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Mesoblast (MSB)

No Bones About Mesoblast

Company Data

ASX Code	MSB
Price	\$1.90
12 month price target	\$3.20
Implied return	68.3%
Shares on issue	107.7m
Market capitalisation	\$204.6m
12 Month price range	\$1.10 - \$2.49
Monthly turnover	4.6m

Cash Flow Summary

Yr to 30 June	2006A	2007A	2008F	2009F
Receipts	2.2	0.7	0	24.5
Interest	0.6	0.9	0.1	0
Oper. Cash Inflow	2.8	1.6	0.1	24.5
Oper. Cash Out	(5.9)	(9.7)	(14.0)	(29.1)
Net Oper Cash	(3.2)	(8.1)	(13.9)	(4.6)
Net Inv. Cashflow	(4.1)	(4.3)	(5.5)	(1.2)
Net Fin. Cashflow	0	16.7	0	0
Inc/(Dec) Cash	(7.2)	4.3	(19.4)	(5.8)
Opening Cash	15.1	7.9	12.1	(7.2)
Closing Cash	7.9	12.1	(7.2)	(13.0)

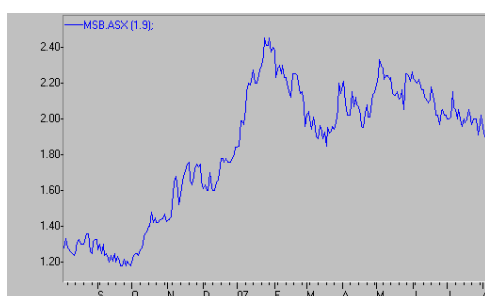
Board of Directors

Michael Spooner	Chairman (Non-Exec)
Silviu Itescu	MD & CEO
Donal O'Dwyer	Non-Exec. Dir.
Byron McAllister	Non-Exec. Dir.

Major Shareholders

Silviu Itescu	34.5%
AMP	11.6%

Share Price Chart



Source: Iress Market Technology

Investment Summary

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 & 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.

Validation of Business Model

Success in demonstrating the clinical utility of allogeneic MPCs will validate MSB's business model. This will allow the company to proceed with the development of "off-the-shelf" stem-cell for a variety of clinical applications. The major advantages of this model are:

- **superior economics** – lower costs and higher margins
- **immediate access** – can be used when needed in the clinic

As a consequence, MSB will be able to offer a superior product with better economics than companies who are currently developing autologous cell-based therapies.

Good Pipeline

MSB has 4 development programs for various orthopaedic applications in progress, while Angioblast is about to commence Phase-2 testing for cardiovascular applications:

- **Spinal fusion** – Phase-2 clinical program commenced
- **Long bone fractures** – Autologous cells effective in patients
- **Knee cartilage** – Preclinical animal studies near completion
- **Intervertebral disc cartilage** – Preclinical program commenced
- **Cardiovascular** – Phase-2 clinical program commenced

We expect the company will be initiating other programs as these progress.

While we have some issues regarding the structuring of the technology into two separate companies, it is possible that this will ultimately end up providing real benefits to MSB shareholders. In the meantime, the development of the underlying technology promises upside.

Valuation

12-month price target of \$3.40

Our current valuation for MSB is **\$2.35**, a 24% premium to the current share price. However, over the next 12-months, we believe the company will be passing a number of key milestones which, if successful, could support a price of **\$3.20**.

We have valued MSB using a risk adjusted discounted cash flow model for the key programs under development in MSB (spinal fusion, fractures, knee cartilage and vertebral cartilage) as well and added the 39.2% stake in Angioblast. We have placed a 75% probability that the current Phase-2 trials will be successful and a 60% probability that the products will eventually reach market. While these rates are higher than success rates for new pharmaceuticals, we believe the preclinical and clinical data to date have reduced the risk of a major adverse event and the nature of cell-based therapies eliminates many of the main causes of drug failure. While the safety issues with MPCs still need to be addressed, the key issue going forward is likely to be demonstration of a clear therapeutic benefit. In this area, the data thus far has been very encouraging.

Uptick in valuation will come from reduction of technical risk

While we believe our current valuation of \$2.35 is a fair reflection of the current risk in developing MSB's cell-based therapeutic products, with 2 Phase-2 trials using allogeneic cells in progress, the key factor that could change over the next 12-months is a significant reduction in the risk of the programs. Positive results, in terms of safety and some indication of efficacy from these trials, will dramatically improve the probability of these products reaching the market. What makes results of these trials significant is that positive safety and efficacy data will reduce the risk for all applications of MPC's. Equally, however, any safety issues identified in the Phase-2 trial will have a significant impact on the use of MPC's in a clinical setting. In view of this, we believe the outcome of these trials will address an important risk factor in MSB's technology and thus justify a significant re-rating of MSB. If positive, this re-rating could easily take the price to above **\$3.20**.

The key market assumptions used in our model are presented below.

Table 1: Market Assumptions for MPC-based Therapies

Indication	Est. Market Entry	Est Price	Final Market Share	Total Market (No. Treatments)
Spinal Fusion	FY13	\$4,000	15%	300,000
Fractures	FY14	\$3,000	15%	600,000
Knee Cartilage	FY13	\$1,250	5%	3,500,000
Vertebral Cartilage	FY15	\$1,500	5%	5,000,000
Cardiovascular	FY13	\$5,000	5%	2,000,000

SOURCE: *Lodge Estimates*

In our model, we have assumed that MSB will fund the development for each indication through Phase-2 clinical testing and then license the remaining development to a third party. Given these products will have demonstrated safety and efficacy in the clinic, we have assumed the royalty rate on end sales of 25%. In addition to probability adjustments to factor in the technical risk, we have used a discount rate of 16% to reflect the market risk.

