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Mesoblast Reports Positive Results Using Intravenously Injected Adult Stem Cells for Type 2 Diabetes

Key Points

- **Single injection of Mesoblast's proprietary allogeneic, or off-the-shelf, Mesenchymal Precursor Cells (MPCs) significantly lowered blood sugar levels for up to eight weeks in non-human primates with Type 2 diabetes**
- **A clear dose-dependent effect was seen, with the highest three MPC doses maintaining significantly reduced blood glucose levels after eight weeks compared with controls**
- **In MPC treated subjects, there was a direct correlation between reductions in fasting blood glucose levels over time and reductions in circulating C-reactive protein (CRP), the major predictor of cardiovascular risk in Type 2 diabetic patients**
- **Highest three MPC doses significantly reduced circulating CRP levels after eight weeks compared with controls, to levels associated with reduced risk for heart attacks and death in Type 2 diabetic patients**
- **Type 2 diabetes will be the first clinical indication to be targeted using Mesoblast's intravenous product formulation**
- **Phase 2 clinical trial in Type 2 diabetes expected to commence first quarter 2012**

Phoenix, United States; 9 November; and Melbourne, Australia; 10 November 2011: Regenerative medicine company, Mesoblast Limited (ASX: MSB), today announced that a single intravenous injection of its proprietary adult stem cells resulted in significant lowering of blood sugar levels for up to eight weeks in a controlled, randomized preclinical trial in non-human primates with Type 2 diabetes. This was accompanied by significant reductions in circulating inflammatory markers to levels associated with protection against heart attacks and death in patients with Type 2 diabetes. Results of the study were presented at the Credit Suisse Healthcare conference in Phoenix, Arizona.

A randomized, placebo-controlled study was performed in 17 non-human primates with dietary-induced Type 2 diabetes to evaluate the effects of a single intravenous injection of Mesoblast's proprietary allogeneic, or off-the-shelf, Mesenchymal Precursor Cells (MPCs) on blood glucose levels over an eight week period. Controls (n=3) received a single saline injection, while 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).

At baseline, the high mean fasting blood glucose levels were not significantly different between any of the Type 2 diabetic groups. Over the eight week period of the study, the control group showed no significant changes in the high levels of fasting blood glucose. In contrast, a single injection of MPCs at every dose tested significantly reduced fasting blood glucose levels as early as two weeks ($p<0.001$ for each dose), with a clinically meaningful reduction in fasting blood sugar levels of up to 80 mg/dl by four weeks. There was a dose-dependent effect, with the highest three MPC doses maintaining sustained reductions in fasting blood glucose over the entire eight week study period, and the lowest MPC dose being least effective. Over the eight weeks, the groups receiving 1 and 2 million MPC/kg maintained significantly lower mean fasting blood glucose levels compared with the control group (respectively, 119 mg/dl and 110 mg/dl vs 154 mg/dl, both $p<0.05$). The mean fasting blood glucose level in the group which received 0.3 million MPC/kg (130 mg/dl) was moderately lower than the controls (154 mg/dl), while the lowest dose at 0.1 million MPC/kg was without effect (160 mg/dl vs 154 mg/dl).

In MPC treated subjects, there was a direct correlation between reductions in fasting blood glucose levels over time and reductions in circulating C-reactive protein (CRP). CRP is a major inflammatory marker which is highly predictive of risk for heart attack and cardiac death when present at levels >3 mg/L in people with Type 2 diabetes. At eight weeks, mean CRP levels were 1.3 mg/L, 1.1 mg/L and 1.6 mg/L in the groups who received 0.3, 1 and 2 million MPC/kg, compared with 3.9 mg/L and 4.9 mg/L in the groups who received saline and 0.1 million MPC/kg, respectively ($p<0.05$ for the pooled highest three doses vs pooled controls and lowest dose).

These results in non-human primates build on an earlier study which showed that a single dose of human MPCs injected into mice with diabetes resulted in a significant increase in blood insulin levels and sustained reduction in blood glucose levels for the entire three-week period of follow-up. This was due to restoration in the damaged pancreas of the balance between insulin-producing beta cells, which reduce blood glucose, and glucagon-producing alpha cells, which increase blood glucose.

Mesoblast Chief Executive, Professor Silviu Itescu, said that the results obtained to date indicate that a single intravenous injection of Mesoblast's MPCs may have a sustained benefit on blood glucose control, reduce inflammation, and improve lipid profile in patients with Type 2 diabetes.

"Mesoblast's cells have the potential to establish a new medical paradigm for the treatment of Type 2 diabetes which is safe and simultaneously targets multiple factors responsible for the disease and its complications.

"Intravenous injection of our MPCs may not only improve blood glucose control, it may concomitantly reduce the significant risk of heart attacks and death that occurs in patients with Type 2 diabetes," Professor Itescu added.

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Mesoblast has an upcoming scheduled meeting with the United States Food and Drug Administration (FDA) to discuss its Phase 2 clinical program in patients with Type 2 diabetes. The company expects to commence a randomized, placebo-controlled Phase 2 trial in the first quarter of 2012.

Type 2 diabetes accounts for 90-95 per cent of the 230 million diabetics in the western world, with its prevalence increasing at an alarming rate. In the United States alone, there were 27 million established cases of Type 2 diabetes in adults aged over 20 in 2010. With a growth rate of 2.6% per year, this number is expected to increase to more than 35 million in 2020.

