mesoblast

Annual General Meeting
Chief Executive's Presentation

NOVEMBER 29, 2021

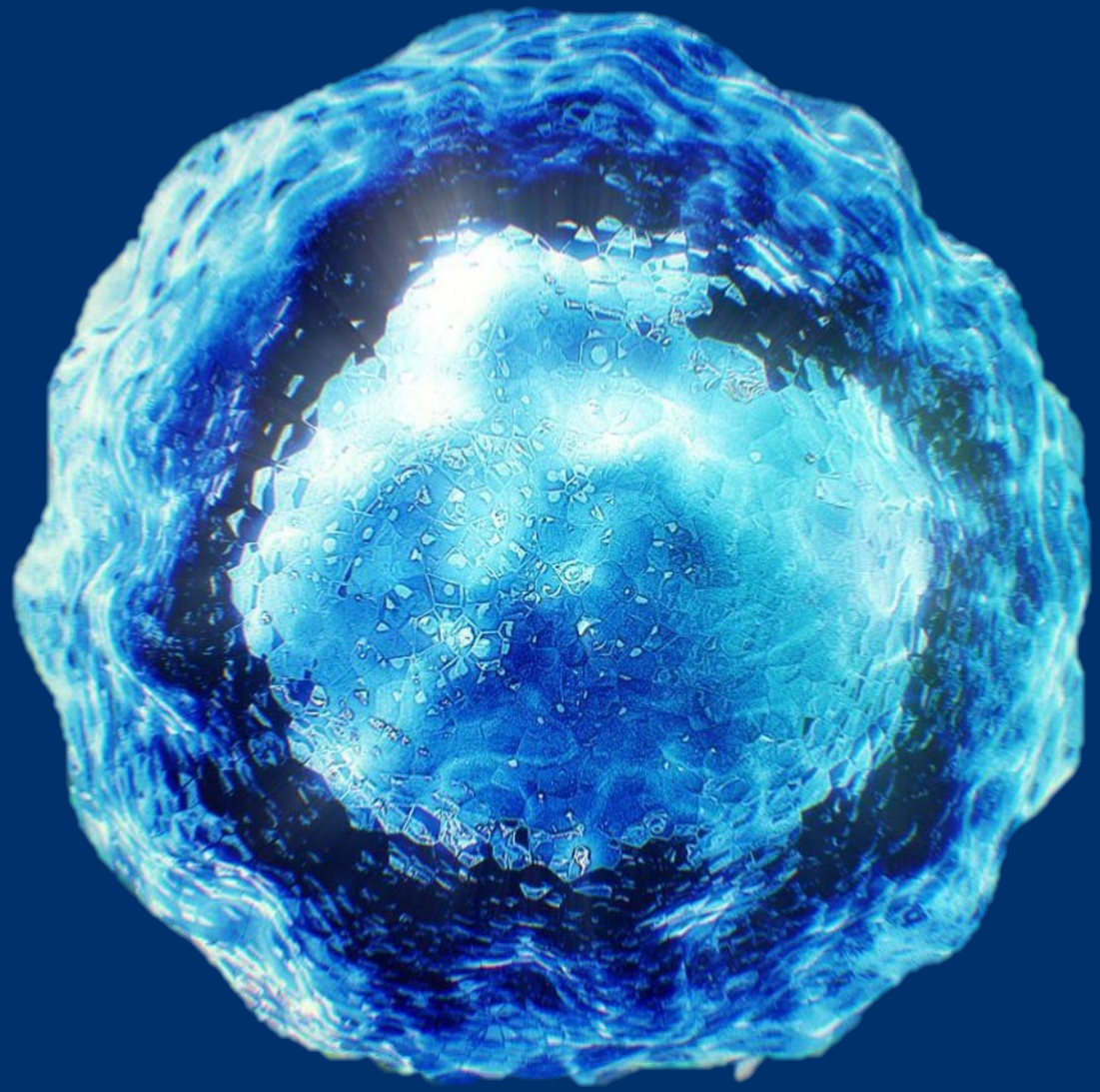
ASX: MSB; Nasdaq: MESO

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.

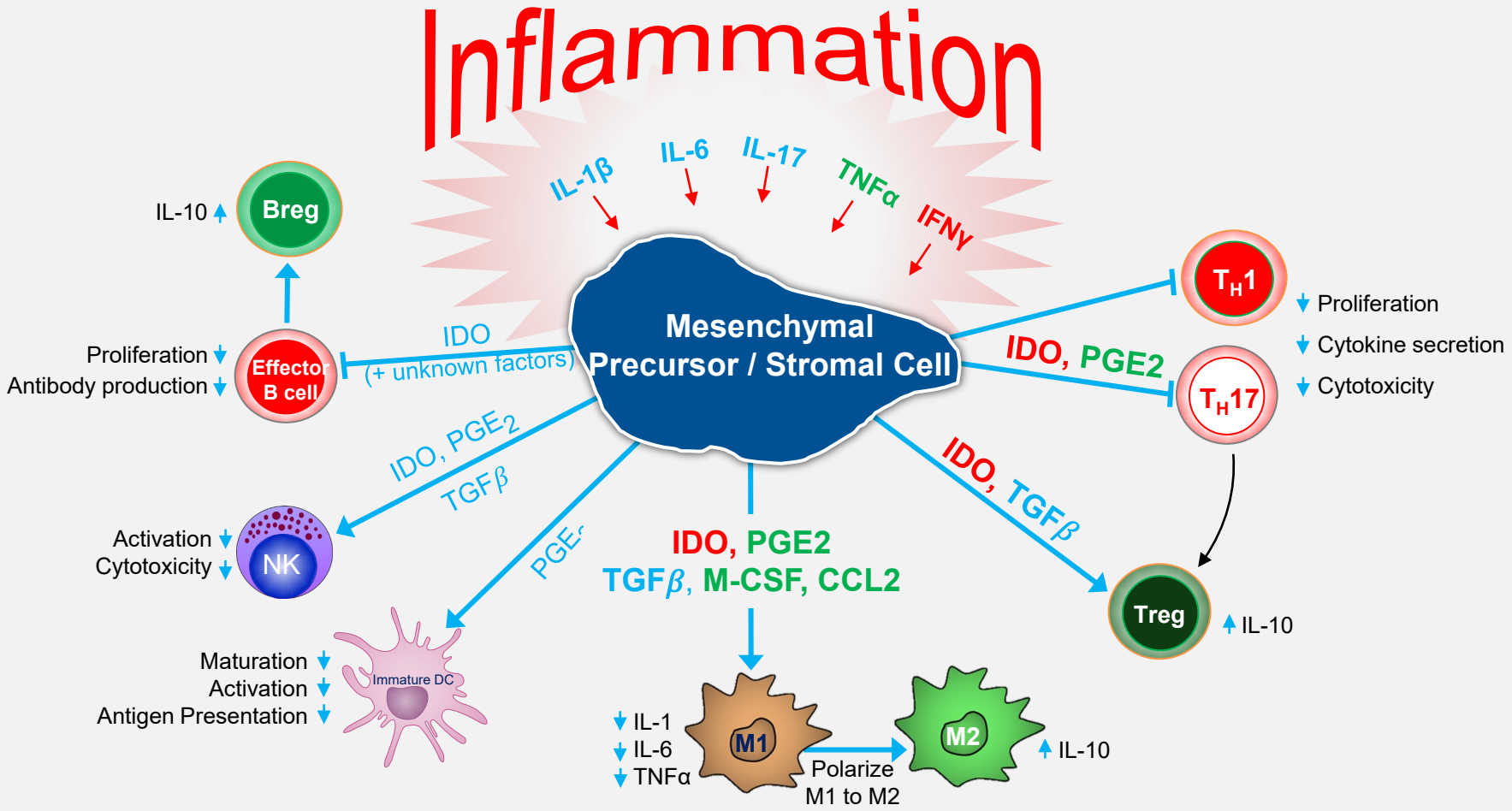
Our Mission

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



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



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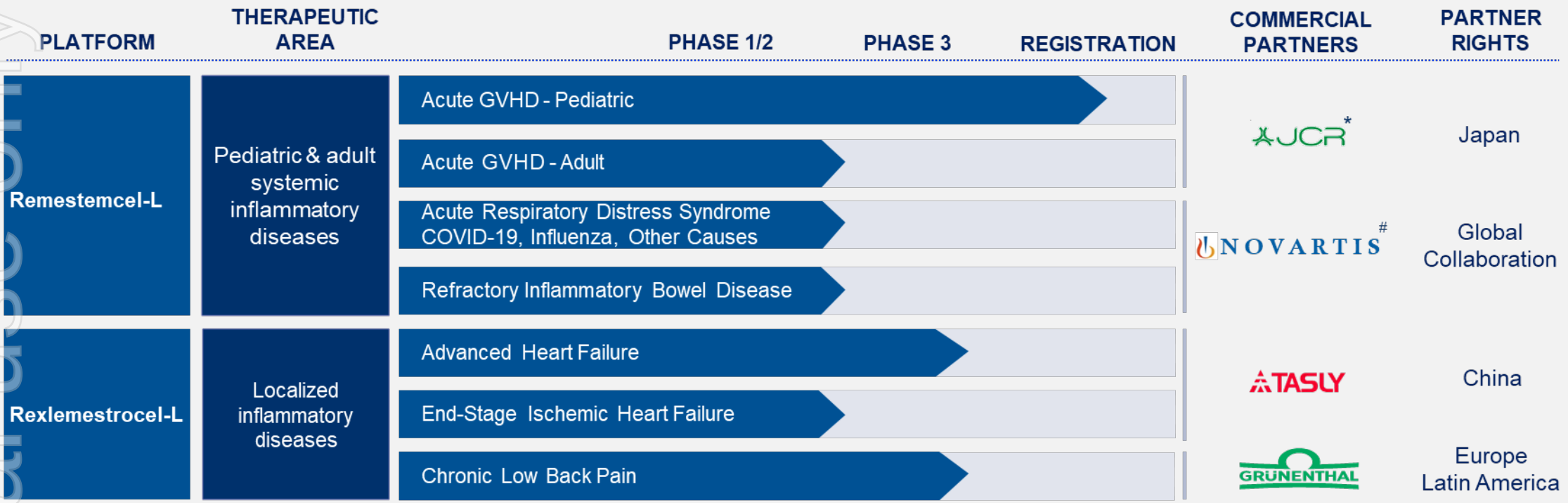
Pipeline



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

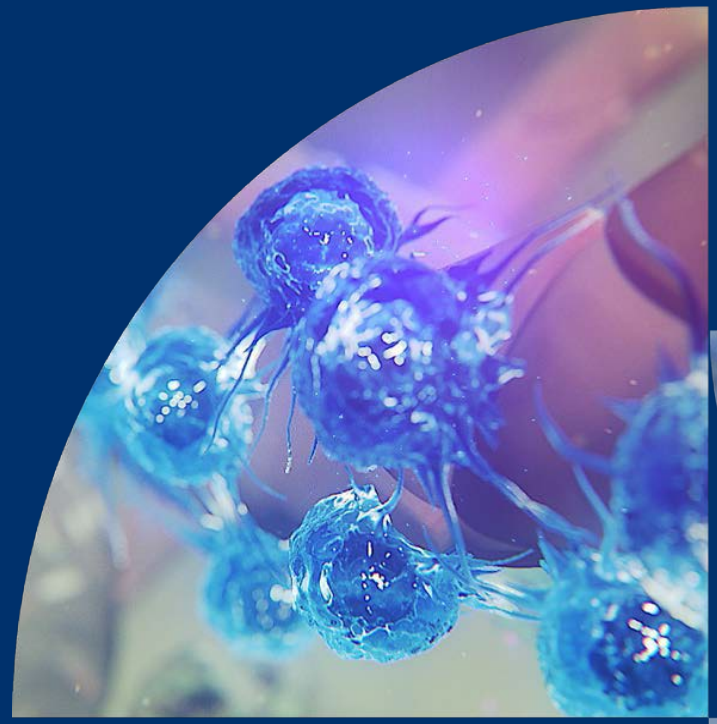
* Mesoblast has the right to use data generated by JCR Pharmaceuticals Co Ltd in Japan to support its development and commercialization plans for remestemcel-L in the US and other major healthcare markets, including for GVHD and Hypoxic Ischemic Encephalopathy

\# The agreement remains subject to certain closing conditions, including time to analyze the results from the COVID-19 ARDS trial

