



# Annual General Meeting November 24, 2020

ASX: MSB; Nasdaq: MESO

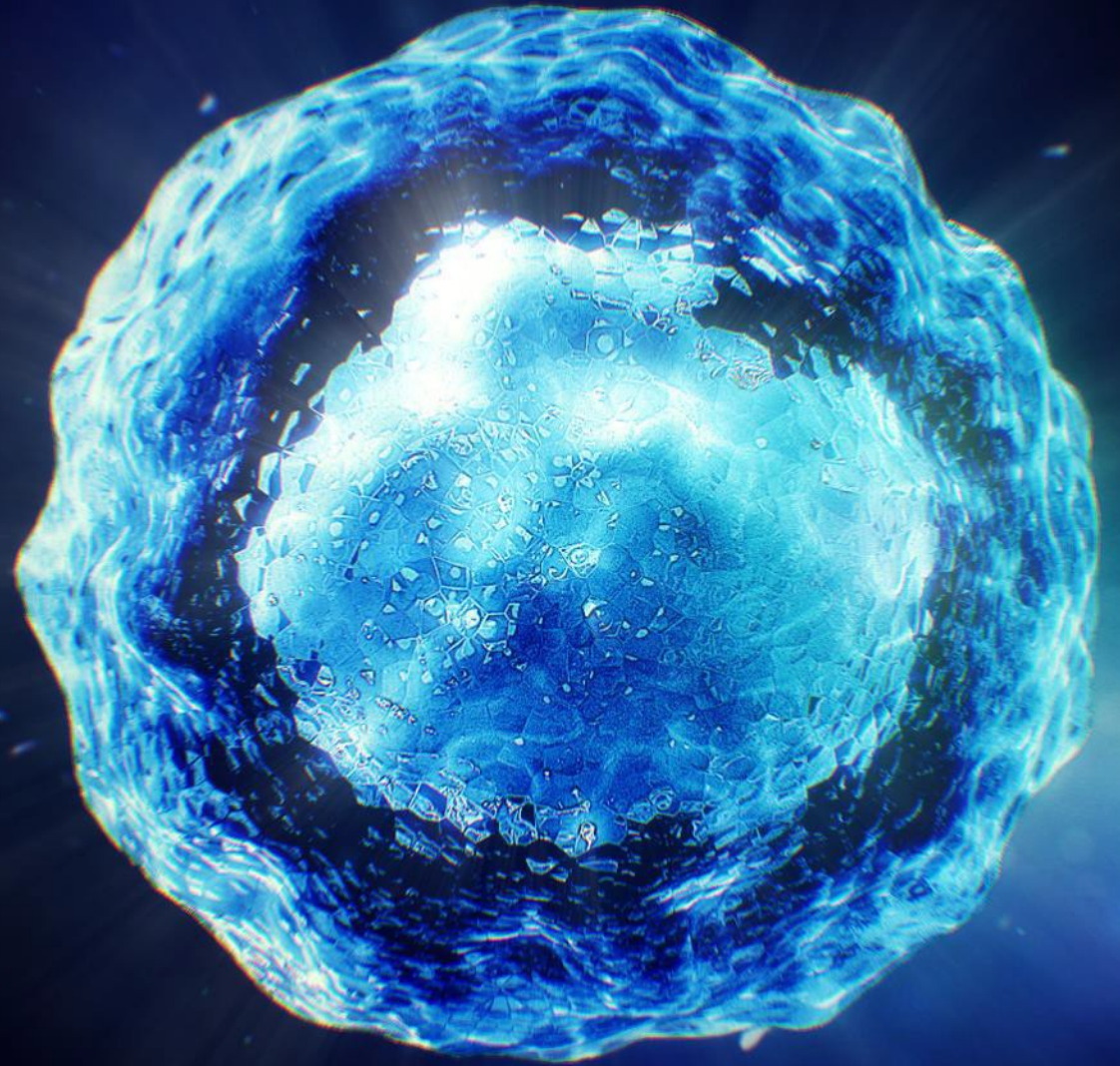


## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS





*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



# Product Pipeline

PRODUCT CANDIDATE	THERAPEUTIC AREA	PHASE 1/2	PHASE 3	REGISTRATION	MESOBLAST COMMERCIAL RIGHTS	COMMERCIAL PARTNERS
Remestemcel-L (RYONCIL™)	Pediatric & adult systemic inflammatory diseases	COVID-19 Acute Respiratory Distress Syndrome (ARDS)			Global Collaboration	
		All Cause ARDS Other Respiratory				
		Refractory Inflammatory Bowel Disease				
		Acute GVHD - Pediatric			Global ex-Japan	
		Acute GVHD - Adult				
Rexlemestrocel (REVASCOR®)	Localized inflammatory diseases	Advanced Heart Failure			Global ex-China	
		End-Stage Ischemic Heart Failure				
Rexlemestrocel (MPC-06-ID)		Chronic Low Back Pain			Global ex-EUR, LATAM	

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

\* Mesoblast has the right to use data generated by JCR Pharmaceuticals Co Ltd in Japan to support its development and commercialization plans for remestemcel-L in the US and other major healthcare markets, including for GVHD, Hypoxic Ischemic Encephalopathy and Epidermolysis Bullosa

# Overview of Collaboration with Novartis for Remestemcel-L

- Worldwide license and collaboration agreement with Novartis for the development, manufacture and commercialization of remestemcel-L
- Initial focus is on the treatment of acute respiratory distress syndrome (ARDS) and other respiratory conditions
- Novartis intends to initiate a Phase 3 study in non-COVID-19-related ARDS after the anticipated closing of the license agreement and successful completion and outcome of the current COVID-19 ARDS study
- Mesoblast will retain full rights and economics for remestemcel-L for graft versus host disease (GVHD), and Novartis has an option to, if exercised, become the commercial distributor outside of Japan
- For most non-respiratory indications, the parties may co-fund development and commercialization on a 50:50 profit-share basis



# Key Terms of Collaboration with Novartis



- Novartis will make a US\$50 million upfront payment including US\$25 million in equity\*
- Mesoblast may receive:
  - A total of US\$505 million pending achievement of pre-commercialization milestones for ARDS indications;
  - Up to an additional US\$50 million reimbursement on the achievement of certain milestones related to the successful implementation of its next-generation manufacturing processes;
  - Additional payments post-commercialization of up to US\$750 million based on achieving certain sales milestones; and
  - Tiered double-digit royalties on product sales
- From the initiation of a Phase 3 trial in all-cause ARDS, Novartis will fully fund global clinical development for all-cause ARDS and potentially other respiratory indications
- Mesoblast will be responsible for clinical and commercial manufacturing and Novartis will purchase commercial product under agreed pricing terms
- Novartis will be responsible for any capital expenditure required to meet increased capacity requirements for manufacture of remestemcel-L

