LONGEVERON

A Regenerative Medicine Company

Investor Presentation

Nasdaq (LGVN) | January 2024



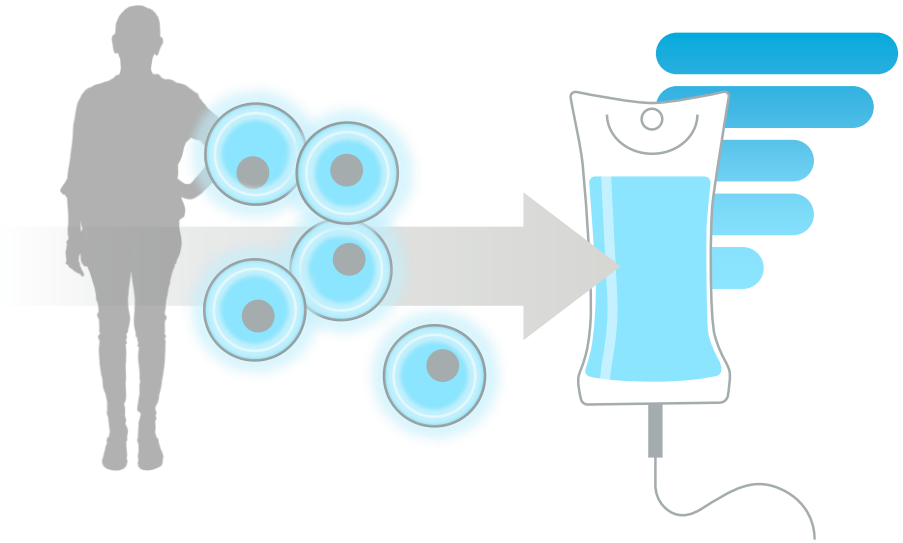
Forward Looking Statements

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, statements regarding the offer and sale of securities, the terms of the offering, about the ability of Longeveron's clinical trials to demonstrate safety and efficacy of the Company's product candidates, and other positive results; the timing and focus of the Company's ongoing and future preclinical studies and clinical trials and the reporting of data from those studies and trials; the size of the market opportunity for the Company's product candidates, including its estimates of the number of patients who suffer from the diseases being targeted; the success of competing therapies that are or may become available; the beneficial characteristics, safety, efficacy and therapeutic effects of the Company's product candidates; the Company's ability to obtain and maintain regulatory approval of its product candidates in the U.S., Japan and other jurisdictions; the Company's plans relating to the further development of its product candidates, including additional disease states or indications it may pursue; the Company's plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available and its ability to avoid infringing the intellectual property rights of others; the need to hire additional personnel and the Company's ability to attract and retain such personnel; the Company's estimates regarding expenses, future revenue, capital requirements and needs for additional financing; the Company's need to raise additional capital, and the difficulties it may face in obtaining access to capital, and the dilutive impact it may have on its investors; the Company's financial performance and ability to continue as a going concern, and the period over which it estimates its existing cash and cash equivalents will be sufficient to fund its future operating expenses and capital expenditure requirements. Additionally, Longeveron makes no assurance that any public offering of its securities as described herein will occur at all, or that any such transaction will occur on the timelines, in the manner, or on the terms anticipated due to numerous factors. Further information relating to factors that may impact the Company's results and forward-looking statements are disclosed in the Company's Quarterly and Annual Reports as filed with the Securities and Exchange Commission. 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.

About Longeveron

- We are a mid-clinical stage company focused on development of Medicinal Signaling Cells (MSCs) for rare diseases and aging-related medical conditions with high unmet need
- We have conducted successful programs in Alzheimer's Disease (AD) through Phase 2, and are conducting active Phase 2 clinical programs in Hypoplastic Left Heart Syndrome (HLHS) and Aging-related Frailty (AF)
- Recently announced postive results from our CLEARMIND Phase 2 trial of Lomecel-B™ in patients with mild-AD
- Presented five-year survival data from Phase 1 trial of Lomecel-B™ in HLHS at AHA 2023

Lomecel-B™ -- A Pipeline in a Product



Allogeneic medicinal signaling cells (MSCs) isolated from bone marrow of healthy young adults

