LONGEVERON

A Regenerative Medicine Company

Cellular therapies for life-threatening and chronic aging-related conditions



Investor Presentation

Nasdaq (LGVN) | March 2025

Forward Looking Statements

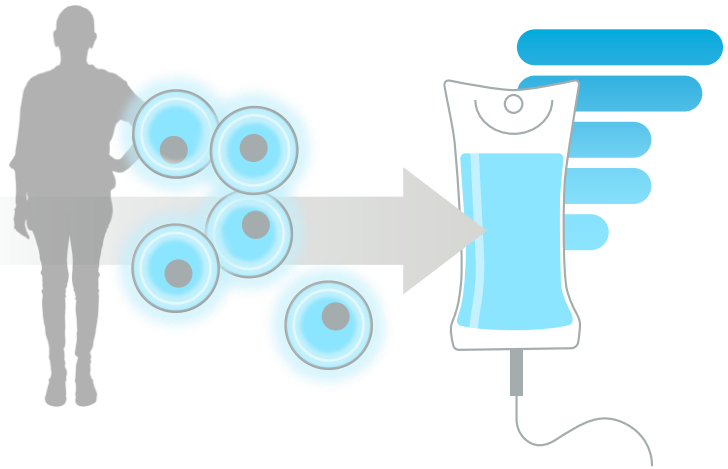
Certain statements in this presentation that are not historical facts are forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, which reflect management's current expectations, assumptions, and estimates of future operations, performance and economic conditions, and involve risks and uncertainties that could cause actual results to differ materially from those anticipated by the statements made herein. Forward-looking statements are generally identifiable by the use of forward-looking terminology such as "believe," "expects," "may," "looks to," "will," "should," "plan," "intend," "on condition," "target," "see," "potential," "estimates," "preliminary," or "anticipates" or the negative thereof or comparable terminology, or by discussion of strategy or goals or other future events, circumstances, or effects. Factors that could cause actual results to differ materially from those expressed or implied in any forward-looking statements in this release include, but are not limited to, our limited operating history and lack of products approved for commercial sale; adverse global conditions, including macroeconomic uncertainty; inability to raise additional capital necessary to continue as a going concern; a history of losses and may not be able to achieve profitability going forward; no FDA-approved allogenic, cell-based therapies for Aging-related Frailty, AD, or other aging-related conditions, nor HLHS or other cardiac-related indications; ethical and other concerns surrounding the use of stem cell therapy or human tissue; the use of our product candidates or future products in individuals may expose us to product liability claims, and we may not be able to obtain adequate product liability insurance; if our trade secret and patent position does not adequately protect our product candidates and their uses, others could compete against us more directly, which could harm our business and have a material adverse effect on our business, financial condition, and results of operations; if certain license agreements are terminated, our ability to continue clinical trials and commercially market products could be adversely affected; inability to protect the confidentiality of our proprietary information, trade secrets, and know-how; third-party claims of intellectual property infringement may prevent or delay our product development efforts; intellectual property rights do not necessarily address all potential threats to our competitive advantage; inability to successfully develop and commercialize our product candidates and obtain the necessary regulatory approvals; we cannot market and sell our product candidates in the U.S. or in other countries if we fail to obtain the necessary regulatory approvals; final marketing approval of our product candidates by the FDA or other regulatory authorities for commercial use may be delayed, limited, or denied, any of which could adversely affect our ability to generate operating revenues; we may not be able to secure and maintain research institutions to conduct our clinical trials; ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations; if we receive regulatory approval of Lomecel-B™ or any of our other product candidates, we will be subject to ongoing regulatory requirements and continued regulatory review, which may result in significant additional expense; being subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our therapeutic candidates; reliance on third parties to conduct certain aspects of our preclinical studies and clinical trials; interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data; the volatility of price of our Class A common stock; provisions in our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our Class A common stock; we have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators; and in order to successfully implement our plans and strategies, we will need to grow our organization, and we may experience difficulties in managing this growth. Further information relating to factors that may impact the Company's results and forward-looking statements are disclosed in the Company's filings with the Securities and Exchange Commission, including Longeveron's Annual Report on Form 10-K for the year ended December 31, 2024, filed with the Securities and Exchange Commission on February 28, 2025, and its Quarterly Reports on Form 10-Q. The forward-looking statements contained in this presentation are made as of the date of this presentation, and the Company disclaims any intention or obligation, other than imposed by law, to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.

Longeveron Overview

- Stem cell therapies for life-threatening and chronic aging-related conditions
- Lead asset Lomecel-B™ has produced multiple positive initial results in 5 clinical trials across 3 indications
- Clinical pipeline in HLHS, Alzheimer's disease and Aging-related Frailty, with large US market opportunities
- FDA Granted HLHS program Rare Pediatric Disease, Orphan Drug and Fast Track Designations
- FDA Granted AD program Regenerative Medicine Advanced Therapy (RMAT) and Fast Track Designations
- Cash and cash equivalents of $19.2 million as of December 31, 2024; no debt
- Proven management, scientific, and manufacturing teams

Cellular Therapy Lomecel-B™ (laromestrocel) -- A Pipeline in a Product

- Stem cell therapy uses stem cells to repair, regenerate or replace damaged or diseased cells in the body
- Allogeneic (donor-derived) medicinal signaling cells (MSCs) isolated from bone marrow of healthy young adults (18 to 45)
- Cells are culture-expanded - replicated under controlled laboratory conditions - into the billions
- After a specific number of expansion cycles called “passages”, the cells are harvested, separated into specific doses (e.g. 50 million cells), and frozen until future use in patients
- Lomecel-B™ development programs:
  - Hypoplastic Left Heart Syndrome (HLHS) - on-going Phase 2b clinical trial
  - Alzheimer’s disease (AD) - completed through Phase 2a
  - Aging-related Frailty (AF) - completed through Phase 2b



