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CLINICAL OUTCOMES USING RYONCIL™ (REMESTEMCEL-L) IN CHILDREN AND ADULTS WITH SEVERE INFLAMMATORY GRAFT VERSUS HOST DISEASE PUBLISHED IN THREE ARTICLES IN BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION

Key points:

- Biology of Blood and Marrow Transplantation, the official publication of the American Society for Transplantation and Cellular Therapy, publishes three peer-reviewed articles detailing results from three separate trials of remestemcel-L in children and adults with acute graft versus host disease
- Publications highlight consistent benefits seen across all three trials in patients with greatest levels of inflammation and the most severe grades of the disease
- Trial results underpin Mesoblast's Biologics License Application to seek approval of its product candidate RYONCIL™ (remestemcel-L) for pediatric steroid-refractory acute graft versus host disease (GVHD), which has been accepted for priority review by the United States Food and Drug Administration (FDA)
- These outcomes also provide the rationale for use of remestemcel-L in other conditions associated with severe inflammation and cytokine release, including COVID-19 infection

Melbourne, Australia; May 25, 2020; and New York, USA; May 24, 2020: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in cellular medicines for inflammatory diseases, today announced that clinical outcomes of its allogeneic mesenchymal stem cell (MSC) medicine RYONCIL™ (remestemcel-L) in children and adults with steroid-refractory acute graft versus host disease (GVHD) have been published in three peer-reviewed articles and an accompanying editorial in the May issue of Biology of Blood and Marrow Transplantation, the official publication of the American Society for Transplantation and Cellular Therapy.

Mesoblast Chief Medical Officer Dr Fred Grossman said: "Results from these three trials show a consistent pattern of safety and efficacy for RYONCIL (remestemcel-L) in patients with the greatest levels of inflammation and the most severe grades of acute GVHD. These clinical outcomes provide a compelling rationale for use of remestemcel-L in children and adults with other conditions associated with severe inflammation and cytokine release, including acute respiratory distress syndrome (ARDS) and systemic vascular manifestations of COVID-19 infection."

In the accompanying editorial, Dr Jacques Galipeau, Professor and Assistant Dean of Medicine at the Stem Cell & Regenerative Medicine Center at the University of Wisconsin–Madison and Chair of the International Society of Cell and Gene Therapy (ISCT) MSC Committee, concluded that after more than a decade of clinical study involving three distinct advanced trials, it appears that remestemcel-L might well have finally met the regulatory requirements for marketing approval in the United States for steroid refractory acute GVHD in children, and it is to be determined whether this industrial MSC product will find utility for adults afflicted by acute GVHD or other indications.

The trials highlighted in the three articles all evaluated the same treatment regimen of RYONCIL, with patients receiving twice weekly intravenous infusions of 2 million cells per kg body weight over a four-week period. RYONCIL was well-tolerated in all studies with no identified safety concerns. The three trials were:

- Study 275: An Expanded Access Program in 241 children across 50 centers in eight countries where RYONCIL was used as salvage therapy for steroid-refractory acute GVHD in patients who failed to respond to steroid therapy as well as multiple other agents.
    - Day 28 Overall Response (OR), the primary endpoint, was achieved in 65% of subjects. Survival through 100 days was significantly greater in patients who achieved a day 28 OR (82%) compared with patients that did not achieve day 28 OR (39%), with 67% overall day 100 survival.

2. Study GVHD001/002: A Phase 3 single-arm trial in 55 children across 20 centers in the United States where RYONCIL was used as the first line of treatment for children who failed to respond to steroids for acute GVHD.

- Consistent with the findings in Study 275, Day 28 OR was achieved in 70% of children. This was statistically significant compared to the pre-specified control value of 45% (70.4% versus 45%, P =0.0003). As in study 275, clinical response at day 28 was highly predictive of improved survival through day 100 (87% compared to 47% in patients that did not achieve day 28 OR P = 0.0001). Similar predictive value of day 28 was also seen in survival through day 180 (79% vs. 43.8%, P= 0.003). Overall survival was 74.1% at day 100 and 68.5% at day 180.