Longeveron Overview

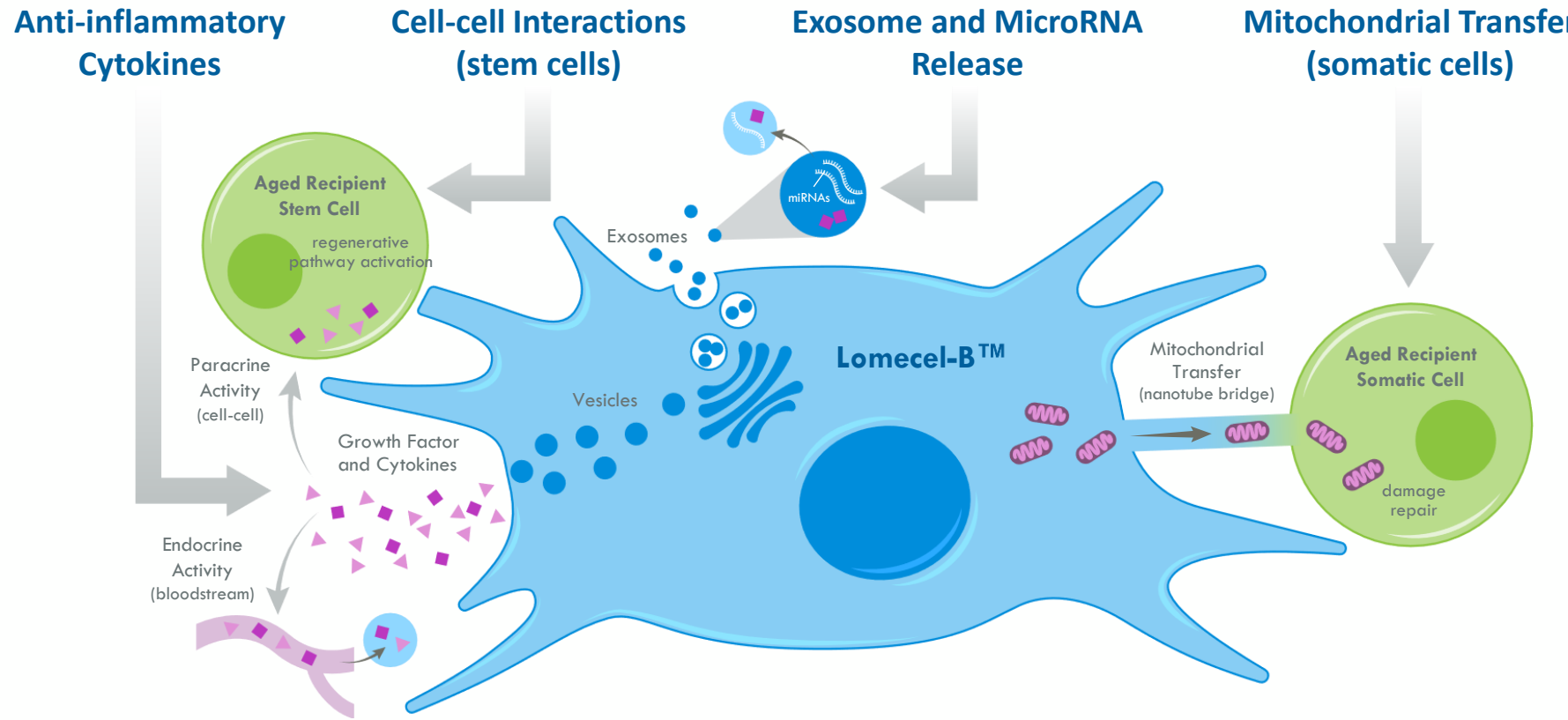
- Developing Medicinal Signaling Cells (MSCs) with Therapeutic Potential in a Range of Unmet Needs
- Postive Mid-Stage Data for Lead Asset Lomecel-B™
- Robust clinical pipeline in HLHS, Alzheimer's Disease and Aging-related Frailty
- On-site GMP Facility for Production of Lomecel-B™ (not dependent on CDMO)
- Balance Sheet Enhanced with Recent Equity Offerings, Significant Insider Ownership, No Debt
- Proven management, scientific, and manufacturing teams

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

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

Lomecel-B™ Key Advantages:

