

mesoblast investor update

ISSUE EIGHT

Mesoblast emerges as a global leader in regenerative medicine

The exciting new field of regenerative medicine offers the promise of halting or reversing major diseases for which conventional drug therapies have either failed or been found severely wanting. In particular, orthopaedic and cardiovascular diseases represent areas of major unmet clinical need throughout the western world where regenerative therapies, and specifically stem cells, may make dramatic inroads.

At Mesoblast, we believe that the key to developing novel regenerative treatments for orthopaedic and cardiovascular diseases can be found in a very rare type of adult cell which is present in all of us throughout our bodies, and is termed a mesenchymal precursor cell (MPC). We are very encouraged by a whole series of trial results generated by both Mesoblast and our sister company in the United States, Angioblast Systems Inc., which have shown that the patented MPC technology has now advanced into a mature stage of clinical development.

Consequently, we are confident of the near-term potential for MPCs to generate a whole range of new treatment modalities capable of repairing bones, cartilage, blood vessels, heart muscle, and other tissues which have deteriorated because of age, disease, or lifestyle.

Point of Differentiation: The Allogeneic Business Model

Mesoblast's core patented technology enables isolation of a unique and highly potent type of adult stem cells which can be derived from a single donor, expanded in culture into very large numbers, and used in many patients without the risk of rejection.

The ability of MPCs to escape immune rejection forms the basis of a business model akin to a pharmaceutical drug, with low costs of goods and high margins. Since listing on the Australian Stock Exchange in December

2004, Mesoblast, and Angioblast in the US, have worked tirelessly to demonstrate the validity and robustness of this business model.

The conclusion from a wide range of preclinical trials in orthopaedic and cardiovascular disease models performed over the past two and a half years is that MPCs derived from a single donor can be used to generate safe and highly effective "off-the-shelf" products for use in thousands of unrelated recipients without the risk of rejection. The results of these preclinical trials have been positively reviewed by the United States Food and Drug Administration (FDA).

Obtaining FDA clearance within 30 days of filing each of two Investigational New Drug (IND) submissions to begin Phase 2 trials using allogeneic MPCs, attests to the robustness of the preclinical and manufacturing results and underscores the rationale of the allogeneic business model.

Both companies have now embarked on Phase 2 clinical trials to validate the allogeneic business model in humans. While Mesoblast concentrates on developing stem cell therapies for orthopaedic applications – a franchise of regenerative products for spine disease, long bone fractures and disorders of cartilage, such as osteoarthritis - our significant equity investment in Angioblast means that Mesoblast shareholders can simultaneously access additional market opportunities in cardiovascular diseases, which are at least as large as the orthopaedic markets.

Both Mesoblast and Angioblast are confident that the preclinical success of the shared allogeneic MPC platform technology will be translated into commercial success by developing "off the shelf" products that will be highly effective in large, pivotal clinical trials.

Being able to immediately provide patients with large numbers of uniform, reproducible, effective, and potentially life-saving stem cells at hospitals and treatment centres means that potentially thousands of patients could benefit from the cells of a single universal donor.

Orthopaedic Applications

Based on solid experimental evidence that Mesoblast's proprietary adult stem cells can generate new bone and cartilage tissues, the company remains firmly focused on the commercialisation of its proprietary technology for orthopaedic indications.

Mesoblast's lead clinical products have focused on indications for bone repair, such as long bone fractures and spinal fusion, while our product pipeline is concentrating on new products for cartilage indications, such as rebuilding degenerating intervertebral discs and repairing or protecting cartilage degeneration in the knee and other joints affected with osteoarthritis.

Bone Repair and Regeneration

Long Bone Fracture Repair Trial - The Royal Melbourne Hospital

Mesoblast is developing a proprietary stem cell product for repair of long bone fractures. By having an "off-the-shelf" stem cell therapy for fracture repair, Mesoblast will be able to provide a regenerative product that surgeons can use as soon as a patient is first brought to a trauma facility with a fracture needing intervention.

The immediate availability of a stem cell therapy for bone repair has great implications for accelerating the healing of sporting injuries as well as preventing deformities and long-term complications following road and other trauma.

Mesoblast's bone repair product will be used together with a bone filler material, and will be applied by surgeons either in an open procedure if the fracture is very large or by direct injection through the skin if the fracture is smaller.