Addressing Unmet Medical Needs of Chronic and Life-threatening Conditions

Hypoplastic Left Heart Syndrome (HLHS)

- One of most severe congenital heart conditions
- Cause unknown
- Devastating for patient & family
- Limited treatment options
  - Series of surgical repairs
  - Heart transplant
- HLHS accounts for 2-3% of all congenital heart disease

Alzheimer's Disease (AD)

- 1 in 3 older adults dies with Alzheimer's or another dementia
- AD kills more than breast cancer and prostate cancer combined
- In 2024, AD and other dementias cost U.S $360 billion
- Between 2000 and 2021, deaths from AD have increased 141% *(deaths from heart disease have decreased 2.1%)*

Aging-related Frailty (AF)

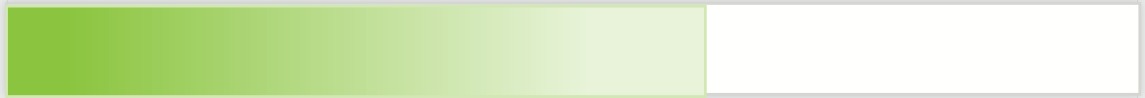
- By 2030, 1 in 6 people in the world > 60 years old, representing over 1.4 billion people
- In 2020, # of people > 60yrs outnumbered children <5yrs
- Accumulation of molecular and cellular damage with the passage of time
- Gradual decrease in physical & mental capacity, a growing risk of disease and death

U.S. Opportunity: Large Markets with Unmet Medical Needs

	Hypoplastic Left Heart Syndrome (HLHS)	Alzheimer's Disease	Aging-related Frailty
U.S. Patient Population	1,000[3]	6.9 million[2]	8.1 million[1]
U.S. Market Potential	Up to $1B[6]	~$5-10B[5]	~$4 – 8B[4]

[1] Company estimate based on US Census Bureau Population ≥65 years old of 54.06 million (2019 estimate) and community-dwelling Aging-related Frailty prevalence estimates over the age of 65 (15%) from Bandeen-Roche et al; *Gerontol A Biol Sci Med Sci*. 2015. Prevalence estimates vary depending on definition criteria used and population studied.
[2] 2024 Alzheimer's Disease Facts and Figures, 2024.
[3] Centers for Disease Control and Prevention estimate. www.cdc.gov/ncbddd/heartdefects/hlhs.html
[4] Assumes 10% penetration and cost of $5,000 to $10,000 per patient
[5] Assumes 20% penetration and cost of $5,000 to $10,000 per patient
[6] Based on Market Analysis from Clearview Healthcare Partners with a wide range to acknowledge that product profile could be limited to functional cardiac improvement but might include survival benefit

Robust Clinical Pipeline

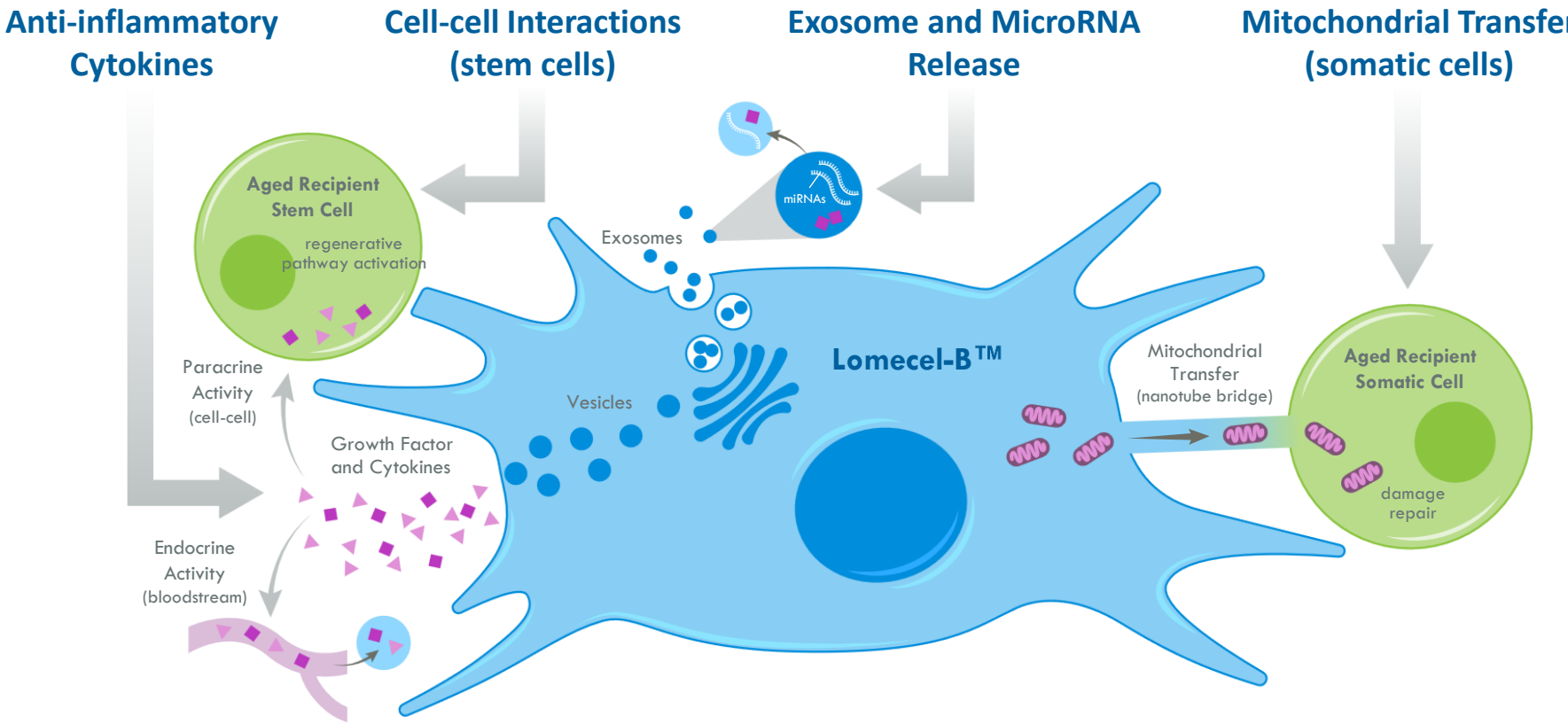
Indication	Geography	Phase 1	Phase 2	Phase 3	Milestones
Hypoplastic Left Heart Syndrome	U.S.				• ELPIS II actively enrolling • ELPIS I LT Transplant-free survival data presented at CHSS (Oct 2024)
Alzheimer's Disease	U.S.				• Positive Phase 2a results presented at AAIC 2024 (July 2024)
Aging-related Frailty	U.S.				• U.S. Phase 2b Single-Dose trial complete