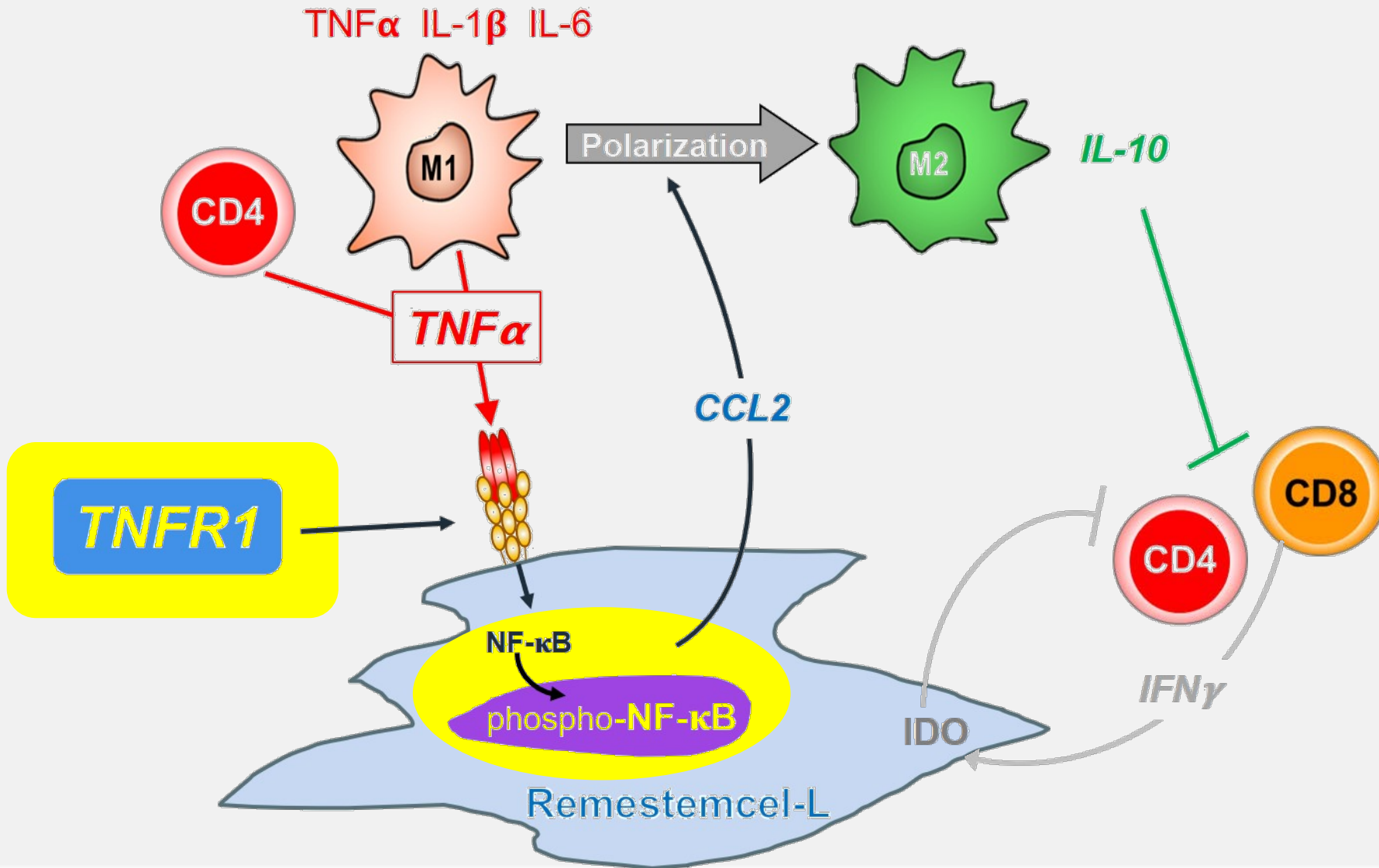
\* The closing of the license agreement is subject to the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act