asx announcement

mesoblast

REXLEMESTROCEL-L SHOWS GREATEST TREATMENT BENEFIT ON MAJOR ADVERSE CARDIOVASCULAR EVENTS IN HIGH-RISK HEART FAILURE PATIENTS WITH DIABETES AND/OR MYOCARDIAL ISCHEMIA

Endpoint in Line with FDA Guidance on Key Outcomes in High-Risk Patients and with Pharma Industry Drugs Approved for Cardiovascular Risk Reduction in Diabetes

Key points:

- Analysis of pre-specified high-risk groups in the DREAM-HF Phase 3 trial of rexlemestrocel-L in patients with chronic heart failure and low ejection fraction (HFrEF) showed greatest treatment benefit in major cardiovascular adverse events (MACE) of cardiovascular mortality or irreversible morbidity (non-fatal heart attack or stroke) in patients with diabetes and/or myocardial ischemia (72% of total treated population)
- This target population is at very high risk for mortality and irreversible morbidity due to micro- and macro-vascular disease despite receiving optimal standard of care therapies [1]
- Rexlemestrocel-L, added to optimal standard of care therapies, reduced the 3-point MACE composite of cardiovascular death or heart attack or stroke by 37% across all HFrEF patients with diabetes and/or ischemia and by 54% in HFrEF patients with systemic inflammation (elevated baseline hs-CRP)
- United States Food & Drug Administration (FDA) has previously accepted 3-point MACE reductions of 12-14% for approval of multiple pharmaceutical industry drugs to reduce cardiovascular risk in diabetic patients [2,3]
- FDA confirmed that reduction in cardiovascular mortality or irreversible morbidity (non-fatal heart attack or stroke) is an acceptable clinically meaningful endpoint for determining the treatment benefit of rexlemestrocel-L for patients with HFrEF
- Mesoblast to formally submit to FDA its new analyses of outcomes in high-risk HFrEF patients with diabetes and/or myocardial ischemia to agree on a potential pathway to approval.

Melbourne, Australia; December 6, and New York, USA; December 5, 2021: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, today provided new analyses from the landmark DREAM-HF Phase 3 trial showing that the greatest treatment benefit from rexlemestrocel-L is in HFrEF patients with diabetes and/or ischemia, who are at high-risk of cardiovascular mortality, heart attacks or strokes.

In recent guidance to Mesoblast, FDA confirmed that reduction in incidence of cardiovascular mortality or irreversible morbidity (non-fatal heart attack or stroke) is a clinically meaningful acceptable endpoint in patients with chronic HFrEF and encouraged Mesoblast to identify the highest-risk group with greatest likelihood of beneficial response to intervention with rexlemestrocel-L in the DREAM-HF Phase 3 trial.

In line with this guidance, Mesoblast performed additional analyses of MACE outcomes in pre-specified high-risk patient groups from the landmark DREAM-HF trial, and the results were presented December 3 by Chief Executive Dr Silviu Itescu at the 18th Global CardioVascular Clinical Trialists Forum (CVCT) in Washington DC.

The data showed that:

- While a single rexlemestrocel-L dose on top of maximal standard of care therapies reduced the composite 3-point MACE in all 537 patients by 33% (p=0.02) over a mean follow-up of 30 months, a hierarchical analysis across pre-specified high-risk subgroups showed greatest benefit in patients with diabetes and/or myocardial ischemia (hazard ratio 0.63, p=0.019)

- Among control patients with HFrEF (n=276) all of whom were treated with maximal available standard of care therapies, risk of 3-point MACE was 1.9-fold higher in controls with diabetes and/or myocardial ischemia (n=192) than controls with neither diabetes nor myocardial ischemia (n=84), p=0.02. This confirmed the ongoing high-risk of 3-point MACE in control patients with diabetes and/or myocardial ischemia due to micro- and macro-vascular disease despite receiving optimal standard of care therapies
- Compared to control patients, rexlemestrocel-L reduced the incidence of 3-point MACE by 37% overall in NYHA class II or III HFrEF patients with diabetes and/or myocardial ischemia (n=385, p=0.02) and by 54% in those with diabetes and/or myocardial ischemia who had evidence of systemic inflammation, as defined by elevated baseline levels of hs-CRP >2mg/L (n=212, p=0.003).

Diabetes Mellitus is not only a significant risk factor in the onset of heart failure, it also increases the risk of mortality and morbidity in patients who have existing heart failure.[1-3] Type 2 diabetes causes structural heart disease and heart failure through myocardial ischemia involving small and large vessels. Importantly, inflammation which is a critical component of the pathophysiology of the disease is also known to accelerate large vessel atherosclerosis.[1]

The 3-point composite MACE is an endpoint the FDA has previously accepted for approval of multiple drugs to reduce cardiovascular risk in diabetic patients. FDA guidance states that reliance on a single study to provide the substantial evidence of effectiveness necessary to support a Biologic License Application (BLA) is generally limited to situations in which a trial has demonstrated a clinically meaningful effect on mortality, irreversible morbidity, or prevention of a disease with potentially serious outcome for which confirmation of the result with a second trial would be practically or ethically impossible. Mesoblast will submit for formal FDA review the new data analyses showing the reduction in mortality and irreversible morbidity by rexlemestrocel-L in HFrEF patients with diabetes and/or myocardial ischemia, to agree on a potential pathway to approval.

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 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 moderate to severe 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. Dunlay SM., et al. Circulation. 2019;140:e294–e324
2. Wang CCL et al. Circulation 2019; 139: 1741-1743.
3. McGuire DK et al. JAMA Cardiol. 2021; 6:148-158.

Mesoblast Limited
ABN 68 109 431 870
www.mesoblast.com

Corporate Headquarters
Level 38
55 Collins Street
Melbourne 3000
Victoria Australia
T +61 3 9639 6036
F +61 3 9639 6030

United States Operations
505 Fifth Avenue
Third Floor
New York, NY 10017
USA
T +1 212 880 2060
F +1 212 880 2061

Asia
21 Biopolis Road
#01-22 Nucleos (South Tower)
SINGAPORE 138567
T +65 6570 0635
F +65 6570 0176

Forward-Looking Statements
This announcement 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. All statements other than statements of historical fact, including our intention to agree with FDA on a potential pathway to approval, are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "likely," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions and variations thereof. 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. The risks, uncertainties and other factors that may impact our forward-looking statements include, but are not limited to: the timing, progress and results of Mesoblast's preclinical and clinical studies; Mesoblast's ability to advance product candidates into, enroll and successfully complete, clinical studies; the timing or likelihood of regulatory filings and approvals; whether the FDA agrees to a regulatory pathway; and the pricing and reimbursement of Mesoblast's product candidates, if approved; 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. 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. Unless required by law, 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.

For more information, please contact:

Corporate Communications / Investors
Paul Hughes
T: +61 3 9639 6036
E: investors@mesoblast.com

Media
Sumit Media
Grant Titmus
T: +61 419 388 161
E: grant@sumitmedia.com.au

Rubenstein
Nadine Woloshin
T: +1 917-699-9456
E: nwoloshin@rubenstein.com