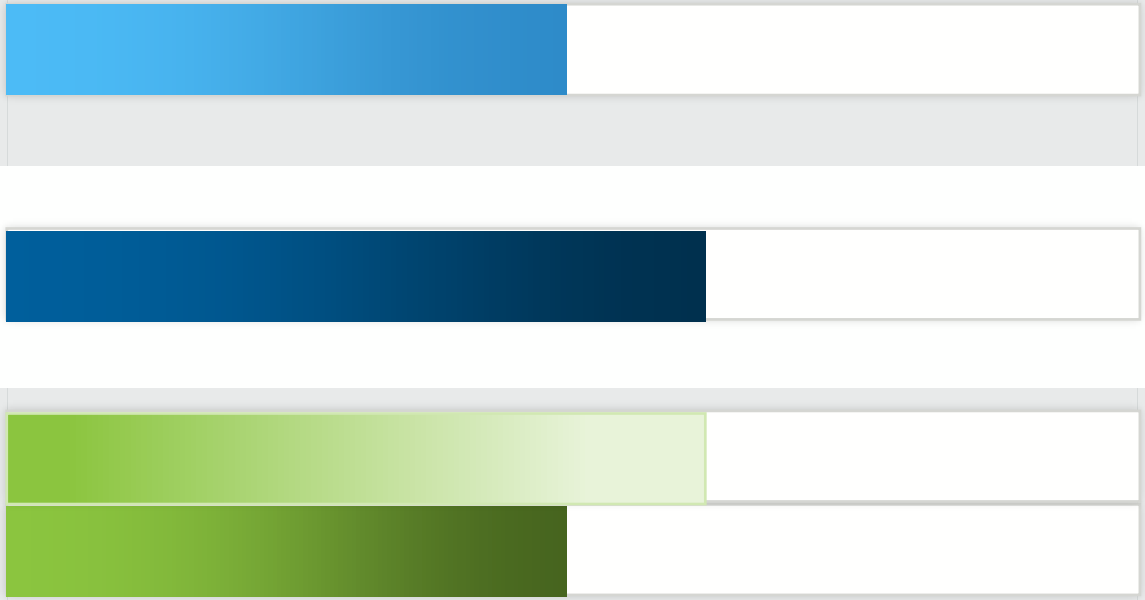
- Superior efficacy for addressing inflammation
- Cells migrate to sites of tissue damage
- Enhanced safety as inherently Immuno-evasive
- Convenient off-the-shelf administration



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.

Robust Clinical Pipeline

Indication	Geography	Phase 1	Phase 2	Phase 3	Milestones
Hypoplastic Left Heart Syndrome	U.S.				• ELIPIS 1 survival data presented at AHA 2023 • ELPIS 2 actively enrolling
Alzheimer's Disease	U.S.				• Positive Phase 2a data announced Q4 2023
Aging-related Frailty	U.S. Japan				• U.S. Phase 2b Single-Dose Trial complete • Ongoing Phase 2 trial in Japan.



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]	5.8 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] Alzheimer's Association estimate: https://www.alz.org/alzheimers-dementia/facts-figures.
[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

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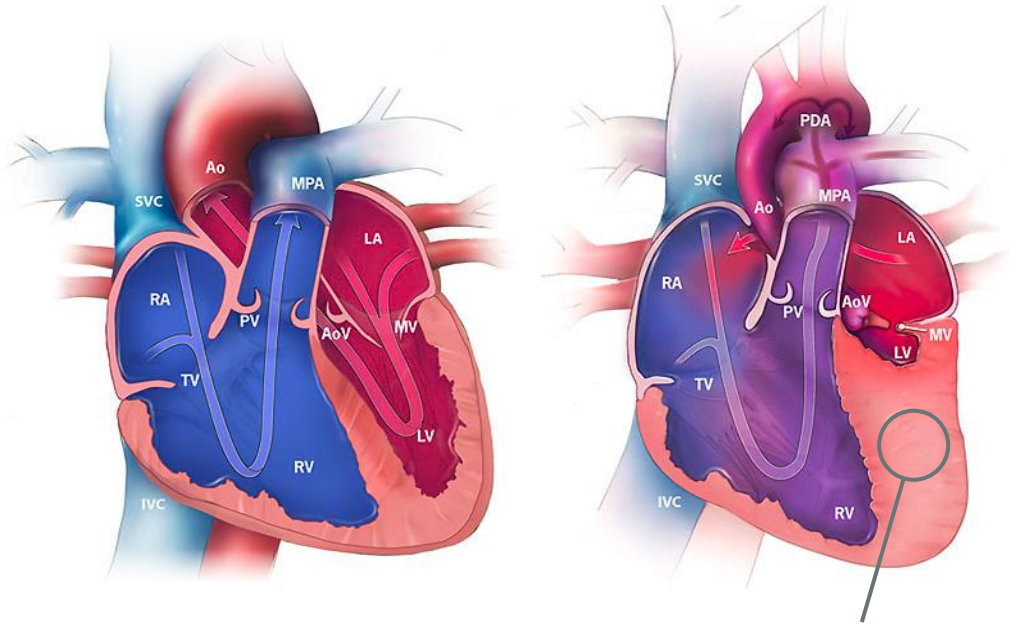
Lomecel-B™
for Hypoplastic Left Heart Syndrome (HLHS)

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]



