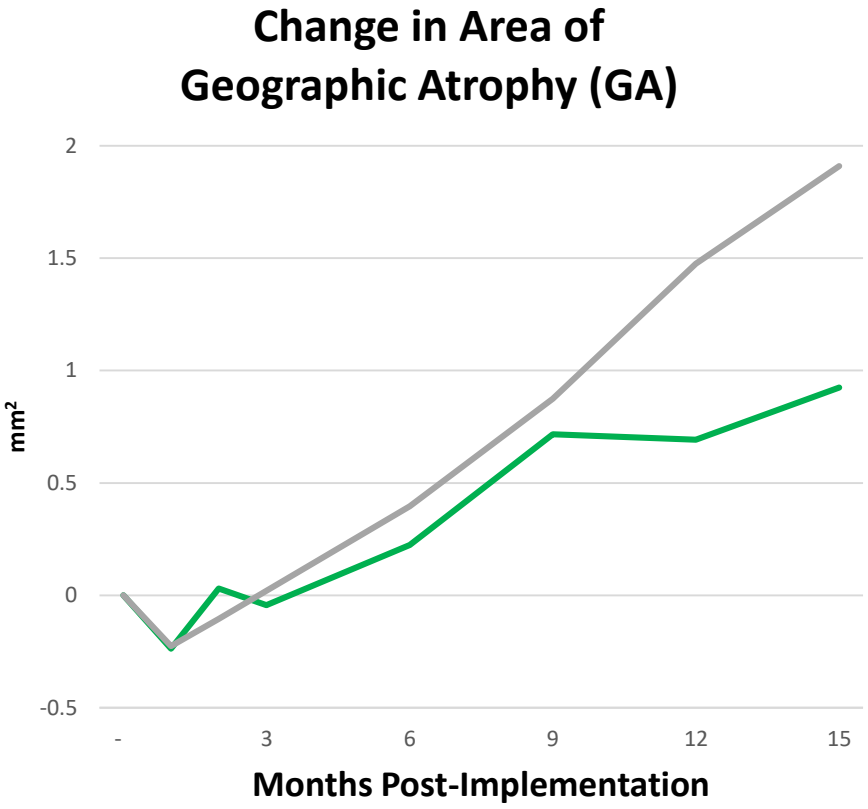
Visual Acuity Case Study (Patient #13)





Treated Eye — Fellow Eye (Control)

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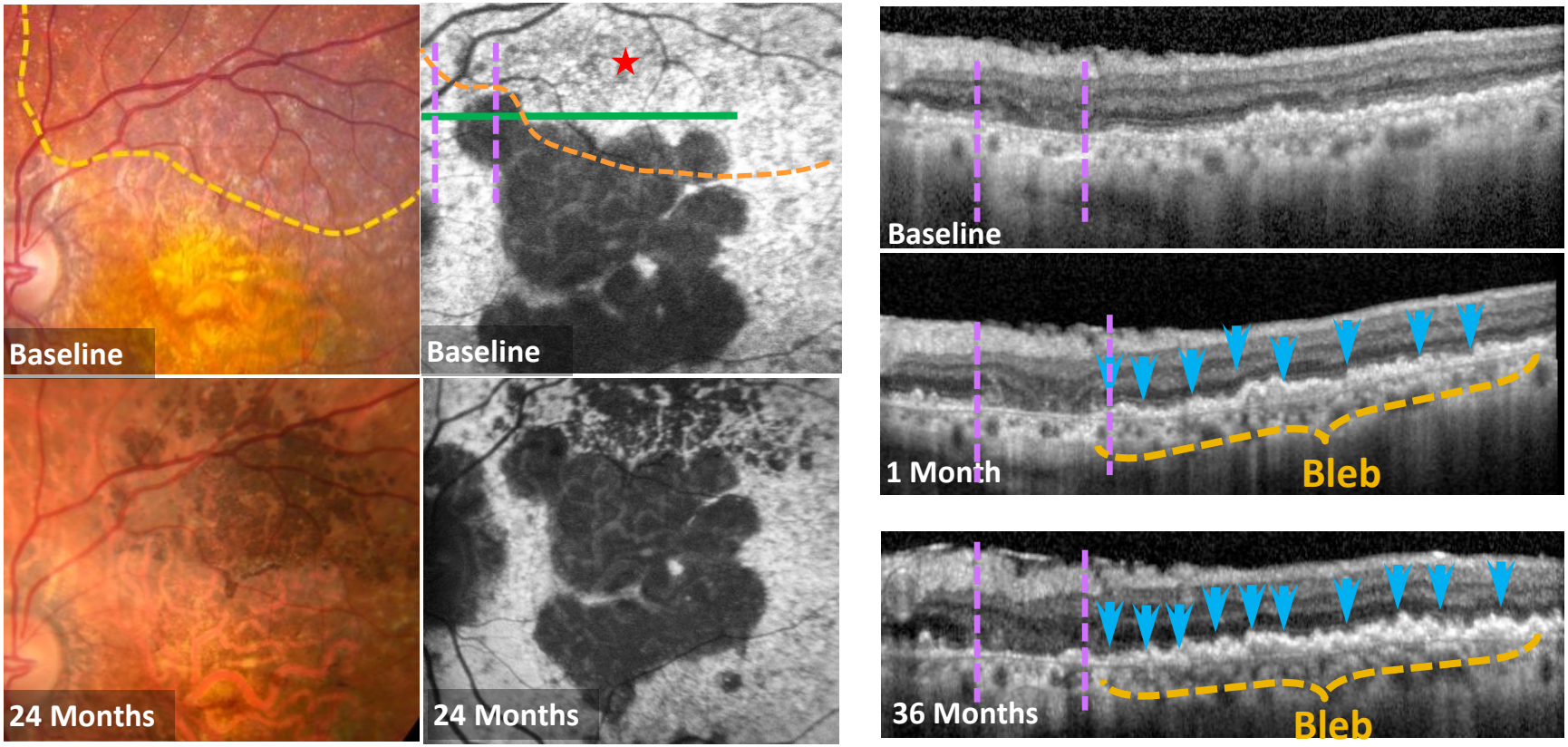
Cell Engraftment - Patient #2

(via PPV)

CFP | FAF | OCT



Bleb border, Subretinal injection location, GA border, Irregular hyper-reflectance