- These results were significantly higher than those from matched control pediatric subjects from the contemporaneous database of the Mount Sinai Acute GVHD International Consortium (MAGIC), accessed to provide an unbiased and independent estimate of response rates and outcomes in matched pediatric control patients treated with institutional standard of care. In the MAGIC controls, Day 28 OR was 43% and Day 100 survival was 57%.

3. Study 280: A Phase 3 randomized placebo-controlled trial in 260 patients, including 28 children, across 72 centers in seven countries where RYONCIL or placebo were added to second line therapy in patients with steroid-refractory acute GVHD who failed to respond to steroid treatment.

- Among high-risk children and adults who had the most severe disease stages, day 28 OR was significantly greater in the RYONCIL treated group (58% versus 37%; P = 0.03) compared to placebo. Among the standard risk patients there was no significant benefit of RYONCIL treatment. Within the pediatric patients in this study (n=28) day 28 OR was significantly greater in the RYONCIL group compared with the placebo group (64% vs 36%, respectively, P=0.05).

- These Phase 3 results provide prospective, randomized controlled data which are supportive for the use of RYONCIL in children and high-risk adults with steroid-refractory acute GVHD.

About Acute Graft Versus Host Disease

Acute GVHD occurs in approximately 50% of patients who receive an allogeneic bone marrow transplant (BMT). Over 30,000 patients worldwide undergo an allogeneic BMT annually, primarily during treatment for blood cancers, and these numbers are increasing.[1] In patients with the most severe form of acute GVHD (Grade C/D or III/IV) mortality is as high as 90% despite optimal institutional standard of care.[2,3] There are currently no FDA-approved treatments in the United States for children under 12 with steroid-refractory acute GVHD.

About RYONCIL™

Mesoblast's lead product candidate, RYONCIL (remestemcel-L), is an investigational therapy comprising culture-expanded mesenchymal stem cells derived from the bone marrow of an unrelated donor. It is administered to patients in a series of intravenous infusions. RYONCIL is believed to have immunomodulatory properties to counteract the inflammatory processes that are implicated in SR-aGVHD by down-regulating the production of pro-inflammatory cytokines, increasing production of anti-inflammatory cytokines, and enabling recruitment of naturally occurring anti-inflammatory cells to involved tissues.

References

1. Niederwieser D, Baldomero H, Szer J. Hematopoietic stem cell transplantation activity worldwide in 2012 and a SWOT analysis of the Worldwide Network for Blood and Marrow Transplantation Group including the global survey. Bone Marrow Transplant 2016; 51(6):778-85.
2. Westin, J., Saliba, RM., Lima, M. (2011) Steroid-refractory acute GVHD: predictors and outcomes. Advances in Hematology 2011;2011:601953.
3. Axt L, Naumann A, Toennies J (2019) Retrospective single center analysis of outcome, risk factors and therapy in steroid refractory graft-versus-host disease after allogeneic hematopoietic cell transplantation. Bone Marrow Transplantation 2019;54(11):1805-1814.

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About Mesoblast
Mesoblast Limited (ASX:MSB; Nasdaq:MESO) is a world leader in developing allogeneic (off-the-shelf) cellular medicines. The Company has leveraged its proprietary mesenchymal lineage cell therapy technology platform to establish a broad portfolio of commercial products and late-stage product candidates. 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's Biologics License Application to seek approval of its product candidate RYONCIL™ (remestemcel-L) for pediatric steroid-refractory acute graft versus host disease (acute GVHD) has been accepted for priority review by the United States Food and Drug Administration (FDA), and if approved, product launch in the United States is expected in 2020. Remestemcel-L is also being developed for other inflammatory diseases in children and adults including moderate to severe acute respiratory distress syndrome. Mesoblast is completing Phase 3 trials for its product candidates for advanced 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 a strong and extensive global intellectual property (IP) portfolio with protection extending through to at least 2040 in all major markets. This IP position is expected to provide the Company with substantial commercial advantages as it develops its product candidates for these conditions.

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

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. 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 include, but are not limited to, statements about the initiation, timing, progress and results of Mesoblast and its collaborators' clinical studies; Mesoblast and its collaborators' ability to advance product candidates into, enroll and successfully complete, clinical studies; the timing or likelihood of regulatory filings and approvals; and the pricing and reimbursement of Mesoblast's product candidates, if approved; the potential benefits of strategic collaboration agreements and Mesoblast's ability to 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. 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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