



# Global Leader in Allogeneic Cellular Medicines for Inflammatory Diseases

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Financial Results and Operational Update for  
the Half-Year Ended December 31, 2023

February 2024

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

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*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. Long-term data shows durability of survival benefit >4 years. New data from second potency assay provided to FDA, meeting scheduled Q1 CY2024.

## Remestemcel-L for *Adult* SR-aGVHD

Market size for adult population approx. 5-fold larger than pediatric. Mesoblast is collaborating with BMT CTN, a body responsible for approximately 80% of all US transplants, to conduct a pivotal trial in adults with SR-aGVHD.

## Rexlemestrocel-L for Heart Disease

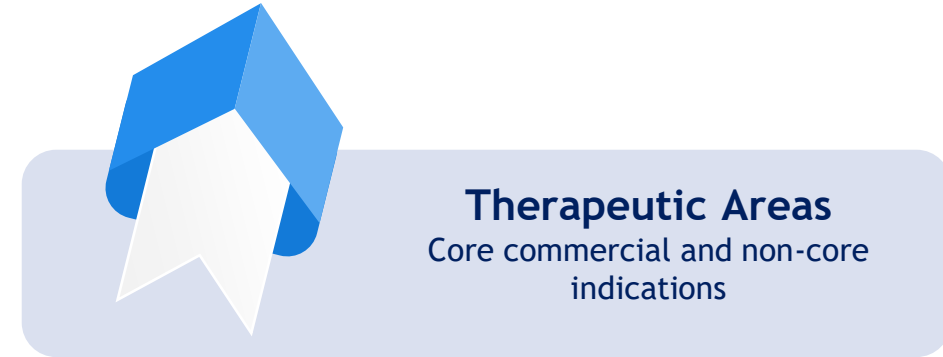
First Phase 3 completed for heart failure with reduced ejection fraction (HFrEF) Class II/III patients. FDA RMAT for end-stage HFrEF patients with an LVAD. Randomized controlled trial in pediatric congenital heart disease published. RPDD & ODD granted by FDA.

## Rexlemestrocel-L for CLBP

First randomized controlled Phase 3 trial completed, RMAT granted by FDA for discogenic pain. Agreement in place for confirmatory trial, 12-month pain reduction endpoint for FDA approval. Pivotal trial activities have commenced.

# 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

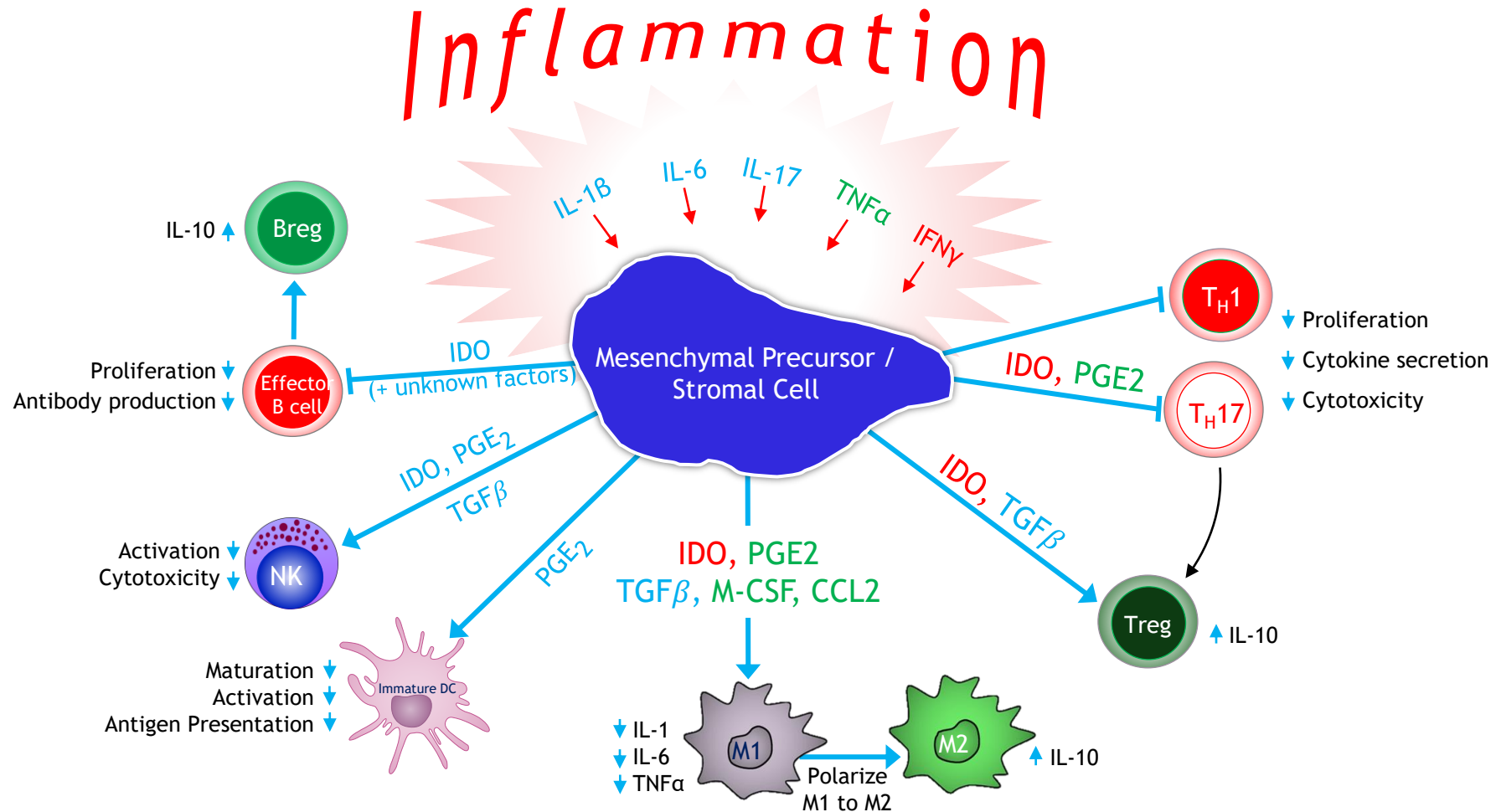
- ▣ Scalable allogeneic “off-the-shelf” cellular platforms
- ▣ Manufacturing meets stringent criteria of international regulatory agencies
- ▣ Robust quality assurance processes ensure final product with batch-to-batch consistency and reproducibility
- ▣ Manufacturing innovations to meet increasing capacity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



