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REVASCOR IMPROVES SURVIVAL AND REDUCES MAJOR MORBIDITY IN HIGH-RISK ISCHEMIC HEART FAILURE PATIENTS WITH INFLAMMATION

Phase 3 trial results published in European Journal of Heart Failure identify key target population for Mesoblast allogeneic cell therapy

Melbourne, Australia; December 3 and New York, USA; December 2, 2024: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, today announced a key publication in the November 2024 online issue of the prestigious peer-reviewed *European Journal of Heart Failure (EJHF)*, which reports that a single intramyocardial injection of the Company's allogeneic cell therapy Revascor® (rexlemestrocel-L) results in improved survival in high-risk patients with ischemic heart failure and inflammation.[1]

Results from the randomized, controlled DREAM-HF trial in patients with chronic heart failure with reduced ejection fraction (HFrEF) identified the control group at highest risk of cardiovascular death as being those with ischemic etiology and inflammation and showed that a single intramyocardial injection of Mesoblast's mesenchymal precursor cell therapy (MPCs; rexlemestrocel-L) resulted in a sustained reduction in cardiovascular mortality in these high-risk patients. This identifies the target HFrEF population that is responsive to REVASCOR therapy.

DREAM-HF's lead investigator, Dr. Emerson C. Perin, MD, PhD, FACC, Medical Director at The Texas Heart Institute, said "Mesoblast's allogeneic MPCs may restore the balance between anti-inflammatory and pro-inflammatory cytokines in the damaged, inflamed heart. A single administration of MPCs appears sufficient to improve survival and other major clinical outcomes in high-risk HFrEF patients with inflammation. These effects are seen on top of existing treatments that target neurohormonal imbalances and congestion, providing a disease-modifying approach not achievable with standard-of-care alone."

The newly published results showed that over a mean follow-up of 30 months in the DREAM-HF trial:

- Factors portending the greatest risk for cardiovascular death in control patients were inflammation (baseline plasma high-sensitivity C-reactive protein ≥2 mg/L; p=0.003) and ischemic HFrEF etiology (p=0.097), with increased cardiovascular death risk of 61% and 38%, respectively.
- A single intra-myocardial MPC administration significantly lowered the risk of cardiovascular death in HFrEF patients with inflammation regardless of whether plasma hsCRP or plasma IL-6 was used as inflammatory biomarker by 80% (p=0.003) and 60% (p=0.037) respectively.
- MPCs reduced 2-point MACE (heart attack or stroke) by 57% (p=0.016) and 3-point MACE (cardiovascular death, heart attack, stroke) by 35% (p=0.049) in patients with ischemic HFrEF (n=303) compared to controls.
- MPCs reduced 2-point and 3-point MACE by 88% (p=0.005) and 52% (p=0.018) respectively, in patients with ischemic HFrEF and inflammation (n=158) compared to controls.

"We are pursuing potential approval pathways for our STRO3-immunoselected and industrially manufactured heart failure product REVASCOR across the continuum from pediatric congenital heart disease to adults with ischemic HFrEF," said Mesoblast Chief Executive Dr. Silviu Itescu. "Earlier this year we received feedback from the U.S. Food and Drug Administration (FDA) providing support for an accelerated approval pathway in end-stage ischemic HFrEF patients with a left ventricular assist device (LVAD). This new publication identifies the larger ischemic HFrEF population which responds to REVASCOR with mortality benefit."

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About Revascor® (rexlemestrocel-L) in Heart Disease
REVASCOR is an allogeneic preparation of immunoselected and culture-expanded mesenchymal precursor cells (MPC) and is being developed as an immunomodulatory therapy to address the high degree of inflammation in the heart and cardiovascular system that is present across the spectrum of HFrEF patients ranging from New York Heart Association (NYHA) class II through end-stage disease, in order to reduce the high rate of major cardiovascular events and complications. This investigational therapy has been evaluated in two large placebo-controlled randomized studies in patients with chronic HFrEF. These consisted of a trial with 537 NYHA class II/III treated patients (DREAM-HF)[2] and a 159-patient trial in end-stage HFrEF patients implanted with a left ventricular assist device (LVAD).

Rexlemestrocel-L has US Food and Drug Administration (FDA) Regenerative Medicine Advanced Therapy (RMAT) and Orphan Drug designations for patients with end-stage HFrEF implanted with an LVAD.

About Chronic Heart Failure
Chronic heart failure (CHF) is characterized by poor heart function resulting in insufficient blood flow to the body's vital organs and extremities. This condition affects approximately 6.5 million people in the United States and 26 million people globally with increasing prevalence and incidence. Chronic heart failure patients are commonly classified according to the New York Heart Association (NYHA) categories based on the patient's physical limitations. Class I (mild) patients have no limitations while Class IV patients (severe/end stage) experience symptoms even at rest.

The mortality rate approaches 50% at 5 years as patients progress beyond NYHA early class II disease in parallel with increasing inflammation in the heart and in the circulation.[3,4] Despite recent approvals of new therapies for HFrEF, NYHA class II/III HFrEF patients with inflammation remain at high risk for cardiovascular death, heart attacks and strokes.

