# >mesoblast

the regenerative medicine company

Cellular Medicines for Intractable Serious and Life-Threatening Diseases

November 2017

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 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. We have based these forward-looking statements largely on our current expectations and future events , recent changes in regulatory laws, and financial rends 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 statements of these forward-looking statements regarding its relationships with current and potential future business partners and future benefits of those relationships; statements concerning Mesoblast's ability to grow its business 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 achievements to be materially different from those which may be expressed or implied by such statements and ability to clinical risks that may cause besoblast's actual results.

## Our Mission:

Mesoblast is committed to bring to market disruptive cellular medicines to treat serious and life-threatening illnesses

#### **Investment Proposition:**

Building a Leading Franchise of Cellular Medicines

- Disruptive Cellular Technology Platform
- Commercial Translation Capabilities
- Advanced Pipeline of Cellular Medicines
- Targeting Serious or Life-Threatening Conditions with Unmet Needs

#### **Disruptive Cellular Medicine Platform**<sup>1-4</sup>

- STRO-1<sup>+</sup> Mesenchymal Precursor Cells (MPCs) are at the apex of the hierarchy of Mesenchymal Lineage cells
- STRO-1/STRO-3 immuno-selection provides a homogeneous population of MPCs with unique receptors that respond to activating inflammation and damaged-tissue signals
- In response to activating signals present in the endogenous environment, MPCs secrete a diverse variety of biomolecules responsible for immunomodulation and tissue repair

# The multi-modal mechanisms of action target multiple pathways

- 1. Simmons PJ and Torok-Storb, B. Identification of stromal cell precursors in bone marrow by a novel monocloncal antibody, STRO-1. Blood. 1991;78:55-62.
- 2. Gronthos S, Zannettino AC, Hay SJ, et al. Molecular and cellular characterisation of highly purified stromal stem cells derived from human bone marrow. J Cell Sci. 2003;116(Pt 9):1827-35.
- 3. See F, Seki T, Psaltis PJ, et al. Therapeutic effects of human STRO-3-selected mesenchymal precursor cells and their soluble factors in experimental myocardial ischemia. J Cell Mol Med. 2011;15:2117-29.
- 4. Psaltis PJ, Paton S, See F, et al. Enrichment for STRO-1 expression enhances the cardiovascular paracrine activity of human bone marrow-derived mesenchymal cell populations. J Cell Physiol. 2010;223(2):530-40.



## **Commercial Translation Capabilities:**

## Technology Positioned for Scalable, Industrialized Manufacturing

Immune privileged nature of STRO-1+ MPCs enables allogeneic "off the shelf" product candidates

Culture expansion scalable to produce commercial quantities of potent and reproducible therapeutic doses

In-house proprietary media formulations and commercial-grade bioreactors to deliver step-change yield improvements

Specific formulations defined for product delineation

Management know how in regulatory activities necessary for product approval and commercial launch

TEMCELL® HS. Inj., first allogeneic cellular medicine received full approval in Japan and successfully launched for acute Graft vs Host Disease<sup>1</sup>



Lonza contract manufacturing facility in Singapore

#### **Portfolio of Advanced Product Candidates:** Three Tier 1 Product Candidates in Phase 3

Platform	Product Candidate	Therapeutic Area	Pre-Clinical/ Pre-IND	Phase 2	Phase 3	Approval	Partnering <sup>1</sup>
MPC	MPC-150-IM	Advanced (Class 3) HF End Stage (Class 4) HF <sup>1</sup>					The soblast the regenerative medicine company
MPC	MPC-06-ID	Chronic Low Back Pain					The regenerative medicine company
MPC	MPC-300-IV	RA DN/Type 2 Diabetes				Japan	the regenerative medicine company
MSC	TEMCELL® HS Inj	Acute GVHD Acute GVHD					<b>∦JCR</b> <b>}meso</b> blast
							the regenerative medicine company

Includes MSC-100-IV (Crohn's disease – biologic refractory), MPC-25-IC (Acute Cardiac Ischemia),

MPC-25-Osteo (Spinal Fusion) and MPC-75-IA (Knee Osteoarthritis)

This chart is figurative and does not purport to show individual trial progress within a clinical program. For product registration purposes, Phase 3 programs may require more than one trial. Tier 1 programs represent our lead programs where we focus the majority of our time and resources. Tier 2 programs are also in development and may advance to Tier 1 depending on the merit of newly generated data, market opportunity or partnering options.

1. Clinical trial is funded by the U.S. National Institutes of Health and the Canadian Health Research Institute.

Commercialization

## The 21<sup>st</sup> Century Cures Act ("Cures Act"):

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

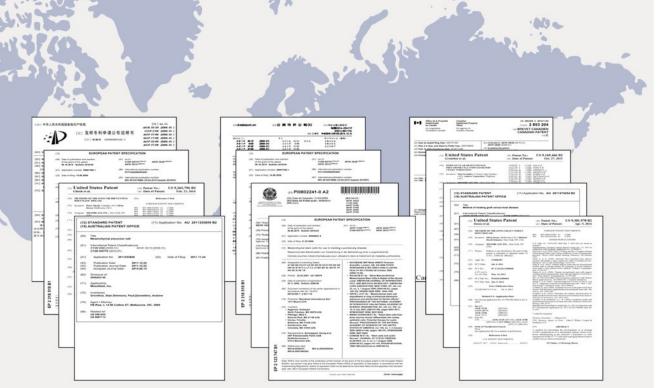
- Cellular medicines may be designated as regenerative advanced therapies, if they are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and there is preliminary clinical evidence indicating the potential to address the unmet medical need
  - Key benefits 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 a patient registry data and other sources of "real world evidence" for post approval studies, subject to approval by the FDA

We Believe Our Portfolio of Advanced Product Candidates is Well Positioned to Achieve Accelerated Approvals Under the Cures Act

#### **Intellectual Property:**

An Extensive Portfolio Covering Composition of Matter, Manufacturing, and Therapeutic Applications of Potent Immuno-selected Mesenchymal Lineage Precursors and Progeny

~ 800 Patents and patent applications across 69 Patent Families. Protection across major markets including the U.S., Europe, Japan and China