and certain other conditions





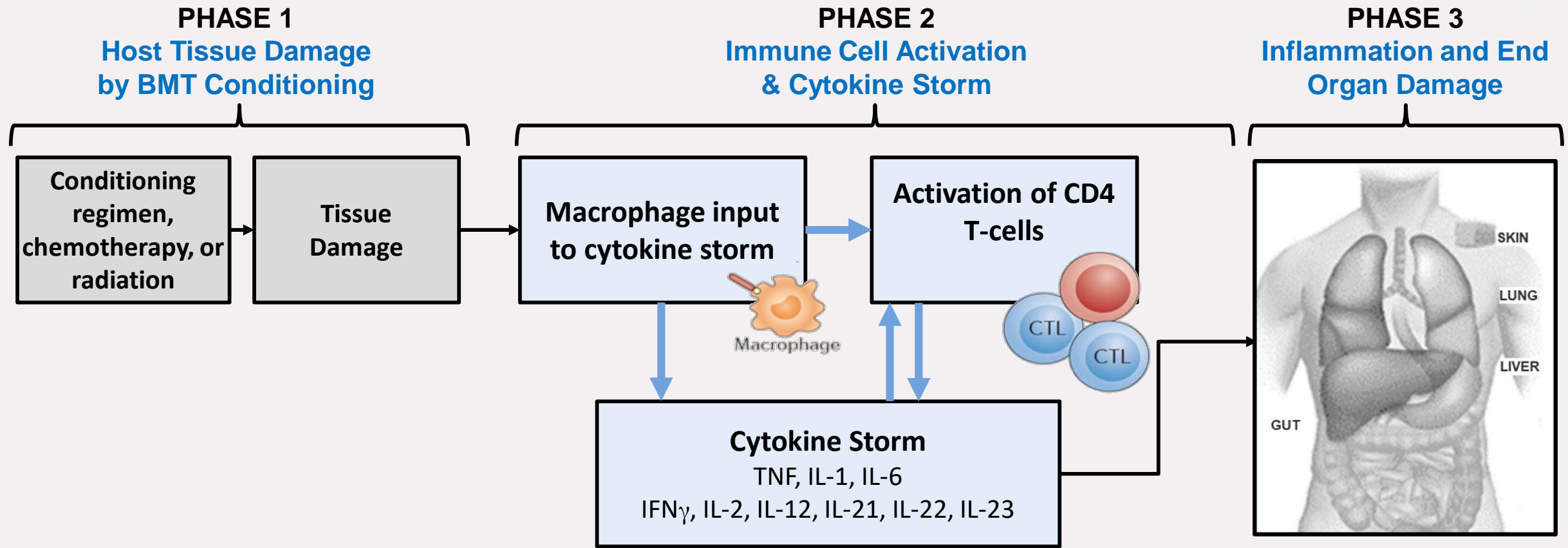
## **Remestemcel-L: Potential Treatment in Severe Inflammatory Conditions**