Financial Highlights

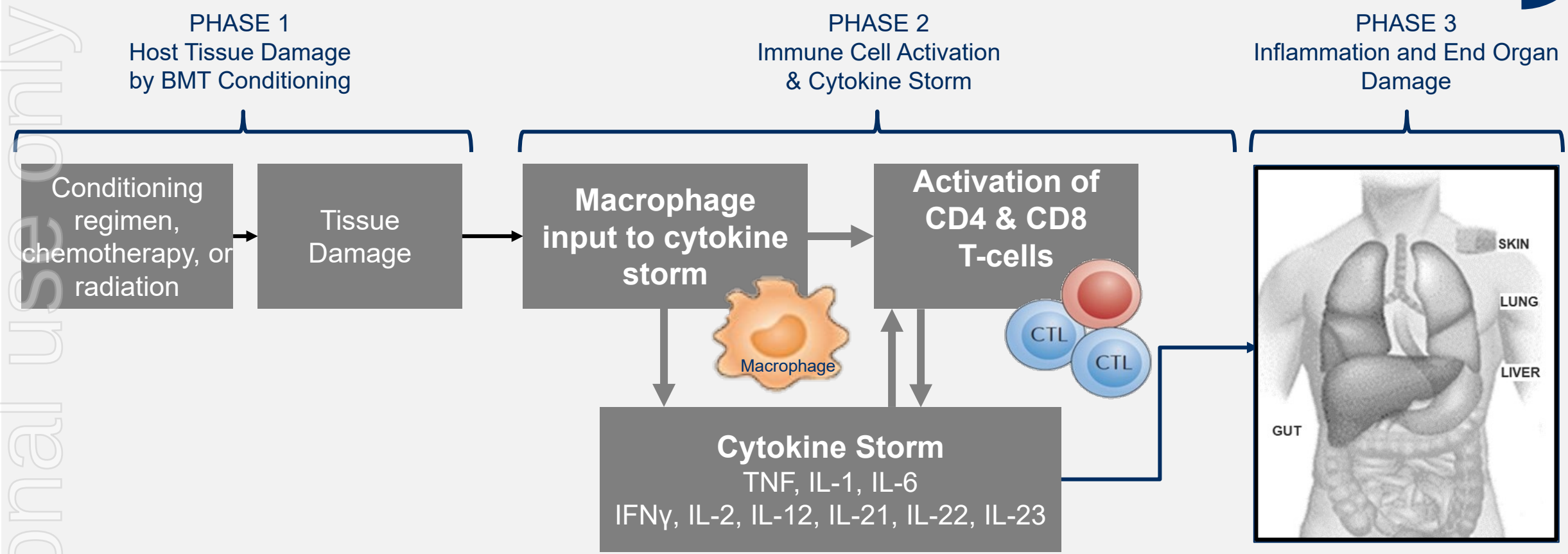
- Successfully entered into a refinancing and expansion of our senior debt facility with Oaktree Capital Management. The new US$90 million, 5-year secured facility has a 3-year interest only period after which time 40% of the principal amortizes over two years and a final payment due no later than November 2026
- Cash on hand at September 30, 2021, the most recent balance sheet date, was US$116.0 million
- Sales of TEMCELL® HS Inj.[1] in Japan by licensee JCR for the treatment of aGVHD have re-established a steady growth trajectory after plant capacity was expanded to meet growing demand[2]
  - Revenue from TEMCELL® royalties increased by 10% from the prior year period to US$7.2 million in the year ended June 30, 2021
  - In the most recent quarter ended September 30, 2021, revenues from TEMCELL® royalties were US$2.4 million, an increase of 22% on the previous quarter, and of 90% on the comparative quarter last year
- In the most recent quarter, net operating cash usage was US$19.6 million, a reduction of US$8.6 million on the comparative quarter
- Approximately 50% of net operating cash usage was to support the regulatory pathway to approval, manufacturing scale-up, and lifecycle management of the remestemcel-L platform

1. TEMCELL® HS Inj. is a registered trademark of JCR Pharmaceuticals Co. Ltd.
2. JCR Pharmaceuticals News Release: *Notice regarding Capital Expenditures to Increase Production Capacity at the Seishin Plant*. July 31, 2020



Remestemcel-L
- Acute Graft versus Host Disease (aGVHD)
- Acute Respiratory Distress Syndrome (ARDS)

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



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

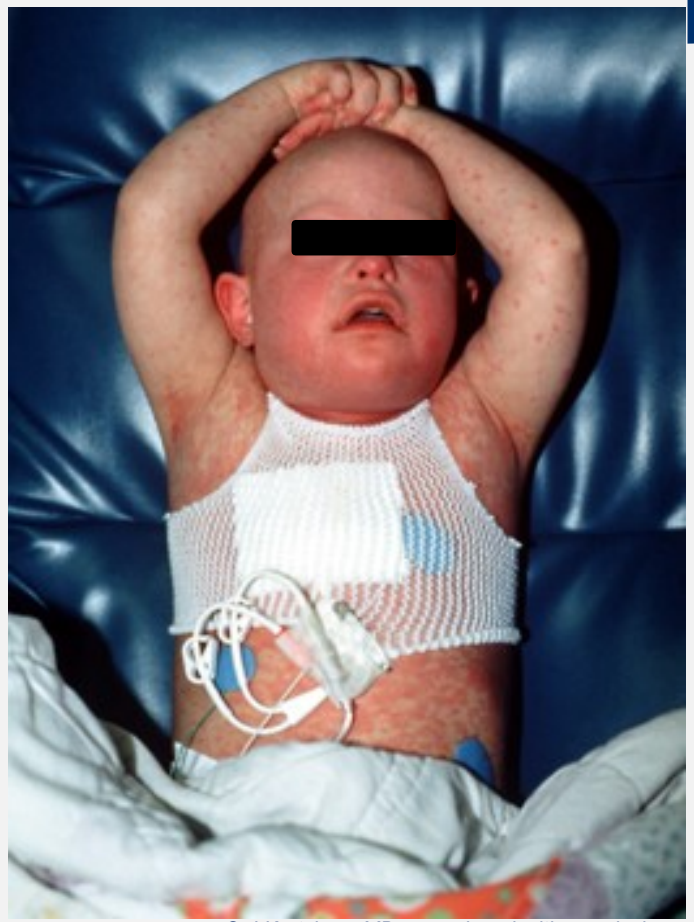
Children with Steroid-Refractory Acute GVHD at High Risk of Treatment Failure and Death

Extremely high unmet medical need

- More than 2,000 allogeneic BMTs in children and adolescents in US[1]
- Despite prophylaxis, ~50% will develop aGVHD[2]
- 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%[2-5] when involving gut and liver



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1. HRSA Transplant Activity Report, CIBMTR, 2019; 2. Westin, J., Saliba, RM., Lima, M. (2011) Steroid-refractory acute GVHD: predictors and outcomes. Advances in Hematology; 3. MacMillan, M.L. et al. Pediatric acute GVHD: clinical phenotype and response to upfront steroids. Bone Marrow Transplant 55, 165–171 (2020); 4. Jagasia, M. et al. Risk factors for acute GVHD and survival after hematopoietic cell transplantation. Blood (2012) 119 (1): 296-307; 5. 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: Prior Clinical Data in Children with SR-aGVHD

Consistent efficacy and safety outcomes in a total of 309 children from three studies:

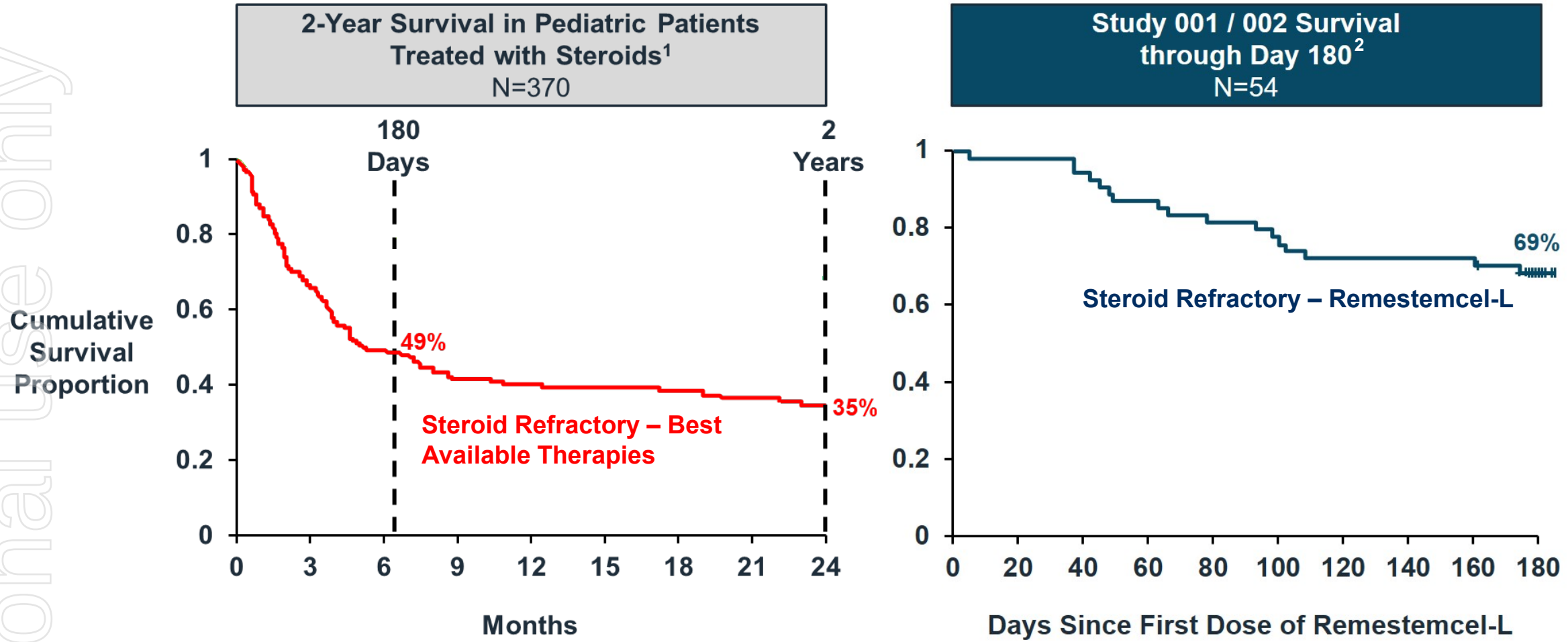
- Remestemcel-L was used as first-line therapy in a randomized controlled Phase 3 trial of 260 patients, with SR-aGVHD, including 27 children
- Remestemcel-L was used as salvage therapy in an expanded access program in 241 children with SR-aGVHD, 80% of whom had Grade C/D disease, and failed institutional 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[1] N=30[2]	Placebo N=13	Remestemcel-L N=14	Remestemcel-L N=241	Remestemcel-L N=54[3]
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.

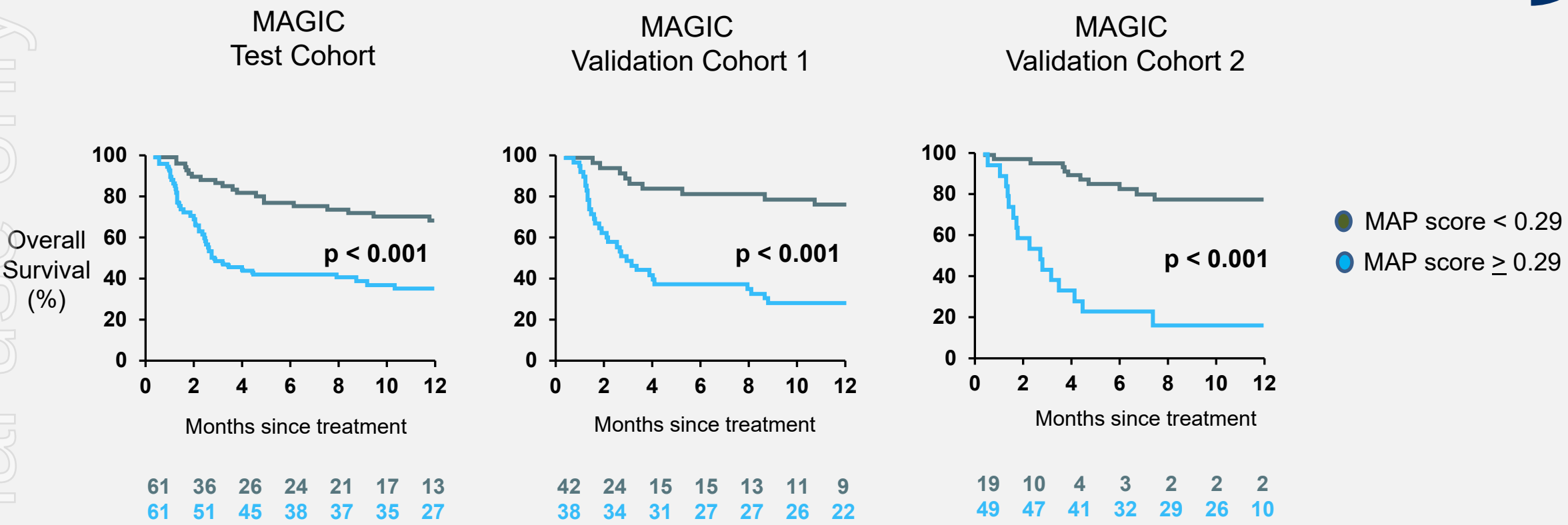
1. Mount Sinai Acute GVHD International Consortium (MAGIC) - a group of ten BMT centers throughout the US and Europe whose purpose is to conduct ground-breaking clinical trials in GVHD, including developing informative biorepositories that assist in developing treatments that can guide GVHD therapy.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



