# mesoblast the regenerative medicine company



Credit Suisse Healthcare Conference 9 November 2011

#### **Forward looking statements**

#### CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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#### **Investment snapshot**

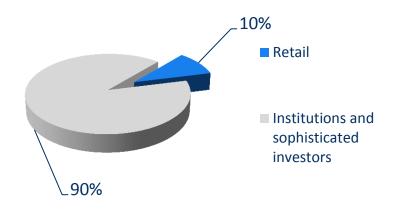
Mesoblast is a public company, listed on the Australian Securities Exchange since 2004

Australian Securities Exchange since 2004.	Current share price	A\$8.23
t is included in the CRD/ACV 200 Index	Cash available (approx)	A\$256m
t is included in the S&P/ASX 200 Index.	Market capitalization	A\$2,300m

**Issued shares** 

Results (\$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**





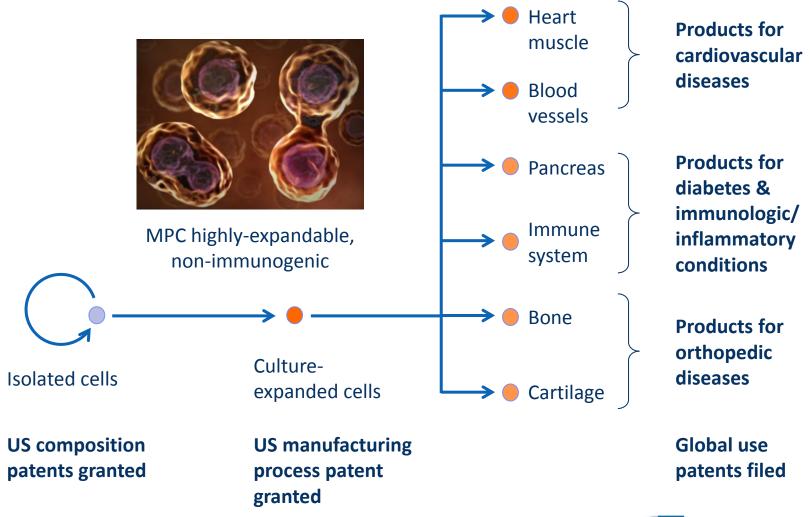
280m

#### Stem cell overview

- 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
- embryonic stem cells
  - pluripotent can form most cells in the body
  - 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
- mesenchymal stem cells
  - multipotent can form limited cell types (skin, bone, fat, muscle, etc)
  - clear of safety and ethical issues
  - may be used allogeneically ("off the shelf")



#### We own the intellectual property on Mesenchymal Precursor Cells





#### Our proprietary adult stem cells

- potent, purified adult mesenchymal precursor cells
  - strong safety profile no immune reactions
  - avoid ethical and safety issues associated with embryonic stem cells
  - backed by strong patent position
- "off the shelf" just like classic pharmaceutical drugs
  - 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



#### The Mesoblast value proposition – the three pillars

#### The Teva alliance

- delivers proven execution capability in major global markets
- drives clinical programs in key therapeutic areas experienced team
- cash from milestone payments to fund Mesoblast pipeline

#### Orthopedic pipeline

- intervertebral disc repair
- stress fractures
- spinal fusion

#### Intravenous product pipeline

- systemically delivered cells
  - Type 2 diabetes
  - immunologic conditions (eg rheumatoid arthritis)
  - inflammatory diseases of various tissues (eg lungs)



#### Teva (Cephalon) strategic alliance

- Cephalon received exclusive worldwide commercialization rights to selected cardiovascular and neurologic indications, and bone marrow transplantation
- Cephalon responsible for funding Phase 2b and Phase 3 clinical development
- Mesoblast receives upfront fee of US\$130 million, plus up to US\$1.7 billion in milestone payments, plus revenue split, retains all manufacturing rights
- Cephalon acquired 19.99% stake in Mesoblast for \$243m outlay
- Mesoblast cash balance of \$263 million to fund other major indications including
  - diabetes
  - immunologic conditions (eg rheumatoid arthritis)
  - inflammatory diseases of various tissues (eg lungs)
  - ophthalmic indications
  - orthopedic cartilage and bone conditions
- Teva acquisition of Cephalon positive for Mesoblast



#### Global 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

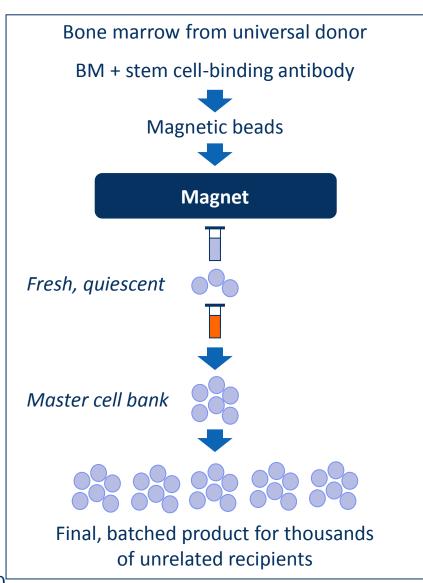
- product delineation for distribution partners
- maintain optimal product pricing differences

