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

# Form 6-K

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

**For the month of November 2018**

**Commission File Number 001-37626**

# Mesoblast Limited

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

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

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

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

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

Form 20-F ☑ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Yes ☐ No ☑

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Yes ☐ No ☑

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

On November 11, 2018, Mesoblast Limited filed with the Australian Securities Exchange a new release announcement, which is attached hereto as Exhibit 99.1, and is incorporated herein by reference.

On November 12, 2018, Mesoblast Limited filed with the Australian Securities Exchange a new investor presentation, which is attached hereto as Exhibit 99.2, and is incorporated herein by reference.

**SIGNATURES**

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

MESOBLAST LIMITED

/s/ Charlie Harrison

Charlie Harrison
*Company Secretary*

Dated: November 15, 2018

**INDEX TO EXHIBITS**

| Item | |
|---|---|
| 99.1 | Press release of Mesoblast Ltd, dated November 11, 2018. |
| 99.2 | Investor presentation of Mesoblast Ltd, dated November 12, 2018. |

asx announcement

mesoblast
the regenerative medicine company

## CLINICALLY MEANINGFUL OUTCOME IN NIH TRIAL OF MPC-150-IM FOR HEART FAILURE LVAD RECIPIENTS PROVIDES PATHWAY FOR POTENTIAL REGULATORY APPROVAL

**New York, USA; November 11, 2018 and Melbourne, Australia; November 12, 2018:** Mesoblast Limited (ASX:MSB; Nasdaq:MESO) today announced that results from a 159-patient randomized, sham-controlled Phase 2 trial in end-stage heart failure patients implanted with a left ventricular assist device (LVAD) showed that Mesoblast's allogeneic cell therapy candidate MPC-150-IM achieved significant reduction in major gastrointestinal (GI) bleeding episodes and related hospitalizations, a complication affecting up to 40% of LVAD recipients.[1]

This clinically meaningful outcome confirms results seen in an earlier 30-patient pilot trial[2] which provided the basis for the Regenerative Medicine Advanced Therapy (RMAT) designation granted to Mesoblast by the United States Food and Drug Administration (FDA) for MPC-150-IM as adjunctive therapy to LVAD implantation.

Under the RMAT designation, Mesoblast received specific guidance from the FDA that reduction in major GI bleeding episodes and related hospitalizations in the current trial is a clinically meaningful outcome with a high unmet need that could meet requirements for an approvable regulatory endpoint. In contrast, the FDA advised that the primary endpoint in the current trial of temporary weaning from full LVAD support is considered a biomarker and is not a clinically meaningful outcome in and of itself.

Results from the United States National Heart, Lung and Blood Institute (NHLBI)-sponsored trial were presented today by the study's independent lead investigator Dr Francis Pagani, Surgical Director of the Adult Heart Transplant Program and Program Director for the Center for Circulatory Support, University of Michigan Medical Center, as a late-breaking trial at the 2018 American Heart Association Scientific Sessions in Chicago.

Dr Pagani said: "This trial, like the previous pilot investigation, demonstrated that intramyocardial allogeneic MPC injections were associated with a significant reduction in GI bleeding, a major cause of morbidity and increased cost in LVAD patient management."

Over the six-month observation period, treatment with MPC-150-IM was associated with the following results:

- the primary endpoint of temporary weaning from full LVAD support was not achieved overall; limitation was that the high rate of pump thrombosis reduced the number of evaluable wean attempts
- significant beneficial effect was observed on the primary endpoint of temporary weaning from full LVAD support in a pre-determined subgroup analysis of ischemic heart failure patients, representing 44% of the total trial population (rate ratio 1.55, p value for interaction =0.02)
- significant reduction in cumulative incidence of major GI bleeding events by 48%, from 33% in controls to 17% (p=0.02)
- significant reduction in rate of major GI bleeding events by 76%, from 15.9/100 patient months to 3.8/100 patient months (p<0.001)
- significant reduction in rate of hospitalization for GI bleeding, a major cause of hospital readmissions, by 65%, from 0.21/100 patient months to 0.07/100 patient months (p=0.03); no significant reduction in all cause readmissions
- no patients experienced a safety-stopping event for the trial
- overall mortality was similar between the two groups, 14% vs 15% at 12 months
- overall time to transplant was similar between the two groups, despite a non-significant increase in anti-HLA class I antibodies in the MPC group (26% vs 9% in controls)

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Full trial results are expected to be published in a peer-reviewed journal.

Major GI bleeding in LVAD recipients is thought to be caused by a general state of inflammation in the heart and abnormal blood vessels in the GI tract.3,4,5 The proposed mechanism of action (MOA) by which Mesoblast's mesenchymal precursor cells (MPCs) are thought to exert their effects in these patients across multiple organ systems is through secretion of biomolecules which reduce damaging inflammation and reverse endothelial dysfunction associated with inflammation.

Mesoblast Chief Executive Dr Silviu Itescu said: "We are very pleased by the results of this independently conducted trial. The clinically meaningful outcome achieved in these very high-risk patients provides a potential pathway to bring our heart failure product candidate MPC-150-IM to market sooner for these patients in great need. In addition, the ability to address inflammation and endothelial dysfunction, mechanisms central to the development and progression of heart failure, may have broader implications for the use of our cells in patients with advanced heart failure."

The Phase 2 trial was conducted by the Cardiothoracic Surgical Trials Network (CTSN) with the International Center of Outcomes and Innovation Research, Mt. Sinai School of Medicine, serving as the coordinating center. The trial was funded and sponsored by the NHLBI of the United States National Institutes of Health and the Canadian Institutes for Health Research.

**MPC-150-IM for Chronic Heart Failure**
Mesoblast's product candidate MPC-150-IM is being developed for patients suffering from chronic heart failure (CHF) and progressive loss of heart function following damage to the heart muscle.
CHF is characterized by an enlarged heart and insufficient blood flow to the organs and extremities of the body due to both progressive dysfunction of heart muscle and dysfunction of blood vessels in the heart and in the peripheral organs. CHF is classified by the severity of the symptoms experienced by the patient. The most commonly used classification system was established by the New York Heart Association (NYHA) and ranges from Class I (mild) to Class IV or end-stage (severe).