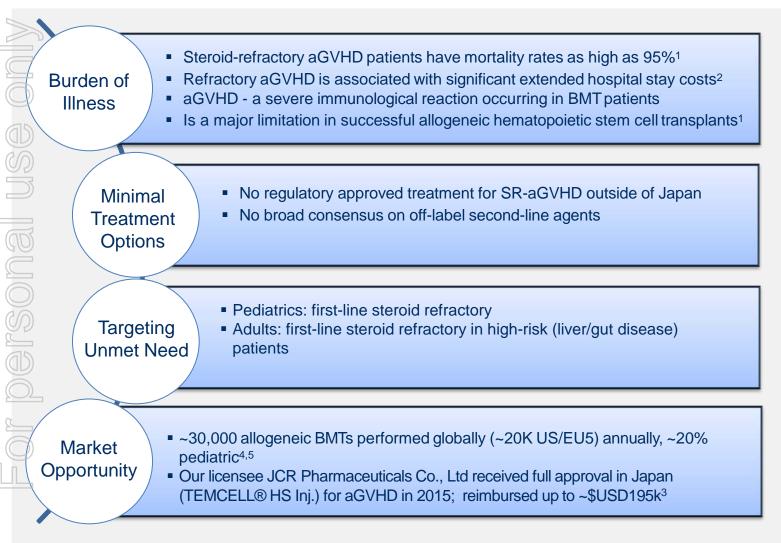
#### Diverse Pipeline of Cellular Medicines



Masdaq

Acute Graft vs Host Disease (aGVHD) MSC-100-IV for Steroid-Refractory aGVHD

## **MSC-100-IV: Market Opportunity for aGVHD**





- 1. West, J., Saliba, RM., Lima, M. (2011) Steroid-refractory acute GVHD: predictors and outcomes. Advances in Hematology.
- 2. Anthem-HealthCore/Mesoblast claims analysis (2016).
- 3. Based on a ¥JPY = \$USD 0.009375 spot exchange rate on as of the market close on November 11, 2016. Amounts are rounded. Source: Bloomberg.
- 4. Gratwohl A et al Quantitative and qualitative differences in use and trends of hematopoietic stem cell transplantation: a Global Observational Study. Haematologica. 2013 Aug;98(8):1282-90.
- 5. CIBMTR, Decision resources GVHD Epi Nov 2012.

## **MSC-100-IV** for aGVHD: Product Development Strategy

#### Target *pediatric* patients with SR-aGVHD first

- Extensive safety and efficacy data generated and published with MSC-100-IV in children with SR-aGVHD<sup>1</sup>
- High economic burden in treatment of children with SR-aGVHD
- Fast-track designation for MSC-100-IV provides pathway for priority review and rolling review process
- Submit single, open-label Phase 3 trial via accelerated approval

#### Seek label extension for high-risk adult patients with SR-aGVHD (liver/gut disease)

- This adult subset has the highest mortality and greatest resistance to other treatment agents
- High economic burden in treating this population subset
- MSC-100-IV has identified efficacy signals in analyses of this subgroup in a Phase 3 randomized control trial

#### Lifecycle potential in *chronic* GVHD (cGVHD)

- Chronic GVHD represents a distinct patient population
- Proof of concept data already published for MSC in cGVHD<sup>2</sup>

Allogeneic Human Mesenchymal Stem Cell Therapy (Remestemcel-L, Prochymal) as a Rescue Agent for Severe Refractory Acute Graft-versus-Host Disease in Pediatric Patients - Biology of Blood and Marrow Transplantation Journal, August 2013.
 Khandelwal P, Teusink-Cross A, Davies S (2017) Ruxolitinib as Salvage Therapy in Steroid-Refractory Acute Graft-versus-Host Disease in Pediatric Hematopoietic Stem Cell Transplant Patients. Biol Blood Marrow Transplant 23; 1122-1127

<sup>2.</sup> Weng JY, Du X, Geng SX, Peng YW, Wang Z, Lu ZS et al. Mesenchymal stem cell as salvage treatment for refractory chronic GVHD. Bone Marrow Transplant 45: 1732-1740 (2010)

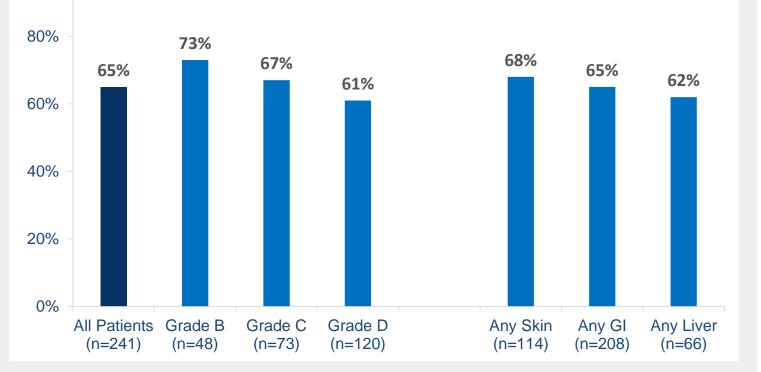
### **MSC-100-IV: Expanded Access Program**

Overall Day 28 Response in Pediatric aGVHD Patients Receiving MSC-100-IV as First-line or Salvage Therapy After Failing Steroids

100%

# Population: steroid-refractory aGVHD pediatric patients

- 241 pediatric patients undergoing HSCT were enrolled and treated at 50 sites in North America and Europe from 2007-2014
- Ages 2 months 17 years
- Acute GvHD grades B-D (CIBMTR)
- Failed steroid treatment and multiple other agents
- aGVHD not improving after at least 3 days of methylprednisolone (at least 1 mg/kg/day or equivalent)



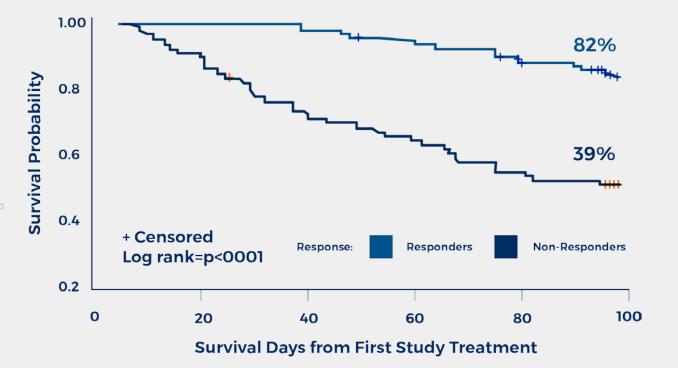
Complete Response was 14%, Partial Response was 51%

 Responses were observed for all GVHD grades and did not differ by baseline organ involvement

### **MSC-100-IV: Expanded Access Program**

Correlation of Day 28 Overall Response with Day 100 Survival, Using MSC-100-IV as First-line or Salvage Therapy After Failing Steroids and/or Additional Treatments

> MSC-100-IV in Children with SR-aGVHD who failed multiple other modalities - Survival of Pediatric Patients Treated with MSC-100-IV 28-Day Responders vs Non-responders n=241