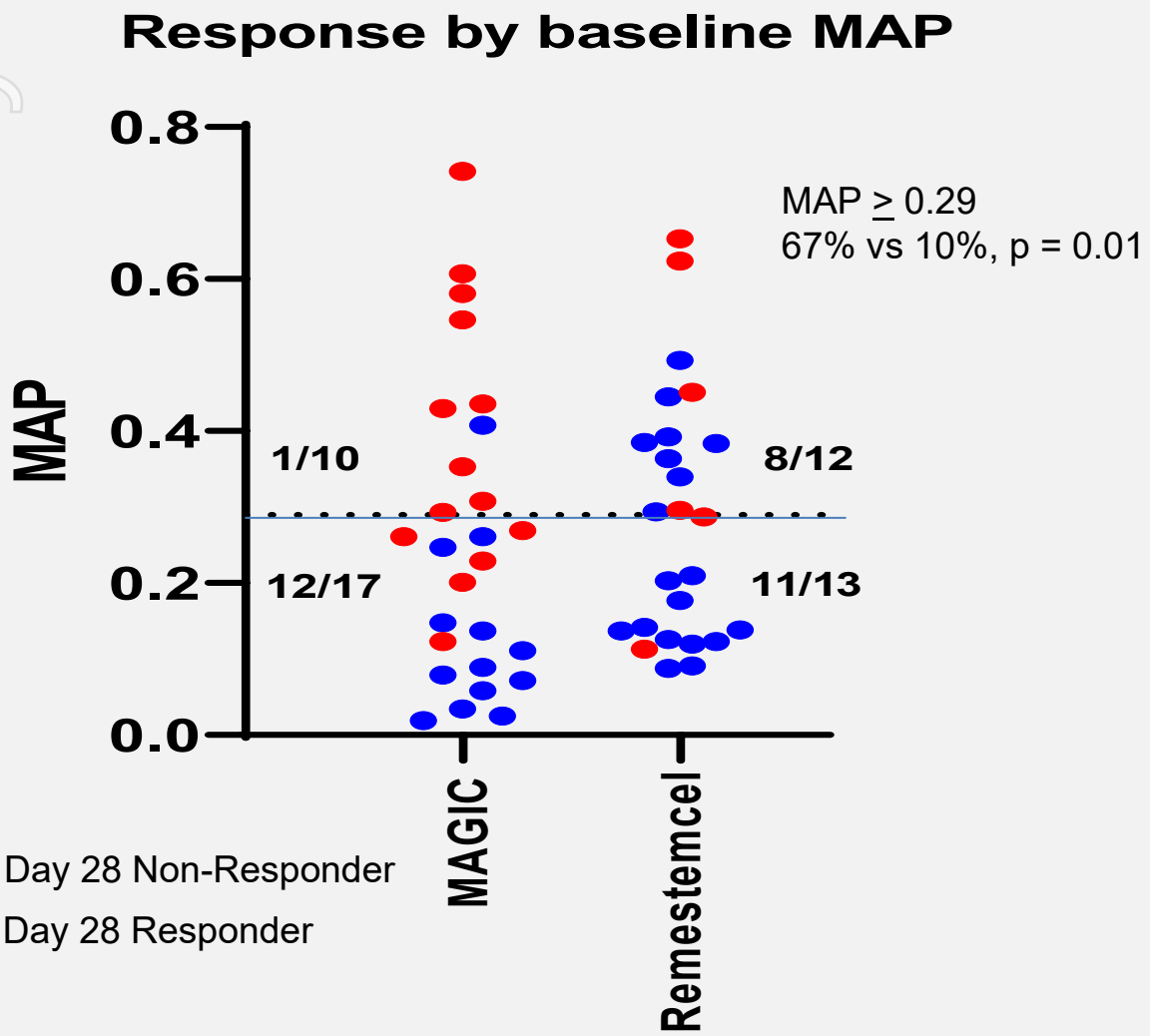
1. Adapted and redrawn from Figure 2 of MacMillan, M.L. et al. Pediatric acute GVHD: clinical phenotype and response to upfront steroids. Bone Marrow Transplant 55, 165–171 (2020); 2. Kurtzberg, J. et al. A Phase 3, Single-Arm, Prospective Study of Remestemcel-L, Ex Vivo Culture-Expanded Adult Human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

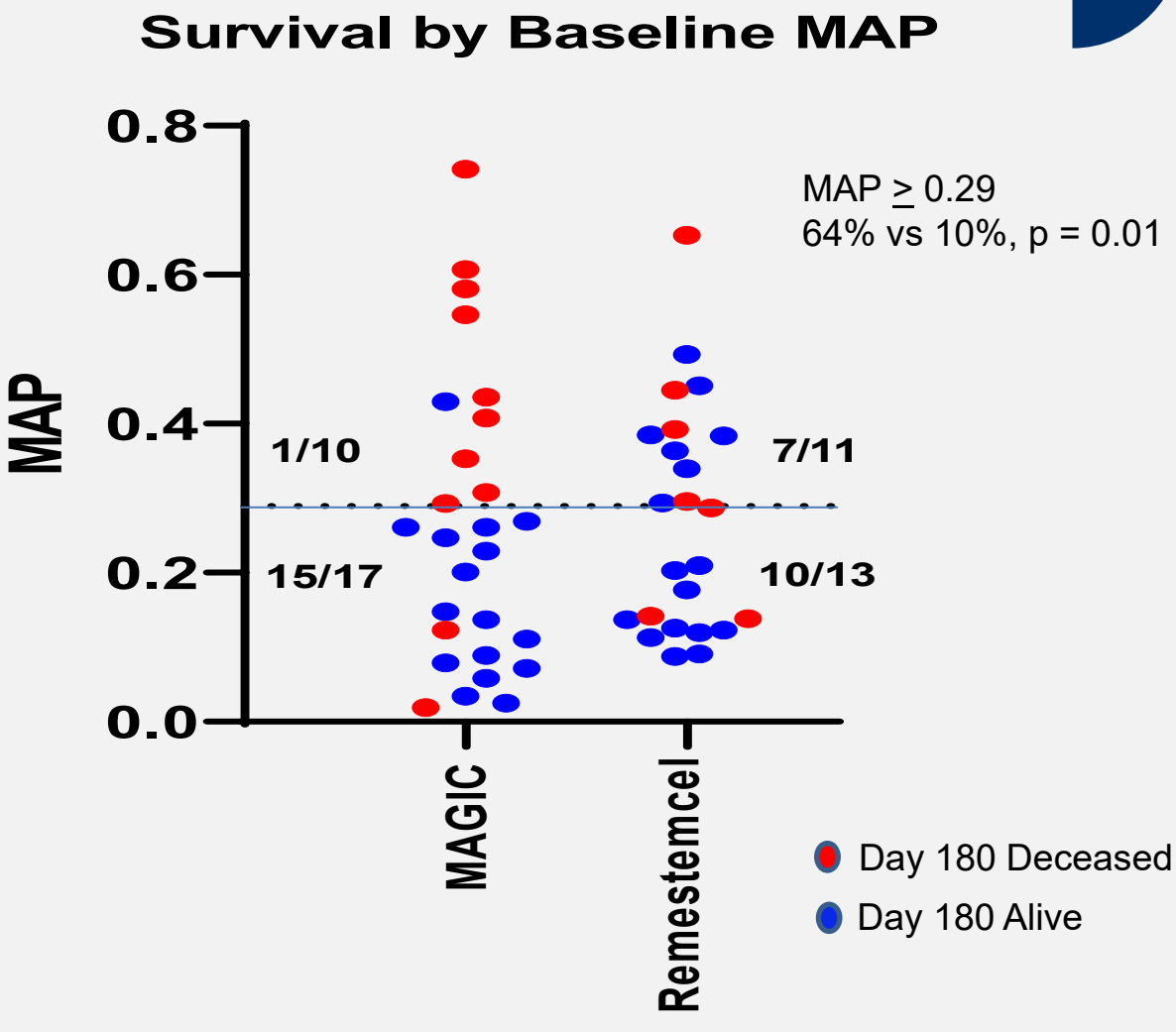
MAGIC Algorithm Probability Biomarker Score (MBS, MAP) > 0.29 is a Validated Threshold Identifying Acute GVHD Patients at High Risk of Non-Response to Treatment and Death



Major-Monfried H, et al. MAGIC biomarkers predict long-term outcomes for steroid-resistant acute GVHD. Blood 2018; 131 (25): 2846-2855

Remestemcel-L Treatment Results in Significantly Greater Day 28 Overall Responses and Day 180 Survival in Steroid-Refractory Patients with Baseline MAP ≥ 0.29





Kasikis S et al. Bone Marrow Transplantation 2021; 56:2869–2870.

Remestemcel-L: Regulatory & Commercial Update for SR-aGVHD

- These data provide further support for the proposed anti-inflammatory mechanism of action of remestemcel-L and its immunomodulatory activity in patients with SR-aGVHD, resulting in improved survival outcomes

- Mesoblast has an upcoming scheduled meeting with United States Food & Drug Administration's (FDA) Office of Tissues and Advanced Therapies (OTAT) to address the appropriateness of potency assays related to remestemcel-L's proposed anti-inflammatory mechanism of action

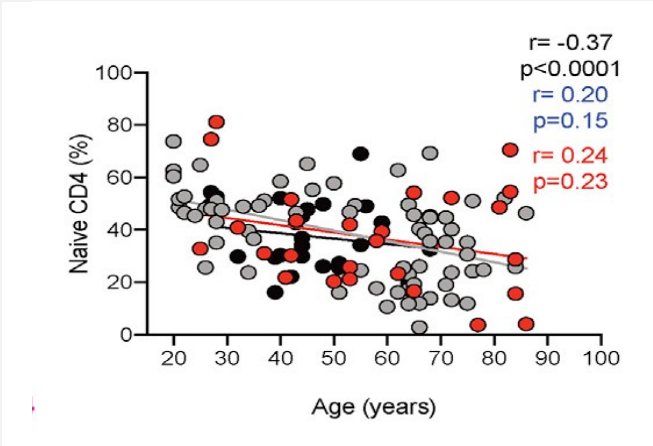
- These discussions are part of the ongoing process to resolve outstanding items with the goal of resubmission of the Biologics License Application (BLA) and ultimately achieving approval for remestemcel-L in the treatment of SR-aGVHD in children

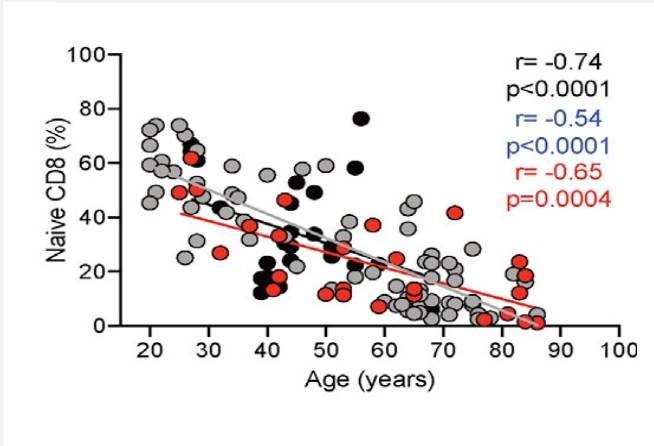
Overview – Remestemcel-L for ARDS due to COVID-19