# Immunomodulatory Activities of Remestemcel-L in Response to Inflammation





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



# Remestemcel-L: Consistent Clinical Outcomes in Children with SR-aGVHD

- Consistent efficacy and safety outcomes in a total of 309 children from three studies:
  - Remestemcel-L was used as first-line therapy in a randomized controlled Phase 3 trial of 260 patients, with SR-aGVHD, including 27 children
  - Remestemcel-L was used as salvage therapy in an expanded access program in 241 children with SR-aGVHD, 80% of whom had Grade C/D disease, and failed institutional standard of care
  - Remestemcel-L was used as first-line therapy in Mesoblast's open-label Phase 3 trial in 54 children with SR-aGVHD, 89% of whom had Grade C/D disease

		Protocol 280 (pediatric)		EAP 275	Study 001
	MAGIC <sup>1</sup> N=30 <sup>2</sup>	Placebo N=13	Remestemcel-L N=14	Remestemcel-L N=241	Remestemcel-L N=54 <sup>3</sup>
Day 28 Overall Response	43%	38%	64%	65%	69%
Day 100 Survival	57%	54%	79%	66%	74%

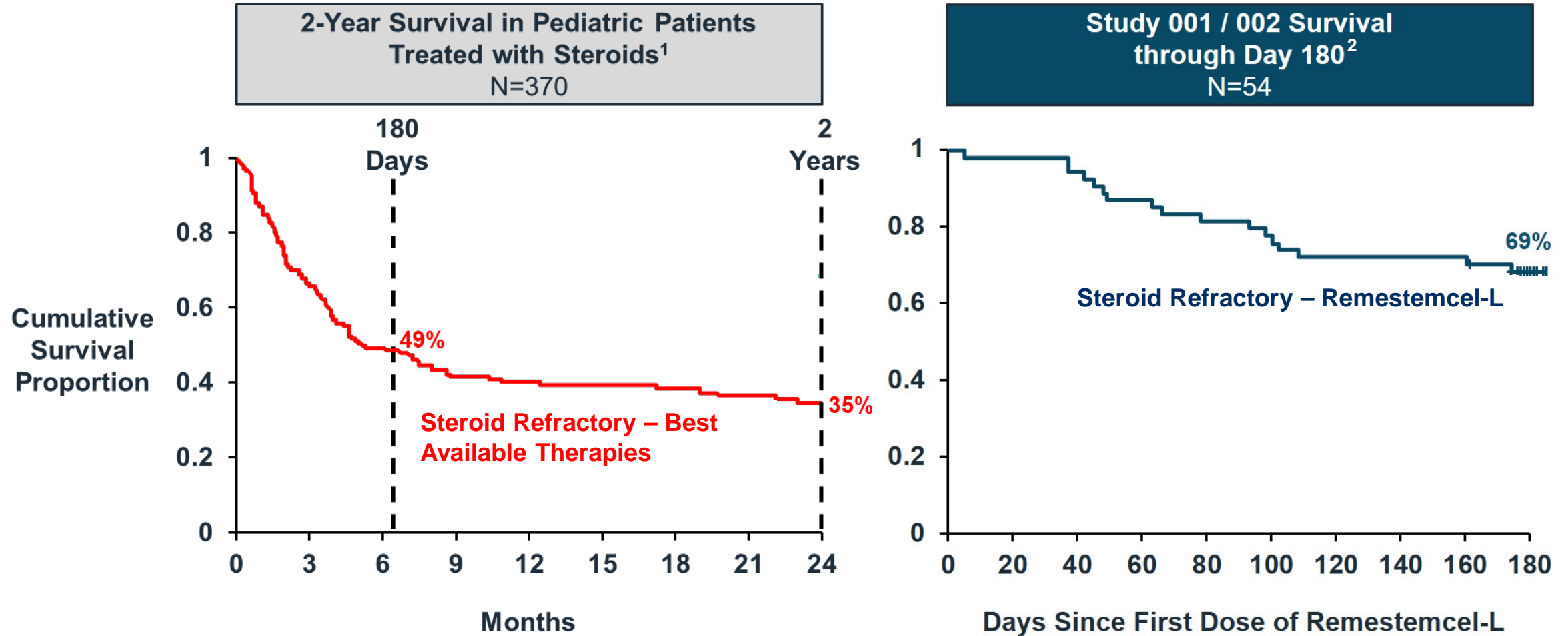
Source: ODAC Advisory Committee Briefing Document and Presentation August 2020.

