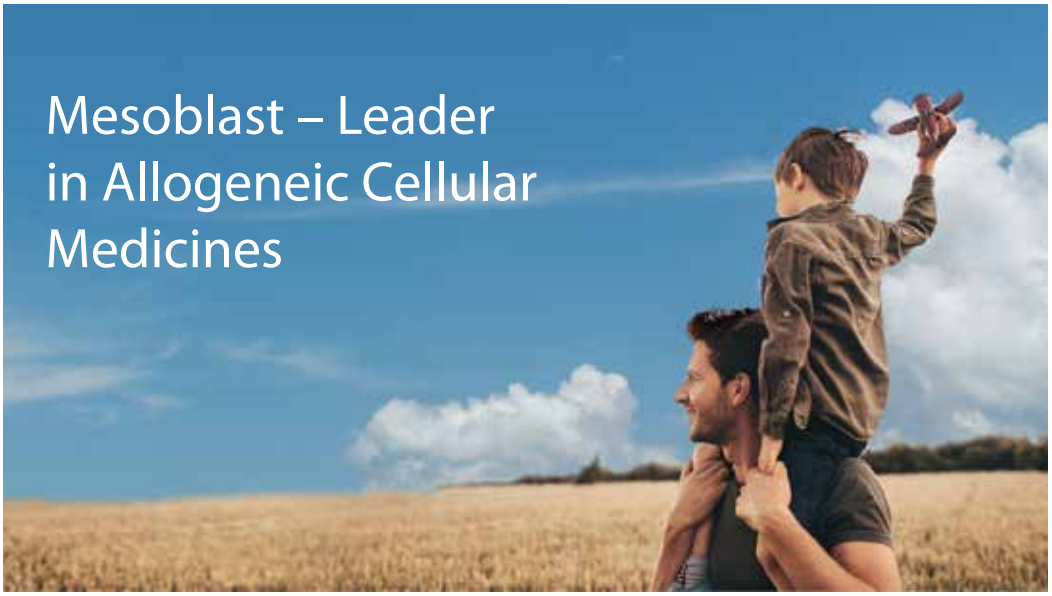
mesoblast



# Mesoblast – Leader in Allogeneic Cellular Medicines

## Mesoblast (ASX:MSB; Nasdaq:MESO) is developing and commercializing allogeneic cellular medicines to treat serious and life-threatening inflammatory diseases with significant, unmet medical needs.

The Company's Phase 3 off-the-shelf mesenchymal lineage cell product candidates are:

- RYONCIL™ (remestemcel-L) for steroid-refractory acute graft versus host disease (acute GVHD)
- Remestemcel-L for moderate to severe acute respiratory distress syndrome (ARDS) due to COVID-19 infection
- REVASCOR® for advanced chronic heart failure, and
- MPC-06-ID for chronic low back pain due to degenerative disc disease.

The United States Food and Drug Administration (FDA) has accepted for priority review Mesoblast's Biologics License Application (BLA) to seek approval of RYONCIL to treat steroid-refractory acute GVHD in children. The FDA has set a Prescription Drug User Fee Act (PDUFA) action date of September 30, 2020, and if approved, Mesoblast will make RYONCIL immediately available in the United States.

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 upon receiving marketing authorizations.

## Phase 3 Product Candidates

| PRODUCT CANDIDATE | THERAPEUTIC AREA | PHASE 1/2 / PHASE 3 / REGISTRATION | MESOBLAST COMMERCIAL RIGHTS | COMMERCIAL PARTNERS |
|---|---|---|---|---|
| RYONCIL™ (Remestemcel-L) | Pediatric & adult systemic inflammatory diseases | Acute GVHD – Pediatric | Global ex-Japan | JCR |
| | | Acute GVHD – Adult | | |
| REMESTEMCEL-L | | Chronic GVHD | Global | |
| | | Acute Respiratory Distress Syndrome (COVID-19; Influenza; Bacterial) | | |
| | | Hypoxic Ischemic Encephalopathy* | Global ex-Japan | JCR |
| | | Epidermolysis Bullosa* | | |
| | | Biologic-refractory Crohn's Disease | Global | |
| REVASCOR® (Rexlemestrocel) | Localized inflammatory diseases | Advanced Heart Failure | Global ex-China | TASLY |
| | | End-Stage Ischemic Heart Failure | | |
| MPC-06-ID (Rexlemestrocel) | | Chronic Low Back Pain | Global ex-EUR, LATAM | GRÜNENTHAL |

