**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, D.C. 20549**

# Form 6-K

**Report of Foreign Private Issuer**
**Pursuant to Rule 13a-16 or 15d-16 under the Securities Exchange Act of 1934**

**For the month of November 2023**

**Commission File Number 001-37626**

# Mesoblast Limited

(*Exact name of Registrant as specified in its charter*)

**Not Applicable**
(*Translation of Registrant's name into English)*

**Australia**
(*Jurisdiction of incorporation or organization)*

**Silviu Itescu**
**Chief Executive Officer and Executive Director**
**Level 38**
**55 Collins Street**
**Melbourne 3000**
**Australia**
(*Address of principal executive offices*)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F:

Form 20-F ☑ Form 40-F ☐

**INFORMATION CONTAINED ON THIS REPORT ON FORM 6-K**

On November 22, 2023, Mesoblast Limited filed with the Australian Securities Exchange a new release announcement, which is attached hereto as Exhibit 99.1, and is incorporated herein by reference.

On November 15, 2023, Mesoblast Limited filed with the Australian Securities Exchange a corporate presentation, which is attached hereto as Exhibit 99.2, and is incorporated herein by reference.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly organized.

Mesoblast Limited
/s/ Niva Sivakumar

Niva Sivakumar
*Company Secretary*

Dated: November 22, 2023

**INDEX TO EXHIBITS**

| Item | |
|---|---|
| 99.1 | Press release of Mesoblast Ltd, dated November 22, 2023. |
| 99.2 | Corporate presentation of Mesoblast Ltd, dated November 15, 2023 |

Exhibit 99.1

asx announcement

mesoblast

**MESOBLAST PARTNERS WITH BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK (BMT CTN) ON PIVOTAL TRIAL IN ADULTS WITH SR-aGVHD**

**Melbourne, Australia; November 22 and New York, USA; November 21, 2023:** Mesoblast Limited (ASX:MSB; Nasdaq:MESO), global leader in allogeneic cellular medicines for inflammatory diseases, today announced that the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), a body including centers responsible for approximately 80% of all US allogeneic BMTs, has entered into an agreement to develop a pivotal trial of Mesoblast's lead product candidate Ryoncil® (remestemcel-L) in the treatment of adults with steroid-refractory acute graft versus host disease (SR-aGvHD). The BMT CTN is funded by the United States National Institutes of Health (NIH).

Dr John Levine, Chair-Elect of the BMT CTN Steering Committee and Professor of Internal Medicine and Pediatrics, Icahn School of Medicine at Mount Sinai, New York said: "We are delighted to be partnering with Mesoblast in this pivotal Phase 3 trial of RYONCIL, a potentially life-saving treatment for adolescents and adults with the most severe form of aGVHD. The clinical data from children treated with RYONCIL which support this trial are very compelling."

In its September 2023 draft guidance to industry for development of agents to treat aGVHD,[1] the US Food and Drug Administration (FDA) stated that a marketing application might be supported by positive results from a single-arm trial in a population with refractory aGVHD where there are no available therapies. The trial to be developed and executed by the BMT CTN intends to evaluate RYONCIL in patients 12 and older who are refractory to both corticosteroids and a second line agent such as ruxolitinib, for whom there are no approved therapies. Prior to implementation, the clinical trial protocol will be reviewed by two independent National Heart, Lung, and Blood Institute (NHLBI)-appointed committees. Mesoblast will then submit the final protocol to FDA, as agreed at the Type A meeting with FDA in September.

Mesoblast also intends to provide FDA with additional potency assay data for RYONCIL product manufactured using the current FDA-inspected process, linking product which was used in the pediatric Phase 3 trial, which met its primary endpoint, with product which will be used in the proposed registration Phase 3 trial in adults. Showing that the product used in the pediatric and adult trials is standardized, together with data showing that future product is well characterized for commercial release, could support approval for the pediatric indication given the absence of any approved therapies for children.

Mesoblast Chief Executive Silviu Itescu said: "We are pleased to be partnering with the premier hematopoietic stem cell transplant network across the United States with the aim of having a product available for adults suffering from aGVHD and who have no other approved therapies."

**About Mesoblast**

Mesoblast (the Company) 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

**About the Blood and Marrow Transplant Clinical Trials Network (BMT CTN)**
The BMT CTN conducts rigorous multi-institutional clinical trials of high scientific merit, focused on improving survival for patients undergoing hematopoietic cell transplantation and/or receiving cellular therapies. The BMT CTN has completed accrual to 52 Phase II and III trials at more than 100 transplant centers and enrolled over 16,600 study participants. BMT CTN is funded by the National Institutes of Health (NIH,), and is a collaborative effort of 20 Core Transplant Centers/Consortia, The Center for International Blood and Marrow Transplant Research (CIBMTR), the National Marrow Donor Program (NMDP) and the Emmes Company, LLC, a clinical research organization. CIBMTR is a research collaboration between the NMDP/Be The Match and the Medical College of Wisconsin (MCW). Together, MCW, NMDP and Emmes have been providing research support to the BMT CTN since 2001, as the Network's data and coordinating center. More information about the BMT CTN can be found at www.bmtctn.net

**About the National Marrow Donor Program® (NMDP)**
The NMDP is the leading global partner working to save lives through cellular therapy. With 35 years of experience managing the most diverse registry of potential unrelated blood stem cell donors and cord blood units in the world, NMDP is a proven partner in providing cures to patients with life-threatening blood and marrow cancers and diseases. Through their global network, they connect centers and patients to their best cell therapy option—from blood stem cell transplant to a next-generation therapy—and collaborate with cell and gene therapy companies to support therapy development and delivery through Be The Match BioTherapies®. NMDP is a tireless advocate for the cell therapy community, working with hematologists/oncologists to remove barriers to consultation and treatment, and supporting patients through no-cost programs to eliminate non-medical obstacles to cell therapy. In addition, they are a global leader in research through the CIBMTR® (Center for International Blood and Marrow Transplant Research®)—a collaboration with Medical College of Wisconsin, investing in and managing research studies that improve patient outcomes and advance the future of care.