Lomecel-B™: Multiple Mechanisms of Action (MOA)

Pro-vascular, Pro-regenerative and Anti-inflammatory: Repairs Tissue and Promotes Healing

Lomecel-B™ Key Advantages:

- Superior efficacy for addressing inflammation
- Cells migrate to sites of tissue damage
- Enhanced safety as inherently Immuno-evasive
- Convenient off-the-shelf administration



Jimenez-Puerta GJ, et al. *Journal of Clinical Medicine*. 2020 Feb;9(2):445.
Mazhari R and Hare JM. *Nature Clinical Practice Cardiovascular Medicine*. 2007 Feb;4(1):S21-6.

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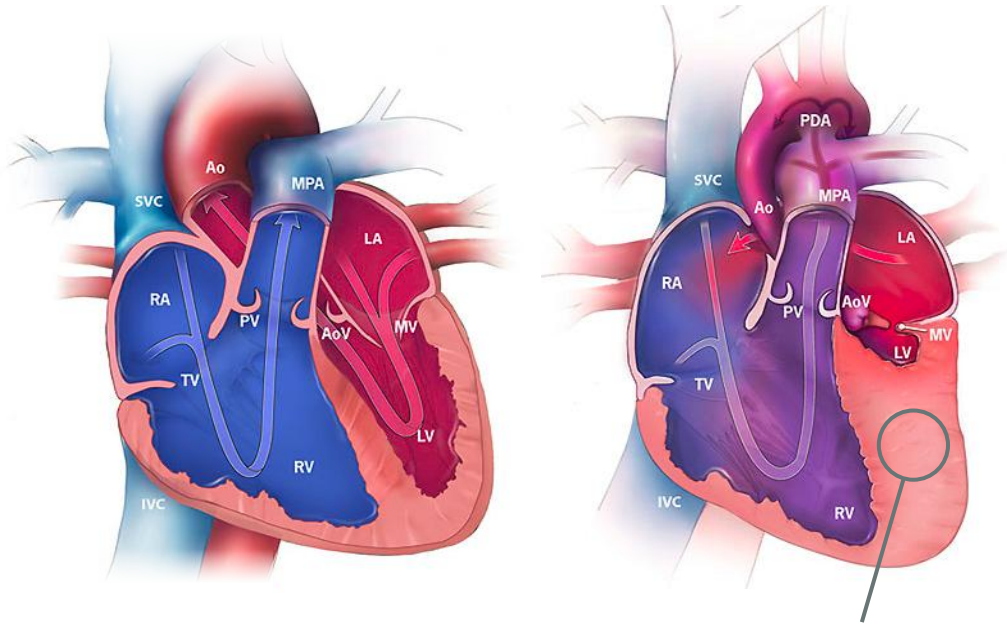
Lomecel-B™
for Hypoplastic Left Heart Syndrome (HLHS)

Significant Unmet Need in HLHS

- **HLHS** is a rare pediatric congenital heart defect in which the left side of the heart fails to normally develop
- Affects ~1,000 babies/year in United States[1]
- Children with HLHS require 3 staged open-heart surgeries in order to survive
    - Norwood Procedure – 10 days of life
    - Glenn Procedure – approximately 4 months
    - Fontan – 3 to 4 years
- Even with surgery, overload on the right ventricle causes it to fail, leading to increased short-term mortality, delayed development, and long-term organ failure
- Overall survival to adolescence estimated at only 50% to 60%[2]
- 5 years transplant-free survival ~80%[3,4]



