# mesoblast the regenerative medicine company

# Leading the world in novel adult stem cell therapies

Jefferies Annual Healthcare Conference New York 2012

### **Forward looking statements**

#### CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This presentation, including any comments made during or following the presentation, may contain forward-looking statements that are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. 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 Teva, Cephalon and Lonza 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. Actual results may differ from the results anticipated in these forward-looking statements, and the differences may be material and adverse. Factors 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.

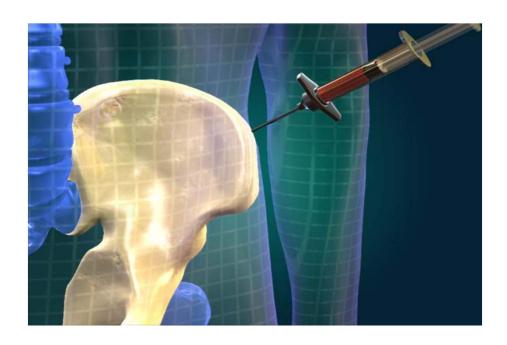


### A risk managed business model

- Proprietary platform technology delivers multi-product pipeline
  - multiple shots on goal
  - not dependent on success of any one product
- corporate partnerships manage execution risk
  - Teva provides global distribution capability, regulatory and clinical trial experience
  - Teva Phase 3 funding alleviates internal cash burn
  - Lonza provides best-in-breed process development & manufacturing capability, alleviates need for internal spend on manufacturing facility
- strong cash position (approx. \$226m) enables simultaneous development of multiple products
  - Mesoblast has sufficient cash to advance new programs in parallel
  - investment in people with expertise in clinical development
- staged development program controls technical risk
  - managed transition from simple to complex indications and delivery modes
  - build on strong preclinical foundations and accumulated clinical experience



# **Technology**



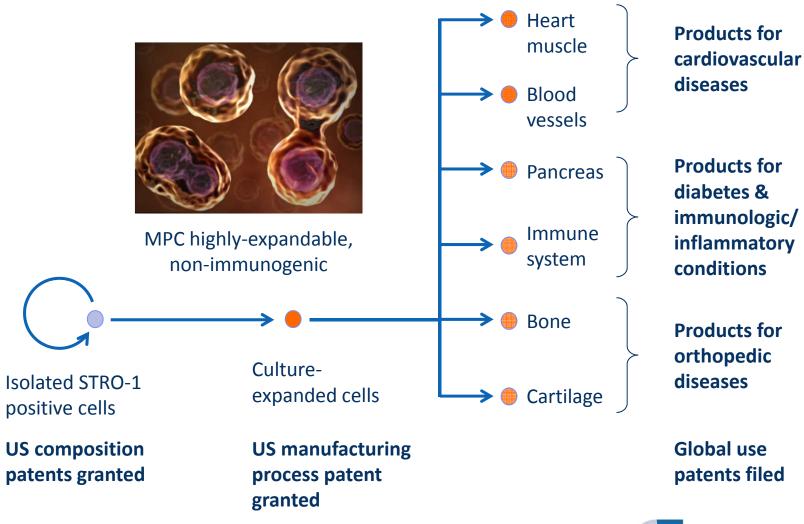


#### Overview of current stem cell universe

- stem cells are unspecialized cells that can renew themselves
  - can mature into specialized cell types such as muscle, nerve, bone, blood cells, etc
  - stem cells constantly renew and repair tissues in the body
- our mesenchymal precursor cells are multipotent and allogeneic, with superior characteristics to alternative stem cell types
- limitations of other stem cell types
  - embryonic stem cells
    - pluripotent can form most cells in the body
    - ethical and safety issues tumor potential
  - hematopoietic stem cells
    - multipotent can form limited cell types (blood cells, immune system)
    - normally only used autologously (patient's own cells) due to immune reactions



### We own the IP on Mesenchymal Precursor Cells (MPCs)





### Our proprietary adult stem cells

- potent, purified adult mesenchymal precursor cells
  - strong safety profile
  - avoid ethical and safety issues associated with embryonic stem cells
  - backed by strong patent position
- "off the shelf" classic pharmaceutical drug model
  - batch to batch consistency
  - clear, rapid regulatory pathway
- easy to expand in large numbers
  - low cost of goods, no supply constraints
  - high margin business model



# **Product Pipeline**





#### **Platform Technology Delivers Multi-Product Pipeline**

#### **Cardiovascular and Neurologic Products**

- Teva alliance delivers proven execution capability in major global markets
- cash from milestone payments to fund rest of Mesoblast pipeline