**About the Medical College of Wisconsin (MCW)**
With a history dating back to 1893, the MCW is dedicated to leadership and excellence in education, patient care, research, and community engagement. More than 1,500 students are enrolled in MCW's medical school and graduate school programs in Milwaukee, Green Bay, and Central Wisconsin. MCW's School of Pharmacy opened in 2017. A major national research center, MCW is the largest research institution in the Milwaukee metro area and second largest in Wisconsin. In the last 10 years, faculty received more than $1.5 billion in external support for research, teaching, training, and related purposes. This total includes highly competitive research and training awards from the National Institutes of Health (NIH). Annually, MCW faculty direct or collaborate on more than 3,100 research studies, including clinical trials. Additionally, more than 1,650 physicians provide care in virtually every specialty of medicine for more than 2.8 million patients annually. It has a long history in hematopoietic transplantation and cellular therapy, including operating an outcomes registry of transplantation and cellular therapy outcomes and facilitating related research since 1972.

**About Emmes**
Founded more than 45 years ago, Emmes is a global, full-service Clinical Research Organization dedicated to excellence in supporting the advancement of public health and biopharmaceutical innovation. The company's clients include numerous agencies and institutes of the U.S. federal government and a wide range of biotechnology, pharmaceutical and medical device companies throughout the world. To learn more about how our research is making a positive impact on human health, go to the Emmes website at www.emmes.com.


**Mesoblast Limited**
ABN 68 109 431 870
www.mesoblast.com

**Corporate Headquarters**
Level 38
55 Collins Street
Melbourne 3000
Victoria Australia
T +61 3 9639 6036
F +61 3 9639 6030

**United States Operations**
505 Fifth Avenue
Third Floor
New York, NY 10017
USA
T +1 212 880 2060
F +1 212 880 2061

**Asia**
21 Biopolis Road
#01-22 Nucleos (South Tower)
SINGAPORE 138567
T +65 6570 0635
F +65 6570 0176

**References / Footnotes**

1. United States Food & Drug Administration. Graft-versus-Host Diseases: Developing Drugs, Biological Products, and Certain Devices for Prevention or Treatment Guidance for Industry. Draft Guidance. September 2023

**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 any future decision that the FDA may make on the BLA for remestemcel-L for pediatric patients with SR-aGVHD), 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.

*For more information, please contact:*

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

***Media***
BlueDot Media
Steve Dabkowski
T: +61 419 880 486
E: steve@bluedot.net.au

Exhibit 99.2

mesoblast

# Global Leader in Allogeneic Cellular Medicines for Inflammatory Diseases

## Corporate Presentation

November 2023

ASX: MSB; Nasdaq: MESO

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This presentation 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. All statements other than statements of historical facts contained in this presentation are forward-looking statements. Words such as, but not limited to, "believe," "expect," "anticipate," "estimate," "intend," "plan," "targets," "likely," "will," "would," "could," and similar expressions or phrases identify forward-looking statements. We have based these forward-looking statements largely on our current expectations and future events , recent changes in regulatory laws, and financial trends that we believe may affect our financial condition, results of operation, business strategy and financial needs. These statements may relate to, but are not limited to: expectations regarding the safety or efficacy of, or potential applications for, Mesoblast's adult stem cell technologies; expectations regarding the strength of Mesoblast's intellectual property, the timeline for Mesoblast's regulatory approval process, and the scalability and efficiency of manufacturing processes; expectations about Mesoblast's ability to grow its business and statements regarding its relationships with current and potential future business partners and future benefits of those relationships; statements concerning Mesoblast's share price or potential market capitalization; and statements concerning Mesoblast's capital requirements and ability to raise future capital, among others. 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. You should read this presentation together with our financial statements and the notes related thereto, as well as the 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, include, without limitation: risks inherent in the development and commercialization of potential products; uncertainty of clinical trial results or regulatory approvals or clearances; government regulation; the need for future capital; dependence upon collaborators; and protection of our intellectual property rights, among others. 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.

# Our Mission

*Mesoblast is committed to bringing to market innovative cellular medicines to treat serious and life-threatening illnesses*

## Investment Highlights

| | |
|---|---|
| Novel Allogeneic Cell Therapy Platform | Developing off-the-shelf, allogeneic cellular medicines based on proprietary mesenchymal stromal cell (MSC) technology platforms to enable treatment without the need for donor matching or immunosuppression |
| Remestemcel-L for *Pediatric* SR-aGVHD | Single-arm pivotal Phase 3 trial completed; primary endpoint successfully met<br>Long-term data shows durability of survival benefit >4 years<br>Additional potency assay data to be presented to FDA |
| Remestemcel-L for *Adult* SR-aGVHD | Market size for adult population approx. 5-fold larger than pediatric<br>The pivotal trial is expected to be conducted by BMT CTN, a body responsible for approximately 80% of all US transplants, at a fraction of the cost of a traditional CRO |
| Rexlemestrocel-L for CLBP | First randomized controlled Phase 3 trial completed, RMAT granted by FDA for discogenic pain<br>Agreement on 12-month pain reduction endpoint for FDA approval, confirmatory trial needed<br>Start-up activities for this trial significantly advanced with investigators, trial sites & CRO |
| Rexlemestrocel-L for HFrEF | RMAT granted by FDA for heart failure with reduced ejection fraction (HFrEF) and LVADs<br>Phase 2b/3 trial in HFrEF LVAD patients completed<br>First Phase 3 trial for HFrEF Class II/III patients completed |

BLA = Biologics License Application
FDA = United States Food and Drug Administration
PDUFA = Prescription Drug User Fee Act
RMAT = Regenerative Medicine Advanced Therapy
LVAD = Left Ventricular Assist Device
CRO = Contract Research Organization

