



From promise to people.

Our mission is to pioneer a new branch of medicine based on the directed differentiation and transplant of allogeneic cells to patients

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Cell Cure Neurosciences
(A subsidiary of Lineage Cell Therapeutics, Inc.)

Forward-Looking Statements

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Lineage Cell Therapeutics

#ReplaceAndRestore™

Broad Capabilities

Cell manufacturing and transplant technology

6

Cell types in development

>200

Cell types for future targeting

Highly Differentiated

Allogeneic product candidates

2

Active clinical trials

~375

Issued and pending patents

Validated Platform

2 funded partnerships and collaborations

Up to \$670M*







Global partnership with Roche for lead asset OpRegen®

\$12M

Research collaboration with William Demant Invest for ReSonance™

* Includes \$50M up front payment received Jan 2022, \$5M milestone received Nov 2025, \$615M of remaining eligible milestones, and tiered double-digit royalties on sales

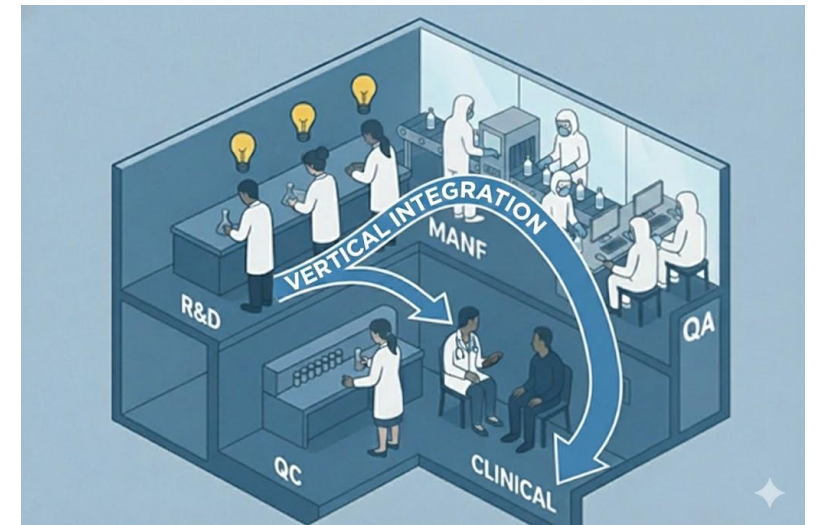
Cell Transplant Pipeline – 100% Allogeneic

FIELD	PROGRAM	PHASE 1	PHASE 2	PHASE 3
 Ophthalmology	OpRegen® Dry AMD with Geographic Atrophy (GA)	24 patients treated	Phase 2a enrolling	Genentech A Member of the Roche Group Development Partner/Study Sponsor
 Demyelination	OPC1 Spinal Cord Injury (SCI)	5 patients treated	25 patients treated	CIRM <small>CALIFORNIA STEM CELL AGENCY</small> Grant Partner
 Neurotology	ANP1 (ReSonance™) Auditory Neuropathy (Hearing Loss)	Preclinical		William Demant Invest Funded Partnership
 Ophthalmology	PNC1 Vision loss; Retinitis Pigmentosa	Research		
 Neurology	RND1 Undisclosed indications	Research	Hypoimmune Line	FACTOR® BIOSCIENCE Gene Editing Partner
 Pancreatic	ILT1 Type 1 Diabetes	Research	Production Scale	

Manufacturing: It's All About the Big Little Things (BLT)