About Mesoblast

Mesoblast Limited (ASX:MSB) is a world leader in commercialising biologic products for the broad field of regenerative medicine. Mesoblast has the worldwide exclusive rights for a series of patents and technologies developed over more than 10 years relating to the identification, extraction, culture and uses of adult Mesenchymal Precursor Cells (MPCs).
www.mesoblast.com

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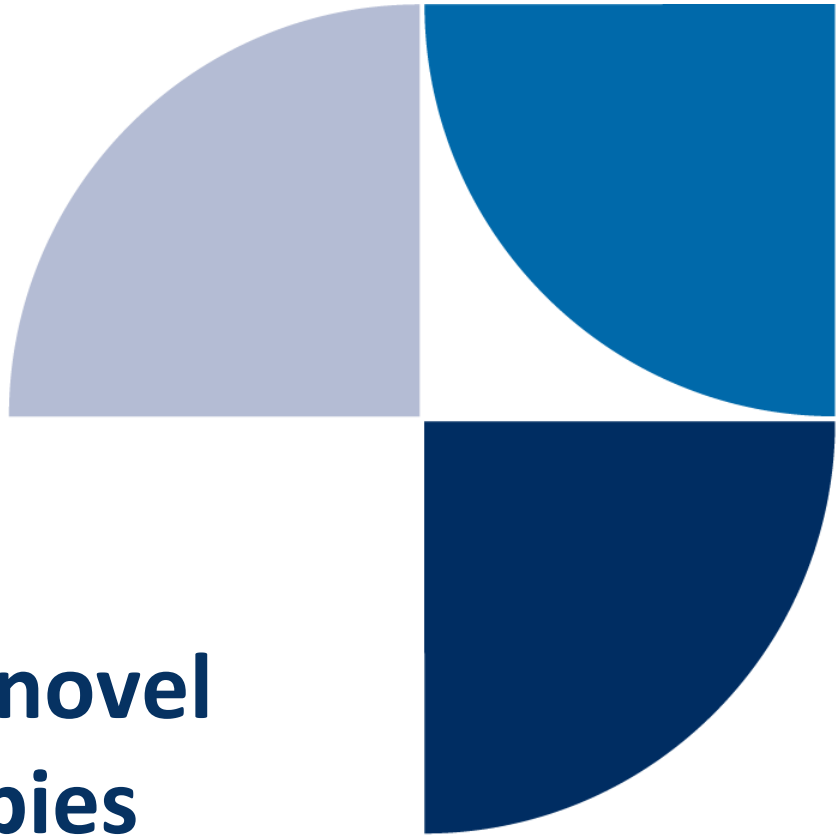

Leading the world in novel adult stem cell therapies

Credit Suisse Healthcare Conference
9 November 2011

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 relationship with Cephalon and future benefits of that relationship; 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.

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Investment snapshot

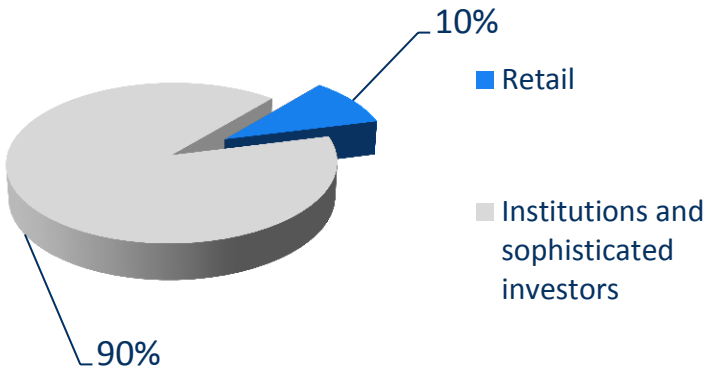
Mesoblast is a public company, listed on the Australian Securities Exchange since 2004.

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

Issued shares	**280m**
Current share price	A$8.23
Cash available (approx)	A$256m
Market capitalization	A$2,300m

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)

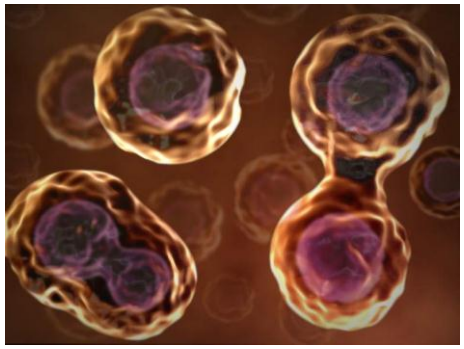
Mesoblast ownership



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



MPC highly-expandable, non-immunogenic

Isolated cells

Culture-expanded cells

- Heart muscle
- Blood vessels
- Pancreas
- Immune system
- Bone
- Cartilage

Products for cardiovascular diseases

Products for diabetes & immunologic/ inflammatory conditions

Products for orthopedic diseases

US composition patents granted

US manufacturing process patent granted

Global use patents filed

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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

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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)

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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

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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

