

mesoblast newsletter

ISSUE TWO

Communicating the story



Mesoblast's Founder & Chief Scientific Adviser, Professor Silviu Itescu, was the keynote speaker at the premier Australian industry seminar, the Australian Biotechnology Summit, held in Sydney in July. He also spoke at the recent Bioshares' Thredbo Biotech Summit.

The vision for Mesoblast – to become the world leader in novel therapeutic approaches for patients with bone and joint diseases, including adult stem cell therapy for bone fractures and spinal disease, and for regeneration of damaged joint cartilage and intervertebral discs. Together with its United States-based investee company, Angioblast Systems Inc, Mesoblast will also seek to develop the adult stem cell therapy as a first-line treatment for a broad range of cardiovascular diseases.

During the second quarter, Mesoblast (ASX:MSB) has made considerable progress in the commercialisation of its proprietary adult stem cell technology for orthopaedic and cardiovascular applications, in line with the company's stated milestones in its December 2004 prospectus.

The company has remained one of the few recent listings to continue trading near the issue price during a very challenging period in the biotechnology sector.

Importantly, the company has sufficient funds to complete all manufacturing and pre-clinical tasks, as outlined in the December 2004 prospectus, necessary for Investigational New Drug (IND) submissions to the United States Food and Drug Administration (FDA) for its stated orthopaedic and cardiovascular clinical applications.

Second quarter highlights include:

- Approval received from the Human Research Ethics Committee of the John Hunter Hospital in Newcastle to begin clinical trials of its adult stem cell therapy in patients with severe coronary artery disease;
- Application submitted to the Human Research Ethics Committee of a second leading Australian hospital to begin clinical trials of its adult stem cell therapy in patients with severe bone fractures;
- Appointment of Clinical and Regulatory Affairs Manager to oversee the upcoming clinical trial programs;
- Identification of a new clinical indication for the proprietary adult stem cells – intervertebral spinal fusion – representing a very large and established global market opportunity
- Entered into agreements with Colorado State University to perform preclinical dose-escalation trials of its proprietary adult stem cells for the treatment of long bone fractures and spinal fusion - these trials will support the company's IND applications for bone repair/regeneration to the FDA;
- Entered into an agreement with a leading United States life sciences company to begin production of Mesoblast's proprietary adult stem cells for clinical trials aimed at obtaining market approval by the FDA;
- Appointment of the Bank of New York to set up a Level 1 American Depository Receipt program; and
- Strengthening and expansion of the company's solid intellectual property portfolio.

Recent Achievements

Regulatory Milestones

The unique immune properties of the type of adult stem cells being developed by Mesoblast mean that they are not recognised as being foreign by the immune cells of an unrelated individual. Consequently, Mesoblast aims to develop "off-the-shelf" therapies using adult stem cells obtained from universal donors, produced in large-scale centralised manufacturing facilities, and used in multiple unrelated recipients. This will result in significantly reduced cost-of-goods, generation of a high margin business model, and the ability to meet pricing limits set by reimbursement authorities, enabling widespread uptake of the new therapies.

As outlined in our prospectus, to file IND applications for use of Mesoblast's universal adult stem cells with the FDA we will have in place documentation from three parallel components: (1) pilot clinical trial data in humans, (2) a manufacturing process for large-scale production of Mesoblast's proprietary adult stem cells to be used in clinical trials aimed at obtaining FDA market approval, and (3) pre-clinical safety and toxicologic data. During the past quarter, continued progress has been made in each of these components, ensuring that Mesoblast remains on track to obtain IND approvals for one or more cardiac and orthopaedic clinical indications.

Pilot Clinical Trial Update

Mesoblast will sponsor at least two clinical trials this calendar year, in the fields of both orthopaedic and cardiovascular diseases. In these first clinical trials, the patients' own bone marrow will be the source of the adult stem cells. The rare mesenchymal precursor cells in the marrow will be isolated and expanded in large numbers using Mesoblast's proprietary technology. All cell isolation and culture will be performed to Good Manufacturing Practice (GMP) standards under contract at Melbourne's Peter MacCallum Cancer Centre's commercial facility, Cell Therapies Limited.

The primary objective of these clinical trials will be to assess the safety of the adult stem cell isolation and culture process. Since the cell culture process for these pilot trials will closely parallel definitive large-scale production for clinical trials aimed at obtaining FDA market approval, the results will form a key component of the company's IND applications to the FDA.

During the second quarter, Mesoblast received approval from the Human Research Ethics Committee at the John Hunter Hospital in Newcastle to begin a clinical trial of its adult stem cell therapy in patients with severe coronary artery disease. The approval is for injection by catheter of Mesoblast's proprietary adult stem cells into the hearts of up to ten patients with severe angina not responsive to optimal medical and surgical therapy.