#### **Commercial benefits**

- reduced COGS
- increased margins on sales price
- R&D support for enhanced second generation products
- leverage new technologies



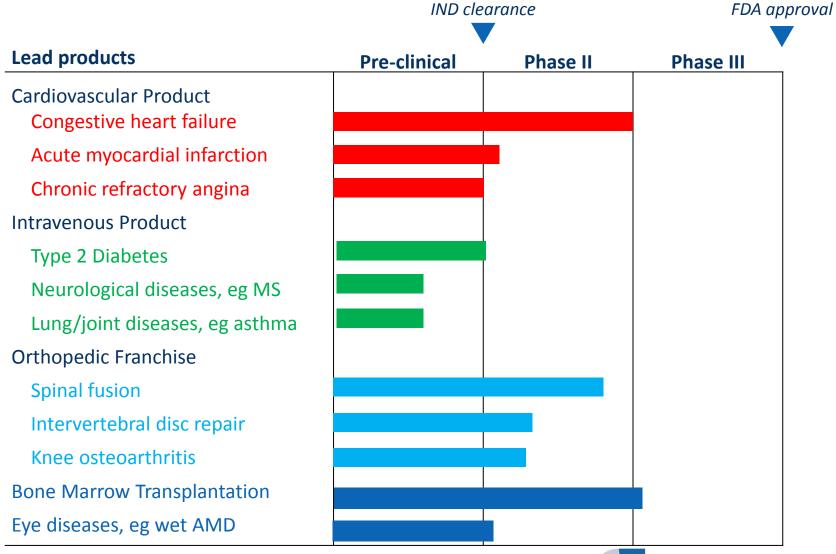
#### Our industrial scale manufacturing process



- homogeneous cell population
- cost-effective large-scale expansion
- batch-to-batch consistency
- stringent release criteria
- potent expanded product



#### "Off-the-shelf" product franchises driving value creation



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

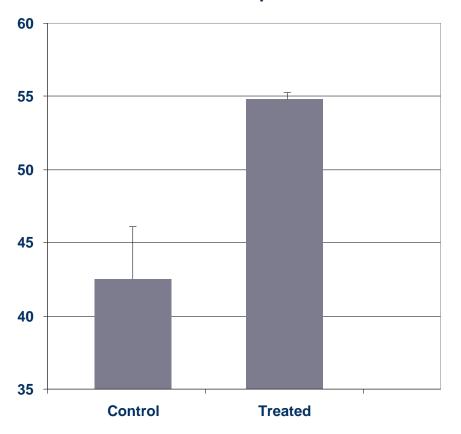
- 60 patient multi-center, randomized, controlled Phase 2 trial
- Class II-IV CHF, ejection fraction < 40% (high 6- and 12-month mortality)</li>
- randomized 3:1 controls to MPCs at 25M, 75M or 150M cell doses
- cells injected by J&J NOGA Myostar™ catheter single injection
- primary endpoint of safety met, no adverse events associated with MPCs at any dose
- key efficacy endpoints after average 18 month follow-up:
  - 50% reduction in serious adverse cardiac events (p=0.001)
  - 80% reduction in major adverse cardiac events (p=0.005)
  - 13% cardiac-related mortality in controls, vs 0% in treated (p=0.059)

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



#### **Cardiovascular franchise – acute myocardial infarction**

## Pre-clinical sheep model Left ventricular ejection fraction at 8 week follow up



#### Phase 2 trial design

- multi-country, 225 patient double blind randomized placebo controlled
- intracoronary infusion, two doses of MPCs vs saline (12.5M and 25M) randomized 1:1:1
- functional parameters MACE, reduction in infarct size
- additional functional efficacy assessments include LVEF, perfusion, volume changes, exercise treadmill test
- 24 month follow up





#### Intravenous franchise – preclinical development

- high value product using systemic administration
- applications:
  - Type 2 diabetes
  - Osteoporosis
  - Lung diseases (asthma)
  - Inflammatory joint diseases (rheumatoid arthritis)
  - Neurological diseases (MS)
- we are generating compelling preclinical data in each of these areas to support early commencement of Phase 2 human trials
  - "best in breed" preclinical models, high predictive value

