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GRECC
Geriatric Research Education and Clinical Center
Honoring Veterans as they Age

Trial Results: Lomecel-B for Aging Frailty

A Phase 2b, Randomized, Blinded and Placebo-Controlled Trial to Evaluate the Safety and Efficacy of Lomecel-B Infusion in Patients with Aging Frailty

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Forward Looking Statements

Certain statements in this presentation that are not historical facts are forward-looking statements that reflect management's current expectations, assumptions, and estimates of future 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. Moreover, forward-looking statements in this release include, but are not limited to, statements about the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results; the timing and focus of our ongoing and future preclinical studies and clinical trials; the size of the market opportunity for our product candidates, the beneficial characteristics, safety, efficacy and therapeutic effects of our product candidates; our ability to obtain and maintain regulatory approval of our product candidates, our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available and our ability to avoid infringing the intellectual property rights of others. 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 SEC. The forward-looking statements contained in this press release are made as of the date of this press release, 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.

Personal Disclosures

None.

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Aging Frailty: Diminishing Health, Independence and Quality of Life

- **Frailty in older adults**
  - ➢Age-associated decline in physiological reserve, with prevalence of ~15% of individuals ≥65
  - ➢Characterized by mobility disability, weakness, fatigue, weight loss, slowness, low activity, etc.
  - ➢At high risk for functional impairment and poor clinical outcomes
  - ➢Highly important unmet need without any approved therapeutic interventions

  (Bandeen-Roche K, et al. *J Gerontol A Biol Sci Med Sci.* 2015)

- **Pathophysiology**
  - ➢Inflammaging
  - ➢Impaired vascular function

*Frailty/Aging Frailty" is currently not a recognized indication by US FDA or Japan PMDA

Frailty in Older Adults

- No approved therapies for frailty
- Current interventions focus on diet and exercise (SPRINTT trial)
- We report on the results of Lomecel-B on aging frailty
  - Enrolled 148 patients
  - Funded by the NIA

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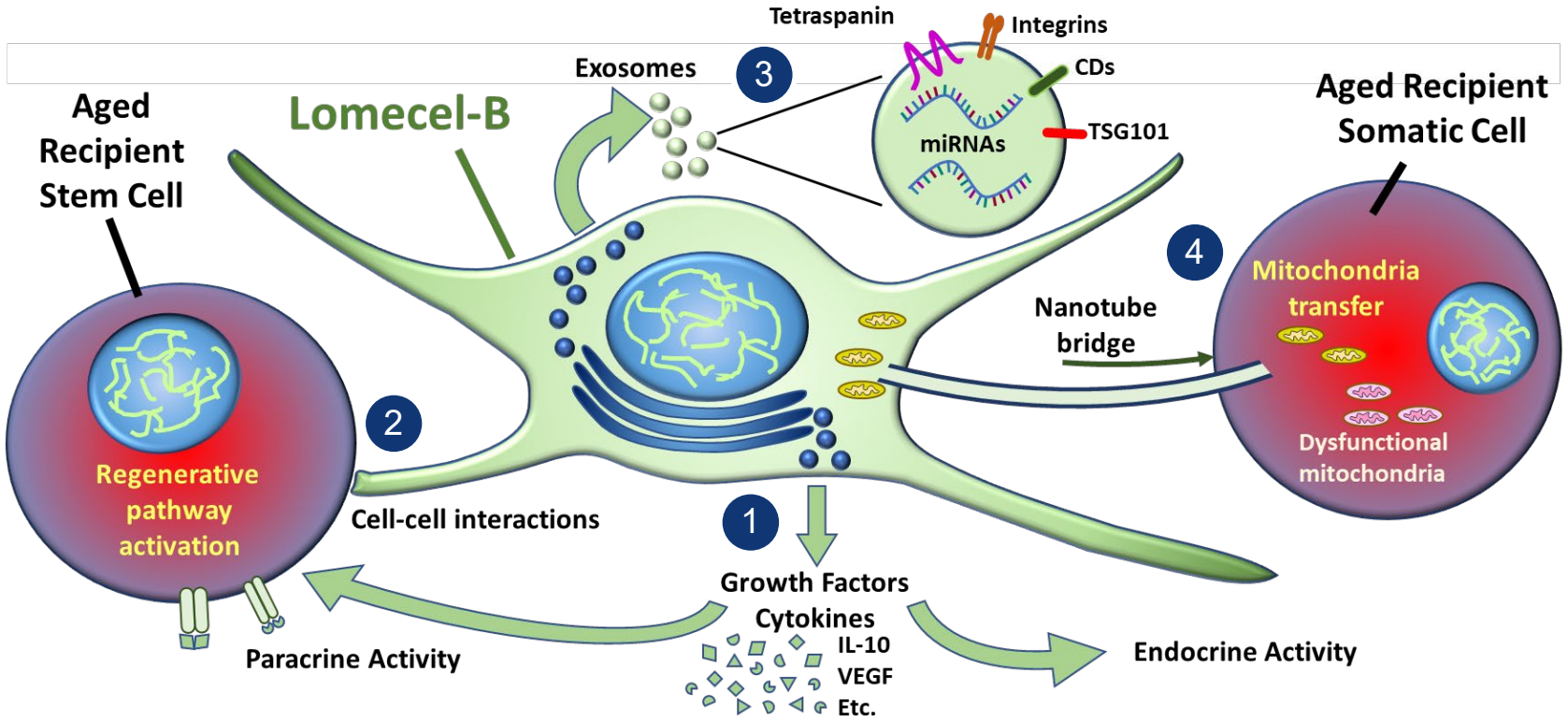
Lomecel-B is a proprietary formulation of allogeneic bone marrow-derived MSCs with pleiotropic mechanisms of action



