asx announcement

mesoblast
the regenerative medicine company

POSITIVE SPINAL DISC REPAIR TRIAL RESULTS USING MESOBLAST ADULT STEM CELLS

Single Injection of Mesenchymal Precursor Cells into Degenerating Intervertebral Discs Reduced Low Back Pain and Improved Function for at Least 12 Months

New York, USA, 29 January and Melbourne, Australia; 30 January 2014: Regenerative medicine company Mesoblast Limited (ASX:MSB; USOTC:MBLTY) today announced positive 12 month outcome results from the 100-patient Phase 2 clinical trial of its proprietary allogeneic, or "off-the-shelf", Mesenchymal Precursor Cells (MPCs) in patients with chronic moderate to severe discogenic low back pain.

The results showed that a single injection of MPCs into degenerating intervertebral discs reduced low back pain and improved function for at least 12 months. When compared with controls, MPC-treated patients used less opioids for pain relief, had greater radiographically-defined disc stability, and underwent less additional surgical and non-surgical treatment interventions. MPC treatments also appeared to be well tolerated during the study.

Mesoblast Chief Executive Silviu Itescu said: "We are very pleased that in a trial primarily designed to assess the safety of Mesoblast's cells for intervertebral disc repair, we have seen strong indications of sustained efficacy across a broad number of clinical and radiographic parameters after a single intra-disc injection. On the basis of these positive results, Mesoblast plans to meet shortly with regulatory authorities in major jurisdictions, including the United States Food and Drug Administration, to discuss product registration trials for the potential treatment of disc degeneration."

Dr Hyun Bae, Clinical investigator and Medical Director, Director of Education, Cedars-Sinai Spine Center, Cedars-Sinai Medical Center, Los Angeles, and Medical Director of Spine Institute, Santa Monica, USA, said: "We are very excited by these results. This is compelling evidence that Mesoblast's stem cell technology has the potential to change the treatment of spinal disease from focusing on surgical reconstruction to biologic regeneration. Physicians and patients are seeking access to a new modality to treat patients with this highly debilitating disease for whom there are limited options. We hope that these outcomes will be replicated in a pivotal trial."

The results of the Phase 2 clinical trial build on and extend previously reported preclinical studies which showed that Mesoblast's highly purified and immunoselected MPCs were able to increase proteoglycan content and improve disc structure in an experimental ovine model of disc degeneration.

Mesoblast's Phase 2 clinical trial enrolled 100 patients with moderate to severe low back pain persisting for more than 6 months and caused by early disc degeneration (<30% disc height loss, 83% below Pfirrmann Grade 5 by MRI). Patients were enrolled across 13 sites in the United States and Australia and randomized to receive direct intra-disc injection of saline (n= 20), hyaluronic acid (HA, n=20), 6 million allogeneic MPCs in hyaluronic acid carrier (6M, n=30) or 18 million allogeneic MPCs in hyaluronic acid carrier (18M, n=30). Patients underwent the outpatient injection for a single painful degenerated lumbar level and are being evaluated for safety and efficacy over a total of 36 months to evaluate long-term treatment effects.

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Key findings at 12 months were:

- Improvement in chronic low back pain

(a) Reduction in mean pain score: While mean pain scores, as measured by a Visual Analog Scale (VAS), were similar for all four groups at baseline (67 points for saline, 72 points for HA, 70 points for 6M MPC, 72 points for 18M MPC), at 12 months MPC treatment resulted in significantly greater pain reduction than was seen in controls. . Mean pain reduction at 12 months was 40 points for the 18M MPC group, 37 points for the 6M MPC group, 27 points for HA controls, and 27 points for saline controls (p=0.046 and p=0.11, respectively, for 18M MPC and 6M MPC vs pooled controls). .

(b) Increased proportion of patients achieving >50% reduction in pain score: Achieving more than 50% reduction in low back pain at 12 months is considered by many patients and physicians as a key target. A significantly greater proportion of MPC treated patients achieved at least a 50% reduction in low back pain at 12 months, as measured by VAS, than controls (6M MPC 69%, 18M MPC 62%, HA 35%, saline 31%, p=0.036 between groups). Both MPC dose groups had a significantly greater proportion of patients with 50% or more reduction in back pain from baseline compared to the pooled controls (6M, p=0.009, 18M p=0.038).

(c) Increased proportion of patients achieving minimal residual back pain: Minimal residual back pain at 12 months was considered if the VAS score was ≤20. A significantly greater proportion of MPC treated patients achieved minimal residual back pain at 12 months than controls (6M group 52%, 18M group 42%, pooled controls 18%, p=0.01 and p=0.05, respectively).