## Pathway to Approval for RYONCIL in Pediatric Patients with SR-aGVHD

- During the Biologics License Application (BLA) review we made substantial progress towards bringing this cutting-edge product to market with a completed FDA inspection of our manufacturing process.
- In August FDA provided a complete response requiring Mesoblast to provide additional potency assay data confirming that product used in the Phase 3 trial is similar to product intended for commercial release, as measured by a standardized potency assay.
- At the Type A meeting in September, Mesoblast presented clinical data indicating that treatment with the improved RYONCIL product version of remestemcel-L, manufactured using the current process inspected by FDA, resulted in consistently high survival rates in children with SR-aGVHD.
- Similarly high survival rates were seen whether using product made for the Phase 3 clinical trial MSB-GVHD001 between 2015-2018 or made with the validated manufacturing process proposed for commercial release and used under Emergency Investigational New Drug (EIND) protocol through 2023.
- Mesoblast believes that the totality of these clinical studies, together with additional potency assay data currently being generated using the IL-2R alpha inhibition potency assay in place during the pediatric Phase 3 trial, will both support approval for the pediatric indication and provide a link between the RYONCIL product that was used in the pediatric Phase 3 trial and available commercial inventory.

## Pathway to Approval for RYONCIL in Adult Patients with SR-aGVHD

- Survival in adults with SR-aGVHD who have failed at least one additional agent, such as ruxolitinib, remains as low as 20-30% by 100 days, a patient population with no approved therapies.[1,2]
- In contrast, 100-day survival was 63% after remestemcel-L treatment was used under expanded access in 71 patients aged 12 and older with SR-aGVHD who failed to respond to at least one additional agent, such as ruxolitinib.
- In its September 2023 draft guidance to industry for development of agents to treat aGVHD, the FDA stated that a marketing application in a population with refractory aGVHD where there are no approved therapies might be supported by positive results from a single-arm trial.[3]
- Mesoblast intends to commence a Phase 3 trial of RYONCIL in adults and adolescents, a market approx. 5-fold larger than pediatric, who are refractory to both corticosteroids and a second line agent such as ruxolitinib, for whom there are no approved therapies.
- The trial is expected to be conducted by the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), a body responsible for approximately 80% of all US transplants, at a fraction of the cost of a traditional contract research organization (CRO).


1. Jagasia M et al. Ruxolitinib for the treatment of steroid-refractory acute GVHD (REACH1): a multicenter, open-label phase 2 trial. Blood. 2020 May 14; 135(20): 1739–1749.
2. Abedin S, et al. Ruxolitinib resistance or intolerance in steroid-refractory acute graft versus-host disease — a real-world outcomes analysis. British Journal of Haematology, 2021;195:429–43.
3. US FDA. Graft-versus-Host Diseases: Developing Drugs, Biological Products, and Certain Devices for Prevention or Treatment Guidance for Industry. Draft Guidance. Sep 2023

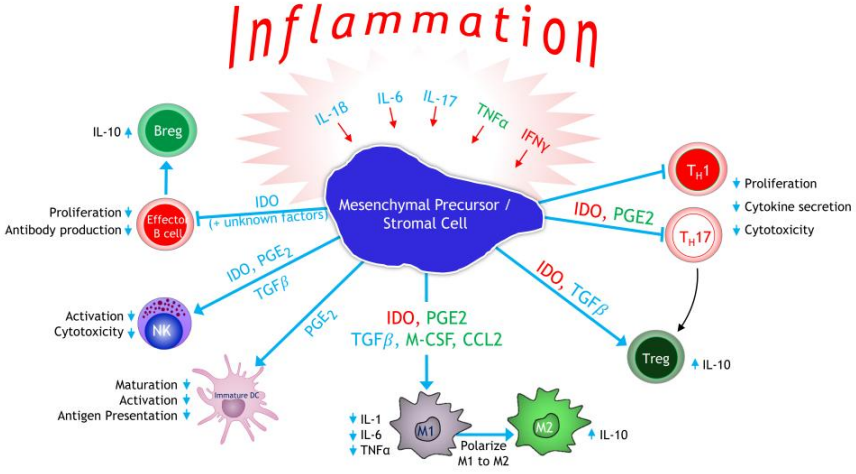
## Financials

- Revenue from royalties, predominantly on sales of TEMCELL® HS Inj.[1] sold in Japan by our licensee, were US$7.5 million for the year ended June 30, 2023.[2]
- Cash balance at September 30, 2023 was US$53.2 million, with net operating cash spend of US$14.2 million for the quarter.
- Management and the Board have put in place a plan that focuses on preservation of cash by implementing significant cost containment strategies and enacting substantial payroll reductions.
- Net operating cash usage over the past two years reduced by 37% to US$63.3 million in FY2023. We have implemented a cost containment plan to achieve a further targeted 23% reduction (US$15 million) in projected FY2024 annual net operating cash spend compared with FY2023, which will be partially offset by investment in our Phase 3 programs for adults with steroid-refractory acute graft versus host disease (SR-aGVHD) and chronic low back pain (CLBP).

1. TEMCELL® HS Inj. is a registered trademark of JCR Pharmaceuticals Co. Ltd.
2. TEMCELL sales by our Licensee are recorded in Japanese Yen before being translated into USD for the purposes of calculating the royalty paid to Mesoblast. Results have been adjusted for the movement of the USD to Japanese Yen exchange rate from 1USD:122.14 Yen for the year ended June 30, 2022 to 1USD:139.76 Yen for the year ended June 30, 2023.