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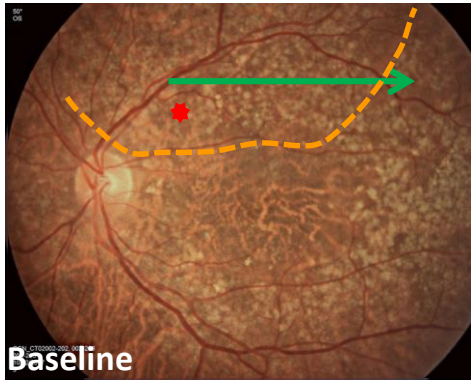
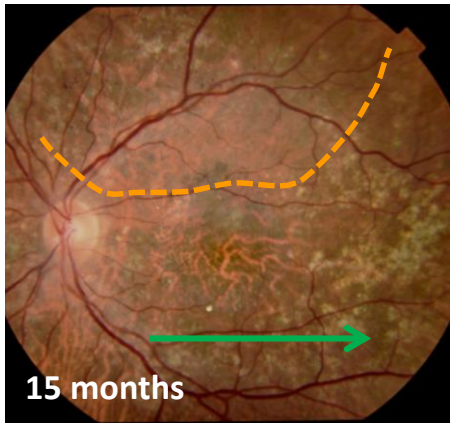
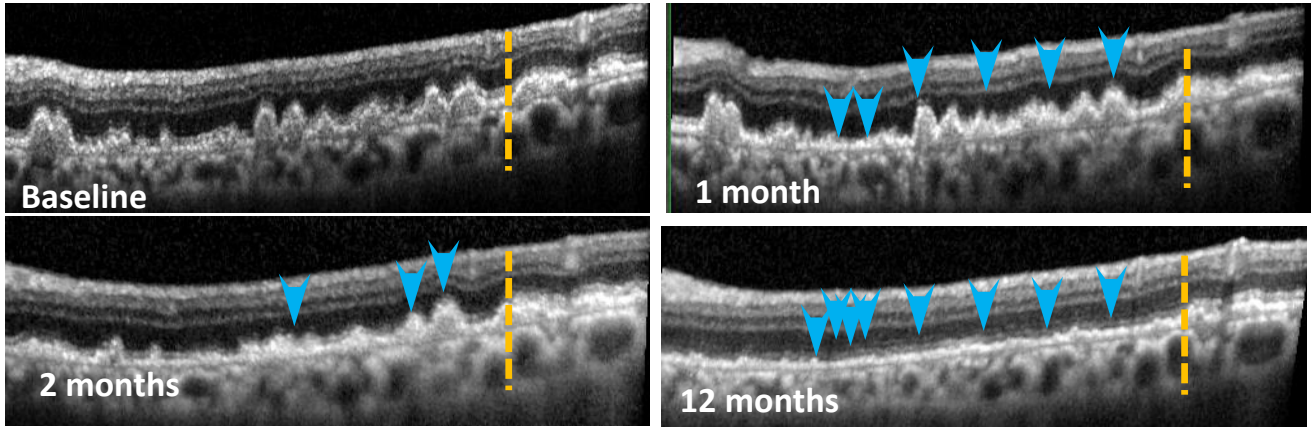
Drusen Reduction in Treated Area – Patient #8

(via PPV)

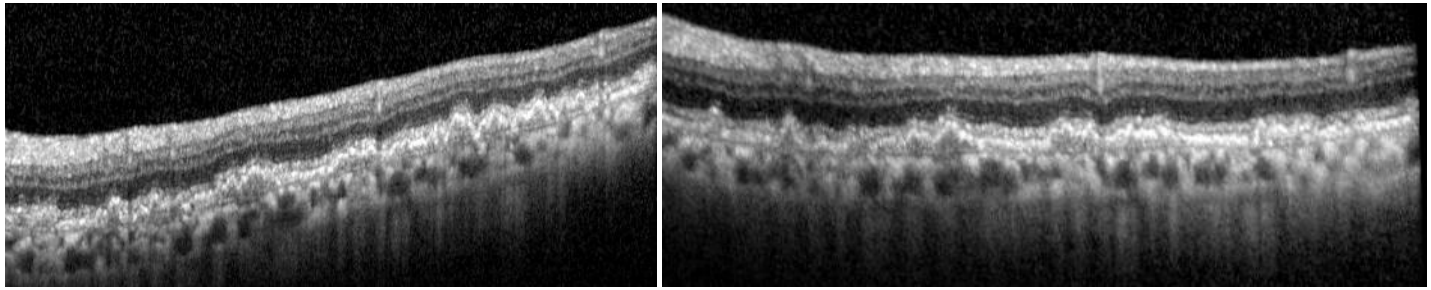




Treated Area



Untreated Area



Bleb border, Subretinal injection location, Irregular hyper-reflectance

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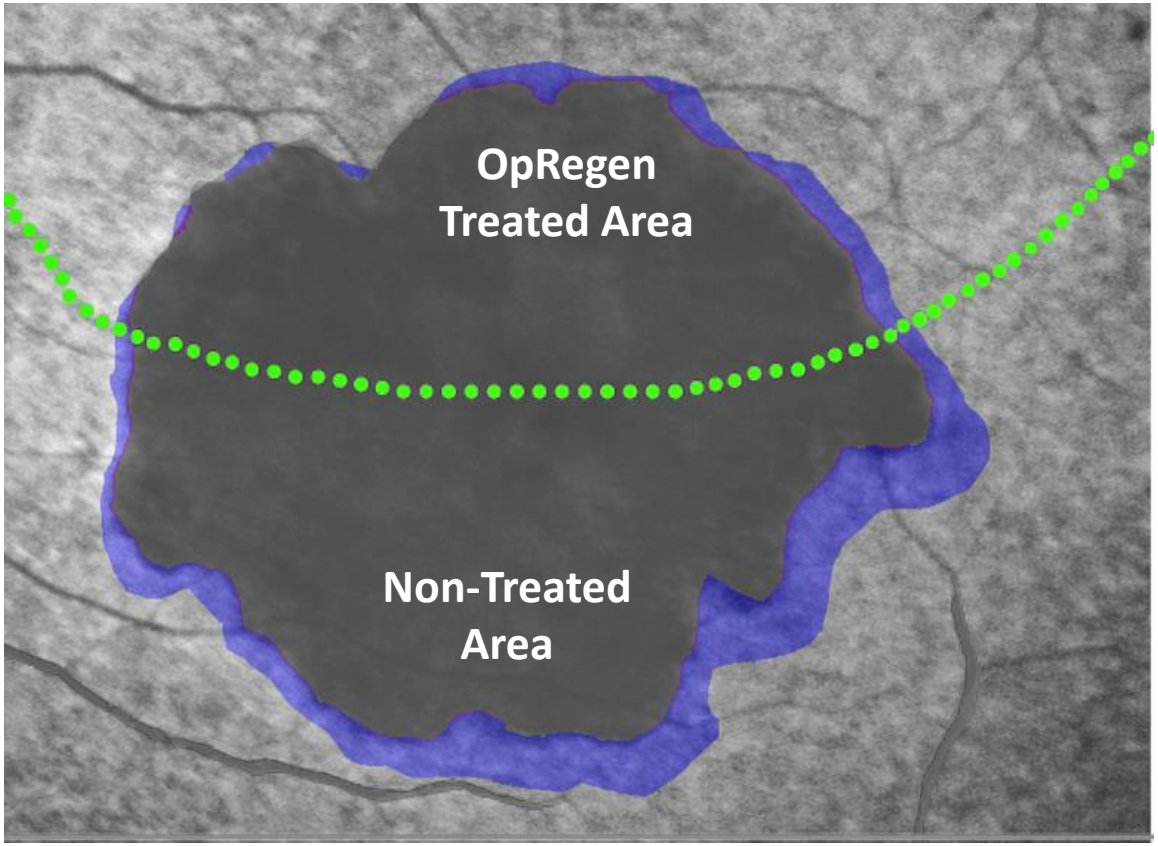
Reduced Growth of GA – Patient #9

(via PPV)

Reduced directional growth in area of GA observed



Bleb border (boundary of transplanted OpRegen cells)

- **Asymmetrical, reduced growth of the area of GA in the OpRegen-treated area was observed at 12 months**

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Data presented at 2019 American Academy of Ophthalmology Annual Meeting

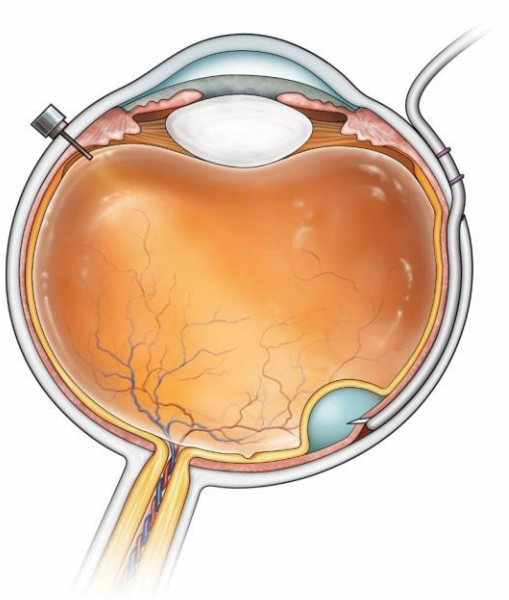
Update on Cohort 4 (Better Visual Acuity Group)