Potential Mechanisms of Action

- Pro-vascular/pro-endothelial
- Anti-inflammatory
- Anti-fibrotic
- Stimulate intrinsic regenerative/repair

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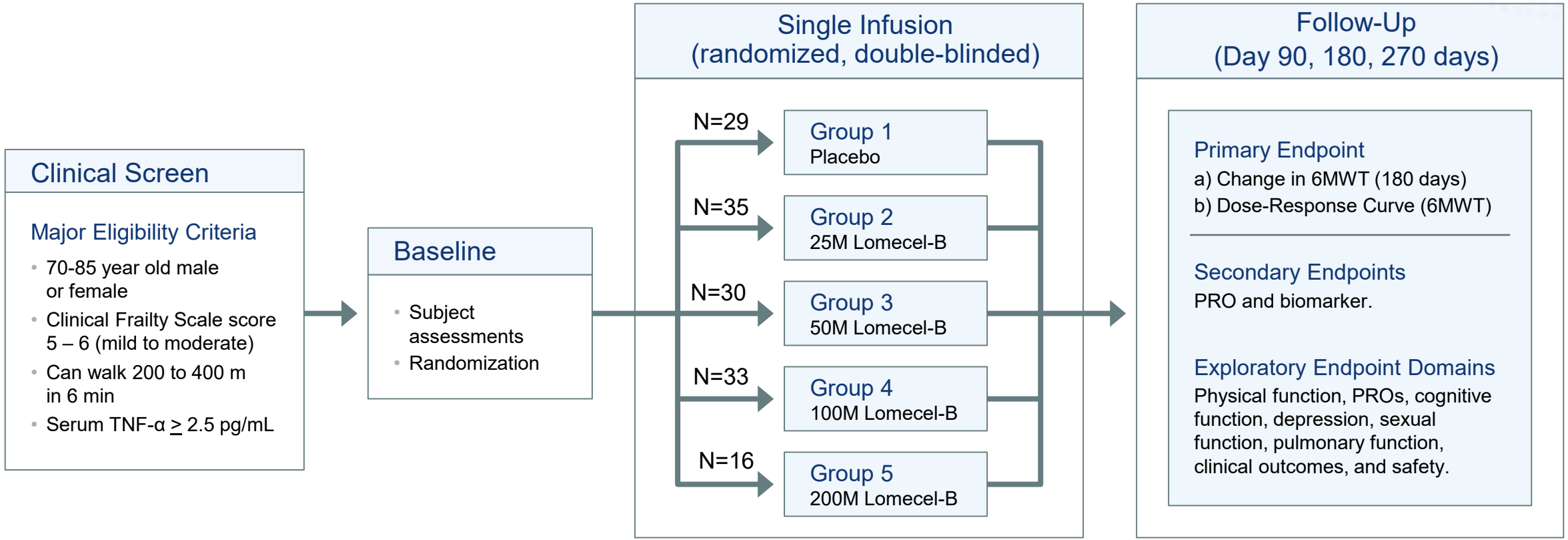
Lomecel-B in Aging Frailty Phase 2b Clinical Trial



Specific Trial Objectives

- Can Lomecel-B improve physical function?
- Is there a dose-response relationship with Lomecel-B?
- Are there patient reported outcomes (PROs) that correlate with change in physical function?
- Are there biomarkers that support the mechanisms of action?
- Can the safety profile from previous allogeneic MSC studies be reproduced using Longeveron-manufactured Lomecel-B?
- Can the potential patient population be refined?
- Can a potency assay be developed for the indication?