## Platform Technology - Mechanism of Action

**Our mesenchymal precursor/stromal cells respond to and are activated by multiple inflammatory cytokines through surface receptors, resulting in orchestration of an anti-inflammatory cascade**

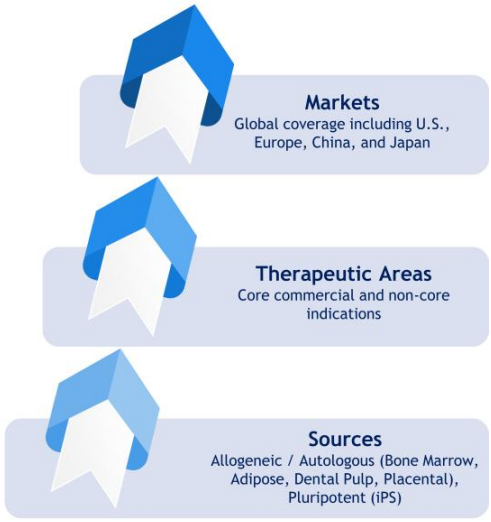





Source: data on file

# Global Intellectual Property (IP) Estate
## Provides Substantial Competitive Advantage

- Extensive patent portfolio with protection extending through 2040
- Over 1,100 patents and patent applications (82 patent families) across all major jurisdictions
- Covers composition of matter, manufacturing, and therapeutic applications of mesenchymal lineage cells
- Provides strong global protection in areas of our core commercial focus against cell-based competitor products
- Outside our core areas, may grant rights to third parties requiring access to our patent portfolio to commercialize their products
- Track record of managing intellectual property
  - Royalty agreement and income received from JCR Pharmaceuticals in Japan for treatment of aGVHD
  - Patent license granted to 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 Crohn's disease



# Commercial-scale Manufacturing Process and Facilities

- Scalable allogeneic “off-the-shelf” cellular platforms
- Manufacturing meets stringent criteria of international regulatory agencies
- Robust quality assurance processes ensure final product with batch-to-batch consistency and reproducibility
- Manufacturing innovations to meet increasing capacity requirements, improve yields and reduce cost of goods
  - Proprietary xeno-free technologies
  - Scaled-up 2D manufacturing
  - 3D bioreactors for high volume indications

**Manufacturing Remestemcel-L**

© Lonza, reproduced with permission

# Late-Stage Clinical Pipeline

## Based on the Proprietary Allogeneic Mesenchymal Stromal Cell Platform


SR-aGVHD = Steroid-Refractory Acute Graft Versus Host Disease; CLBP = Chronic Low Back Pain; HFrEF = Heart Failure with Reduced Ejection Fraction

*This chart is figurative and does not purport to show individual trial progress within a clinical program*

Notes:

- JCR Pharmaceuticals Co., Ltd. (JCR), has the right to develop mesenchymal stromal cells (MSCs) in certain fields for the Japanese market, including for the treatment of hematological malignancies, such as Graft vs Host Disease, and for hypoxic ischemic encephalopathy (HIE).
- Grünenthal has an exclusive license to develop and commercialize rexlemestrocel-L for chronic low back pain in Europe and Latin America/Caribbean.
- Tasly Pharmaceuticals has exclusive rights for rexlemestrocel-L for the treatment or prevention of chronic heart failure in China.



mesoblast

# Rexlemestrocel-L

Chronic Low Back Pain due to Degenerative Disc Disease (CLBP)

mesoblast

# Chronic Low Back Pain Due to Degenerative Disc Disease (CLBP) Impacts 7M+

## Rexlemestrocel-L represents a potential new paradigm for the treatment of CLBP

### Burden of Illness

- Back pain causes more disability than any other condition[1]
- Inflicts substantial direct and indirect costs on the healthcare system,[1] including excessive use of opioids in this patient population

### Treatment Options

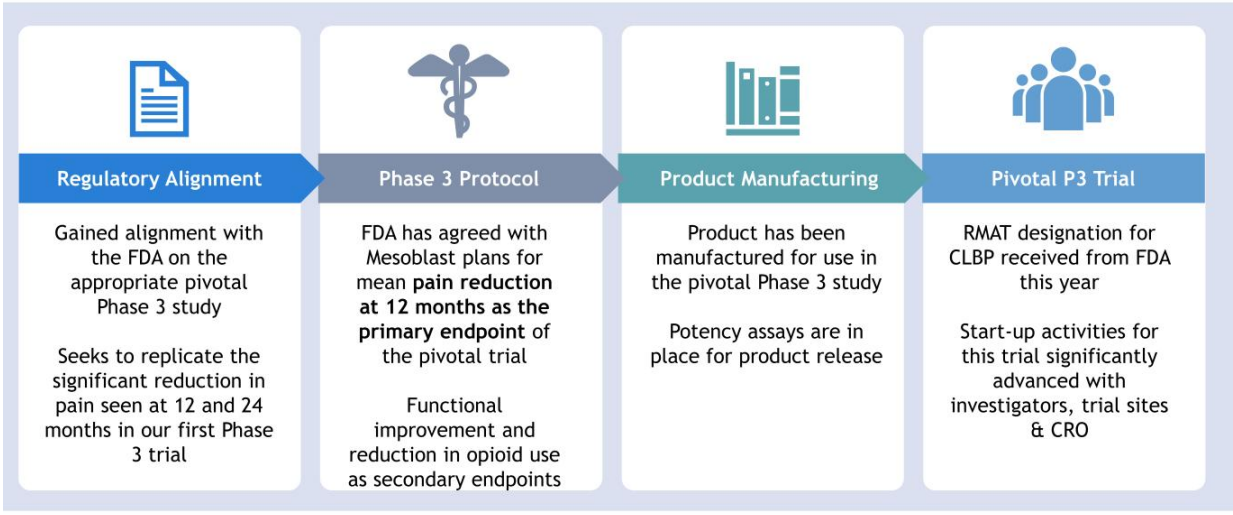
- Minimal treatment options for patients with chronic low back pain (CLBP) who fail conservative therapy include opioids and surgery
- 50% of opioid prescriptions are for CLBP[2]
- Durable improvement in pain has potential to reduce opioid use and prevent surgical intervention

### Market Opportunity

- Over 7m patients are estimated to suffer from CLBP due to degenerative disc disease (DDD) in each of the U.S. and E.U.5 [2-4]

1. Williams, J., NG, Nawi, Pelzter, K. (2015) Risk factors and disability associated with low back pain in older adults in low-and middle-income countries. Results from the WHO Study on global ageing and adult health (SAGE). PloS One. 2015; 10(6): e0127880., 2.Decision Resources: Chronic Pain December 2015., 3. LEK & NCI opinion leader interviews, and secondary analysis., 4. Navigant: Commercial Assessment for a Proprietary Cell-Based Therapy for DDD in the U.S. and the EU3 - August 2014.

