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the regenerative medicine company

MESOBLAST CELL THERAPY REDUCES INFLAMMATION AND REVERSES CORONARY ARTERY DYSFUNCTION IN RHEUMATOID ARTHRITIS PRECLINICAL STUDY

New York, USA, and Melbourne, Australia; 12 May 2015: Mesoblast Limited (ASX: MSB, USOTC:MBLTY) today announced publication of results in the May issue of the peer-reviewed journal *PLOS One* showing that its proprietary allogeneic mesenchymal precursor cells (MPCs) can reduce inflammation and reverse abnormal function of blood vessels, including the coronary arteries, in a previously published sheep model of rheumatoid arthritis. Since patients with rheumatoid arthritis have an approximately 50% higher risk of death from cardiovascular disease than the general population, these results suggest that the anti-inflammatory effect of MPC therapy may have an additional benefit in reducing cardiovascular risk associated with rheumatoid arthritis.

The scientific publication, entitled 'Effect of Mesenchymal Precursor Cells on the Systemic Inflammatory Response and Endothelial Dysfunction in an Ovine Model of Collagen-Induced Arthritis', can be viewed at http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0124144

Rheumatoid arthritis is a chronic disease driven by multiple cytokines, including TNF-alpha, interleukin-6, and interleukin-17, produced by pro-inflammatory monocytes/macrophages and activated T cells. While existing biologic therapies target these pathways individually, none target all concomitantly. In contrast, MPCs concurrently modulate both pro-inflammatory monocytes and activated T cells to reduce multiple pro-inflammatory cytokines produced by these cell types in the inflammed joints.

Mesoblast is currently conducting a double-blinded, randomized, placebo-controlled, dose-escalation Phase 2 trial of its allogeneic MPCs in patients with biologic-refractory rheumatoid arthritis in the United States and Australia. The 48 patient trial is evaluating the safety, tolerability and effectiveness of a single intravenous infusion of either of two MPC dose levels versus placebo for the treatment of active rheumatoid arthritis in patients who have failed at least one biologic agent, including TNF-alpha or IL-6 inhibitors.

The high cardiovascular mortality in rheumatoid arthritis is thought to be due to persistent inflammation and endothelial dysfunction of the coronary arteries leading to thrombosis and plaque rupture. The study in *PLOS One* showed that a single intravenous infusion of allogeneic MPCs significantly reduced the systemic inflammation present in a sheep model of rheumatoid arthritis, increased circulating levels of the anti-inflammatory cytokine IL-10, and reversed the abnormal endothelial dysfunction present in the coronary arteries and the digital arteries in these animals. The authors concluded that MPCs show significant promise in modulating not only local disease activity in chronic inflammation such as a poly or mono-arthritis, but also the systemic sequelae of the condition.

Mesoblast Chief Executive Silviu Itescu said: "Endothelial dysfunction caused by chronic inflammation is particularly important in rheumatoid arthritis where there is a significantly increased risk of coronary artery disease and death, and in diabetes where it is a major contributor to both kidney failure and cardiovascular events. These results suggest that our intravenously delivered product candidate, MPC-300-IV, may have a clear therapeutic role in addressing the consequences of diseases of chronic systemic inflammation."

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About Rheumatoid Arthritis
Rheumatoid arthritis is a chronic progressive disease causing inflammation in the joints and resulting in painful deformity and immobility, especially in the fingers, wrists, feet, and ankles. It affects approximately 1.7 million people in the United States. The incidence increases with age, climbing from 8.7 per 100,000 for those 18-34 years of age, to 89 per 100,000 for those 65-74 years of age. Rheumatoid arthritis is responsible for up to 250,000 hospitalizations and 9 million physician visits per year. Risk of death from cardiovascular causes is approximately 50% higher in patients with rheumatoid arthritis than the general population.

If left untreated, rheumatoid arthritis can lead to joint destruction, deformity, disability, and decreased quality of life. Existing biologic therapies have made major inroads to the treatment of rheumatoid arthritis; however, despite the variety of options available, approximately one third of patients either do not respond or cannot tolerate these therapies. Additionally, as these therapies carry a significant risk of opportunistic infections or malignancies, there is a need for an alternative therapeutic approach which is both safe and effective.

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. The lead therapeutic product candidates under investigation include MPC-150-IM for chronic congestive heart failure; MPC-06-ID for chronic discogenic low back pain, MSC-100-IV for acute graft versus host disease, and MPC-300-IV for biologic refractory rheumatoid arthritis, and diabetic nephropathy.

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