#### **Products for Type 2 Diabetes and Metabolic Disease**

- early diabetics
- kidney/heart/liver complications

#### **Inflammatory/Immunomodulatory Products**

- lung diseases (e.g. Pulmonary Fibrosis)
- Inflammatory joint diseases (e.g. Rheumatoid Arthritis)

#### **Orthopedic products**

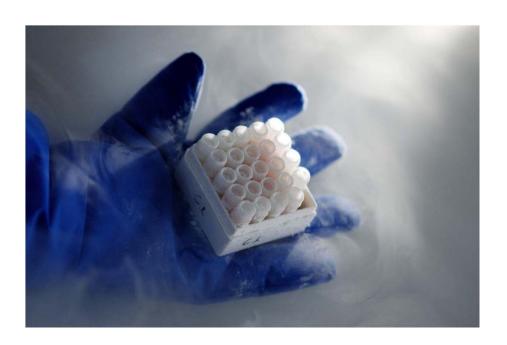
- intervertebral disc repair
- stress fractures
- spinal fusion



#### "Off-the-shelf" products IND clearance FDA approval **Lead products Pre-clinical** Phase III Phase II Cardiovascular Product Congestive heart failure Acute myocardial infarction Chronic refractory angina **Neurologic Products** Stroke/Parkinson's/Huntington's/MS Diabetes/Metabolic Disease Product Early Type 2 Diabetes Diabetic Complications (kidney/liver) Immunomodulatory/Inflammatory Product Lung diseases/Rheumatoid Arthritis **Orthopedic Products** Spinal fusion Intervertebral disc repair **Bone Marrow Transplantation** Eye diseases – wet AMD



## **Strategic Partnerships**





#### **Teva strategic alliance**

- Teva has exclusive rights to Mesoblast cardiovascular, neurologic, BMT products
- Teva holds 19.99% stake in Mesoblast
- 1. Cardiovascular Products:

Bone marrow derived MPC (Mesoblast granted composition patents)
congestive heart failure (CHF) set to commence Phase 3 in US, EU,
Asia/Pac
acute myocardial infarction (AMI) Phase 2 in EU
chronic refractory angina
critical limb ischemia (CLI)

2. Neurologic Products:

Dental Pulp Stem Cells (Mesoblast exclusive world-wide license to granted composition patents)

Huntington's Disease Parkinson's Disease spinal cord injury stroke

3. Bone Marrow Transplant Cord Blood Product:

Non-core niche market, FDA-cleared Phase 3 program
EU is the major transplant market, plan for early EU regulatory approval by Q1 2013



### **Dental Pulp Stem Cells (DPSC)**

- 1. Mesoblast has exclusively licensed world-wide commercial rights to granted composition of matter patents covering DPSC.
- 2. DPSC are a STRO-1 positive subset of Mesoblast's STRO-1 MPC patented technology platform
- 3. DPSC differ from bone marrow-derived MPC in their neural crest origin
- 4. DPSC have been shown to produce significantly greater levels of neurotrophic factors and to be significantly more effective than other adult stem cell types for neural differentiation and neural network repair
- 5. Published studies show DPSC may be effective for protection and repair of cells and tissues involved in Parkinson's disease, acute spinal cord injury, and stroke
- 6. Huntington's disease may provide opportunity for accelerated DPSC market entry



#### Lonza manufacturing alliance is central to profitability

#### State-of-the-art manufacturing plant via strategic alliance with Lonza

- Lonza will supply clinical and long-term commercial MPC product needs globally
- Lonza to construct a purpose-built manufacturing facility exclusively for Mesoblast
- Mesoblast can buy out this facility at a pre-agreed purchase price
- Mesoblast will have exclusive access to Lonza's cell therapy facilities in Singapore

#### Mesoblast retains control of manufacture for all products

- product delineation for distribution partners
- maintain optimal product pricing differences

#### **Commercial benefits**

- reduced COGS, increased margins on sales price
- state-of-the-art, industrialized manufacturing process
  - R&D support for enhanced second generation products
  - leverage new technologies