MPC-150-IM is also being evaluated by catheter-based delivery in patients with NYHA Class IIb-III CHF. This ongoing events-driven Phase 3 trial has enrolled approximately 85% of approximately 600 total patients.

**End-Stage Heart Failure and Left Ventricular Assist Devices**
In the United States, there are approximately 250,000–300,000 patients annually who suffer from advanced systolic heart failure (NYHA Class IIIb–IV) who despite optimal medical therapy (excluding mechanical assist devices) have a one-year mortality >25% and exceeding 50% in class IV patients.6 The only options to increase survival in these patients are the use of cardiac assist devices or heart transplants. Due to the decline in organ donations and limited availability of healthy donor hearts, the treatment of CHF with mechanical circulatory support devices such as LVADs is gaining momentum, with 4,500–5,500 assist devices implanted annually in the United States.7,8,9 However, rehospitalization is frequent in patients with an LVAD ranging from 2.1–2.7 times per year. The majority of patients rehospitalized for non-device related causes are as a result of GI bleeding (34%-44%) and infections (36%-44%).10,11

**References**


1. Kataria R, Jorde UP. GI Bleeding During CF-LVAD Support: State of the Field. Cardiol Rev. 2018 May 9 [Epub ahead of print] PubMed PMID: 29746258
2. Ascheim DD, Gelijns AC, Goldstein D, et al. Mesenchymal precursor cells as adjunctive therapy in recipients of contemporary left ventricular assist devices. Circulation 2014; 129 2287-96
3. Grosman-Rimon L, McDonald MA, Jacobs I, et al. Markers of inflammation in recipients of continuous-flow left ventricular assist devices. ASAIO J 2014;60:657-663
4. Patel SR, Madan S, Saeed O, et al. Association of nasal mucosa vascular alterations, gastrointestinal arteriovenous malformations, and bleeding in patients with continuous-flow left ventricular assist devices. J Am Coll Cardiol: Heart Failure 2016;4:962-970
5. Tabit CE, Coplan MJ, Chen P, et. al. Tumor necrosis factor-α level and non-surgical bleeding in continuous-flow left ventricular assist devices. J Heart Lung Transplant. 2018 Januray; 37(1): 107-115



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6. Gustafsson F, Rogers JG. Left ventricular assist device therapy in advanced heart failure: patient selection and outcomes. European Journal of Heart Failure 2017;19:595-602
7. United Network for Organ Sharing
8. Agency for Healthcare Research and Quality – Healthcare Cost and Utilization Project – Claims Analysis ICD-9 37.6
9. Data on file
10. Chatterjee A, Feldmann C, Hanke JS (2018) The momentum of HeartMate 3: a novel active magnetically levitated centrifugal left ventricular assist device (LVAD). J Thorac Dis 10 (Suppl 15): S1790-S1793
11. Mehra, MR Salerno C, Cleveland JC (2018) Health care resources use and cost implications in the MOMENTUM 3 long-term outcome study: a randomized controlled trial of a magnetically levitated cardiac pump in advanced heart failure

**Conference Call**
Mesoblast will host a conference call to discuss the results beginning at 8.00am EST; 1.00pm BST Monday, November 12; and 12:00am AEDT Tuesday, November 13, 2018.

The live webcast can be accessed via http://webcasting.boardroom.media/broadcast/5bdfe30db7b1cf2eab18cf12

To access the call only, dial 1 855 881 1339 (toll-free United States), 0800 051 8245 (toll-free United Kingdom), 1 800 558 698 (toll-free Australia) or +61 2 9007 3187 (outside of the United States and Australia).

The conference identification code is 867444.

The archived webcast will be available on the Investor page of the Company's website – www.mesoblast.com

**About Mesoblast**
Mesoblast Limited (ASX:MSB; Nasdaq:MESO) is a world leader in developing allogeneic (off-the-shelf) cellular medicines. The Company has leveraged its proprietary technology platform to establish a broad portfolio of late-stage product candidates with three product candidates in Phase 3 trials – acute graft versus host disease, chronic heart failure and chronic low back pain due to degenerative disc disease. Through a proprietary process, Mesoblast selects rare mesenchymal lineage precursor and stem cells from the bone marrow of healthy adults and creates master cell banks, which can be industrially expanded to produce thousands of doses from each donor that meet stringent release criteria, have lot to lot consistency, and can be used off-the-shelf without the need for tissue matching. Mesoblast has facilities in Melbourne, New York, Singapore and Texas and is listed on the Australian Securities Exchange (MSB) and on the Nasdaq (MESO). www.mesoblast.com

**Forward-Looking Statements**
This announcement includes forward-looking statements that relate to future events or our future clinical development and financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward -looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward- looking statements should not be read as a guarantee of future performance or results, and actual results may differ from the results anticipated in these forward-looking statements, and the differences may be material and adverse. Forward-looking statements include, but are not limited to, statements about the timing, progress and results of Mesoblast and its collaborators' preclinical and clinical studies; Mesoblast and its collaborators' ability to advance product candidates into, enroll and successfully complete, clinical studies; the timing or likelihood of regulatory filings and approvals; and the pricing and reimbursement of Mesoblast's product candidates, if approved. You should read this press release together with our risk factors, in our most recently filed reports with the SEC or on our website. Uncertainties and risks that may cause Mesoblast's actual results, performance or achievements to be materially different from those which may be expressed or implied by such statements, and accordingly, you should not place undue reliance on these forward-looking statements. We do not undertake any obligations to publicly update or revise any forward-looking statements, whether as a result of new information, future developments or otherwise.

