



# **Financial Results for First Quarter Ended September 30, 2020**

***Strategic Collaboration with Novartis***

ASX: MSB; Nasdaq: MESO

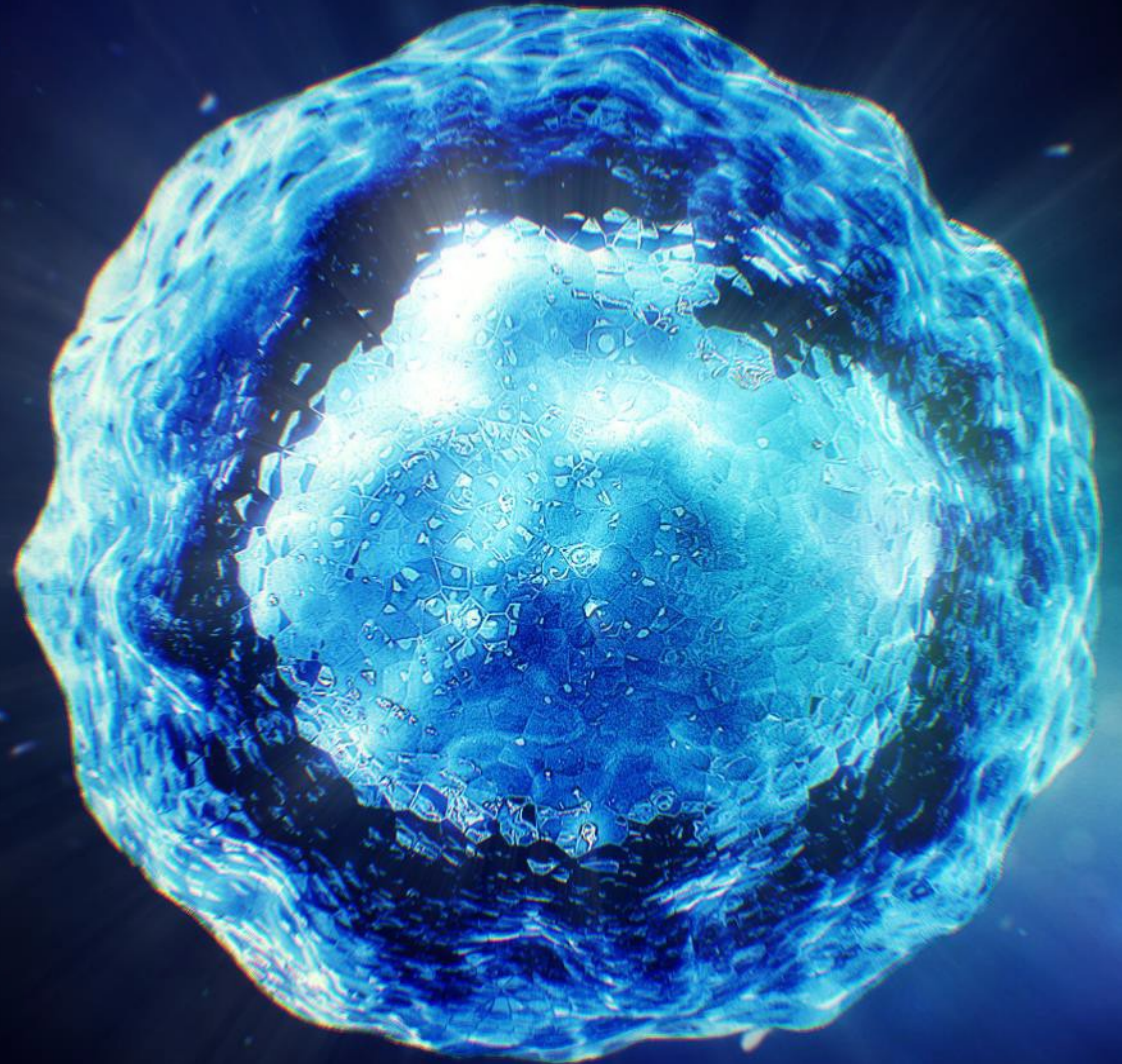


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## Our Mission

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



# Strategic Collaboration with Novartis, Initial Focus on Respiratory Indications



- In early 2020, Mesoblast recognized that the extensive safety data of remestemcel-L and its anti-inflammatory mechanism of action made a compelling rationale for evaluating its potential to reduce the high mortality due to severe inflammation in COVID-19 ARDS
- Capital raised in May 2020 allowed increased investment in both clinical development and manufacturing to facilitate the potential availability of remestemcel-L for patients with COVID-19 ARDS
- Ongoing Phase 3 randomized, placebo-controlled trial of remestemcel-L in up to 300 ventilator-dependent patients with moderate to severe COVID-19 ARDS aims to show a reduction in mortality within 30 days
- The trial's independent data safety monitoring board (DSMB), recommended the continuation of the trial after each of two interim analyses
- Enrollment has now surpassed 180 patients
- Novartis will provide the commercial and manufacturing strength to bring this important cellular medicine to the many patients with COVID-19 and its life-threatening complication of ARDS
- The collaboration establishes a new respiratory focus targeting inflammatory lung conditions

# 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 ARDS, including that associated with COVID-19, and other respiratory conditions
- ARDS is an area of significant unmet need, with a high mortality rate despite current standard of care, which includes prolonged ICU treatment and mechanical ventilation.
- 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



