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MESOBLAST RESUBMITS BIOLOGIC LICENSE APPLICATION (BLA) TO FDA FOR REMESTEMCEL-L IN CHILDREN WITH STEROID-REFRACTORY ACUTE GRAFT VERSUS HOST DISEASE (SR-aGVHD)

Validation of Remestemcel-L Potency Assay used in the Phase 3 Trial which Measures In-Vivo Activity based on Mechanism of Action

Assay Identifies High-Potency Product Lots Associated with Enhanced Survival

New Data Show that Remestemcel-L Improves Inflammatory Biomarkers and Survival in Children at Highest Risk of Mortality

New 4-Year Data from the Phase 3 Trial Shows Durable Long-Term Survival Outcomes

BLA Resubmission will have a Review Period up to Six-Months from Filing upon Acceptance by FDA

If Approved, Remestemcel-L would be the First Treatment Available for Children Under 12 Years Old with SR-aGVHD, a Devastating Disease with Very High Mortality

New York, USA; January 31, 2023 and Melbourne, Australia: Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, announced today it has resubmitted to the U.S. Food and Drug Administration (FDA) its Biologics License Application (BLA) for approval of remestemcel-L in the treatment of children with steroid-refractory acute graft versus host disease (SR-aGVHD).

Survival outcomes have not improved over the past two decades for the most severe forms of SR-aGVHD, a life-threatening complication of an allogeneic bone marrow transplant following treatment for blood cancers and other conditions.[1-3] The lack of any approved treatments for children under 12 means that there is an urgent need for a therapy that improves the dismal survival outcomes. If remestemcel-L receives FDA approval, it will be the first allogeneic "off-the-shelf" cellular medicine to be approved in the United States, and the first therapy for children under 12 years old with SR-aGVHD.

The resubmission contains substantial new information as required by FDA in the Complete Response Letter (CRL) received in September 2020 to the BLA for remestemcel-L. Mesoblast has maintained an active dialogue with FDA since receiving the CRL and in October 2022 provided a high-level synopsis of the substantial new information under its Investigational New Drug (IND) application for remestemcel-L. FDA granted remestemcel-L Fast Track designation, a process to facilitate the development and expedited review of therapies for serious conditions that fill unmet medical needs, and Priority Review designation, which is given to drugs that treat a serious condition and provide a significant improvement in safety or effectiveness over existing treatments. The BLA resubmission will have a review period up to six months from filing upon acceptance by FDA.

Mesoblast has responded to the CRL and the further guidance it has received from the FDA and has generated and provided new data and analyses in the resubmission which we believe provide substantial evidence of remestemcel-L's effectiveness in pediatric SR-aGVHD. Specifically, the resubmission contains the following:

- new long-term survival data of children enrolled in the Phase 3 trial showing durability of treatment effect through at least four years,
- new data showing remestemcel-L's treatment benefit in high-risk disease activity and on survival in propensity-matched studies of children in the Phase 3 trial and controls stratified by validated biomarkers for high-risk disease,

- new analyses of data obtained prospectively showing that the validated potency assay which was in place and used to release product for the 54-patient Phase 3 clinical trial measures a key product attribute which reflects the primary mechanism of action of remestemcel-L in children with SR-aGVHD, correlates with the product's *in vivo* bioactivity, and predicts overall survival outcomes,
- new analyses of data obtained prospectively relating manufacturing changes during product development prior to Phase 3 to progressive increases in potency and to improved survival outcomes in larger studies of remestemcel-L under expanded access in children with SR-aGVHD,
- new data showing that the validated potency assay has low variability and can adequately demonstrate manufacturing consistency and reproducibility, and
- establishment of a new specification for release of commercial product based on extensive clinical data which provides assurance that future batches of remestemcel-L will have attributes supportive of expected survival outcomes.

"There is an urgent need for a therapy that improves the dismal survival outcome in children with SR-aGVHD" said Dr. Silviu Itescu, Chief Executive of Mesoblast. "Our team has worked tirelessly over the past two years to provide a comprehensive response to the FDA. We are grateful for the agency's active dialogue and constructive feedback that will ensure a high bar is met in terms of product consistency and predictability of clinical outcomes."

About Steroid-Refractory Acute Graft Versus Host Disease
Survival outcomes have not improved over the past two decades for children or adults with the most severe forms of SR-aGVHD.[1-3] The lack of any approved treatments for children under 12 means that there is an urgent need for a therapy that improves the dismal survival outcomes in children.

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, including about 20% in pediatric patients.[4,5] SR-aGVHD is associated with mortality as high as 90% and significant extended hospital stay costs.[6,7] There are currently no FDA-approved treatments in the US for children under 12 with SR-aGVHD.

About Remestemcel-L
Mesoblast's lead product candidate, Remestemcel-L, is an investigational therapy comprising culture expanded mesenchymal stromal cells derived from the bone marrow of an unrelated donor. It is administered to patients in a series of intravenous infusions. Remestemcel-L 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.

The original BLA submission contained clinical outcomes of 309 children with SR-aGVHD treated with remestemcel-L showing consistent treatment responses and survival across three separate trials. The data were reviewed by the agency's panel of the Oncologic Drugs Advisory Committee (ODAC) which voted in favor 9:1 that the available data support the efficacy of remestemcel-L in pediatric patients with SR-aGVHD.

The BLA resubmission now contains additional clinical and biomarker data, including from a propensity-matched study of children with high-risk disease, based on the validated MAP biomarker score, comparing outcomes in 25 children from Mesoblast's Phase 3 trial and 27 control children treated with various biologics, including ruxolitinib, from the Mount Sinai Acute GvHD International Consortium (MAGIC) database. The study showed that 67% of high-risk children treated with remestemcel responded positively to treatment within 28 days and were alive after 180 days compared to just 10% in both categories in the MAGIC group.

The BLA resubmission also contains results of a 4-year survival study performed by the Center for International Blood and Marrow Transplant Research (CIBMTR) on 51 evaluable patients with SR-aGVHD who were enrolled in the Phase 3 trial. The results demonstrated durability of the early day 180 survival

benefits, with 63% survival at 1 year and 51% at 2 years in a group of children with predominantly grade C/D disease (89%) and with expected 2 year survival of just 25-38% using best available therapy.[1,8-9]

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 allogeneic stromal cell technology platforms. Remestemcel-L is being developed for inflammatory diseases in children and adults including steroid refractory acute graft versus host disease, biologic-resistant inflammatory bowel disease, and 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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