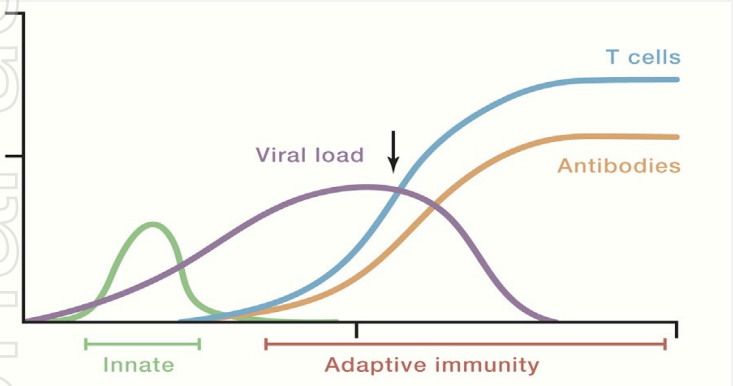
- COVID-19 is a respiratory virus with a high mortality due to a severe inflammatory condition of the lungs called acute respiratory disease syndrome (ARDS)
- ARDS is caused by cytokine storm in lungs of patients infected with COVID-19 and is the primary cause of death
- The extensive safety data of 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

Age > 65 years is Associated with Reduced Naïve T Cell Response to SARS-CoV-2, Delayed Viral Clearance and Greater Disease Severity

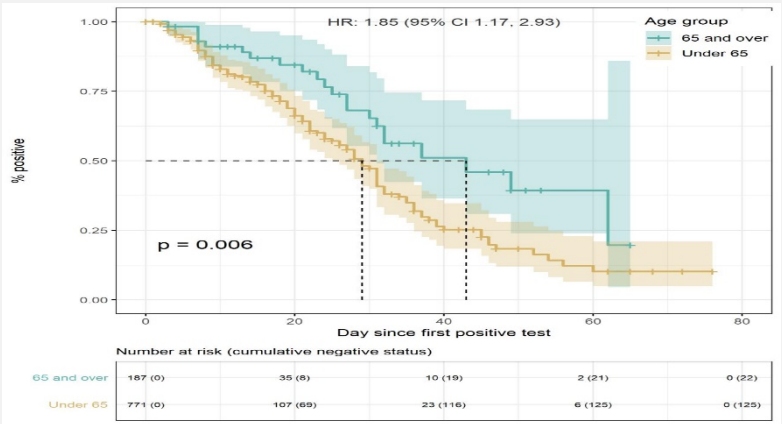
Naïve CD4 and CD8 T Cells reduced in age > 65





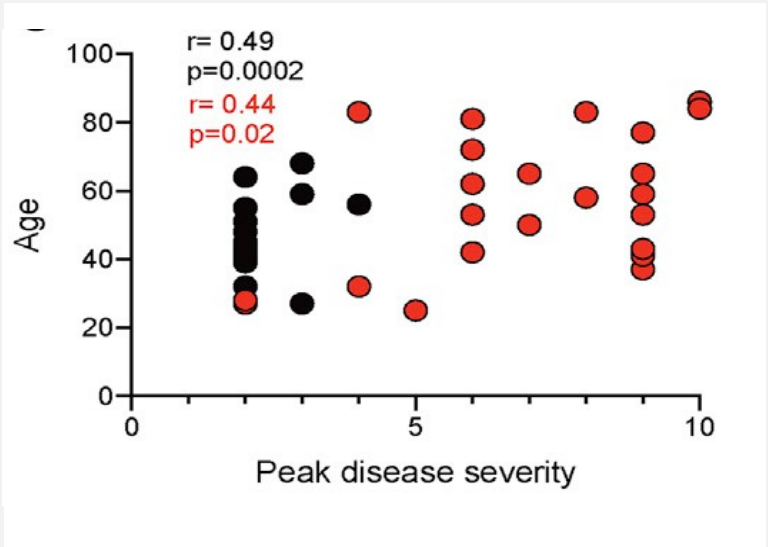


SARS-CoV-2-specific CD4 T cells and CD8 T cells limit disease severity



Median duration to negative status longer in subjects over 65 years (43 days) compared with under 65 years (29 days)

Age > 65 associated with greater COVID-19 peak disease severity



Rydyznski Moderbacher et al., Antigen-Specific Adaptive Immunity to SARS-CoV-2 in Acute COVID-19 and Associations with Age and Disease Severity. 2020, Cell 183, 996–1012; doi.org/10.1016/j.cell.2020.09.038
Stehlik P et al. Repeat testing for SARS-CoV-2: persistence of viral RNA is common, and clearance is slower in older people. Medical Journal of Australia 2021; doi:10.5694/mja2.51036

Clinical Experience with Remestemcel-L in COVID-19 ARDS

Emergency IND in Ventilator-Dependent COVID-19 ARDS

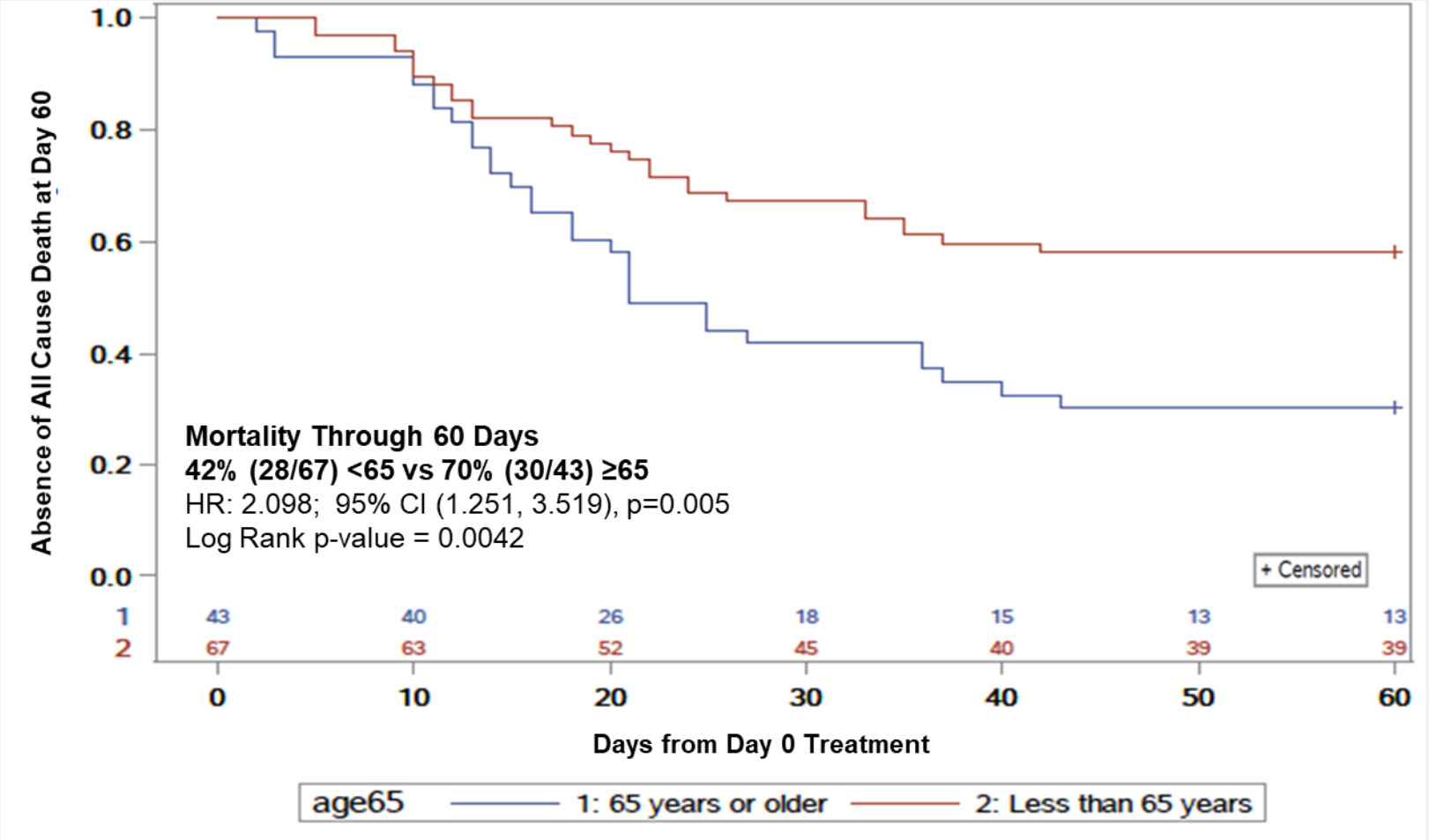
- **11 patients (10/11 were < 65 years)** with moderate/severe ARDS on ventilators at Mt. Sinai Hospital in New York
- Patients received two infusions of remestemcel-L 2 million cells/kg within five days
- Nine patients (82%) successfully came off ventilator and were discharged from the ICU
- Experience under the emergency IND informed the dosing regimen for the randomized controlled Phase 2b/3 trial, however no data on this dosing regimen in patients ≥ 65 years

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
- 222 patients enrolled before the study was stopped by DSMB as unlikely to meet primary endpoint of 43% overall mortality reduction
- **The median age increased from 59 in the first half of the trial to 67 in the second half (p<0.0001)**
- Preliminary results based on 60-day patient follow-up post randomization
- Pre-specified analysis of results stratified by age < or ≥ 65: 125 patients < 65 years, 97 patients ≥ 65 years

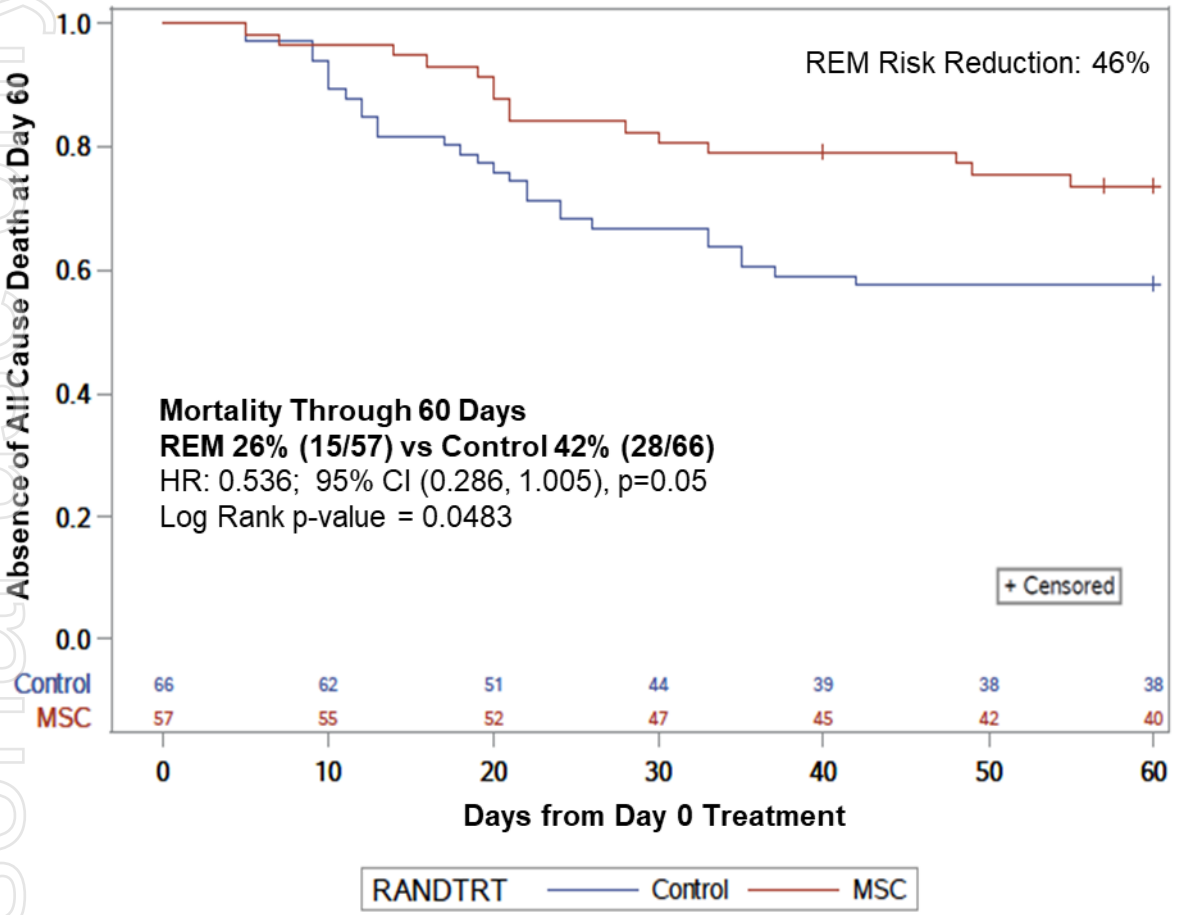
Greater Mortality through Day 60 in Control Patients Older than 65, Consistent with Other Trials