The Company also has a promising pipeline of product candidates and next generation technologies.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## Innovative technology

Mesoblast is developing immuno-selected, culture expanded cellular medicines based on mesenchymal precursor cells (MPCs) and their progeny, mesenchymal stem cells (MSCs). These are rare cells (approximately 1:100,000 in bone marrow) found around blood vessels that are central to blood vessel maintenance, repair and regeneration. Preclinical studies have shown that these cells respond to damaged tissue, secreting mediators that promote tissue repair and modulate immune responses. This mechanism of action enables the targeting of multiple disease pathways in complex diseases with major, unmet medical needs. A key feature of Mesoblast's patented mesenchymal lineage cells is that they are administered without the need for donor–recipient matching or recipient immune suppression, and therefore are often referred to as 'off-the-shelf' cellular medicines.

## Steroid-refractory Acute Graft Versus Host Disease, a Life-threatening Inflammatory Condition

Mesoblast has filed a Biologics License Application (BLA) with the FDA for RYONCIL™ in the treatment of pediatric steroid-refractory acute GVHD. This life-threatening disease 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. In patients with the most severe form of steroid-refractory acute GVHD (Grade C/D or III/IV) mortality is as high as 90% despite optimal standard of care. There are currently no FDA-approved treatments in the United States for children under 12 with steroid-refractory acute GVHD. Aggregated results from 309 children treated with RYONCIL were presented at the annual meeting of the 2020 American Society for Transplantation Cellular Therapy and the Center for International Blood & Bone Marrow Transplant Research meeting. The data showed that treatment with RYONCIL across three separate trials resulted in consistent treatment responses and survival outcomes in children with steroid-refractory acute GVHD.

Key findings and conclusions were:

- Consistent safety and efficacy were observed across the continuum from first-line treatment after steroid failure through the most challenging patients who received RYONCIL as salvage after exhausting all other options
- In the aggregated dataset, 204 of the 309 (66%) patients achieved an overall response at Day 28 following a four-week course of RYONCIL
- Results were consistent across all grades of disease, including most severe (IBMTR Grade C/D or Glucksberg Grade 3/4)
- In the most severe patients (Grade C/D), who accounted for 82% of all treated patients, Day 28 overall response was 65%
- Overall response at Day 28 was strongly predictive of survival at Day 100 and Day 180
- Day 28 responders were more than twice as likely to survive as non-responders (84% vs 39% at Day 100, and 83% vs 38% at Day 180)
- RYONCIL was well tolerated with no infusion-related toxicity and no identified safety concerns.

If approved, RYONCIL has the potential to be an effective and safe therapy to significantly improve survival outcomes in the most vulnerable population of children with severe forms of this disease.

Underpinning Mesoblast's confidence in the United States market access plan for RYONCIL is the Japan experience, where Mesoblast's licensee, JCR Pharmaceuticals, sells TEMCELL®[1] HS Inj. for children and adults with aGVHD. The continued growth in revenues of TEMCELL in Japan is an important indicator for the potential of RYONCIL in the United States market, where Mesoblast has established a targeted commercial team to bring RYONCIL to market. An agreement was entered into with Lonza in Singapore, Mesoblast's manufacturing partner, for the commercial manufacture of RYONCIL to facilitate inventory build ahead of the planned United States market launch and for commercial supply to meet Mesoblast's long-term market projections.

The Company has put in place a lifecycle extension strategy to generate evidence-based clinical outcomes to leverage the experience of bringing RYONCIL to market and to maximize the value of remestemcel-L in other pediatric and adult rare diseases that have shorter timelines to gain marketing authorization and do not require large distribution channels. Investigator-initiated clinical trials for chronic GVHD and other indications will be expanded.