1. Mount Sinai Acute GVHD International Consortium (MAGIC) – 30 children matched for the same inclusion criteria as Study 001 and treated with institutional standard of care.

2. Two subjects in the MAGIC cohort had follow-up <100 days; these subjects are excluded from the respective survival analyses.

3. Study 001 had 55 randomized patients, however one patient dropped out before receiving any dose of remestemcel-L

# Remestemcel-L Improved Dismal Survival in Children with SR-aGVHD



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. Kurtzberg, J. et al. A Phase 3, Single-Arm, Prospective Study of Remestemcel-L, Ex Vivo Culture-Expanded Adult Human Mesenchymal Stromal Cells for the Treatment of Pediatric Patients Who Failed to Respond to Steroid Treatment for Acute Graft-versus-Host Disease. Biol Blood Marrow Transplant 26 (2020) 845-854

# SR-aGVHD Regulatory & Commercial Update



- On August 13 2020, results from 309 children with SR-aGVHD treated with remestemcel-L were presented to the Oncologic Drugs Advisory Committee (ODAC) of the United States Food and Drug Administration (FDA)
- The ODAC panel voted 9:1 that the available data support the efficacy of remestemcel-L in pediatric patients with SR-aGVHD\*
- Despite the overwhelming ODAC vote, on September 30, the FDA provided Mesoblast with a Complete Response Letter
- On November 17, a Type A meeting was held with the FDA to discuss the review of the Biologics License Application for remestemcel-L and a potential pathway for accelerated approval with a post-approval requirement to conduct an additional randomized controlled study in patients 12 years and older
- The definitive outcome of the Type A meeting will not be known until Mesoblast receives the formal minutes which are expected within 30 days of the meeting, however it appears that the current FDA review team will not agree to accelerated approval
- If accelerated approval is not agreed to by the current review team, Mesoblast will request a further Type A meeting to initiate the well-established FDA dispute resolution pathway

\* This vote includes a change to the original vote by one of the ODAC panel members after electronic voting closed