Phase 2b Study Aging Frailty Study Design



NIH National Institute on Aging

1R44AG062015-01

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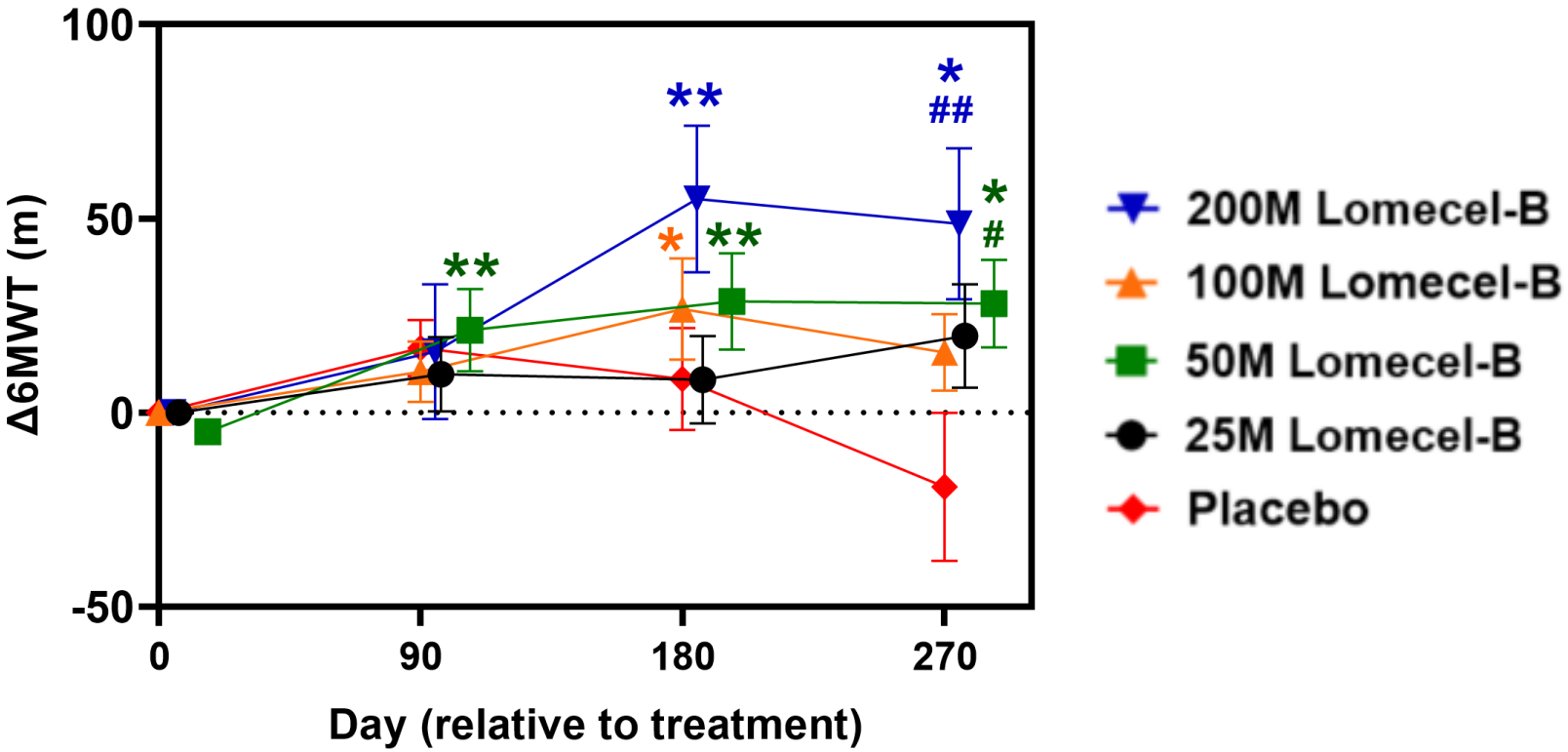
Lomecel-B Infusion Improved Walking Distance Over 9 Months