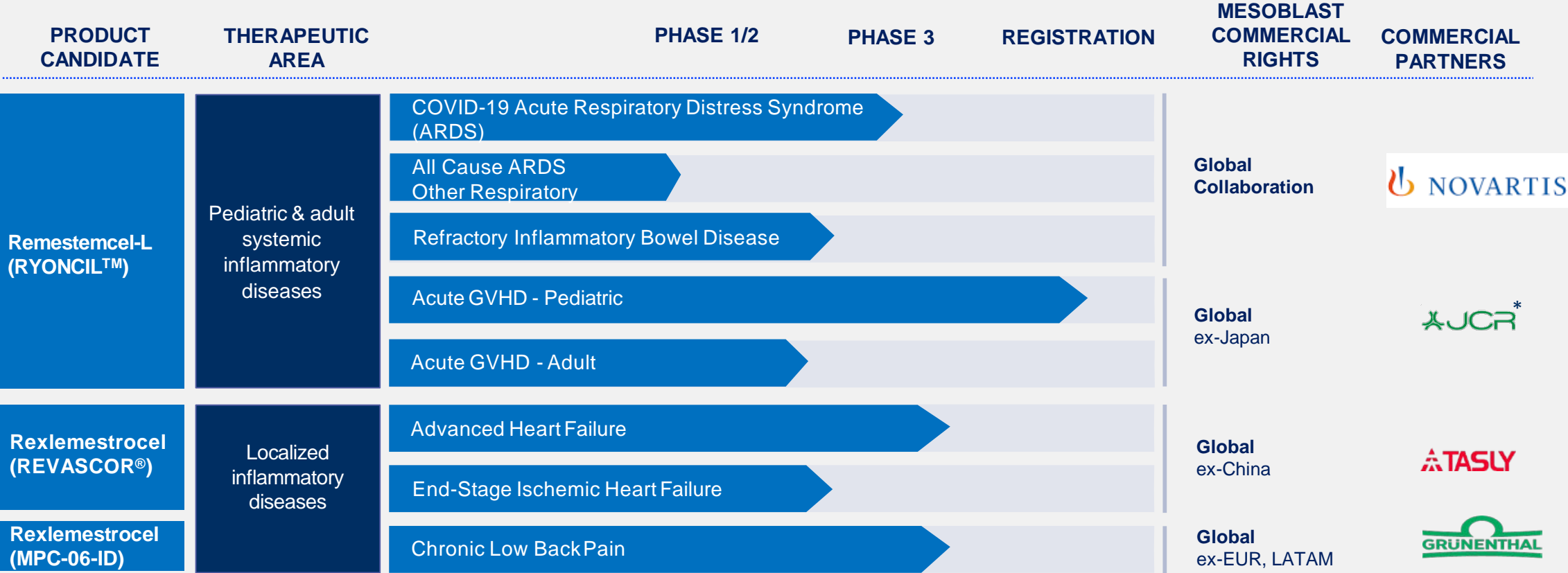
# Key Terms of Collaboration with Novartis



- 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
- Mesoblast may receive 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 reimburse Mesoblast up to US\$50 million on the achievement of certain milestones related to the successful implementation of its next-generation manufacturing processes using its proprietary media and three-dimensional bioreactors aimed at delivering substantial manufacturing efficiencies
- 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