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# Platform Technology - Shared Mechanism of Action Across Our Products

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



# Late-Stage Clinical Pipeline

## Based on the Proprietary Allogeneic Mesenchymal Stromal Cell Platform

Product	Indication	Phase 2	Phase 3	Regulatory Filing	Approved	
Remestemcel-L	Pediatric SR-aGVHD					
Remestemcel-L	Adult SR-aGVHD Crohn's					
Rexlemestrocel-L	HFrEF					
Rexlemestrocel-L	CLBP					

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.
- Tasy Pharmaceuticals has exclusive rights for rexlemestrocel-L for the treatment or prevention of chronic heart failure in China.



# Clinical Program Milestones - 2024

**RYONCIL**  
Adult & Pediatric  
SR-aGVHD  
(remestemcel-L)

- Additional potency assay data provided to FDA
- FDA meeting regarding potency assay data for the pediatric BLA
- Completion and submission to FDA of protocol for adult SR-aGVHD Phase 3 trial in partnership with BMT CTN
- Commence patient enrollment for adult SR-aGVHD trial

Target Date

Status

Q1 CY2024

Achieved

Q1 CY2024

Scheduled

Q1 CY2024

Achieved

Q2 CY2024

Planned

**REVASCOR**  
Adult & Pediatric  
Heart Disease  
(rexlemestrocel-L)

- Meet with the FDA under RMAT to discuss the potential pathway to approval in adults with HFrEF based on LVAD and DREAM-HF trials
- Meet with FDA on congenital heart disease pathway to approval in pediatric patients based on results of randomized, controlled trial

Q1 CY2024

Achieved

Q2 CY2024

Planned

**Inflammatory  
Pain**  
(rexlemestrocel-L)

- CLBP Phase 3 trial start-up activities with investigators, trial sites & contract research organization (CRO)
- Phase 3 CLBP patient screening/enrollment initiates and completes

Q4 CY2023

Achieved

Q1-Q4  
CY2024

Ongoing

# Regulatory Status for RYONCIL in Pediatric Patients with SR-aGVHD

## FDA Meeting Scheduled for March

- Mesoblast has an upcoming meeting scheduled for March with the United States Food and Drug Administration (FDA).
- Mesoblast has provided the agency with new data from a second potency assay for its product Ryoncil® (remestemcel-L) that provides additional product characterization as requested by FDA.
- The new data show that the RYONCIL product made with the current manufacturing process that has undergone successful inspection by FDA, demonstrates greater potency than the earlier generation product, providing context to its greater impact on survival.

# 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.<sup>1,2</sup>
- In contrast, 100-day survival was 67% after RYONCIL treatment was used under expanded access in 51 adults and children with SR-aGVHD who failed to respond to at least one additional agent, such as ruxolitinib.
- 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.
- Mesoblast is collaborating with the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), a body responsible for approximately 80% of all US transplants, to conduct the trial.

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.

# REVASCOR in Adults with Chronic Heart Failure with Reduced Ejection Fraction (HFrEF), Including End-Stage Patients with a Left Ventricular Assist Device (LVAD)

## FDA Meeting Regarding Regulatory Path to Approval

- REVASCOR has shown the potential to reduce major adverse cardiac events (MACE) such as heart attack and cardiovascular death in high-risk patients with HFrEF and inflammation.
- REVASCOR has also shown the potential to improve major outcomes in high-risk patients with end-stage HFrEF, inflammation and LVADs.
- Mesoblast met with FDA this quarter to address potential pathways to approval for REVASCOR under our Regenerative Medicine Advanced Therapies (RMAT) designation. The discussion covered both Class II/III HFrEF ischemic patients with inflammation from the Phase 3 DREAM-HF 565 patient study and Class IV ischemic LVAD patients with inflammation from the 159 patient LVAD study.
- Mesoblast discussed with FDA the mechanism of action by which REVASCOR is able to improve major outcomes, including mortality, across the continuum of heart failure with inflammation.
- Minutes of the meeting are expected from FDA next month.