* Change from baseline: $p<0.05$

** Change from baseline: $p<0.01$

\# Versus placebo: $p<0.05$

\#\# Versus placebo: $p<0.01$

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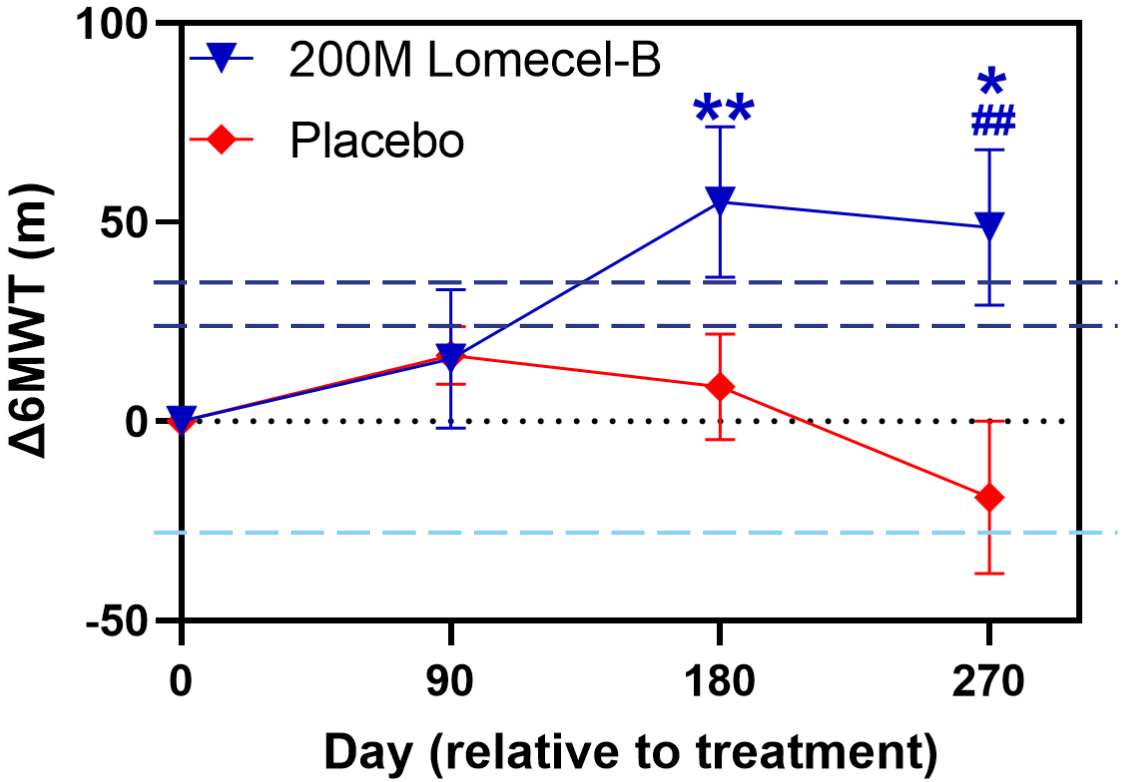
Lomecel-B led to ~ 50 meter increase in walking distance (200 million cell dose group)



Day 270 Δ6MWT (200M vs Placebo) = 63.4 meters ($CI_{95\%}$ 17.1 – 109.62), *p=0.0077*

32m MCID[4] (CHF patients)

17.8m MCID[2] and 20m MCID[3]

-30m Δ = 19% increased mortality[1] (CHF patients)

*** Change from baseline; p<0.05**

**** Change from baseline; p<0.01**

Versus placebo; p<0.01

MCID: Minimal Clinically Important Difference

[1] R. Boxer, A. Kleppinger, A. Ahmad, K. Annis, D. Hager, A. Kenny. The 6-MinuteWalk Is Associated With Frailty and Predicts Mortality in Older Adults With Heart Failure. (2010) *Congest Heart Fail.* 16:208.

[2] B.C. Kwok,Y.H Pua, K. Mamun, W.P. Wong. The minimal clinically important difference of six-minute walk in Asian older adults. (2013) *BMC Geriatrics* 13:23

[3] S. Perera, S.H. Mody, R.C. Woodman, S.A. Studenski Meaningful Change and Responsiveness in Common Physical Performance Measures in Older Adults. (2006) *J Am Geriatr Soc* 54:743.

[4] M.J. Shoemaker, A.B. Curtis, E. Vangsnes, M.G. Dickinson. Clinically Meaningful Change Estimates for the Six-Minute Walk Test and Daily Activity in Individuals With Chronic Heart Failure. (2013) *Cardiopulmonary Physical Therapy J.* 24:21.