- In 241 Children under EAP, Overall Response (CR+PR) at Day 28 was
   65% (95% CI: 58.9%, 70.9%)
- Day 100 survival correlated with overall response, and was significantly improved in those who responded at Day 28 (82% vs. 39%, p<0.0001)</li>

**MSC-100-IV:** 

#### Prior Clinical Results<sup>1</sup> Support Ongoing Phase 3 Trial in Children with Steroid Refractory Acute GVHD (SR-aGVHD)

MSC-100-IV as first line therapy in children with SR-aGVHD

Product-Limit Survival Estimates

Response at Day 28	Randomized Placebo Controlled Trial		Expanded Access Program
	Placebo	MSC-100-IV	MSC-100-IV
Responder	3/14 (21.4%)	9/14 (64.3%)	29/36 (81%)
Non-responder	11/14 (78.6%)	5/14 (35.7%)	7/36 (19%)
	(com	p-value=0.00 nbined treated v	

- These combined study results demonstrate that compared with placebo control patients, MSC-100-IV produced superior overall response at day 28, a clinically meaningful endpoint (p=0.0014) when used as first line therapy in these children with SR-aGVHD
- FDA agreement on ongoing Phase 3 trial design and its eligibility for accelerated approval pathway
- Enrollment criteria: MSC-100-IV being evaluated as first line therapy in children with SR-aGVHD
- 1. Protocols 275 (NCT00759018) and 280 (NCT00366145).

+ Censored

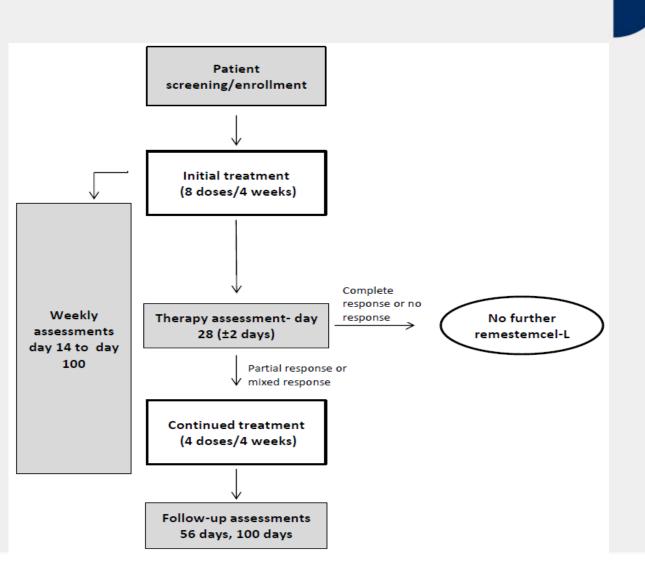
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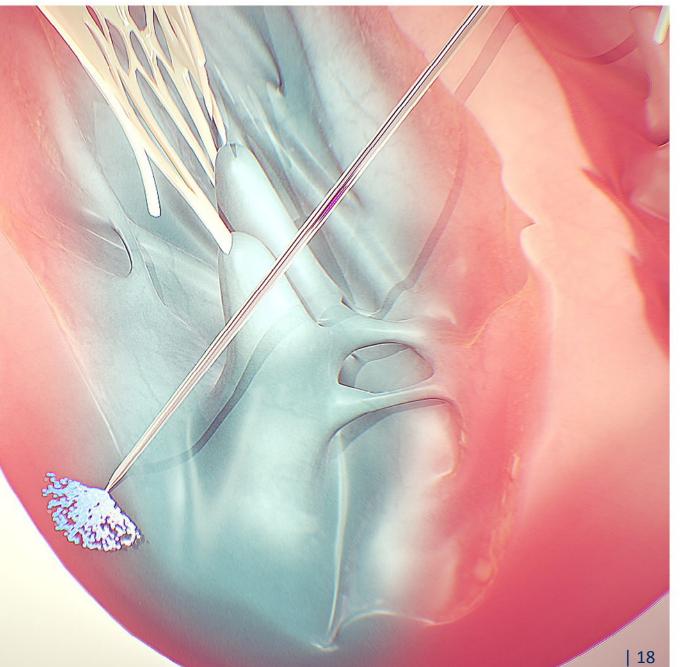
#### **MSC-100-IV:** Phase 3 Pediatric Trial as First-line Therapy in aGVHD After Failing Steroids

- Multi-center, Single-Arm, Open-Label to evaluate efficacy and safety to day 100 (001) and from day 100 to day 180 (002)
- Up to 60 pediatric patients (2 months to 17 years)
- aGVHD following allogeneic HSCT failing systemic corticosteroid therapy
- Grades C and D aGVHD involving skin, liver and/or GI tract
- Grade B aGVHD involving liver and/or GI tract with or without concomitant skin disease
- Primary endpoint: Overall response at Day 28
- Key secondary endpoint: Survival at Day 100 in responders at Day 28
- Interim futility analysis of primary endpoint successful Nov 2016

Enrollment Complete (Q4 CY17) Primary Endpoint Day 28 (Q1 CY18) Day 100 survival data (Q2 CY18)

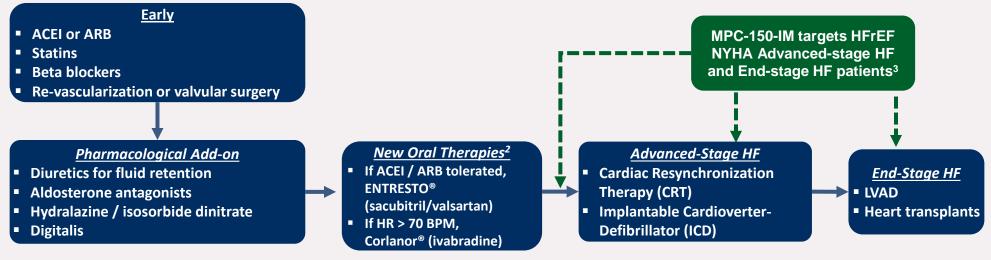


# **MPC-150-IM Chronic Heart Failure** (CHF) Program



#### **MPC-150-IM:** Targeting Patients with Worsening HF Despite Optimal Standard of Care

#### **Common Treatment Pathway in CHF<sup>1</sup>**



**Class** I

Class IV

#### Heart Failure Disease Progression

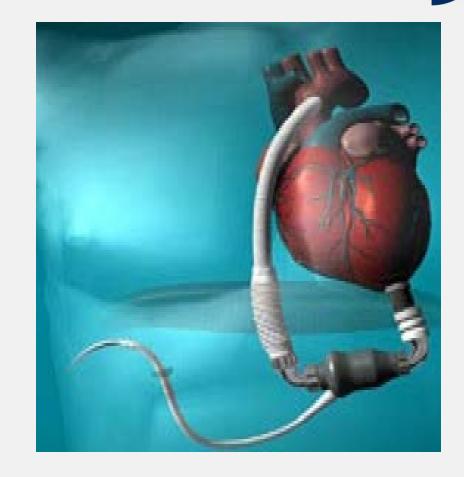
- 1. Source: Simon-Kucher & Partners 2017. Primary research 2017; Payers n=35, KOLs n=15, Cath lab managers n=4.
- 2. Corlanor® (ivabradine) approved by FDA (April 2015). ENTRESTO® (sacubitril/valsartan) approved by FDA (July 2015).
- 3. GlobalData-PharmaPoint Heart Failure (2016); McMurray et al., 2012; Yancy et al., 2013, 2016 ACC/AHAHFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure.