# Pediatric Congenital Heart Disease - Hypoplastic Left Heart Syndrome (HLHS)

## Awarded FDA Rare Pediatric Disease Designation (RPDD) and Orphan Drug Designation (ODD)

- During the quarter FDA granted Mesoblast's cardiovascular product, REVASCOR, both RPDD and ODD. This followed submission of results from the randomized controlled trial in children with hypoplastic left heart syndrome (HLHS), a potentially life-threatening congenital heart condition.
- Results from a blinded, randomized, placebo-controlled prospective trial of REVASCOR conducted in the US in children with HLHS were published in the December 2023 issue of the peer reviewed *The Journal of Thoracic and Cardiovascular Surgery Open (JTCVS Open)*.<sup>1</sup>
- As noted in the JTCVS publication the fact that 100% of REVASCOR-treated children compared with 57% of controls had large enough LVs to accommodate the full BiV conversion suggests that REVASCOR treatment may help increase the ability to 'better grow' the HLHS LV after LV recruitment surgery.
- Mesoblast plans to meet with FDA to discuss the regulatory path to approval for REVASCOR in children with this life-threatening condition.



# Financial Results

for the 6 months ended December 31, 2023

Manufacturing Remestemcel-L

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# Financial Highlights

## Cash Reserves

At December 31, 2023, cash-on-hand was US\$77.6 million (A\$113.5 million), after completing Institutional Placement and Entitlement Offer of A\$60.3 million. Strengthened Balance Sheet through delivering on cost containment strategies.

## Cash Burn

Reduction in net cash usage for operating activities:

- For the three months ended December 31, 2023, net cash usage was US\$12.3 million, a 25% reduction versus the comparative quarter in FY2023.
- For the six months ended December 31, 2023, net cash usage was US\$26.6 million, a 14% reduction versus the comparative period in FY2023.

## Reduction in Loss

Loss after tax reduced by 21% for the six months ended December 31, 2023, versus the comparative period to December 31, 2022.

# Reduction in Manufacturing, R&D and Management Administration; Improved Loss Before Tax

P&L for the six months ended (US\$m)	Dec 31, 2023	Dec 31, 2022
<b>Total Revenue</b>	3.4	3.4
Research and development	(12.6)	(13.4)
Manufacturing	(6.7)	(12.8)
Management & administration	(11.5)	(13.3)
Revaluation of contingent consideration	(0.3)	6.0
Revaluation of warrant liability	4.4	(0.7)
Other operating income & expenses	1.1	(0.0)
Finance costs	(10.3)	(10.7)
<b>Loss before tax</b>	<b>(32.6)</b>	<b>(41.5)</b>
Income tax benefit	0.1	0.1
<b>Loss after tax</b>	<b>(32.5)</b>	<b>(41.4)</b>

**Revenue:** Revenue predominately from royalties on sales of TEMCELL® HS Inj.<sup>1</sup> sold in Japan by our licensee.

**Reduction in Manufacturing Expenditure:** reduced by 47% for the six months ended December 31, 2023, from \$12.8 million to \$6.7 million. Costs in the current period include new potency and characterization data for the remestemcel-L product, as requested by FDA, which have been submitted ahead of our upcoming meeting with FDA next month.

**Finance Costs** include \$6.9 million of non-cash expenditure for the six months ended December 31, 2023 comprising accruing interest and borrowing costs.

Figures have been rounded.