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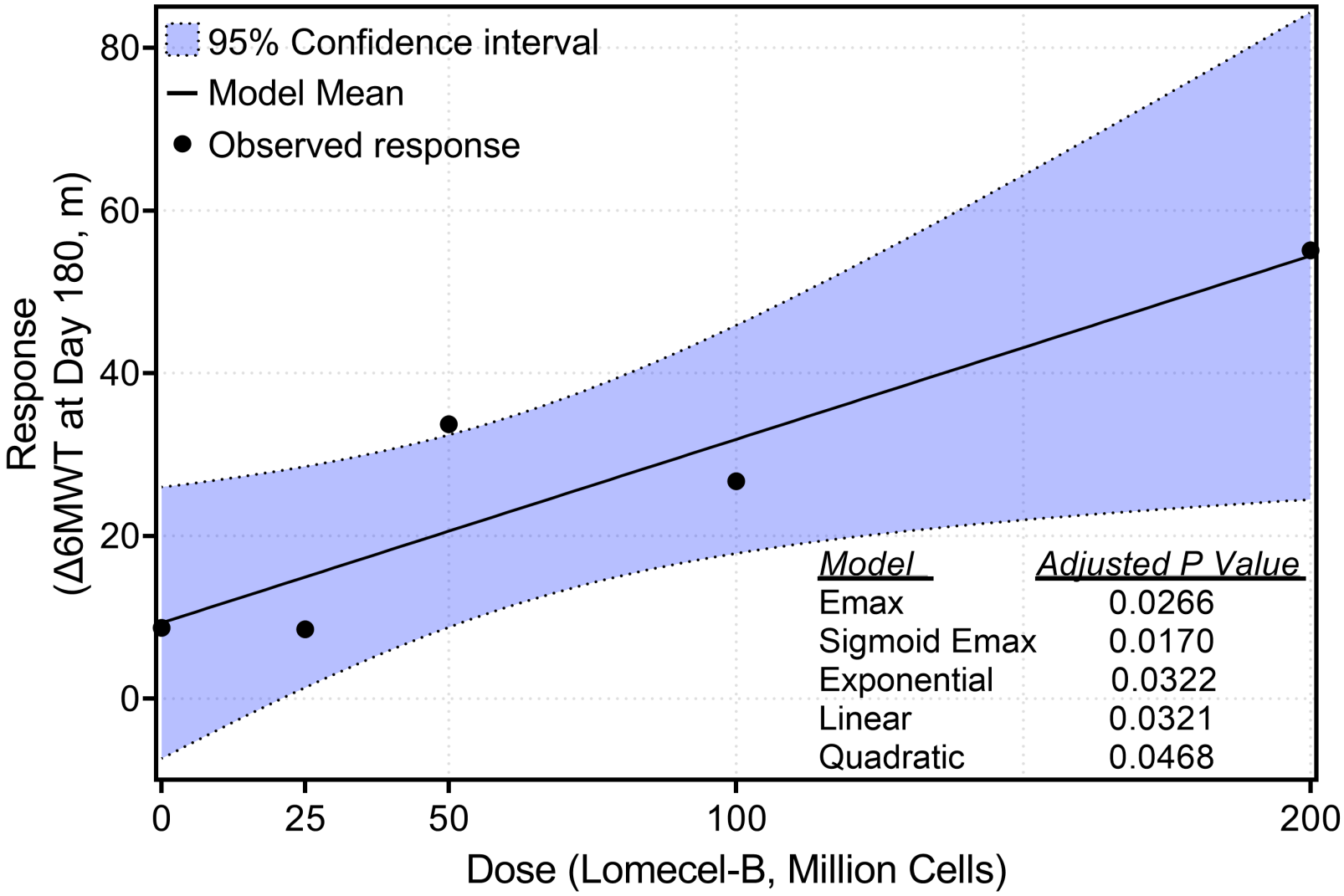
Statistically-significant dose response using 6MWT at 180 days.



