

mesoblast newsletter

ISSUE THREE

Today's clinical and commercial reality

There is significant global interest in Mesoblast and its proprietary adult stem cell technology. Over the past three quarters since listing we have demonstrated that our stem cell technology has real clinical promise, and that we know how to take the right steps towards rapid clinical development and product commercialisation.

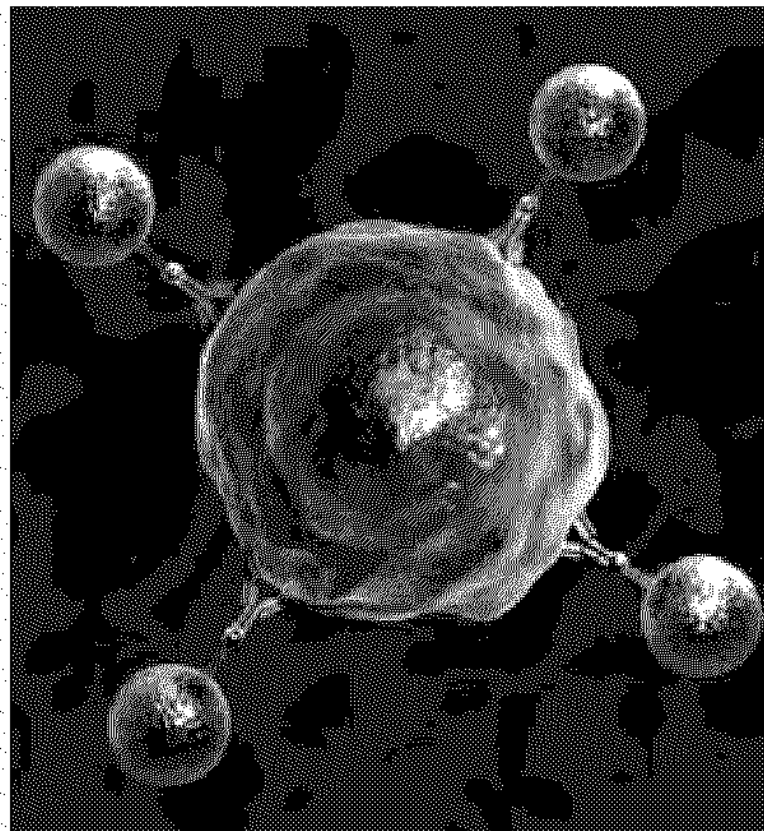
Our opportunity lies in tackling diseases and injuries that impact us all at some stage during our lives. These diseases and injuries represent a massive cost to the global health community. Most importantly though, they are diseases and injuries that cause substantial pain to millions of people, they dramatically impact the quality of life for sufferers and can often significantly reduce life spans.

Our goal therefore is to deliver a safe, affordable biological medical therapy to treat many diseases and injuries and to dramatically improve the quality of life for literally millions of people around the world.

We believe we can bring this new and exciting technology to patients in a remarkably short period of time, progressively unlocking shareholder value as effectively and rapidly as possible.

Highlights of company's activities during the third quarter 2005

- acceleration of clinical program, following Mesoblast's formal pre-Investigational New Drug (IND) discussions with the United States Food & Drug Administration (FDA) which enabled direct progression to Phase II clinical trials without the need for Phase I studies
- obtained ethics committee approval to commence an orthopaedic Pilot Clinical Trial at The Royal Melbourne Hospital
- joined forces with Cordis Corporation, a Johnson & Johnson company, for the upcoming cardiovascular Pilot Clinical Trial at Newcastle's John Hunter Hospital
- entered into a pre-clinical collaborative agreement with a leading international medical device company
- entered into commercial manufacturing agreement with Cambrex Inc: a world leading biologics manufacturer
- appointed an Executive Chairman, Mr Michael Spooner.



Why did we have a pre-IND meeting with the FDA and what was the outcome?

In order to ensure that Mesoblast receives timely IND approvals from the FDA for our clinical programs, we have been interacting regularly with the FDA to receive early input and assurance that our regulatory development strategy is appropriate and acceptable.

In addition to this type of informal interaction, companies are required to have formal pre-IND meetings with the FDA so that the proposed activities leading to an IND submission can be ratified. As announced on 17 October, Mesoblast had a formal pre-IND meeting to enable the FDA to evaluate Mesoblast's science, technology, pre-clinical programs, manufacturing strategy, and proposed clinical program for repair of long bone fractures.

At this meeting, we demonstrated that our cell therapy product is very well characterised. This is due specifically to the inherent advantages of our proprietary technology which ensures a high purity of stem cells in the starting material (up to 1000-fold purer than competitive technologies) and to the manner in which we safely expand our stem cells in culture.