# **Program Update**





### Cardiovascular franchise – congestive heart failure (CHF)

prevalence 6.2 million in US, > 670,000 new patients annually

- 60 patient multi-center, randomized, controlled Phase 2 trial
- Class II-IV CHF, ejection fraction < 40% (high 6- and 12-month mortality)</li>
- randomized 3:1 controls to MPCs at 25M, 75M or 150M cell doses
- cells injected by J&J NOGA Myostar™ catheter single injection
- primary stated endpoint of trial was safety and feasibility
- primary endpoint of safety successfully met, no adverse events associated with MPCs at any dose
- no clinically relevant immune responses to donor cells



#### **Congestive heart failure Phase 3 program**

"In general, Phase 3 studies should use endpoints such as mortality and cardiovascular or heart failure hospitalizations, whereas endpoints, such as ejection fraction, that have not been validated as surrogates for clinical outcome are not considered to be acceptable as primary efficacy endpoints for pivotal trials."

US FDA, Guidance for Industry, Cellular Therapy for Cardiac Disease October 2010

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- End of Phase 2 meetings held with United States Food and Drug Administration (FDA) and European Medicines Agency (EMA)
- Alignment between agencies on Phase 3 trial design, primary endpoint, secondary endpoints
- Phase 3 trial powered for efficacy based on primary composite endpoint of heart failure hospitalization and mortality
- Phase 3 dose selection of 150 million MPC based on concordance of dose effect in Phase 2 trial and preclinical ischemic and non-ischemic sheep heart failure studies
- Phase 2 results showed that 150 million MPC dose caused concordant effects on primary and secondary endpoints

0 vs. 20% event rate in primary composite endpoint over mean 18 month follow-up, significant reduction in end systolic volumes (positive remodelling effects) and significant improvement in functional capacity as measured by > 50 meter increase in walking distance over 6 minutes

# Allogeneic MPCs For Treatment Of Type 2 Diabetes And Metabolic Complications

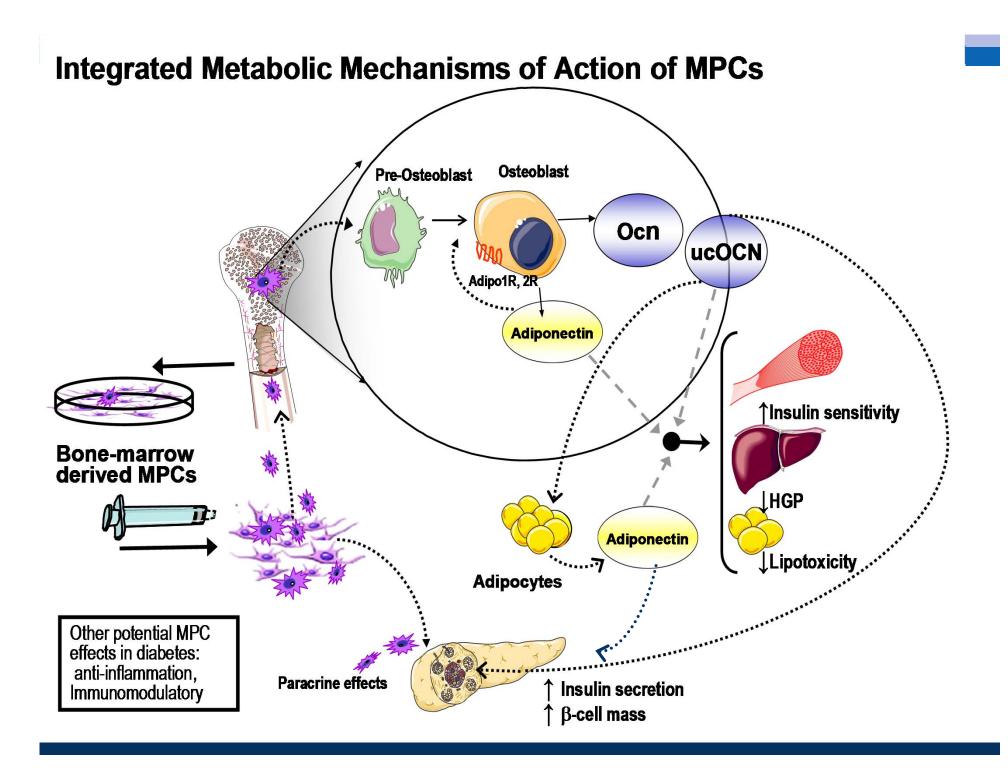
- Potential Mechanisms of Action
- immunomodulatory/anti-inflammatory effects (reduce CRP, IL-1, IL-17)
- direct effects on pancreas

increased islet cells beta cell regeneration improved glucose sensing restoration of normal insulin production