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



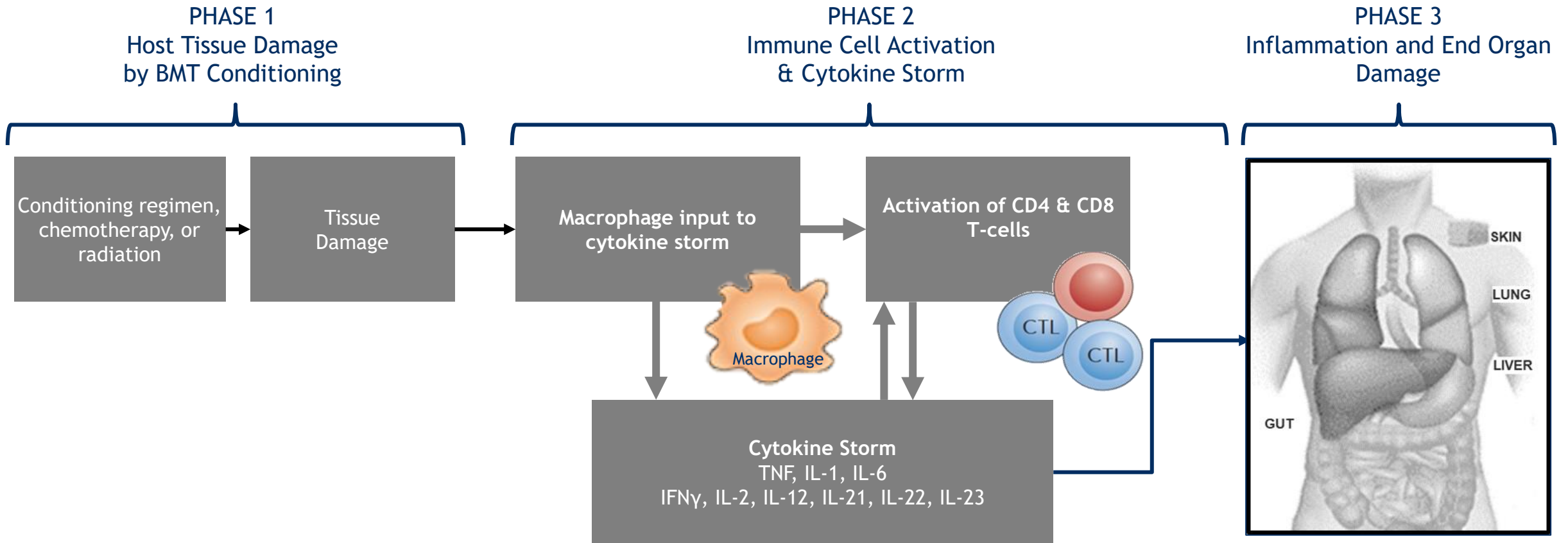


# Remestemcel-L

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

# Acute Graft Versus Host Disease (aGVHD)

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



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

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

### Treatment Options

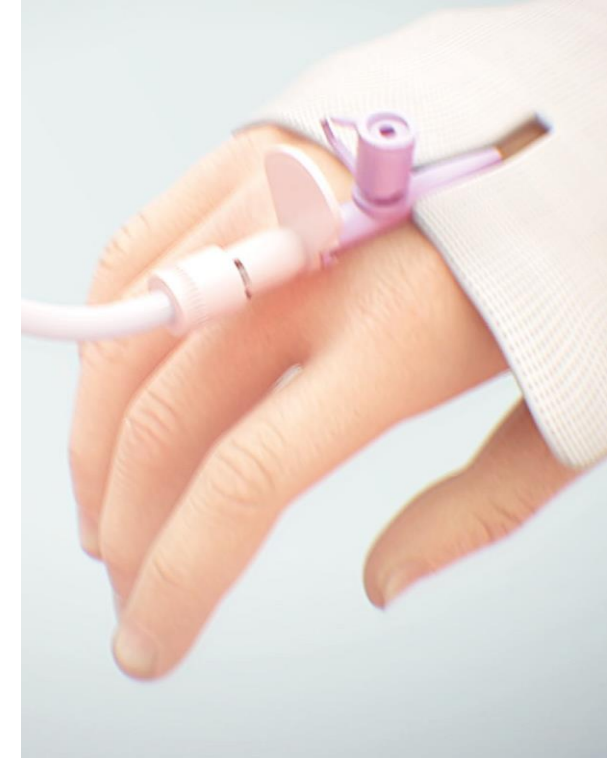
- Corticosteroids are first-line therapy for aGVHD
- There is only one approved treatment for disease refractory to steroids and no approved treatment in the US for children under 12 years old
- In Japan, Mesoblast's licensee received the first product approval for SR-aGVHD in both children and adults

### Burden of Illness

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

### Market Opportunity

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



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*.