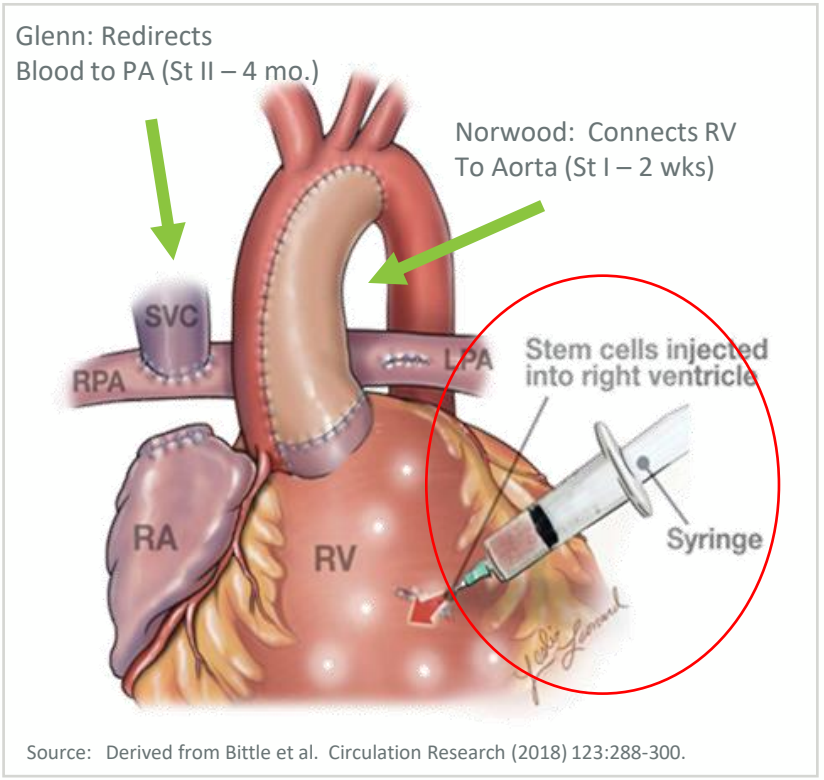
Normal Heart HLHS

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 2 ELPIS II Trial (n=38)
  - Primary Objective: To evaluate the clinical efficacy of Lomecel-B™ in HLHS to improve ejection fraction (EF) of the right ventricle and assess transplant-free survival benefit.
  - Primary endpoint: Change in RV ejection fraction (RVEF) measured between baseline and 12 months after the Stage II surgery; assessed via cardiac magnetic resonance (CMR).
  - Head-to-head trial vs current Standard of Care

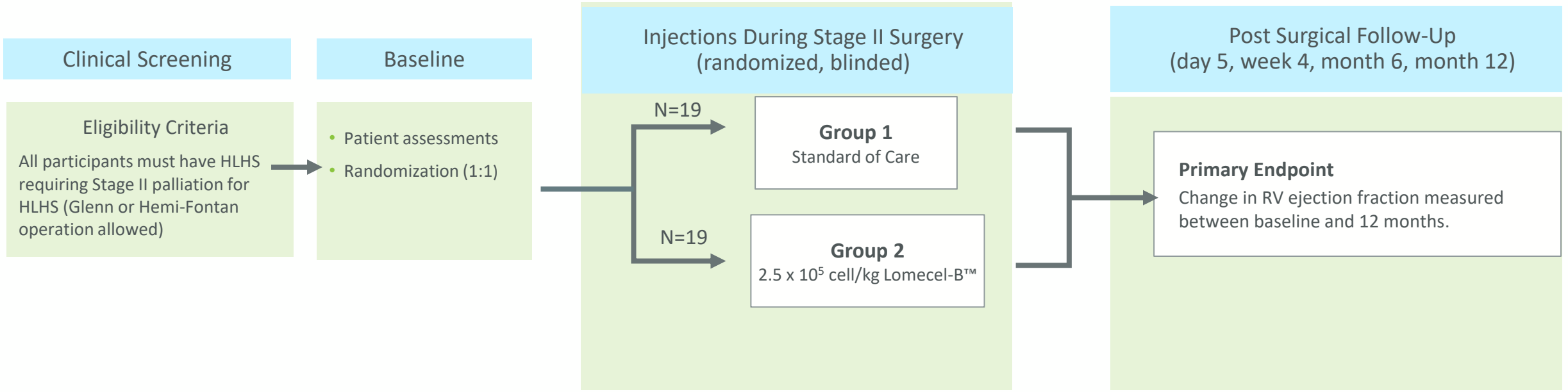


Source: Derived from Bittle et al. Circulation Research (2018) 123:288-300.