## Rexlemestrocel-L / CLBP - Program Summary



## Regenerative Medicine Advanced Therapy (RMAT) Designation Granted by FDA for Rexlemestrocel-L in the treatment of CLBP

- RMAT designation provides all the benefits of Breakthrough and Fast Track designations, including rolling review and eligibility for priority review on filing of a Biologics License Application (BLA)

Results from the trial showed that:

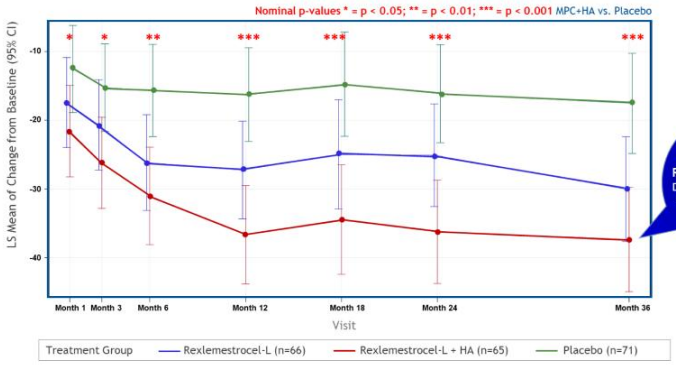
- A single injection of rexlemestrocel-L+HA into the lumbar disc resulted in significant reduction in pain compared with saline control at 12 and 24 months across all subjects (n=404)
- Pain reduction through 36 months was seen in the subset of patients using opioids at baseline (n=168) with the rexlemestrocel-L+HA group having substantially greater reduction at all time points compared with saline controls
- Among patients on opioids at baseline, despite instructions to maintain existing therapies throughout the trial, at 36 months 28% who received rexlemestrocel-L+HA were not taking an opioid compared with 8% of saline treated controls

# Phase 3 Trial Outcomes based on a Single Injection of Rexlemestrocel-L + HA

## Results in More than Three Years of Pain Reduction

Greatest pain reduction was observed in the pre-specified population of subjects with CLBP duration shorter than the baseline study median of 68 months (n=202) with significantly greater reduction (nominal p-value < 0.05) at all time points analyzed over 36 months compared with saline controls

**LS Mean VAS Change in Low Back Pain from Baseline - Duration CLBP < 68 Month Median Baseline Duration (n=202)**




**Duration < Median**

**Rexlemestrocel-L +HA** Demonstrated significant reductions in pain over 36-months

VAS=Visual Analog Score; HA=Hyaluronic Acid



mesoblast

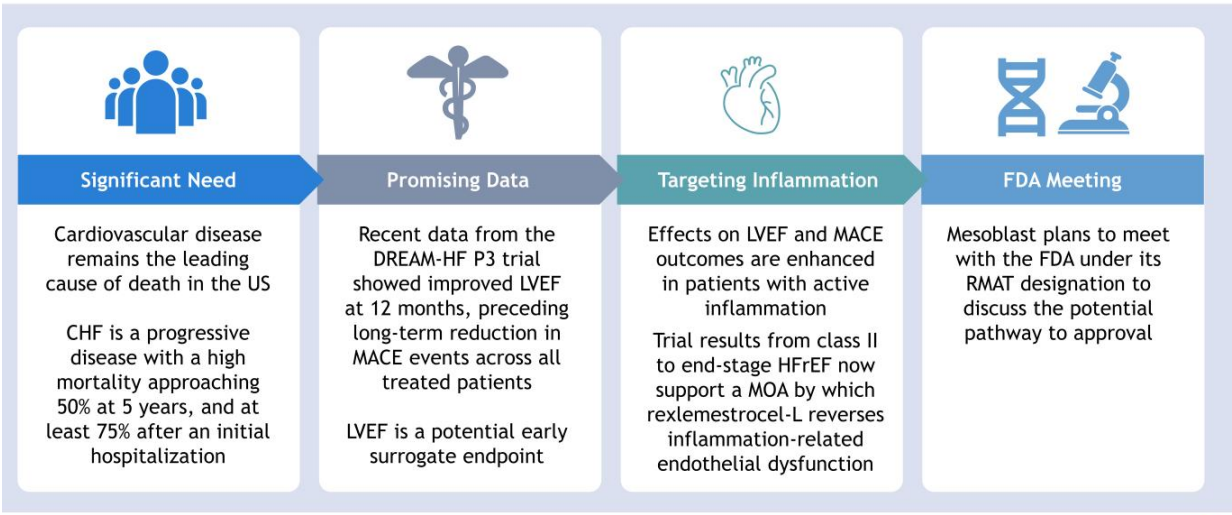
# Rexlemestrocel-L

Chronic Heart Failure Reduced Ejection Fraction (HFrEF)

