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the regenerative medicine company

PHASE 2 TRIAL RESULTS SHOW MESOBLAST CELL THERAPY HAS GREATEST CARDIOPROTECTIVE EFFECT IN PATIENTS WITH ADVANCED HEART FAILURE

New York; USA; and Melbourne, Australia; 30 September 2015: Mesoblast Limited (ASX: MSB; USOTC:MBLTY) today announced that additional Phase 2 trial results of its lead product candidate for the treatment of chronic heart failure (CHF) were presented at the 19th Annual Scientific Meeting of the Heart Failure Society of America in National Harbor, MD, USA held from 26 - 29 September. The results showed that Mesoblast's mesenchymal precursor cell (MPC) therapy had the greatest cardioprotective effect in the subset of patients with more advanced heart failure.

A post-hoc analysis was performed in 30 patients from the Phase 2 trial who had been randomized to receive either placebo or a single administration of 150 million MPCs (MPC-150-IM). The results suggest that patients with advanced heart failure may be an optimal target population for treatment with Mesoblast's MPC therapy.

The objective of the analysis was to evaluate the efficacy of MPC-150-IM in patients with advanced heart failure, as defined by substantial baseline left ventricular (LV) contractile abnormality (LV end systolic volume, LVESV, >100 ml). LVESV >100 ml is more than three standard deviations above normal LVESV and is a predictor of poor long-term outcomes in patients with CHF. A further sensitivity analysis across every decile in baseline LVESV between 70 ml and 120 ml confirmed the findings seen in the stratification using a LVESV >100 ml. Cardiac remodeling by echocardiography at baseline and 6 months, time-to-first heart failure-related major adverse cardiovascular event (HF-MACE) by Kaplan-Meier analysis and incidence of total (recurrent) HF-MACE over 36 months were assessed.

Key findings were:

- control patients with baseline LVESV >100 ml had the greatest deterioration (adverse remodeling) over 6 months in terms of worsening in both LVESV and left ventricular end diastolic volume (LVEDV), and loss of left ventricular ejection fraction (LVEF)
- over a 6 month follow-up period, the 150 million MPC dose resulted in placebo-corrected significant reductions in LVESV of 57 ml ($p=0.007$) and LVEDV of 54 ml ($p=0.004$), and an increase in LVEF of 8.1 absolute percentage points ($p=0.068$) in patients with baseline LVESV >100 ml
- all of the HF-MACE seen over 36 months in the Phase 2 trial occurred in control patients with baseline LVESV > 100 ml; the annualized HF-MACE rate was 24% in this group, with an overall 71% HF-MACE rate over 36 months
- in contrast, no HF-MACE were seen over the entire 36 months in 150 million MPC-treated patients with baseline LVESV >100 ml ($p=0.0007$ when analyzed by Kaplan-Meier time-to-first-event analysis and $p<0.0001$ by incidence analysis for total/recurrent HF-MACE, 0 versus 11 events).

Key conclusions are:

- baseline LVESV >100 ml identified a rapidly deteriorating sub-group of CHF patients with LV systolic dysfunction who experience a high rate of adverse outcomes
- in these patients, a single administration of 150 million MPCs resulted in a significant cardioprotective effect and prevention of any HF-MACE over 36 months of follow up
- patients with baseline LVESV >100 ml may be an optimal target group for the potential cardioprotective benefits of MPC therapy.

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An ongoing Phase 3 trial, using a time-to-first-event analysis of HF-MACE as the primary endpoint, is being conducted in 1,165 patients by Mesoblast's development and commercial partner, Teva Pharmaceutical Industries Ltd, across multiple sites in North America to investigate the use of MPC-150-IM in patients with advanced CHF.

The Phase 3 trial is enriched for patients with high baseline levels of NT-proBNP and a heart failure hospitalization within the last nine months, two inclusion criteria known to predict adverse outcomes in CHF. This enrichment is expected to result in the majority of enrolled patients having LV systolic dysfunction, baseline LVESV >100 ml and high rates of HF-MACE.

Following recent discussions with the United States Food and Drug Administration, an interim analysis will be performed when 50% of the HF-MACE have occurred which will include a test for superiority allowing for the possibility of stopping of the trial early based on overwhelming efficacy.

The trial's Principal Investigator and lead author of the study, Dr Emerson C. Perin, Director of Research in Cardiovascular Medicine and Medical Director of the Stem Cell Center at the Texas Heart Institute, said: "Patients with advanced chronic heart failure and severe systolic contractile dysfunction represent a major medical need despite ongoing advances in cardiovascular medicine. The post-hoc analysis shows that this is an appropriate target population for Mesoblast's MPC therapy, and we hope to reproduce these findings in our ongoing Phase 3 trial."

Chronic Heart Failure
CHF is characterized by an enlarged heart and insufficient blood flow to the organs and extremities of the body. The condition, which affects 2% of the adult population of the United States, is progressive and can be caused by many factors that put an excess demand on the heart muscle such as high blood pressure, faulty valves, infections or congenital heart problems. CHF prevalence is expected to grow 46% by 2030, affecting more than 8 million Americans.

Mesoblast Limited
Mesoblast Limited (ASX: MSB; USOTC: MBLTY) is a global leader in regenerative medicine. The Company has leveraged its proprietary technology platform, which is based on specialized cells known as mesenchymal lineage adult stem cells, to establish a broad portfolio of late-stage product candidates. Mesoblast's allogeneic or 'off-the-shelf' cell product candidates target significantly advanced stages of diseases where there are highly unmet medical needs, including cardiovascular conditions, orthopedic disorders, immunologic/inflammatory disorders and oncology/hematology conditions.

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