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Exhibit 99.2

mesoblast
the regenerative medicine company

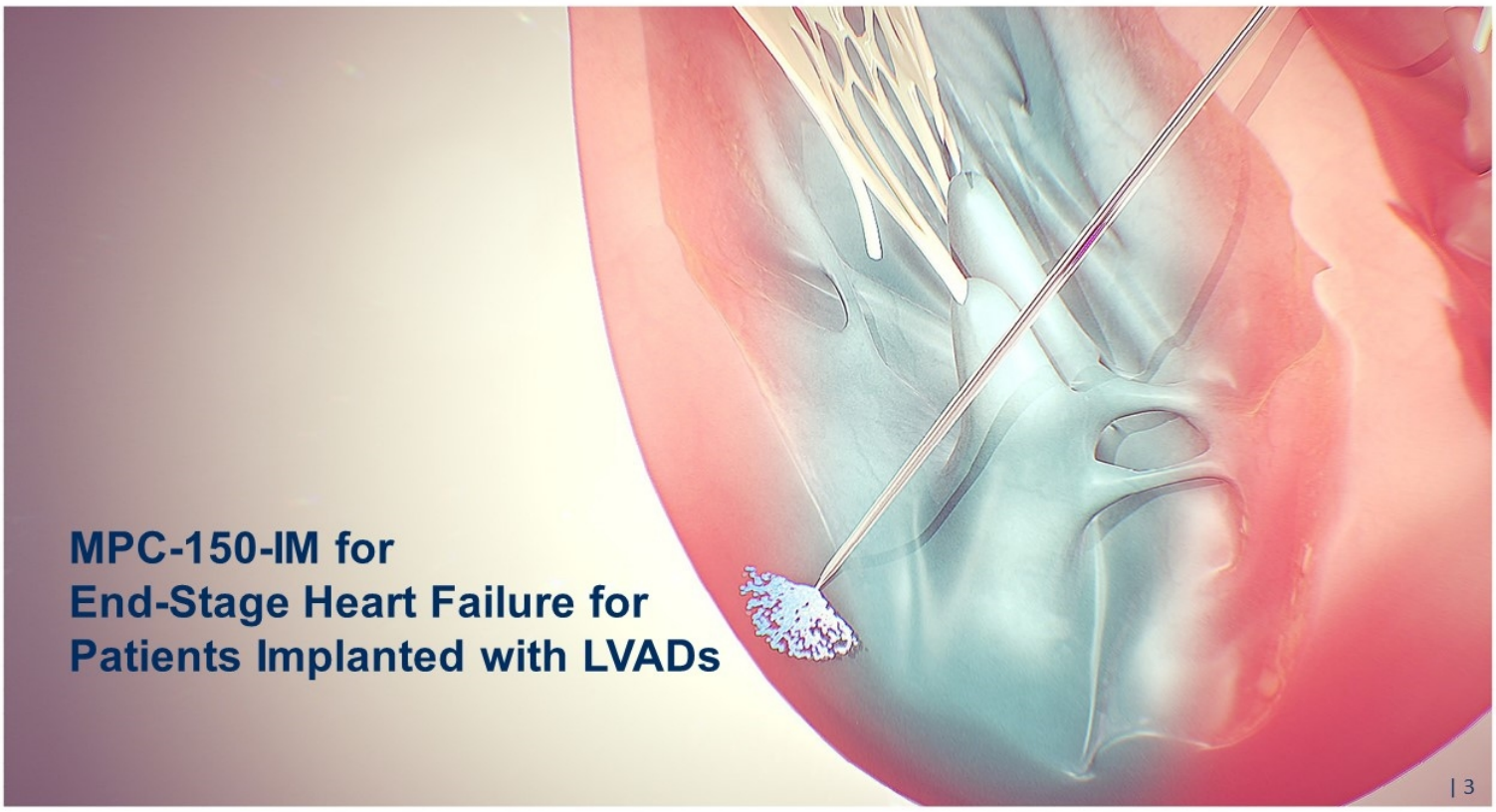
# Clinically Meaningful Outcome in Phase 2b Trial of MPC-150-IM in LVAD Recipients Provides Pathway for Regulatory Approval

12 November 2018

**Nasdaq: MESO ASX: MSB**

## 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.*


MPC-150-IM for
End-Stage Heart Failure for
Patients Implanted with LVADs

# MPC-150-IM: Adjunctive Therapy to Improve Clinical Outcomes in LVAD Patients

**Burden of Illness**

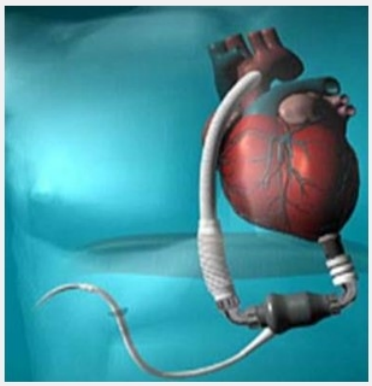
- In the USA, there are approximately 250,000–300,000 patients annually who suffer from advanced systolic heart failure (NYHA Class IIIb–IV). [1]
- Despite optimal medical therapy (excluding mechanical assist devices) Class IIIb have a one-year mortality >25% and exceeding 50% in class IV patients.[1]

**Ongoing Unmet Need**

- LVADs have improved survival, but high morbidity remains high with patients on average experiencing greater than two hospitalization annually.[2]
- Gastrointestinal (GI) bleeding is a leading cause of device attributable hospitalizations[2]
- **Device attributable major adverse events (DAEs) can cost on average from up to $46.5k per hospitalization[2]**

**Market Opportunity**

- ~4,500 – 5,500 assist devices are implanted annually in the Untied States.[3, 4]
- **US LVAD market is growing double-digit CAGR and represents > $500m market opportunity[3,4]**
- Orphan indication with US targeted commercial footprint provides low cost market entry



[1]Gustafsson G, Rogers J. (2017) Left ventricular assist device therapy in advanced heart failure: patient selection and outcomes, [2] Mehra, MR Salerno C, Cleveland JC (2018) Health care resources use and cost implications in the MOMENTUM 3 long-term outcome study: a randomized controlled trial of a magnetically levitated cardiac pump in advanced heart failure, [3]Agency for Healthcare Research and Quality – Healthcare Cost and Utilization Project – claims analysis using ICD-9 37.6 implantation of heart and circulatory assist systems, [4] Data on File

