

## MESOBLAST RECEIVES CLEARANCE TO BEGIN PHASE 2 CLINICAL TRIAL OF MESENCHYMAL PRECURSOR CELLS IN DIABETIC NEPHROPATHY

### Key Points:

- Mesoblast has received ethics approvals to begin a clinical trial of its proprietary allogeneic, or "off-the-shelf", adult Mesenchymal Precursor Cells (MPCs) in people with chronic kidney disease and type 2 diabetes
- Trial is a randomized, double-blind placebo-controlled dose escalation study to evaluate the safety, tolerability and effectiveness of a single intravenous infusion of MPCs over an initial period of three months in patients with Stage 3b or 4 diabetic nephropathy
- Mechanisms of action, based on preclinical studies, may include immunomodulation and reduction of kidney inflammation, reversal of abnormal kidney blood flow, and repair/regeneration of kidney tissue
- Mesoblast's intravenous product is currently being evaluated in a range of inflammatory/immunologic conditions where the immunomodulatory properties of MPCs may provide substantial benefits, including diabetic nephropathy, early type 2 diabetes, and rheumatoid arthritis.

**Melbourne, Australia; 26 June 2013:** Regenerative medicine company Mesoblast Limited (ASX:MSB; USOTC:MBLTY) today announced that it has received approvals from Australian ethics committees to commence a Phase 2 trial evaluating a single intravenous infusion of its proprietary allogeneic or "off-the-shelf" adult Mesenchymal Precursor Cells (MPCs) in patients with type 2 diabetes and advanced kidney disease, or diabetic nephropathy.

Ethics approvals for the two selected doses were obtained after safety data were reviewed from the ongoing 60-patient Phase 2 trial evaluating a single intravenous infusion of MPCs in people with early type 2 diabetes without kidney disease.

The randomized, placebo-controlled, dose-escalating Phase 2 trial will evaluate the safety and efficacy of 150 million or 300 million intravenously-injected MPCs against placebo in 30 people with advanced diabetic nephropathy. Over a 12-week period, the effects of an MPC infusion will be evaluated on kidney function and protein loss, kidney blood flow, glucose control and markers of inflammation.

Diabetes is the leading cause of kidney failure, accounting for more than 40% of all cases of end stage kidney disease. According to GlobalData, the 2011 United States prevalence of chronic kidney disease (CKD) is estimated at 15 million, with approximately 250,000 incident cases of CKD Stages 3b and 4, the target patient population for MPC therapy.

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Diabetic kidney disease or diabetic nephropathy is associated with longstanding inflammation of various tissues, including the kidneys, vascular dysfunction of the kidney as a result of the inflammatory environment, and loss of normally functioning kidney tissue. Mesoblast's preclinical studies in both diabetic and non-diabetic animal models have shown that intravenously delivered allogeneic MPCs can both reduce systemic inflammation and reverse vascular endothelial dysfunction. Additional studies in rodent models of diabetic kidney disease have shown that intravenously administered mesenchymal lineage stem cells can directly reverse abnormal kidney pathology and improve function via secretion of factors that enhance regeneration and repair of kidney tissue.

Together with the glucose-lowering effects that Mesoblast has observed following intravenously administered MPCs in both mice and non-human primates with experimental and natural models of type 2 diabetes, these additional mechanisms of action suggest that MPCs may have an important potential benefit on the principal complication of type 2 diabetes, diabetic kidney disease.

Mesoblast Chief Executive Professor Silviu Itescu said: "The prognosis for patients with diabetic kidney disease is grim. Despite advances in dialysis and kidney transplantation, fewer than 50% of those with end stage kidney disease are alive five years after diagnosis. We believe that our proprietary MPCs may provide a benefit to patients suffering from diabetic nephropathy."

### **About Diabetic Nephropathy**

The definition of chronic kidney disease (CKD) is based on the presence of kidney damage or decreased kidney function for three months or more, irrespective of clinical diagnosis. About 40% of people with diabetes are eventually affected by kidney disease. CKD leads to progressive deterioration in the body's ability to remove excess fluid and metabolic wastes as defined by the glomerular filtration rate. Ultimately, this leads to end stage renal disease or Stage 5 CKD with renal replacement therapy (kidney transplantation or dialysis) currently the only options.

Diabetic nephropathy remains by far the most common cause of end stage renal disease (ESRD) for which the only treatment options are dialysis or kidney transplant. Diabetes accounts for 40% to 45% of ESRD cases (94% type 2 diabetes, 6% type 1 diabetes), and for more than 20% of kidney transplants in the United States.

Diabetes mellitus currently affects over 8% of the world's adult population. It has been predicted that the coming global increase in diabetes mellitus will be 2.7%, a level 1.7 times the anticipated annual growth in the world's population.

**References:** *Williams M. Diabetic Kidney Disease. Med Clin N Am 97 (2013); Levey AS, Eckardt KU, Tsukamoto Y et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005; 67: 2089–2100; Levey AS, Coresh J. Chronic kidney disease. Lancet 2012; 379: 165–180.*

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## **About Mesoblast**

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 technologies include its proprietary adult Mesenchymal Precursor Cell (MPC) technology platform for bone marrow and adipose tissue derived products, Dental Pulp Stem Cells (DPSCs) and expanded Hematopoietic Stem Cells (HSCs). Mesoblast's allogeneic or 'off-the-shelf' regenerative medicine products focus on repair of damaged tissues and modulation of inflammatory responses in conditions with significant unmet medical needs. The lead product candidates use its MPC platform in three major and distinct areas - systemic inflammatory conditions, cardiovascular diseases and orthopedic diseases of the spine. [www.mesoblast.com](http://www.mesoblast.com)

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