# Product Pipeline

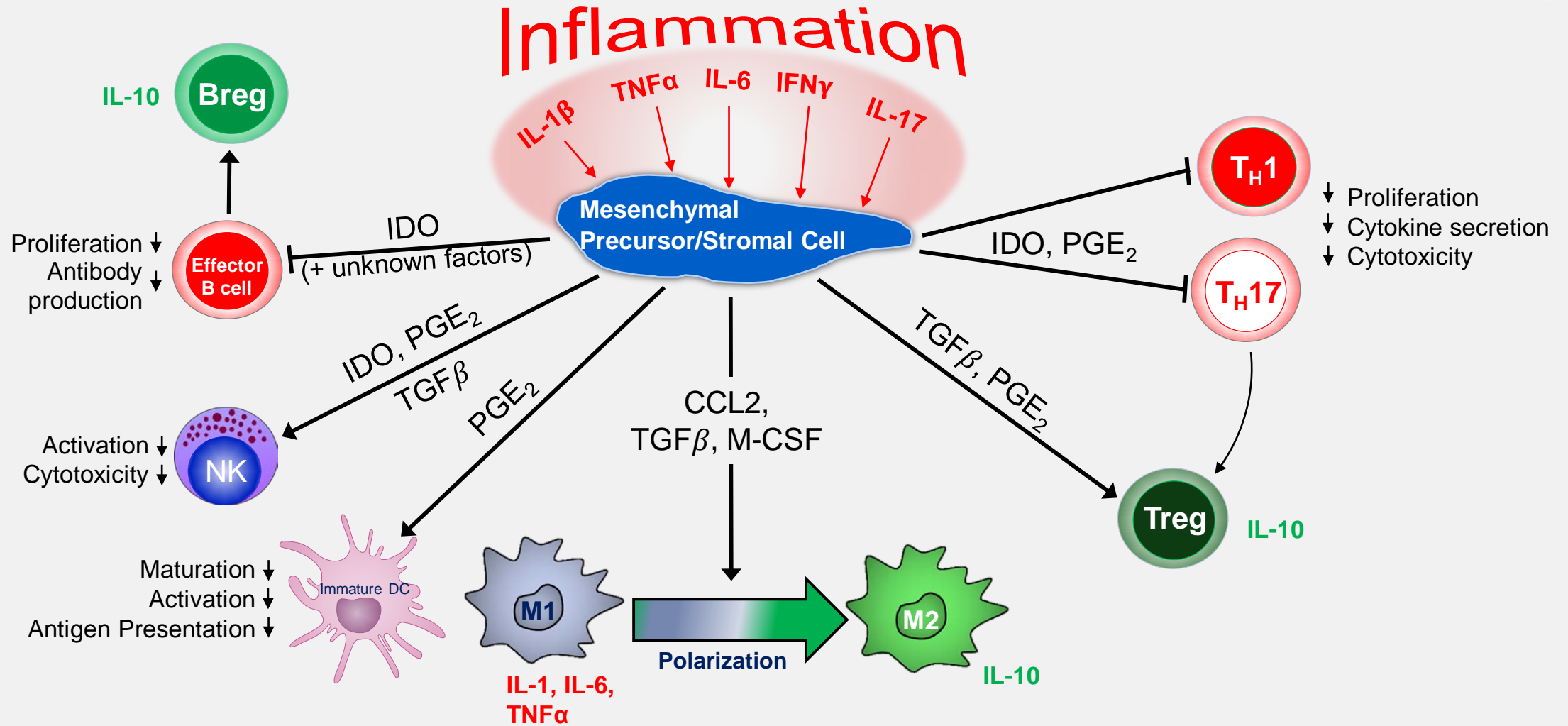


*This chart is figurative and does not purport to show individual trial progress within a clinical program*

\* 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

# 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





# Commercial Scale Manufacturing Capability

- 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
- Projected increase in capacity requirements for maturing pipeline, including COVID-19 ARDS
  - Proprietary xeno-free technologies will increase yields and output
  - Moving to 3D bioreactors will reduce labor and improve manufacturing efficiencies
  - These innovations will significantly reduce cost of goods

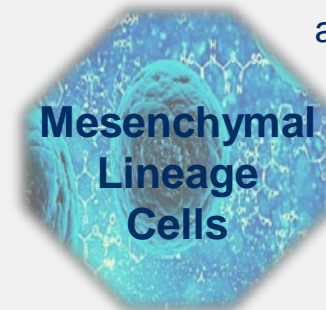
*Manufacturing Remestemcel-L*



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# Global IP Estate Provides Substantial Competitive Advantage

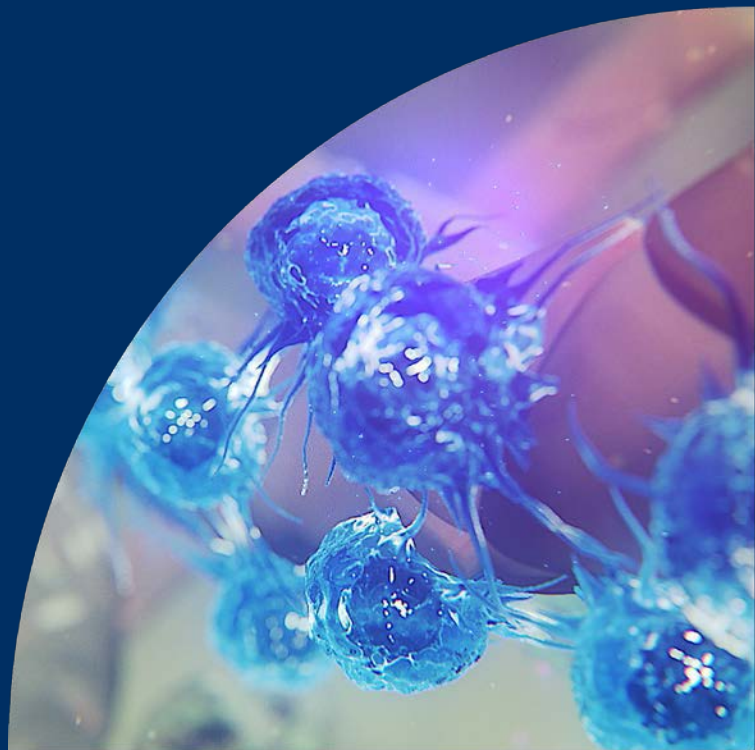
- Extensive patent portfolio with protection extending through 2040 in all major markets
- Over 1,100 patents and patent applications (82 patent families) across all major jurisdictions
- Covers composition of matter, manufacturing, and therapeutic applications of mesenchymal lineage cells
- Provides strong global protection in areas of our core commercial focus
- Grant rights to third parties who require access to our patent portfolio to commercialize their products, when outside our core commercial areas
- Mesoblast receives royalty income from its patent licensee TiGenix, S.A.U., a wholly owned subsidiary of Takeda, on its worldwide sales of its product Alofisel® for the treatment of complex perianal fistulas in adult patients with Crohn's disease, as well as milestone payments



**Markets**  
Global coverage including U.S., Europe, China, and Japan

**Sources**  
Allogeneic / Autologous (Bone Marrow, Adipose, Dental Pulp, Placental), Pluripotent (iPS)

**Therapeutic Areas**  
Core commercial and non-core indications



# Financial Results for the Quarter Ended September 30, 2020

# Strengthened Balance Sheet



- At September 30, 2020, cash on hand was US\$108.1 million
- Proforma cash on hand of US\$158.1 million includes an additional US\$50 million upfront payment from the collaboration with Novartis\*
- Over the next 12 months Mesoblast, pending achievement of certain milestones, may receive additional payments under the collaboration with Novartis
- Up to an additional US\$67.5 million may be available through existing financing facilities and other strategic partnerships over next 12 months