Controls Age < 65 vs ≥ 65 (n=110)

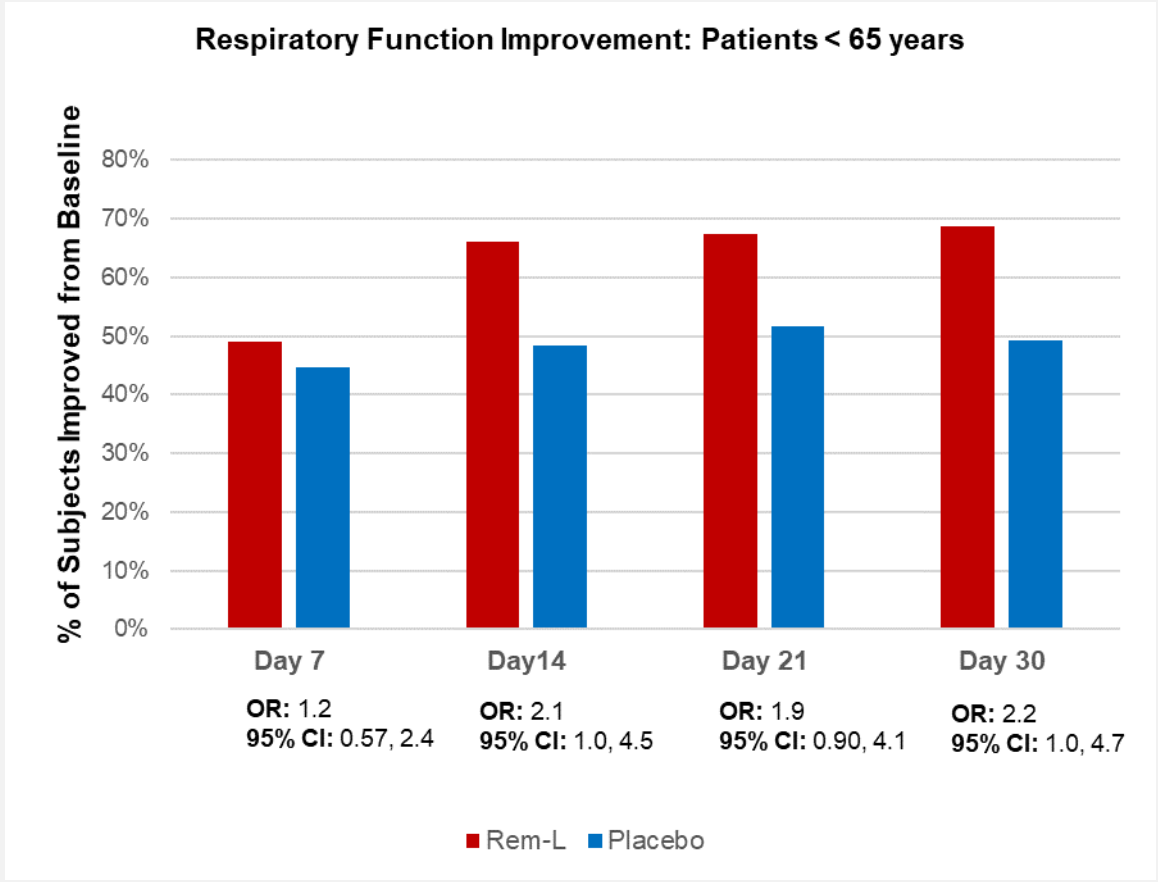


Greatest Mortality Reduction Improved ARDS Severity* Seen in Remestemcel-L Treated Patients < 65 years

Modified Intent to Treat (mITT) Patients **< 65 years old** (n=123), Remestemcel-L vs Control



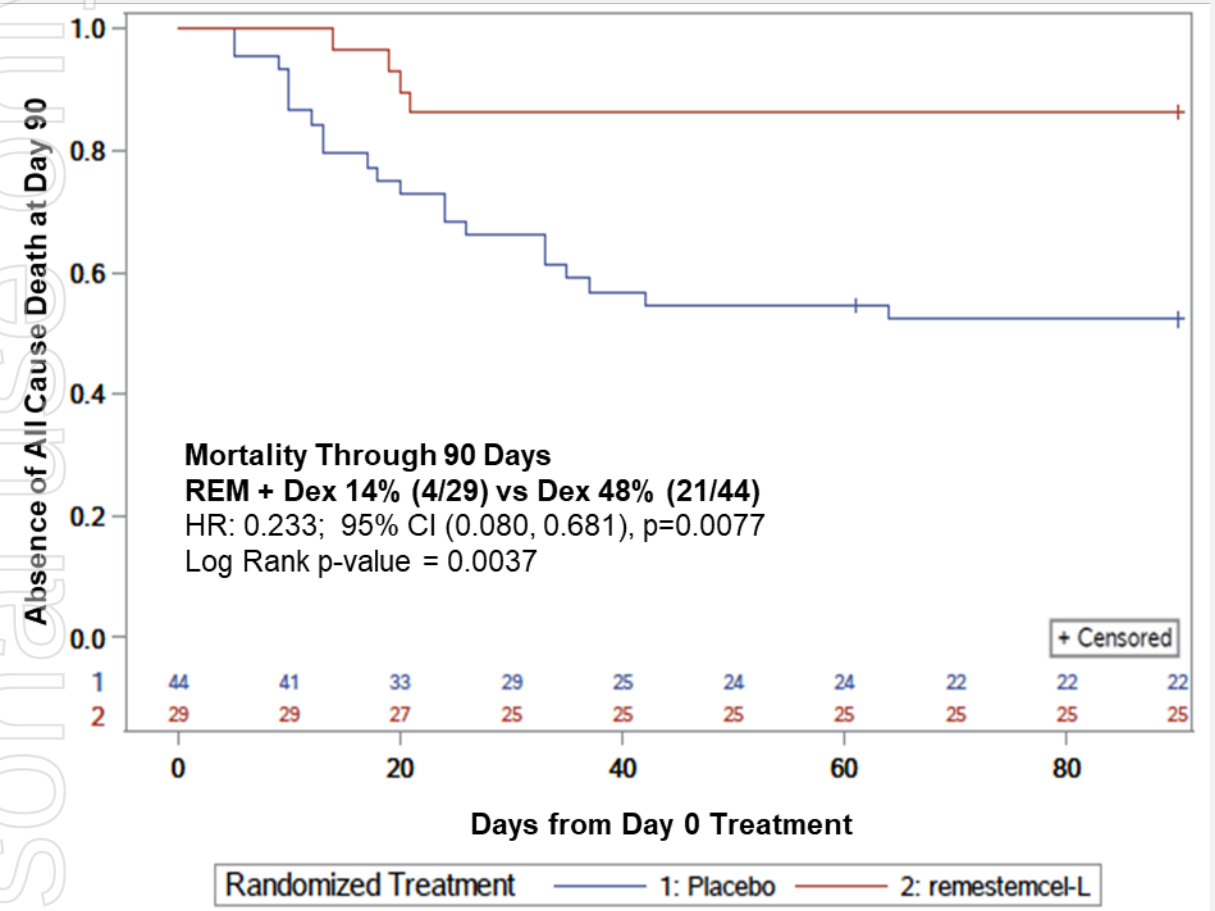
Treated Patients (mITT) **< 65 years old** (n=123) Remestemcel-L vs Control



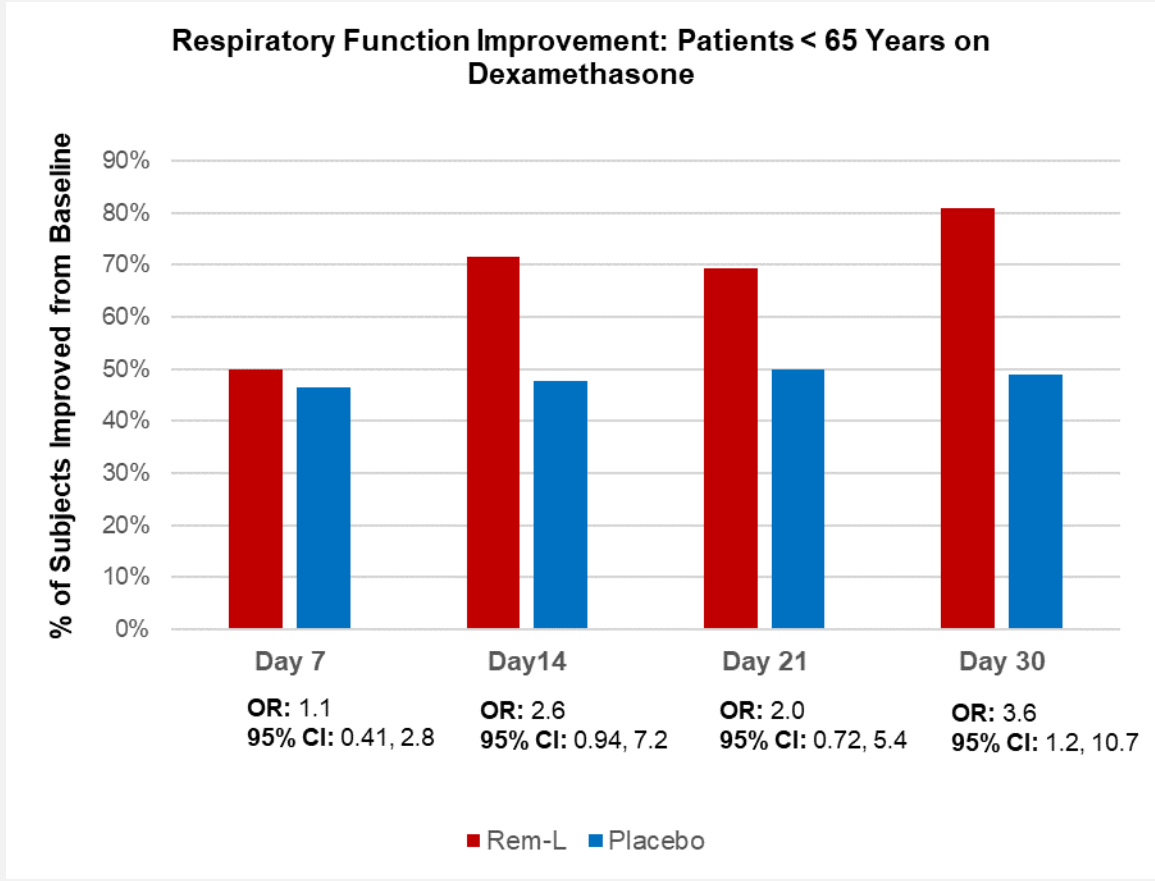
* Measured as resolution and/or improvement of ARDS as defined by the Berlin criteria at Days 7, 14, 21, and 30 post-randomizations

Remestemcel-L Plus Dexamethasone Shows Synergy in Mortality Reduction and Improvement in ARDS Severity in Exploratory Population < 65 years old

Treated Patients (mITT) < 65 years old on Dexamethasone (n=73) through 90-Days



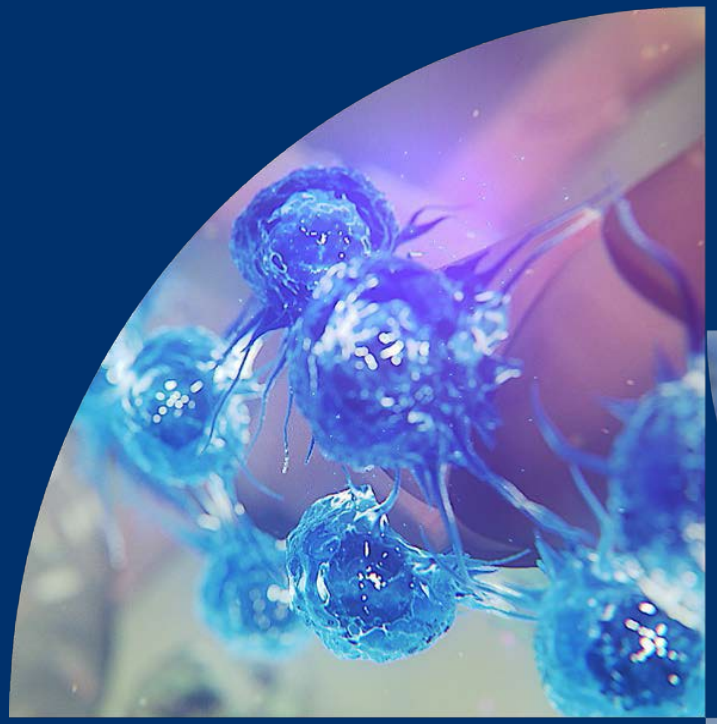
Treated Patients (mITT) < 65 years old on Dexamethasone (n=73)