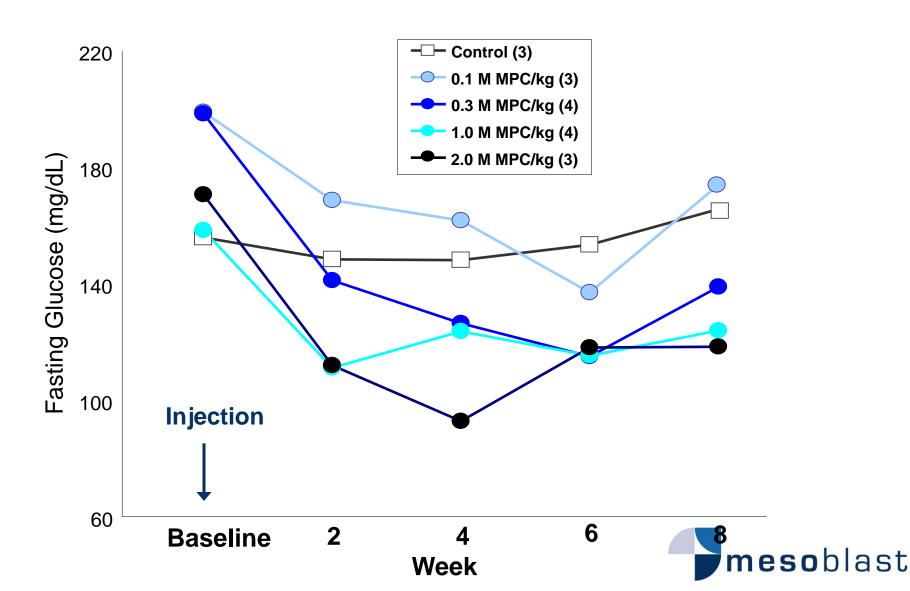


#### Intravenous franchise – Type 2 Diabetes Pre-Clinical Study

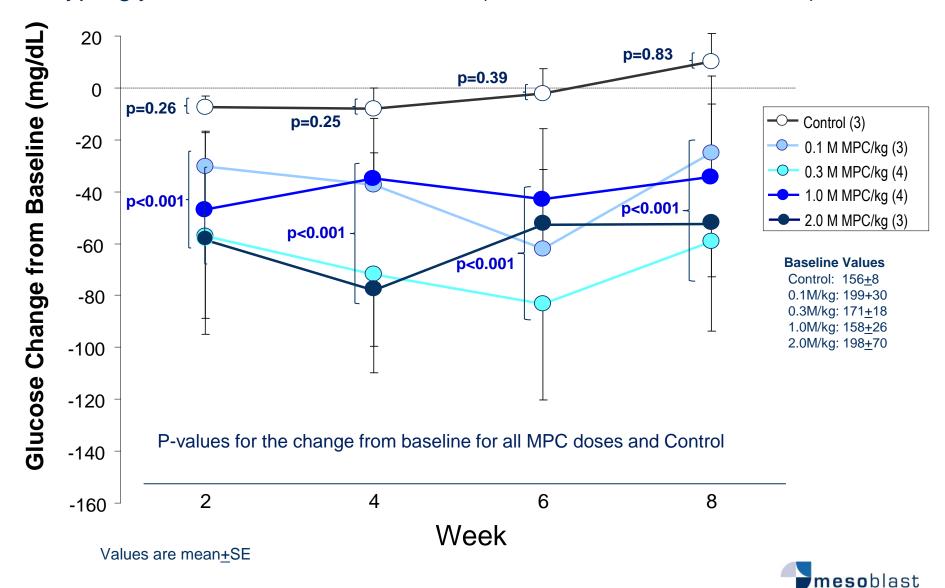
- 17 non-human primates with dietary induced Type 2 diabetes
- Dose-ranging study evaluating effect of single intravenous injection of Mesoblast's allogeneic MPCs over eight weeks
- Controls (n=3) received a single saline injection, four groups of treated subjects (3-4 per group) received one of 4 escalating doses of MPCs (0.1, 0.3, 1 and 2 million MPCs/kg).
- Fasting blood glucose and C-reactive protein measured at 0, 2,
   4, 6, 8 weeks



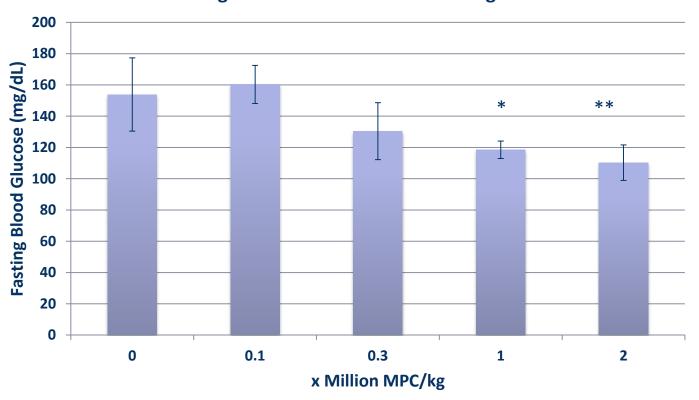
### Effect of MPC or Saline Injection on Fasting Glucose in Nonhuman Primates With Type 2 Diabetes