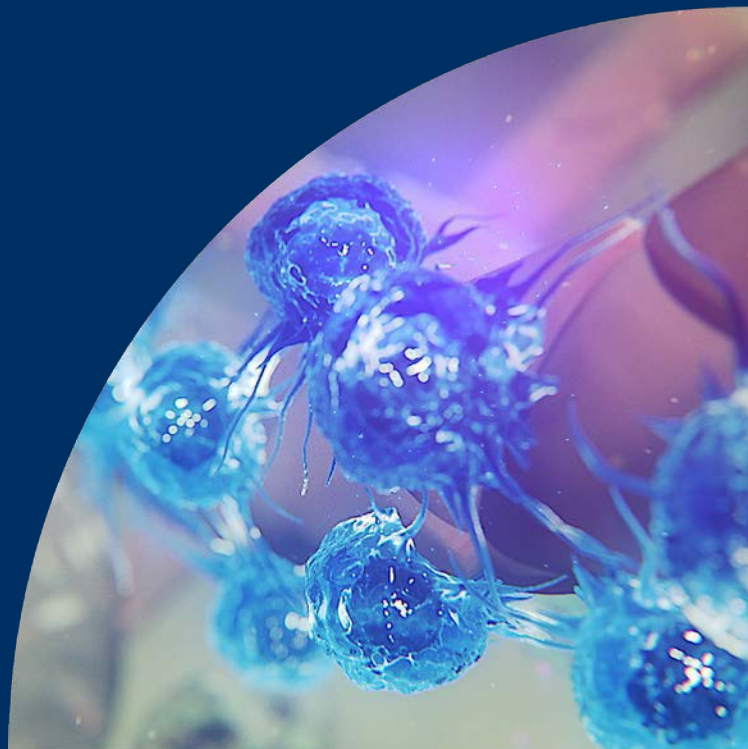
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\* The closing of the license agreement is subject to the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act and certain other conditions

# Capital Raised in May 2020 Supported Increased Investment in COVID-19 Related R&D and Manufacturing

Profit and Loss for the three months ending (US\$m)	September 30, 2020	September 30, 2019
Commercialization revenue	1.3	1.9
Milestone revenue	-	15.0
Interest revenue	-	0.2
<b>Total Revenue</b>	<b>1.3</b>	<b>17.0</b>
Research and development	(19.3)	(12.4)
Manufacturing	(11.9)	(2.7)
Management & administration	(7.7)	(5.5)
Contingent consideration	15.1	(0.3)
Other operating income & expenses	2.0	(0.2)
Finance costs	(4.8)	(3.5)
<b>Loss before tax</b>	<b>(25.3)</b>	<b>(7.4)</b>
Income tax benefit	0.7	1.9
<b>Loss after tax</b>	<b>(24.5)</b>	<b>(5.5)</b>

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# **Remestemcel-L: Potential New Treatment Paradigm in Inflammatory Respiratory Conditions**