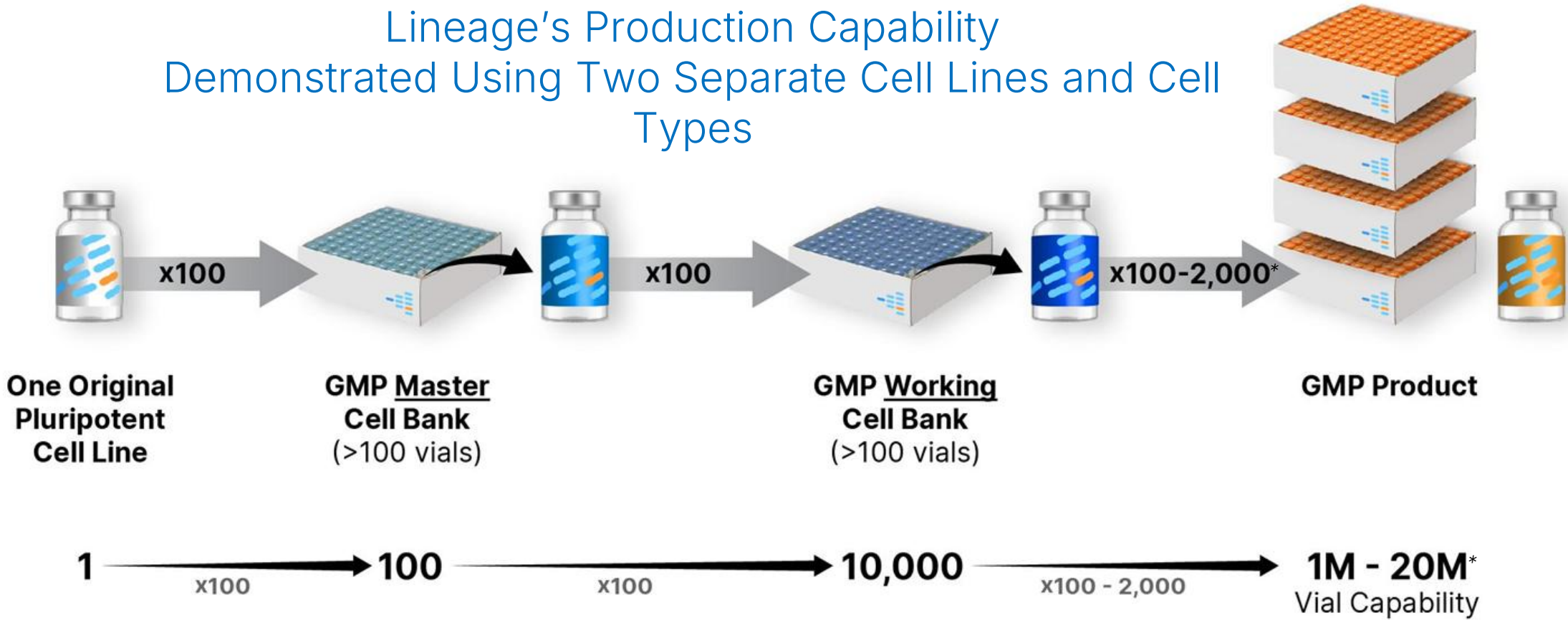
- Our platform is a fundamental shift in the traditional approach to cell therapy product development.
- Key steps in manufacturing with biological risk are resolved prior to nomination of a product line.
- Minimal Viable Product profile determined for commercial utility.
- Control and quality of the lines and differentiation process contributes to a pure and stable product.
- Hands-on engineered 4 programs; recycled these insights and innovations to subsequent programs.
- Intimate/internal tech Transfer from R&D to GMP.
- Our disciplined approach reimagines stem cell-based therapy as an off-the-shelf and affordable product.

Vertical integration allows for solving quality, purity, scale, dose and COGS at the beginning



Successfully Reduced-to-Practice A Commercial-Scale, Cell-Based, GMP Production Process

Lineage's Production Capability Demonstrated Using Two Separate Cell Lines and Cell Types



