asx announcement

mesoblast

# NINETY DAY SURVIVAL OUTCOMES IN COVID-19 ARDS TRIAL OF REMESTEMCEL-L PRESENTED AT ISCT MEETING ON ADVANCES IN CELL & GENE THERAPIES FOR LUNG DISEASES

**Melbourne, Australia and New York, USA; July 19, 2021:** Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, presented 90-day survival outcomes from the 222-patient randomized controlled trial of remestemcel-L in ventilator-dependent COVID-19 patients with moderate/severe acute respiratory distress syndrome (ARDS) at an invited presentation on July 17 to the International Society for Cell & Gene Therapy (ISCT) Scientific Signatures Series on Cell and Gene Therapies in Lung Diseases and Critical Illnesses. The results showed that two doses of remestemcel-L at days 3-5 conferred durable survival benefit through at least 90 days in the pre-specified subgroup of patients under age 65.

Key presentation findings were:

- Remestemcel-L significantly reduced mortality by 48% at 90 days compared to controls in a pre-specified analysis of 123 treated patients under 65 years old, 26% vs 44%, Hazard Ratio (HR) 0.52, 95% CI (0.277, 0.964), p=0.038.[1,2] This compares favourably with the 46% mortality reduction reported at 60 days (p=0.048)[1,2] and indicates a durable treatment benefit in this patient population.
- Remestemcel-L was even more effective when evaluated in an exploratory analysis in patients on dexamethasone as part of their standard of care, with 90-day mortality being reduced by 77% compared to controls under 65 who received dexamethasone, 14% vs 48%, HR 0.23, 95% CI (0.080, 0.681), p=0.0037[1,2]
- These survival benefits were accompanied by significant improvements relative to controls in pre-specified secondary endpoints of ventilator-free days, respiratory function as assessed by ARDS severity, and overall clinical improvement on a 7-point ordinal scale.
- Despite a treatment-related improvement in respiratory function at day 7, there was no mortality reduction in the 97 treated patients over age 65, suggesting the need for more prolonged or higher dosing of anti-inflammatory therapy in these patients who may have a more exuberant inflammatory response associated with defective immune-mediated viral clearance mechanisms.

Recently published guidance to industry by the U.S. Food and Drug Administration (FDA)[3] has recommended demonstration of mortality benefit for at least 60 days in critically ill patients. Mesoblast will be meeting shortly with the FDA to discuss the durable mortality reduction seen in patients under 65 years old who received remestemcel-L in this randomized controlled trial, and the regulatory pathway for remestemcel-L in this patient population.

Mesoblast entered into a license and collaboration agreement with Novartis for the development, manufacture, and commercialization of remestemcel-L, with an initial focus on the treatment of acute respiratory distress syndrome (ARDS), including that associated with COVID-19. The agreement remains subject to certain closing conditions, including time to analyze the results from this COVID-19 ARDS trial.

## About the Trial of Remestemcel-L in Acute Respiratory Distress Syndrome (ARDS) due to COVID-19

The trial enrolled 222 mechanically ventilated COVID-19 patients with moderate/severe ARDS across the US, of whom 217 were randomized 1:1 and received either standard of care alone or standard of care plus 2 intravenous infusions of remestemcel-L at a dose of 2 million cells/kg 3-5 days apart. This was the same remestemcel-L dosing regimen used in the earlier compassionate use program where 11 of 12 patients were younger than 65 and 75% successfully came off ventilatory support.

Tha trial was halted in December 2020 after the Data Safety Monitoring Board (DSMB) performed a third interim analysis on the trial's first 180 patients, noting that the trial was not likely to meet the 30-day mortality reduction endpoint at the planned 300 patient enrolment. The trial was powered to achieve a primary endpoint of 43% reduction in mortality at 30 days for treatment with remestemcel-L on top of maximal care. The DSMB recommended that the trial complete with the enrolled 222 patients, and that all be followed-up as planned.

At follow-up through day 60, remestemcel-L showed a positive but non-significant trend in overall mortality reduction across the entire population of treated patients (n=217). In the pre-specified population of patients under age 65 (n=123), remestemcel-L reduced mortality through day 60 by 46%, but not in patients 65 or older (n=94). In an exploratory analysis through day 60, remestemcel-L reduced mortality by 75% and increased days alive off mechanical ventilation in patients under age 65 when combined with dexamethasone, in comparison with controls on dexamethasone.

**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 2040 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 has completed Phase 3 trials of rexlemestrocel-L for advanced chronic heart failure and chronic low back pain. 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. 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

**Footnotes**
1. All p-values are descriptive and not adjusted for multiplicity
2. Hazard Ratios calculated using Cox regression proportional hazards model without adjustment; p-value from log rank test
3. COVID-19: Developing Drugs and Biological Products for Treatment or Prevention - Guidance for Industry. *U.S. Department of Health and Human Services; Food and Drug Administration; Center for Drug Evaluation and Research (CDER); Center for Biologics Evaluation and Research (CBER)*. February 2021

**Forward-Looking Statements**
This announcement 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. All statements other than statements of historical fact, including our intention to discuss a regulatory pathway with the FDA, are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "likely," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions and variations thereof. 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. The risks, uncertainties and other factors that may impact our forward-looking statements include, but are not limited to: the timing, progress and results of Mesoblast's preclinical and clinical studies; Mesoblast's ability to advance product candidates into, enroll and successfully complete, clinical studies; the timing or likelihood of regulatory filings and approvals; whether the FDA agrees to a regulatory pathway; and the pricing and reimbursement of Mesoblast's product candidates, if approved; 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. 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. Unless required by law, 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.

*For more information, please contact:*

***Corporate Communications / Investors***
Paul Hughes
T: +61 3 9639 6036
E: investors@mesoblast.com

***Media***
Sumit Media
Grant Titmus
T: +61 419 388 161
E: grant@sumitmedia.com.au

Kristen Bothwell
T: +1 917 613 5434
E: kbothwell@rubenstein.com