# Overview – Remestemcel-L for ARDS due to COVID-19

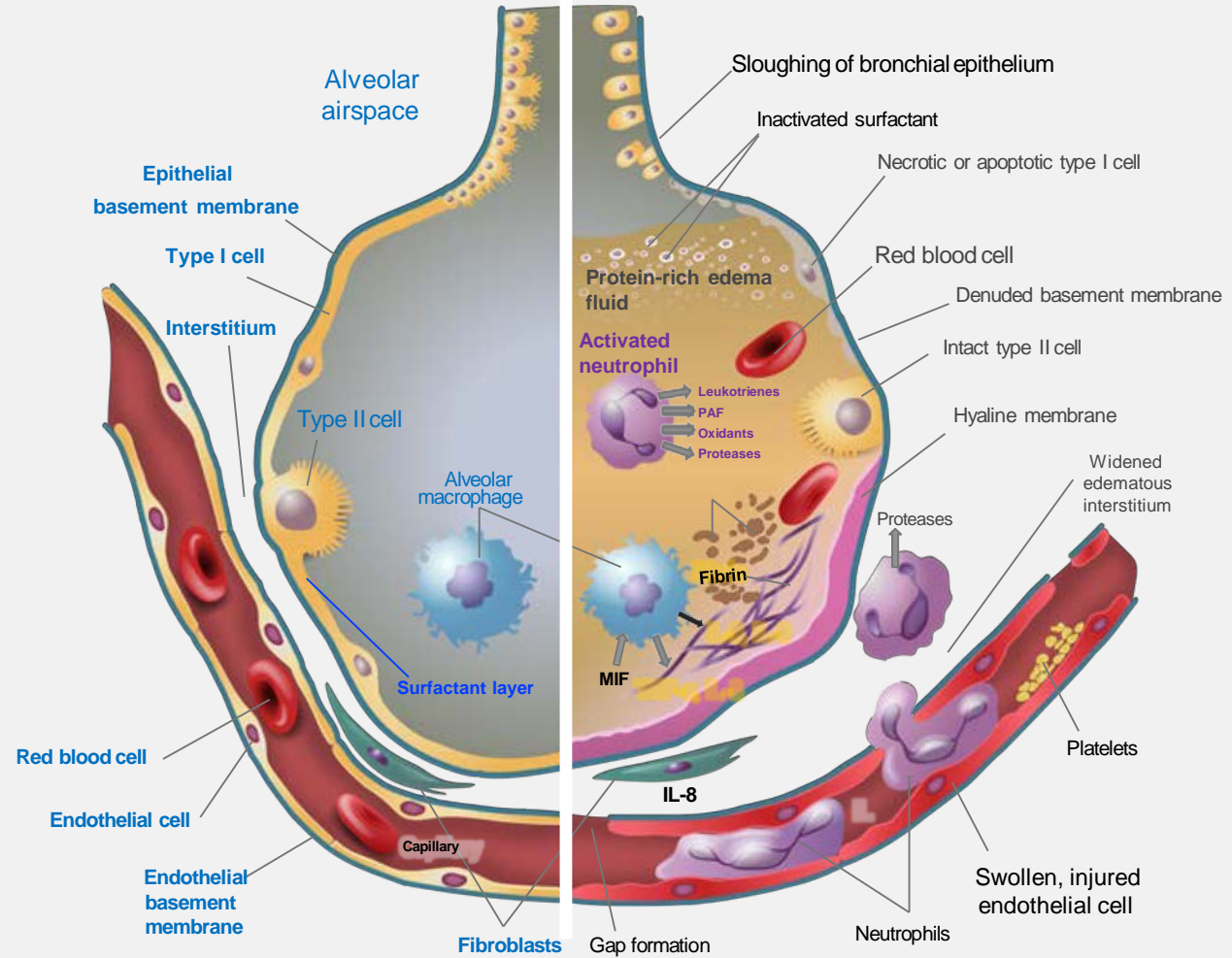


- COVID-19 is a respiratory virus with a high mortality due to a severe inflammatory condition of the lungs called acute respiratory distress syndrome (ARDS)
- ARDS is caused by cytokine storm in lungs of patients infected with COVID-19 and is the primary cause of death
- The extensive safety data of remestemcel-L and its anti-inflammatory effects in aGVHD makes a compelling rationale for evaluating remestemcel-L in COVID-19 ARDS
- Intravenous delivery of remestemcel-L results in selective migration to the lungs making inflammatory lung disease an ideal target for this therapy
- Remestemcel-L has the potential to tame the cytokine storm in ARDS and may offer a life-saving treatment for those suffering from COVID-19

# ARDS due to COVID-19, Influenza & Bacterial Infection – Major Unmet Need

Normal alveolus

Injured alveolus during the acute phase



Source: Matthay MA, Zimmerman GA. Am J Respir Cell Mol Biol. 2005;33:319-27

## Acute respiratory distress syndrome (ARDS)

- A major area of unmet medical need
- Multiple triggers including viral/bacterial infections such as coronavirus or influenza
- Typically requires extended ICU hospitalization and intervention by ventilation
- ~40-80% mortality in viral induced ARDS (influenza & COVID-19, respectively)<sup>1-4</sup>