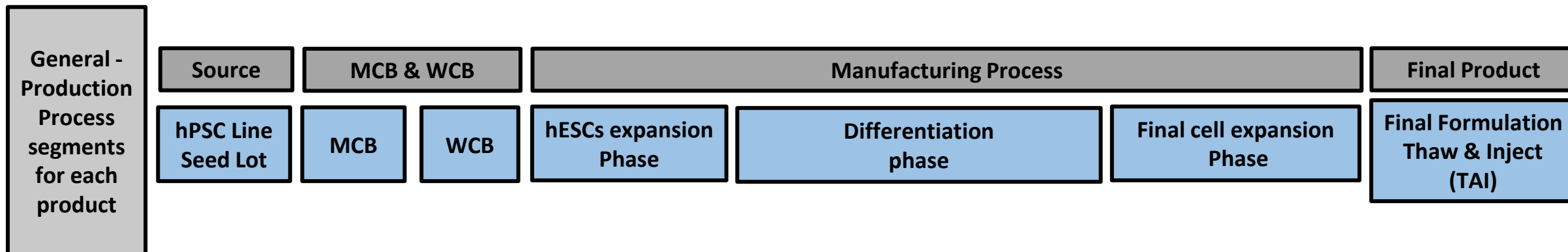
Developed and demonstrated the expertise to produce a cost-effective, scalable, and consistent supply of allogeneic cell transplant product candidates for itself or others, including for indications requiring large cell doses

**Upper end of range requires the addition of automated fill-finish equipment*

Our Production Process Scheme

Process Segments Applicable to Each of Our Products

- **Source Material:** Defined origin and characterization of the relevant starting material.
- **MCB and WCB:** Establishment and qualification of Master and Working Cell Banks.
- **Manufacturing Process:**
 - **hPSC Expansion Phase**
 - **Differentiation Phase** – segmented steps with structured biological queues
 - **Final Cell -Type Expansion Phase** – segmented to # of expansion cycles to meet required scale
- **Drug Product Formulation:** Preparation, stabilization, and configuration of the final therapeutic product.



CMC Requirements for a Successful Cell Therapy



Control (Safety) & Reproducibility

- Source line characterization, cell banking, versatile expansion systems
- Differentiation process development; closed system culturing conditions, optimization
- Analytical methods, in-process controls, release criteria
- Raw material quality

Purity / Identity

- Clinically compatible post-production processing
- Analytical method development for process control and product release

Potency

- Functionality and performance testing, reflecting MOA
- Enhancements; genetic modification (optional), various expression systems