mesoblast

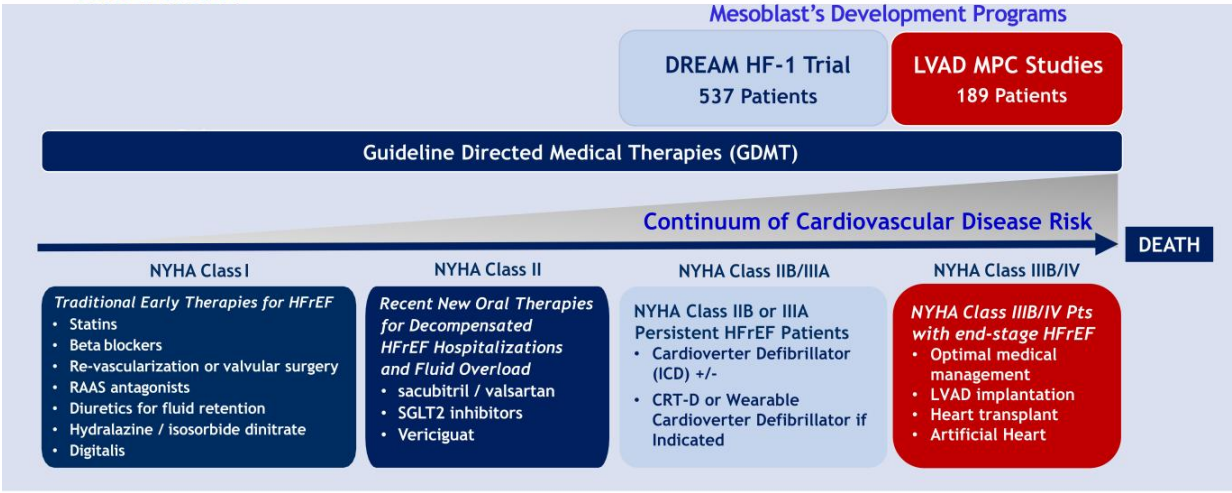
# Rexlemestrocel-L / HFrEF - Program Summary

## Defining the Regulatory Path to FDA Approval



# Patients Experience Progressive Vascular Dysfunction and Heart Failure

## Rexlemestrocel-L has the potential to improve endothelial dysfunction in patients from Class II thru IV



ORIGINAL INVESTIGATIONS

# Randomized Trial of Targeted Transendocardial Mesenchymal Precursor Cell Therapy in Patients With Heart Failure

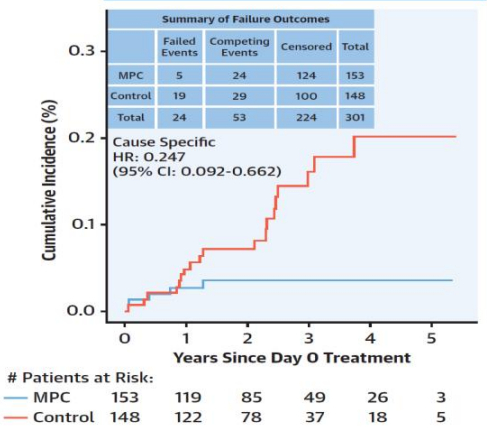
JACC JOURNALS

Emerson C. Perin, MD, PhD,[a] Kenneth M. Borow, MD,[b] Timothy D. Henry, MD,[c] Farrell O. Mendelsohn, MD,[d] Leslie W. Miller, MD,[e] Elizabeth Swiggum, MD,[f] Eric D. Adler, MD,[g] David H. Chang, MD,[h] R. David Fish, MD,[a] Alain Bouchard, MD,[a] Margaret Jenkins, BSc (Hons),[a] Alex Yaroshinsky, PhD,[a] Jack Hayes, MA,[a] Olga Rutman, PhD,[a] Christopher W. James, PA,[a] Eric Rose, MD,[a] Silviu Itescu, MD,[a] Barry Greenberg, MD[a]

Randomized, double-blind, controlled, 537 patient Phase 3 trial of rexlemestrocel-L over mean follow-up of 30 months showed:

- Improved LVEF from baseline to 12 months in all patients - maximal benefit seen in patients with active inflammation
- Reduced risk of MI or stroke by 57% in all treated patients, and by 75% in patients with inflammation
- Reduced risk for time-to-first Major Adverse Cardiac Event (MACE), defined as cardiovascular death, MI or stroke, by 28% in all patients, and by 37% in patients with inflammation

**FIGURE 4** Risk of Myocardial Infarction or Stroke






mesoblast

# Rexlemestrocel-L – Two Pivotal Studies in Chronic Heart Failure (CHF)

## Mesoblast's Development Programs Assess the Impact of Intra-cardiac Administration of Rexlemestrocel-L Across the Continuum of Disease from Mild/Moderate to End-stage Severity

| MPC Study Design | LVAD-MPC Study #2 | DREAM-HF Trial |
|---|---|---|
| **Treated Patients** | **159** | **537** |
| Study Design | Prospective, randomized, Multi-center, double-blinded, single dose, sham-controlled, parallel group efficacy & safety studies of allogeneic mesenchymal precursor cells (MPCs) | |
| Pathologies of ↑ed Importance | LV Systolic Function, Inflammation, Mortality, Major Morbidities | |
| Product | Mesenchymal Precursor Cells with defined Cardiac Potency (Rexlemestrocel-L) | |
| Cell Preparation, Manufacturing, Central Storage and Shipping | Same facilities and vendors in both studies | |
| Physical Location Used for Cell Administration at the Study Site | Operating room | Cardiac catheterization laboratory |
| Patient Analysis Population | End-stage chronic HFrEF candidate for LVAD implant (NYHA Class IIIB or IV), ischemic or non-ischemic etiology (N=159: MPC=106, CTRL=53) | Chronic HFrEF (Late NYHA Class II or IIIA), ischemic or non-ischemic etiology (N=537: MPC=265, CTRL=272) |
| Cell Dose in MPC | 150 million cells administered as 15-20 individual injections during a single procedure | |
| Route of Cell Administration | Epicardial injection | Transendocardial injection |
| Target of Cell Administration | Mid-wall of left ventricle | |