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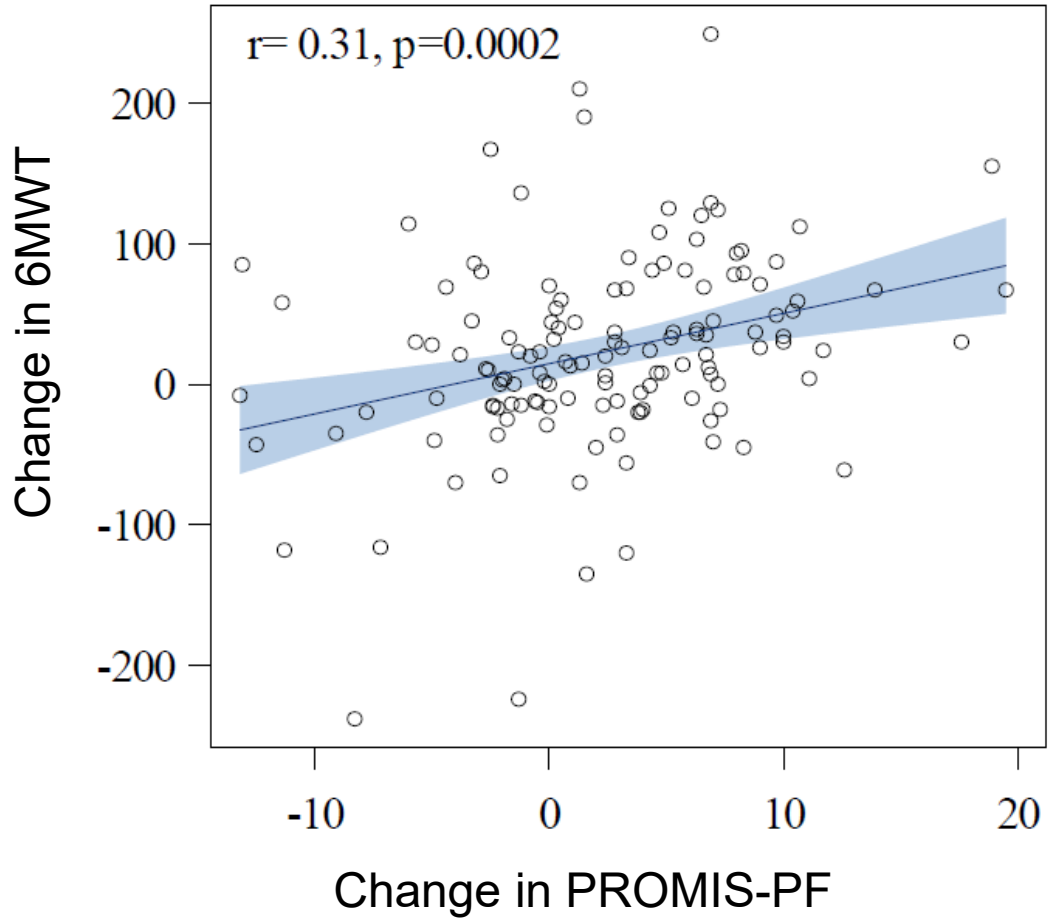
Change in PROMIS-Physical Function SF-20 correlated with change in 6MWT when all Lomecel-B combined



PROMIS-PF: Patient-Reported Outcome Measurement Information System-Physical Function