Over 100,000 patients annually in the US progress to end-stage heart failure (NYHA class IIIB/IV). These patients have a one-year mortality exceeding 50%.[5] Use of LVADs in end-stage heart failure patients to improve survival is gaining momentum, with approximately 2,000 LVADs implanted as destination therapy annually in the US,[6] the majority of whom have an ischemic etiology.

About Mesoblast
Mesoblast (the Company) is a world leader in developing allogeneic (off-the-shelf) cellular medicines for the treatment of severe and life-threatening inflammatory conditions. The Company has leveraged its proprietary mesenchymal lineage cell therapy technology platform to establish a broad portfolio of late-stage product candidates which respond to severe inflammation by releasing anti-inflammatory factors that counter and modulate multiple effector arms of the immune system, resulting in significant reduction of the damaging inflammatory process.

Mesoblast has a strong and extensive global intellectual property portfolio with protection extending through to at least 2041 in all major markets. The Company's proprietary manufacturing processes yield industrial-scale, cryopreserved, off-the-shelf, cellular medicines. These cell therapies, with defined pharmaceutical release criteria, are planned to be readily available to patients worldwide.

Mesoblast is developing product candidates for distinct indications based on its remestemcel-L and rexlemestrocel-L allogeneic stromal cell technology platforms. Remestemcel-L is being developed for inflammatory diseases in children and adults including steroid refractory acute graft versus host disease, and biologic-resistant inflammatory bowel disease. Rexlemestrocel-L is being developed for advanced chronic heart failure and chronic low back pain. Two products have been commercialized in Japan and Europe by Mesoblast's licensees, and the Company has established commercial partnerships in Europe and China for certain Phase 3 assets.

Mesoblast has locations in Australia, the United States and Singapore and is listed on the Australian Securities Exchange (MSB) and on the Nasdaq (MESO). For more information, please see www.mesoblast.com, LinkedIn: Mesoblast Limited and Twitter: @Mesoblast

References / Footnotes

1. Perin EC. Et al. Mesenchymal precursor cells reduce mortality and major morbidity in ischaemic heart failure with inflammation: DREAM-HF. *Eur J Heart Fail* 2024. https://doi.org/10.1002/ejhf.3522
2. Perin EC. Et al. Randomized Trial of Targeted Transendocardial Mesenchymal Precursor Cell Therapy in Patients with Heart Failure. *JACC* Vol. 81, No. 9, 2023. https://doi.org/10.1016/j.jacc.2022.11.061
3. AHA's 2017 Heart Disease and Stroke Statistics

4. Ponikowski P., et al. Heart Failure: Preventing disease and death worldwide. *European Society of Cardiology*. 2014; 1: 4-25
5. Gustafsson F, Rogers JG. Left ventricular assist device therapy in advanced heart failure: patient selection and outcomes. European Journal of Heart Failure 2017;19:595-602.
6. Yuzefpolskaya M et al. Ann Thorac Surg 2023; 115:311-28

Forward-Looking Statements

This press release includes forward-looking statements that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements should not be read as a guarantee of future performance or results, and actual results may differ from the results anticipated in these forward-looking statements, and the differences may be material and adverse. Forward-looking statements include, but are not limited to, statements about: the initiation, timing, progress and results of Mesoblast's preclinical and clinical studies, and Mesoblast's research and development programs; Mesoblast's ability to advance product candidates into, enroll and successfully complete, clinical studies, including multi-national clinical trials; Mesoblast's ability to advance its manufacturing capabilities; the timing or likelihood of regulatory filings and approvals (including any future decision that the FDA may make on the BLA for remestemcel-L for pediatric patients with SR-aGVHD), manufacturing activities and product marketing activities, if any; the commercialization of Mesoblast's product candidates, if approved; regulatory or public perceptions and market acceptance surrounding the use of stem-cell based therapies; the potential for Mesoblast's product candidates, if any are approved, to be withdrawn from the market due to patient adverse events or deaths; the potential benefits of strategic collaboration agreements and Mesoblast's ability to enter into and maintain established strategic collaborations; Mesoblast's ability to establish and maintain intellectual property on its product candidates and Mesoblast's ability to successfully defend these in cases of alleged infringement; the scope of protection Mesoblast is able to establish and maintain for intellectual property rights covering its product candidates and technology; estimates of Mesoblast's expenses, future revenues, capital requirements and its needs for additional financing; Mesoblast's financial performance; developments relating to Mesoblast's competitors and industry; and the pricing and reimbursement of Mesoblast's product candidates, if approved. You should read this press release together with our risk factors, in our most recently filed reports with the SEC or on our website. Uncertainties and risks that may cause Mesoblast's actual results, performance or achievements to be materially different from those which may be expressed or implied by such statements, and accordingly, you should not place undue reliance on these forward-looking statements. We do not undertake any obligations to publicly update or revise any forward-looking statements, whether as a result of new information, future developments or otherwise.

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