The conclusions of the meeting were:

- the FDA is satisfied that we will be able to demonstrate safety to a sufficient degree of confidence through our proposed pre-clinical programs and manufacturing process because of the careful characterisation of our proprietary stem cells
- the FDA will evaluate the results of these studies in the IND submissions and, provided they demonstrate an anticipated safety profile, will support direct commencement of Phase II Clinical Trials, without the need for additional Phase I safety studies
- the FDA will consider each additional IND submission on a case by case basis

What does this mean for Mesoblast?

The results of our pre-IND meeting are of great importance to Mesoblast. Whilst the meeting related specifically to certain orthopaedic indications, the ability to progress straight to Phase II clinical trials is likely to apply to all of the company's clinical activities. This is because the proposed pre-clinical studies and manufacturing process are structured in such a way as to support the safety profile of the proprietary stem cell therapy for each separate orthopaedic and cardiovascular clinical indication.

Therefore, the conclusions of this pre-IND meeting are likely to mean the following for Mesoblast:

- substantial savings in dollars and years of work
- immediate unlocking of significant value for shareholders as a later stage clinical development company which is proceeding through clinical trials at a much faster rate
- earlier commercial partnerships and collaborative arrangements with global dominant players in our areas of interest

Clinical Trial Update

We firmly intend to undertake at least two Pilot Clinical Trials, one orthopaedic and one cardiovascular, each incorporating up to 10 patients.

Our overarching focus will be to work closely with the hospitals and clinicians involved in these trials to ensure that the privacy and well being of all patients involved in the Clinical Trials is protected.

The purpose of these trials is to provide early safety data in humans and validate our Standard Operating Procedures in a clinical environment. Data collected as a result of these Pilot Trials will provide useful supplementary information in support of our FDA submissions.

The orthopaedic Pilot Clinical Trial is for repair of large fractures of the tibia that have failed to properly heal, a condition called non-union. Failure to properly heal broken bones impacts thousands of Australians and millions of people in developed countries worldwide annually. Affected persons are crippled and have a poor quality of life and have few options available to them. The Trial will commence shortly and will be performed at The Royal Melbourne Hospital.

The cardiovascular Pilot Clinical Trial is for patients suffering severe multi-vessel coronary artery disease. This condition affects millions of people worldwide and can cause crippling chest pain and poor quality of life. Eventually, it can lead to heart failure and death. The Trial will be performed at the John Hunter Hospital in New South Wales and is due to commence shortly.

Agreement with Cordis Corporation

On 7 November, we announced a collaborative agreement with Cordis Corporation, a Johnson & Johnson company.

Cordis Corporation is a worldwide leader in developing and manufacturing interventional vascular technology, including the drug-eluting Cypher stent. Through the company's innovation, research and development, they manufacture intravenous delivery systems for clinicians. These systems are used effectively in treating patients with heart disease by delivering drugs to affected areas in the heart and by unclogging blocked arteries.

Cordis' latest generation heart catheter system has been specifically developed to deliver cells or other biologics to the heart. This latest heart catheter system will receive its first worldwide test in patients in conjunction with our proprietary adult stem cells during our imminent cardiovascular Pilot Clinical Trial.

Why did Cordis choose Mesoblast's trial to test its newest generation catheter system?

To obtain regulatory approvals and subsequent sales of its newest heart catheter system, Cordis seeks to identify an optimal cell therapy product that is safe and effective when injected into the heart. Through a confidentiality agreement, Cordis was provided with data on the inherent advantages of our proprietary technology, including product characterisation, purity, scale-up and manufacturing, and, importantly, pre-clinical results of heart function studies performed to date. Consequently, we believe that Cordis' choice to use Mesoblast's Pilot Clinical Trial as the first test of its newest generation catheter delivery system for cell therapy is a significant endorsement of both the clinical and commercial potential of our proprietary adult stem cell technology.

What is the implication for Mesoblast?

Our stem cells delivered via catheter into the heart may prove to be a market dominant therapy in the treatment of cardiovascular disease and heart failure giving rise to a potentially massive market opportunity.

Mesoblast's strategy is to have the strongest possible approach to commercialising our technology by working closely with global dominant players in our areas of interest. The relationship with the Johnson & Johnson companies, Cordis and Biosense Webster, is indicative of this strategy.

Catheter systems for delivering stem cells to the heart have already been developed by a number of other large device manufacturers with major global presences in the cardiovascular markets. We will continue to develop and commercialise our technology and will look to enter into a commercial relationship with one or more of these catheter companies at a time that will maximise shareholder value.

Mesoblast and its American sister company, Angioblast Systems Inc, will retain all intellectual property rights to the platform stem cell technology during the course of our collaboration, and will remain free to pursue all commercial options.

Pre-clinical orthopaedic studies for FDA submissions

The economic burden of bone fractures on the US economy alone is US\$13billion annually, with US\$2.3billion spent annually on medical costs directly associated with internal fixation materials.