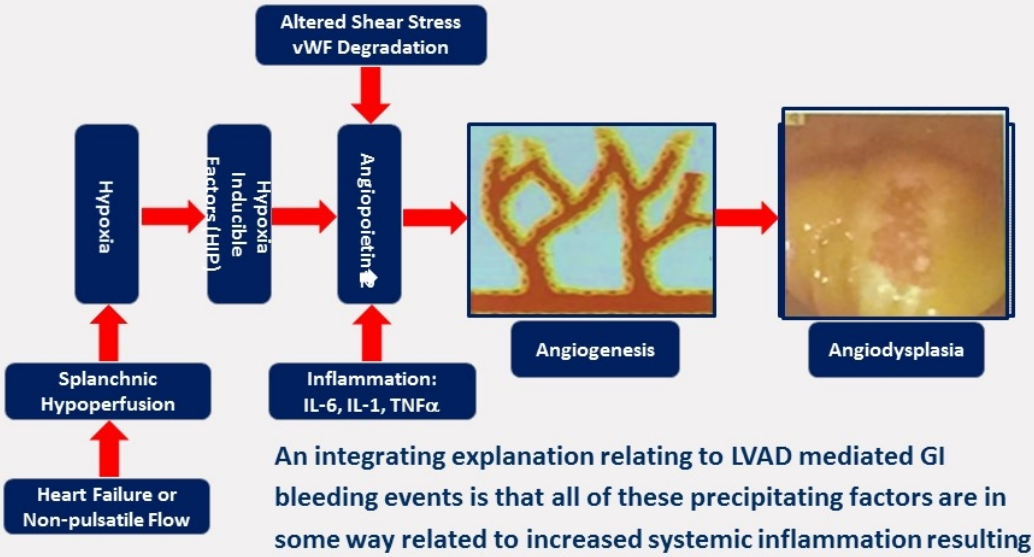
# INTERMACS* Adverse Event Rates in LVAD Patients: Most Common Cause of Non-surgical Hospitalization is Major GI Bleeding[1]

| Adverse Event | Events | Rate |
|---|---|---|
| Bleeding | 4,420 | 7.79 |
| Cardiac/vascular | | |
| Right-sided heart failure | 276 | 0.49 |
| Myocardial infarction | 34 | 0.06 |
| Cardiac arrhythmia | 2,303 | 4.06 |
| Pericardial drainage | 305 | 0.54 |
| Hypertension | 115 | 0.20 |
| Arterial non-CNS thrombosis | 94 | 0.17 |
| Venous thrombotic event | 286 | 0.50 |
| Hemolysis | 314 | 0.55 |
| Infection | 4,132 | 7.28 |
| Stroke | 916 | 1.61 |
| Renal dysfunction | 876 | 1.54 |
| Hepatic dysfunction | 326 | 0.57 |
| Respiratory failure | 1,551 | 2.73 |
| Wound dehiscence | 96 | 0.17 |
| Psychiatric episode | 525 | 0.93 |
| Total burden | 16,569 | 29.20 |

*Interagency Registry for Mechanically Assisted Circulation (INTERMACS): Events per 100 Patient-Months in the First 12 Months Post-Implant, based on 7,286 patients with CF-LVADs between 2012-2014.

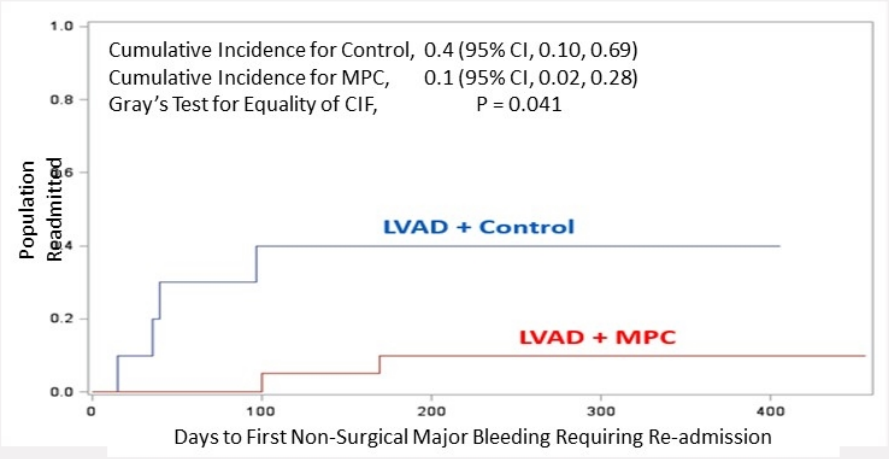
1.Left Ventricular Assist Devices for Lifelong Support Pinney SP, et al. JACC 2017;69:2845-61.

# Proposed Pathway of Angiogenesis and Non-surgical GI Bleeding During CF-LVAD




An integrating explanation relating to LVAD mediated GI bleeding events is that all of these precipitating factors are in some way related to increased systemic inflammation resulting in increased serum levels of angiopoietin-2, a well-documented agent that causes vascular disruption and destabilization.

# MPCs Reduced Major GI Bleeding in 30 Patient Pilot Trial[1]




- MPC group had significantly longer time to first hospitalization due to major GI bleeding ($p<0.05$, Kaplan-Meier statistics)
- 71% reduction in number of patients with at least one hospitalization from GI bleeding through 6 months (16% in LVAD group vs 55% in controls, $p=0.03$ by chi-square test)
- 70% reduction in rate of hospitalizations due to GI bleeding per 100 patient-months of follow-up (4.2 in LVAD group vs 14.2 in controls, $p=0.06$ by binomial test)

1. Source: Data on file.

# The 21st Century Cures Act (Cures Act)

## Legislation for An Expedited Approval Path for Cellular Medicines Designated as Regenerative Medicine Advanced Therapies (RMAT)

- Cellular medicines may be designated as regenerative advanced therapies, if they are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and there is preliminary clinical evidence indicating the potential to address the unmet medical need

- Key benefits of the legislation for cell-based medicines, designated as regenerative advanced therapies, include:
  - Potential eligibility for priority review and accelerated approval
  - Potential to utilize surrogate endpoints for accelerated approval
  - Potential to utilize patient registry data and other sources of "real world evidence" for post approval studies, subject to approval by the FDA