# Remestemcel-L for ARDS – Major Unmet Need

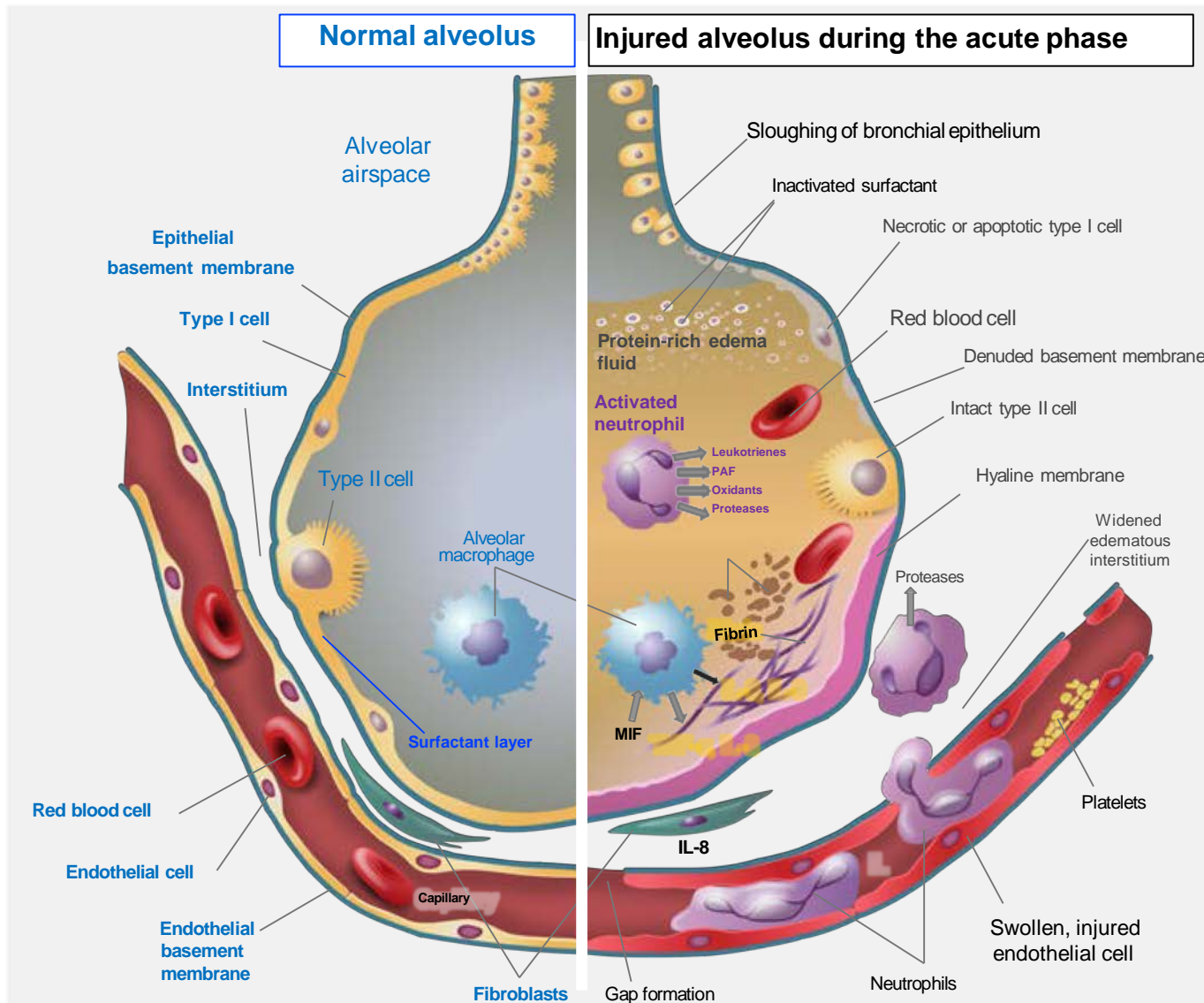


- Multiple triggers including viral (COVID-19, influenza) or bacterial infections
- Typically requires extended ICU hospitalization and intervention by ventilation
- ~40-80% mortality in viral induced ARDS<sup>1-4</sup>
- Up to 61,000 deaths per year in US alone from influenza ARDS<sup>5</sup>
- Intravenous delivery of remestemcel-L results in selective migration to the lungs making inflammatory lung disease an ideal target for this therapy
- COVID-19 ARDS has the highest mortality due to the most severe inflammatory cytokine storm in the lungs
- The extensive safety data of remestemcel-L and its anti-inflammatory effects in aGVHD makes a compelling rationale for evaluating remestemcel-L in COVID-19 ARDS