Our ultimate goal is to generate a commercial product that consists of a clinically effective dose of our stem cells available on demand to clinicians, hospital and trauma units immediately as needed at the time of an acute event or a surgical procedure. Our stem cell product will provide a cost effective and, more importantly, a timely solution aimed at improving the quality of life for patients that often have a poor prognosis or may have life long pain and suffering.

Consequently, our initial Phase II Orthopaedic Clinical Trial will utilise stem cells obtained from a universal, or allogeneic, donor to treat unrelated patients with severe long bone fractures with a high propensity for non-

union, or lack of healing. To support our IND submission to the FDA for this Phase II clinical trial, in August we began preclinical trials at the Colorado State University in the US. Data collected as a result of these trials will be essential to our IND submissions to the FDA for the clinical trial outlined above and for other orthopaedic applications related to bone regeneration.

Two specific large animal studies are being completed that utilise universal, or allogeneic, donor stem cells (the use of cells from totally unrelated donors). Stem cells harvested from one strain of sheep have now been implanted into a number of sheep from a completely different strain.

Outcomes associated with these studies include both safety and efficacy and are essential to proving Mesoblast's core technology and to obtaining FDA IND approvals. Progress toward completing these studies has been extremely rapid with initial results expected by no later than the first quarter of 2006.

Collaboration in pre-clinical orthopaedic studies with global device leader

As part of these pre-clinical orthopaedic studies, we entered into a collaborative agreement with a major global device manufacturer to provide carrier materials which enable our proprietary stem cells to fill the bone defect adequately and enhance their ability to form bone. In this collaborative agreement, Mesoblast will retain all intellectual property rights to the platform stem cell technology, and will remain free to pursue all commercial options.

If our proprietary stem cells prove to be safe and effective when delivered into the bone defects with these carrier materials, we believe there will be strong impetus for the two parties to enter into a formal commercial relationship.

However, as with heart catheter systems, similar carrier materials have already been developed by a number of other large device manufacturers with major global presences in the orthopaedic markets, and we anticipate that the results obtained with our cells during this collaboration will be able to be broadly translated to these other orthopaedic carrier materials.

Mesoblast will be in a position to use the data from these pre-clinical trials in subsequent discussions with a variety of potential commercial partners.

Status of stem cell manufacturing process

Mesoblast has entered into an agreement with Cambrex Inc in the US to commence the process of gearing up for large scale manufacturing of the company's adult stem cells.

The ability to consistently manufacture in commercially viable quantities will be an essential element to our IND submissions to the FDA. We will establish Good Manufacturing Process (GMP) that includes rigid quality assurance and quality control guidelines. Additionally, an important outcome for us will be the determination of Standard Operating Procedures (SOP) that will continue to guide the overall manufacturing process.

Under the agreement, Cambrex will produce commercial quantities of clinical grade cells to GMP standards for our US-based human clinical trials.

It should be noted that cells produced under the same manufacturing process at the Peter MacCallum Cancer Institute's Cell Therapies Pty Ltd in Australia will be used in Mesoblast's human Pilot Clinical Trials scheduled to commence soon.

Our Team

Our focus is on excellence and in particular attracting and retaining the best possible people. Since listing Mesoblast and our US-based sister company Angioblast Systems Inc have built a highly qualified team of regulatory and clinical specialists with substantial experience in successfully preparing regulatory submissions to the FDA. We have also bolstered our internal business and project management capabilities to meet our management and overall control needs. Our goal, however, will be to maintain a strict and constant control over costs. Accordingly, and where ever possible, we look to outsource work to best of breed specialists and partner organisations that have the skills and experience necessary to assist us in achieving our goals.

Funding

At 30 September 2005, Mesoblast had around \$13.6 million of funds. Importantly, Angioblast Systems has cash reserves of \$2.68 million bringing the total cash available for the joint development of the companies' adult stem cell technology to over \$16.04 million.

Mesoblast believes it has sufficient funds in place to complete those tasks associated with preclinical and clinical trials necessary to complete IND submission to the FDA.

The Board of Directors is confident that with its strong cash balance, Mesoblast will be able to deliver on its technical and commercial milestones in a disciplined and strategic manner.

Next Quarter Goals

Our goals for this quarter ending 31 December 2005 are:

- Commence Pilot Clinical Trials for both an orthopaedic indication and a cardiovascular indication
- Transfer manufacturing and SOPs to Cambrex Inc for commercial scale-up of stem cells
- Maintain constructive dialogue with key regulatory authorities
- Continue constructive engagement with key medical opinion leaders and end-users of Mesoblast's technology
- Report on initial results from pre-clinical trials at the Colorado State University



Mesoblast and its Founder & Chief Scientific Adviser, Professor Silviu Itescu, were highlighted in the inaugural edition of Forbes Asia magazine.

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:

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