mesoblast

the regenerative medicine company



CEO presentation

Annual General Meeting Melbourne, 29 November 2012

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Corporate overview



Shareholder value and ownership

Market valuation	
Issued shares	287 million
Current share price*	\$5.74
Market capitalization (approx)	\$1,647 million

Shareholder ownership



- Institutions/sophisticatedilnvestors
- Retail investors
- Management
- Strategic Investors



* 28 November 2012

Cash and development spend

Cash 30 September 2012 = \$190 million

Cash spend for FY 2012		\$ million
Clinical programs		19.9
Clinical trialsCell production	10.0 9.9	
Research & development		13.0
Manufacturing processesResearch & translational programs	7.7 5.3	
People (labour)		19.4
Support (overheads) & I.P.		12.9
Total cash spend on operations (before tax and interest)		65.2
Cash on hand (30 June)		206.7



Our people ... the most valuable asset





Major accomplishments – highlights of 2012

- 1. Clinical and preclinical development of intravenous product formulation for a wide range of systemic diseases
 - generated positive preclinical results in primate model of type 2 diabetes
 - commenced Phase 2 trial for type 2 diabetes and its complications
 - generated positive preclinical results in large animal model of inflammatory arthritis, showing concomitant effects on multiple pathways of joint inflammation
 - plans underway to initiate Phase 2 clinical program in rheumatoid arthritis
 - additional planned applications, including diabetic kidney disease, lung diseases
- 2. Completed enrollment in the Phase 2 trials for non-surgical treatment of degenerative lumbar disc disease and for spinal fusion surgery

Continued



Major accomplishments – highlights of 2012

- 3. Completed Phase 2 trial in congestive heart failure (CHF), identifying an MPC dose which prevented any hospitalization or death for a mean follow-up period approaching three years
- 4. Held positive meetings, together with Teva, with FDA and EMA to discuss a proposed Phase 3 clinical trial protocol for CHF with primary endpoint of reduction in hospitalization or death
- 5. Implemented product manufacturing strategy to facilitate scale-up, meet regulatory compliance for Phase 3, and provide commercial supply
- 6. Reached agreement with FDA on the manufacturing process to supply MPCs for use in the upcoming Phase 3 trial for congestive heart failure, in Phase 3 trials for other indications, and on path forward for commercial supply



Corporate partnerships manage execution risk – Teva alliance

- Partnership focus on neurologic, cardiovascular diseases
- Lead product for congestive heart failure number 1 cause of hospitalization in industrialized world
- Provides Phase 3 clinical and regulatory expertise
- Provides funding for partnered programs
- Provides global distribution strength
- Allows Mesoblast to focus on manufacturing optimization



Corporate partnerships manage execution risk – Lonza alliance

- Lonza partnership provides global process development and manufacturing capability
- Exclusive access to state-of-the-art Lonza Singapore facility for allogeneic cell manufacture
- New Singapore site will support clinical trial and early commercial supply
- Partnership alleviates need for Mesoblast internal spend on manufacturing facility, and will provide significantly larger facility for commercial supply on first product approval





Mesenchymal Precursor Cell (MPC) technology



Our proprietary MPC technology platform

- 1. Patented adult stem cell technology platform for Stro-1/Stro-3 cells
- 2. Highly purified populations of earliest precursors of mesenchymal lineage cells present in multiple tissue sites, e.g. bone marrow, adipose, dental pulp
- 3. Scientific advantages based on high degree of potency and effectiveness of this purified cell type across multiple disease targets
- 4. Commercial advantages derive from high degree of expansion potential and relative non-immunogenicity...allogeneic cell therapy



Leveraging our proprietary MPC technology platform

- Products specifically target major medical conditions where proprietary technology offers unique scientific and clinical advantages
- Multiple products developed in parallel to increase probability of success
- Strong cash position enables simultaneous product development
- Probability of success enhanced through strategic partnerships
- Potential to deliver significant and sustainable revenues via either direct product sales or through profitable manufacturing operations



MPC technology platform delivers product diversity

- 1. Products in partnership with Teva, primarily in cardiovascular and neurological diseases
- 2. Products for intravenous delivery in type 2 diabetes and its complications including kidney disease
- 3. Products delivered intravenously for immunologic/inflammatory conditions, such as lung and joint diseases
- 4. Products locally administered for orthopedic diseases of the spine, and vascular and inflammatory eye conditions





Product manufacturing



Product manufacturing strategy

Our objectives are to ensure:

- Regulatory compliance with best practice
- Product delineation supporting partnering/reimbursement
- New product development
- Commercial scale-up
- Capacity for commercial product supply
- Reduced COGS



Regulatory compliance with best manufacturing practice

Agreement reached with United States Food and Drug Administration (FDA) for supply of MPCs in Phase 3 clinical trials and on a clear pathway for commercial manufacturing supply

The FDA agreed:

- That Mesoblast's extensive characterization and testing of its MPC technology platform was acceptable and consistent with expectations for Phase 3 clinical supplies
- With Mesoblast's proposed assays to demonstrate potency for its MPC product, a key requirement for entry into Phase 3 trials
- With the scope of product comparability studies needed to support manufacturing optimization and scale-up as clinical and commercial supply demands increase



Control of manufacturing ensures product delineation

Mesoblast can delineate products to support and separate partner markets, optimize reimbursement strategies, and manage product lifecycles.