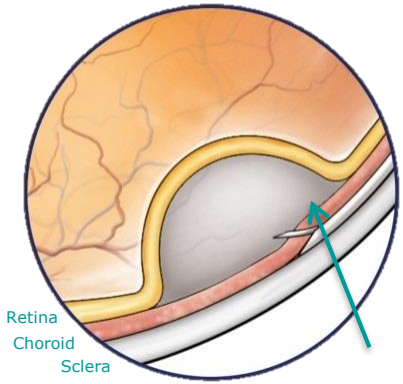
- **Ongoing recruitment – 4 enrolled (planned total of 12)**
- **BCVA between 20/250-20/64 in the study eye, smaller area of GA**
- **Two formulations**
  - OpRegen BSS Plus (3 subjects enrolled using PPV route)
  - OpRegen 'Thaw-And-Inject' (TAI) uses CryoStor CS5, a serum-free, animal-free GMP grade cryopreservation solution (1 subject enrolled to date using Orbit SDS)

OpRegen TAI & Orbit SDS Update

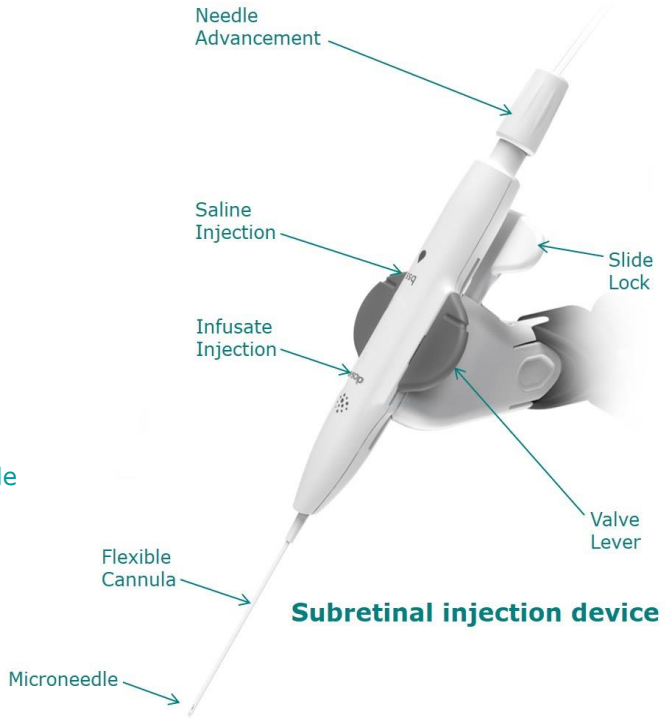
Update on Cohort 4 (Better Visual Acuity Group)
(cont)

- **New approach to subretinal delivery uses the Orbit SDS to access the subretinal space via a suprachoroidal route**
  - Avoids need for vitrectomy and retinotomy
  - Better dose control and fewer AEs due to cell efflux
  - FDA 510k cleared device





Extended microneedle



Subretinal injection device

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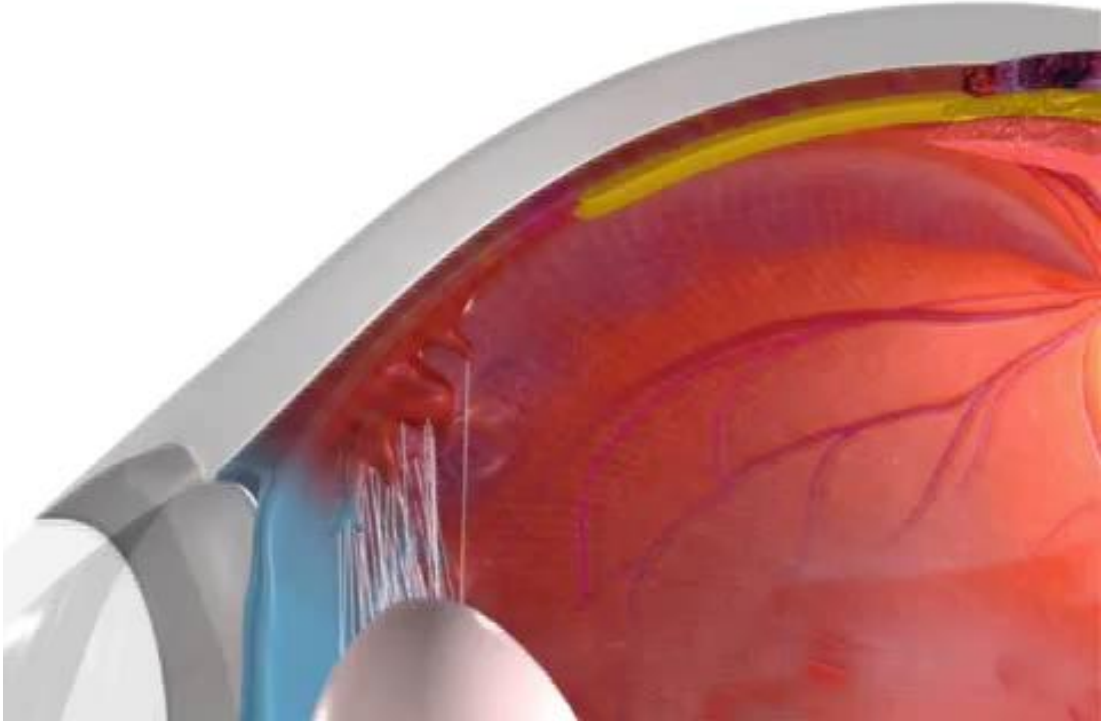
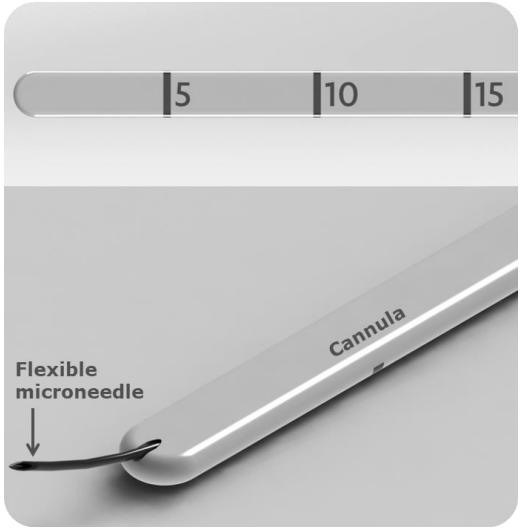
Subretinal Delivery via the Suprachoroidal Space