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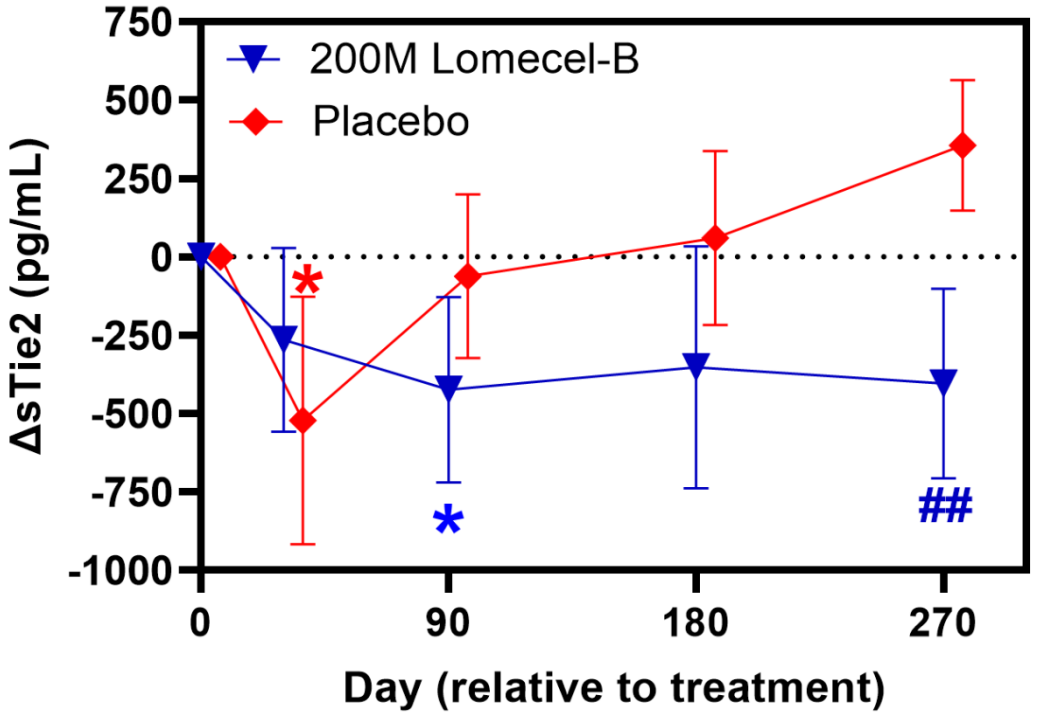
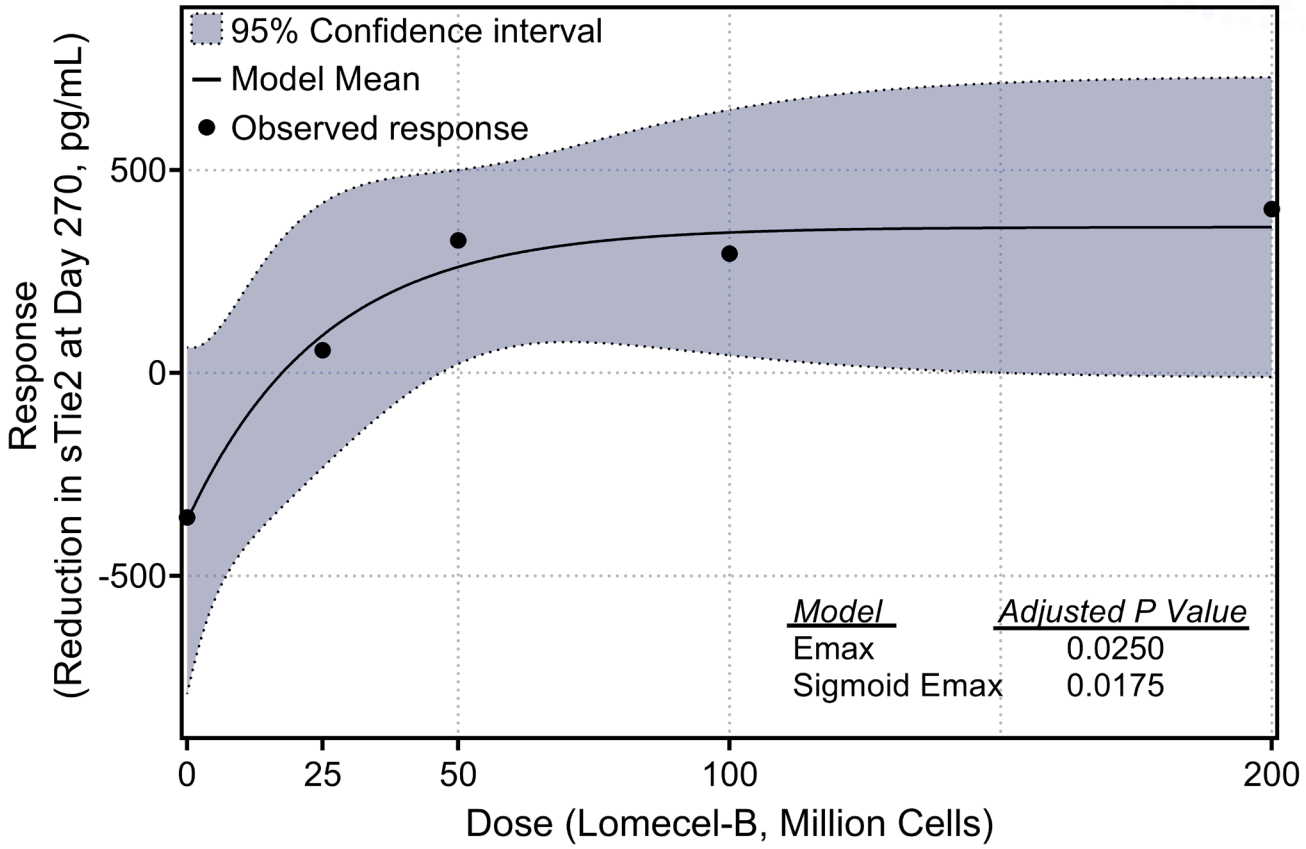
Lomecel-B 200M arm showed decreased serum levels of soluble Tie2 (sTie2): supports pro-vascular and anti-inflammatory MOAs