VINO

## **MPC-150-IM: Class IV Market Opportunity**

<ul> <li>250K – 300K patients/yr suffer from advanced systolic HF (NYHA Class IV)<sup>1</sup></li> <li>50k patients/yr have end-stage heart failure</li> <li>Despite optimal medical therapy, 1-year mortality exceeds 50% in end-stage heart failure patients<sup>1</sup></li> <li>Only ~2K heart transplants are performed in U.S. annually due to limited donors<sup>2</sup></li> <li>LVADs have improved survival, but 1-year mortality remains at 20-30%<sup>1</sup></li> <li>Number of destination (permanent) LVADs implanted/yr are &lt;5K due to associated high morbidity (e.g. GI bleeding and infection)</li> <li>Strengthen native heart muscle</li> <li>Reduce re-hospitalizations</li> <li>Increase survival</li> </ul>	
Minimal Treatment Options	
Unmet Need   Reduce re-hospitalizations	
<ul> <li>Market</li> <li>US LVAD market growing double-digit CAGR<sup>4</sup></li> <li>US targeted commercial footprint (top 40 centers represent 75% of volume) provides low cost market entry<sup>3</sup></li> </ul>	

Gustafsson G, Rogers J. (2017) Left ventricular assist device therapy in advanced heart failure: patient selection and outcomes. European Journal of Heart Failure 19, 595-602.,
 Agency for Healthcare Research and Quality: HCUPnet: ICD-9 principal procedure code 27.51 2014., 3. Medicare provider charge inpatient-DRGALL-FY2014., St. Jude Medical-2016-analyst and investor day



## **LVAD MPC Pilot Trial Proof of Concept:**

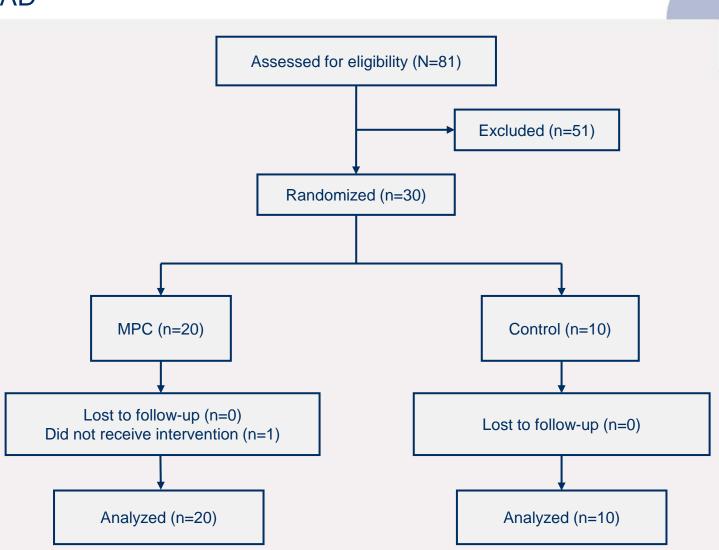
Evaluating 25M MPCs as Adjunct to LVAD<sup>1-2</sup>

- 57.4 yrs (±13.6)
- 83% Male

only

personal use

- LVEF 18.1% (± 4.3)
- 37% Ischemic,
   63% Non-ischemic
- 67% Destination, 33% Bridge to Transplant



1. Source: Ascheim DD et al. Circulation. 2014;129:2287-2296.

2. Study is sponsored Mt. Sinai and funded by the United States National Institutes of Health (NIH) and Canadian Institutes for Health Research, and conducted by the NIH-funded Cardiothoracic Surgical Trials Network (CTSN).



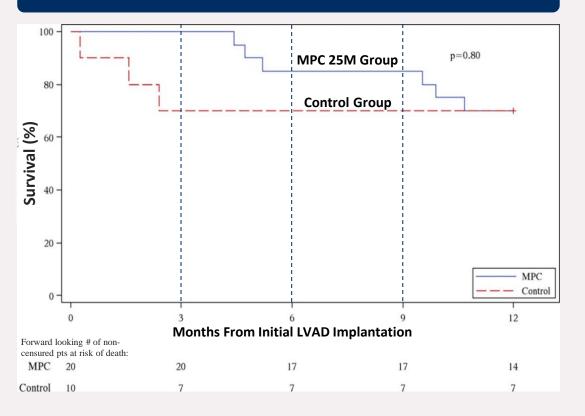
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#### LVAD MPC Pilot Trial Outcomes: 25M MPCs Increased Ability to be Weaned off LVADs and Increased Short-Term Survival<sup>1</sup>

- No cell-related safety events observed
- Median time to first hospitalization was 91 days in the MPC group vs 51 days in the control group
- 50% of MPC vs. 20% of control patients tolerated temporary wean at 90 days despite low dose of cells deployed
- Total number of temporary weans tolerated by MPC group was more than double that of the control group
- Using Bayesian approach, posterior probability that MPCs increased likelihood of successful wean at 90 days was 93%
- At 90 days, 30% (3/10) of controls expired compared to 0% (0/20) treated patients

1. Source: Ascheim DD et al. Circulation. 2014;129:2287-2296.





The 159-patient, double-blind, placebo-controlled 2:1 randomized trial, is evaluating the safety and efficacy of injecting MPC-150-IM into the native myocardium of LVAD recipients

Enrollment completed in Q3, CY2017

Primary efficacy endpoint of the study is the number of temporary weans from LVAD tolerated over 6 months

Secondary efficacy endpoints over 12 months include:

- Time to re-hospitalization
- Patient survival

**MPC-150-IM**:

Various quality of life measurements

Study is sponsored by Icahn School of Medicine, funded by the United States National Institutes of Health (NIH) and Canadian Health of Research Institute, and conducted by the NIH-funded Cardiothoracic Surgical Trials Network (CTSN)

- Phase 2B Class IV trial six-month primary endpoint reached (Q1 CY18)
- Phase 2B Class IV trial full data read-out (Q3 CY18)

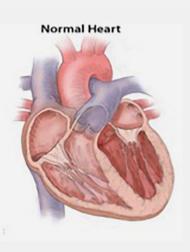
## **MPC-150-IM: Commercial Strategy**

- Leverage data for potential earlier market entry opportunity for MPC-150-IM in end-stage heart failure patients (more than 5K/yr)
  - evaluate potential to reduce LVAD morbidity, increase survival and increase LVAD use as destination therapy (DT)
  - targeted product launch strategy would require minimal investment (top 40 centers represent ~75% of volume)\*
  - if product strengthens native heart muscle, Bridge to Recovery (BTR) represents a future high-growth market opportunity for temporary LVAD use and explantation in end-stage, Class-IV heart failure patients (~50k/yr)

In addition to the Class IV heart failure patients, we will seek to bridge to a larger Class III heart failure population via label extension using our Phase 3 results

## MPC-150-IM: Class III Heart Failure Market Opportunity

<ul> <li>Burden of Illness</li> <li>Globally, 17-45% of heart failure patients die within 1 year of hospital admission</li> <li>Majority die within 5 years of admission<sup>1</sup></li> <li>MPC-150-IM to target advanced HFrEF NYHA Class II-III with the objective of reducing major cardiovascular events (e.g. mortality and hospitalizations)</li> </ul>
Minimal Treatment Options - Despite recent advancements in pharmacotherapy, limited treatment options are available for patients with advanced NYHA Class II-IV Heart Failure with Reduced Ejection Fraction (HFrEF) <sup>2</sup>
Unmet Need  • Therapy that reduces major cardiovascular events (e.g. mortality and hospitalizations) in patients with advanced HFrEF NYHA Class II – III
<ul> <li>NYHA Class II-IV patients with LVEF&lt;40% in the US alone<sup>3</sup></li> <li>Over \$60.2bn/yr in U.S. direct costs when this illness is identified as a primary diagnosis<sup>4</sup></li> <li>- \$115bn as part of a disease milieu<sup>4</sup>; hospitalizations result in ~69% of expenditures<sup>5</sup></li> </ul>



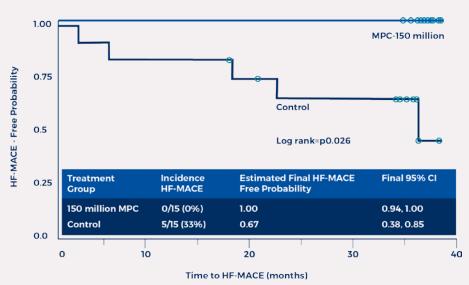
**Systolic Heart Failure** 

Less blood pumped out of ventricles guezza swell

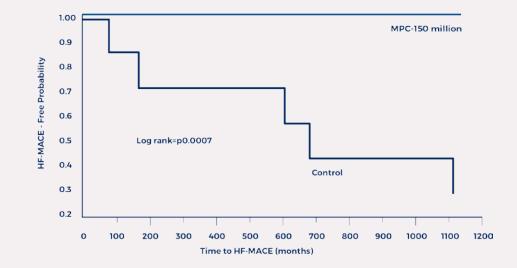
1. Heart Failure: Preventing disease and death worldwide – European Society of Cardiology 2014., 2. ACC/AHAHFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure., 3. Gurwitz JH, Magid DJ, Smith DH, et al. Contemporary Prevalence and Correlates of Incident Heart Failure with Preserved Ejection Fraction. The American Journal of Medicine. 2013;126(5):393-400. Derived by applying a HF-REF prevalence rate of 32.6% to the U.S. rate of 5.7m U.S. patients., 4.A Reevaluation of the Costs of Heart Failure and its Implications for Allocation of Health Resources in the United States. Voigt J. Clinl.Cardiol. 37, 5, 312-321 (2014)., 5.The Medical and Socioeconomic Burden of Heart Failure: A Comparative Delineation with Cancer. Dimitrios, F. International Journal of Cardiology (2015), doi: 10.1016/j.ijard.2015.10.172.,



% HF-MACE Kaplan-Meier Curve over 36 months following treatment in all patients<sup>1</sup>



#### HF-MACE Kaplan-Meier Curve over 36 monthsfollowing treatment in patients with LVESV>100ml<sup>2</sup>



- Over 36 months, patients receiving 150M MPC had significantly greater probability of remaining free of a first HF-MACE vs. controls (0% vs. 33%, p = 0.026 by log-rank)
- All HF-MACE events occurred in controls with baseline Left Ventricular End Systolic Volume (LVESV)>100ml, where the treatment effect size was even greater (0% vs. 71%, p = 0.0007 by log rank)
- Controls with baseline LVESV>100ml had 11 total/recurrent HF-MACE events over 36 months vs. 0 in matched patients receiving 150M MPCs (p=0.0007)

1. HF-MACE is defined as a composite of cardiac related death or non-fatal heart failure hospitalisations. 2. Circ Res. 2015; 117:576-584. Perin E et al. A Phase II Dose-Escalation Study of Allogeneic Mesenchymal Precursor Cells in Patients With Ischemic or Non-Ischemic Heart Failure 3. Journal of Cardiac Failure 2015; Vol 21(8): S107; 19<sup>th</sup> Annual Scientific Meeting of the Heart Failure Society of America, Emerson et al.

NYHA class II/III patients with large baseline LVESV and advanced heart failure are at highest risk of heart failure-related major adverse cardiac events (HF-MACE)

- Have increased likelihood of having recurrent HF hospitalizations
- Existing therapies are limited and economic burden is greatest

#### The ongoing Phase 3 trial is enriched for HF patients with high risk of HF-MACE

- Enrichment for these patients based on heart failure hospitalization in the past 9 months and/or significantly elevated baseline NT-proBNP
- Primary endpoint is a comparison of recurrent non-fatal HF-MACE between cell-treated NYHA class II/III patients and controls
  - Terminal events (such as death, implantation of a mechanical heart assist device or a heart transplant) are also being analyzed as they relate to non-fatal recurrent HF-MACE