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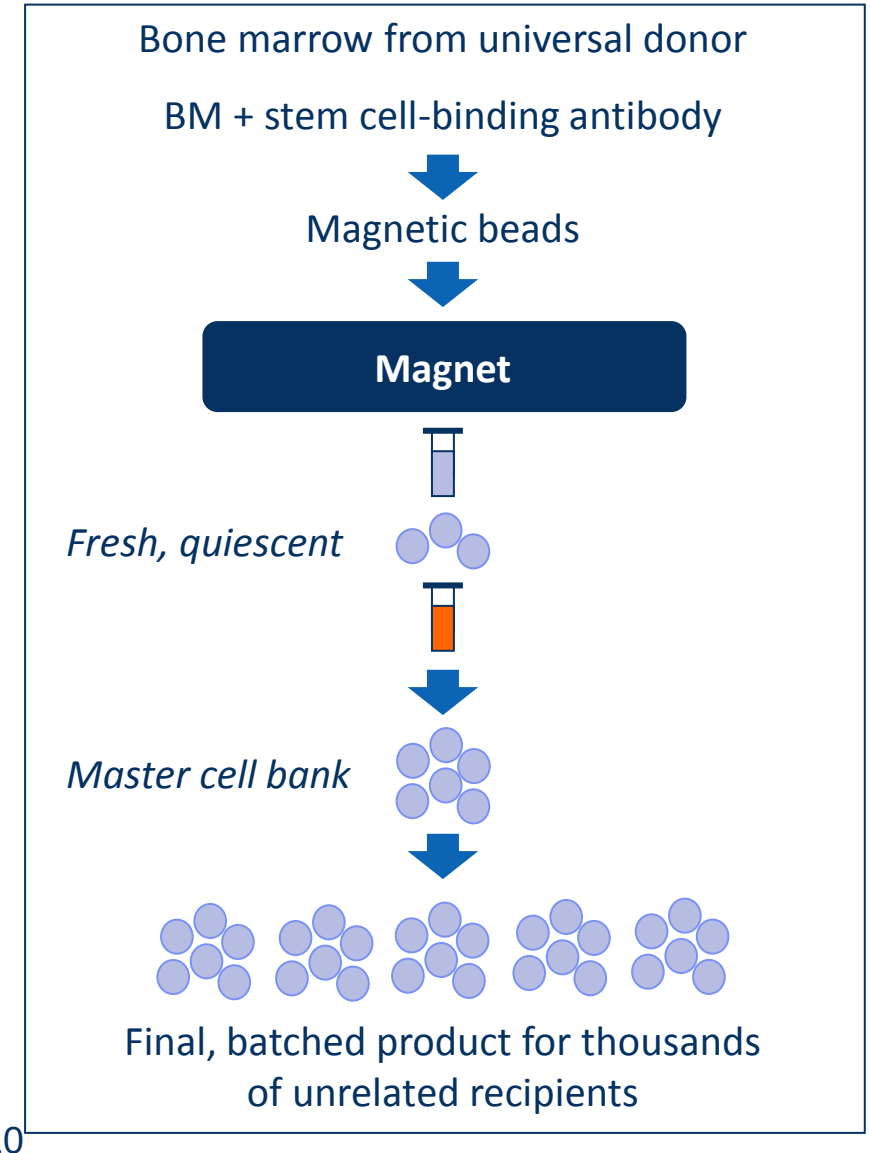
Our industrial scale manufacturing process