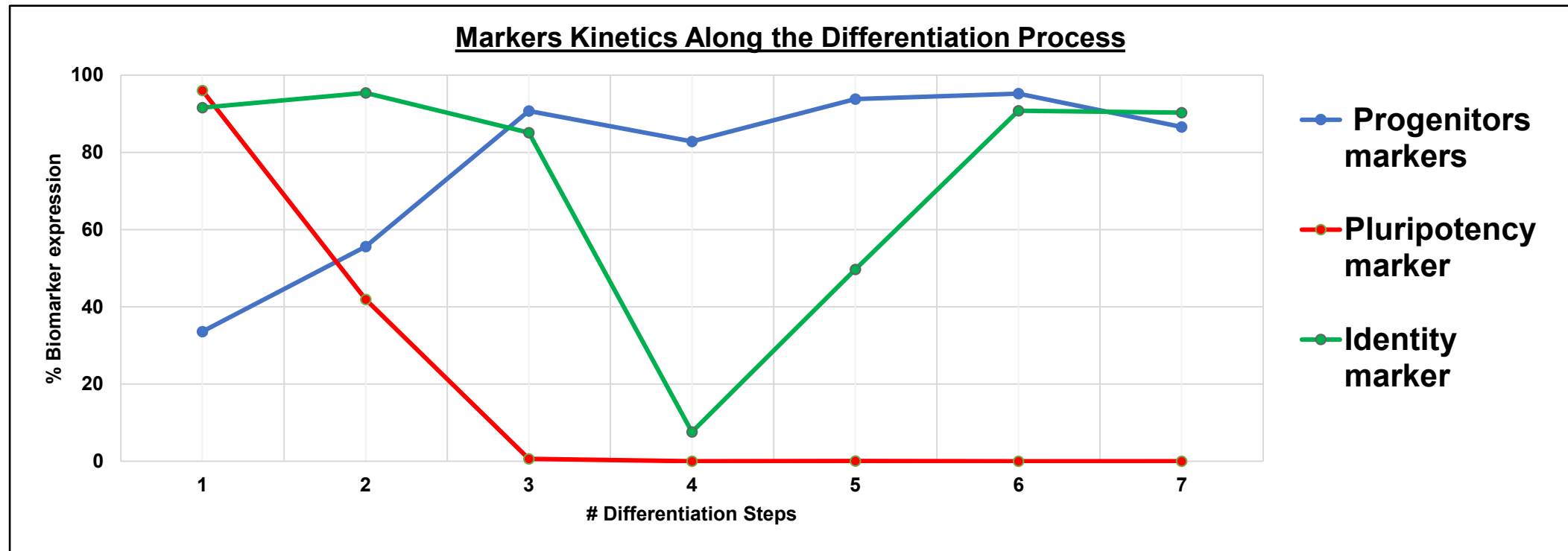
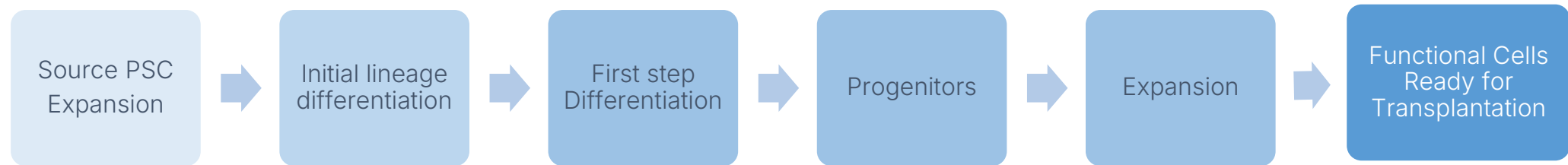
Scalability

- Scale-up closed systems modalities, substrates, harvesting protocols
- Clinical and commercial throughputs for drug process and product
- Commercially-attractive cost of goods

Delivery

- Compatibility with the drug product and the TAI format
- Minimal use of drug product
- Adjustment based formulation

Focus on Control and Tight Follow Up of Differentiation Kinetics



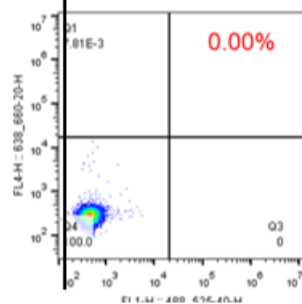
Induction of progenitor markers
Elimination of pluripotency markers