**MPC-150-IM for End-Stage Heart Failure Patients with LVADs Received RMAT Designation**

# FDA Regulatory Interaction for MPC-150-IM using LVADs

| | |
|---|---|
| **December 2017** | FDA grants RMAT designation for Mesoblast's novel MPC therapy for the treatment of heart failure due left ventricular systolic dysfunction of either ischemic or non-ischemic etiology in patients with LVADs. Based on pilot trial data that demonstrated:<br>• Successful weans in MPCs compared to control<br>• Reduction in hospitalization due to GI bleeding |
| **June 2018** | FDA meeting (Type B meeting) to discuss regulatory pathway for MPC-150-IM in an LVAD population. Feedback:<br>1. Non-surgical GI bleeding and/or epistaxis are clinically meaningful issues for patients with LVADs and represents an unmet clinical need<br>2. Temporary wean considered a biomarker and not a clinically meaningful outcome in and of itself<br>– Weaning to explantation is a clinically meaningful outcome but it is a rare event and is limited to select center<br>o Not clear that successful weans would reasonably predict explantation outcome<br>o Concerns about interpretability of binary wean data<br>3. Need to show the adverse event, including allosensitization, and survival are not unfavorably affected by the MPC product<br>4. Need sufficient safety database for adverse event analysis of meaningful subgroups |

# Can MPCs Reduce GI Bleeding Complications in End-Stage Heart Failure Patients with LVADs?

## Rationale

- Intra-myocardial injections of allogeneic MPCs may reduce myocardial and systemic inflammation
- MPCs improve coronary and systemic artery endothelial dysfunction in ovine systemic inflammation
- MPCs may reverse endothelial dysfunction in the heart and GI vascular beds in LVAD-related inflammation


# 2018 American Heart Association Scientific Sessions - *Late Breaking*

# Objective and Target Population

***Objective*** : To assess whether one-time injections of high dose MPCs into the native myocardium of LVAD recipients is safe and improves cardiac recovery

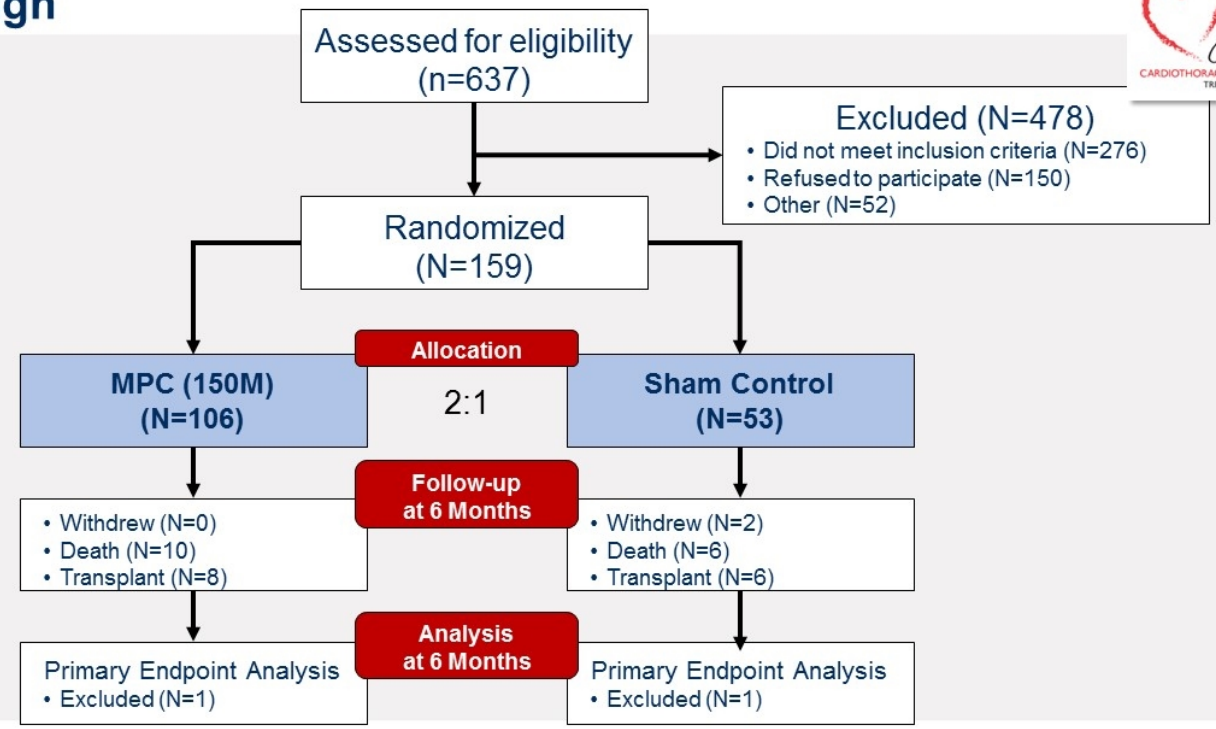
## Inclusion Criteria

- Adults with advanced HF
  - Ischemic
  - Non-ischemic
- Scheduled for implantation of an FDA- or HC-approved LVAD for
  - BTT
  - DT

## Exclusion Criteria

- Percutaneous LVAD or BV support
- Planned ablation or aortic valve intervention
- Recent CT surgery or prior cardiac Tx
- LV reduction surgery or cardiomyoplasty
- >10% anti-HLA antibody titers with known specificity to MPC-donor HLA antigens
- Prior cell therapy for cardiac repair