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

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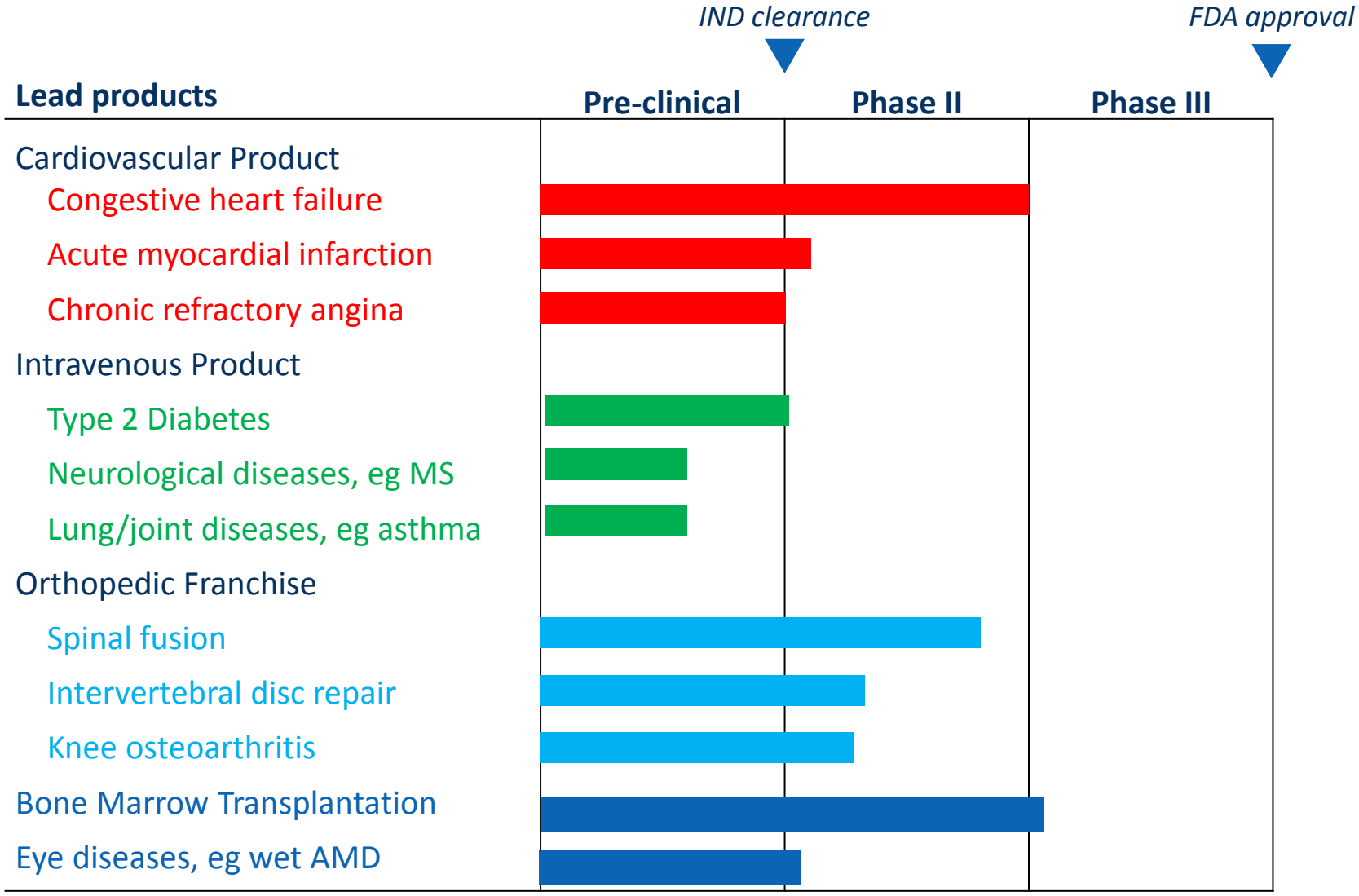
“Off-the-shelf” product franchises driving value creation



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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)
- 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

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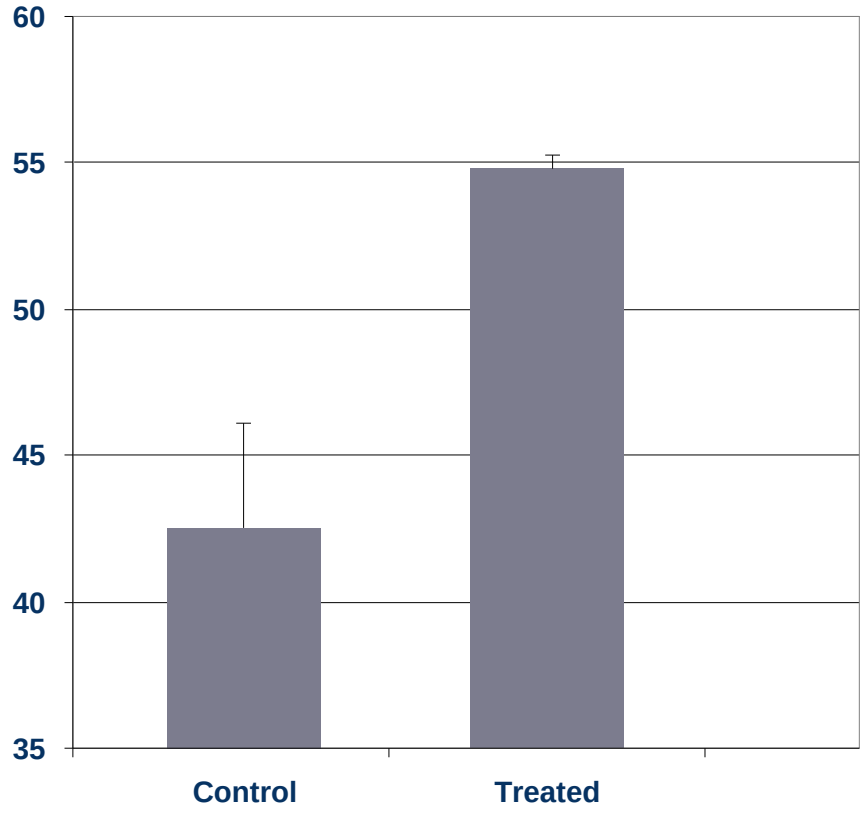
Cardiovascular franchise – acute myocardial infarction

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

1.2 million new patients annually in US alone

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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

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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