## **MPC-150-IM:**

#### Operational Update for Phase 3 Trial in NYHA Class II-III Advanced CHF Patients

- Trial has enrolled more than 400 of approximately 600 patients
- In April 2017, a pre-specified interim futility analysis of the efficacy endpoint in the Phase 3 trial's first 270 patients was successfully achieved
- After completing the interim analysis, the trial's Independent Data Monitoring Committee (IDMC) formally recommended the trial be continued as planned
- Phase 3 trial targeted enrollment completion (2H CY18)

# Chronic Low Back Pain (CLBP) Due to Disc Degeneration

#### MPC-06-ID: a non-Opioid alternative for Chronic Low Back Pain due to **Degenerative Disc Disease**

<ul> <li>Burden of Illness</li> <li>Back pain causes more disability than any other condition<sup>1</sup></li> <li>Inflicts substantial direct and indirect costs on the healthcaresystem<sup>1</sup>, including excessive use of opioids in this patient population</li> </ul>	
<ul> <li>Minimal Treatment Options</li> <li>Treatment options for patients with CLBP who fail conservative therapy include opioids and surgery</li> <li>50% of opioid prescriptions are for chronic low back pain (CLBP)</li> </ul>	
<ul> <li>Disease modifying therapy for durable improvement in pain and function has potential to prevent progression to opioid use or surgical intervention</li> </ul>	
Market Opportunity <ul> <li>In 2016, over ~7m U.S. patients are estimated to suffer from CLBP due to degenerative disc disease (DDD)<sup>3,4,5</sup></li> <li>MPC-06-ID development program targets over ~3.2m patients</li> </ul>	

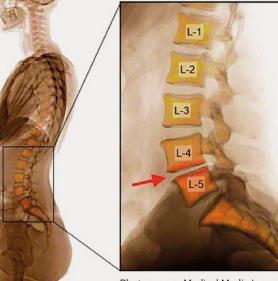


Photo source: Medical Media Images.

Degenerative Disc Disease

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.

## **The Opioid Epidemic**

- 50% of opioid prescriptions are for chronic low back pain (CLBP)
- Over 1,000 people are treated in U.S. emergency departments everyday for misusing prescription opioids
- Over 33,000 people in the U.S. died of prescription opioid related overdoses in 2016
- Opioid epidemic declared a public health emergency by U.S. President Trump in October, 2017
- A non-opioid solution for CLBP is imperative

The 21<sup>st</sup> Century Cures Act includes measures to combat opioid dependence and accelerated approval for non-opioid pain reducing drugs

Information derived from

Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999-2015 on CDC WONDER Online Database, released December, 2016. Available at: http://wonder.cdc.gov/ucdicd10.html

Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2015 National Survey on Drug Use and Health. Online Database, released September, 2016. Available at: https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2015/NSDUH-FFR1-2015/NSDUH-FFR1-2015.htm

Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers - United States, 2002-2004 and 2008-2010. Drug Alcohol Depend. 2013 Sep 1;132(1-2):95-100. doi: 10.1016/j.drugalcdep.2013.01.007. Epub 2013 Feb 12.

#### MPC-06-ID: Phase 2 Trial Results Support Phase 3 Program

- 100 patients with >6 months of CLBP due to DDD and unresponsive to conservative therapies (incl. opioids and epidural steroids) were evaluated in a blinded, randomized, placebo controlled Phase 2 trial
- Pre-specified analyses for change in pain from baseline using VAS and change in function using ODI
- Primary endpoint composite over 24 months using pain and function thresholds (p<0.05 for 6 million MPCs vs saline using Intent to Treat Analysis and p=0.08 by Per Protocol Analysis)<sup>1</sup>

#### both 12 & 24 Months - PP1 50.0% 45.0% 40.7% 40.0% 34.6% 35.0% 30.0% 25.0% 20.0% 17.7% 15.0% 12.5% 10.0% 5.0% 0.0% Saline Hyaluronic Acid 6-million MPC 18-million MPC

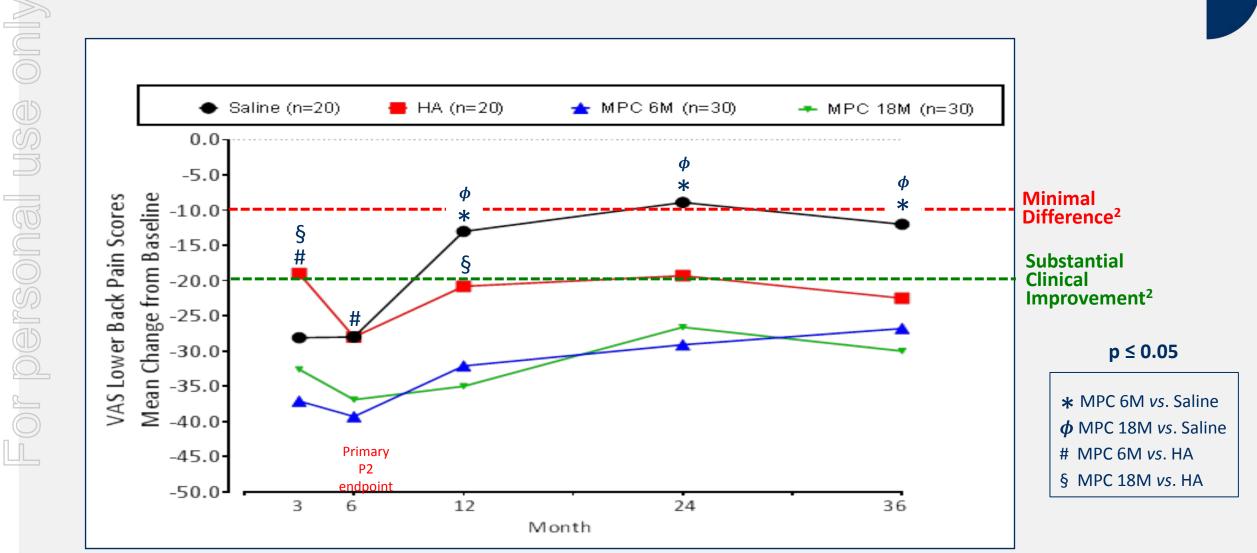
**Composite Responders at** 

#### 1. Source Mesoblast Ltd; PP = Per Protocol population. A Composite Responder must have an optimal pain (50% reduction in VAS) AND function (15 point reduction in ODI) response AND no additional intervention.