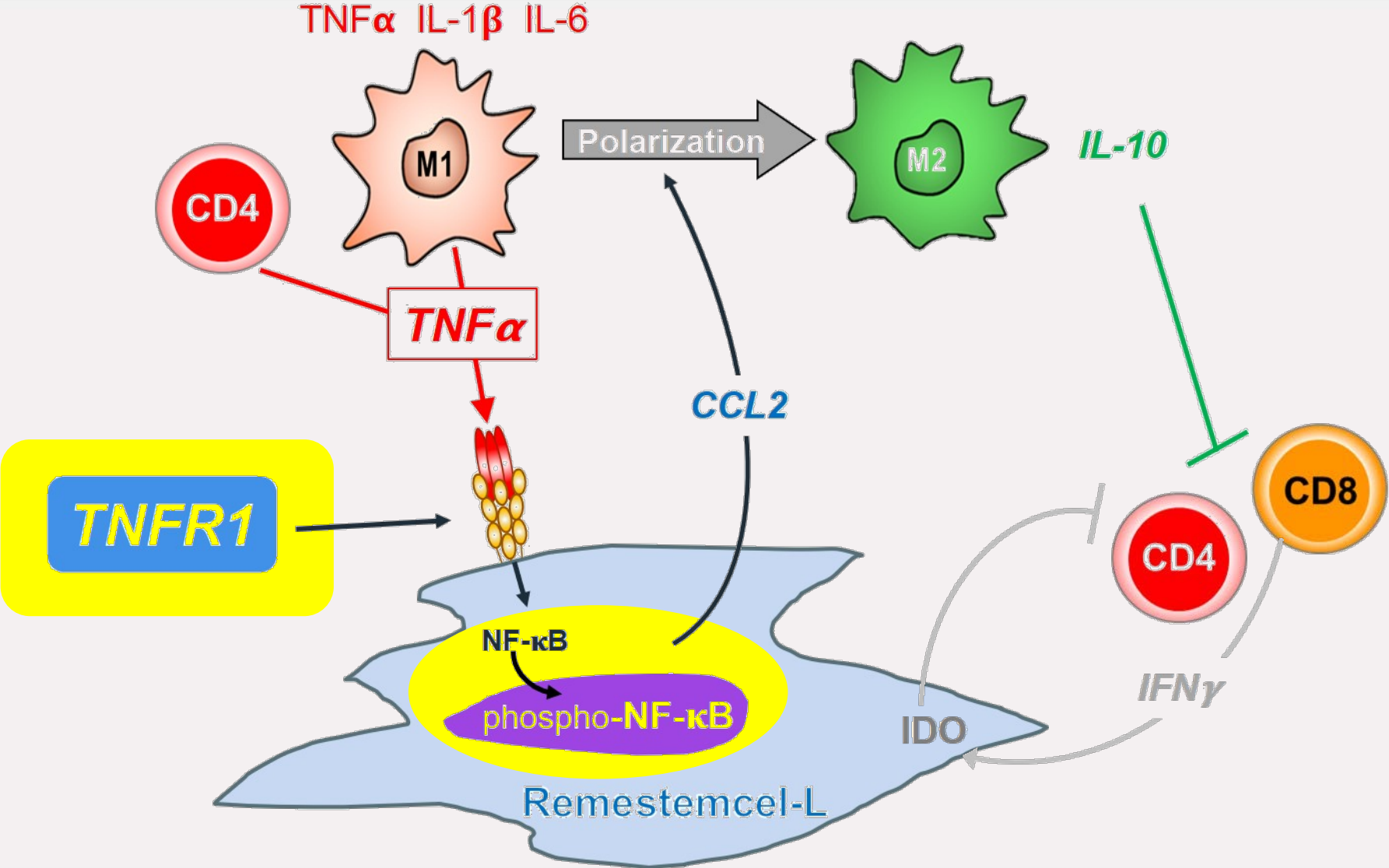
## Pathophysiology

- 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

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



# Immunomodulatory Activities of Remestemcel-L in Response to Inflammation



# 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

1 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>

2. 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

# Remestemcel-L: Phase 3 Randomized Controlled Trial in COVID-19 ARDS

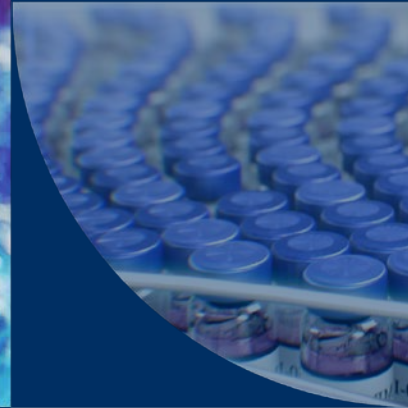
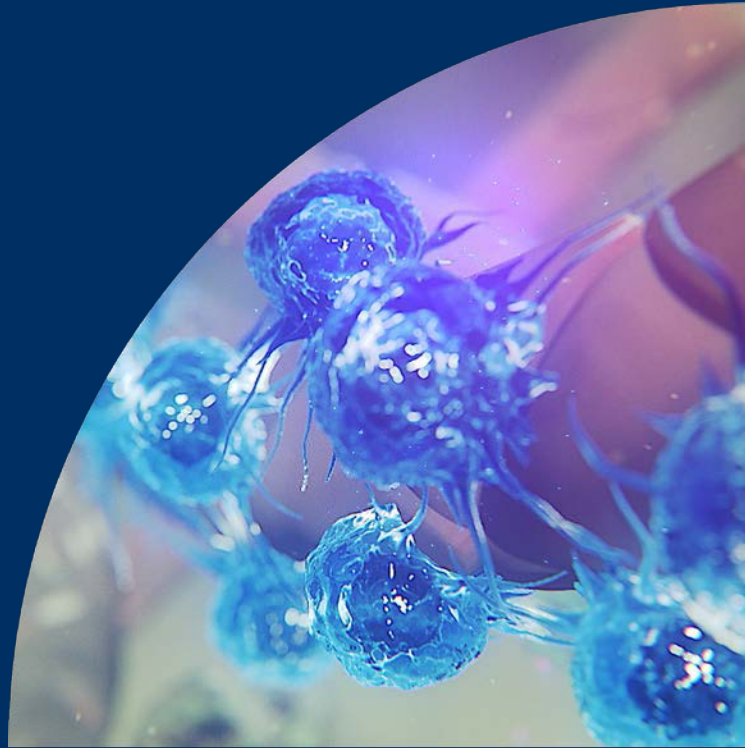


- Multi-center, randomized, controlled, blinded study to assess safety and efficacy of remestemcel-L versus placebo in ventilator-dependent patients with moderate/severe ARDS due to COVID-19
- Up to 300 patients randomized 1:1 to receive placebo or two infusions of remestemcel-L within 3-5 days
- Primary endpoint all cause mortality up to 30 days; key secondary endpoint days alive off ventilator within 60 days
- Trial designed to have three interim analyses for potential early stoppage due to futility or overwhelming efficacy
- Full recruitment expected to complete during Q1 CY2021