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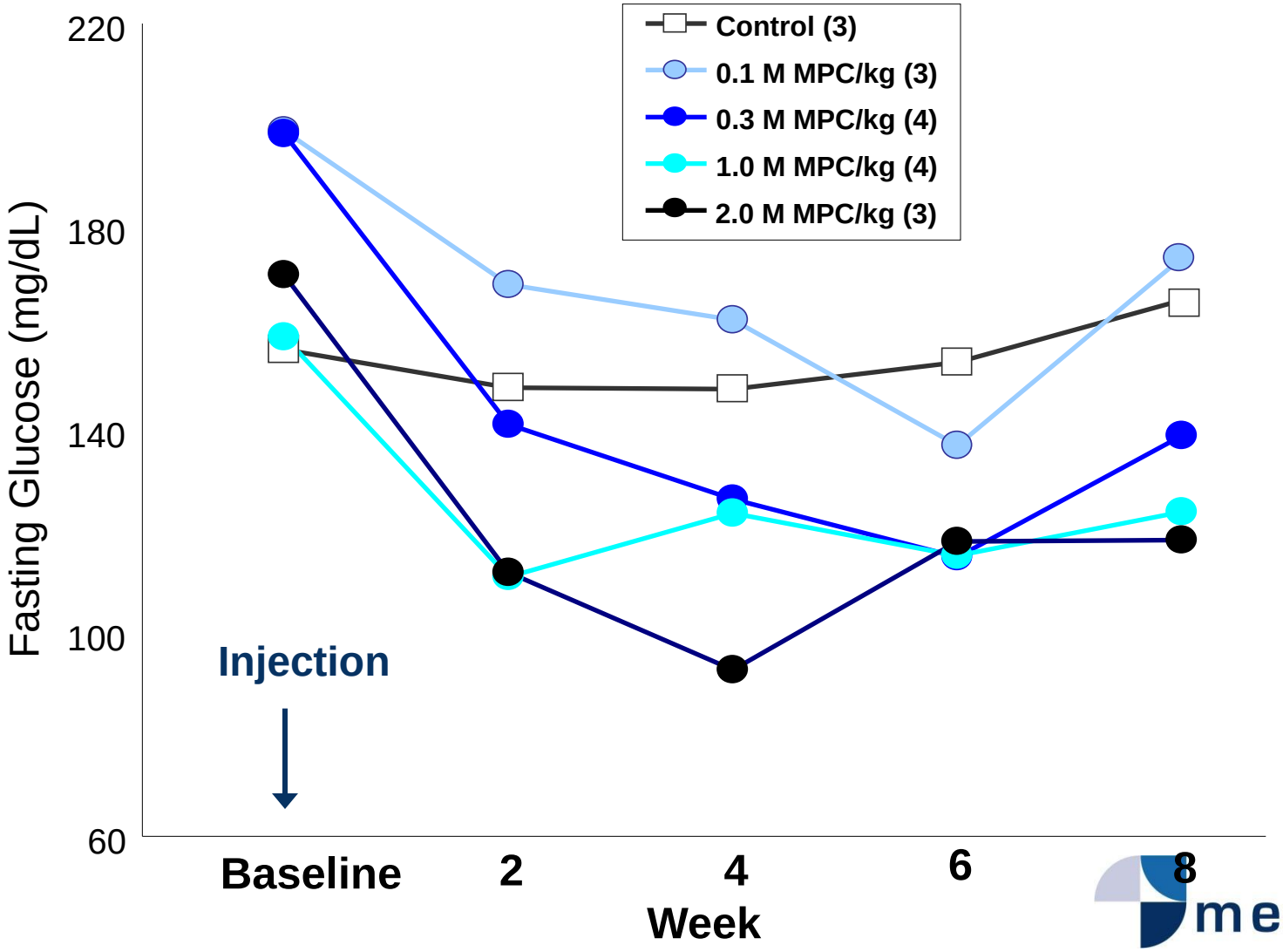
Effect of MPC or Saline Injection on Fasting Glucose in Nonhuman Primates With Type 2 Diabetes