Comprehensive Drug Product Characterization

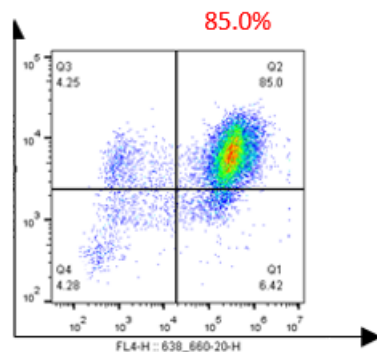
Bio-Analytical Assessments

Functional Assessments

Impurities

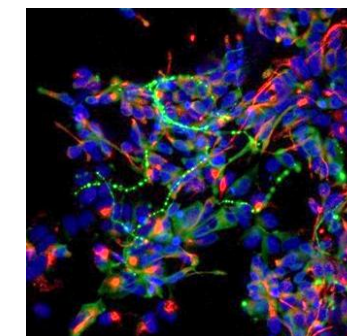


Purity



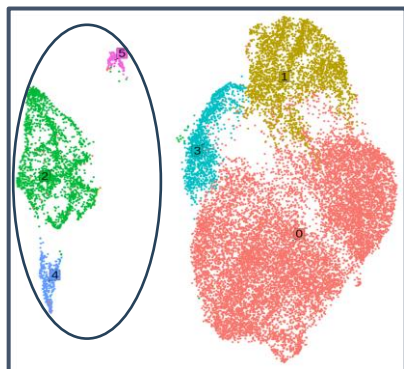
LCT-XXX

Morphology /IHC

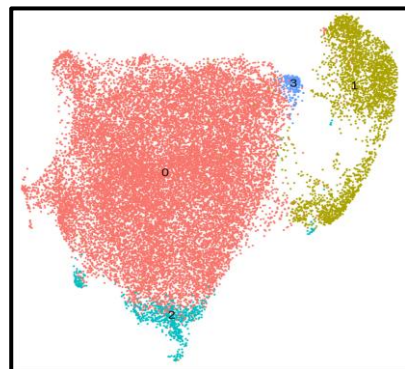


Beta Tubulin/
Synapsin1/
DAPI

LCTXX1.0

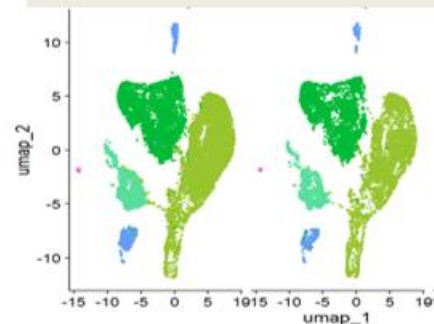


LCTXX1.2



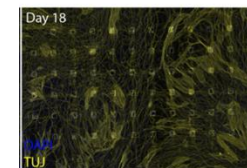
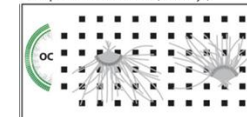
Comparability

LCTXX Batch1 LCTXX Batch2

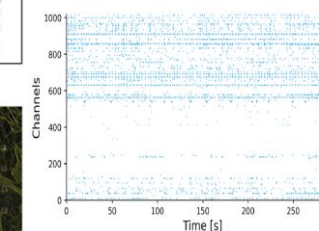


Potency

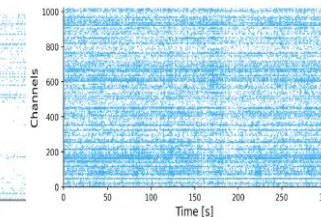
SG explant culture on MEA (6-18 days)



Day 19 in vitro



Day 29 in vitro



Functional Measurements



Effective Cell Replacement Therapy Delivery Considerations

Major Hurdles in Cell Therapy Delivery

– **Cell Survival and Integration**

- Ensuring that the transplanted cells survive in the environment and integrate properly

– **Immune Rejection**

- Immunosuppressive strategies / hypoimmune cell line
- RPEs have inherent immune protection mechanisms

– **Delivery Methods**

- Safe and effective delivery of cells to the precise location within the right area
 - i.e. subretinal delivery to areas of geographic atrophy

– **Functionality of the transplanted cells**

- Differentiation state; potency

– **Efficacy**

- Achieving meaningful clinical benefit requires not just cell survival but functional integration and (possibly) tissue restoration

Lineage Delivery Experience

– **Lineage programs span various indications, and each require a specific cell replacement approach:**

- Dry AMD – Subretinal RPE placement into the areas of atrophy
- Spinal Cord injury – OPC1 placement/fill into the spinal cavity at the injury site using a novel proprietary device
- Hearing loss – Resonance cell placement into a specific compartment in the inner ear
- Undisclosed pre-clinical program

– **Requirements for delivery in each indication may vary by dose/volume and physical properties of the delivery of device (controlled release)**

– **Adjustments and/or tailor-made solutions are developed when needed (such as for OPC1 program)**