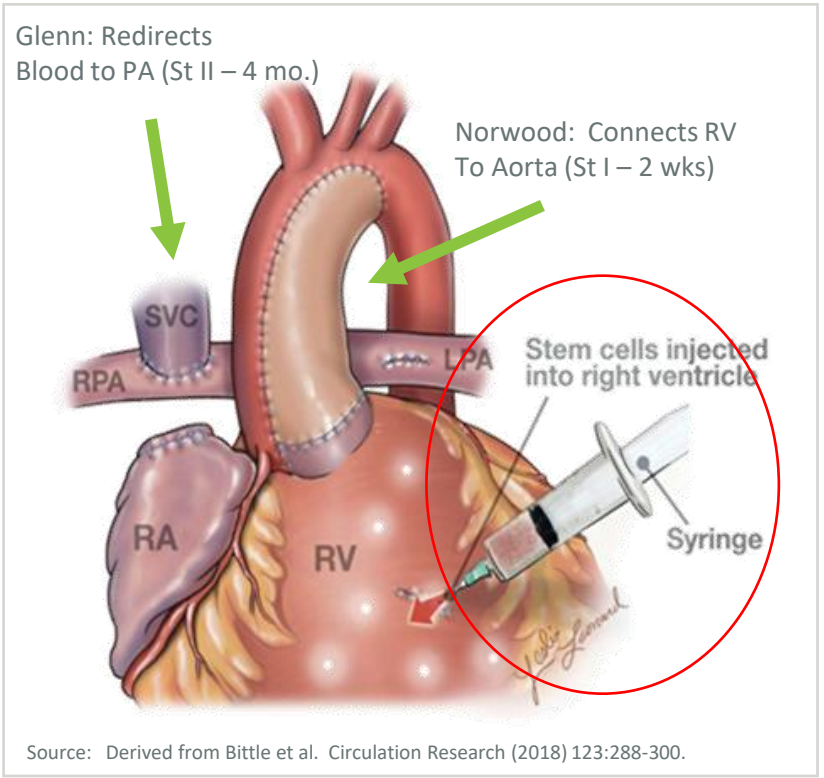
Normal Heart HLHS

1. Ohye RG, et al. Comparison of shunt types in the Norwood procedure for single-ventricle lesions. The New England journal of medicine (2010) 362:1980-92. 2. Newburger JW, et al. Transplant-Free Survival and Interventions at 6 Years in the SVR Trial. Circulation(2018) 137:2246-2253. 3. Kaushal S, et al. Long-Term Transplant-Free Survival is Improved in Hypoplastic Left Heart Syndrome with Cell-Based Therapy. 2023 American Heart Association Scientific Meeting. Philadelphia, PA (11 – 14 Nov 2023). 4 Lynch et al. Outcomes of Children with Hypoplastic Left Heart Syndrome and Heart Failure on Medical Therapy (2024) JACC: Advances 3:100811.

Clinical Approach to HLHS with Lomecel-B™

Improving Cardiac Function through Regenerative Effect of MSCs

- Dysfunction of the systemic right ventricle (RV) remains an independent risk factor for death or heart-transplant
- Lomecel-B™ injected into myocardium of right ventricle during Stage II surgery at approximately 4 months of age ("Glenn or Hemi-Fontan Procedure")
- Phase 1 ELPIS I Trial (n=10) completed
- Phase 2 ELPIS II Trial (n=38) on-going
- **U.S. FDA has granted Lomecel-B™ for HLHS:**
  - Rare Pediatric Disease Designation
    - Approval may come with transferable Priority Review Voucher
  - Orphan Drug Designation
  - Fast Track Designation



Source: Derived from Bittle et al. Circulation Research (2018) 123:288-300.

Lomecel-B™ administered directly into heart at approximately four months during second surgery

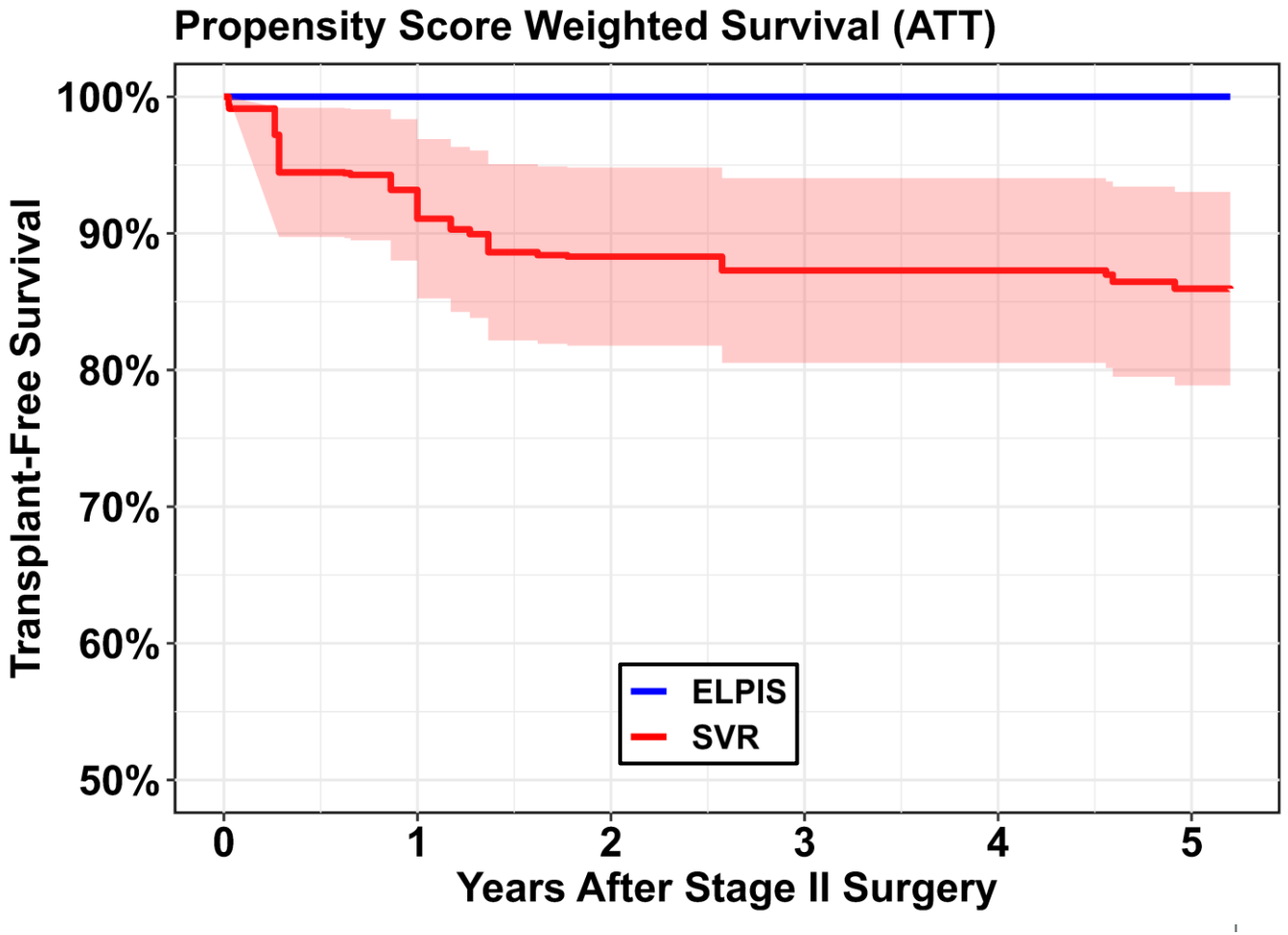
Long-term Survival Data Presented at 2024 Congenital Heart Surgeon's Society Ann Mtg