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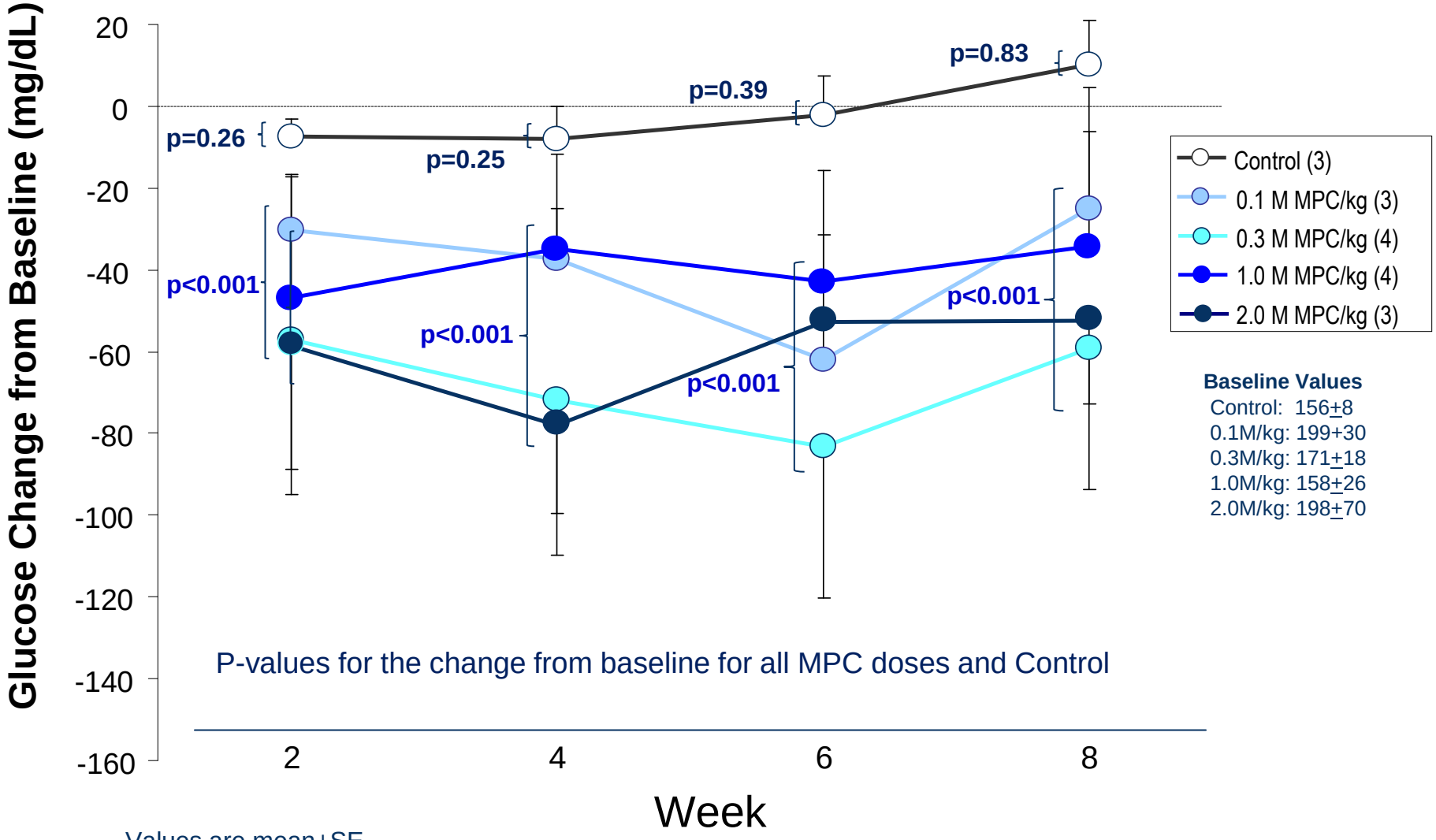
Fasting Glucose Change from Baseline Over Time in Obese, Hyperglycemic Nonhuman Primates (AB205/AB206 Pooled Data)



Values are mean±SE

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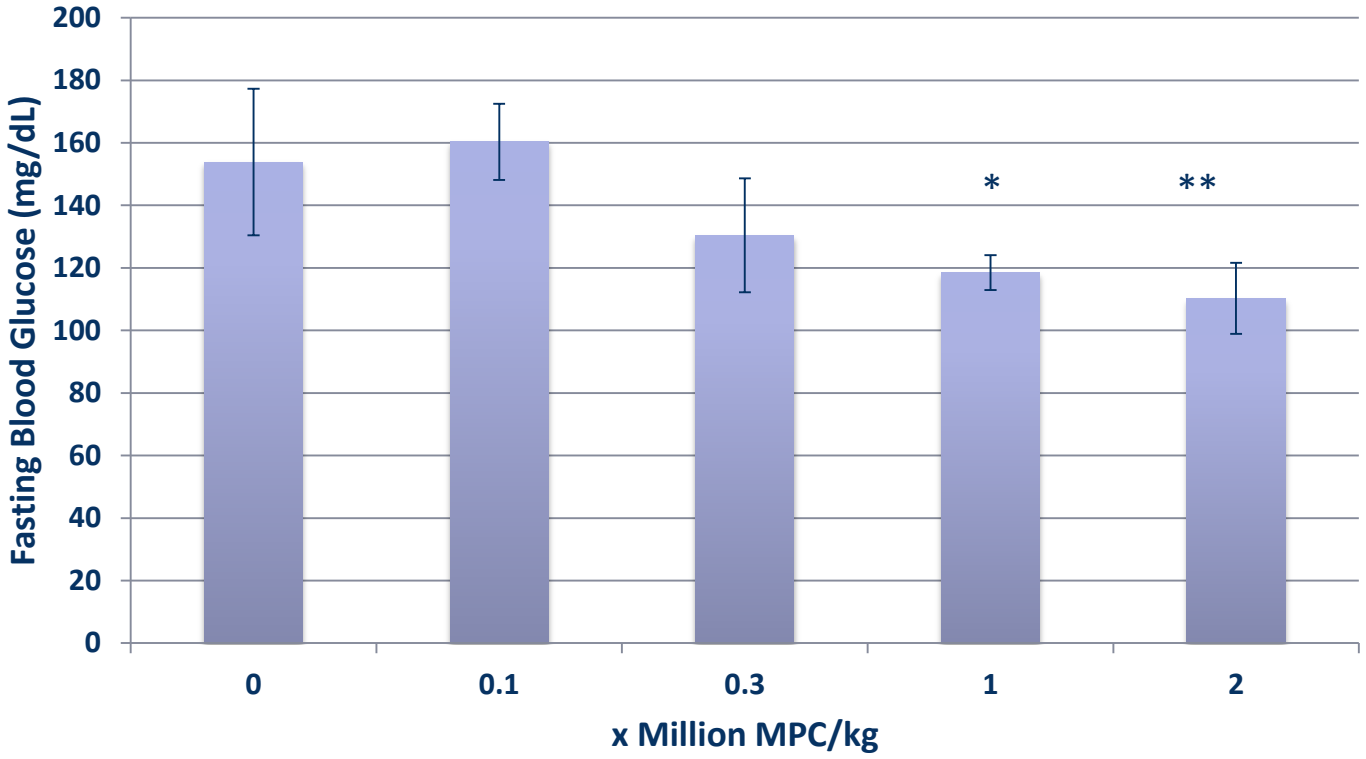
Dose-Dependent Effect Of Single Intravenous MPC Injection On Mean Fasting Blood Glucose Levels Over Eight Weeks