% Responder Rate

#### **MPC-06-ID:** Phase 2 Clinical Trial Results:

Substantial Reduction in Low Back Pain Through 36 Months After Single Dose

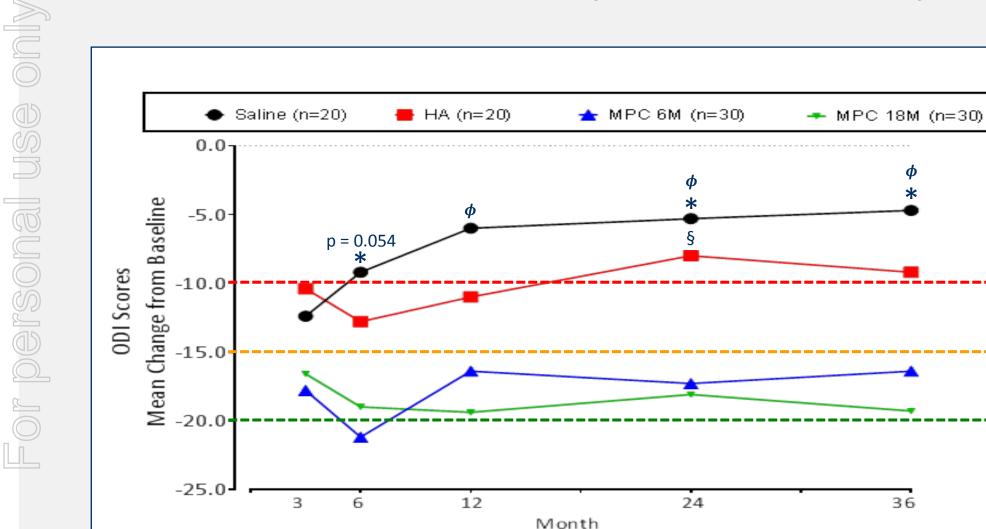


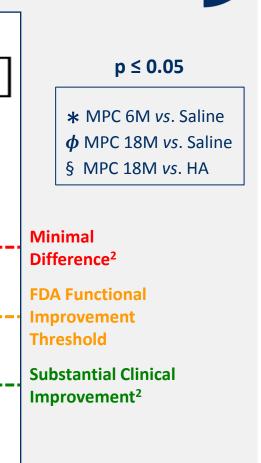
1. ITT Population. Subjects failing therapy due to intervention had BOCF imputed for all visits after the intervention. Patients with missing data were considered treatment failures, so BOCF imputed for all missing values.

 Abdel Shaheed Christina, Maher Chris G, Williams Kylie A, Day Richard, McLachlan Andrew J. Efficacy, Tolerability, and Dose-Dependent Effects of Opioid Analgesics for Low Back Pain: A Systematic Review and Meta-analysis. JAMA Internal Medicine . American Medical Association; 2016 Jul 1;176(7):958-68.

### **MPC-06-ID:** Phase 2 Clinical Trial Results

#### Reduction in Functional Disability Through 36 Months After Single Dose





36

ITT Population. Subjects failing therapy due to intervention had BOCF imputed for all visits after the intervention. Patients with missing data considered treatment failures, so BOCF imputed for all missing values. 1.

Abdel Shaheed Christina, Maher Chris G, Williams Kylie A, Day Richard, McLachlan Andrew J. Efficacy, Tolerability, and Dose-Dependent Effects of Opioid Analgesics for Low Back Pain: A Systematic Review and Meta-analysis. JAMA Internal Medicine . 2. American Medical Association; 2016 Jul 1;176(7):958-68.

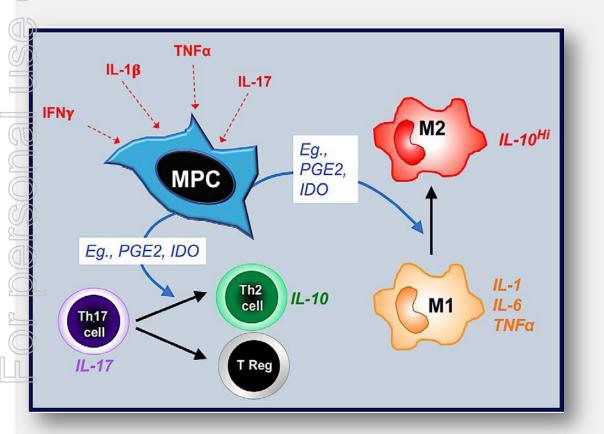
#### MPC-06-ID: Phase 3 Trial Update

- A 360-patient Phase 3 trial across U.S. and Australian sites
- Targeted to complete recruitment early Q1 CY18
- FDA has provided written guidance:
  - Use of a composite primary endpoint at 12 and 24 months is acceptable
  - Agreed thresholds for pain (50% decrease in VAS) and function (15 point improvement in ODI)
  - No additional intervention at the treated level through 24 months

If the P3 results replicate P2 results in pain and function, leverage this product candidate as a potential non-opioid treatment option for chronic low back pain

# Our inflammatory diseases portfolio (MPC-300-IV)

#### Cellular product candidate that responds to multiple inflammatory signals



#### **Phase 2 Clinical Data in Immune Mediated Diseases**

- 60 patients, type 2 diabetes with inadequately controlled glucose:
  - Randomized, placebo controlled dose-ranging study completed
  - Positive dose-dependent effects seen on reduction in HbA1c at 3 months<sup>1</sup>
- **30** patients, diabetic kidney disease:
  - Randomized, placebo controlled dose-ranging study completed
  - Positive effects seen on glomerular filtration rate and on inflammatory biomarkers over 6 months<sup>2</sup>
- 48 patients, biologic-refractory rheumatoid arthritis:
  - Randomized, placebo controlled, dose-ranging study over 52 weeks

1. Allogeneic Mesenchymal Precursor Cells in Type 2 Diabetes: A Randomized, Placebo-Controlled, Dose-Escalation Safety and Tolerability Pilot Study - Diabetes Care, July 2015

2. Allogeneic Mesenchymal Precursor Cells (MPC) in Diabetic Nephropathy: A Randomized, Placebo-controlled, Dose Escalation Study - E BioMedicine, October 2016

## MPC-300-IV: Biological Refractory Rheumatoid Arthritis (RA) Market Opportunity

Burden of illness	In the US alone in 2016 <sup>1,2</sup>					
Treatr	Low disease activity or remission is seen in low numbers of natients					
Unmet N	<ul> <li>Need for disease-modifying therapies that are well tolerated and induce low disease activity or remission in a greater percentage of patients as early as possible in the disease management</li> </ul>					
Market Opportunity	<ul> <li>In 2016, sales of RA agents, predominantly TNF inhibitors exceeded \$19 billion globally. Projections of over \$22.5 billion by 2025, due to sales of oral JAK inhibitors, TNF biosimilars<sup>3</sup></li> </ul>					



- 1. GlobalData©: Rheumatoid Arthritis Global Forecast 2015-2025 0- January 2017.
- 2. Decision Resources Rheumatoid Arthritis Dec 2015.
- 3. Decision Resources Rheumatoid Arthritis April 2016.
- 4. Decision Resources: Unmet Need Immune and Inflammatory Disorders Rheumatoid Arthritis April 2016.