The John Hunter Hospital is the only medical centre in Australia to have the state-of-the-art NOGA catheter system, marketed by Biosense Webster Inc, a Johnson and Johnson operating company. The trial's Principal Investigator, Dr Suku Thambur, has had extensive experience with this catheter system for myocardial injection of human bone marrow. Mesoblast anticipates first patient recruitment to occur during the current quarter, with the proviso that all clinical decisions are ultimately the domain of the hospital and the Principal Investigator.

This approval indicates not only strong support by clinicians for human trials using Mesoblast's proprietary adult stem cells, but also the rapid progress being made by Mesoblast in implementing its commercialisation program.

Mesoblast has also made a clinical trial submission to the Human Research Ethics Committee of a second leading Australian hospital to test its proprietary adult stem cells in patients with severe long-bone fractures. Mesoblast anticipates receiving ethics committee approval during the current quarter, with first patient recruitment expected to occur shortly thereafter.

In view of Mesoblast's rapid implementation of its clinical trial programs and their anticipated expansion, the company appointed Dr Tamara Lewis as Clinical and Regulatory Affairs Manager on 14 June. Dr Lewis has expertise in the global commercialisation of pharmaceuticals and medical devices, having worked closely with the FDA and Australia's Therapeutic Goods Administration (TGA). Before joining Mesoblast, Dr Lewis was Regulatory and Clinical Affairs Manager with Australian heart assist device company, Ventracor Limited, and a senior member of Kende's regulatory, development and commercialisation team. Her specialty areas include design and oversight of clinical trials and the identification of key regulatory issues for biological therapeutics.

First Cardiovascular Clinical Trial

The first cardiovascular clinical trial of Mesoblast's proprietary adult stem cell technology will evaluate the safety of injecting cultured adult stem cells in up to 10 patients suffering from severe, debilitating chest pain due to multi-vessel coronary artery disease (CAD) that has not responded to other therapies.

CAD occurs when the arteries that supply blood to the heart muscle (coronary arteries) become hardened and narrowed in a process called atherosclerosis due to the build-up of plaque on the inner walls or lining of the arteries. Blood flow to the heart is reduced as the arteries become narrower until it ceases, resulting in a heart attack.

Medications commonly used to treat CAD include cholesterol-lowering medications, anticoagulants, aspirin, ACE inhibitors, beta blockers and nitroglycerine, but many patients fail to respond to these and may require invasive surgical procedures. In many instances even coronary artery bypass grafting will not be sufficient to improve symptoms of chest pain (angina) or heart failure.

Mesoblast and Angioblast Systems aim to reduce the number of patients requiring such surgery through the development of cardiovascular therapy that targets these conditions using our proprietary adult stem cell technology. In addition, we envision combining our stem cell therapy with coronary artery bypass grafting to improve the outcome of this procedure.

Pre-clinical trials in which adult stem cells were injected into hearts soon after a heart attack have shown substantial increases in the number and type of blood vessels that carry blood to healthy, but susceptible, heart muscle and significant improvement in heart function.

It is hoped that Mesoblast's proprietary culture-expanded adult stem cells will stimulate the growth of new blood vessels and improve disabling chest pain, thereby greatly improving the patient's quality of life.

Fast facts : CAD is the most common type of heart disease. It is the leading cause of death in the United States in both men and women. Approximately 7 million people in the United States suffer from CAD and 500,000 die from it each year.

Pre-Clinical Regulatory Update

Much work has progressed during the past quarter both in Australia and in the United States with respect to a cell culture/expansion manufacturing process meeting GMP standards.

During the past quarter, Mesoblast entered into an agreement with a leading United States life sciences company to begin process development for large scale production of Mesoblast's proprietary adult stem cells.

As discussed above, the cell culture process for the pilot human clinical trials to be performed in Australian medical centres will closely parallel definitive large scale production for clinical trials aimed at obtaining United States FDA market approval. Therefore, Mesoblast will facilitate smooth transfer of the process being optimised under contract at Cell Therapies to its large scale contract manufacturer in the United States in preparation for its IND applications to the FDA.

Mesoblast's IND applications to trial its universal adult stem cells will provide data to show that progressively increasing doses are safe when placed in the precise location where therapeutic effect is desired, e.g. at the site of a long bone fracture, in the intervertebral space, in the knee, or in the heart.

Mesoblast's adult stem cell technology lends itself for use in combination with a broad range of delivery devices and mechanical tools that are currently used in the treatment of various orthopaedic and cardiovascular diseases. Combining our adult stem cells with existing delivery devices and mechanical tools will enhance the outcome of the medical procedure, will garner support from physicians and other key stakeholders such as reimbursement authorities, and will open the possibility to strategic partnerships with international device manufacturers and market leaders.