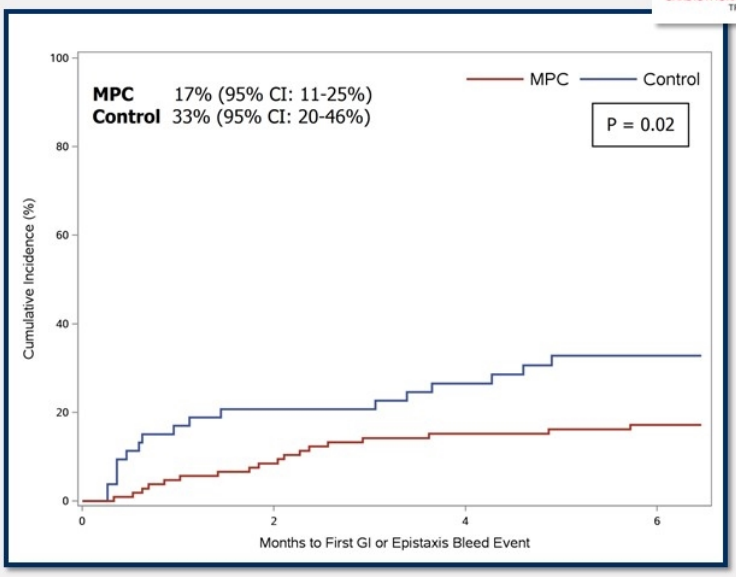
# Trial Design



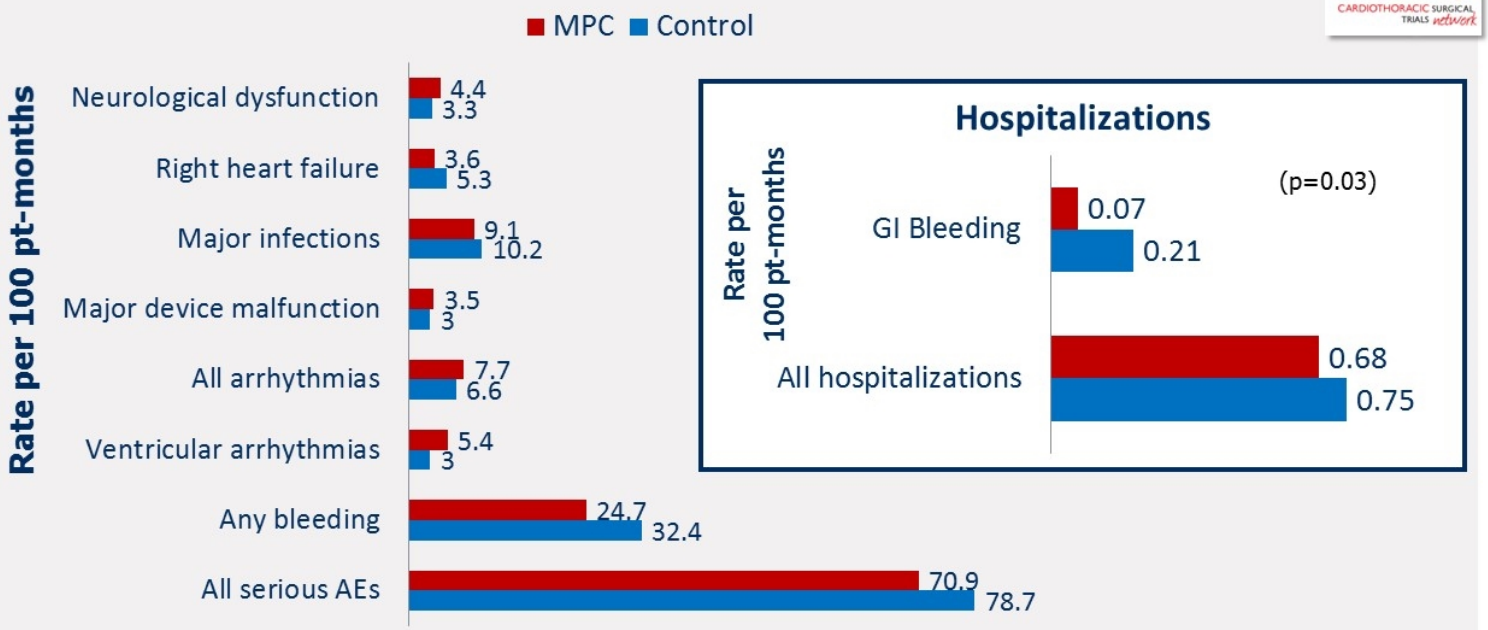
# Mucosal Bleeding at 6 Months

## Rate of GI/Epistaxis Bleeding

| MPC (n = 106) | Control (n = 53) | P-value |
|---|---|---|
| Event Rate (100-Pt-Months) | Event Rate (100-Pt-Months) | |
| **3.8** | **15.9** | **<0.001** |

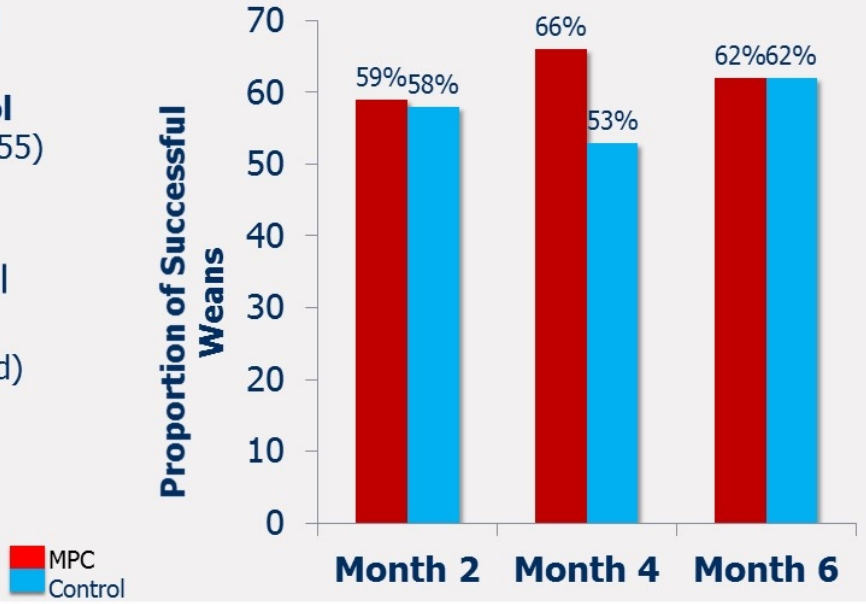


# Serious AEs & Hospitalizations at 6 Months



# Successful Temporary Weans from LVAD Support

- Average proportion of successful temporary weans:
  - **61% in MPC vs. 58% in control**
  - RR=1.08 (95% CI 0.83-1.41; p=0.55)
- Posterior probability that MPC increased likelihood of successful weaning:
  - **69%** (<80% pre-defined threshold)



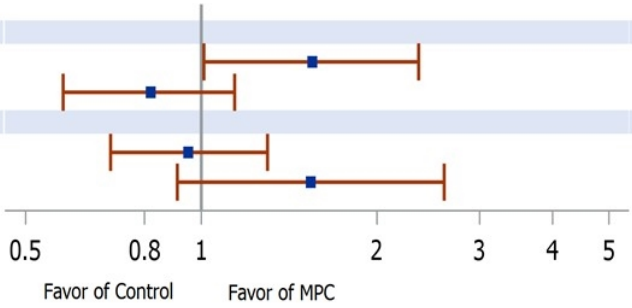
# Limitations

- High rate of pump thrombosis reduced number of evaluable wean attempts
- Enrolled heterogeneous study population
  - Ischemic/non-ischemic HF, BTT/DT, 2 types of devices
  - Increased variability may have reduced likelihood of detecting Rx effect
- Although all bleeding events & transfusions were adjudicated, we did not routinely collect INR, platelets, and anticoagulation regimens

