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SINGLE INTERVENTION WITH REXLEMESTROCEL-L IMPROVES LEFT VENTRICULAR EJECTION FRACTION AT 12 MONTHS, PRECEDING LONG-TERM REDUCTION IN MAJOR ADVERSE CARDIOVASCULAR EVENTS

Key points:

- Improvement in left ventricular ejection fraction (LVEF) at 12 months was shown after a single intervention with rexlemestrocel-L in the 565-patient randomized controlled trial in New York Heart Association (NYHA) class II/III chronic heart failure (CHF) with reduced ejection fraction (HFrEF)
- Increased LVEF preceded long-term reduction in major adverse cardiovascular events (MACE) and associated recurrent hospitalizations for non-fatal heart attack or stroke
- LVEF improvement at 12 months may be an appropriate early surrogate endpoint for long-term reduction in MACE
- Effects on LVEF and MACE outcomes were even more pronounced in 301 HFrEF patients with high baseline levels of inflammation as measured by hsCRP
- Results from three randomized controlled trials in class II/III HFrEF and in end-stage HFrEF with left ventricular assist devices (LVADs) support the idea of a common mechanism of action (MOA) by which rexlemestrocel-L reverses inflammation-related endothelial dysfunction and reduces adverse clinical outcomes across the spectrum of HFrEF patients
- Rexlemestrocel-L has regenerative medicine advanced therapy (RMAT) designation from the US Food and Drug Administration (FDA) for treatment of chronic heart failure with left ventricular systolic dysfunction in patients with an LVAD. Mesoblast now intends to meet with FDA under the RMAT framework to discuss the totality of the data and the evidence of a common rexlemestrocel-L MOA across the broader HFrEF spectrum.

Melbourne, Australia; July 19, and New York, USA; July 18, 2022: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, today announced that treatment of HFrEF patients with rexlemestrocel-L, its allogeneic "off-the-shelf" product candidate for the treatment of chronic heart failure with reduced ejection fraction, resulted in greater improvement in the pre-specified analysis of left ventricular ejection fraction at 12 months relative to controls in the DREAM-HF Phase 3 trial. Improvement in LVEF was most pronounced in the setting of inflammation and preceded long-term reduction in the 3-point MACE of cardiovascular death, non-fatal heart attack or stroke. These results were recently highlighted in a heart failure panel discussion titled "Late-Stage Advancements in Heart Failure Therapeutics and Management."

Rexlemestrocel-L is an immunomodulatory therapy developed to target the high degree of inflammation and resultant endothelial dysfunction present across the spectrum of HFrEF, from NYHA class II through end-stage CHF on LVADs. This MOA is postulated to improve systolic function and LVEF in HFrEF patients and reduce the high rate of major cardiovascular events and complications, notably 3-point MACE in NYHA class II/III patients and gastrointestinal (GI) tract ischemia, abnormal GI blood vessels, and life-threatening GI bleeding events in LVAD patients. Rexlemestrocel-L has already been granted FDA RMAT and Orphan Drug designations for treatment of chronic heart failure with left ventricular systolic dysfunction in patients with an LVAD.

Results from two large placebo-controlled randomized studies in patients with HFrEF, a disease associated with inflammation, a 565-patient trial in NYHA class II/III patients (DREAM-HF) and a 159-patient trial in end-stage heart failure patients implanted with an LVAD, as well as in an earlier 30-patient trial in LVAD patients, provide support for a common MOA for rexlemestrocel-L across the spectrum of HFrEF. New data from the DREAM-HF trial shows that a single intervention with rexlemestrocel-L resulted in improvement from baseline to 12 months in LVEF, which preceded and correlated with long-term reduction in MACE across a mean follow up of 30 months. This suggests that early improvement in LV systolic function, as measured by LVEF change from baseline to 12 months, could be an appropriate surrogate endpoint predictive of adverse long-term clinical outcomes in this patient population.