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

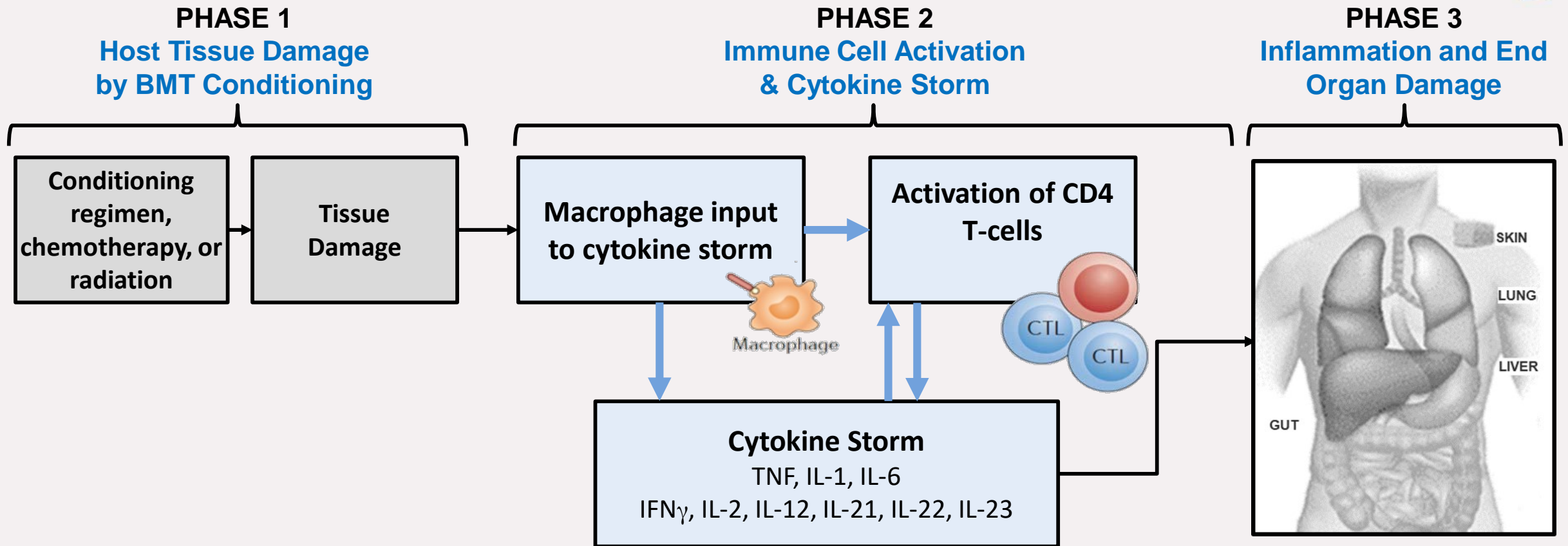


- DSMB recommended continuation of the trial after reaching first (30%) and second (45%) interim analyses
- Trial enrollment has now surpassed 180 patients
- Plan to seek Emergency Use Authorization (EUA) subject to positive data read-out
- Manufacturing scale-up to meet projected increase in capacity requirements for maturing pipeline, including ARDS due to COVID-19 and other causes, additional respiratory indications
  - Increase manufacturing footprint for capacity expansion
  - Implement proprietary xeno-free technologies to increase yields and output
  - Plan for long-term move to 3D bioreactors to reduce labor and improve manufacturing efficiencies



# Remestemcel-L: Acute Graft Versus Host Disease

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



# Children with Steroid-Refractory Acute GVHD at High Risk of Treatment Failure and Death

## Extremely high unmet medical need

- More than 2,000 allogeneic BMTs in children and adolescents in US annually<sup>1</sup>
- Despite prophylaxis, ~50% will develop aGVHD<sup>2</sup>
- First-line treatment is corticosteroids
- Response rate is ~50%
- Children < 12 years of age have no approved treatment for steroid-refractory acute GVHD

## Acute GVHD Primarily Affects Skin, GI Tract, and Liver

- Classic skin rash; Abdominal cramps; Large volumes of diarrhea
- Rising serum bilirubin (indicative of liver damage or disease)
- Mortality as high as 70 – 90%<sup>2-5</sup> when involving gut and liver



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# Remestemcel-L: Prior Clinical Data 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>
<b>Day 28 Overall Response</b>	<b>43%</b>	<b>38%</b>	<b>64%</b>	<b>65%</b>	<b>69%</b>
<b>Day 100 Survival</b>	<b>57%</b>	<b>54%</b>	<b>79%</b>	<b>66%</b>	<b>74%</b>

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

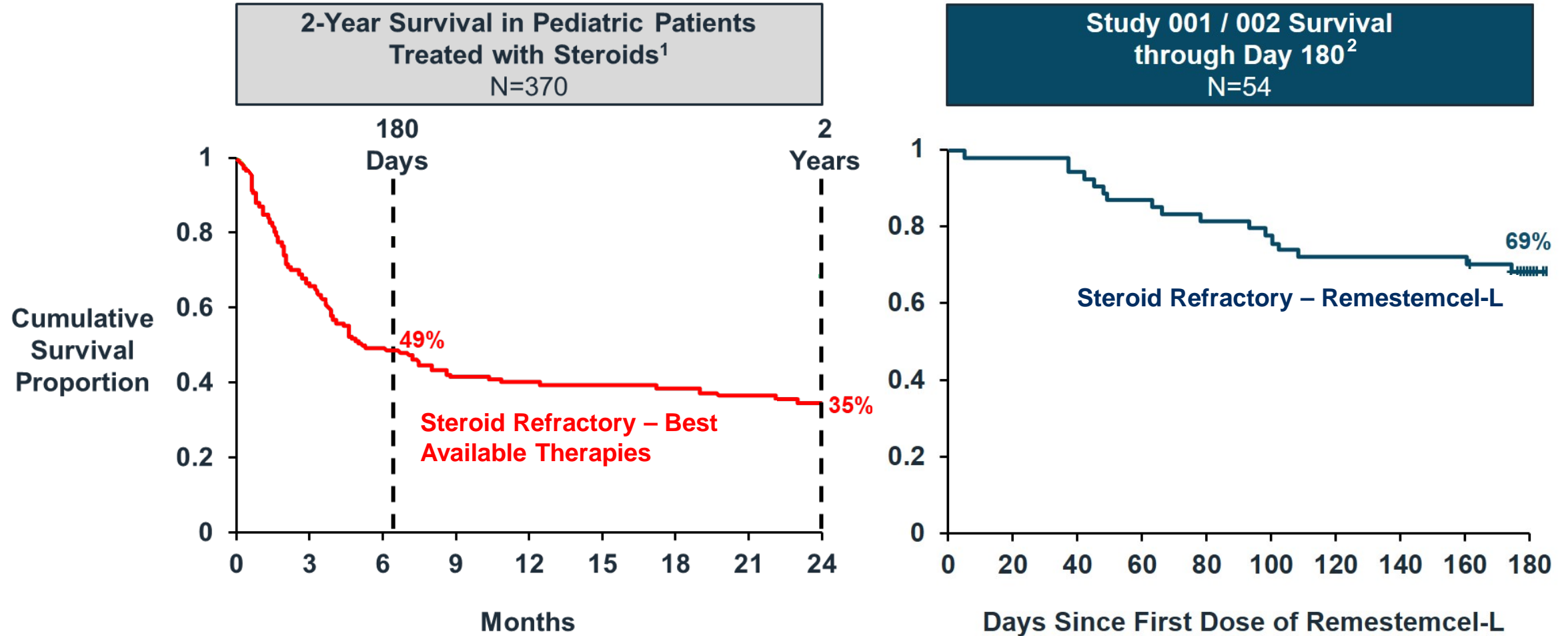
1. Mount Sinai Acute GVHD International Consortium (MAGIC) - a group of ten BMT centers throughout the US and Europe whose purpose is to conduct ground-breaking clinical trials in GVHD, including developing informative biorepositories that assist in developing treatments that can guide GVHD therapy.