Efficient Practical Approach from Production to Clinical Administration

- Stable and reproducible production process at scale with strong analytics
- Defined set of release criteria – quality/purity and function
- Drug product safety profile
 - Orthogonal evaluation non-targeted cell population and residual PSC via protein markers and scRNAseq
- Drug product compatibility with delivery modality (cell integrity post administration)
- Use of surrogate labeled cell to optimize delivery (in preclinical setting)
- Ready to administer (Thaw and Inject -TAI) Drug Product :
 - Cryopreservation in a bed side easy thaw format
 - Dosage (volume, cell concentration, container) with versatile compatibility:
 - with different formulation (i.e.) suspension / but also scaffold compatible
 - or devices (e.g. subretinal cannulas for dry AMD including PPV and transchoroidal approaches)

Administration Device Qualifications

—**Delivery Precision**

- The device should reliably and accurately deliver cells to the intended location within the body (e.g., specific retinal layer for eye diseases, precise area in the injury spinal cord).

—**Cell Viability and Potency**

- Minimizes damage to the cells during delivery
 - Shear stress, time at RT

—**Compatibility**

- The device should be compatible with the cell product formulation (e.g., suspension, scaffold) to ensure proper cell delivery.

—**Regulatory Compliance**

- Meet all applicable regulatory requirements and standards for medical devices.



OpRegen[®] Cell Therapy

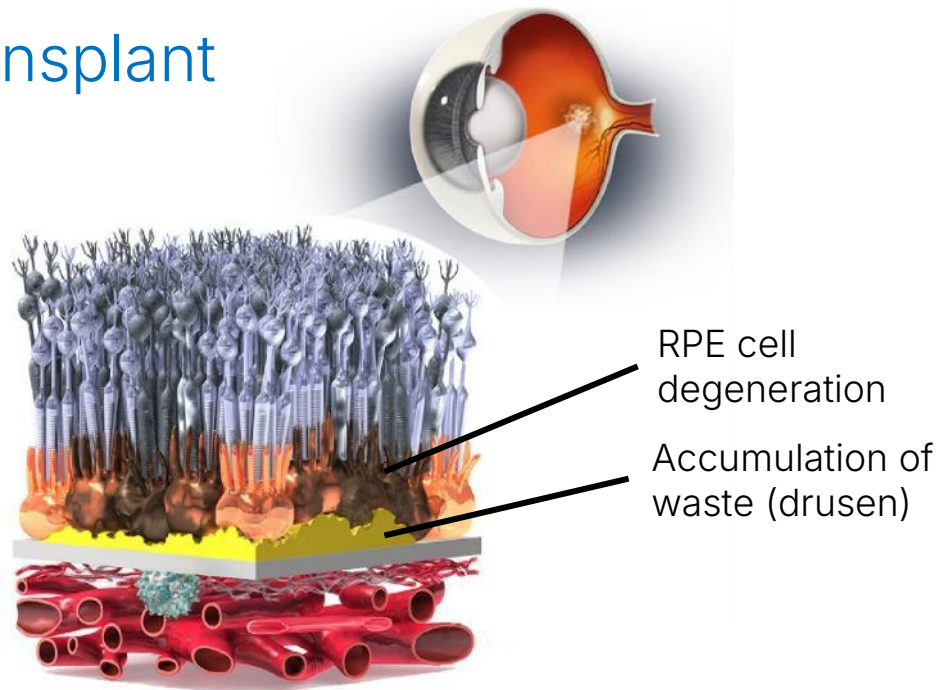
RPE Cell Transplant to Treat Dry AMD with GA
Improving structure *and* function, durably, from
a single dose