## Remestemcel-L for Moderate to Severe Acute Respiratory Distress Syndrome due to COVID-19 Infection

COVID-19 is a respiratory virus with a high mortality due to a severe inflammatory condition of the lungs called acute respiratory disease syndrome (ARDS). It is caused by a cytokine storm in the lungs of patients infected with COVID-19 and is the primary cause of death. ARDS is a major area of unmet need that typically requires extended ICU hospitalization and intervention by mechanical ventilation. There are multiple triggers including viral and bacterial infections such as coronavirus or influenza with 40-80% mortality in viral-induced ARDS (influenza & COVID-19, respectively).

The extensive safety data of remestemcel-L and its anti-inflammatory effects in acute GVHD makes a compelling rationale for evaluating remestemcel-L in COVID-19 ARDS. Intravenous delivery of remestemcel-L results in selective migration to the lungs contributing to the potential for remestemcel-L to tame the cytokine storm in ARDS.

During the period March-April 2020, 12 ventilator-dependent COVID-19 patients with moderate/severe COVID-19 ARDS were treated with two infusions of remestemcel-L within the first five days under emergency compassionate use at New York City's Mt Sinai hospital. Nine patients successfully came off ventilator support at a median of 10 days and were discharged from hospital. These results contrast with only 9% of ventilator-dependent

1 TEMCELL® HS Inj. is a registered trademark of JCR Pharmaceuticals Co. Ltd

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**Manufacturing Remestemcel-L**

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COVID-19 patients being able to come off ventilators with standard of care treatment at two major referral hospital networks in New York during the same time period.

This compassionate use treatment experience informed the design of the clinical protocol for the randomized, placebo-controlled Phase 3 trial of remestemcel-L in ventilator-dependent COVID-19 moderate/severe ARDS patients in North America. Enrollment in up to 30 leading medical centers began in May and is expected to complete within three to four months. Interim analyses are planned, which could result in stopping the trial early for efficacy or futility.

The trial will randomize up to 300 ventilator-dependent patients in intensive care units to either remestemcel-L or placebo (1:1) on top of maximal care, in line with specific guidance provided by the FDA for robust statistical analysis. The primary endpoint is all-cause mortality within 30 days of randomization, with the key secondary endpoint being the number of days alive and off mechanical support.

## REVASCOR® for Advanced and End-stage Heart Failure

Mesoblast is developing REVASCOR® to fill the treatment gap for both advanced and end-stage chronic heart failure. The objective is to use REVASCOR to prevent or delay further progression of heart failure or cardiac death in patients who are no longer responsive to maximal standard of care heart failure drugs.

After surpassing the number of primary endpoints required for the completion of the Phase 3 trial of REVASCOR for advanced chronic heart failure, final study visits for all surviving patients have been completed in this cardiovascular-outcomes trial in 566 patients. An ongoing quality review of all data is being finalized at the study sites, with a data readout planned for mid-2020.

The independent Data Monitoring Committee overseeing this Phase 3 trial held its 10th and final scheduled meeting and recommended that the trial continue as planned. The DMC reviewed available data from the 566 randomized patients, including components of the trial's primary and secondary endpoints, and all safety data.

The Phase 3 trial results will be considered pivotal to support regulatory approval in the United States, as well as in China through a partnership with Tasly Pharmaceuticals to develop and commercialize the product for advanced chronic heart failure.

The American Heart Association journal Circulation Research published a Special Article highlighting the important potential clinical benefits of REVASCOR in patients with advanced chronic heart failure, stating that there is a biologic rationale for the use of this product in targeting cardiac inflammation in order to improve heart failure outcomes.

## MPC-06-ID for Chronic Low Back Pain due to Degenerative Disc Disease

Mesoblast's Phase 3 trial of MPC-06-ID in 404 patients with chronic low back pain due to degenerative disc disease has a primary composite endpoint of improvement in pain and function through 24 months. Final study visits for all patients have been completed, with an ongoing quality review of all data being finalized at the study sites. A data readout is planned for mid-2020.