# Remestemcel-L for Children with SR-aGVHD

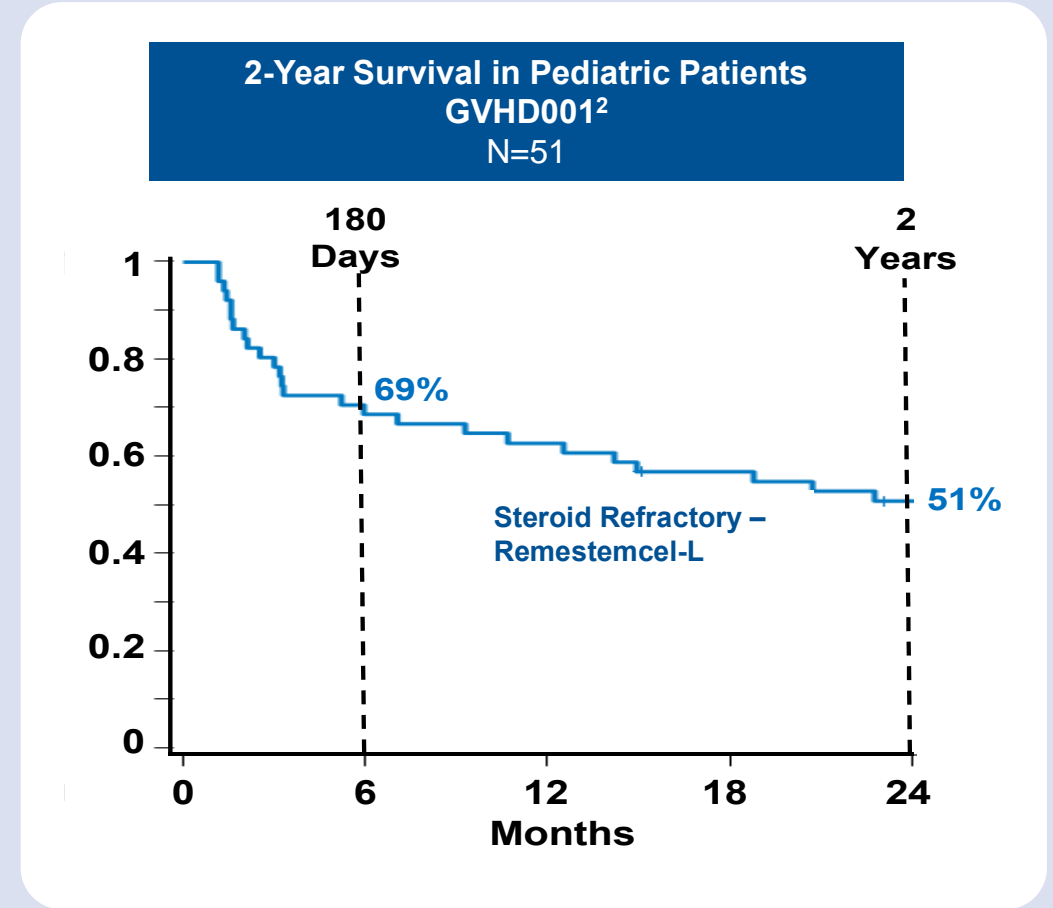
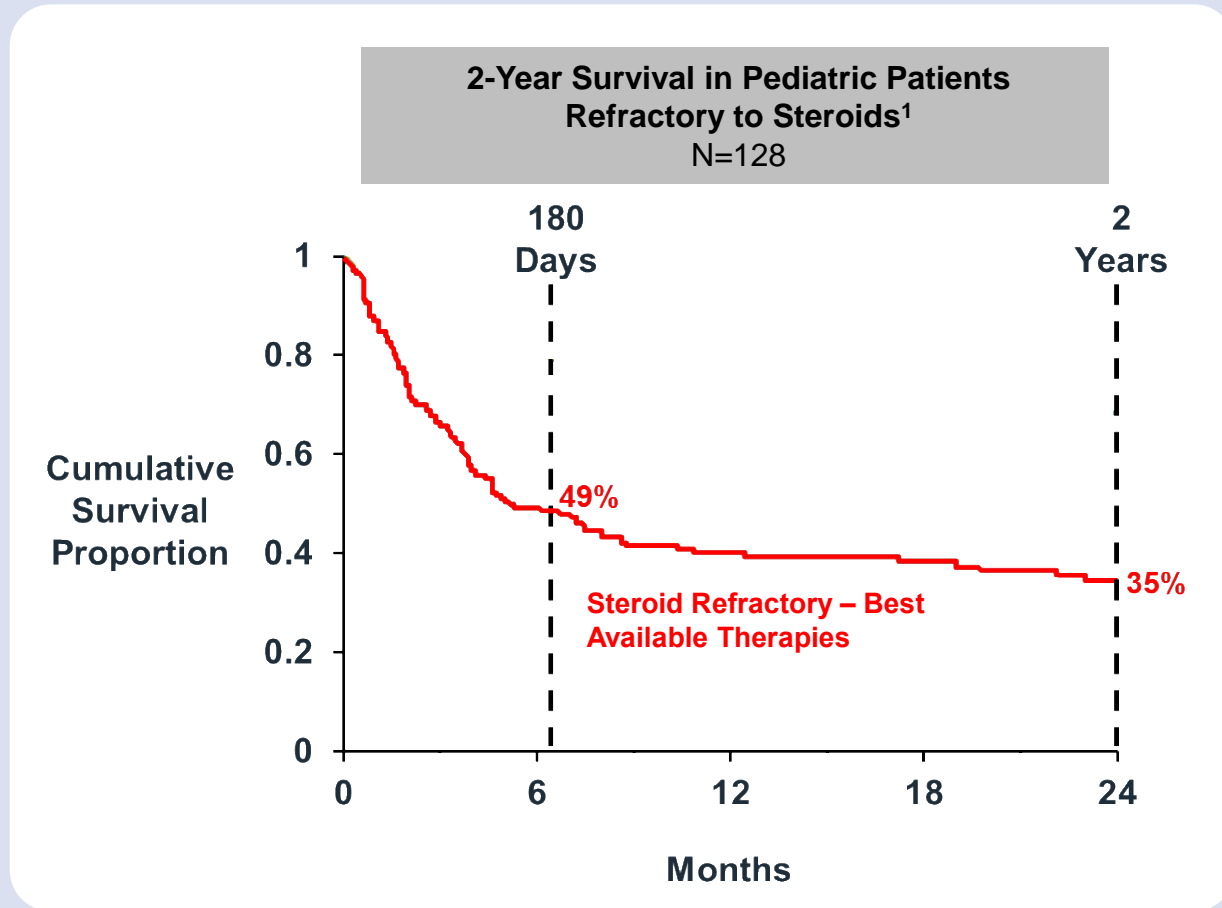
Improved Early Survival Across Three Studies involving more than 300 Treated Children