Roche/Genentech Alliance

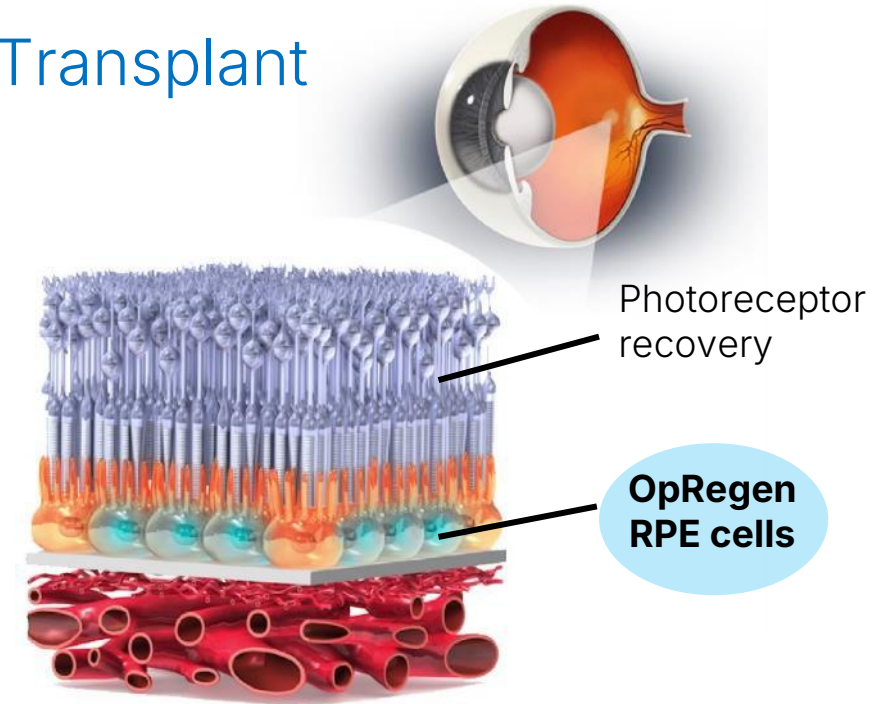
Lineage Approach - OpRegen Cell Therapy, a "Complete" Approach

OpRegen cell therapy is a one-time injection of fully mature and functional RPE cells currently in development for: 1) replacement and restoration of retinal tissue (anatomy), and 2) preservation or improvement of vision (function)