In the DREAM-HF study, among the 537 patients who were randomized and received either treatment or sham, a single injection of rexlemestrocel-L resulted in the following:[1]

- 52% greater increase in LVEF from baseline to 12 months compared with controls. While both groups had similar LVEF at baseline (28.7% and 28.6%), at 12 months least squared mean change from baseline was 5.0 for the rexlemestrocel-L group and 3.3 for controls (p=0.021)
- 65% reduction in 2-point MACE (non-fatal heart attack or stroke) compared to controls, 4.6% vs 13.0%, p=0.001, across a mean follow-up of 30 months
- 33% reduction in 3-point MACE compared to controls, 20.3% vs 30.1%, p=0.021, across a mean follow-up of 30 months
- 68% reduction in the rate of recurrent hospitalizations from non-fatal heart attacks or strokes compared with controls (p=0.0002)

Outcomes were even more pronounced in the pre-specified subgroup of 301 NYHA class II/III HFrEF patients with detectable circulating evidence of inflammation as measured by elevated baseline hsCRP, where a single injection of rexlemestrocel-L resulted in the following:[1]

- 86% greater increase in LVEF from baseline to 12 months compared with controls: while both groups had similar LVEF at baseline (29.1% and 28.2%), at 12 months least squared mean change from baseline was 5.6 for the rexlemestrocel-L group and 2.9 for controls (p=0.005)
- 79% reduction in 2-point MACE compared to controls, 2.6% vs 12.2%, p=0.004, across a mean follow-up of 30 months
- 45% reduction in 3-point MACE compared to controls, 19.0% vs 32.4%, p=0.012, across a mean follow-up of 30 months

Outcomes in a second HFrEF population with high levels of inflammation, 159 patients with end-stage heart failure and LVAD implantation, showed that a single intervention with rexlemestrocel-L reduced life-threatening mucosal bleeding events requiring hospitalization through 6 months (GI or epistaxis) compared with controls, 17% vs 33%, p=0.02. These results confirmed the observed reduction in major GI bleeding events seen in an earlier 30-patient randomized study. The FDA has indicated that a reduction in life-threatening mucosal bleeding events is an important clinical outcome in patients implanted with an LVAD.

These results are consistent with a postulated mechanism of action by which rexlemestrocel-L targets inflammation and endothelial dysfunction across the spectrum of HFrEF with the potential to reduce major adverse clinical events in HFrEF patients from NYHA class II/III through to end-stage disease and LVADs. Mesoblast now intends to meet with FDA under the RMAT framework to discuss the totality of the data, the evidence of a common MOA across the broad HFrEF spectrum, and how the outcomes from each trial may support the regulatory approval pathway for rexlemestrocel-L.

About Heart Failure

Heart failure affects approximately 6.5 million people in the United States and 26 million people globally, with increasing prevalence and incidence. The mortality rate approaches 50% at 5 years as patients progress beyond NYHA class II disease in parallel with increasing inflammation in the heart and in the circulation.[2,3] Despite recent approvals of new therapies for HFrEF, including SGLT2 inhibitors, that have reduced hospitalizations due to reversible volume-related events, NYHA class II/III HFrEF patients with inflammation remain at high risk for cardiac death, heart attacks and strokes. Over 60,000 patients annually in the US progress to end-stage heart failure (NYHA class IV) and these patients have a one-year mortality exceeding 50%.[4] Use of LVADs in end-stage heart failure patients to improve survival is gaining momentum, with approximately 5,500 LVADs implanted annually in the US.[5-7] However, systemic inflammation associated with major life-threatening gastrointestinal bleeding high rates of rehospitalization remain a major obstacle to greater LVADsuse.[8,9]

About Mesoblast

Mesoblast 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, biologic-resistant inflammatory bowel disease, and acute respiratory distress syndrome. Rexlemestrocel-L is in development 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

Footnotes

1. LVEF, 2-point MACE, and recurrent hospitalizations due to heart attack or stroke were pre-specified endpoints and the 3-point MACE was a post-hoc analysis of pre-specified endpoint components
2. AHA's 2017 Heart Disease and Stroke Statistics
3. Ponikowski P., et al. Heart Failure: Preventing disease and death worldwide. *European Society of Cardiology*. 2014; 1: 4-25
4. 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.
5. United Network for Organ Sharing
6. Agency for Healthcare Research and Quality – Healthcare Cost and Utilization Project – Claims Analysis ICD- 37.6.
7. Data on file
8. Chatterjee A, Feldmann C, Hanke JS (2018) The momentum of HeartMate 3: a novel active magnetically levitated centrifugal left ventricular assist device (LVAD). J Thorac Dis 10 (Suppl 15): S1790-S1793.
9. Mehra, MR Salerno C, Cleveland JC (2018) Health care resources use and cost implications in the MOMENTUM 3 long-term outcome study: a randomized controlled trial of a magnetically levitated cardiac pump in advanced heart failure.

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 BLA resubmission), 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.

Release authorized by the Chief Executive.

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