ELPIS I - 100% transplant-free survival for 10 patients up to 5 years post Glenn surgery

- ELPIS I met its primary endpoint of safety through 1-year post-treatment, with 100% survival rate, 100% transplant-free and patients maintained expected rate of growth one year after treatment
- 5 years survival data are available
- None of the 10 treated patients required heart transplant up to 5 years post Stage 2 surgery
- 5-year transplant-free survival is 100% in Lomecel-B™ treated cohort compared to 80% in a propensity-matched historical control group.[1,2,3,4]
- No Lomecel-B™ related safety issues were reported
- No Major Adverse Cardiovascular Events (MACE) were reported during the study
- Findings support the use of Lomecel-B™ as a potential adjunct to HLHS reconstruction surgery to improve transplant-free survival

1. Ohye RG, et al. Comparison of shunt types in the Norwood procedure for single-ventricle lesions. The New England journal of medicine (2010) 362:1980-92. 2. Newburger JW, et al. Transplant-Free Survival and Interventions at 6 Years in the SVR Trial. Circulation(2018) 137:2246-2253. 3. Kaushal S, et al. Long-Term Transplant-Free Survival is Improved in Hypoplastic Left Heart Syndrome with Cell-Based Therapy. 2023 American Heart Association Scientific Meeting. Philadelphia, PA (11 – 14 Nov 2023). 4 Lynch et al. Outcomes of Children with Hypoplastic Left Heart Syndrome and Heart Failure on Medical Therapy (2024) JACC: Advances 3:100811.

Long-term Survival in HLHS from ELPIS I Trial of Lomecel-B™



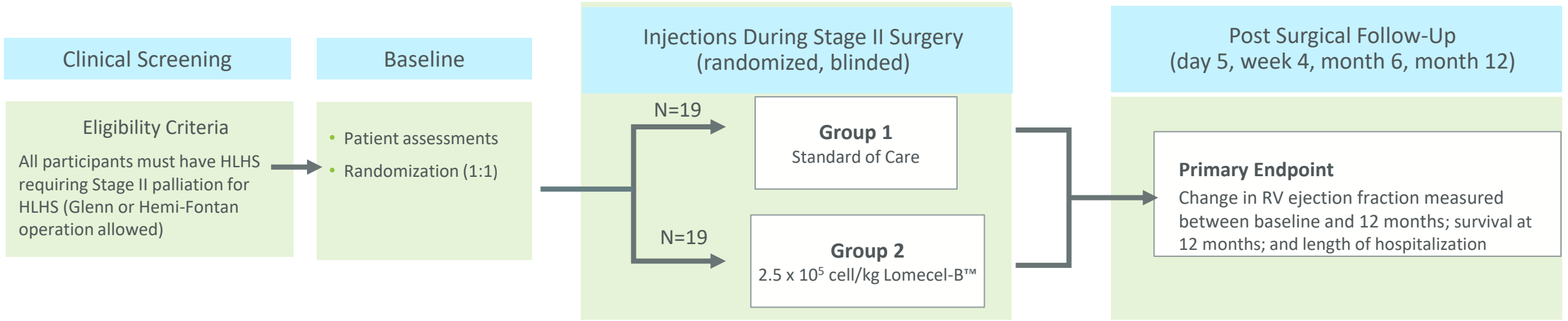
- Results from ELPIS I trial showed 100% survival (transplant-free) in Lomecel-B™ treated patients at up to 5 years
- In SVR historically matched controls, 5-year mortality was ~15%

The NIH/NHLBI Pediatric Heart Network Single Ventricle Reconstruction Trial dataset was used in preparation of this work. Data were downloaded from https://www.pediatricheartnetwork.com/pud_login.asp?study_id=SVR on 05/09/2023