## Fasting Glucose Change from Baseline Over Time in Obese, Hyperglycemic Nonhuman Primates (AB205/AB206 Pooled Data)



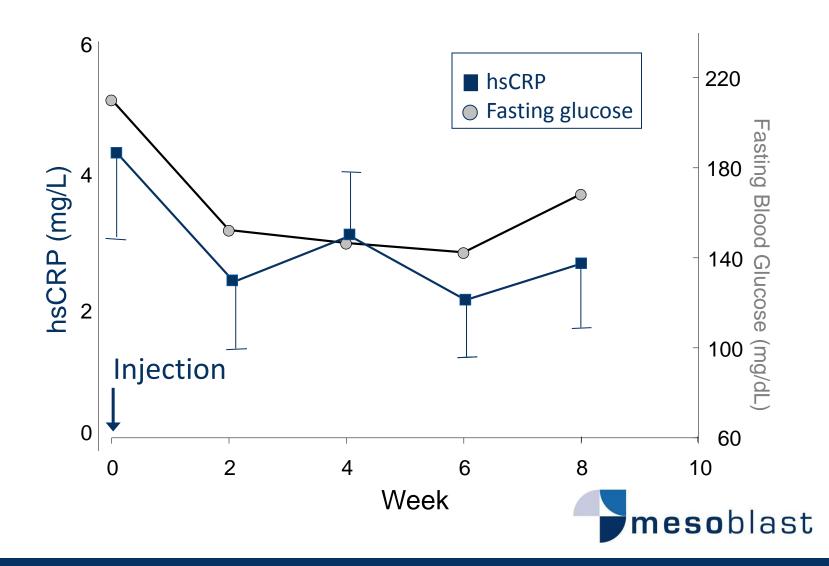
### Dose-Dependent Effect Of Single Intravenous MPC Injection On Mean Fasting Blood Glucose Levels Over Eight Weeks



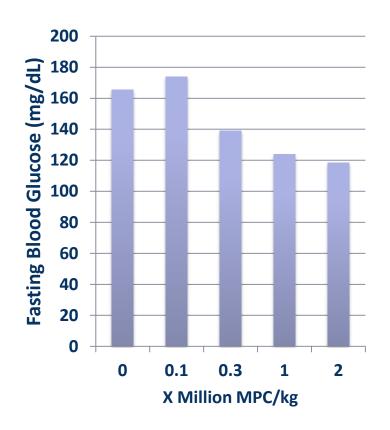
\*\* P<0.05 compared to controls

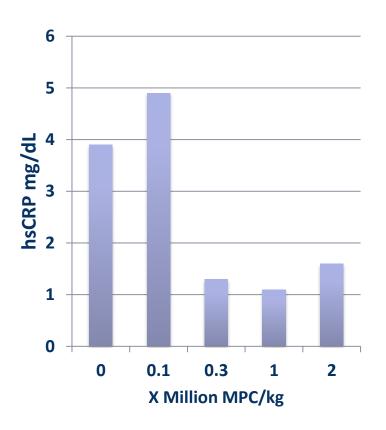


## AB206: C-Reactive Protein and Fasting Glucose over Time All MPC Doses Pooled (n=9)



## Dose-Dependent Effects On Reduced Mean Fasting Blood Glucose and Reduced CRP Levels At Eight Weeks After A Single Intravenous Injection Of Allogeneic MPC







#### 2011 - major accomplishments to date

- executed strategic alliance with Cephalon Inc. for selected product commercialization
- Executed strategic alliance with Lonza for long-term manufacturing capacity
- expanded cardiovascular franchise to cover heart failure, heart attack and chronic angina
- Completed congestive heart failure Phase 2 trial
  - special presentation at American Heart Association meeting
- Expanded spine franchise: commenced degenerative disc repair Phase 2 trial,
   complements ongoing Phase 2 spinal fusion trials
- Completed pre-clinical Type 2 diabetes study in preparation to begin first Phase 2 trial for intravenous product
- Commenced Phase 2 trial in wet age-related macular degeneration
- Commenced Phase 3 trial in bone marrow transplantation



#### Value inflexion points – near term

- completion of Phase 2 heart failure trial progression to Phase 3 pivotal trial
- completion of two orthopedic Phase 2 spinal fusion trials
- completion of disc repair Phase 2 trial
- moving diabetes into Phase 2 trials
- building the intravenous franchise
- further partnering opportunities optimal timing



# mesoblast the regenerative medicine company

Leading the world in novel adult stem cell therapies