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

ELPIS II: Phase 2b Study Design

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

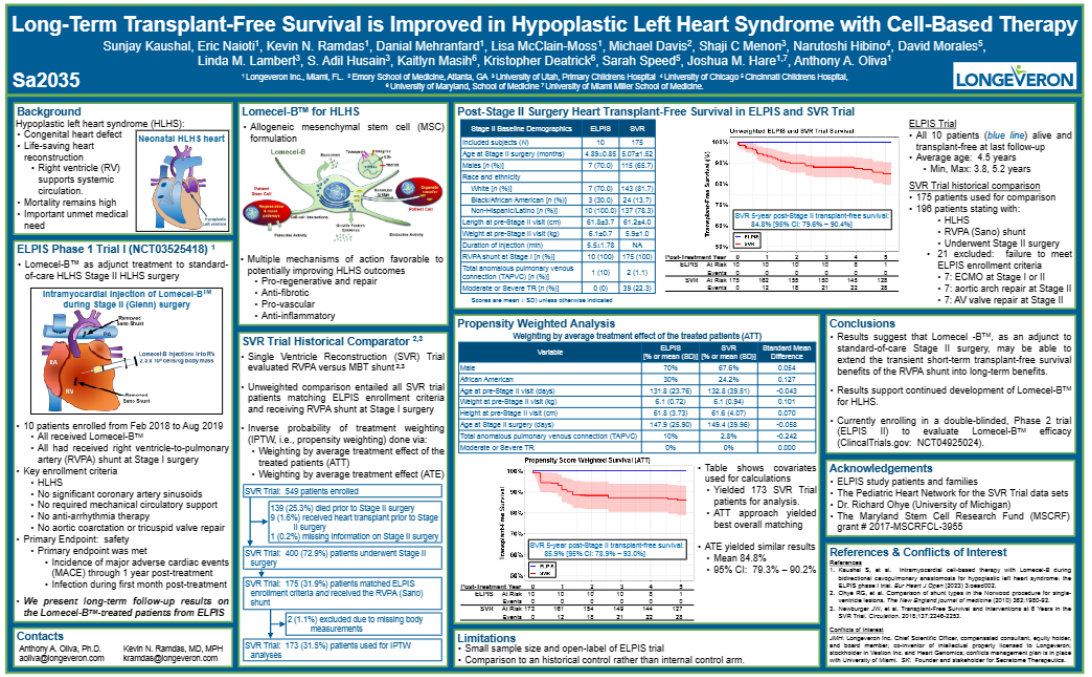


- ELPIS II is being conducted at leading clinical centers, including Boston Children's Hospital, Lurie's Children's Hospital, Children's Hospital of Los Angeles, Children's Healthcare of Atlanta, UTHealth-McGovern Medical School, Cincinnati Children's Hospital Medical Center, and Primary Children's Hospital at University of Utah
- ELPIS II is being conducted with the support of the National Heart, Lung, and Blood Institute (NHLBI)

Phase 1 Long-term Survival Data Presented at the 2023 American Heart Association

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

- Long-term follow-up beyond the initial study ELPIS is ongoing
- 5 years survival data are available
- None of the 10 treated patients required heart transplant up to 5 years post Stage 2 surgery
- Average age at last follow up 4.5 years
- Acceptable safety profile
- 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]



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.

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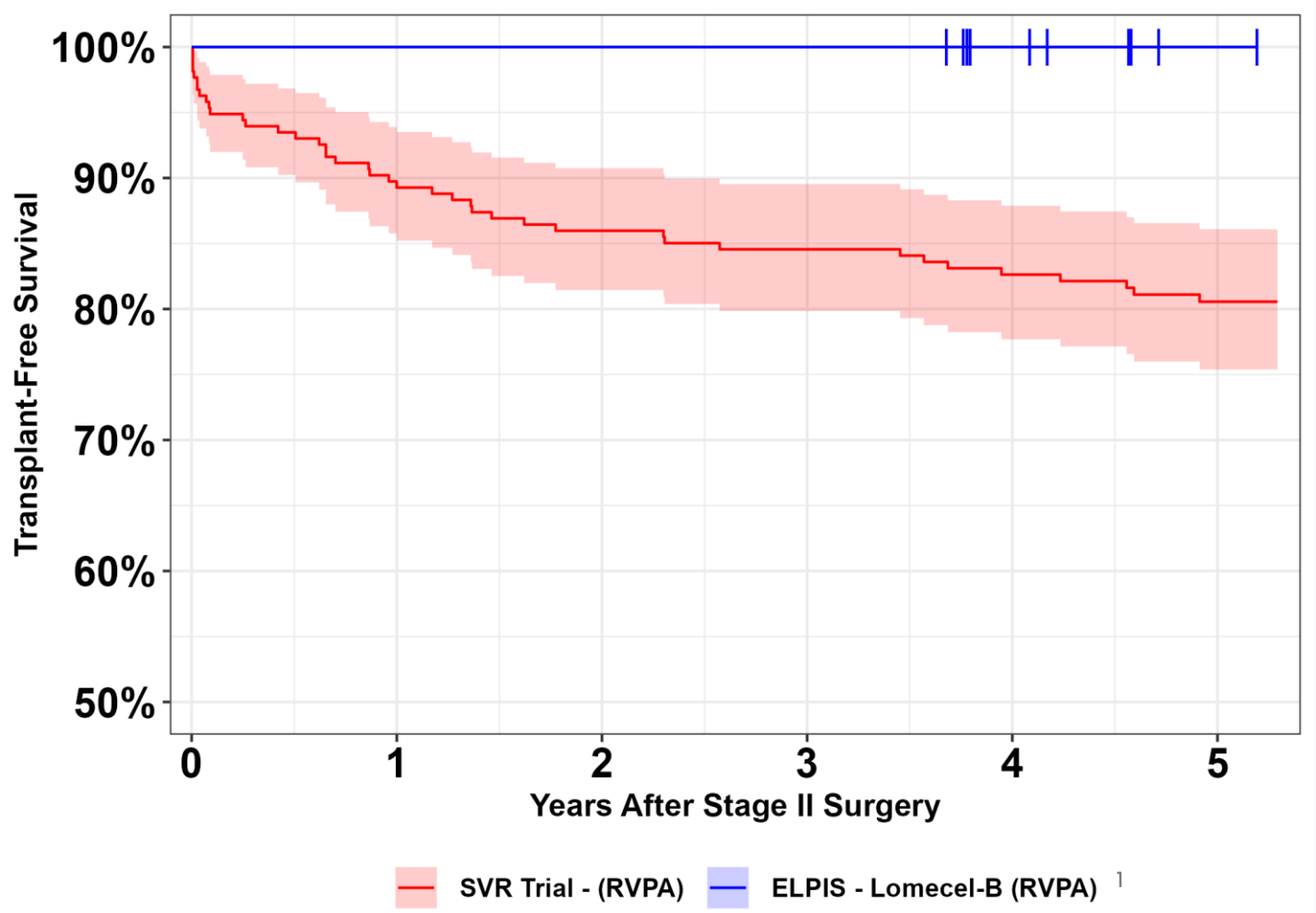
Long-term Survival in HLHS from ELPIS I Trial of Lomecel-B™



