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MESOBLAST RECEIVES FDA CLEARANCE FOR PHASE 2 CLINICAL TRIAL OF MESENCHYMAL PRECURSOR CELLS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

Key Points:

- Mesoblast receives clearance from United States Food and Drug Administration (FDA) to begin Phase 2 trial of proprietary allogeneic, or "off-the-shelf", Mesenchymal Precursor Cells (MPCs) in patients with active Rheumatoid Arthritis (RA)
- Trial will be randomized, double-blind placebo-controlled dose escalation study to evaluate the safety, tolerability and effectiveness of a single intravenous infusion of two MPC dose levels over an initial period of 3 months in patients who have had poor or incomplete responses to biologic inhibitors of the TNF-alpha pathway
- Mesoblast's MPCs have been shown in preclinical studies to have a broad immunomodulatory mechanism of action (MOA), simultaneously inhibiting T cells and monocytes involved in inflammation and autoimmunity
- In an animal model of RA, MPC treatment significantly decreased the T cell and monocyte-derived inflammatory cytokines TNF-alpha, IL-6 and IL-17 in the diseased joint and reduced tissue pathology
- MOA provides the rationale for strategic development of MPCs in RA both in patients with incomplete responses to biologic inhibitors of the TNF-alpha pathway alone and as a first-line biologic treatment in those not responding to conventional anti-rheumatic agents
- In addition, a second Phase 2 trial of MPCs as a first-line biologic treatment for active RA is planned to commence in Europe in 1H 2013.

Melbourne, Australia; 30 January 2013: Regenerative medicine company Mesoblast Limited (ASX:MSB; USOTC:MBLTY), today announced that it has received clearance from the United States Food and Drug Administration (FDA) to commence a Phase 2 clinical trial evaluating a single intravenous infusion of allogeneic, or "off-the-shelf", Mesenchymal Precursor Cells (MPCs) for the treatment of active rheumatoid arthritis.

The randomized, double-blind placebo-controlled trial is expected to commence during the second quarter 2013, and will recruit across multiple sites in the United States and Australia. The trial will compare the effects of a single intravenous infusion of allogeneic MPCs dosed at 1 or 2 million cells/kg compared with placebo in 48 patients who have had an incomplete or inadequate response to a biologic inhibitor of the TNF-alpha pathway for active rheumatoid arthritis. Safety and effectiveness of the MPC therapy will be assessed at multiple time points with the primary endpoints defined as 3 months.

RA is an autoimmune disease caused by aberrant activation of multiple immune pathways involving both monocytes and T cells, ultimately resulting in joint destruction. Existing biologic treatments target only single immune pathways, resulting in incomplete responses, need for chronic administration, and potentially unacceptable infectious adverse events.

In contrast, Mesoblast's MPCs have been shown in preclinical studies to have a broad immunomodulatory mechanism of action (MOA), simultaneously inhibiting T cells and monocytes involved in inflammation and autoimmunity. The broader effects of Mesoblast's MPCs on multiple immune pathways suggest that they may be particularly useful agents for reducing the inflammation and permanent joint damage associated with progression of RA.

In a randomized, placebo-controlled study in 30 sheep with collagen-induced arthritis, a model that manifests joint damage characteristic of human RA, treatment with Mesoblast's MPCs resulted in reduced TNF-alpha, IL-6, and IL-17 in the diseased joint. In comparison with saline treated controls, synovial tissue from arthritic sheep 30 days after receiving a single intravenous injection of 2 million MPCs/kg showed 88% reduction in IL-6 levels ($p=0.029$), 83% reduction in TNF-alpha levels ($p=0.049$), 53% reduction in IL-17 levels ($p=0.005$), and 43% reduction in infiltrating monocytes/macrophages ($p=0.018$). MPC-treated animals had a 31% reduction in histopathology severity scores compared with controls ($p<0.025$).

These findings show that MPCs can concomitantly inhibit both Th17 T cells and pro-inflammatory monocytes, and improve synovial tissue pathology. This provides a rationale for their potential use as both a first-line biologic treatment in those not responding to conventional anti-rheumatic agents and in patients with incomplete responses to biologic inhibitors of the TNF-alpha pathway alone.

Mesoblast Chief Executive Professor Silviu Itescu said: "We believe that the broad immunomodulatory effects of our MPCs could provide a tangible benefit to patients with debilitating autoimmune diseases, including RA. This is the first in a series of programs designed to establish the credentials of our intravenous product formulation for a broad-based spectrum of inflammatory and immunologic conditions."

About Rheumatoid Arthritis

RA is a chronic systemic disease characterized by progressive joint deformity and joint destruction driven by synovial inflammation and hyperplasia in which cytokines play central pathogenic roles. The prevalence of RA is estimated to be 0.8% worldwide, with women twice as likely to develop the disease as men. In the United States, RA afflicts 1.3 million people. It is responsible for 250,000 hospitalizations and 9 million physician visits each year. According to Global Data, the RA therapeutics market was valued at $10.3 billion globally in 2010, and has doubled over a four-year period after growing at a Compound Annual Growth Rate (CAGR) of 12.3%.

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Mesoblast Limited
Mesoblast Limited is a world leader in the development of biologic products for the broad field of regenerative medicine. Mesoblast's patented Mesenchymal Precursor Cell technology is being developed for a broad range of major clinical diseases, including inflammatory and immunologic conditions, diabetes and its complications, orthopedic spine conditions, and cardiovascular disorders. www.mesoblast.com

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