*** P<0.05 compared to controls***

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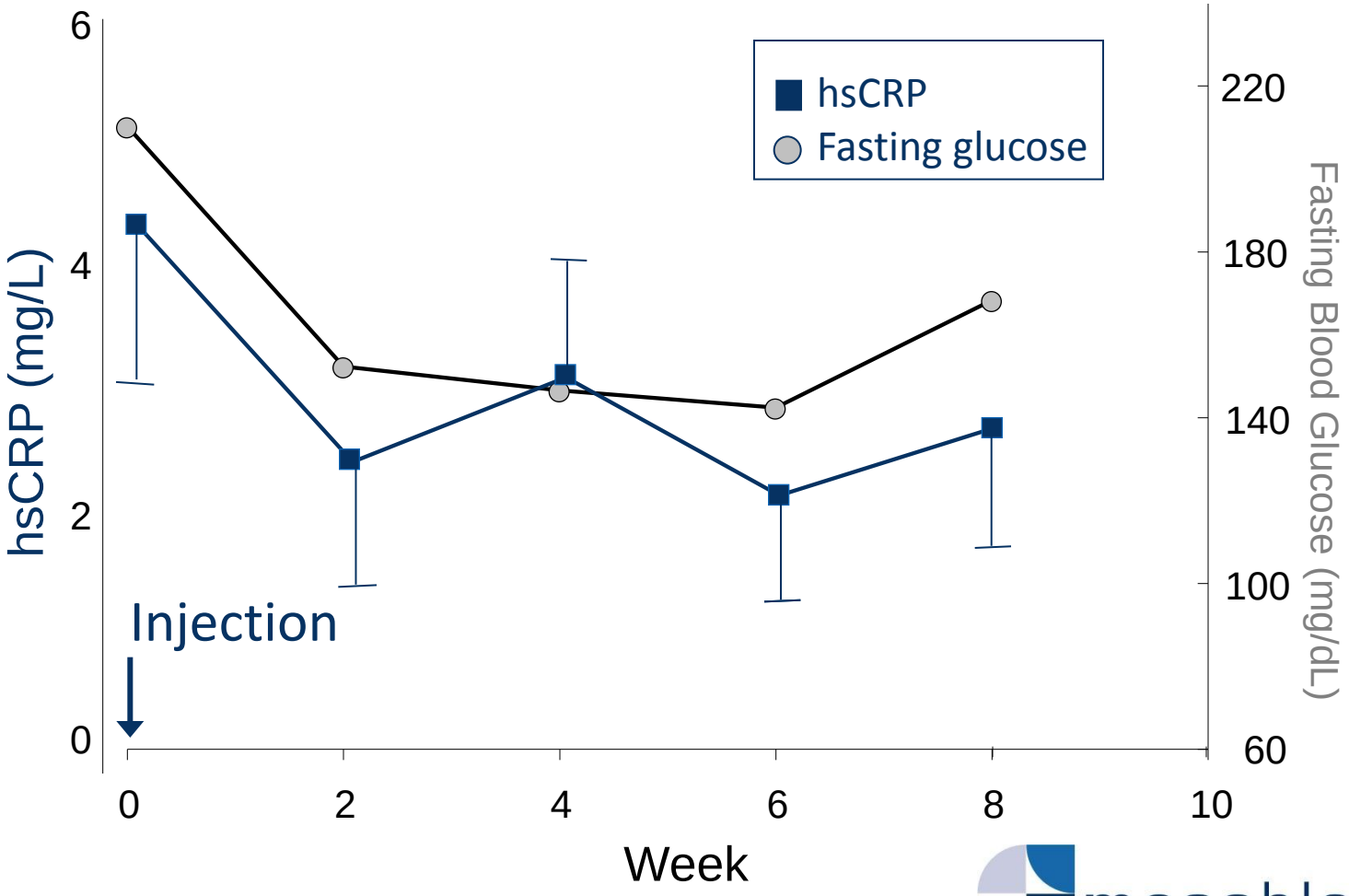
AB206: C-Reactive Protein and Fasting Glucose over Time
All MPC Doses Pooled (n=9)