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

3. GVHD001 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



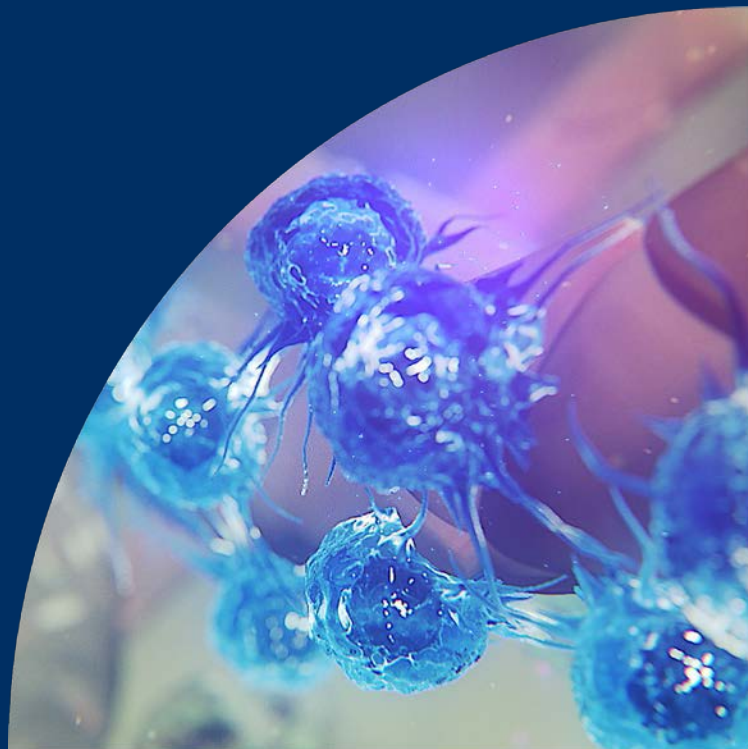
1. Adapted and redrawn from Figure 2 of MacMillan, M.L. et al. Pediatric acute GVHD: clinical phenotype and response to upfront steroids. Bone Marrow Transplant 55, 165–171 (2020); 2. Kurtzberg, J. et al. A Phase 3, Single-Arm, Prospective Study of Remestemcel-L, Ex Vivo Culture-Expanded Adult Human 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



- As part of the broad license and collaboration agreement with Novartis for remestemcel-L, Mesoblast will retain full rights and economics for GVHD
- 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. At the current time it appears that the FDA review team will not agree to accelerated approval. However, 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
- If the current review team does not agree to accelerated approval, Mesoblast will request a further Type A meeting to initiate the well-established FDA dispute resolution pathway
- Under the terms of the license and collaboration agreement, Novartis has an option to become the commercial distributor for remestemcel-L in SR-aGVHD outside of Japan

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



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

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

# Partnerships and License Agreements

## Phase 3 Product Candidates for Heart Failure and Chronic Low Back Pain

### MPC-06-ID



- Strategic partnership to develop and commercialize MPC-06-ID in Europe & Latin America
- Mesoblast will receive up to US\$150 million in upfront and milestone payments prior to product launch
- Milestone payments could exceed US\$1 billion depending on patient adoption
- Mesoblast will also receive tiered double digit royalties on product sales

### CHRONIC LOW BACK PAIN - DEGENERATIVE DISC

PREVALENCE  
EUROPE  
~7.0 MILLION



### REVASCOR™



- Exclusive cardiovascular rights in China
- Mesoblast received US\$40 million in an upfront payment and equity placement
- Eligible for additional milestones and royalties

### CARDIOVASCULAR – CHRONIC HEART FAILURE

PREVALENCE  
CHINA  
~4.5 MILLION



# REVASCOR® for Advanced and End-Stage Heart Failure

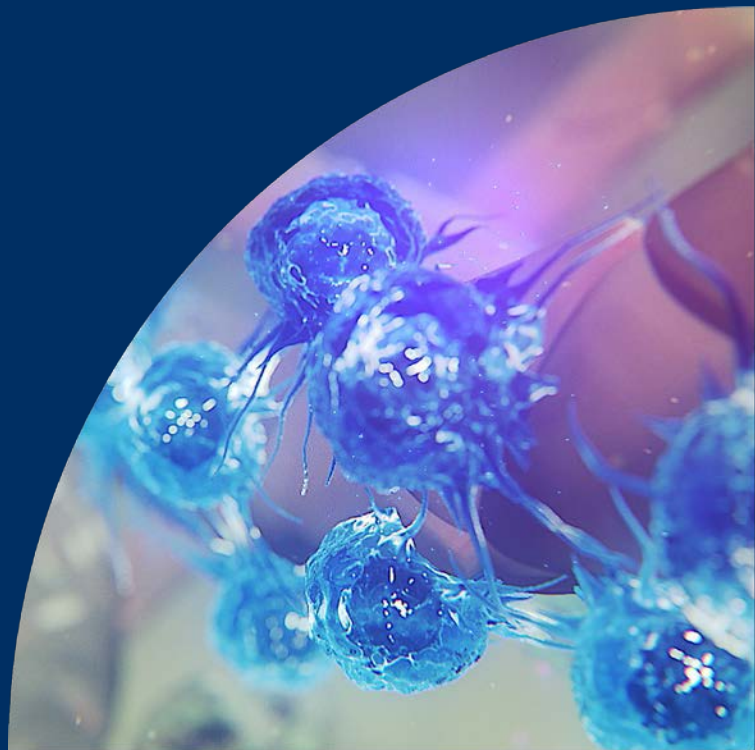


- In December 2019, the Phase 3 trial in advanced heart failure surpassed the number of primary endpoint events required for trial completion
  - Final study visits for all surviving patients have been completed
  - Ongoing quality review of all data is being completed at the study sites
  - Data readout 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**