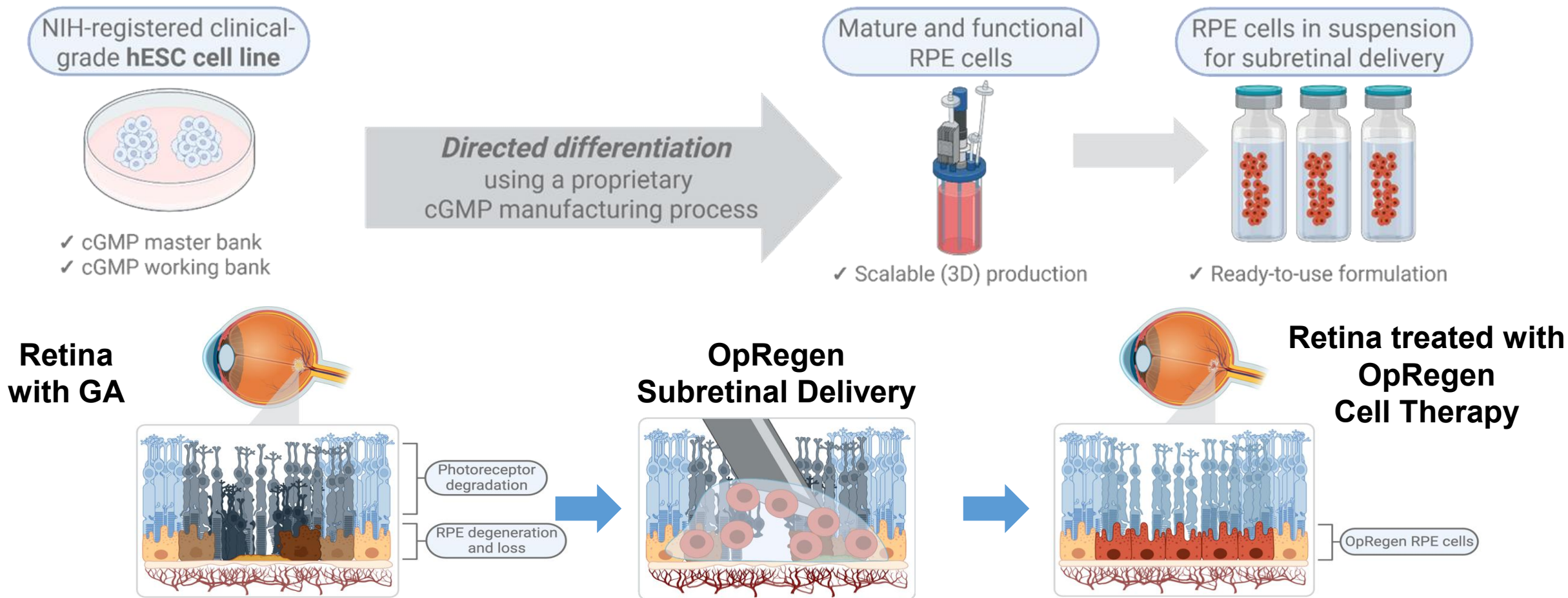
Pre-Transplant



Post-Transplant



OpRegen Cell Therapy – A Suspension of Allogeneic RPE Cells With the Potential to Counteract RPE Cell Dysfunction & Loss in GA

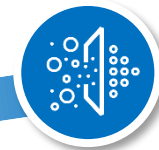
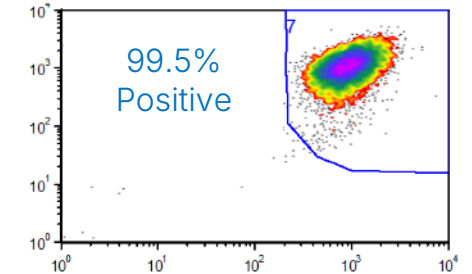


Repeating Success – OpRegen as a Case Study and Guide



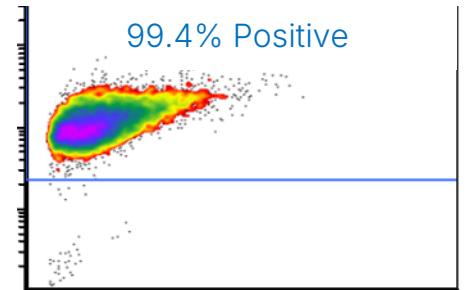
Control (Safety) & Reproducibility

- Multiple clinical batches generated and released
- Comparability testing performed on batches
- Single source, master bank cell line
- No reports of transplant rejection to date



Purity/Identity

- Highly pure RPE via flow cytometry
- Multiple identity markers utilized
- No residual PSCs detectable (orthogonal methods)



Potency/Functionality

- Phagocytosis assay
- Trans-epithelial resistance (polarization)
- Differential apical and basal growth factor secretion



Clinical Applicability

- 2 delivery methods evaluated
- Ready to Inject Drug Product



Scalability

- Dynamic culturing system (3D, not 2D)
- Bioreactor and microcarriers for expansion and scale-up



OpRegen Program - Main Delivery Learnings

- **Anatomical and functional benefits** reported at 1 and 2 years have **continued to persist at 3 years** post OpRegen treatment
- Patients with **extensive coverage** of their area of atrophy with the OpRegen surgical bleb **showed evidence of retinal structure improvement**
 - The retinal structure improvement was accompanied by sustainable gains in visual acuity
- OpRegen TAI has been qualified for use and administration as a suspension across different delivery systems
- OpRegen was delivered subretinally with two modalities
 - Transvitreal (vitrectomy/retinotomy) and transchoroidal approaches
- Well-tolerated
 - No cases of rejection to date (~3 month immunosuppression)
- Being developed under worldwide collaboration and license agreement with **Roche/Genentech**



Key Takeaway for the Lineage Approach

In certain settings, replacing whole cells may provide restorative benefits beyond the reach of traditional approaches

#ReplaceandRestore™



Our Inspiration.

View their stories at
lineagecell.com/media