- 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 ~20%

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

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

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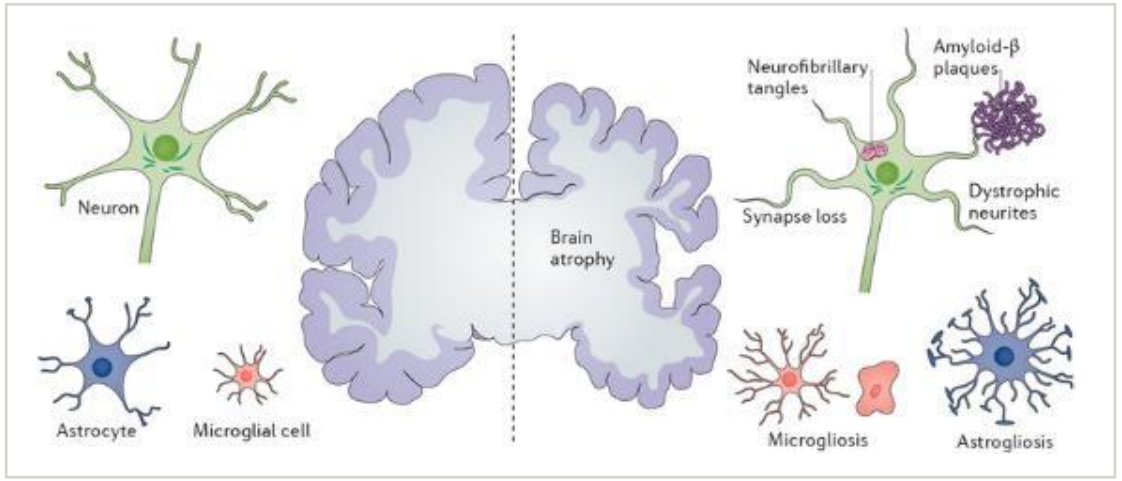
Lomecel-B™ for Alzheimer's Disease