Innovative R&D delivers product delineation through:

- Changes in formulation or dosage
- Products derived from different tissue sources (e.g. bone marrow, adipose, dental pulp)
- Combination therapies using different modes of delivery or devices
- Biologic modifications of cells





Product pipeline



Platform delivers multi-product pipeline





Products for intravenous administration

Intravenous products to treat prevalent systemic disorders affecting the metabolic, inflammatory and immune systems

- type 2 early diabetes
- kidney failure and cardiovascular complications
- liver fibrosis

Inflammatory/immune mediated diseases

- inflammatory joint diseases rheumatoid arthritis
- Iung diseases asthma, pulmonary fibrosis

Intravenous formulation of MPCs can be delivered once or multiple times for disorders that affect multiple organs



Integrated metabolic mechanisms of action of MPCs



Intravenous delivery – Type 2 diabetes

- Randomized, placebo-controlled Phase 2 trial in 60 patients with type 2 diabetes actively recruiting under FDA guidance
- Patients evaluated over 12 weeks for blood glucose control and inflammatory markers such as C-reactive protein (C-RP)
- Objective to find optimal dose for both glucose control and reduction in inflammation parameters

Trial will set foundation for evaluating MPCs in treating patients with advanced diabetes and life-threatening complications such as renal failure and cardiovascular disease



Intravenous delivery – renal complications of diabetes

- Plan to evaluate whether single dose of MPCs can stabilize or reverse end-stage kidney disease
- Nearly 10% annual rate of cardiovascular disease and death in diabetic patients with end-stage kidney disease
- Non-human primate study showed circulating C-RP levels significantly reduced after single MPC dose (C-RP is major predictor of cardiovascular risk in diabetes)

Plan to evaluate whether intravenous MPC therapy has potential to offer cardioprotective and renal benefits in these patients



Intravenous delivery – immune-mediated diseases

- Preclinical data indicate MPCs have immunomodulatory properties
- Single intravenous injection may provide sustained benefits for immunemediated diseases
- Mechanism of action (MOA) may be unique, shutting down multiple cytokine pathways simultaneously:
 - TNF-alpha, IL-6, IL-17 are mediators that drive autoimmune diseases such as rheumatoid arthritis, Crohn's disease, multiple sclerosis
 - existing treatments require chronic administrations; may cause unacceptable infectious adverse events

Initial targets are inflammatory joint and lung diseases

Randomized, placebo-controlled Phase 2 trials of MPCs for patients with RA planned as either first line treatment or rescue after failure with other biologics



Products for local administration – cardiovascular

With Teva, developing therapies for cardiovascular diseases including congestive heart failure (CHF) and acute myocardial infarction (AMI)

- Phase 2 trial for CHF showed patients treated with single intra-cardiac injection of highest dose of MPCs have had no hospitalization for decompensated heart failure or cardiac-related deaths over nearly 3 years of follow-up
- Teva and Mesoblast met with FDA and European Medicines Association to discuss aligned Phase 3 trial with endpoint of reduction in hospitalization and death
- Teva and Mesoblast are working closely on a detailed Phase 3 trial design involving an early interim analysis to evaluate evidence of efficacy
- Phase 2 AMI trial ongoing in Europe and Australia
- Additional potential areas include chronic refractory angina



Products for local administration – spine disease

Diseases of the spine represent largest growing market segment in orthopedics

- Spinal fusion product for patients with advanced disc degeneration who need surgery
 - Phase 2 spinal fusion trials completed enrollment
 - 12-month follow-up results for lumbar fusion to be announced shortly
- Larger market for restoration of early disc damage
 - Phase 2 study completed enrollment of 100 patients with intervertebral disc disease
 - results expected mid 2013

Spinal franchise will likely be optimized with one strategic partner, leveraging distribution and market strengths



Other products – eye diseases and bone marrow transplantation

Developing stem cell therapeutic product for treating various vascular and inflammatory diseases of the eye including wet and dry age-related macular degeneration (AMD)

- Wet and dry AMD are the major causes of blindness in the elderly
- Phase 2 trial wet AMD study currently enrolling patients at sites in Singapore and Australia

Developing stem cell therapeutic product to improve bone marrow transplant outcomes and provide a therapy for patients who cannot find a donor and may otherwise die

- Ongoing Phase 3 clinical trial using MPCs to expand hematopoietic precursors from cord blood for transplantation in cancer patients whose bone marrow has been destroyed by high dose chemotherapy
- Aim is to increase 3-4 fold the number of unrelated donor transplants



The year ahead, what we expect:

- Commencement of Phase 3 trial for congestive heart failure involving an early interim analysis to evaluate evidence of efficacy
- Clinical results in Phase 2 trials with early type 2 diabetes, spinal fusion and intervertebral disc repair
- Ongoing Phase 2 trial for AMI and Phase 3 for BMT
- Expand focus on intravenous product franchise with commencement of Phase 2 trials for
 - diabetic kidney disease
 - rheumatoid arthritis
 - lung diseases
- Additional partnering opportunities optimal timing



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Leading the world in novel adult stem cell therapies

