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RAPID IMPROVEMENT AND REMISSION IN PATIENTS WITH REFRACTORY ULCERATIVE COLITIS AND CROHN'S COLITIS AFTER DIRECT INJECTION OF REMESTEMCEL-L BY COLONOSCOPY

Results of First Patient Cohort from Randomized Controlled Study Presented at Congress of European Crohn's and Colitis Organisation (ECCO)

Melbourne, Australia; February 21, and New York, USA; February 20, 2022: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, today announced positive results from an interim analysis of the first patient cohort in the randomized, controlled study of remestemcel-L by direct endoscopic delivery to areas of inflammation in patients with medically refractory ulcerative colitis or Crohn's colitis. A single local delivery of remestemcel-L by colonoscopy resulted in rapid mucosal healing and disease remission in these refractory patients at high risk of progression to surgery.

The results of the first cohort of patients were presented at the 17th Congress of European Crohn's and Colitis Organisation (ECCO), February 16-19, by the trial's lead investigator Dr. Amy L. Lightner, Associate Professor of Surgery in the Department of Colon and Rectal Surgery at Cleveland Clinic and were published in the *Journal of Crohn's and Colitis.*[1,2]

"Mesenchymal stromal cells (remestemcel-L) offer a safe therapeutic for the treatment of medically refractory Ulcerative Colitis and Crohn's colitis," said Dr. Lightner. "Early data suggests improved clinical and endoscopic scores as early as two weeks following remestemcel-L delivery."

The study at Cleveland Clinic will randomize up to 48 patients with medically refractory ulcerative colitis or Crohn's colitis in a 2:1 fashion to receive a single intervention with remestemcel-L at a dose of 150-300 million cells or placebo delivered via direct injection using a 23 G sclerotherapy needle at the time of colonoscopy. Medically refractory ulcerative colitis and Crohn's colitis patients are defined as having active disease for at least 6 months and having lost response to at least one monoclonal antibody (anti-TNF or anti-integrin). Medically refractory Crohn's colitis patients exclude small bowel involvement and colorectal strictures. Outcomes are evaluated by validated endoscopic and clinical scoring systems at 2 weeks, 6 weeks, and 3 months post intervention.[3,4]

Key results of the interim analysis performed in the first 12 enrolled patients were as follows:

- Colonoscopic delivery of remestemcel-L was not associated with any treatment-related adverse events
- All ulcerative colitis patients treated with remestemcel-L had improved clinical and endoscopy scores within two weeks, as defined by the Mayo clinical score and Mayo endoscopic severity (MES) score, and all achieved clinical and endoscopic remission by six weeks
- All ulcerative colitis patients were extremely satisfied or satisfied with remestemcel-L treatment at three months, based on the inflammatory bowel disease patient reported treatment impact (IBD-PRTI), and response was described as excellent or good in all patients
- All Crohn's colitis patients treated with remestemcel-L showed treatment remissions or responses by three months, as measured by the Simple Endoscopy Score for Crohn's Disease (SES-CD) (mean score 17 at baseline decreased to 5 at three months)
- Remestemcel-L treatment resulted in reduction of fecal calprotectin, a validated biomarker of disease activity,[5] from mean of 231 at baseline to 67 at three months, indicative of remission
- In controls with ulcerative colitis and Crohn's colitis over three months, endoscopy scores increased, fecal calprotectin levels increased from a mean of 330 to 505, and clinical responses were described as poor or unchanged

Mesoblast Chief Medical Officer, Dr. Eric Rose said, "We are delighted to be involved with Dr. Lightner and her team at Cleveland Clinic in this latest cutting-edge study. This randomized controlled trial is the first to evaluate local delivery of remestemcel-L directly into the inflamed colon, using objective endoscopic measures of mucosal healing, in patients with colitis who are at high risk of surgical resection of their colon."

About Inflammatory Bowel Disease
According to recent estimates, more than three million people (1.3%) in the US alone have inflammatory bowel disease, with more than 33,000 new cases of Crohn's disease and 38,000 new cases of ulcerative colitis diagnosed every year.[6-8] Despite recent advances, approximately 30% of patients are primarily unresponsive to anti-TNFα agents and even among responders, up to 10% will lose their response to the drug every year. Up to 80% of patients with medically-refractory Crohn's disease and 20% of patients with medically-refractory ulcerative colitis eventually require surgical treatment of their disease,[9,10] which can have a devastating impact on quality of life.