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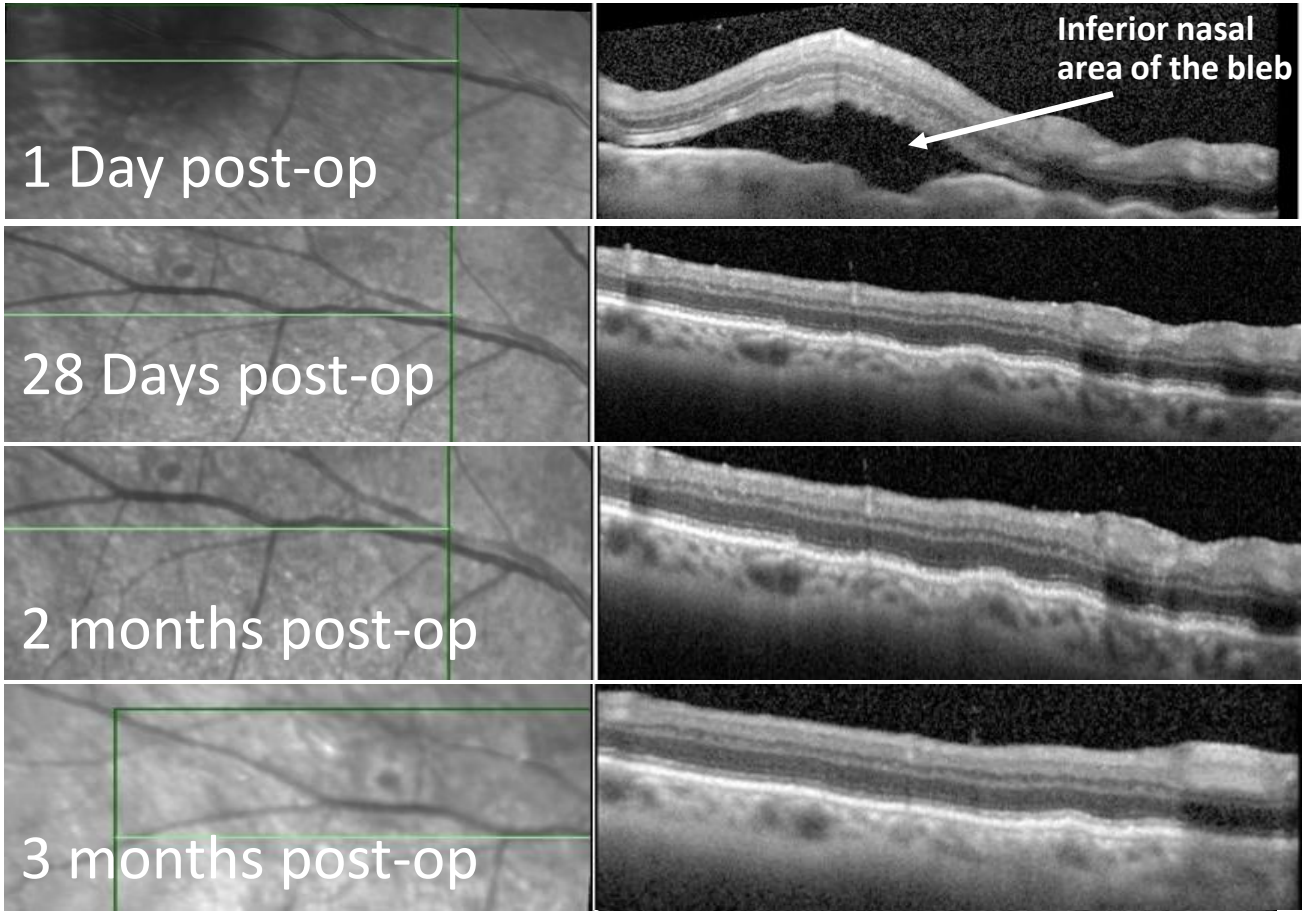
Suprachoroidal to Subretinal Delivery

Phase I/IIa OpRegen Clinical Study: Orbit SDS Case Study

- **Subretinal injection of OpRegen suspension performed July 2019**
  - No operational complications
  - No unexpected post-op complications
  - Subject doing well, no unexpected AEs as of 4.5 months post-op

- **Subject has demonstrated signs of improved visual acuity in treated eye**
  - 13 letter improvement in ETDRS letters at 4.5 months post-injection

Patient #16 (via Orbit SDS) – Bleb Area



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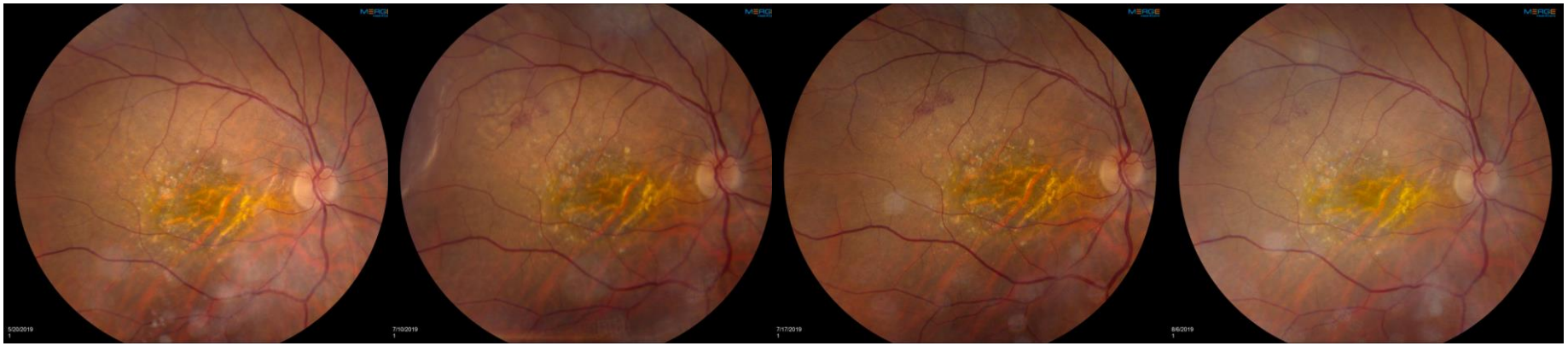
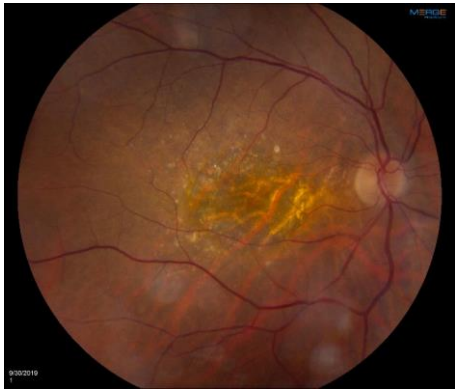
Patient #16 – First OpRegen TAI & Orbit SDS Subject



Screening | 1 Day post-op | 7 Days post-op | 28 Days post-op



3 Months post-op

- Mild subretinal hemorrhage – Completely resolved and absorbed by 3 months post-op

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Summary (Part I)

- Following transplantation of OpRegen cells, there is rapid healing of the injection sites
- Subretinal pigmentation in the treated area was present in 10/15 PPV-treated subjects, and has remained stable for up to 3 years in some subjects
- There are additional signs of RPE engraftment in the area of implantation; subretinal hyper-reflective areas on OCT in humans and in pigs (in pigs this correlated with transplanted cells via histology)
- New or worsening ERMs observed in 13/15 PPV-treated subjects, most mild to moderate in severity. One severe ERM was peeled 10 weeks post-transplant with full recovery. After peeling, complete recovery to baseline BCVA and evidence of structural improvement on GA borders was observed
- There was one case of retinal detachment in a PPV-treated subject 2 weeks post-op, unknown whether a result of surgical procedure, implanted cells, or a combination of events

Summary (Part II)

- Subretinal transplantation of OpRegen appears well-tolerated with signs of improved retinal structure in the treated areas in some cases
- Asymmetrical, reduced directional growth of the GA in the treated area was observed in 3 subjects. This requires long term follow-up because GA expansion is a progressive, but slow process
- Drusen reduction in area of transplant was observed in 2 subjects
- Possible improvement in outer retinal structure has been observed in some subjects
- Cohort 4 is ongoing in subjects with better baseline vision (<20/64), smaller areas of GA, and a known history of disease progression
- An alternative procedure to access the subretinal space via the Orbit SDS is ongoing with promising early results

Next Steps

- Second Orbit SDS patient is scheduled for surgery in early December
- DSMB will meet to review the case 1 month following
- Possible removal of protocol mandated stagger, which will allow open, concurrent enrollment
- Updated data will be presented at the 2020 ARVO meeting in Baltimore

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www.lineagecell.com

Spinal Cord Injury Overview

John Steeves, B.Sc., Ph.D.