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+

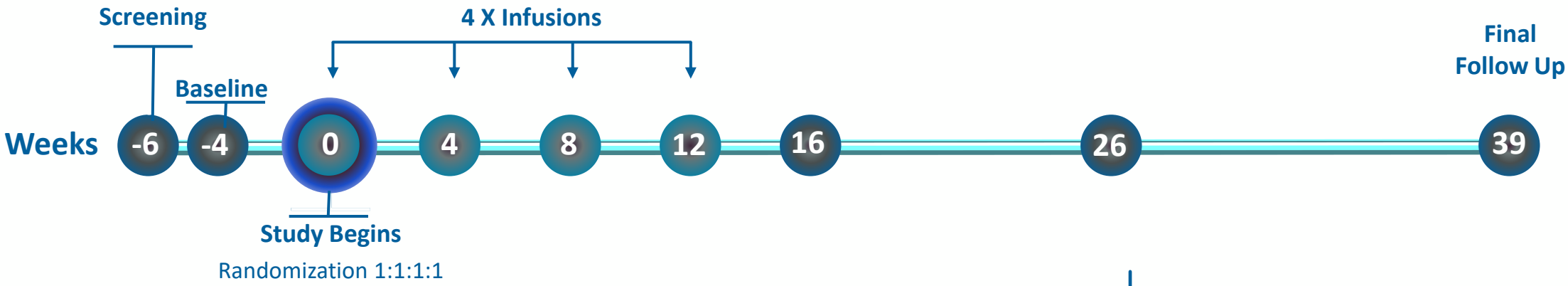


- MSCs effect in animal models of Alzheimer's Disease:
  - Cross the blood brain barrier (BBB)
  - ↓ pro-inflammatory; ↑ anti-inflammatory biomarkers
  - Improve immune functioning
  - Promote neurogenesis
  - Improve endothelial function

*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



Randomization 1:1:1:1

- Group 1: Placebo
- Group 2: Single Dose Lomecel-B™ (25M)
- Group 3: Multi dose Lomecel-B™ (25M)
- Group 4: Multi dose Lomecel-B™ (100M)

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

- Results Announced Q4 2023
- Lomecel-B™ demonstrated positive benefit/risk profile
- No Alzheimer's Disease related imagine abnormalities, hypersensitivity, infusion-related reactions, interruptions of infusions, or death
- Pre-specified secondary endpoint, a composite Alzheimer's Disease score (CADS), met its endpoint of superiority compared to placebo ($P<0.1$)
- Specific components of the CADS – hippocampal volume and ADS-QOL - were also statistically significant compared to placebo at $P<0.05$

CLEAR MIND Phase 2a Conclusions

- Data suggest Lomecel-B™ may:
  - Prevent disease worsening and even possibly improve cognitive function (based on the MoCa and MMSE indices)
  - Improve quality of life based on caregiver assessment (ADRQL)
- Lomecel-B™ was also associated with reduction of loss in brain volume in areas associated with Alzheimer's Disease (TBV, Hippocampus, Ventricles, Thalamus), decreases neuroinflammation as assessed by DTI, and improves cerebral blood flow
- Results of CLEAR MIND study provide a clear foundation for further development of Lomecel-B™ in mild Alzheimer's Disease patient population

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

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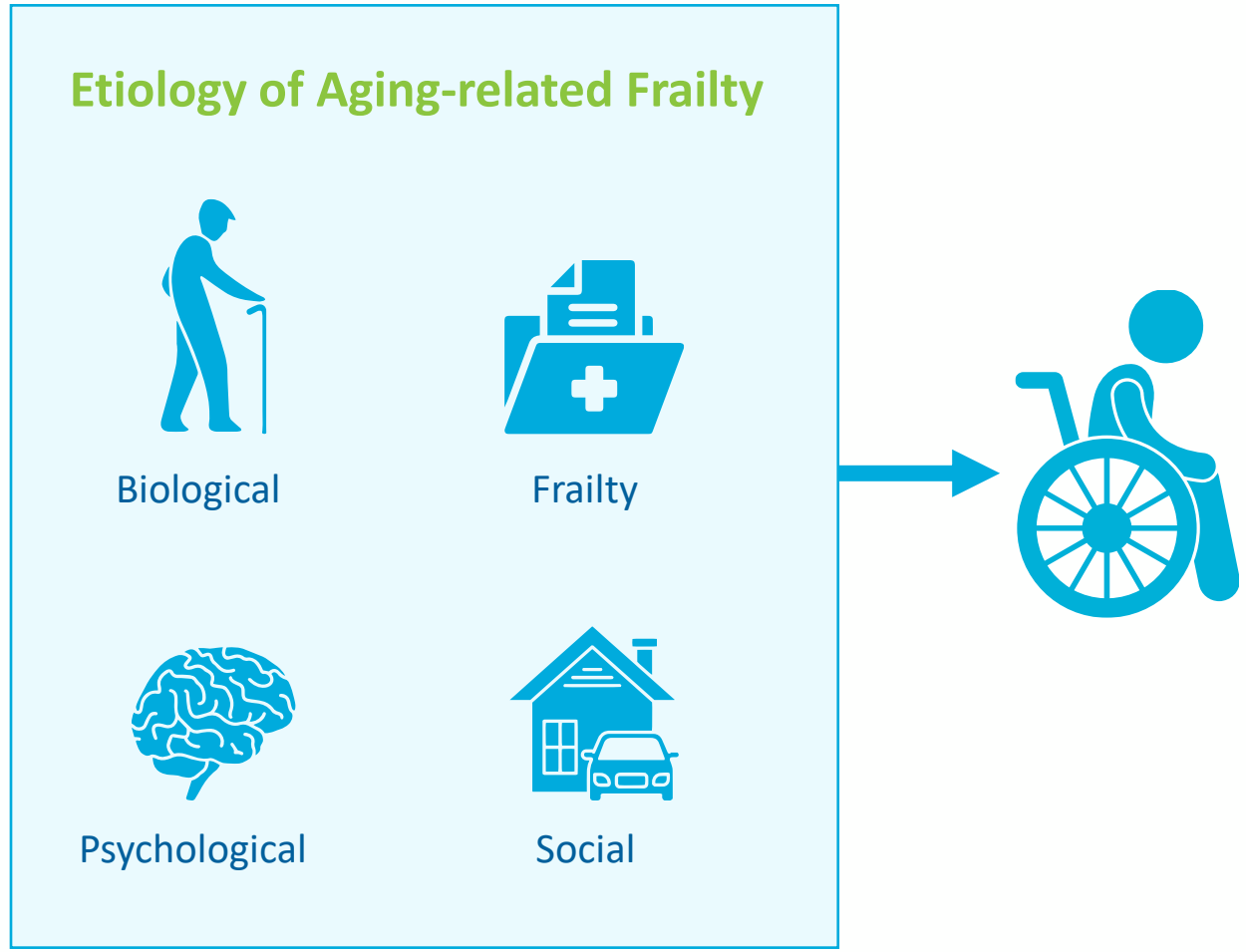
Aging-related Frailty*