(d) Reduced opioid use for pain relief: At 12 months, mean daily use of opioid medications for back pain was reduced by as much as 42% in the 18M MPC group compared with the saline control group (p=0.17). Mean opioid use was 1.00 tablet/day saline group, 0.94 tablet/day HA group, 0.77 tablet/day 6M MPC group, and 0.58 tablet/day 18 MPC group. Mean opioid use was also over two-fold higher in saline and HA controls achieving ≥50% reduction in pain score than in MPC treated patients, indicating that pain reduction in the controls may have been due to high opioid intake rather than to any biologic effect (mean opioid use 1.3 and 1.2 tablets/day in saline and HA controls compared with 0.7 and 0.6 tablets/day for the 6M and 18M MPC groups).

(e) Reduced need for additional surgical and non-surgical interventions for persistent pain: MPC-treated patients had a significantly reduced need for additional interventions at the treated disc level, including surgical intervention (spine fusion, discectomy or artificial disc replacement) or injection (epidural steroid injection, rhizotomy or transforaminal injections), than saline controls. By 12 months, 25% saline controls had undergone an additional intervention, compared with 10% HA controls, 6.9% of 6M MPC and only 3.3% of 18M MPC treated patients. By Kaplan-Meier analysis of time to a first additional treatment intervention, treatment with either 6M or 18M MPC significantly reduced the need for additional interventions compared with saline treatment (p=0.024 and p=0.010, respectively).

- Improvement in function

  (a) Reduction in mean disability score: At 12 months, MPC treatment resulted in greater improvement in function than was seen in controls, as measured by the Oswestry Disability Index (ODI). Mean reduction in the ODI functional disability score was 43% for the 18M MPC group, 35% for the 6M MPC group, 30% for HA controls, and 28% for saline controls (p=0.09 for 18M MPC group vs saline).

  (b) Increased proportion of patients achieving minimal residual functional disability: Minimal residual functional disability at 12 months was considered if the ODI score was $\leq$20. A greater proportion of MPC treated patients achieved minimal residual functional disability at 12 months than controls (18M group 39%, 6M group 36%, pooled controls 18%, p=0.14 and p=0.14, respectively).

- Improvement in disc stability

  In patients with early disc degeneration (Pfirrmann MRI degenerative grades below 5), increased translational movement of the disc is a potential indicator of instability associated with early disc degeneration and annular fissures seen on MRI and pathologic examination. At 12 months, MPC-treated patients demonstrated a significant reduction in radiographically-determined translational movement of the disc, suggesting a treatment effect on disc degeneration, anatomy, and improved disc stability. The 18M MPC group had a mean translational movement of only 1.3%, the 6M MPC group 2%, the HA group 2.5%, and the saline group 3.5% (p=0.021 between groups). When adjusting translation per degree of rotation (TPDR), a similar treatment effect on reduced translational movement was seen in both the 6M and 18M MPC groups.

- Safety:

  Allogeneic MPC treatment was well tolerated with the most frequently reported adverse event, back pain, occurring across all treatment groups.

About Chronic Degenerative Intervertebral Disc Disease

More than 6 million patients in the United States alone are currently dealing with chronic back pain that has persisted for at least three months, with around 3.5 million people affected by moderate or severe degenerative intervertebral disc disease. The United States Centers for Disease Control and Prevention's National Center for Health Statistics reported in 2010 that low back pain was the leading cause of pain, affecting 28% of American adults, and the second most common cause of disability in American adults. The United States lifetime prevalence of low back pain is estimated to be at least 60-84%. Total costs of low back pain are estimated to be between $100 billion and $200 billion annually, two thirds of which are due to decreased wages and productivity. Treatment for chronic back pain of discogenic origin includes conservative treatment, analgesia, anti-inflammatory agents, epidural steroid injections, and ultimately surgical intervention. Discogenic back pain is the end result of a complex process initiated by degeneration and loss of proteoglycan and water content of the nucleus pulpous, and increased stress on and fissure formation of the annulus fibrosis.

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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 proprietary technologies include its highly purified, immunoselected Stro-1/Stro-3 positive Mesenchymal Precursor Cells (MPCs), culture-expanded Mesenchymal Stem Cells (MSCs), Dental Pulp Stem Cells (DPSCs), and expanded Hematopoietic Stem Cells (HSCs). Mesoblast's protein technologies are based on factors derived from its proprietary cellular platforms, including Stromal Derived Factor-1 (SDF-1). Mesoblast's allogeneic or 'off-the-shelf' regenerative medicine products are being developed for the treatment of conditions with significant unmet medical needs. Product development focus is in four major and distinct areas - systemic diseases with an underlying inflammatory and immunologic etiology; cardiac and vascular diseases; orthopedic diseases of the spine; and improving outcomes of bone marrow transplantation associated with oncology or genetic conditions. www.mesoblast.com

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