John Steeves, Professor and Founding Director

ICORD (International Collaboration On Repair Discoveries)
UBC & Vancouver General Hospital (VGH)

- **Appointed University of British Columbia (UBC) since 1979**
- **Founded ICORD in 1995, generated $50 million for Blusson Spinal Cord Center**
- **ICORD is engaged in all aspects of SCI research (~35 faculty + 150 trainees)**
- **President of NeuroTherapeutics Inc. (1999-2002)**
- **ISCoS Scientific Chair and ISCoS Executive**
- **ASIA Board Member and ASIA Program Committee Chair**
- **International Neurological Standards Committee**
- **Distinguished Scholar, Peter Wall Institute of Advanced Studies, UBC**
- **Founded and Co-Chair of SCOPE (2006 -)**

Blusson Spinal Cord Center at VGH (home of ICORD)

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Why Spinal Cord Injury (SCI) Matters

Lucas Linder was paralyzed from the neck down following a vehicle accident.

One year following treatment with OPC1, he had regained significant motor function and threw out the first pitch at a Major League Baseball game.

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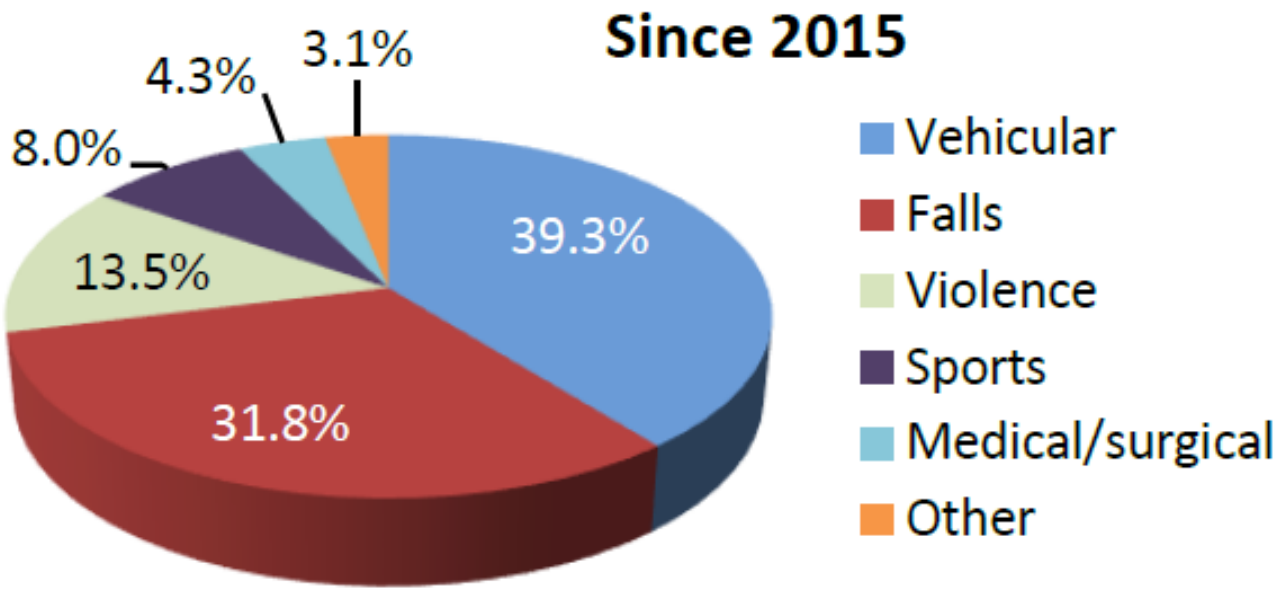
Spinal Cord Injury (SCI) Statistics*

- **<u>Incidence</u>: Approximately 18,000 new cases each year**
- **<u>Prevalence</u>: Between 249,000 and 363,000 people in the US**
- **<u>SCI causes:</u>**



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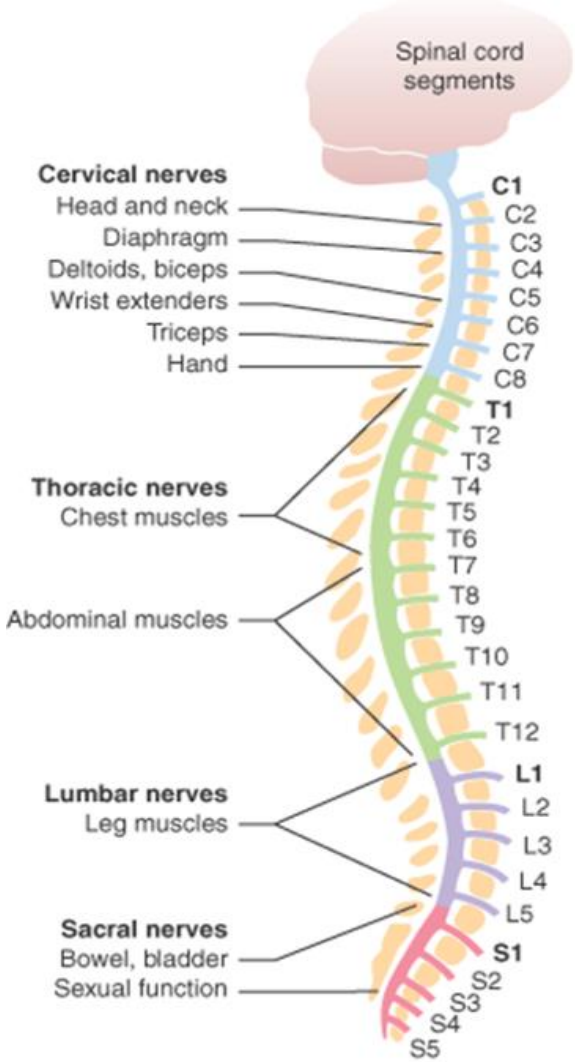
** Source: National Spinal Cord Injury Statistical Center*

SCI Overview

- **SCI creates a significant burden for patients and caregivers***
  - **67% of patients are unemployed 10 years post-injury**
  - **Lifetime healthcare costs can reach $5 million for one patient**
- **Motor level improvements can translate into clinically significant improvements in self-care and reductions in cost of care**
- **The therapeutic goal is to restore additional arm, hand, and finger function, increasing independence and quality of life**