The company has been testing its proprietary stem cell therapy in a Pilot Clinical Trial at The Royal Melbourne Hospital in patients suffering from non-healing, long bone fractures.

Interim results indicated strong bone regeneration and fracture union in every one of the first five patients implanted with Mesoblast's proprietary cells. The success of the stem cell therapy in these patients eliminated the need for a second operation to harvest bone from their hips. There have been no reported cell-related adverse events.

A detailed update on the effectiveness of the stem cell therapy and the outcome in all patients in the trial will be made in due course. The extremely encouraging interim results, together with earlier preclinical trial results, strongly support Mesoblast's plan to advance the long bone repair program into Phase 2 clinical trials under the umbrella of an IND submission to the US FDA. We expect this submission to be filed during Q1 2008.

Phase 2 Spinal Fusion Trial - United States

A second major application of Mesoblast's bone regenerating stem cell technology is for induction of spinal fusion in end-stage intervertebral disc disease, a major orthopaedic market. Over 300,000 spinal fusion procedures are performed in the United States alone each year, with the number expected to grow to over 500,000 by 2009. Current fusion therapies use bone harvested from a patient's own hip (termed autograft), that requires a second surgical procedure which frequently results in long-term complications such as chronic pain and infection.

Mesoblast's preclinical trials conducted at Colorado State University showed that the company's allogeneic, or "off-the-shelf", cells were equal to, or even more, robust in creating bony spinal fusion around the disc site than autograft hip bone.

On the basis of these and other exceptional preclinical, manufacturing and safety studies, Mesoblast received rapid clearance from the US FDA for its IND submission to commence a Phase 2 clinical trial of its NeoFuse™ allogeneic adult stem cell product for spinal fusion.

The Phase 2 trial investigating the treatment of degenerative intervertebral disc disease is based at New York's Hospital for Special Surgery, a leading global orthopaedic, rheumatologic and rehabilitation speciality hospital. The trial team is being led by Dr Joseph Lane, who is Professor of Orthopaedic Surgery and Assistant Dean at Weill Medical College at Cornell University. Interim data from this trial is expected to be provided by the company during Q1 2008.

Cartilage Repair and Regeneration

Rebuilding the Intervertebral Disc

Low back pain is present in 15-25% of the general population, and affects 70-90% of people at some stage in their lifetime, most often due to a degenerating intervertebral disc.

While spinal fusion remains the therapeutic goal for end-stage disc degeneration, a less invasive approach would be preferable to address the needs of the much larger population with early-stage disc disease.

To address this major market opportunity, Mesoblast is developing an allogeneic or "off the shelf" adult stem cell product which can be injected by a minimally invasive approach into degenerating discs of unrelated recipients in order to repair and regenerate disc cartilage, increase disc space height, and improve the biomechanics of the native disc.

During the last quarter, Mesoblast commenced preclinical trials of its patented adult stem cell technology for repair and regeneration of vertebral disc cartilage. These trials signal Mesoblast's expansion of its line of products for spinal diseases and its strategic aim to build a robust franchise for the very large global spinal disease market. The results of these trials, expected early 2008, will be closely reviewed and, if positive, will result in an IND submission to the FDA to commence human clinical trials.

Regenerating Knee Joint Cartilage - Osteoarthritis

Regeneration and protection of cartilage in large joints of patients with osteoarthritis represents a major disease indication targeted by our proprietary stem cell technology.

Inflammatory diseases of the joints, such as osteoarthritis, affect over 43 million people annually in the United States alone. More than 10 million people in the US currently suffer from osteoarthritis of the knee, making it the most common joint disease. Access Economics estimated that in Australia osteoarthritis affects more than 3.4 million people, costing the community billion of dollars annually in direct and indirect costs.

Osteoarthritis is a condition where irreversible loss of joint cartilage occurs through age-related degeneration or through injury. Current treatments attempt to alleviate painful symptoms but are unable to restore the cartilage lining the joint. Joint replacement is often the only option for restoring function.

We recently reported highly successful interim results of our first large joint cartilage repair program in osteoarthritis, conducted at Western Australia's Murdoch University and facilitated by a \$2.7 million Commercial Ready Grant awarded to Mesoblast in December 2005 by the Australian Government.

The results of the preclinical trial showed that injection of our allogeneic, or "off-the-shelf", stem cells into damaged knee joints resulted in significant protection of the knee cartilage against destruction and improvement in osteoarthritis. After just three months, stem cell treated knee joints had significantly thicker and stronger cartilage compared with control joints.