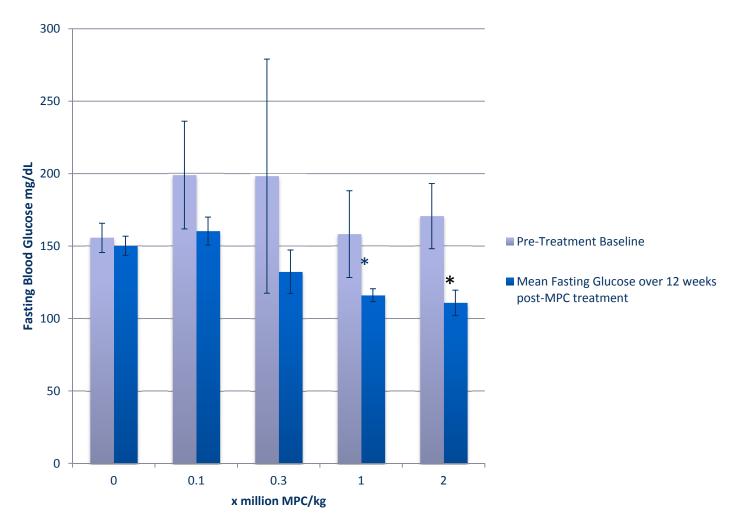
effects on peripheral endocrine organs

increased osteocalcin from bones improved adipose tissue sensitization to insulin





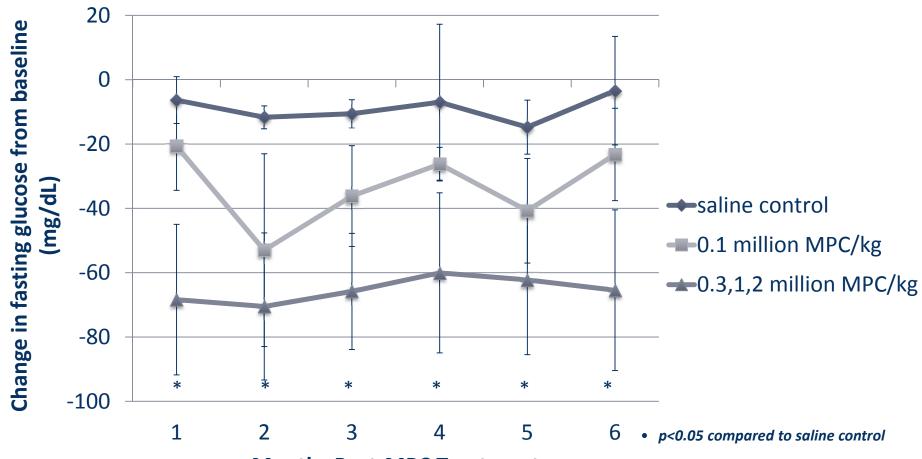
# Mean Fasting Blood Glucose levels over 12 weeks following single MPC injection in non-human primates with type 2 diabetes



<sup>\*</sup> Significant at P<0.05 compared to respective baseline



# Highest doses show sustained glucose lowering effect for 6 months in nonhuman primates with early type 2 diabetes (AB206)