* Change from baseline; p<0.05

Versus placebo; p<0.01

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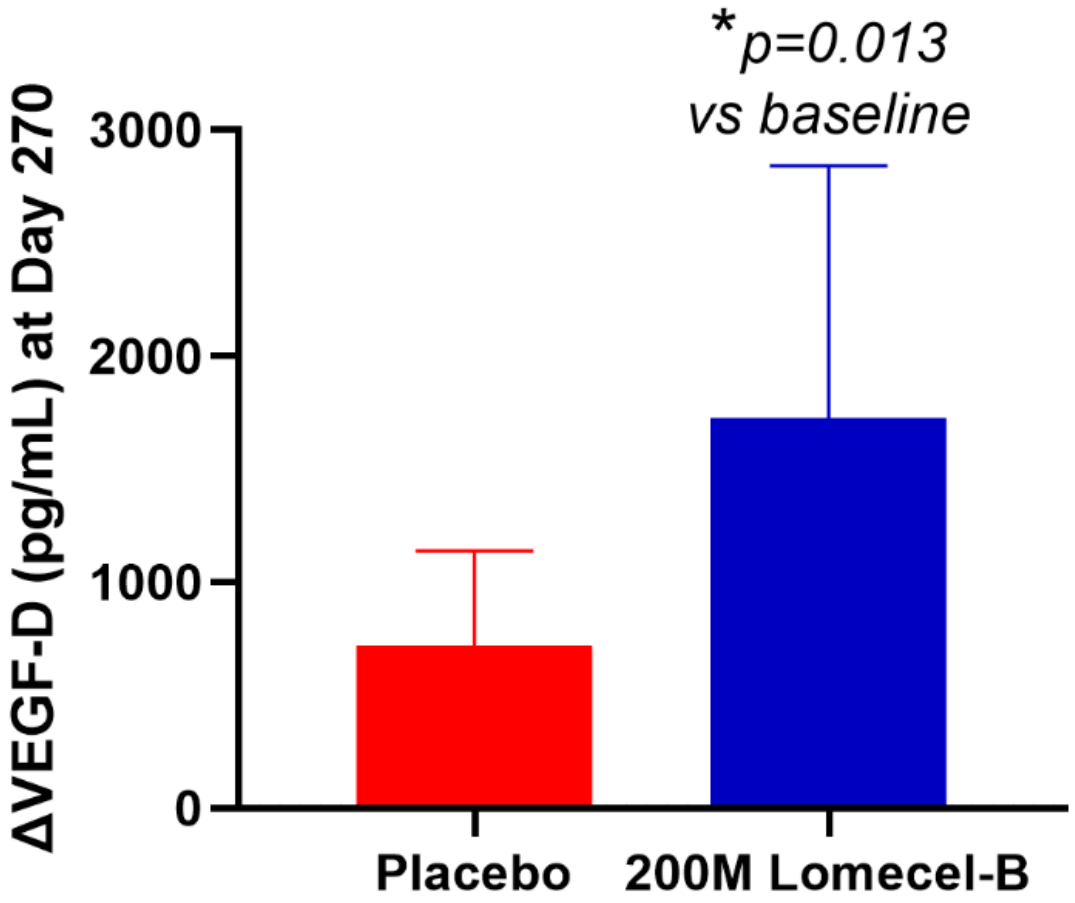
Lomecel-B 200M arm showed increased VEGF-D: supports pro-vascular MOA



VEGF-D: Vascular endothelial growth factor-D

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Safety Findings

- No product-related serious adverse events (SAEs)
- No clinically significant issues identified via laboratory evaluations
- Consistent with prior safety results

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Summary of Results and Objectives

Significant improvement in 6MWT (functional capacity endpoint) over 9 months……

Demonstrated dose response curve → suggests biological activity……

Patient-reported outcomes that correlate with functional changes……

Biomarkers supporting mechanisms of action…… **Further biomarker analysis pending**

Reproduced safety profile of Lomecel-B……

Refine the patient population…… …… **Population stratification analysis pending**

Develop a potency assay…… **Ongoing process**

Acknowledgements

- We thank the many patients who volunteered for this study

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  - Pedro Ylisastigui, MD: Clinical Physiology Associates – Ft. Myers, FL

- Longeveron staff and numerous others

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Thank You
and
Panel Discussion

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