# Exploratory Subgroup Analyses

## Interaction of Rx and Pre-determined Subgroups on Wean Success Rate over 6 Months

| Subgroup Analysis | Wean Rate Ratio (95% CI) | P-value for Interaction |
|---|---|---|
| Cardiomyopathy | | 0.02 |
| Ischemic | 1.55 (1.01, 2.36) | |
| Non-ischemic | 0.82 (0.58, 1.14) | |
| Indication for LVAD | | 0.12 |
| BTT | 0.95 (0.70, 1.30) | |
| DT | 1.54 (0.91, 2.61) | |



# Primary Safety Endpoint & Sensitization

- No patients developed a primary safety stopping event
- Allosensitization to Class I HLA antigens
  - 26% MPC vs 9.4% Control
  - Between-group difference: 16.5% (95% CI: 5 to 28%)
- Allosensitization to Class II HLA antigens
  - Similar in control and MPC patients at all time points

# Conclusions

- Succeeded in achieving the FDA identified clinically meaningful outcome of reduction in GI bleeding and related hospitalization
- Results confirm the previous pilot trial, which also demonstrated significant reduction in GI bleeding and related hospitalization in MPC treated LVAD patients
- Company intends to meet with the FDA to provide full study data and discuss potential BLA filing
- While trial did not meet the overall primary endpoint of temporary weaning, MPC treatment did significantly improve weaning in ischemic patients
  - Weaning, in and of itself, is a biomarker and not a clinically meaningful outcome
- LVAD patients with ischemic heart failure closely resemble the majority of patients in DREAM-HF in terms of age and etiology; however, the LVAD patients are more advanced with end stage disease and have more severe endothelial dysfunction presenting as GI Bleeding

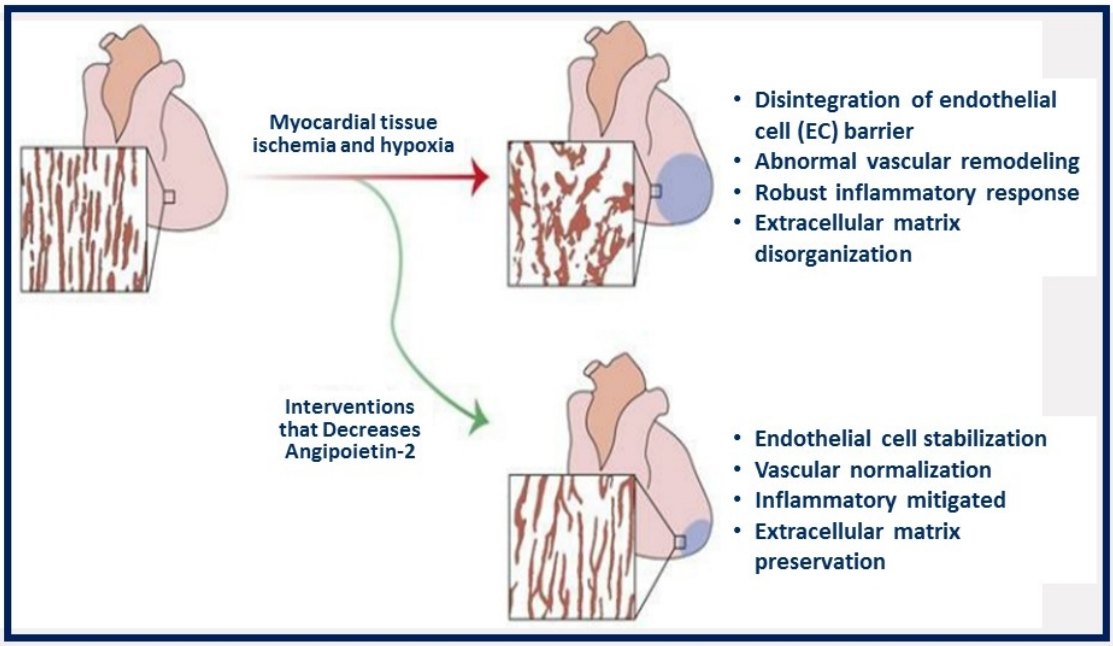
# Acknowledgements


- This trial was supported by a cooperative agreement (U01-HL088942) funded by NHLBI and NINDS, of the National Institutes of Health (NIH), and the Canadian Institutes for Health Research (CIHR)
- Mesoblast provided MPCs and cryoprotective medium
- We would like to thank the patients, their families, doctors, nurses and research personnel for participating in this trial


## Questions & Answers


# Appendix

# Roles of Angiopoietin-2 in Exacerbating Cardiac Hypoxia and Inflammation in Association with Myocardial Ischemia

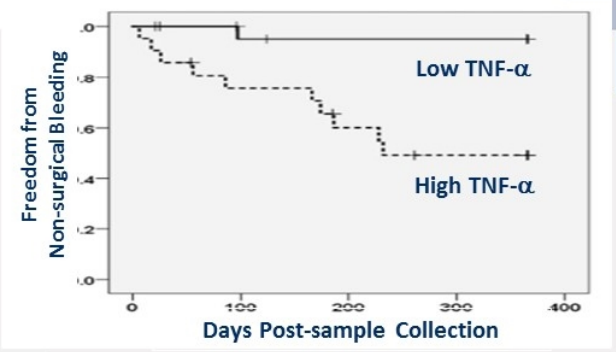



Source: Modified from Lee SJ, et al. Angiopoietin-2 exacerbates cardiac hypoxia and inflammation after myocardial infarction. J Clin Invest 2018:128:5018-5033