#### MPC-300-IV: Phase 2 Study Design

#### **Inclusion Criteria**

- Inadequate response to at least 1 anti-TNF +/- other biologics
- On a stable regimen methotrexate for >4 months +/- DMARDs for >3 months

#### **Randomisation Scheme**

- MPC 1 million cells/kg (N=16)
- MPC 2 x million cells/kg(N=16)
- Placebo (N=16)

#### **Objectives**

- Primary: Safety and tolerability of a single intravenous MPC infusion through a 12-week primary endpoint
- Secondary: Clinical efficacy at week 4, 12, 39 and 52, primary efficacy endpoint at week 12
  - Pre-specified analyses were applied to the whole study population and the pre-specified exploratory subgroup based on whether the subjects had previously received 1-2 or >3 biologic agents and included:
  - American College of Rheumatology (ACR 20/50/70, ACR-N) composite clinical responses
  - Health assessment questionnaire-disability index (HAQ-DI)
  - Disease Activity Score (DAS28) composite measurement
  - Short-form health survey (SF-36), an assessment of health-related quality-of-life

<sup>\*\*</sup> ClinicalTrials.gov Identifier: NCT01851070.

### **MPC-300-IV**:

Phase 2 trial in biologic refractory Rheumatoid Arthritis shows early and durable effects after single dose

- Infusions were well-tolerated and there were no treatment-related serious adverse events reported, with the safety profile comparable among the placebo and two MPC treatment groups.
- A single intravenous MPC infusion in biologic refractory RA patients resulted in dose-related improvements in clinical symptoms, function, disease activity and patient-reported outcomes. Efficacy signals were observed for each of ACR 20/50/70, ACR-N, HAQ-DI, SF-36 and DAS-28 disease activity score.
- 2 million MPC/kg dose showed greatest overall treatment responses. Onset of treatment response occurred as early as 4 weeks, peaked at 12 weeks, was sustained through 39 weeks, and waned by 52 weeks.
- Greatest benefits over 52 weeks were seen in patients who had failed less than 3 biologics (1-2 biologic sub-group) prior to MPC treatment, identifying this as a potentially optimal target population.
  - Phase 2 trial clinical responses along with the safety profile position MPC-300-IV as an early treatment option in RA patients who are resistant or intolerant to anti-TNF or other biologics
  - Future studies will evaluate whether higher doses can induce even greater rates of low disease activity or remission within 12 weeks





## Financials & Milestones

# Q1 FY18

#### Cash Position and Cash Flows for three months ending 30 Sep 2017 (US\$m)

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	30 Sep 2017	30 Sep 2016	\$Change	
Operating cash outflows	(20.3)	(20.8)	0.5	
Investing cash outflows	(0.6)	(0.3)	(0.3)	
Financing cash inflows/(outflows)	38.4	(0.1)	38.5	
Forex	(0.3)	0.6	(0.9)	
Net increase (decrease) in cash	17.2	(20.6)	37.8	

Cash outflows from Operating activities have reduced 2.3% (\$0.5 million)

	30 Sep 2017	30 Jun 2017	\$Change
Cash on Hand	62.9	45.7	17.2

Cash on hand increased by \$17.2 million (38%) due to net financing cash inflows of \$38.4m in the quarter as a result of the successful September 2017 entitlement offer of 36.2 million shares

## Q1 FY18 - Profit and Loss for the three months ending 30 Sep 2017 (US\$m)

For the three months ending	30 Sep 2017	30 Sep 2016	\$ Change	%
Revenue	1.2	0.4	0.8	197%
Research and Development	(15.4)	(14.0)	(1.4)	(10%)
Manufacturing Commercialization	(0.9)	(3.3)	2.4	73%
Management & Administration	(5.0)	(5.5)	0.4	8%
Contingent Consideration	9.5	(1.0)	10.5	NM
Other Operating Income & Expenses	0.7	0.5	0.2	41%
Loss Before Tax	(9.9)	(22.9)	13.0	57%

Revenue increased by \$0.8 million (197%) vs comparative period in FY17

- Commercialization revenue increased by 178% (\$0.4 million) due to an increase in royalty income on sales of TEMCELL® Hs. Inj., versus the comparative period
- A sales milestone of \$0.5 million was recognized as TEMCELL® Hs. Inj., reached a cumulative sales milestone in the three months ended 30 September 2017. No milestones were recognized in the comparative quarter

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Overall management contained spend whilst increasing its R&D investment in Tier 1 clinical programs by deferring manufacturing production and constraining management and administration costs

- **R&D expenses increased by \$1.4 million (10%)** as management invested in Tier 1 clinical programs
- Manufacturing Commercialization decreased by \$2.4 million (73%) sufficient clinical grade product on hand enabled the number of production runs to be reduced in the period vs the comparative quarter
- Management & Admin costs reduced by \$0.4 million (8%) as management contained rent and IT costs

# **Targeted Upcoming Milestones and Catalysts**

#### **MSC-100-IV for Pediatric Acute GVHD**

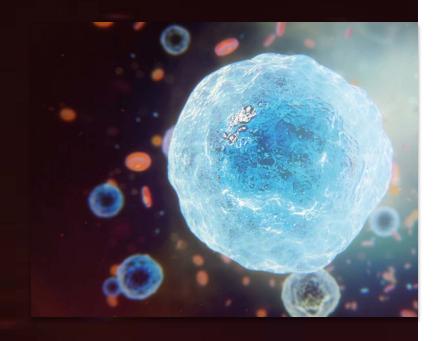
- Phase 3 expected to complete enrollment (Q4 CY17)
- Day 28 primary endpoint data read-out (Q1 CY18)
- Day 100 survival data (Q2 CY18)

#### MPC-150-IM for Advanced and End-Stage Heart Failure

- Phase 2B Class IV trial six-month primary endpoint reached (Q1 CY18)<sup>1</sup>
- Phase 2B Class IV trial full data read-out (Q3 CY18)<sup>1</sup>
- Phase 3 trial for Class II/III targeted enrollment completion (H2 CY18)

#### MPC-06-ID for Chronic Low Back Pain

- Phase 3 trial expected to complete enrollment (early Q1 CY18)
- **Potential Corporate Partnerships**



1. Study is funded by the United States National Institutes of Health (NIH) and the Canadian Health Research Institute (CHRI), and conducted by the NIH-funded Cardiothoracic Surgical Trials Network (CTSN).