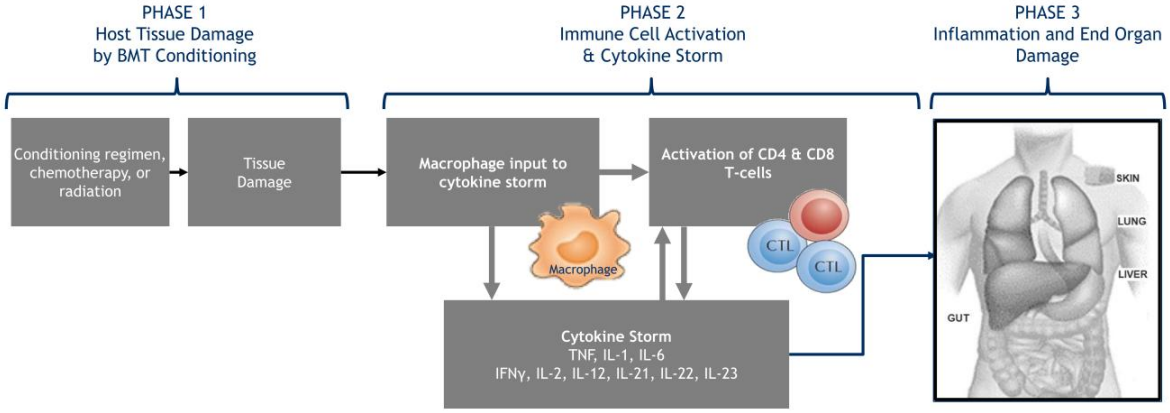
# Remestemcel-L

Steroid-Refractory Acute Graft Versus Host Disease (SR-aGVHD)

mesoblast

# Acute Graft Versus Host Disease (aGVHD)

## Serious and Fatal Complication of Allogeneic Bone Marrow Transplantation (BMT)






Modified from Blazar et al., Nature Reviews Immunology 12: 443 - 458

mesoblast

# Remestemcel-L: Steroid-Refractory Acute Graft Versus Host Disease (SR-aGVHD)

## SR-aGVHD is associated with mortality rates as high as 90%

### Treatment Options

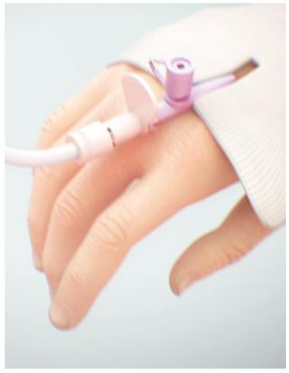
- Corticosteroids are first-line therapy for aGVHD
- There is only one approved treatment for disease refractory to steroids and no approved treatment in the US for children under 12 years old
- In Japan, Mesoblast's licensee received the first product approval for SR-aGVHD in both children and adults

### Burden of Illness

- Acute GVHD is a life-threatening complication that occurs in ~50% of patients receiving allogeneic bone marrow transplants (BMTs)[1]
- Acute GVHD primarily affects skin, GI tract, and liver
- Steroid-refractory aGVHD is associated with mortality rates as high as 90%[1,4] and significant extended hospital stay costs[2]

### Market Opportunity

- More than 30,000 allogeneic BMTs performed globally (>20K US/EU) annually, ~20% pediatric[2,3]
- Approx. 9,000 -10,000 allogeneic BMTs performed in the US annually
- Approx. 1,500 allogenic BMTs are in children and adolescents in US[3]



1. Westin, J., Saliba, RM., Lima, M. (2011) Steroid-refractory acute GVHD: predictors and outcomes. Advances in Hematology. 2. Niederwieser D, Baldomero H, Szer J. (2016) 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. 3. HRSA Transplant Activity Report, CIBMTR, 2020 4. 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.



mesoblast

# Remestemcel-L for Children with SR-aGVHD

## Improved Early Survival Across Three Studies involving more than 300 Treated Children

| Day 100 Survival | | | |
|---|---|---|---|
| **Remestemcel-L Protocol** | **Remestemcel-L** | **Matched Controls** | **Matched Control Protocol** |
| **First Line Therapy after Steroids Treatment Setting** | | | |
| **Pediatric Subset of Protocol 280:** randomized controlled P3, n=27 w/SR-aGVHD | 79% | 54% | Study Control Arm (n=13) |
| **Study 001**, open-label P3, n=54[1] with 89% Grade C/D disease | 74% | 57% | **MAGIC[2] cohort**, n=30[3] propensity-controlled subset |
| **Salvage Therapy Treatment Setting** | | | |
| **Expanded Access Protocol (EAP275)**, n=241 | 66% | na | |
| **EAP275**, n=51 Grade D subset | 51% | 31% | **CIBMTR dbase**, n=327[4] propensity controlled subset |

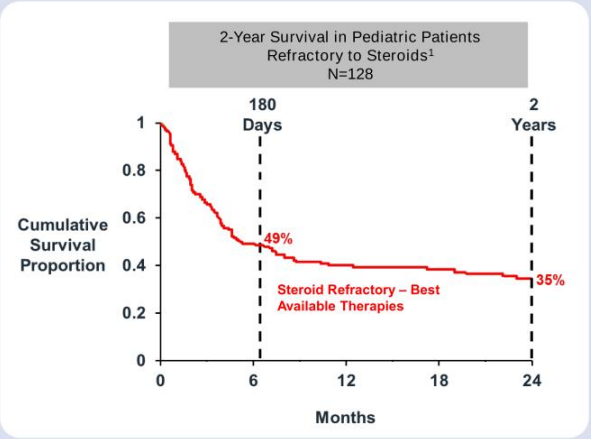
1. GVHD001 had 55 randomized patients, however one patient dropped out before receiving any dose of remestemcel-L; 2. Mount Sinai Acute GVHD International Consortium (MAGIC) - a group of ten BMT centers throughout the US and Europe whose purpose is to conduct ground-breaking clinical trials in GVHD, including developing informative biorepositories that assist in developing treatments that can guide GVHD therapy; 3. Two subjects in the MAGIC cohort had follow-up <100 days; these subjects are excluded from the respective survival analyses; 4. Data on file