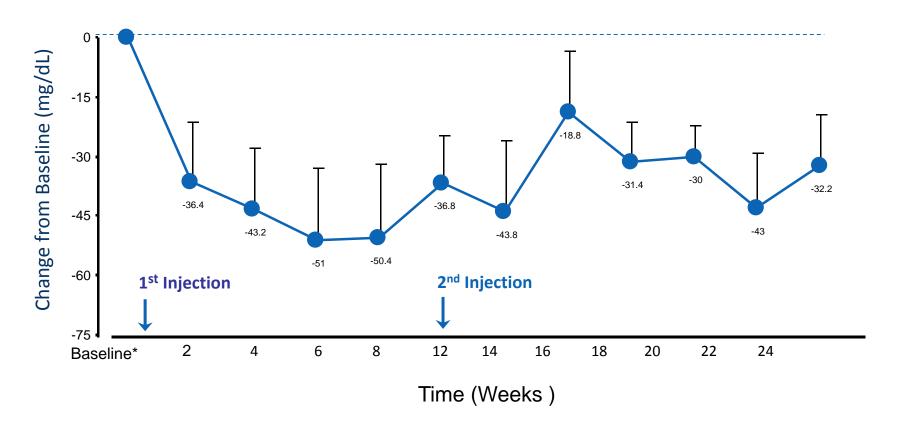


**Months Post-MPC Treatment** 

Saline control: N=3
0.1 million MPC/kg: N=3
0.3, 1, 2 million MPC/kg: N=6



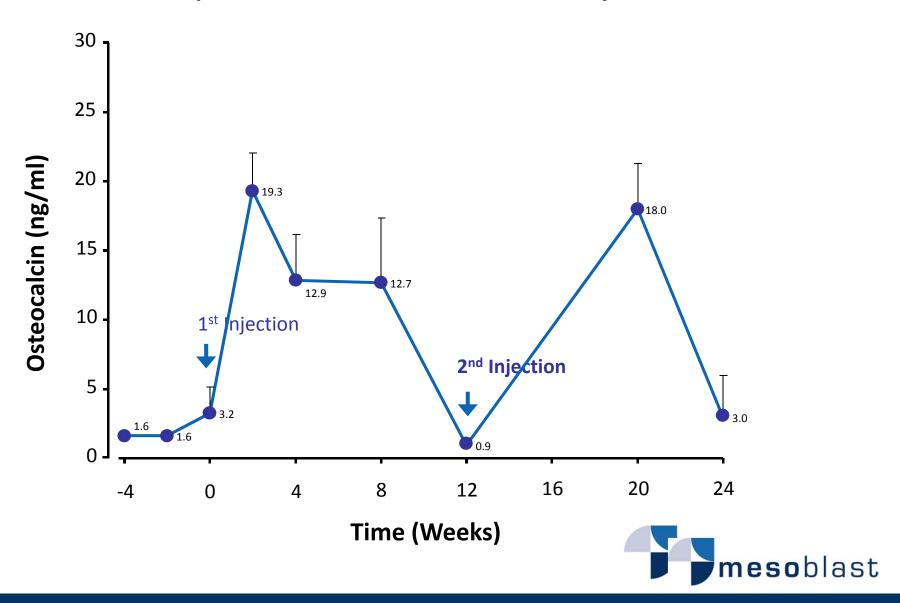
#### Repeat Dosing In AB205 (0.3, 1, or 2 M MPC/kg): Mean (+SEM) Blood Glucose Changes from Baseline over Time



<sup>\*</sup>Baseline clinical chemistry drawn at week -2; 1st MPC injection on Day 0



Repeat Dosing In AB205 (0.3, 1, or 2 M MPC/kg): Mean Osteocalcin levels have similar inductive peaks and kinetics after 1<sup>st</sup> and 2<sup>nd</sup> injections



### **Conclusions From Diabetic Primate Studies**

- Sustained 6-month durability of glucose lowering effect by single intravenous injection of allogeneic MPC at 0.3, 1 or 2 million MPC/kg;
- Accompanying sustained reductions in CRP levels suggest a potential cardioprotective effect of the MPC
- Repeat dosing was safe and resulted in parallel peaks and kinetics of osteocalcin induction
- This was associated with normalization of fasting insulin levels and maintenance of low fasting blood glucose levels



## **Corporate Overview**





### **Investment snapshot**

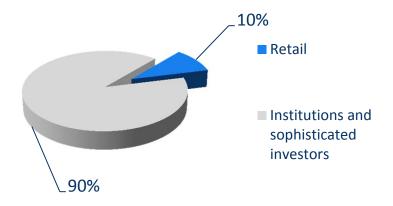
Mesoblast is a public company, listed on the Australian Securities Exchange since 2004.

It is included in the S&P/ASX 200 Index.

Issued shares	280m
Current share price	US\$6.50
Cash available (approx)	US\$226m
Market capitalization (approx)	US\$1,700m

Results (A\$m except per share data)	2011	2010
Total revenue & other income	120.9	0.8
Operating expenses		
R&D	15.3	7.6
Management	11.8	3.6
Other	1.5	4.4
Profit / losses (before tax)	92.2	(14.8)
EPS basic – cents per share	41.8	(10.5)
EPS diluted – cents per share	39.8	(10.5)

#### Mesoblast ownership





#### Value inflexion points – near term

- commencement of Phase 3 trial in congestive heart failure
- completion of Phase 2 spinal fusion trials
- completion of Phase 2 disc repair trial
- completion of Phase 2 trial in type 2 diabetes
- commencement of neurologic preclinical trials using dental pulp stem cells
- expanding the intravenous product franchise, e.g. lung diseases, rheumatoid arthritis
- further partnering opportunities optimal timing



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