[1]Right Ventricle-Pulmonary Artery Shunt

ELPIS II: Phase 2b Study Design

Phase 2b, Randomized, Multi-center study to Evaluate Lomecel-B™ Injection in Patients with HLHS



- ELPIS II is being conducted at leading clinical centers, including Boston Children's Hospital, Lurie's Children's Hospital, Children's Hospital of Los Angeles, Children's Healthcare of Atlanta, UTHealth-McGovern Medical School, Cincinnati Children's Hospital Medical Center, Primary Children's Hospital at University of Utah, Children's Hospital of Colorado, Children's Nebraska, Children's Hospital of Philadelphia
- ELPIS II is being conducted in collaboration with the National Heart, Lung, and Blood Institute (NHLBI) through grants from the National Institutes of Health (NIH)

Lomecel-B™ for HLHS Regulatory Path Clarified

Successful Type C Meeting with U.S. FDA in August 2024

- On-going Phase 2b clinical trial (ELPIS II) deemed pivotal and, if positive, acceptable for Biological License Application (BLA) submission for potential full traditional approval
- Alignment with FDA on ELPIS II primary and secondary endpoints
- Alignment with FDA on CMC and Potency Assay plan and requirements

Potential for ELPIS II to serve as the foundation for a BLA submission potentially significantly reduces the time to reach submission and potential approval of Lomecel-B™ as an HLHS adjunct therapy

Lomecel-B™
for Alzheimer's Disease (AD)

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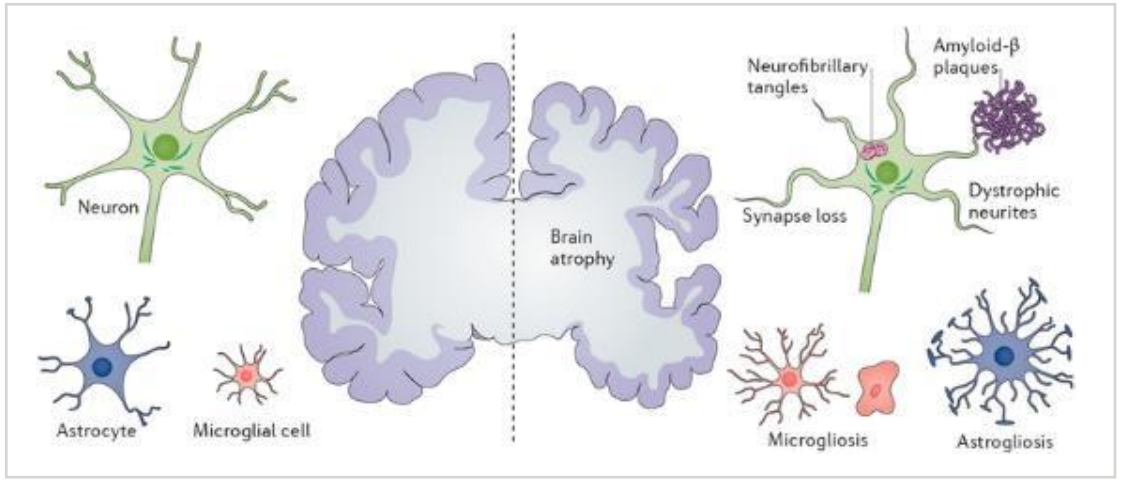
Lomecel-B™ for Alzheimer's Disease

Targeting CNS Inflammation

- Previous therapies targeted amyloid plaques (b-secretase inhibitors and anti-amyloid antibodies) or neurofibrillary tangles (antibodies) with little evidence of disease state improvement
- Inflammation is increasingly recognized as a major pathway to the pathology leading to neurodegeneration in AD
- Genetic evidence for inflammation being important in AD comes from *TREM2* (an important protein in multiple immune cells) variants associated with AD*
- Inflammatory responses in brain to the pathologies of AD are increasingly recognized to drive the pathogenesis of the disease+
- **U.S. FDA has granted Lomecel-B™ for AD:**
  - Regenerative Medicine Advanced Therapy (RMAT) Designation
  - Fast Track Designation

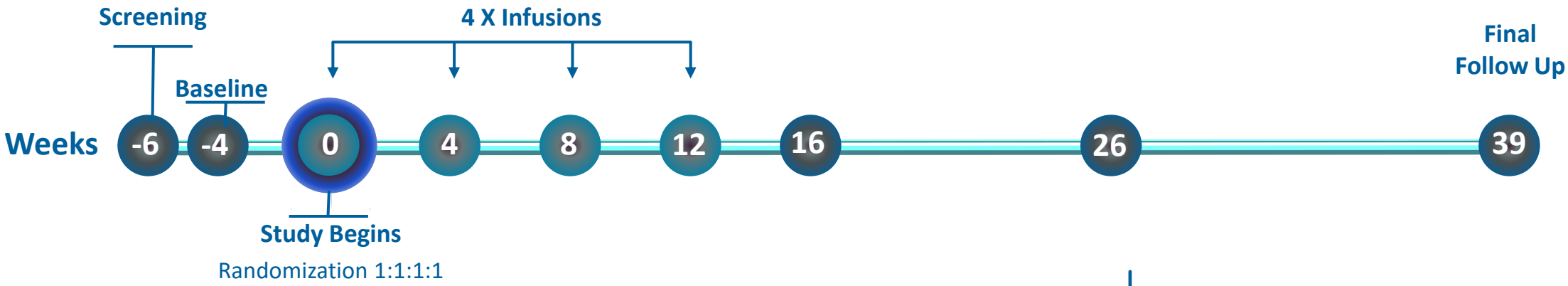


- MSCs effect in animal models of Alzheimer's Disease:
  - Cross the blood brain barrier (BBB)
  - ↓ pro-inflammatory; ↑ anti-inflammatory biomarkers
  - Improve immune functioning
  - Promote neurogenesis
  - Improve endothelial function

*Shi Y, Holtzman DM (December 2018). *Nature Reviews. Immunology*. 18 (12): 759–772
+Heppner FL; Ransohoff RM; Becher B (2015).. *Nature Reviews Neuroscience*. 16 (6): 358–372

Figure from Congdon EE, Sigurdsson EM. Tau-targeting therapies for Alzheimer disease. *Nat Rev Neurol.* 2018 Jul;14(7):399-415.