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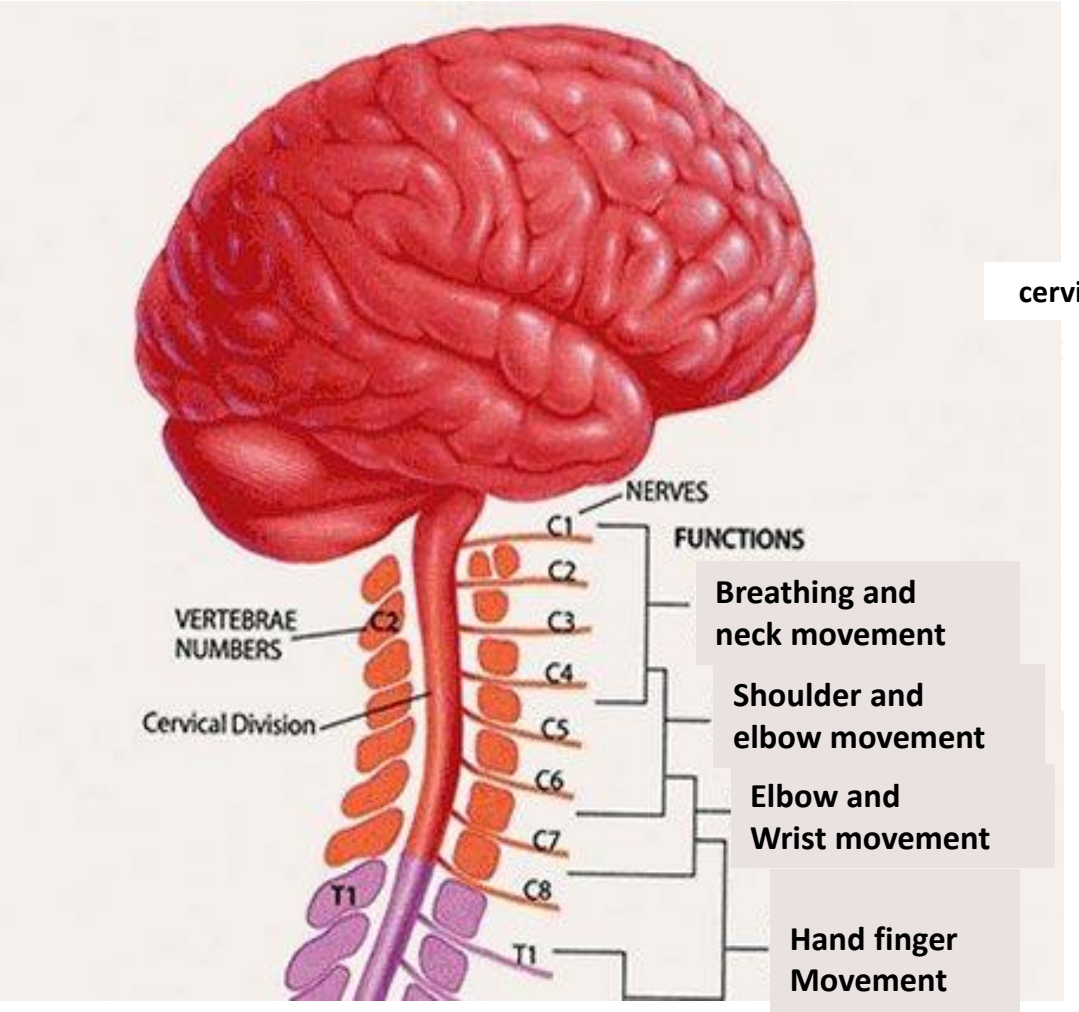
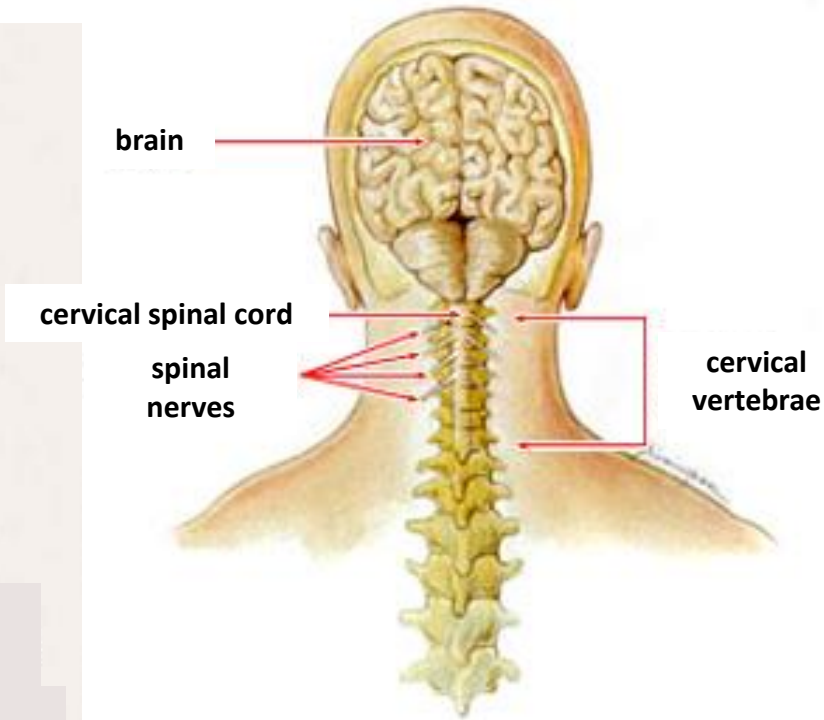
(*) National SCI Statistical Center, 2019 SCI Data Sheet.

Cervical Spinal Cord Motor Functions





C5 – elbow flexors

C6 – wrist extensors

C7 – elbow extensors

C8 – hand finger flexors

T1 – small finger abductor

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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

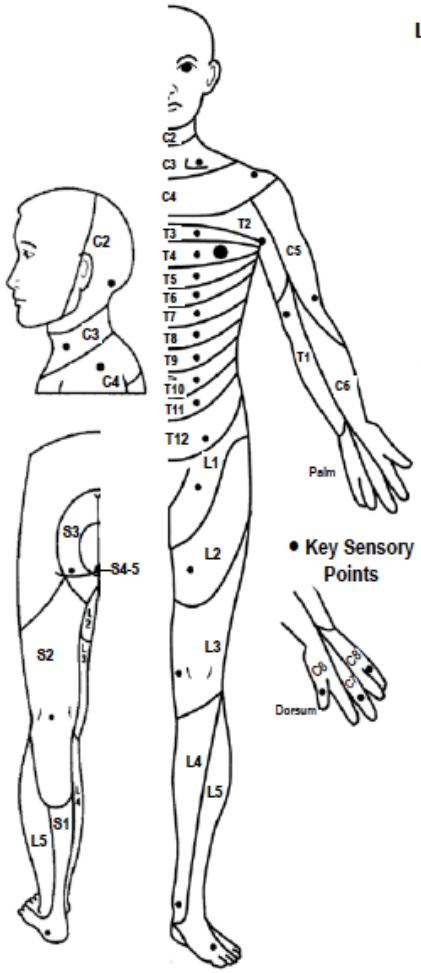
MOTOR KEY MUSCLES		SENSORY KEY SENSORY POINTS Light Touch (LT)	Pin Prick (PP)
	C2		
	C3		
	C4		
Elbow flexors	C5		
Wrist extensors	C6		
Elbow extensors	C7		
Finger flexors	C8		
Finger abductors (little finger)	T1		
	T2		
	T3		
	T4		
	T5		
	T6		
	T7		
	T8		
	T9		
	T10		
	T11		
	T12		
	L1		
Hip flexors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

UER (Upper Extremity Right)

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

LER (Lower Extremity Right)

(VAC) Voluntary anal contraction (Yes/No)



LEFT

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

UEL (Upper Extremity Left)

LEL (Lower Extremity Left)

(DAP) Deep anal pressure (Yes/No)

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
1 = altered
2 = normal
NT = not testable

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		

Functional Recovery Requires Return of Motor Activity

- **The ISNCSCI motor score evaluates strength of contraction by key muscles**
- **Upper Extremity Motor Score (UEMS)**
  - **5 muscles x max. strength score of 5 x 2 sides = maximum 50 points**
- **Motor Level:**
  - **Defined by the lowest key muscle function that has a grade of at least 3, providing the key muscle functions represented by segments above that level are judged to be intact (graded as a 5)**
- **SCAR Spinal Cord Ability Ruler**
  - **Quantitative linear measure of functional ability based on motor function from the ISNCSCI exam and the ability to perform certain activities of daily living as assessed by the Spinal Cord Independence Measure (SCIM) exam**

Activities of Daily Living (ADLs)

ADLs across different levels of motor function after cervical complete SCI

+2 Motor Level Improvement

Function	Capability				
	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**

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(modified from Whiteneck et al. 1999)

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OPC1

A Cell Therapy Approach to Treating Spinal Cord Injury

OPC1 Overview

- **OPC1 consists of oligodendrocyte progenitor cells**
- **RMAT Designation**
- **Orphan Drug Designation**
- **>$14M in support from CIRM**

OPC1 Injection Procedure

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OPC1: Oligodendrocyte Progenitor Cells (OPCs)

- **Cells are derived from an NIH-registered cell line (allogeneic, not from the patient)**
- **OPCs are precursors to cells which provide electrical insulation for nerve axons in the form of a myelin sheath**
- **Cryopreserved "off the shelf" administration**
- **Treatment occurs between 21-42 days post-injury**
- **Potential application to other neurodegenerative diseases**
- **Three identified functions:**
  - **Produces neurotrophic factors**
  - **Induces remyelination**
  - **Induces vascularization**