During the past quarter, Mesoblast entered into agreements with Colorado State University to perform preclinical dose-escalation trials of its proprietary adult stem cells for the treatment of long bone fractures and spinal fusion. These trials will be led by Professor Simon Turner, a world leading authority in these fields, and will be performed using standard surgical techniques, mechanical tools, and FDA approved delivery devices. These trials are scheduled to commence in August, with initial results expected within five months. They will support the company's IND applications for bone repair/regeneration to the FDA.

Fast facts According to figures from the US, more than one sixth of the annual 5.6 million bone fractures fail to heal properly, particularly when segments of bone are physically missing at the site of the fracture. Almost 300,000 spinal fusion procedures are performed annually in the United States alone. For both poorly healing fractures and spinal fusions, surgeons generally use a patient's own bone tissues. It is hoped that Mesoblast's universal adult stem cells could provide a more effective alternative for both poorly healing fractures and for intervertebral bone regeneration without the associated pain and other complications of a bone graft.

Targeting United States Investors

Mesoblast Limited has appointed The Bank of New York to establish and maintain a Level 1 American Depositary Receipt (ADR) program.

This follows significant interest in the company from US investors, who have a high and informed understanding of the potential benefits and markets of adult stem cell therapies. The US is already an important market for Mesoblast because its 33%-owned sister company, Angioblast Systems Inc. is based there. Angioblast is developing adult stem cell technology for cardiovascular applications.

The ADR program will ensure that Mesoblast is more accessible to US private investors and increase liquidity in the stock for a US investor base. An ADR program also creates the possibility of investment by institutions that are only permitted to buy US-based securities.

Market Guidance for 3rd Quarter, 2005

Mesoblast's programs for pilot clinical trials of its proprietary adult stem cells for major orthopaedic and cardiovascular diseases are scheduled to commence in the current quarter.

Clinical trial commencement will signify one of the most significant steps undertaken by the company in commercialisation of its world-leading technology. The trials will seek to establish safety of the technology in patients, and, possibly, early efficacy. They will lay the groundwork for subsequent FDA applications and for initiating discussions with multinational strategic partners.

Competitive Advantages of Mesoblast's Technology

- The adult stem cells that form the basis of Mesoblast's technology do not cause an immune response, and do not have the issues that constrain development of embryonic stem cells (ethical concerns and high risk of cancer formation).
- Clinical confirmation of lack of immune activation will open the way for Mesoblast to produce an off-the-shelf therapy, rather like the pharmaceuticals available today.
- Adult stem cells obtained from a universal donor could be multiplied and grown in the laboratory, packaged in therapy-sized doses, shipped to hospitals for immediate administration and used to treat large numbers of unrelated patients.
- This will enable Mesoblast to develop a low cost, high-margin business model.
- For all envisaged applications, effective use of Mesoblast's technology will have marked therapeutic advantages over any treatments currently available. The adult stem cells will replace damaged or diseased tissue to hasten the healing as well as improve the blood supply to bone or heart muscle.
- The therapy will achieve functional improvement, rather than simply arresting the progression of disease.

Mesoblast at a glance

An Australian biotechnology company committed to the development of novel treatments for orthopaedic conditions, including the commercialisation of a unique adult stem cell technology aimed at the regeneration and repair of bone and cartilage.

ASX code: MSB

What are adult stem cells?

Adult stem cells are found in small numbers in various tissues of the body. They repair and maintain the tissue in which they are found. Scientists have discovered that adult stem cells also have the ability to become various other

tissues of the body, as a result of which they have the potential to be used in the treatment of various diseases and injuries.

How do adult stem cells differ from embryonic stem cells?

Embryonic stem cells are found only in the embryo. Their removal destroys the embryo. Adult stem cells therefore overcome the ethical concerns associated with the origins of embryonic stem cells. Adult stem cells have less capacity than embryonic stem cells uncontrolled growth, so are less likely to cause the formation of tumours.

What differentiates Mesoblast from other cell companies?

Mesoblast's proprietary technology involves efficient isolation and expansion of Mesenchymal Precursor Cells that are the only type of adult stem cell that can regenerate bone, cartilage, fat, muscle and arteries. These cultured cells are 1000-fold purer than existing or competing technologies.

Potential for Mesoblast's Cell Therapy in Treatment of Sports Injuries



Professor Itescu discusses Mesoblast's world-leading adult stem cell technology with the panel on Channel Nine's 'The Footy Show'. The company's technology is being considered to accelerate bone regeneration and improve outcomes for Australian footballers, and other elite athletes, with severe bone fractures. Banking an elite player's own cultured stem cells may provide a novel insurance policy to safeguard against potential career-threatening orthopaedic injuries.

Images: Courtesy Channel 9

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.

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