CLEAR MIND Phase 2a Study Design



- Group 1: Placebo [N=12]
- Group 2: Single Dose Lomecel-B™ (25M) [N=13]
- Group 3: Multi dose Lomecel-B™ (25M) [N=13]
- Group 4: Multi dose Lomecel-B™ (100M) [N=11]

Primary Endpoint	Percentage of patients with at least 1 SAE 4 weeks from any infusion
Secondary Endpoint	CADS composite imaging and neurocognitive testing scores
Exploratory Endpoints	Change from baseline cognitive tests, MRI biomarkers

CLEAR MIND Phase 2a Results for Alzheimer’s Disease

- Trial results selected for featured research oral presentation at the 2024 Alzheimer's Association International Conference (AAIC) July 2024
- Lomecel-B™ demonstrated positive benefit/risk profile
- Lomecel-B™ treated patients showed an overall slowing/prevention of disease worsening compared to placebo
- The trial achieved the primary safety and secondary efficacy endpoints and showed statistically significant improvements in pre-specified clinical and biomarker endpoints in specific Lomecel-B™ groups compared to placebo
- The established safety profile of Lomecel-B™ for single and multiple dosing regimens was demonstrated in study data that showed no incidence of hypersensitivity, infusion-related reactions, and no cases of amyloid-related imaging abnormalities (ARIA)
- Administration of Lomecel-B™ was associated with slowing cognitive and functional decline as demonstrated by statistically significant results in the Montreal Cognitive Assessment and statistical trending improvements compared to placebo in CDR-SB and MMSE
- There was a statistically significant improvement relative to placebo observed in the Alzheimer’s Disease Cooperative Study Activities of Daily Living (ADCS-ADL)
- Brain MRI results demonstrated a 49% reduction in brain volume loss and improvement in cerebral blood flow

CLEAR MIND Phase 2a Conclusions and Next Steps

- Results of CLEAR MIND clinical trial support the therapeutic potential of Lomecel-B™ in the treatment of mild Alzheimer's disease and provided evidence-based support for further clinical development
- The Company anticipates meeting with the FDA in the first quarter of 2025 to review future clinical and regulatory strategy for Lomecel-B™ in Alzheimer's disease
- The Company is currently seeking partnerships and non-dilutive funding to support further development of Lomecel-B™ in Alzheimer's disease

Lomecel-B™
for Aging-related Frailty (AF)

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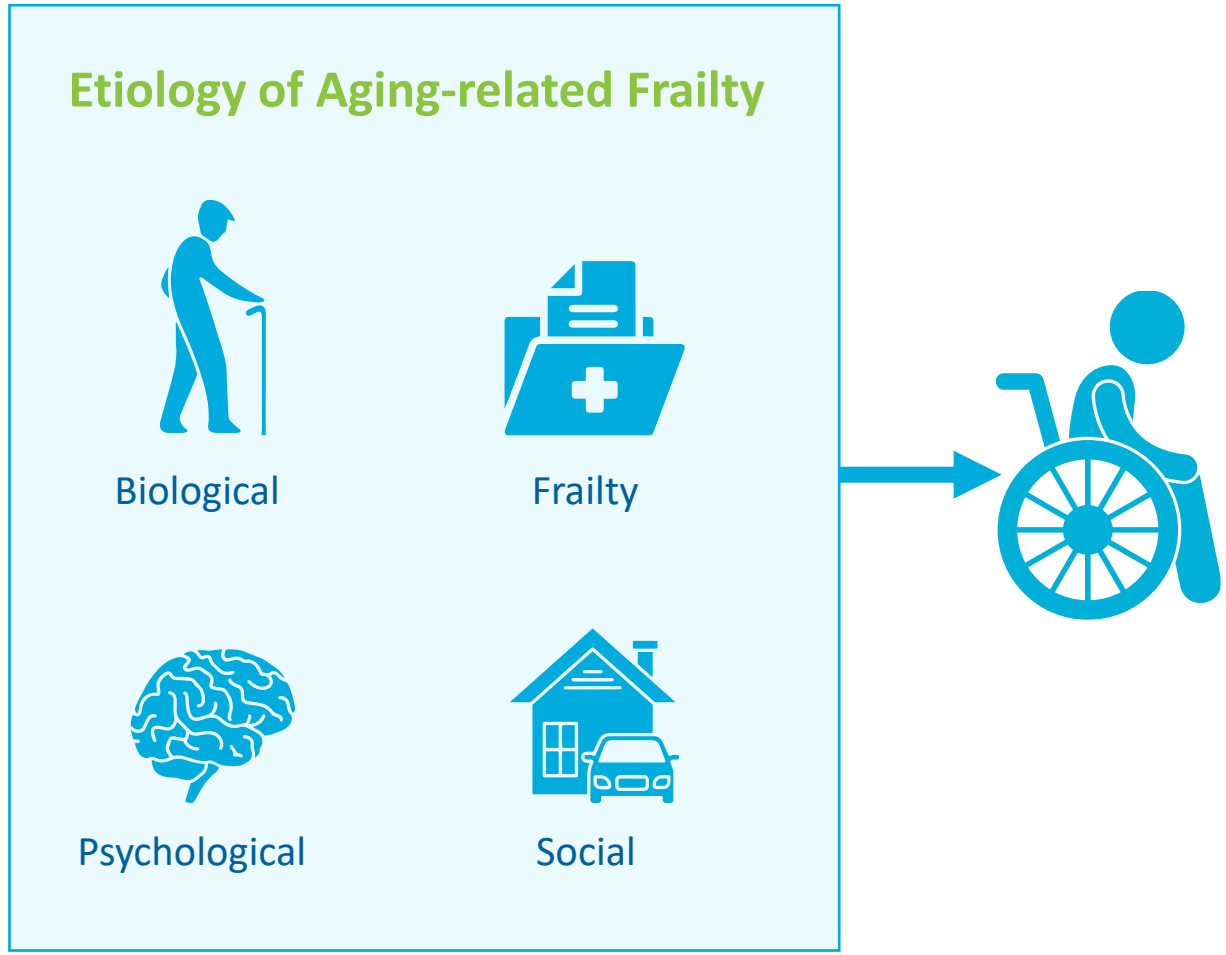
Aging-related Frailty*