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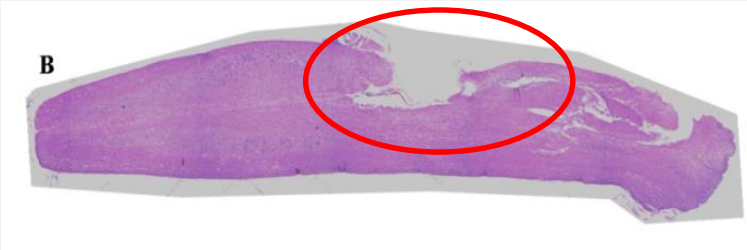
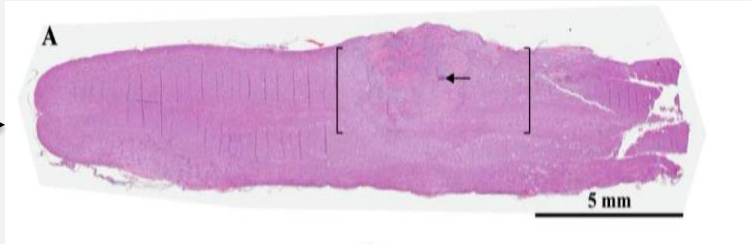
OPC1 Potential Mechanisms of Action

Prevention of Cavitation

Control

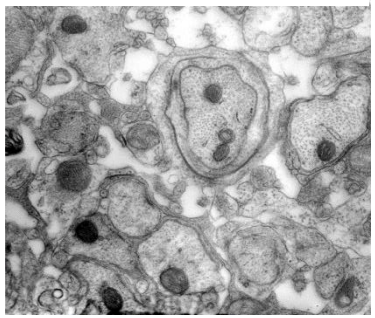


OPC1

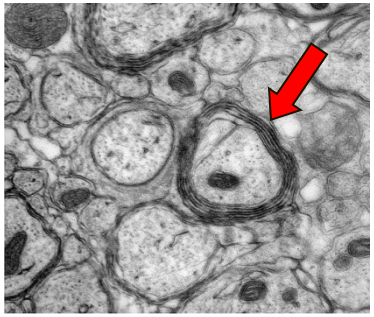


Myelination of axons

shiverer mouse

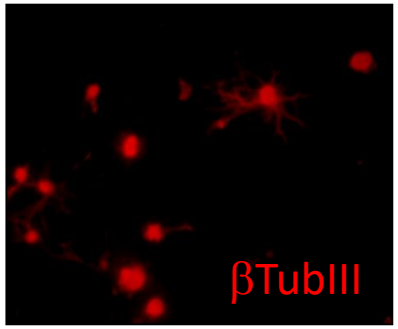


shi mouse + OPC1

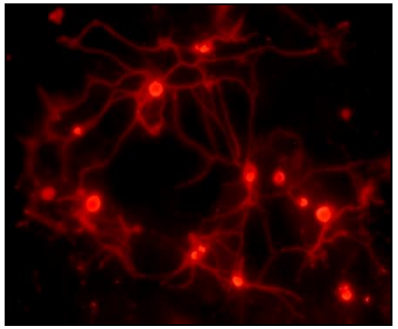


Secretion of neurotrophic factors

Control Media



OPC1



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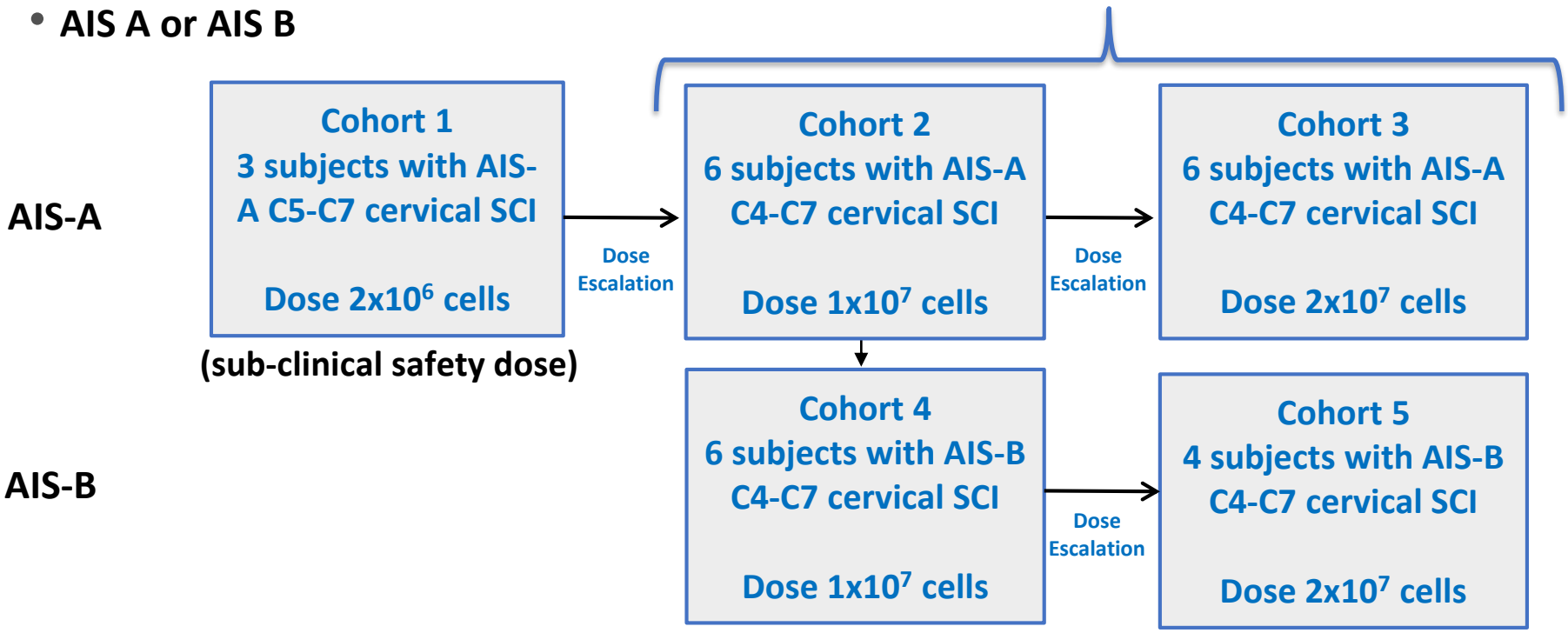
SCiStar Study Enrollment & Cohort Progression

- Open Label (n=25)
- Traumatic cervical SCI (C4-C7)
- Dosed 21-42 days post injury
- Ages 18-69
- AIS A or AIS B

- Primary Assessment: Safety
- Secondary Assessment: Neurological Function (ISNCSCI exams)
- Exploratory Assessments: SCIM, GRASSP



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SCiStar Study - Summary of Adverse Events

Majority of adverse events were mild to moderate in severity (12 months)