About Objective Measures of Disease Activity in Patients with Inflammatory Bowel Disease

Objective measurement of disease activity can be achieved by endoscopy, histopathology, imaging, and biomarkers.[3] Fecal calprotectin is a very sensitive biomarker for inflammation in the gastrointestinal tract, with the presence of calprotectin a result of neutrophil migration into the gastrointestinal tissue due to an inflammatory process.[5] It is used for the diagnosis of inflammatory bowel disease, including ulcerative colitis and Crohn's disease, for monitoring disease activity and response to treatment, for prediction of disease relapse and post-operative recurrence in inflammatory bowel disease, and for predicting those patients at highest risk of progressing to bowel resection.[5]

Regulatory guidance recommends that registration trials of potential therapies for ulcerative colitis use primary endpoints incorporating both endoscopy and patient-reported outcomes (PROs).[3] Clinical trials for ulcerative colitis most commonly use the Mayo endoscopic subscore (MES) and the composite Mayo Clinic Score. FDA has consistently recommended the inclusion of endoscopic evaluation of mucosal healing in Crohn's disease as a co-primary endpoint to ensure that a clinical improvement is accompanied by a benefit in the underlying disease process. Simple Endoscopic Score for Crohn's Disease (SES-CD) is a reliable and responsive instrument,[4] but correlates poorly with symptoms. The current regulatory recommendation for trial eligibility is an SES-CD score $\geq$ 6 to define baseline endoscopic disease severity, with endoscopic remission defined by an SES-CD score of 0 to 2, and endoscopic response defined by a 50% reduction in the SES-CD score from baseline.

About Mesoblast
Mesoblast is a world leader in developing allogeneic (off-the-shelf) cellular medicines for the treatment of severe and life-threatening inflammatory conditions. The Company has leveraged its proprietary mesenchymal lineage cell therapy technology platform to establish a broad portfolio of late-stage product candidates which respond to severe inflammation by releasing anti-inflammatory factors that counter and modulate multiple effector arms of the immune system, resulting in significant reduction of the damaging inflammatory process.

Mesoblast has a strong and extensive global intellectual property portfolio with protection extending through to at least 2041 in all major markets. The Company's proprietary manufacturing processes yield industrial-scale, cryopreserved, off-the-shelf, cellular medicines. These cell therapies, with defined pharmaceutical release criteria, are planned to be readily available to patients worldwide.

Mesoblast is developing product candidates for distinct indications based on its remestemcel-L and rexlemestrocel-L stromal cell technology platforms. Remestemcel-L is being developed for inflammatory diseases in children and adults including steroid refractory acute graft versus host disease and moderate to severe acute respiratory distress syndrome. Rexlemestrocel-L is in development for advanced chronic heart failure and chronic low back pain. Two products have been commercialized in Japan and Europe by Mesoblast's licensees, and the Company has established commercial partnerships in Europe and China for certain Phase 3 assets.

Mesoblast has locations in Australia, the United States and Singapore and is listed on the Australian Securities Exchange (MSB) and on the Nasdaq (MESO). For more information, please see www.mesoblast.com, LinkedIn: Mesoblast Limited and Twitter: @Mesoblast

References / Footnotes

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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. Forward-looking statements include, but are not limited to, statements about: the initiation, timing, progress and results of Mesoblast's preclinical and clinical studies, and Mesoblast's research and development programs; Mesoblast's ability to advance product candidates into, enroll and successfully complete, clinical studies, including multi-national clinical trials; Mesoblast's ability to advance its manufacturing capabilities; the timing or likelihood of regulatory filings and approvals (including BLA resubmission), manufacturing activities and product marketing activities, if any; the commercialization of Mesoblast's product candidates, if approved; regulatory or public perceptions and market acceptance surrounding the use of stem-cell based therapies; the potential for Mesoblast's product candidates, if any are approved, to be withdrawn from the market due to patient adverse events or deaths; the potential benefits of strategic collaboration agreements and Mesoblast's ability to enter into and maintain established strategic collaborations; Mesoblast's ability to establish and maintain intellectual property on its product candidates and Mesoblast's ability to successfully defend these in cases of alleged infringement; the scope of protection Mesoblast is able to establish and maintain for intellectual property rights covering its product candidates and technology; estimates of Mesoblast's expenses, future revenues, capital requirements and its needs for additional financing; Mesoblast's financial performance; developments relating to Mesoblast's competitors and industry; and the pricing and reimbursement of Mesoblast's product candidates, if approved. 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.

Release authorized by the Chief Executive.

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