Mesoblast Limited (MESO) Reports Positive Phase 2 Results of Mesenchymal Precursor Cells in Patients with CLBP-Related Intervertebral Disc Degeneration

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Today announced 36-month results from the randomized, placebo-controlled 100-patient Phase 2 trial of its proprietary allogeneic Mesenchymal Precursor Cells (MPCs) in patients with chronic low back pain (CLBP) due to intervertebral disc degeneration. A single intra-discal injection of 6 million MPCs resulted in meaningful improvements in both pain and function that were durable for at least 36 months.

“The sustained benefits on pain and function over three years seen with a single injection of Mesoblast’s cell therapy have the potential to transform the treatment paradigm for chronic low back pain due to disc degeneration,” said trial investigator Dr Hyun Bae, Professor of Surgery and Director of Education at the Cedars Sinai Spine Center, and Director of the Spine Institute in Los Angeles, CA. “Instead of replacing or fusing the disc, there is mounting compelling evidence that we can use this regenerative medicine to heal the disc. We are fast approaching this inflection point in the treatment of low back pain, which is particularly important in view of the epidemic of opioid abuse."

The durable outcomes seen from a single MPC injection in patients with degenerative disc disease who have failed conservative measures are consistent with an overarching mechanism of action that may also be evident in treatment of other chronic diseases where a single MPC dose has resulted in sustained benefits, including advanced chronic heart failure and biological-resistant rheumatoid arthritis. In each of these diseases, MPCs are thought to be activated by signals in the damaged tissues to release factors that both inhibit damaging inflammation and induce a pro-reparative state.

The Phase 2 trial compared a single intra-discal injection of 6 million or 18 million MPCs against two placebo arms, saline or hyaluronic acid, using a pre-specified Per Protocol (PP) population analysis. The primary endpoint composite was the same as is being used in the ongoing Phase 3 trial, a 50% reduction in the Visual Analog Scale (VAS) pain score and a 15-point reduction in the Oswestry disability index (ODI), with no additional intervention, at both 12 and 24 months.

In line with United States Food and Drug Administration (FDA) guidance for the ongoing Phase 3 trial, the 24-month primary endpoint composite was additionally analyzed using an intent to treat (ITT) population. The 36-month analysis aimed to determine the proportion of patients who maintained treatment success beyond the 24-month primary evaluation.

Key trial results were:

- the primary endpoint composite over 24 months was achieved by 41% of patients who received 6 million MPCs, 35% of the 18 million MPC group, 18% of the

hyaluronic acid group, and 13% of the saline group, using the pre-specified PP population analysis- pain responder criteria (50% pain reduction with no additional intervention at both 12 and 24 months) was achieved by 52% of the 6 million MPC group compared with 13% of the saline group ($p<0.05$)- functional responder criteria (15-point reduction in ODI and no additional intervention at both 12 and 24 months) was achieved by 48% of the 6 million MPC group compared with 13% of the saline group ($p<0.05$)

- similar results were seen for the primary endpoint composite over 24 months using the ITT analysis, with 38% of the 6 million MPC group achieving this outcome compared with 10% of the saline group ($p<0.05$)- 82% of the 6 million MPC group who achieved the primary endpoint composite over 24 months maintained treatment success using this composite endpoint at 36 months- 86% of the 6 million MPC group who successfully met the pain responder criteria (50% pain reduction with no additional intervention at both 12 and 24 months) remained pain responders through 36 months- 92% of the 6 million MPC group who met the functional responder criteria (15-point reduction in ODI and no additional intervention at both 12 and 24 months) remained functional responders through 36 months
- there were no significant differences in measurements of safety between cell-treated patients and controls over 36 months

The 36-month Phase 2 trial results support the ongoing 360-patient Phase 3 trial of Mesoblast's product candidate MPC-06-ID for CLBP by reinforcing the rationale for MPC dose selection, use of saline control, and the trial's primary endpoint composite over 24 months. If similar clinical durability is seen in the Phase 3 program, it is anticipated such data will translate into meaningful health economic benefits including increased productivity that may support attractive product reimbursement.

In December 2016, Mesoblast and Mallinckrodt Pharmaceuticals entered into an agreement to exclusively negotiate a commercial and development partnership for MPC-06-ID in the treatment of chronic low back pain due to disc degeneration.