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

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

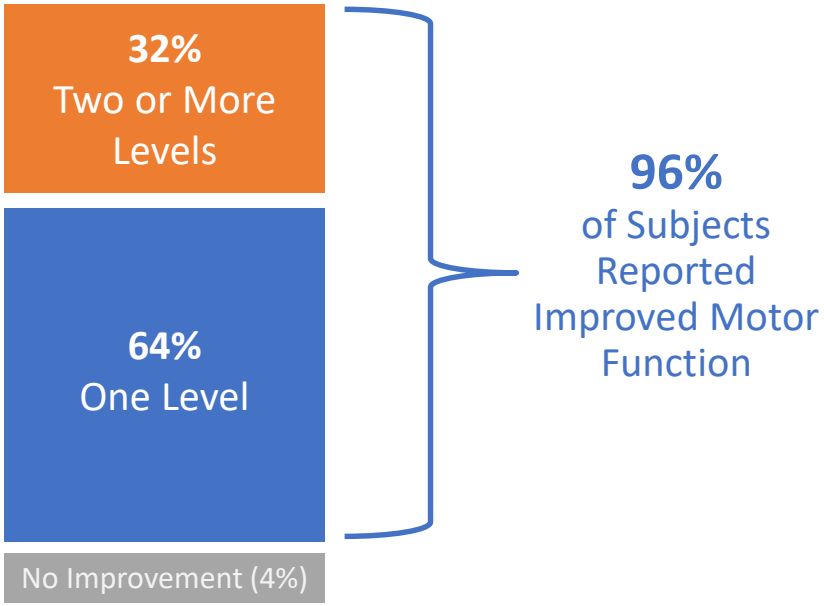
SCiStar Study - Engraftment and Efficacy Results

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

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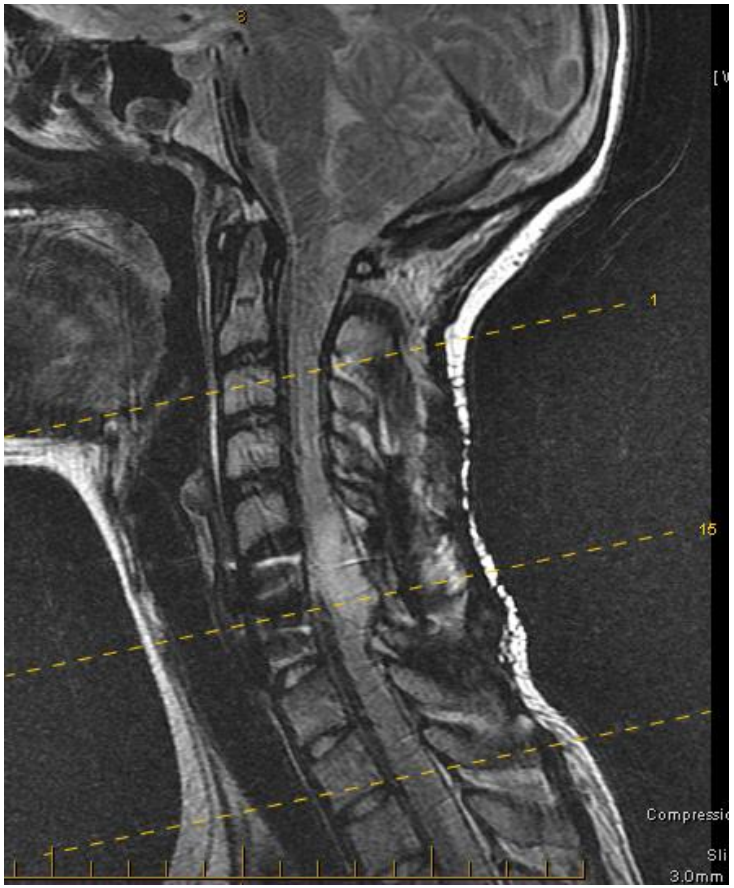
SCiStar Study - MRI Results

12 Month MRI Results Indicate Durable Engraftment

- **Cystic cavitation occurs in ~80% of cases**
- **96% (24/25) of SciStar subjects had serial MRI scans that indicated <u>no sign</u> of a lesion cavity at 12 months**
- **The MRI results suggest formation of a tissue matrix at the injury site, supporting that OPC1 cells have durably engrafted to help prevent cavitation at the injury site[1]**



Day 365 – weighted sagittal MRI

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(1) Wirth et al, Exp Neurology 1995

SCiStar Study – Motor Recovery and Upper Extremity Motor Score (UEMS)

Motor Recovery and UEMS in Cohorts 2-5 at 12 Months

	+2 Motor Levels		UEMS Improvement	
	6 Months	12 Months	6 Months	12 Months
Cohort 2	2/6	4/6	9.7	12.3
Cohort 3	1/6	1/6	6.0	9.2
Cohort 4	1/6	1/6	5.5	6.7
Cohort 5	0/4	1/4	5.8	6.8
Cohorts 2-5	4/22	7/22	6.8	8.9 +/- 4.2

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Cohort 1 (n=3) received $2x10^6$ cells; Cohorts 2-5 (n=22) received $1x10^7$ or $2x10^7$ cells.

Next Study Design Considerations: Analysis of Patients with the Least UEMS Recovery

Subject	UEMS Change from Baseline to 12 mo	2 Motor Level Gain Y/N	Cohort	Dose	Baseline AIS	NLI Baseline
2207	7	N	5	20 million	B	C4
2203	6	N	3	20 million	A	C6
2105	6	N	3	10 million	A	C4
2004	5	N	4	10 million	B	C6
2007	4	N	4	10 million	B	C4
2307	4	N	5	10 million	B	C5
2303	3	N	4	10 million	B	C6

- **Two patients had cord compression subsequent to injection (Day 7, Day 30)**
- **Three patients had a C4 NLI (lowest intact neurological level) at Baseline**

Key Takeaway:

C4 and cord compression issues can be addressed in the next trial.

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SCiStar Study – 2 Year Results
(Nov 2019 Update)

- **Overall safety profile continues to be excellent (21 subjects)**
  - **MRI scans show no evidence of adverse changes**
  - **No unexpected serious adverse events related to the OPC1 cells**
  - **No study subjects had worsening of neurological function**

- **Motor Level Improvements**
  - **Cohort 1 subjects continue to be stable 2-4 years out post treatment**
  - **5 Cohort 2 subjects achieved at least 2 motor levels of improvement over baseline on at least one side (formerly 4 of 6)**
  - **1 Cohort 2 subject achieved 3 motor levels of improvement on one side over baseline on at least one side; maintained through 36 month visit**

- **Upper Extremity Motor Score (UEMS)**
  - **Additional improvement in average UEMS score for Cohort 2**

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SCiStar Study - Overall Summary

- **Excellent overall safety profile**
- **96% durable engraftment through 1 year post-injection**
- **MRI scans available through 24 months show no evidence of adverse changes (21 subjects)**
- **No subjects had a decline in motor function from Year 1 to Year 2**
- **95% of patients exhibited robust motor recovery in the upper extremities at 1 year (at least 1 motor level on at least 1 side)**
- **Significant motor improvements achieved in five of six Cohort 2 subjects**
- **Results support further evaluation in a randomized, controlled study**

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Comparative Trial – Primary Endpoint Considerations

- **Upper Extremity Motor Score (UEMS)**
- **Improvement of 2 or more motor levels on at least one side**
- **Spinal Cord Independence Measure (SCIM)**
- **Spinal Cord Ability Ruler (SCAR)**
- **Capabilities of Upper Extremities Test (CUE-T) – new**
- **Spinal Cord Injury Functional Index (SCI-FI) – new**

Spinal Cord Outcomes Partnership Endeavor

SCOPE is an Industry, Academic and Community Roundtable for Spinal Cord Injury Research

- Workshops & publications
- Enrollment initiatives
- Functional outcome assessments

<u>SCOPE Mission</u>:

Enhance the development of clinical trial and human study protocols that will accurately validate therapeutic interventions for spinal cord injury (SCI) and facilitate improved best practices.

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SCOPE Role in SCI Clinical Development

- **SCOPE has published peer-reviewed guidelines for SCI clinical trials that have had a significant impact on FDA guidance for industry sponsors**

- **SCOPE has identified outcome measures for complete cervical SCI which link recovery of neurological function to improvements in functional ability**

- **SCOPE provides a path to pivotal trials in which both clinical and statistical significance can be demonstrated with manageable numbers of patients and a reasonable time frame**

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The future of cell therapy.