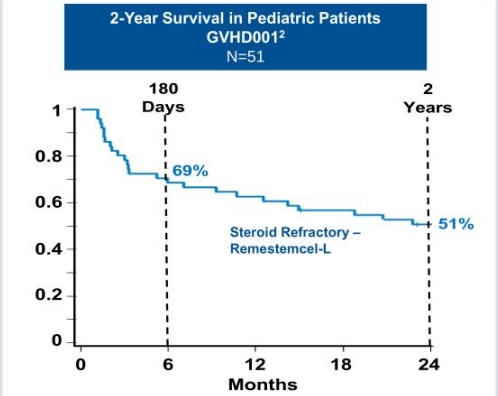


mesoblast

# Long term Survival in Pediatric Patients with SR-aGVHD Treated with Remestemcel-L

## Presented at the 2023 Tandem Meeting of ASTCT and CIBMTR




1.Adapted and redrawn from Figure 2 of MacMillan, M.L. et al. Pediatric acute GVHD: clinical phenotype and response to upfront steroids. Bone Marrow Transplant 55, 165–171 (2020);
2.CIBMTR – Center for International Blood & Bone Marrow Transplantation Research. Clinical Outcomes of Pediatric Patients Treated with Remestemcel-L for Steroid-Refractory Acute Graft Versus-Host Disease on a Phase 3, Single- Arm, Prospective Study (Nov 2022)
ASTCT = American Society for Transplantation and Cellular Therapy; CIBMTR = Center for International Blood and Marrow Transplant Research



mesoblast

# Extended Survival Data in Children with SR-aGVHD

## Remestemcel-L Treatment Resulted in Durable Survival Over 4 Years

**Survival Outcomes in Pediatric & Adult SR-aGVHD**

(Remestemcel-L data from the Center for International Blood and Marrow Transplant Research (CIBMTR) dbase)

| Study | GVHD001 | MacMillan et al[1] | Rashidi et al[2] | REACH2[3] | REACH2[3] | REACH1[4] |
|---|---|---|---|---|---|---|
| Treatment | Remestemcel-L | BAT[5] | BAT[5] | BAT[5] | Ruxolitinib | Ruxolitinib |
| N= | 51 | 128 | 203 | 155 | 154 | 71 |
| Subjects | Children | Children | Adults | Adults | Adults | Adults |
| aGVHD Grade | 88% Grade C/D | 22% Grade 3/4 | 54% Grade 3/4 | 63% Grade 3/4 | 63% Grade 3/4 | 68% Grade 3/4 |
| Year 1 Survival | 63% | 40% | -- | 44% | 49% | 43% |
| Year 2 Survival | 51% | 35% | 25% | 36% | 38% | -- |
| Year 3 Survival | 49% | | | | | |
| Year 4 Survival | 49% | | | | | |

1. MacMillan ML et al. Pediatric acute GVHD: clinical phenotype and response to upfront steroids. Bone Marrow Transplant 2020; 55(1): 165-171
2. Rashidi A et al. Outcomes and predictors of response in steroid-refractory acute graft-versus-host disease: single-center results from a cohort of 203 patients. Biol Blood Bone Marrow Transplant 2019; 25(11):2297-2302.
3. Zeiser R et al. Ruxolitinib for Glucocorticoid-Refractory Acute Graft-versus-Host Disease. N Engl J Med 2020;382:1800-10.
4. Jagasia M et al. Ruxolitinib for the treatment of steroid-refractory acute GVHD (REACH1): a multicenter, open-label phase 2 trial. Blood. 2020 May 14; 135(20): 1739–1749
5. BAT = Best Available Treatment



mesoblast

## Pathway to Approval for RYONCIL in Pediatric Patients with SR-aGVHD

- During the Biologics License Application (BLA) review we made substantial progress towards bringing this cutting-edge product to market with a completed FDA inspection of our manufacturing process.
- In August FDA provided a complete response requiring Mesoblast to provide additional potency assay data confirming that product used in the Phase 3 trial is similar to product intended for commercial release, as measured by a standardized potency assay.
- At the Type A meeting in September, Mesoblast presented clinical data indicating that treatment with the improved RYONCIL product version of remestemcel-L, manufactured using the current process inspected by FDA, resulted in consistently high survival rates in children with SR-aGVHD.
- Similarly high survival rates were seen whether using product made for the Phase 3 clinical trial MSB-GVHD001 between 2015-2018 or made with the validated manufacturing process proposed for commercial release and used under Emergency Investigational New Drug (EIND) protocol through 2023.
- Mesoblast believes that the totality of these clinical studies, together with additional potency assay data currently being generated using the IL-2R alpha inhibition potency assay in place during the pediatric Phase 3 trial, will both support approval for the pediatric indication and provide a link between the RYONCIL product that was used in the pediatric Phase 3 trial and available commercial inventory.

## RYONCIL for Adults with SR-aGVHD

- Commercial strategy is to progress to adults who have failed steroids and a first-line agent, including ruxolitinib
- Market opportunity approximately five times larger than pediatric
- Approximately 45% of ruxolitinib patients are non-responders [1]
- Survival in adults with SR-aGVHD who have failed at least one additional agent, such as ruxolitinib, is 20-30% by 100 days [1,2]
- In contrast, 100-day survival was 63% after remestemcel-L treatment was used under compassionate care in 71 patients aged 12 and older with SR-aGVHD who failed to respond to at least one additional agent, such as ruxolitinib
- In its September 2023 draft guidance to industry for development of agents to treat aGVHD, the FDA stated that a marketing application in a population with refractory aGVHD where there are no approved therapies might be supported by positive results from a single-arm trial.[3]
- The Blood and Marrow Transplant Clinical Trials Network (BMT CTN), a body responsible for approximately 80% of all US transplants, is expected to conduct the pivotal trial of RYONCIL in this adult population at a fraction of the cost of a traditional contract research organization (CRO)


1. Jagasia M et al. Ruxolitinib for the treatment of steroid-refractory acute GVHD (REACH1): a multicenter, open-label phase 2 trial. Blood. 2020 May 14; 135(20): 1739–1749
2. Abedin S, et al. Ruxolitinib resistance or intolerance in steroid-refractory acute graft versus-host disease — a real-world outcomes analysis. British Journal of Haematology, 2021;195:429–43
3. US FDA. Graft-versus-Host Diseases: Developing Drugs, Biological Products, and Certain Devices for Prevention or Treatment Guidance for Industry. Draft Guidance. Sep 2023

mesoblast

# Thank You



mesoblast