

FDA PROVIDES GUIDANCE ON CLINICAL PATHWAY TO MARKETING APPLICATION FOR REVASCOR IN END-STAGE HEART FAILURE PATIENTS WITH AN LVAD

Primary Endpoint of Confirmatory Trial to be Reduction in Major Mucosal Bleeding Events

Melbourne, Australia; August 27, 2019, and New York, USA, August 26, 2019: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in cellular medicines for inflammatory diseases, announced today positive outcomes from its recent meeting with the United States Food and Drug Administration (FDA) on the pathway for marketing authorization of its allogeneic cell therapy product candidate Revascor in end-stage heart failure patients implanted with a left ventricular assist device (LVAD).

Key outcomes were:

- FDA reiterated that a reduction in major gastrointestinal bleeding events and/or epistaxis, collectively termed major mucosal bleeding events, is an important clinical outcome in patients implanted with an LVAD.
- FDA confirmed that data from the recently completed 159-patient placebo-controlled trial showing that Revascor reduced major mucosal bleeding events can support product marketing authorization through a Biologics License Application (BLA), with confirmatory clinical data.
- FDA agreed on a confirmatory Phase 3 trial of Revascor in LVAD patients, with a primary endpoint of reduction in major mucosal bleeding events, and key secondary endpoints demonstrating improvement in various parameters of cardiovascular function.

The confirmatory trial is planned to be conducted with the International Center for Health Outcomes Innovation Research (InCHOIR) at the Icahn School of Medicine at Mount Sinai in New York, in line with an existing Memorandum of Understanding.

Mesoblast Chief Executive Dr Silviu Itescu said: “The FDA guidance on the pathway to registration for our heart failure product candidate in LVAD patients is a major step forward for our cardiovascular program. We will work closely with the FDA and InCHOIR to generate the confirmatory clinical data needed for full marketing approval of Revascor in the prevention of this life-threatening inflammatory complication of an LVAD implant in end-stage heart failure patients.”

Revascor is being developed for these patients under existing FDA Regenerative Medicine Advanced Therapy (RMAT) and Orphan Drug Designations.

About Orphan Drug Designation

The FDA’s Orphan Drug Designation Program provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases and disorders that affect fewer than 200,000 people in the United States. Orphan drug designation qualifies the sponsor for various development incentives, including eligibility for seven years of market exclusivity upon regulatory approval, exemption from FDA application fees, tax credits for qualified clinical trials, and other potential assistance in the drug development process.

About RMAT Designation

The FDA’s RMAT designation program under the 21st Century Cures Act aims to expedite the development of regenerative medicine therapies intended for the treatment of serious diseases and life-threatening conditions. RMAT designation allows for multi-disciplinary, comprehensive interactions with the FDA to support efficient development of and potential accelerated approval pathway for cell therapy candidates. The RMAT designation also offers eligibility for priority review.

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About End-Stage Heart Failure and LVADs

In the United States, over 60,000 patients annually suffer from end-stage heart failure, and despite optimal medical therapy these patients have a one-year mortality exceeding 50%.¹ The only options to increase survival in these patients are the use of left ventricular assist devices (LVADs) or heart transplants.

Due to the decline in organ donations and limited availability of healthy donor hearts, the use of LVADs in end-stage heart failure patients is gaining momentum, with approximately 5,500 LVADs implanted annually in the United States.^{2,3,4} However, high rates of rehospitalization remain a major obstacle to greater LVAD use, with up to 40% of patients being rehospitalized as a result of major gastrointestinal bleeding.^{5,6}

About Revascor in Heart Failure

Mesoblast's investigational cell therapy Revascor consists of 150 million allogeneic mesenchymal precursor cells (MPCs) and is being developed for injection into heart muscle of patients with moderate-advanced or end-stage chronic heart failure.

Revascor for End-Stage Heart Failure Patients with LVADs

In a 30-patient placebo-controlled pilot trial in end-stage heart failure patients with LVADs, conducted by the United States National Institutes of Health (NIH), a single intra-myocardial dose of Revascor resulted in a 70% reduction in GI bleeding and associated hospitalizations. The results of this pilot trial were the basis of the RMAT designation granted in December 2017 by the FDA for use of Revascor in LVAD patients. In a subsequent meeting in 2018, the FDA advised Mesoblast that the defined endpoint of reduction in major GI bleeding and rehospitalization is an appropriate clinically meaningful endpoint and could be the basis of an approved indication for use of Revascor given the life-threatening nature of the condition, and the RMAT designation under which Revascor is being regulated. In November 2018, NIH investigators presented results of a 159-patient randomized placebo-controlled Phase 2 clinical trial at the American Heart Association Scientific Sessions. In the Phase 2 trial, a single intra-myocardial injection of Revascor at the time of LVAD implantation resulted in a 76% reduction in major GI bleeding events and 65% reduction in related hospitalizations in the overall patient population studied. In a post-hoc analysis in patients with an ischemic cause of their heart failure, these effects of Revascor were even greater, as well as an observed significant increase in the ability to wean off device support, suggesting strengthening of the native heart muscle.

Revascor in Patients with Moderate to Advanced Heart Failure

Revascor is being evaluated in a placebo-controlled Phase 3 trial which has enrolled 566 patients with New York Heart Association Class II/III moderate to advanced heart failure across multiple sites in North America. The objectives of this Phase 3 events-driven trial are to evaluate the ability of Revascor to meet the primary endpoint of reduction in recurrent heart failure-related major adverse cardiac events (HF-MACE) in patients with left ventricular dysfunction, as well as delay or prevent disease progression to terminal cardiac events, defined as death, left ventricular assist device (LVAD) implantation, or cardiac transplant. The trial has accrued and validated approximately 90% of its required target of primary endpoint events. It is expected that all the required primary endpoint events will be accrued and validated by the end of CY 2019. In April 2017, the Phase 3 trial was successful in a pre-specified futility analysis of the primary efficacy endpoint in the first 270 patients.

About Mesoblast

Mesoblast Limited (ASX: MSB; Nasdaq: MESO) is a world leader in developing allogeneic (off-the-shelf) cellular medicines. The Company has leveraged its proprietary technology platform to establish a broad portfolio of late-stage product candidates with three product candidates in Phase 3 trials – acute graft versus host disease, chronic heart failure and chronic low back pain due to degenerative disc disease. Through a proprietary process, Mesoblast selects rare mesenchymal lineage precursor and stem cells from the bone marrow of healthy adults and creates master cell banks, which can be industrially expanded to produce thousands of doses from each donor without the need for tissue matching. Mesoblast has facilities in Melbourne, New York, Singapore and Texas and is listed on the Australian Securities Exchange (MSB) and on the Nasdaq (MESO). www.mesoblast.com

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References

¹ 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.

²United Network for Organ Sharing.

³Agency for Healthcare Research and Quality – Healthcare Cost and Utilization Project – Claims Analysis ICD- 37.6.

⁴Data on file.

⁵Chatterjee 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.

⁶Mehra, 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 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. 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 timing, progress and results of Mesoblast and its collaborators' clinical studies for LVAD patients; Mesoblast and its collaborators' ability to advance its product candidates into, enroll and successfully complete, clinical studies for LVAD patients; and the timing or likelihood of regulatory filings and approvals for use in LVAD patients. 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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