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; however, it is likely that safety as observed in the proposed Phase 2 trial in Japan combined with the US Frailty 2b study will result in ASRM approval

[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)

Lomecel-B™ for Aging-related Frailty

Japan Clinical Trial Strategy Offers Fast Track for Regenerative Medicine

Regenerative Medicine (Gene and Cell Therapies)

The Act on the Safety of Regenerative Medicine (ASRM)



- Comprises all medical technologies for which the safety and efficacy have not yet been established
- Only approved for medical care and clinical research use and not intended for marketing
- Treatment at one's own expense with no insurance coverage unless part of clinical research[1]

The Act on Pharmaceuticals and Medical Devices (PMDA)



- Required for the production and marketing of regenerative and cellular therapeutic products by drug manufacturers for use nationally
- Conditional approval possible with clinical trials indicating a prediction of efficacy and assurance of safety

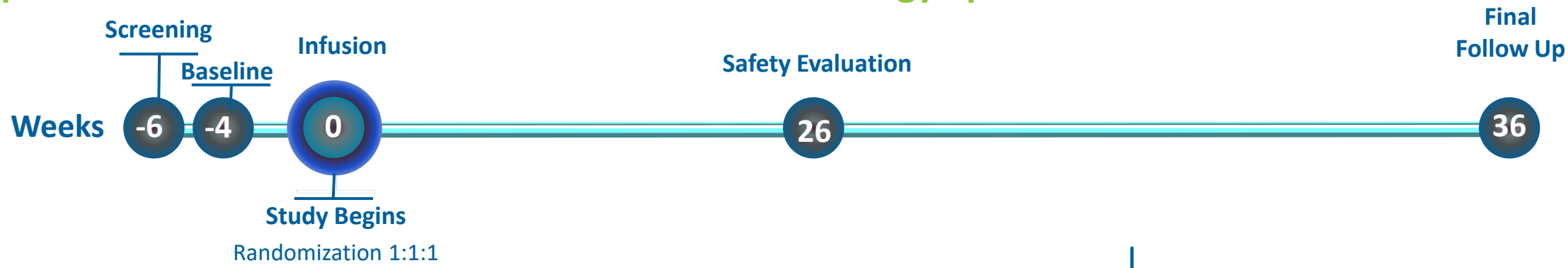
ASRM approval can lead to revenue generation years before BLA application with FDA or conditional approval by PMDA

[1] Will be funded by hospitals

Source: Ministry of Health, Labour and Welfare website; ClearView Analysis.

Aging-related Frailty Study Design

Japanese National Center for Geriatrics and Gerontology-sponsored trial



Randomization 1:1:1

- Group 1: Placebo (N=15)
- Group 2: Single Dose Lomecel-B™ (50M) (N=15)
- Group 3: Single Dose Lomecel-B™ (100M) (N=15)

Primary Endpoint

Percentage of patients with at least 1 SAE 4 weeks from infusion

Exploratory Endpoint

Change from Baseline in the Six Minute Gait Test (6 MWT)

- Patient population: 70-85 years old; MMSE >=25
- Amended protocol accepted by PMDA 8/2022

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.

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Thank You

Website
www.longeveron.com

Chief Financial Officer
Lisa Locklear
llocklear@longeveron.com

Investor Relations
Mike Moyer
LifeSci Advisors
(617) 308-4306
mmoyer@lifesciadvisors.com



LONGEVERON

Social Media

@LGVNSocial
@Longeveron
@Longeveron Inc

Converge Miami
1951 NW 7th AVENUE
Suite 520
Miami, FL 33136

844-470-2550
longeveron.com