Grünenthal, a global leader in pain management, and Mesoblast entered into a strategic partnership to develop and commercialize MPC-06-ID for the treatment of chronic low back pain associated with degenerative disc disease in patients who have exhausted conservative treatment options in Europe and Latin America. The companies have agreed on an overall development plan for the product to meet European regulatory requirements. As part of this plan, they are collaborating on the study design for a confirmatory Phase 3 trial in Europe, with the results of the two Phase 3 trials expected to support both FDA and European Medicines Agency regulatory approvals for MPC-06-ID.

## Scalable Manufacturing

The inherent technical properties of Mesoblast's mesenchymal lineage cells allow for scalable culture expansion to produce anticipated commercial quantities with batch to batch consistency and reproducibility. Proprietary media formulations, advances in development of 3D bioreactor technology and automation are intended to deliver step-changes improvement in product yield.

## Evidence-based Science and Translational Medicine

Mesoblast's approach to product development is to ensure rigorous scientific investigations are performed with well-characterized cell populations in order to understand mechanisms of action for each potential indication. Extensive preclinical translational studies guide clinical trials that are structured to meet stringent safety and efficacy criteria set by international regulatory agencies. All trials are conducted under the continuing review of independent Data Safety Monitoring Boards comprised of independent medical experts and statisticians. These safeguards are intended to ensure the integrity and reproducibility of results, and to ensure that outcomes observed are scientifically reliable.

## Robust Intellectual Property Estate

Mesoblast has an extensive patent portfolio comprising approximately 1,000 patents and patent applications with protection extending through 2040 in all major markets. This intellectual property portfolio covers composition of matter, manufacturing, and therapeutic applications of mesenchymal lineage cells. The Company believes this patent estate provides strong global protection in areas of its core commercial focus.

## Global Operations

Mesoblast has locations in the United States, Australia and Singapore and is listed on the Australian Securities Exchange (MSB) and on the Nasdaq (MESO).

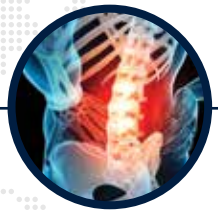
## Markets Opportunities for Lead Products

### Acute Graft Versus Host Disease

- >30,000 allogeneic bone marrow transplants performed globally (>20K US/EU) annually, ~20% pediatric
- Steroid-refractory aGVHD represents >USD $700m U.S./EU market opportunity

### Advanced Heart Failure

- U.S. healthcare costs for NYHA class II-IV patients $115bn/year
- Hospitalizations account for ~69% of expenditure
- Multi-billion dollar annual market opportunity in in the U.S.



### Chronic Low Back Pain Due to Disc Degeneration

- MPC-06-ID development focused on over ~3.2m patients in U.S. alone
- U.S. market opportunity >USD $1 billion

## Corporate History

Mesoblast has more than a decade of scientific, manufacturing, clinical development and corporate development experience targeted at bringing to market allogeneic, off-the-shelf cellular medicines for inflammatory diseases.

**2004** Mesoblast founded in Melbourne, Australia and listed on the ASX

**2010** Entered into strategic alliance with Cephalon to develop and commercialize MPC therapeutics

**2011** Entered into manufacturing partnership with Lonza Group in Singapore for MPC medicines

**2013** Acquired MSC business from Osiris Therapeutics with future earnouts

**2014** Granted manufacturing pioneer status by Economic Development Board of Singapore

**2015** Dual listed on the Nasdaq

**2016** TEMCELL® HS Inj (MSC medicine) launched in Japan by Mesoblast licensee JCR

**2017** Mesoblast receives royalty income from its patent licensee TiGenix, S.A.U., a wholly owned subsidiary of Takeda, on its worldwide sales of its product Alofisel® for the treatment of complex perianal fistulas in adult patients with Crohn's disease, as well as milestone payments.

**2018** Entered into strategic partnership agreement with Tasly for cardiovascular assets in China

**2019** Smith & Nephew acquired Osiris Therapeutics, and will receive future earn-outs on MSC business

**2019** Entered into strategic partnership with Grünenthal for chronic low back pain asset in Europe & Latin America

**2020** Filed first BLA submission to US FDA; RYONCIL™ (remestemcel-L) for steroid-refractory acute graft versus host disease in children

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