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Mesoblast Reports Positive Results Using Intravenously Injected Adult Stem Cells for Type 2 Diabetes

Key Points

- **Single injection of Mesoblast's proprietary allogeneic, or off-the-shelf, Mesenchymal Precursor Cells (MPCs) significantly lowered blood sugar levels for up to eight weeks in non-human primates with Type 2 diabetes**
- **A clear dose-dependent effect was seen, with the highest three MPC doses maintaining significantly reduced blood glucose levels after eight weeks compared with controls**
- **In MPC treated subjects, there was a direct correlation between reductions in fasting blood glucose levels over time and reductions in circulating C-reactive protein (CRP), the major predictor of cardiovascular risk in Type 2 diabetic patients**
- **Highest three MPC doses significantly reduced circulating CRP levels after eight weeks compared with controls, to levels associated with reduced risk for heart attacks and death in Type 2 diabetic patients**
- **Type 2 diabetes will be the first clinical indication to be targeted using Mesoblast's intravenous product formulation**
- **Phase 2 clinical trial in Type 2 diabetes expected to commence first quarter 2012**

Phoenix, United States; 9 November; and Melbourne, Australia; 10 November

2011: Regenerative medicine company, Mesoblast Limited (ASX: MSB), today announced that a single intravenous injection of its proprietary adult stem cells resulted in significant lowering of blood sugar levels for up to eight weeks in a controlled, randomized preclinical trial in non-human primates with Type 2 diabetes. This was accompanied by significant reductions in circulating inflammatory markers to levels associated with protection against heart attacks and death in patients with Type 2 diabetes. Results of the study were presented at the Credit Suisse Healthcare conference in Phoenix, Arizona.

A randomized, placebo-controlled study was performed in 17 non-human primates with dietary-induced Type 2 diabetes to evaluate the effects of a single intravenous injection of Mesoblast's proprietary allogeneic, or off-the-shelf, Mesenchymal Precursor Cells (MPCs) on blood glucose levels over an eight week period. Controls (n=3) received a single saline injection, while four groups of treated subjects (3-4 per group) received one of 4 escalating doses of MPCs (0.1, 0.3, 1 and 2 million MPCs/kg).



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At baseline, the high mean fasting blood glucose levels were not significantly different between any of the Type 2 diabetic groups. Over the eight week period of the study, the control group showed no significant changes in the high levels of fasting blood glucose. In contrast, a single injection of MPCs at every dose tested significantly reduced fasting blood glucose levels as early as two weeks ($p < 0.001$ for each dose), with a clinically meaningful reduction in fasting blood sugar levels of up to 80 mg/dl by four weeks. There was a dose-dependent effect, with the highest three MPC doses maintaining sustained reductions in fasting blood glucose over the entire eight week study period, and the lowest MPC dose being least effective. Over the eight weeks, the groups receiving 1 and 2 million MPC/kg maintained significantly lower mean fasting blood glucose levels compared with the control group (respectively, 119 mg/dl and 110 mg/dl vs 154 mg/dl, both $p < 0.05$). The mean fasting blood glucose level in the group which received 0.3 million MPC/kg (130 mg/dl) was moderately lower than the controls (154 mg/dl), while the lowest dose at 0.1 million MPC/kg was without effect (160 mg/dl vs 154 mg/dl).

In MPC treated subjects, there was a direct correlation between reductions in fasting blood glucose levels over time and reductions in circulating C-reactive protein (CRP). CRP is a major inflammatory marker which is highly predictive of risk for heart attack and cardiac death when present at levels > 3 mg/L in people with Type 2 diabetes. At eight weeks, mean CRP levels were 1.3 mg/L, 1.1 mg/L and 1.6 mg/L in the groups who received 0.3, 1 and 2 million MPC/kg, compared with 3.9 mg/L and 4.9 mg/L in the groups who received saline and 0.1 million MPC/kg, respectively ($p < 0.05$ for the pooled highest three doses vs pooled controls and lowest dose).

These results in non-human primates build on an earlier study which showed that a single dose of human MPCs injected into mice with diabetes resulted in a significant increase in blood insulin levels and sustained reduction in blood glucose levels for the entire three-week period of follow-up. This was due to restoration in the damaged pancreas of the balance between insulin-producing beta cells, which reduce blood glucose, and glucagon-producing alpha cells, which increase blood glucose.

Mesoblast Chief Executive, Professor Silviu Itescu, said that the results obtained to date indicate that a single intravenous injection of Mesoblast's MPCs may have a sustained benefit on blood glucose control, reduce inflammation, and improve lipid profile in patients with Type 2 diabetes.

"Mesoblast's cells have the potential to establish a new medical paradigm for the treatment of Type 2 diabetes which is safe and simultaneously targets multiple factors responsible for the disease and its complications.

"Intravenous injection of our MPCs may not only improve blood glucose control, it may concomitantly reduce the significant risk of heart attacks and death that occurs in patients with Type 2 diabetes," Professor Itescu added.



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Mesoblast has an upcoming scheduled meeting with the United States Food and Drug Administration (FDA) to discuss its Phase 2 clinical program in patients with Type 2 diabetes. The company expects to commence a randomized, placebo-controlled Phase 2 trial in the first quarter of 2012.

Type 2 diabetes accounts for 90-95 per cent of the 230 million diabetics in the western world, with its prevalence increasing at an alarming rate. In the United States alone, there were 27 million established cases of Type 2 diabetes in adults aged over 20 in 2010. With a growth rate of 2.6% per year, this number is expected to increase to more than 35 million in 2020.

About Mesoblast

Mesoblast Limited (ASX:MSB) is a world leader in commercialising biologic products for the broad field of regenerative medicine. Mesoblast has the worldwide exclusive rights for a series of patents and technologies developed over more than 10 years relating to the identification, extraction, culture and uses of adult Mesenchymal Precursor Cells (MPCs).

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