# Effects of CF-LVAD on TNF-α, ANG-2 and ANG-1 on GI Bleeding

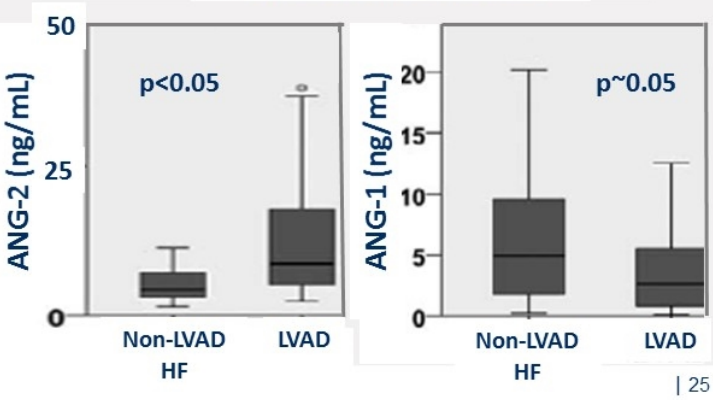
## TNF-α in CF-LVAD Patients[1]

- Elevated TNF-α level is a key regulator of altered angiogenesis, pericyte apoptosis and expression of tissue factor
- High TNF-α levels are associated with increased risk of non-surgical bleeding, predominantly GI in origin




## ANG-2 and ANG-1 In CF-LVAD Patients[2]

- ↑ANG-2 and ↓ANG-1 levels occur compared to non-LVAD HF patients
- ↑ANG-2 level is associated with higher rate of non-surgical bleeding, predominantly GI in origin





1. Tabit CE, et al. J Heart Lung Transplant 2018;37-107-115
2. Tabit CE, et al. Circulation 2016;134:141-152

# MPCs Improve Coronary Artery Endothelial Dysfunction In A Sheep Model of Systemic Inflammation

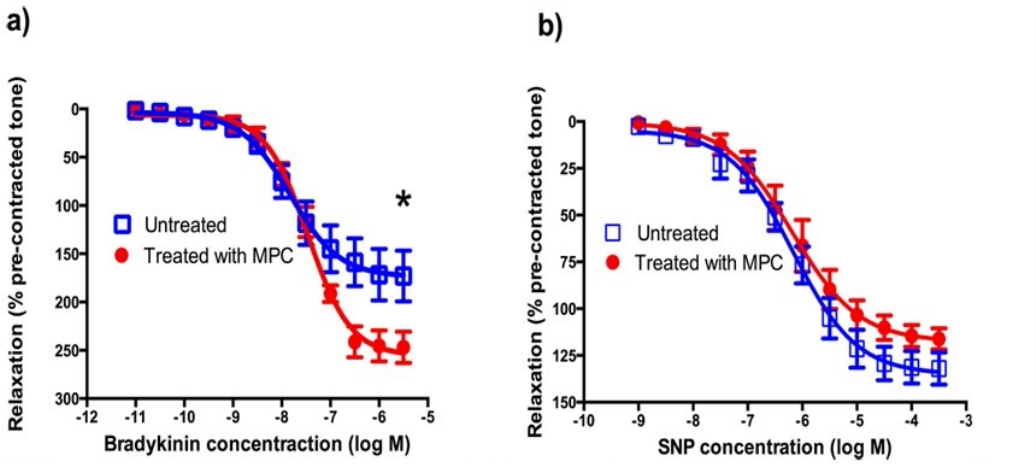



**Fig 3. Comparison of vasorelaxation in ovine coronary arteries in arthritic sheep treated and untreated with mesenchymal precursor cells (MPC).** Arterial rings were contracted with endothelin-1, and relaxation responses to cumulatively increasing concentrations of (A) Bradykinin (BK), (B) Sodium nitroprusside (SNP), were expressed as a percentage relaxation of pre-contracted tone. Each point represents the mean ±SEM from 8 animals. * Indicates statistically significant difference ($p < 0.05$) in the maximum response for the dilation to bradykinin between treated and untreated animals (see Table 1).

Source: Dooley et al. Effect of MPCs on the systemic inflammatory response and endothelial dysfunction in an ovine model of collagen-induced arthritis. PLOS One, May 7, 2015.

# MPCs Improve Digital Artery Endothelial Dysfunction In A Sheep Model of Systemic Inflammation

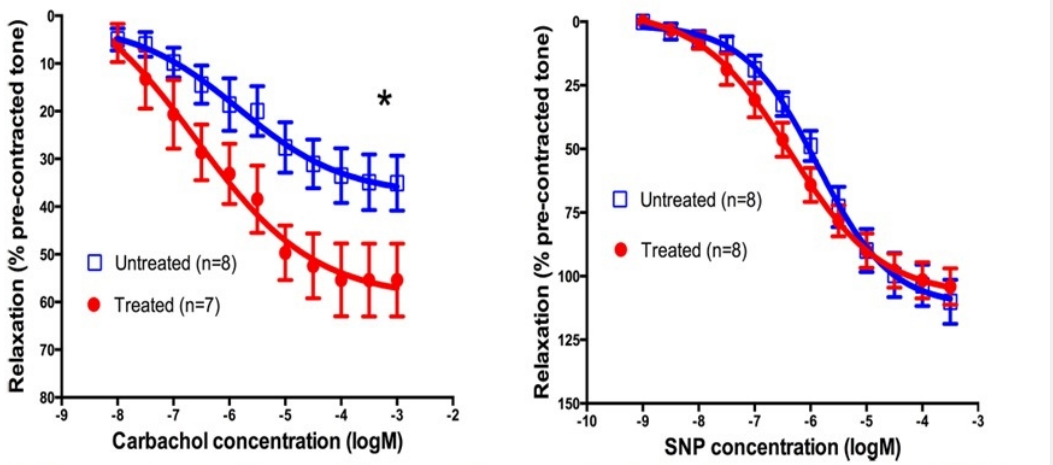



**Fig 4. Comparison of vasorelaxation in ovine digital arteries in arthritic sheep treated and untreated with mesenchymal precursor cells (MPC).** Arterial rings were contracted with 5-hydroxytryptamine (5-HT), and relaxation responses to cumulatively increasing concentrations of (A) Carbachol and (B) Sodium Nitroprusside (SNP) were expressed as a percentage relaxation of pre-contracted tone. Each point represents the mean ±SEM from 7–8 animals. * Indicates statistically significant difference ($p < 0.05$) in the maximum response for the dilation to carbachol between treated and untreated animals (See Table 2).

Source: Dooley et al. Effect of MPCs on the systemic inflammatory response and endothelial dysfunction in an ovine model of collagen-induced arthritis. PLOS One, May 7, 2015.