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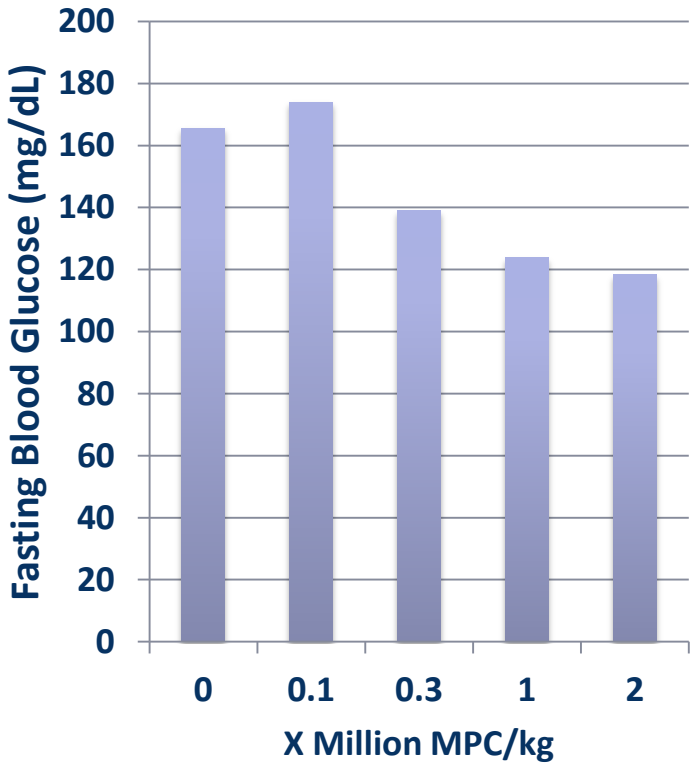
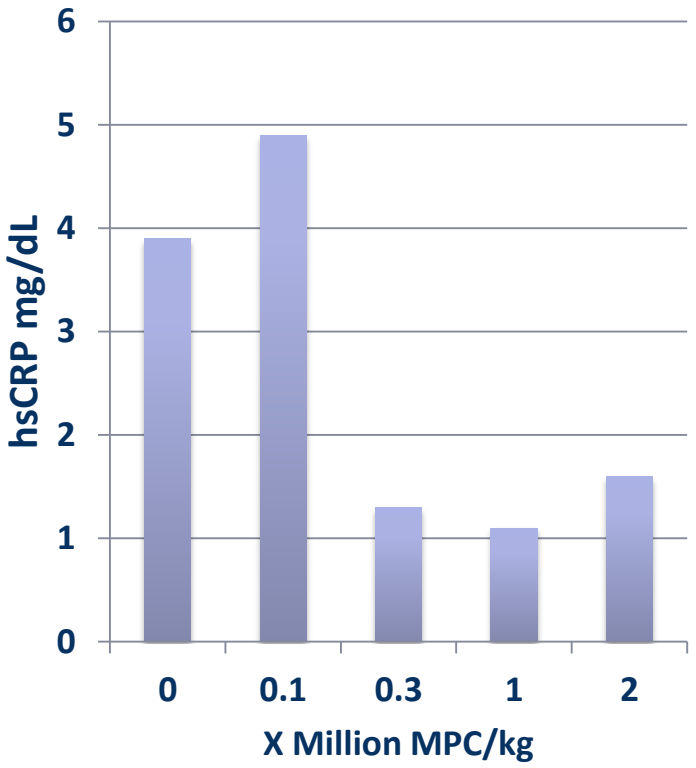
Dose-Dependent Effects On Reduced Mean Fasting Blood Glucose and Reduced CRP Levels At Eight Weeks After A Single Intravenous Injection Of Allogeneic MPC





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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

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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

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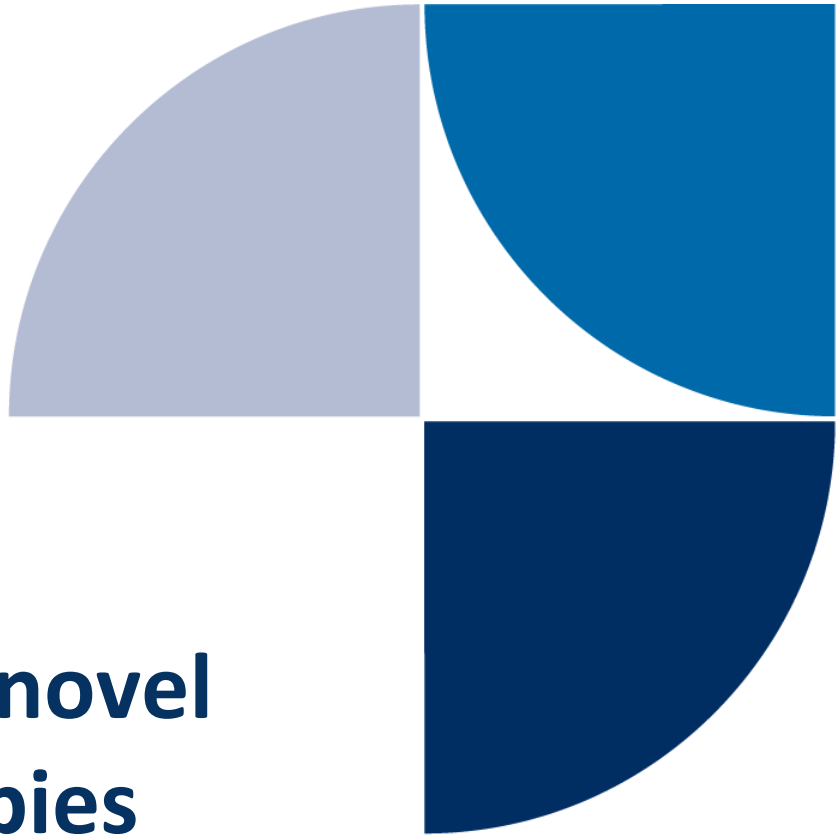

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