1. Matthay MA., et al. Acute Respiratory Distress Syndrome. Nature 2019 5:18. doi: [10.1038/s41572-019-0069-0](https://doi.org/10.1038/s41572-019-0069-0); 2. Bellani G, Laffey JG, Pham T, et al. Epidemiology and patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA 2016;315:788-800; 3. Petrilli CM et al. Factors associated with hospitalization and critical illness among 4,103 patients with Covid-19 disease in New York City. MedRxiv 2020; 4. Gibson PG., et al. COVID-19 ARDS: clinical features and differences to “usual” pre-COVID ARDS. Med J Aust. 24 April 2020 5. Centers for Disease Control and Prevention. Disease Burden of Influenza. <https://www.cdc.gov/flu/about/burden/index.html>



# ARDS due to COVID-19, Influenza & Bacterial Infection - Pathophysiology



- Activation of alveolar M1 macrophages results in cytokine storm
- Influx of neutrophils results in proteolytic destruction
- Aberrant secretion of fluid by alveolar cells
- Interstitial edema, cell death and influx of inflammatory cells

# Promising Pilot Data in Adults & Children with COVID-19



## Compassionate Use Emergency IND in Ventilator-Dependent Adults with COVID-19 ARDS

- 12 patients with moderate or severe ARDS received two infusions of remestemcel-L within five days at Mt. Sinai Hospital in New York City
- Nine patients (75%) successfully came off ventilator support at a median of 10 days and were discharged from hospital
- This contrasts with only 9% of all COVID-19 patients able to be extubated and a 12% survival rate in two major NY hospital networks during same time period<sup>1,2</sup>

## Children with Multisystem inflammatory Syndrome (MIS-C) due to COVID-19

- In approximately 50% of cases, MIS-C is associated with significant cardiovascular complications that directly involve heart muscle and may result in decreased cardiac function
- Mesoblast has established an EAP which provides physicians with access to remestemcel-L in COVID-19 infected children aged 2 months-17 years with cardiovascular and other complications of MIS-C
- Two children with significant cardiac dysfunction, normalized after two infusions and discharged from the hospital

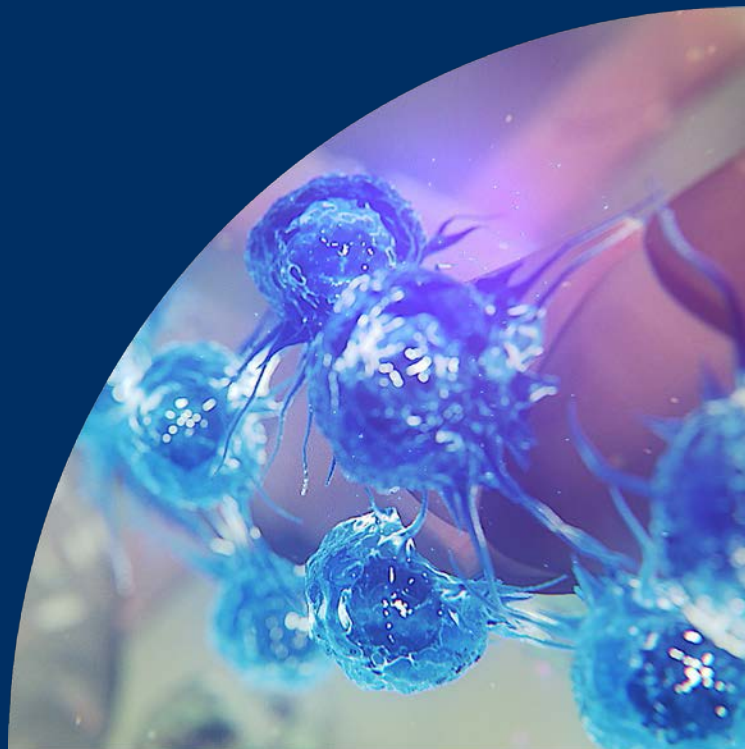
<sup>1</sup> Petrilli CM et al. Factors associated with hospitalization and critical illness among 4,103 patients with Covid-19 disease in New York City. MedRxiv 2020 doi: <https://www.medrxiv.org/content/10.1101/2020.04.08.20057794v1.full.pdf>

<sup>2</sup> Richardson S et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020. doi:10.1001/jama.2020.6775

