

PUBLISHED STUDY RESULTS SHOW THAT MESOBLAST CELLS ADMINISTERED INTRAVENOUSLY SIGNIFICANTLY AMELIORATE JOINT DISEASE IN MODEL OF EARLY RHEUMATOID ARTHRITIS

Study provides translational and mechanistic support for Phase 2 trial results of Mesoblast’s cell therapy in patients with biologic refractory rheumatoid arthritis

Melbourne, Australia and New York, USA; February 13, 2017: Mesoblast Limited (ASX: MSB; Nasdaq: MESO) today announced results of a new study published in the current issue of the peer-reviewed journal *Stem Cell Research & Therapy*, showing that a single intravenous infusion of 150 million of the Company’s proprietary allogeneic “off-the-shelf” STRO-3 immunoselected Mesenchymal Precursor Cells (MPCs) significantly improved clinical disease severity, reduced joint cartilage erosions, and improved synovial inflammation and histopathology in a large animal model of early rheumatoid arthritis (RA).¹

This is the first study to show that intravenously administered STRO-1/STRO-3 immunoselected MPCs can ameliorate clinical and histopathologic disease severity in a large animal model of collagen-induced arthritis, a highly relevant and predictive model of human RA. The study’s lead investigators, from the Faculty of Veterinary and Agricultural Sciences, University of Melbourne, compared treatment with a single intravenous infusion of either 150 million allogeneic, STRO-3 immunoselected and culture-expanded sheep MPCs or saline in 16 sheep with early collagen-induced arthritis. This well-established large animal model of human RA is driven by multiple pro-inflammatory cytokines produced by synovial fibroblasts, T cells and monocytes, and progresses from monoarthritis early in the disease to inflammation of multiple joints (polyarthritis), cartilage erosions, and joint destruction.²

Mesenchymal lineage precursors and stem cells have been shown to be capable of targeting mechanistic pathways that are central to the process of progressive RA in humans, including by inhibiting the joint synovial fibroblast pro-inflammatory factor NF-kappaB that is implicated in synovial proliferation, inflammation, and joint destruction, and by polarizing pro-inflammatory monocytes and T cells to anti-inflammatory states. Notably, STRO-1 positive MPCs have been shown to be at least 10-fold more potent inhibitors of T-cell activation and proliferation than conventional plastic-adherent Mesenchymal Stem Cells (MSCs).³

Key clinical, immunologic, and histopathologic outcomes of the study were:

- Within two days, the MPC-treated group showed significantly faster decline of elevated neutrophil numbers in the blood than saline-treated controls, a white blood cell type that plays a critical role in the clinical manifestations of RA, gout and other inflammatory joint diseases in humans
- Within four days, and over the two-week study period, the MPC-treated group had a significantly lower composite clinical score of lameness, joint swelling and pain compared with saline-treated controls, with significant improvements seen in each of these clinical parameters
- Markers of inflammation in the blood (interleukin 17 and Activin A) were significantly reduced in the MPC-treated group compared with saline-treated controls over the two-week study period
- At the end of the study, the MPC-treated group showed significantly less joint destruction and joint inflammation compared with saline-treated controls, as evidenced by:
 - significantly reduced joint cartilage erosions
 - significantly reduced levels of activated synovial fibroblasts and fibrosis
 - significantly reduced infiltration of synovial tissues with monocytes and CD4 T cells, and;
 - significantly reduced blood vessel formation within the synovial tissues

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- All of these histopathologic components ameliorated by MPC treatment are key features associated with progressive joint disease and destruction in patients with active RA.

This study shows that Mesoblast's MPCs administered intravenously can significantly ameliorate inflammatory arthritis, and provides important mechanistic and translational support for the improved clinical outcomes previously reported in the ongoing Phase 2 trial with Mesoblast's product candidate MPC-300-IV in patients with RA who are refractory to TNF-alpha inhibitors and other biologic agents.⁴

¹ Abdalmula et al. Stem Cell Research & Therapy (2017) 8:22. Available at: <https://stemcellres.biomedcentral.com/articles/10.1186/s13287-016-0460-7>.

² Abdalmula et al, Vet Immunol Immunopathol. (2014); 159:83.

³ Nasef et al. Int. Jnl. Lab. Hem. (2009) 31, 9.

⁴ Trial NCT01851070. Additional information available at: <https://clinicaltrials.gov/show/NCT01851070>

About Mesoblast

Mesoblast Limited (ASX:MSB; Nasdaq:MESO) is a global leader in developing innovative cell-based medicines. The Company has leveraged its proprietary technology platform, which is based on specialized cells known as mesenchymal lineage adult stem cells, to establish a broad portfolio of late-stage product candidates. Mesoblast's allogeneic, 'off-the-shelf' cell product candidates target advanced stages of diseases with high, unmet medical needs including cardiovascular diseases, immune-mediated and inflammatory disorders, orthopedic disorders, and oncologic/hematologic conditions.

Forward-Looking Statements

This press release includes forward-looking statements that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements should not be read as a guarantee of future performance or results, and actual results may differ from the results anticipated in these forward-looking statements, and the differences may be material and adverse. You should read this press release together with our risk factors, in our most recently filed reports with the SEC or on our website. Uncertainties and risks that may cause Mesoblast's actual results, performance or achievements to be materially different from those which may be expressed or implied by such statements, and accordingly, you should not place undue reliance on these forward-looking statements. We do not undertake any obligations to publicly update or revise any forward-looking statements, whether as a result of new information, future developments or otherwise.

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