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

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

# 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

# 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 <sup>1</sup>	Rashidi et al <sup>2</sup>	REACH2 <sup>3</sup>	REACH2 <sup>3</sup>	REACH1 <sup>4</sup>
Treatment	Remestemcel-L	BAT <sup>5</sup>	BAT <sup>5</sup>	BAT <sup>5</sup>	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

# Regulatory Status for RYONCIL in Pediatric Patients with SR-aGVHD

## FDA Meeting Scheduled for March

- Mesoblast has an upcoming meeting scheduled for March with the United States Food and Drug Administration (FDA).
- Mesoblast has provided the agency with new data from a second potency assay for its product Ryoncil® (remestemcel-L) that provides additional product characterization as requested by FDA.
- The new data show that the RYONCIL product made with the current manufacturing process that has undergone successful inspection by FDA, demonstrates greater potency than the earlier generation product, providing context to its greater impact on survival.

# 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.<sup>1</sup>
- Survival in adults with SR-aGVHD who have failed at least one additional agent, such as ruxolitinib, is 20-30% by 100 days.<sup>1,2</sup>
- In contrast, 100-day survival was 67% after remestemcel-L treatment was used under expanded access in 51 children and adults with SR-aGVHD who failed to respond to at least one additional agent, such as ruxolitinib.
- Mesoblast is collaborating with the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), a body responsible for approximately 80% of all US transplants, to conduct a pivotal trial in this patient population.

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.





# Rexlemestrocel-L

Chronic Heart Failure Reduced Ejection Fraction (HFrEF)

# Rexlemestrocel-L / HFrEF - Program Summary

## Defining the Regulatory Path to FDA Approval



### Significant Need

Cardiovascular disease remains the leading cause of death in the US

CHF is a progressive disease with a high mortality approaching 50% at 5 years, and at least 75% after an initial hospitalization



### Promising Data

Recent data from the DREAM-HF P3 trial showed improved LVEF at 12 months, preceding long-term reduction in MACE events across all treated patients

LVEF is a potential early surrogate endpoint



### Targeting Inflammation

Effects on LVEF and MACE outcomes are enhanced in patients with active inflammation

Trial results from class II to end-stage HFrEF now support a MOA by which rexlemestrocel-L reverses inflammation-related endothelial dysfunction



### FDA Meeting

Mesoblast met with the FDA under its RMAT designation to discuss the potential pathway to approval

FDA formal minutes due in March

# Patients Experience Progressive Vascular Dysfunction and Heart Failure

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

## Mesoblast's Development Programs

DREAM HF-1 Trial  
537 Patients

LVAD MPC Studies  
189 Patients

## Guideline Directed Medical Therapies (GDMT)

## Continuum of Cardiovascular Disease Risk

DEATH

### NYHA Class I

- Traditional Early Therapies for HFrEF*
- Statins
  - Beta blockers
  - Re-vascularization or valvular surgery
  - RAAS antagonists
  - Diuretics for fluid retention
  - Hydralazine / isosorbide dinitrate
  - Digitalis

### NYHA Class II

- Recent New Oral Therapies for Decompensated HFrEF Hospitalizations and Fluid Overload*
- sacubitril / valsartan
  - SGLT2 inhibitors
  - Vericiguat

### NYHA Class IIB/IIIA

- NYHA Class IIB or IIIA Persistent HFrEF Patients
- Cardioverter Defibrillator (ICD) +/-
  - CRT-D or Wearable Cardioverter Defibrillator if Indicated

### NYHA Class IIIB/IV

- NYHA Class IIIB/IV Pts with end-stage HFrEF*
- Optimal medical management
  - LVAD implantation
  - Heart transplant
  - Artificial Heart

