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REMESTEMCEL-L REDUCES MORTALITY IN PATIENTS LESS THAN 65 YEARS OLD WITH MODERATE/SEVERE COVID-19 ARDS: TOPLINE 60-DAY RESULTS FROM RANDOMIZED CONTROLLED TRIAL

- Remestemcel-L reduced mortality through 60 days in the pre-specified population under 65 years old
- In these patients the benefit was further increased when remestemcel-L was used with dexamethasone as part of standard of care
- Mortality reduction by remestemcel-L was accompanied by increased days alive off mechanical ventilation and reduced days in hospital
- Plan to meet with U.S. Food and Drug Administration (FDA) to discuss potential next steps

Melbourne, Australia; April 30 and New York, USA; April 29, 2021: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, today announced the 60 day results from the randomized controlled trial of remestemcel-L in 222 ventilator-dependent COVID-19 patients with moderate/severe acute respiratory distress syndrome (ARDS) which had been halted after the third interim analysis, as previously announced. Remestemcel-L reduced mortality through day 60 by 46% in the pre-specified group below age 65, but not in patients 65 or older. 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.

"Reduction in mortality in mechanically ventilated patients under 65 years old remains a critical unmet need since as many as 72% of currently hospitalized patients across the US with COVID-19 are in this age category.[1]" said Mesoblast Chief Executive, Silviu Itescu. "This is similar to other causes of viral ARDS such as influenza where 70-80% of patients in intensive care units are under 65.[2,3] The reduction in mortality seen with remestemcel-L in this age group highlights the potential to make a meaningful difference in the treatment of diseases of excessive inflammation."

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.

During the course of the trial, as the pandemic evolved, numerous changes occurred in treatment regimes. As a result, the referral pool of patients into the trial became progressively older with comorbidities and refractory to treatment. The median age in the trial increased from 59 in the first half to 67 in the second half, $p<0.0001$[4,5]. This may have impacted the outcome of the third interim analysis which resulted in the trial's early conclusion. It is possible that to achieve mortality reduction in patients over 65 with comorbidities will require a different dosing regimen than that which may be effective in patients under 65.

Key findings in the trial were:

- Remestemcel-L reduced mortality by 46% through day 60 in the pre-specified population of 123 treated patients under age 65, 26% vs 42%, Hazard Ratio (HR) 0.54, 95% CI (0.286, 1.005), $p=0.048$[5,6]
- Remestemcel-L had similar treatment effects on mortality in these patients with either moderate ARDS (HR 0.56)[6,7] or severe ARDS (HR 0.56)[6,7]
- Standard of care changed during the course of the trial to incorporate dexamethasone, with only 2% of the first 50 patients enrolled receiving dexamethasone compared with 84% of the subsequent 172 patients; this allowed for additional exploratory analyses of remestemcel-L treatment effects in patients who received dexamethasone as part of their standard of care

- Remestemcel-L reduced mortality through day 60 by 75% compared to controls in patients under 65 who received dexamethasone as part of their standard of care, 14% vs 45%, HR 0.25, 95% CI (0.085, 0.727), p=0.006[5,6]

- Remestemcel-L increased days alive off ventilator within 60 days and reduced time to discharge from initial hospitalization compared to controls in patients under 65 who received dexamethasone as part of their standard of care, p=0.01 and p=0.005, respectively[5,8]

"The mortality benefit observed with remestemcel-L in ventilator-dependent patients younger than 65, particularly in combination with dexamethasone, has the potential to change the treatment regimen in this critical patient population," said Dr Fred Grossman, Chief Medical Officer of Mesoblast. "As cases continue to surge in younger patients across the US, we plan to meet with the FDA to discuss next steps in the regulatory process."

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.

Additional secondary endpoints, which include days in intensive care, and cardiac, neurological, and pulmonary organ damage, together with measures of circulating cytokines and inflammatory markers, are being evaluated and will be reported when completed.

Conference Call
There will be a webcast today, beginning at 9.00am AEST (Friday, April 30); 7.00pm EDT (Thursday, April 29, 2021). It can be accessed via:
https://webcast.boardroom.media/mesoblast-limited/20210427/NaN60874bd69634a7001901f0a6

The archived webcast will be available on the Investor page of the Company's website:
www.mesoblast.com

About Remestemcel-L
Remestemcel-L is an investigational therapy comprising culture-expanded mesenchymal stromal cells derived from the bone marrow of an unrelated donor. Remestemcel-L is thought to have immunomodulatory properties to counteract the cytokine storms that are implicated in various inflammatory conditions by downregulating the production of pro-inflammatory cytokines, increasing production of anti-inflammatory cytokines, and enabling recruitment of naturally occurring anti-inflammatory cells to involved tissues.

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. The Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET). Centers for Disease Control and Prevention
2. Martin-Loeches et al. Pandemic and post-pandemic Influenza A (H1N1) infection in critically ill patients *Critical Care* 2011, 15:R286
3. Bonmarin I et al. Intensive care unit surveillance of influenza infection in France: the 2009/10 pandemic and the three subsequent seasons. *Euro Surveill*. 2015;20(46)
4. two sample t-test
5. All p-values are descriptive and not adjusted for multiplicity
6. Hazard Ratios calculated using Cox regression proportional hazards model without adjustment; p-value from log rank test
7. Interaction term between remestemcel-L treatment and ARDS severity in Cox regression proportional hazards model was not significant (p=0.98), indicating that treatment effect is not confounded by disease severity
8. Wilcoxon rank sum test

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 potential next steps 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 path forward; 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
Kristen Bothwell
T: +1 917 613 5434
E: kbothwell@rubenstein.com