Diminishing Health, Independence and QoL

- Frailty
  - Age-associated decline in reserve and function across multiple physiologic systems leading to inability to cope with stressors
  - Characterized by mobility disability, weakness, fatigue, weight-loss, slowness, low activity, etc.
- Higher risk for poor clinical outcomes
  - Infections, falls, fracture, hospitalizations, death
- High unmet need and high prevalence
- No approved treatments for Frailty
  - General prevalence of ~15% of individuals >65 using CHS Frailty Phenotype definition.[1]

Etiology of Aging-related Frailty



*Frailty/Aging-related Frailty" presently does not have a consensus definition of the indication for regulatory purposes

[1]Bandeen-Roche K, et al. J Gerontol A *Biol Sci Med Sci.* 2015

Lomecel-B™ for Aging-related Frailty

Completed U.S. Phase 2b Study Aging-related Frailty Study (N=143)

- Designed to determine whether there was a dose response to a single infusion of Lomecel-B™ in Aging-related Frailty
- There were 5 treatment groups: placebo and 4 different doses of Lomecel-B™: 25, 50, 100 and 200 million cells
  - Note: highest dose treatment group added after start of study
- Patients were defined as aged 70 to 85, with evidence of inflammation by elevated TNF-a levels at baseline, and with mild to moderate frailty (by CHS scale) and impaired mobility
- Primary efficacy endpoint measure was 6MWT – a test of physical endurance (distance walked in 6 minutes)

Results

There was a statistically significant increase in 6MWT in multiple Lomecel-B™ treatment groups 9 months after a single infusion of Lomecel-B™ compared to placebo

- There was also a dose-response to Lomecel-B™ as measured in 6MWT at 6 months
- There were no SAEs attributed to treatment with Lomecel-B™ and most AEs were related to the process of administration (associated with the insertion of a catheter for IV infusion)

Financial Position

$19.2 M
(as of 12/31/24)

Cash and cash equivalents

~14.9 M
(as of 12/31/24)

Shares of common stock outstanding;
~6.8M shares of common stock exercisable under outstanding warrants

Experienced and Successful Leadership



Wa'el Hashad

CHIEF EXECUTIVE OFFICER

- 35+ years as an executive leader in the biotechnology and pharmaceutical industries. His diverse global expertise encompasses leading early-stage companies focusing on drug approval and commercialization, as well as effectively overseeing mergers and acquisitions, and driving business development.



Joshua M. Hare, MD

CO-FOUNDER & CHIEF SCIENCE OFFICER

- A pioneer and world leader in stem cell research, he is the founding director of the Interdisciplinary Stem Cell Institute at the University of Miami's Miller School of Medicine and a Fellow of various esteemed associations, including the American Heart Association and the prestigious National Academy of Inventors.



Lisa Locklear

EVP & CHIEF FINANCIAL OFFICER

- Considerable CFO and global executive leadership experience in finance and accounting at Avanir Pharmaceuticals, GSN Games, CoreLogic, Ingram Micro, the Walt Disney Company, and Price Waterhouse (now PwC). She is also a recipient of the notable Healthcare Businesswoman's Association Luminary Award.



Nataliya Agafonova, MD

CHIEF MEDICAL OFFICER

- Extensive senior leadership experience in the biotechnology and pharmaceutical industries. Her successful cross-therapeutic expertise in drug development helped bring several products to the U.S. and EU markets.



Paul Lehr

GENERAL COUNSEL & SECRETARY

- Over 25 years of senior legal/executive roles in corporate and research settings. Former CEO of HeartGenomics, a cardiac biotech firm. Former President & General Counsel of a cardiac rehabilitation company, negotiating a master franchise agreement with 100+ facilities in India/the Middle East and securing Medicare approval with CMS.



Devin Blass

CTO & SVP, CMC

- Over 15 years of experience in the development and manufacture of advanced therapies. Mr. Blass served as SVP of Comprehensive Cell Solutions, the CDMO of New York Blood Center Enterprises (NYBCe). There, he oversaw the CDMO business unit, encompassing Technical Operations, Business Development, and Cell Sourcing.

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Thank You

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