asx announcement

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the regenerative medicine company

IMPROVED OUTCOMES USING MESOBLAST CELLS IN END-STAGE HEART FAILURE

Trial Results Published in American Heart Association Journal Circulation

New York, USA, and Melbourne, Australia; 25 June 2014: Regenerative medicine company Mesoblast Limited (ASX: MSB, USOTC: MBLTY) today announced that trial results evaluating a low dose of Mesoblast's proprietary mesenchymal precursor cells (MPCs) in patients with end-stage or class IV New York Heart Association (NYHA) heart failure who receive a left ventricular assist device (LVAD) have been published in the June issue of the American Heart Association journal *Circulation.* The trial was sponsored and funded by the United States National Institutes of Health (NIH) and coordinated by the NIH-funded Cardiothoracic Surgical Trials Network (CTSN).

The multi-center, randomized, placebo-controlled trial compared outcomes in 30 end-stage or NYHA class IV heart failure patients requiring LVAD mechanical support who received either a single low dose injection into damaged heart muscle of allogeneic, or off-the-shelf, MPCs or a placebo injection. The trial investigators concluded that administration of a low MPC dose appeared to be safe and there was a potential signal of efficacy. The trial results showed that a single low dose MPC injection was associated with increased ability to maintain circulation without LVAD support, reduced early mortality, and reduced rehospitalization rates compared with control injections.

The American Heart Association reports that of the more than six million people in the United States with diagnosed heart failure about 10% have end-stage or NYHA class IV disease. The only treatment options for end-stage or class IV heart failure are a heart transplant or mechanical support with an LVAD. Heart transplants cannot meet the large need due to limited donor availability, with only 2,332 transplants performed in the United States in 2012[1]. Major limitations to permanent LVAD use include life-threatening infections and gastrointestinal bleeding, which is the most common cause of rehospitalization in this population[2-4]. Consequently, major objectives of using MPCs in end-stage heart failure patients are to improve native heart muscle function sufficiently to reduce the need for LVAD support, and to improve the long-term complications of permanent LVAD support.

At the trial's 90-day primary endpoint for safety and exploratory efficacy, a single low-dose injection of MPCs (25 million cells) into the damaged heart muscle resulted in:

- decreased rate of immunization and allosensitization (10% vs 30% in controls)
- increased proportion of patients successfully weaned from their LVAD mechanical support (50% vs 20% in controls)
- decreased mortality rate (0% vs 30% in controls).

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Over 12 months of follow-up, MPC treatment resulted in:

- no cell-related immune responses or adverse events
- longer duration of successful LVAD wean than in controls at each time point evaluated
- increased proportion of patients tolerating one or more LVAD weans (85% versus 40% in controls)
- longer median time to first re-hospitalization (91 days vs 51 days in controls)
- decreased number of patients re-hospitalized over one year (22% vs 38% in controls)
- decreased rehospitalization rate from major gastrointestinal bleeding episodes (event rate/patient-year 0.55 vs 0.93 in controls)
- similar survival rates to controls.

The CTSN investigators stated that the results were promising and are planning next studies to evaluate the potential for higher or additional MPC doses to enhance the ability to wean LVAD recipients off mechanical support.

Sources:

[1] The National Heart, Lung and Blood Institute; The Organ Procurement and Transplantation Network; The United Network for Organ Sharing; The American Heart Association; WebMD; Gale Encyclopedia of Surgery: A Guide for Patients and Caregivers. [2-3] Forest SJ, Bello R, Friedmann P, Casazza D, Nucci C, Shin JJ, D'Alessandro D, Stevens G, Goldstein DJ. Readmissions after ventricular assist device: etiologies, patterns, and days out of hospital. *Ann Thorac Surg*. 2013; 95:1276–1281;Hasin T, Marmor Y, Kremers W, Topilsky Y, Severson CJ, Schirger JA, Boilson BA, Clavell AL, Rodeheffer RJ, Frantz RP, Edwards BS, Pereira NL, Stulak JM, Joyce L, Daly R, Park SJ, Kushwaha SS. Readmissions after implantation of axial flow left ventricular assist device. *J Am Coll Cardiol*. 2013; 61:153–163. [4] Stulak JM, Lee D, Haft JW, Romano MA, Cowger JA, Park SJ, AaronsonKD, Pagani FD. Gastrointestinal bleeding and subsequent risk of thromboembolic events during support with a left ventricular assist device. *J Heart Lung Transplant*. 2014; 33:60–64.

Mesoblast Limited

Mesoblast Limited (ASX:MSB; USOTC:MBLTY) is a world leader in the development of biologic products for the broad field of regenerative medicine. The Company's proprietary technologies include its highly purified, immunoselected Stro-1/Stro-3 positive Mesenchymal Precursor Cells (MPCs), culture-expanded Mesenchymal Stem Cells (MSCs), Dental Pulp Stem Cells (DPSCs), and expanded Hematopoietic Stem Cells (HSCs). Mesoblast's protein technologies are based on factors derived from its proprietary cellular platforms, including Stromal Derived Factor-1 (SDF-1). Mesoblast's allogeneic or 'off-the-shelf' regenerative medicine products are being developed for the treatment of conditions with significant unmet medical needs. Product development focus is in four major and distinct areas - systemic diseases with an underlying inflammatory and immunologic etiology; cardiac and vascular diseases; orthopedic diseases of the spine; and improving outcomes of bone marrow transplantation associated with oncology or genetic conditions. www.mesoblast.com

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