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

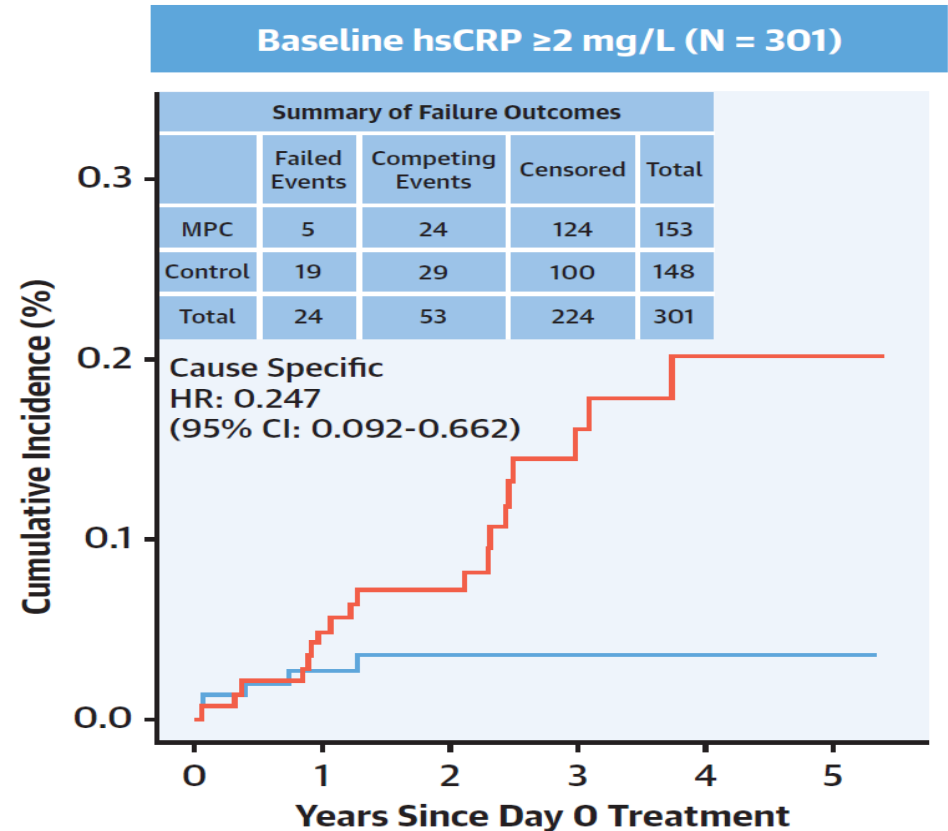


Perin EC, Borow KM, Henry TD, et al. Randomized Trial of Targeted Transcatheter Mesenchymal Precursor Cell Therapy in Patients With Heart Failure. *Journal of the American College of Cardiology*. 2023;81(9):849-863.

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**



# Patients at Risk:

— MPC	153	119	85	49	26	3
— Control	148	122	78	37	18	5

# REVASCOR As Treatment For Severe Congenital Heart Disease

## Awarded FDA Rare Pediatric Disease Designation and Orphan Drug Designation

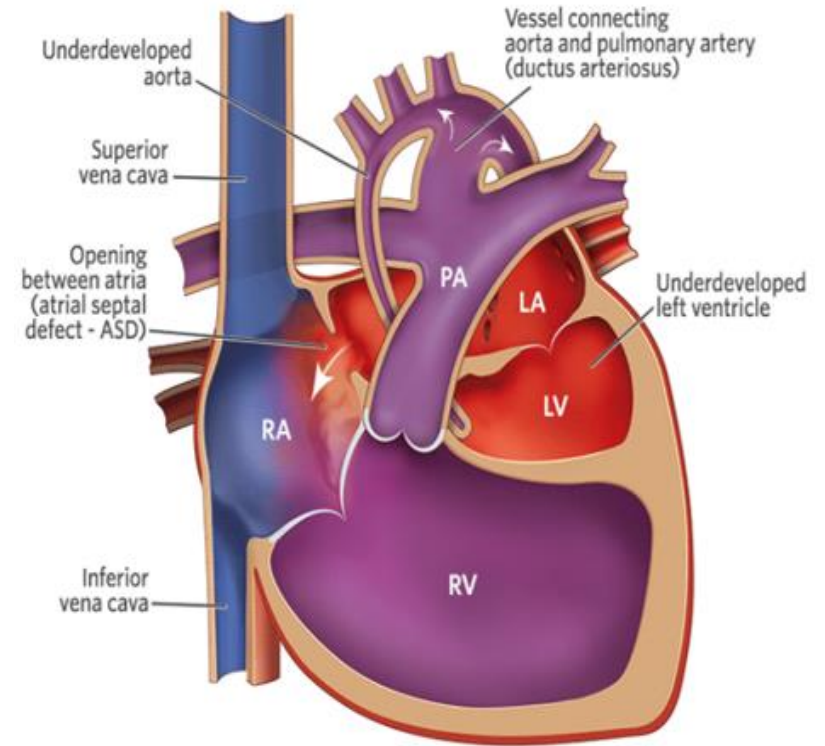
REVASCOR has multiple mechanisms-of-action that may be beneficial to children with congenital heart disease including neovascularization, anti-fibrosis, and reduction in inflammation.

Hypoplastic left heart syndrome (HLHS) is a severe congenital heart disease in which the left side of the heart does not fully develop and effective pumping of oxygenated blood by the left ventricle to the rest of the body is reduced.

Achievement of life-saving surgery creating a two-ventricle series circulation with the left ventricle (LV) pumping blood to the body and the right ventricle pumping blood to the lungs is limited by the inability in most patients for the left ventricle to grow sufficiently to support the circulation to the body.

Clinical trial at Boston Children's Hospital evaluated whether REVASCOR could enhance LV size to support circulation to the body.

### Anatomy of hypoplastic left heart syndrome



# REVASCOR As Treatment For Severe Congenital Heart Disease

## Awarded FDA Rare Pediatric Disease Designation and Orphan Drug Designation

- In the HLHS randomized controlled single-center US trial in 19 patients, a single intramyocardial administration of REVASCOR at the time of staged surgery resulted in significantly increased LV systolic and diastolic volumes over 12 months compared with control.<sup>1</sup>
- These changes are indicative of clinically important growth of the small left ventricle that can help facilitate a subsequent surgical correction allowing for a normal two ventricle circulation.
- Improvement in left ventricular functional outcomes with REVASCOR may encourage more widespread use of surgical procedures to create a functioning left ventricle in children with HLHS resulting in reduction in long-term morbidity and mortality compared with other medical and/or surgical approaches.
- A Rare Pediatric Disease (RPD) designation demonstrates that the disease is serious or life-threatening and the manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents, and that the disease is a rare disease or condition.
- On FDA approval of a Biologics Licensing Application (BLA) for REVASCOR for the treatment of HLHS, Mesoblast may be eligible to receive a Priority Review Voucher (PRV) that can be redeemed for any subsequent marketing application or may be sold or transferred to a third party.