* Respiratory Function Improvement measured as resolution and/or improvement of ARDS as defined by the Berlin criteria at Days 7, 14, 21, and 30 post-randomizations; Clinical Improvement was assessed based on a 7-point ordinal scale at baseline and on Days 7, 14, 21, and 30 and discharge from hospital

Remestemcel-L: Regulatory Pathway to Potential EUA for COVID-19 ARDS

- Mesoblast met with the FDA in regard to potential Emergency Use Authorization (EUA) for remestemcel-L in the treatment of ventilator-dependent patients with moderate or severe ARDS due to COVID-19
- The FDA advised that an additional clinical study in COVID ARDS, if statistically positive, could provide a dataset in conjunction with the recently completed 222 patient clinical study that might be sufficient to support an EUA
- FDA indicated that potency assays must be established and agreed prior to commencement of the proposed Phase 3 clinical trial
- FDA provided guidance that the existing COVID ARDS Investigational New Drug (IND) file and future submissions for remestemcel-L in this indication may continue to cross-reference manufacturing information in BLA for pediatric SR-aGVHD
- Mesoblast has an upcoming meeting with FDA's OTAT regarding potency assays for remestemcel-L in relation to SR-aGvHD, attributes which we believe to be also relevant to COVID ARDS
- Mesoblast plans to move forward with an additional Phase 3 trial in COVID-19 ARDS with the next step being to agree with the FDA the final protocol and potency assay



Rexlemestrocel-L

- Chronic Low Back Pain (CLBP)
- Chronic Heart Failure (CHF)

Rexlemestrocel-L: A New Paradigm for Treatment of Chronic Low Back Pain due to Degenerative Disc Disease

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

Minimal Treatment Options

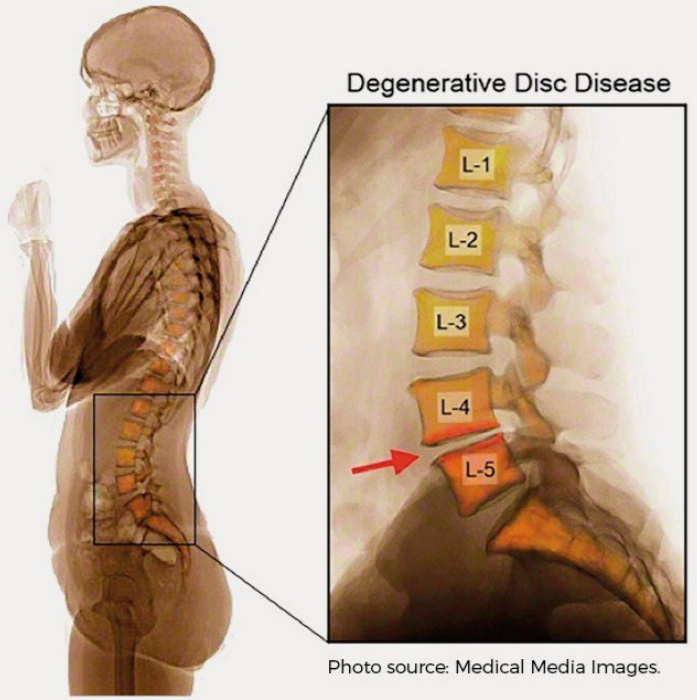
- Minimal treatment options for patients with chronic low back pain (CLBP) who fail conservative therapy include opioids and surgery
- 50% of opioid prescriptions are for CLBP

Unmet Need

- Disease modifying therapy for durable improvement in pain and function has potential to prevent progression to opioid use or 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 [3,4,5]
- MPC-06-ID development program targets over 3.2m patients in U.S. and 4m in E.U.5 with moderate to severe disease



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. Simon, J., McAuliffe, M., Shamim, F. (2015) Discogenic Low Back Pain. Phys Med Rehabil Clin N Am 25 (2014)305–317., 3.Decision Resources: Chronic Pain December 2015., 4. LEK & NCI opinion leader interviews, and secondary analysis., 5. Navigant: Commercial Assessment for a Proprietary Cell-Based Therapy for DDD in the U.S. and the EU3 – August 2014., 6. HealthCare Utilization and Cost of Discogenic Lower Back Pain in the US – Anthem/HealthCore.

Single Injection of Rexlemestrocel-L + HA in Phase 3 Trial, Results in at Least Two Years of Pain Reduction with Opioid Sparing Activity in Patients with CLBP

- Achievement of substantial and durable reductions in CLBP through 24 months across the entire evaluable study population (n=391) compared with saline controls
- Greatest pain reduction observed in the pre-specified population with CLBP of shorter duration than the study median of 68 months (n=194), substantially greater reduction at all time points (1, 3, 6, 12, 18 and 24 months) compared with saline controls
- Significantly greater pain reduction in the pre-specified patient subset of opioid users (n=168) at all time-points compared with saline controls and by 24 months there was a 40% reduction in opioid use
- Rexlemestrocel-L may provide a safe, durable, and effective opioid-sparing therapy for patients with chronic inflammatory back pain due to degenerative disc disease, and that greatest benefits are seen when administered earlier in the disease process

Chronic Heart Failure: Rising Incidence & High Mortality

- Cardiovascular disease remains the leading cause of death in the United States[1]
- Heart failure affects 6.5 million patients in the US and 26 million patients globally. As populations age, the prevalence is increasing[2]
- Chronic heart failure (CHF) is a progressive disease with a high mortality that approaches 50% at 5 years[2,3], and at least 75% after an initial hospitalization[4]
- Patients with heart failure are also at high risk of recurrent major adverse cardiac events involving large vessels (heart attacks / strokes)

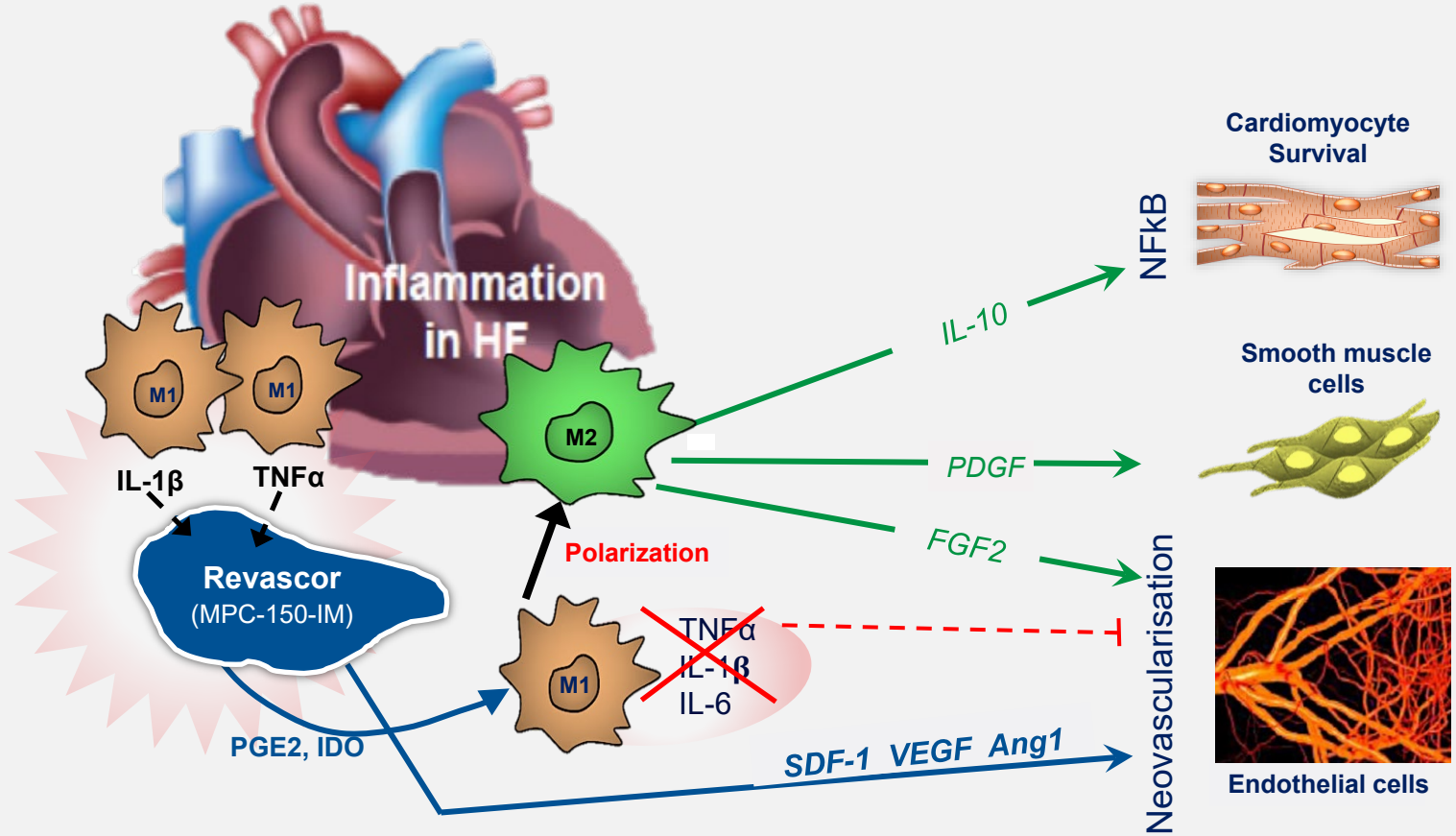
New therapies for chronic heart failure reduce recurrent hospitalizations due to cardiac decompensation, however they do not materially improve cardiac mortality or major ischemic events (heart attacks/strokes)

1. Muntner BEJ, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation.* Feb 19, 2019. 2. United States Food & Drug Administration. Treatment for Heart Failure: Endpoints for Drug Development. Draft Guidance. June 2019. 3. Taylor CJ, et al. Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population-based cohort study. *BMJ.* 2019;364:l223. 4. Shah KS, et al. Heart Failure with Preserve, Borderline, and Reduced Ejection Fraction; 5-Year Outcomes. *JACC*. 2017;Nov12.

Proposed Mechanism of Action of Intra-Cardiac MPC Administration in Treatment of both Heart Failure & Large Vessel Atherosclerosis

Mesenchymal precursor cells (MPC) key mechanisms of action thought to beneficially impact the heart and the systemic vasculature:

- Reduction in cardiac and systemic inflammation
- Reversal of endothelial dysfunction
- Induction of microvascular network within viable heart muscle
- Reduction in heart muscle death



Borow KM, Yaroshinsky A, Greenberg B, Perin E. Phase 3 DREAM-HF Trial of Mesenchymal Precursor Cells in Chronic Heart Failure: A Review of Biological Plausibility and Implementation of Flexible Clinical Trial Design. *Circ Res.* 2019;125:265-281

Late Breaking Presentation at American Heart Association Annual Meeting

- Data from the randomized, controlled Phase 3 trial of rexlemestrocel-L in 565 patients with NYHA class II and class III HFrEF were presented as a late breaking presentation at the AHA annual Scientific Sessions during a featured program titled ‘Building on the Foundations of Treatment: Advances in Heart Failure Therapy’

- The trial’s co-principal investigator Dr Emerson Perin, Medical Director of Texas Heart Institute, and Clinical Professor, Baylor College of Medicine, gave the presentation titled *‘Randomized Trial of Targeted Transendocardial Delivery of Mesenchymal Precursor Cells in High-Risk Chronic Heart Failure Patients with Reduced Ejection Fraction’*