These results strongly support Mesoblast's plan to progress with a wide-ranging Australian and US-based clinical trial program to implant the allogeneic MPC into osteoarthritic knees by either arthroscopy or direct needle injection. On completion of the preclinical trials, all data will be submitted to the FDA as part of an IND submission to commence the Phase 2 trials in patients with knee osteoarthritis. We expect this IND submission to be filed by the end of Q2 2008.

Cardiovascular Applications

In parallel with Mesoblast's activities in the orthopaedic arena, Angioblast has accumulated extensive experimental evidence that the shared platform technology can repair and regenerate damaged blood vessels and heart tissue. Angioblast's lead clinical products are focussed on the treatment of coronary artery disease, angina (chest pain), heart failure, and heart attacks. Other products in pipeline development include products for the treatment of peripheral artery disease and for diabetic vascular disease.

These are all extremely large market opportunities, with vast patient populations whose medical needs are unmet and where existing therapies are inadequate or absent.

Heart Failure Pilot Trial - John Hunter Hospital, New South Wales

In conjunction with Angioblast, Mesoblast has concluded a pilot clinical trial at John Hunter Hospital in Newcastle, Australia, in patients with multi-vessel coronary artery disease and heart muscle damage. The company's proprietary stem cells were injected into damaged heart muscle using the latest generation of myocardial catheters provided by Johnson & Johnson's companies, Cordis Corporation and Biosense Webster.

The primary endpoint of safety was achieved and there were no cell-related adverse events. Importantly, heart muscle recovery was seen in all six patients within three months of cell implantation, as defined by either improvement in symptoms of heart failure or heart function.

In addition, all patients demonstrated reduced episodes of chest pain (angina) and reduced need for anti-anginal medications, suggesting that the stem cell therapy had improved blood flow to the damaged heart muscle.

These very exciting results have now encouraged Angioblast to progress its cardiovascular clinical program into Phase 2 trials for patients with chronic coronary artery disease and heart muscle dysfunction. The markets for patients with chronic coronary artery disease are extremely large and wholly unmet, with over 500,000 new heart failure patients treated annually and over 500,000 bypass surgical procedures for coronary artery disease performed annually in the United States alone. Angioblast intends to target both of these markets, and is expected to file an IND submission to commence a Phase 2 trial in patients with heart muscle damage during Q1 2008.

Phase 2 Heart Attack Trial - United States

During the 2007 reporting year, Angioblast announced positive results from preclinical trials of its adult stem cells injected by catheter directly into the damaged heart muscle of sheep after a heart attack. The success of the trials established the safety and effectiveness of the stem cells in a clinically relevant and widely applicable protocol, which used the latest generation myocardial catheters from the Johnson and Johnson companies, Cordis Corporation and Biosense Webster, to implant the cells in the damaged heart muscle of sheep.

The studies focused on the treatment of heart attacks using cells from an allogeneic donor which had been expanded and frozen: in effect, testing the "off-the-shelf" stem cell product. These preclinical studies established that the allogeneic stem cells can be implanted safely by cardiac catheter and are effective when used in combination with standard-of-care therapies to improve vascular blood flow, such as balloon angioplasty.

The results of this catheter-based protocol were subsequently used to support Angioblast's recent successful IND submission to the US FDA to begin a Phase 2 clinical trial at the Texas Heart Institute. This will be the world's first catheter-based allogeneic stem cell trial in heart attack patients. Angioblast expects to have interim data results from this trial available by the end of Q1 2008.

Funding and Strategic Partnerships

At 30 June 2007, cash available to support the clinical and preclinical activities outlined above was \$12.5 million. These cash reserves will enable the company to significantly advance clinical development of its adult stem cell platform, file additional IND submissions, and bring the technology to a stage of proven clinical maturity. Significantly greater funds will be required to progress the technology through pivotal trials and product registration, and we expect that in large part these funds will come via strategic corporate relationships.

We remain committed to identifying the best and most appropriate global strategic partners to enter into exclusive co-development, distribution, or licensing agreements. While the partnerships we have entered into with major international medical device companies to date have been limited in scope, they have proven to be very useful from a collaborative aspect. We believe the clinical validation of the platform technology during execution of the Phase 2 clinical trials will place the company at a particularly advantageous position in concluding definitive discussions with potential strategic partners.