# Key Milestones for Remestemcel-L in COVID-19 ARDS



- Phase 3 multi-center, randomized, controlled trial of remestemcel-L versus placebo in ventilator-dependent patients with moderate/severe ARDS due to COVID-19
- Up to 300 patients randomized 1:1 to receive placebo or two infusions of remestemcel-L within 3-5 days
- Primary endpoint all cause mortality up to 30 days; key secondary endpoint days alive off ventilator within 60 days
- Full recruitment expected to complete during Q1 CY2021
- DSMB recommended continuation of the trial after reaching first (30%) and second (45%) interim analyses
- Trial enrollment has now surpassed 180 patients
- Plan to seek Emergency Use Authorization (EUA) subject to positive data read-out



## **Update on Other Phase 3 Product Candidates**

- **Heart Failure**
- **Chronic Low Back Pain**

# REVASCOR® for Advanced and End-Stage Heart Failure



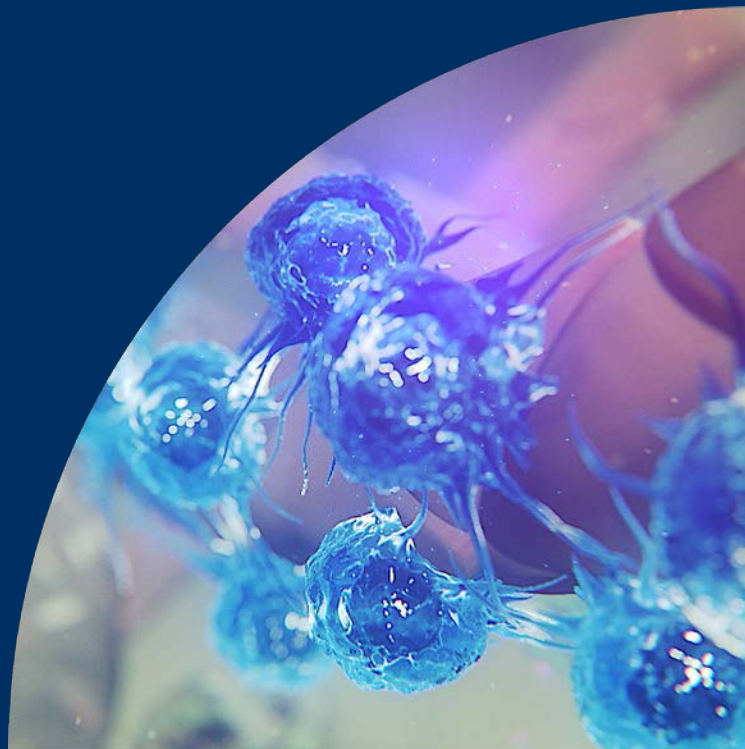
- In December 2019, the Phase 3 trial in advanced heart failure surpassed the number of primary endpoint events required for trial completion
  - Final study visits for all surviving patients have been completed
  - Ongoing quality review of all data is being completed at the study sites
  - Data readout expected during Q4 CY2020
  - Results may support regulatory approval in the US
- Results from a sub-study of 70 patients with end-stage ischemic heart failure and a Left Ventricular Assist Device (LVAD), of 159 randomized patients who received either REVASCOR or saline, were presented at the American College of Cardiology (ACC) Virtual Scientific Sessions
  - Conclusions from the study included MPCs had a beneficial effect on LVAD weaning, major mucosal bleeding, serious adverse events, and readmissions in ischemic heart failure patients
  - End-stage ischemic heart failure patients with LVADs are older and have co-morbidities such as diabetes, thereby closely resembling the majority of patients in Mesoblast's 566-patient Phase 3 trial of REVASCOR for advanced chronic heart failure



# MPC-06-ID for Chronic Low Back Pain



- Phase 3 trial of MPC-06-ID for chronic low back pain in 404 patients:
  - Final study visits for all patients have been completed
  - Ongoing quality review of all data is being completed at the study sites
  - Data readout expected during Q4 CY2020
- Continued operational progress in strategic partnership for chronic lower back pain with Grünenthal in Europe to complete clinical protocol design, obtain regulatory input, and receive clearance from European regulatory authorities to begin European Phase 3 trial
- Results from the Phase 3 trials will be considered pivotal to support regulatory approval in the US, as well as in Europe



 **mesoblast**