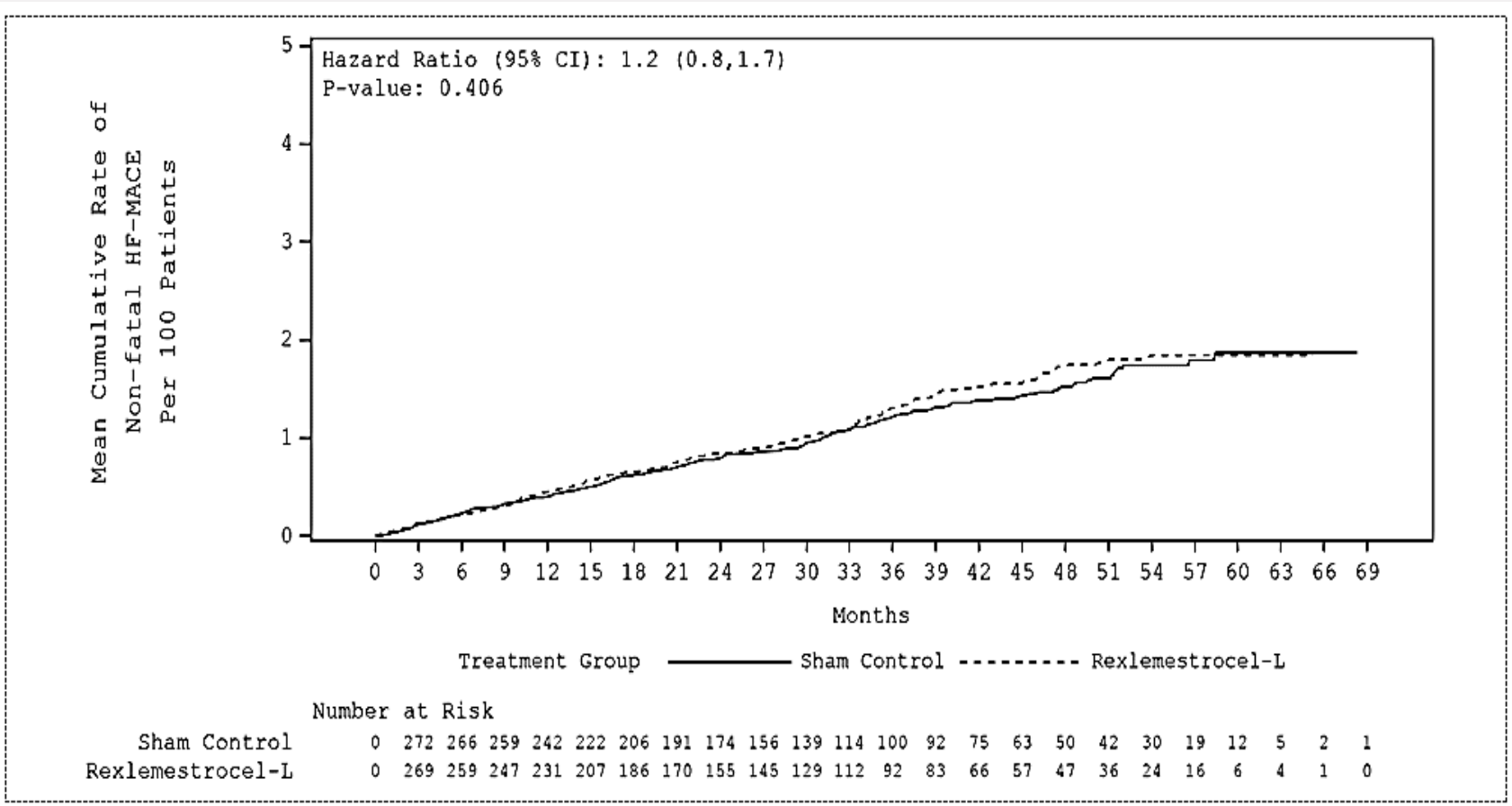
- Newly presented data from the landmark study showing a significant relationship between presence of systemic inflammation as quantified by high-sensitivity C-reactive protein (hs-CRP) and treatment benefit with rexlemestrocel-L on risk of cardiovascular mortality, heart attacks or strokes

Rexlemestrocel-L Did Not Further Reduce Frequency of Hospitalization for Worsening HF Symptoms Over Maximal Standard of Care

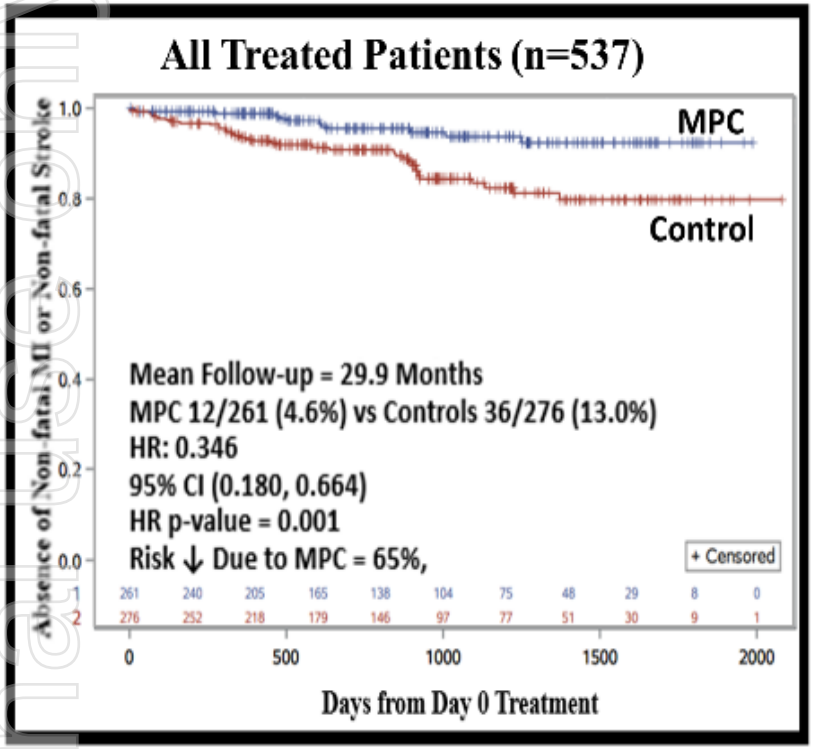
All Patients (n=537)

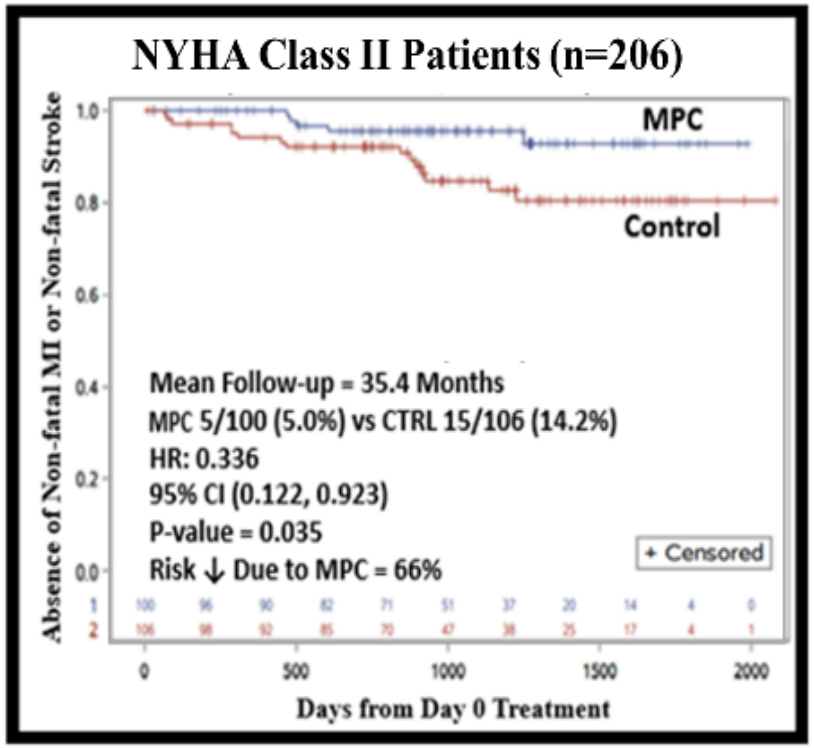
HR: 1.2

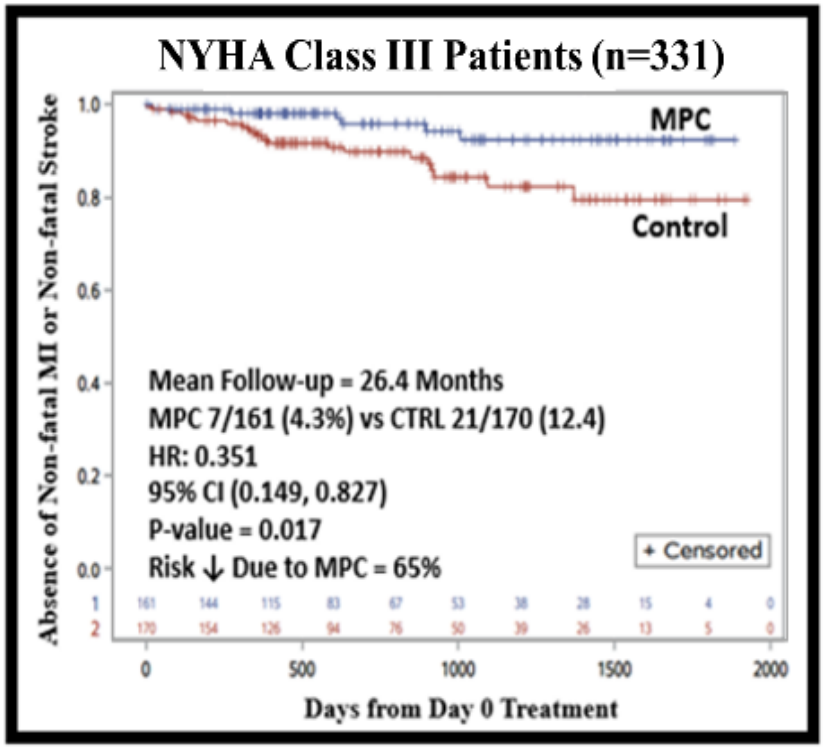
p=0.4



Rexlemestrocel-L Reduced Incidence of Non-fatal MI or Non-fatal Stroke Over Standard of Care Alone