Patent Protection

During the 2007 financial year, the United States Patent and Trade Mark Office (USPTO) granted a key patent to Angioblast which delivers a major commercial advantage and offers long term protection for the company's platform technology.

The patent ensures that only Mesoblast and Angioblast can commercialise our proprietary adult stem cells, termed Mesenchymal Precursor Cells, in the US, the world's largest market for regenerative medicines.

Conclusion

The significant achievements over the past year are a reflection of the rapid technical and clinical progress being made by Mesoblast and its sister company, Angioblast Systems Inc. in the United States.

Both companies are well positioned to capitalise on the leading edge, shared platform technology, and are supported by robust patent protection, good management and corporate governance, sufficient funds, and solid communication capabilities.

As highlighted above, both companies have now progressed to the stage of mature clinical stage commercial development. By the middle of 2008, it is anticipated that a total of five Phase 2 clinical trial IND submissions for orthopaedic and cardiovascular indications will have been filed, and that at least two Phase 2 trials will be significantly advanced with a further three commencing.

These characteristics underpin the emergence of both companies as global leaders in the exciting field of regenerative medicine.

What they say...

Reporter: And after just three months, (the patient) had no chest pain at all.

Patient: I feel like I'm probably going to live forever now.

Channel 9 News

Reporter: He's had a heart attack, a stroke and four bypasses but today (the patient) feels 10 years younger.

Patient: It is a miracle, yes. It's wonderful too.

Channel 7 News

No Bones about Mesoblast

We initiate coverage of MSB with a current valuation of \$2.35 and a 12-month price target of \$3.20. Our 12-month price target is based on the significant reduction in the technical risk for MSB's cell-based therapies with positive results from the current Phase 2 clinical trials.

The preclinical and clinical testing to date have provided two pieces of critical data:

- allogeneic MPCs are safe & effective in animals
- autologous MPCs are safe & effective in humans.

The current Phase-2 trials will put the final piece in the jigsaw, namely demonstrate allogeneic MPCs are safe and effective in humans.

Positive results from these trials will have favourable implications for all of the clinical applications for MSB's stems cells (hence the significant reduction in risk) as well as validate MSB's business model. In addition, we would expect that the reduction in technical risk will attract the interest of potential licensees with delivery platforms.

Lodge Partners

Adults Only

MSB aims to capitalise on its patents around adult MPCs. More than 1m of the 5.6m fractures occurring annually in the US are associated with healing difficulties and MSB's product has the potential to be helpful in these types of fractures. Buy. Target price \$2.48.

ABN Amro

Mesoblast was ranked 16th in the inaugural BRW Biotech Top 50 rankings, announced in August 2007.

Stem Cell Breakthrough

Embryo research is illegal in many nations including Australia, but research based on adult stem cells is producing some wonderful results, as a highly successful Hunter Medical Research Institute (HMRI) trial at the John Hunter Hospital has shown. HMRI and its partner Mesoblast Limited say that six seriously ill heart patients have shown significant improvements in various aspects of their conditions after stem cells were injected into their hearts. This is all the more exciting given that the main purpose of the trial was to weigh the medical safety of the procedure...This is indeed a brave new world of medical accomplishment, and a notable success for HMRI and its team of talented researchers.

The Newcastle Herald

Biotech Benefit for Knees

Once in a blue moon a stock market announcement arrives that could impact on AFL football. Yesterday it was biotechnology company Mesoblast which has arrived at a therapy with wide application for our great game ... Given that knee complaints are the most common joint disease and that there are no effective therapies that target cartilage, the company will now rapidly advance a new clinical program for knee osteoarthritis.

Herald Sun

Stem Cells Fix Broken Hearts

"This trial was set up to test the safety of using these rare stem cells in humans, so to get some preliminary efficacy as well is very exciting. We now know that these stem cells have the potential to form new heart muscle, and they can certainly revitalise existing heart muscle," (interventional cardiologist) Dr (Suku) Thambar said. "And it is all Australian work."

Sydney Morning Herald



Newsletters

This Mesoblast newsletter is available online on Mesoblast's website – www.mesoblast.com

Announcements to the Australian Stock Exchange and other public announcements are posted on a timely basis on the Mesoblast website.

If you would like to be informed of Mesoblast's progress by e-mail, please register by sending your contact details to: info@mesoblast.com



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