1. Wittenberg RE, Gauvreau K, Leighton J, Moleon-Shea M, Borow KM, Marx GR, Emani SM, Prospective randomized controlled trial of the safety and feasibility of a novel mesenchymal precursor cell therapy in hypoplastic left heart syndrome, JTCVS Open (2023), doi: <https://doi.org/10.1016/j.xjon.2023.09.031>.



# Rexlemestrocel-L

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

# 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<sup>1</sup>
- Inflicts substantial direct and indirect costs on the healthcare system,<sup>1</sup> 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<sup>2</sup>
- 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.<sup>3-4</sup>



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



## Regulatory Alignment

Gained alignment with the FDA on the appropriate pivotal Phase 3 study

Seeks to replicate the significant reduction in pain seen at 12 and 24 months in our first Phase 3 trial



## Phase 3 Protocol

FDA has agreed with Mesoblast plans for mean **pain reduction at 12 months as the primary endpoint** of the pivotal trial

Functional improvement and reduction in opioid use as secondary endpoints



## Product Manufacturing

Product has been manufactured for use in the pivotal Phase 3 study

Potency assays are in place for product release



## Pivotal P3 Trial

RMAT designation for CLBP received from FDA

Pivotal trial activities, including investigators, trial sites & CRO have commenced

# 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)

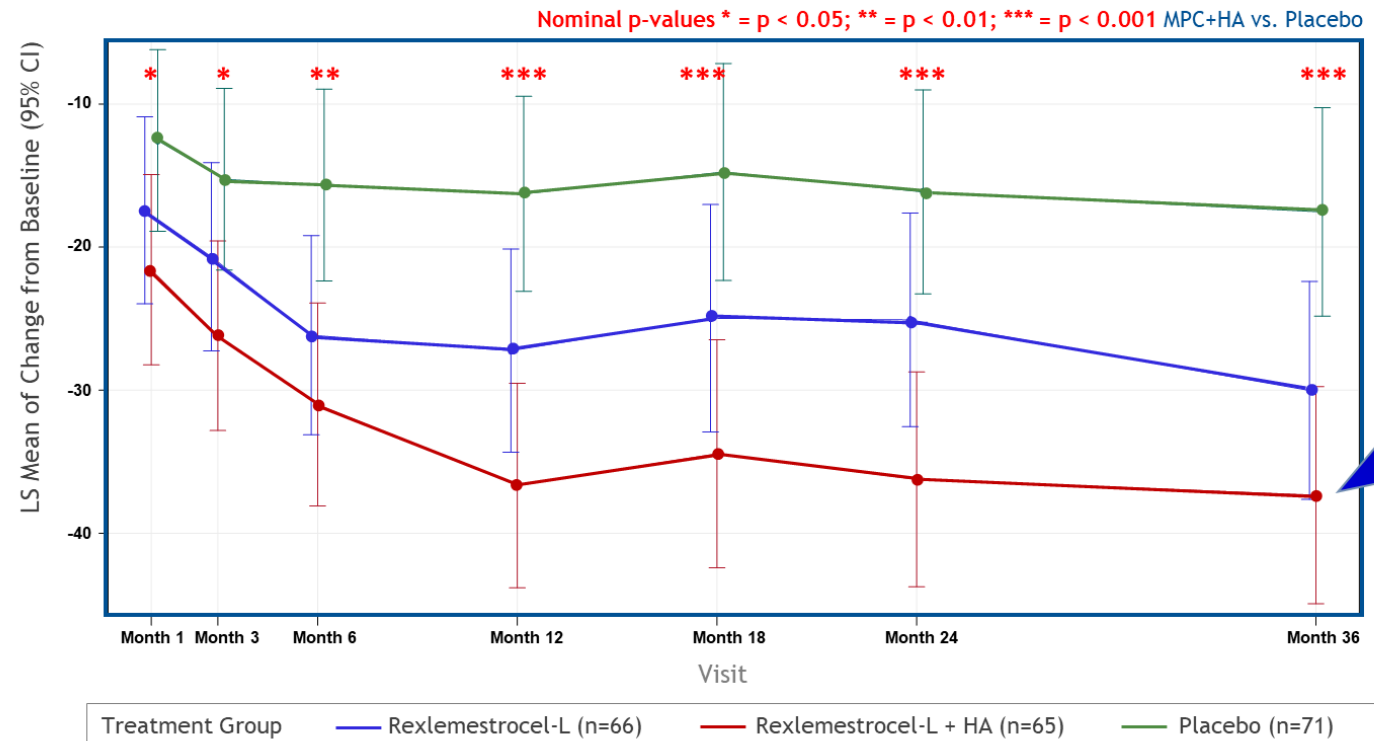
Results from the trial showed that:

- 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

Thank You