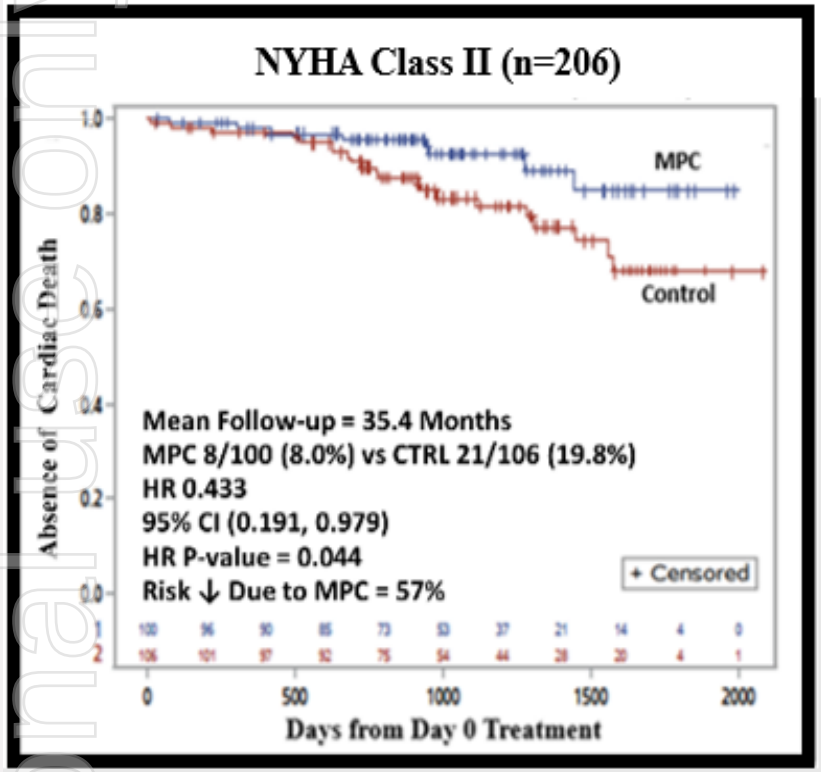


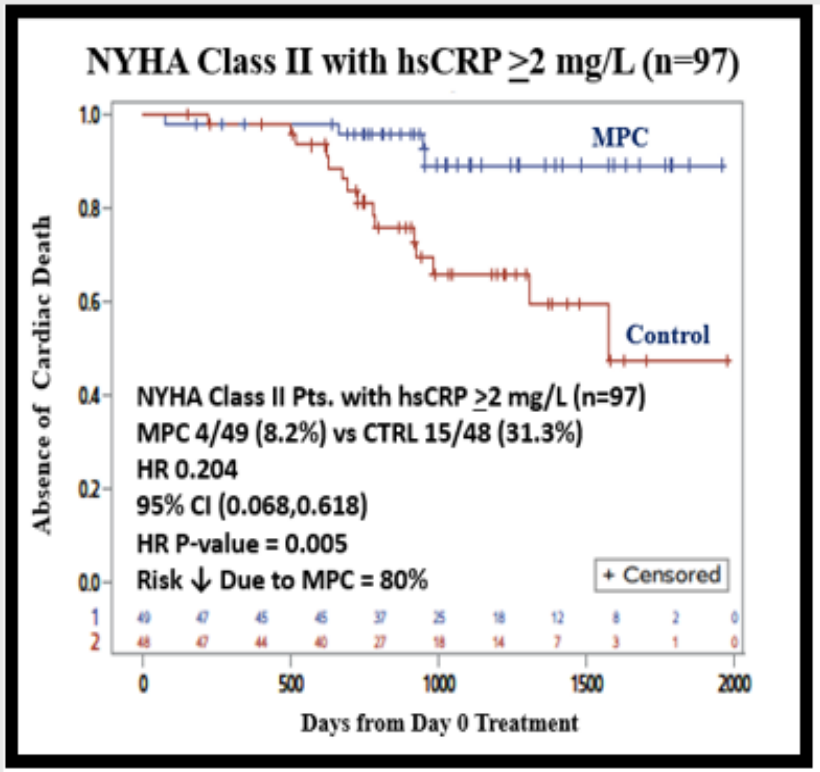


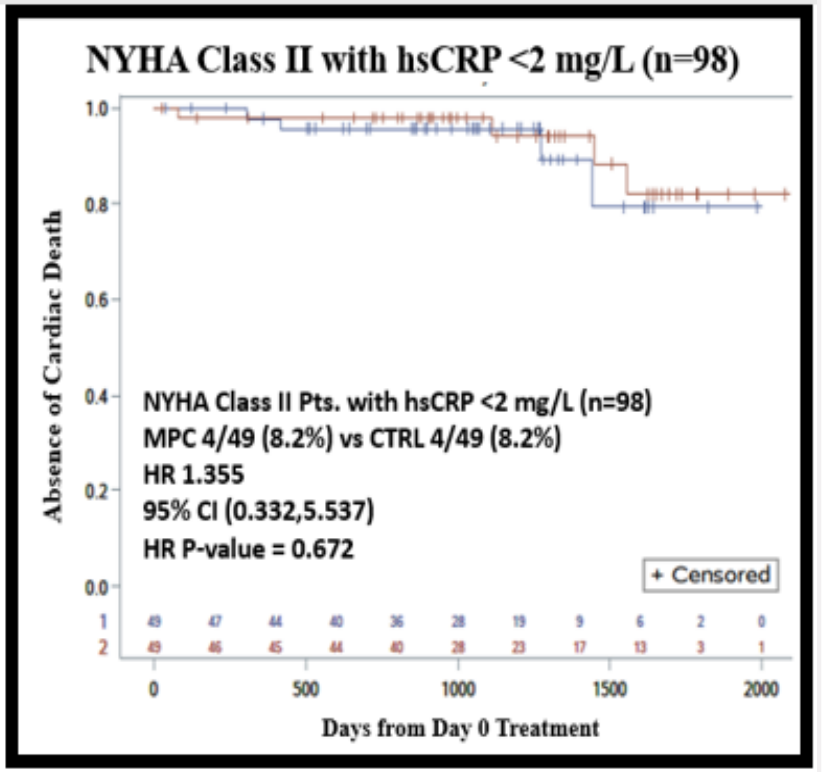


Rexlemestrocel-L Reduced Incidence of Cardiac Death, Particularly in Patients with Inflammation

Time-to-Cardiac Death in NYHA Class II Patients

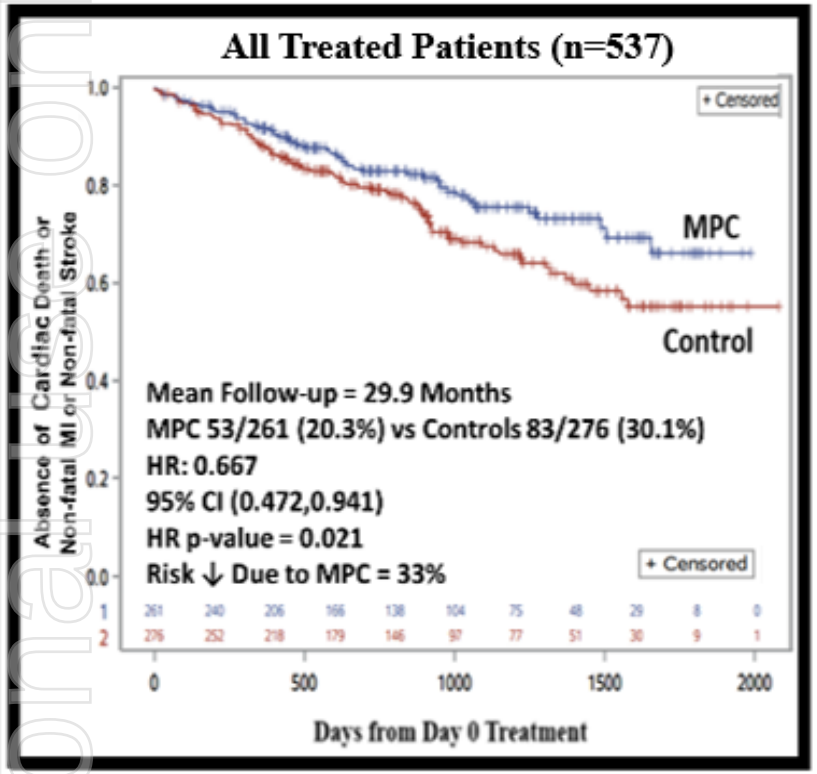


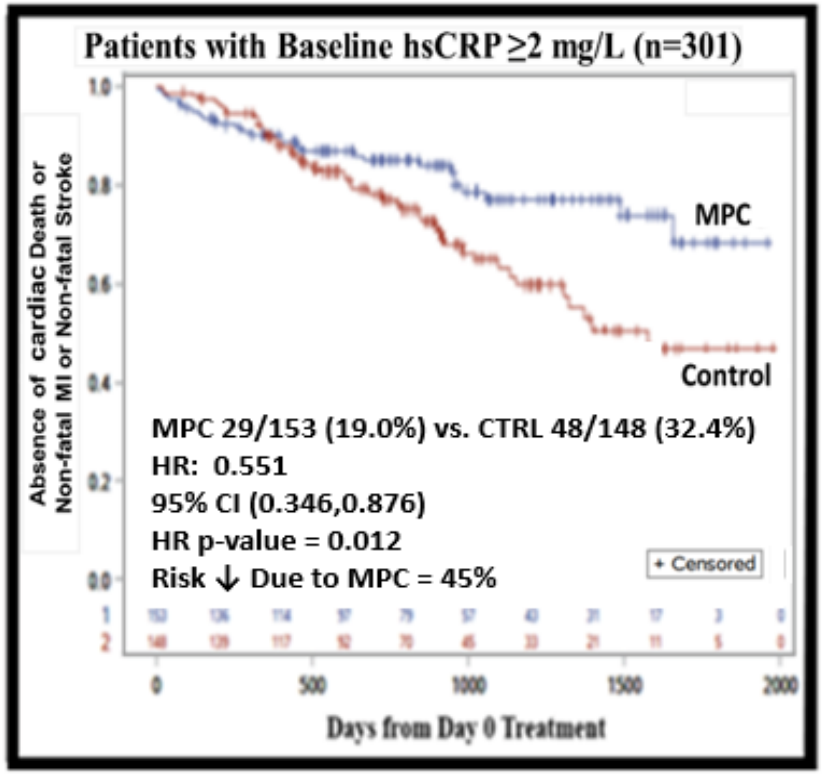


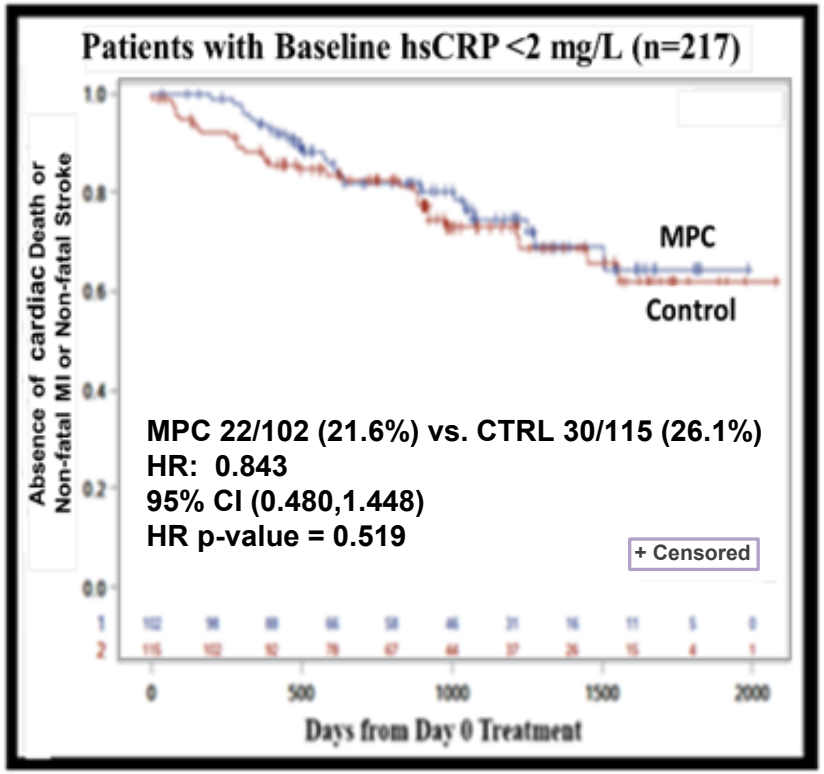


Rexlemestrocel-L Reduced Incidence of 3-Point MACE (Cardiac Death or MI or Stroke) in all 537 Treated Patients, and Especially in Those with Inflammation

Time-to-First-Event for Cardiac Death or Non-fatal MI or Non-fatal Stroke

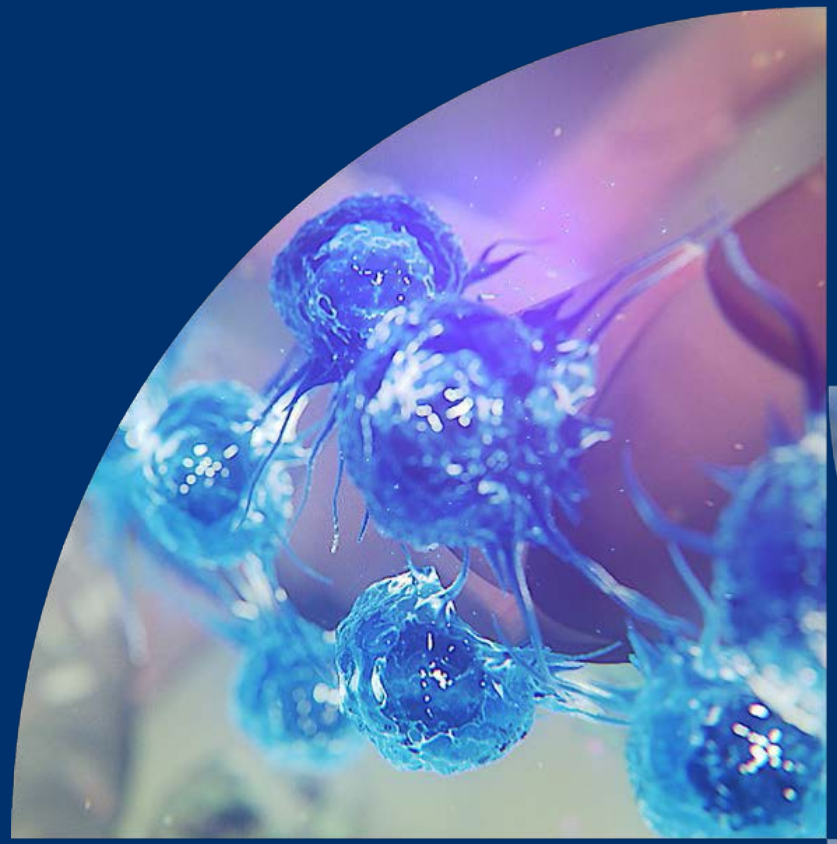






Conclusions

- Transendocardial delivery of 150 million allogeneic MPCs (rexlemestrocel-L) was safe and did not elicit any clinically meaningful immune-related responses
- Over a mean follow-up of 30 months, a single rexlemestrocel-L dose added to maximal standard of care significantly reduced:
  - Non-fatal MI or non-fatal stroke in NYHA class II & class III
  - Cardiac death in NYHA class II
  - Composite of cardiac death or non-fatal MI or non-fatal stroke in all 537 patients
  - Benefits of MPC therapy were most evident in 301 patients with baseline inflammation (plasma hsCRP ≥2 mg/L)
  - Rexlemestrocel-l did not further reduce frequency of hospitalization for worsening HF symptoms over maximal standard of care



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