Valuation comparable with overseas players

Our valuation for MSB of A\$2.35 (MCap A\$254m) can be compared with MSB's nearest competitor Osiris (MCap US\$347m). While Osiris has a product in the market, sales of this product are limited by supply and, because of the nature of the product, the gross margin of 55% is considerably less than MSB will be able to achieve. Osiris has another product in Phase-3 clinical testing and two other products at an earlier stage. In our view, positive safety and efficacy data from MSB's Phase-2 trials will make it comparable, if not more, attractive than Osiris. Thus we feel comfortable with our re-rated target price for MSB of \$3.20 reflecting a MCap of A\$345m.

Prior to the results from the two Phase-2 trials being available, MSB should progress its cartilage programs (knee and vertebral) which we would expect to have a positive impact on its valuation. There is also the potential for the company to initiate programs for other therapeutic applications.

Re-rating will provide upside for investors

Thus, while we believe MSB is trading at a slight discount (20%) to its current fair value, we anticipate there are a number of near term events that would support a significant re-rating of the stock and potential upside for investors.

Investment Thesis

Good preclinical and clinical data

With two Phase-2 clinical trials using allogeneic (unrelated) mesenchymal stem cells (MPCs) commencing, MSB is poised to validate the technology-basis for its business model; namely the development of cell therapies using “off-the-shelf” stem cells. In our view, this validation should support a significant re-rating of MSB through the reduction of technological risk and also from increasing the attractiveness of the company’s technology to potential licensees.

While it is never possible to be certain on the outcome of any clinical testing program, the studies to date bode well for a favourable outcome from these Phase-2 trials:

- Allogeneic MPCs have proven to be safe and effective in large animal studies
- Autologous MPCs have proven to be safe and effective in human clinical trials

Phase-2 is the final step in the jigsaw

If successful, the two Phase-2 programs (spinal fusion by Mesoblast and heart attacks by Angioblast) will put the final piece in place, namely:

- Allogeneic MPCs shown to be safe and effective in human patients

In addition to validating MSB’s business model of providing lower cost, off-the-shelf stem cells for regenerative, clinical applications, this final demonstration is likely to attract the interest of industry partners. Thus, while MSB’s products are still several years away from market sales, we would anticipate the company will be in a strong position to secure favourable licensing arrangements for the various applications of its technology that will generate near term income for the company.

In our view, the data to date has significantly reduced the risk of these clinical trials and positive results from these trials should support a re-rating of the stock.

Technology Approach –All Stem Cells Are Not Equal

MSB is using adult stem cells which are....

MSB’s technology is based on multipotent stem cells which can be isolated from various adult tissues (bone marrow, adipose, skin) and have the potential to differentiate into various types of connective tissue such as bone, cartilage, muscle, fat and tendon. These cells are called Mesenchymal Precursor Cells or MPCs.

...safer...

MPCs are very different from Embryonic Stem Cells (ES cells) which have been the focus of much media attention and public debate. ES cells are derived from very early stage embryos known as blastocysts, which are a ball of 50-150 cells formed 5 days after fertilisation. Unlike multipotent cells which can only form a few types of tissues, ES cells are pluripotent and have the ability to develop into any cell-type found in the body. In addition to ethical concerns regarding access and use of ES cells, the pluripotency of these cells has also raised safety concerns due to their potential to form ectopic tumours.

...multipotent...

MSB’s MPCs are multipotent stem cells from adult, rather than embryonic, tissues. As stem cells, they are able to divide to produce more stem cells and are also able to develop into tissue-specific cell types. As multipotent cells, MPCs are able to form several other cell types however the types of cells they can mature into is restricted. As a consequence, these cells are often called progenitor or precursor cells.

There are essentially two main types of adult stem cells: haematopoietic and mesenchymal. Haematopoietic stem cells can develop into the various cells that are found in blood such as red blood cells, lymphocytes, leukocytes etc. By comparison, the fate of mesenchymal stem cells (MSCs) is restricted to becoming one of the cell types found in various connective tissues in the body.

...but rare!

One of the richest sources of adult stem cells (both haematopoietic and mesenchymal) is the bone marrow. However, even within this tissue the stem cells are very rare, estimated to only represent 0.001% of all the cells present. Thus, while a number of research groups and companies have attempted to use various bone marrow preparations for cell therapy, in general these remain mixed populations of cell types with only limited number of actual mesenchymal stem cells present.

The results of the preclinical and clinical studies undertaken by MSB as well as other groups have shown that MPC’s can facilitate the growth and regeneration of specific tissues.

MPC's probably induce "self-healing"

Precisely how this is achieved is not known. However, the evidence indicates that much of the growth is not from the MPC's themselves, but from their ability to stimulate the cells which are already present at the site of treatment to start growing. Thus, very few, if any, of the implanted cells actually end up in the regenerated tissue. Instead the implanted MPCs provide various signals and growth factors that prompt the damage tissue to heal itself.

This is probably the most elegant form of cell therapy and removes some of the safety and ethical concerns associated with cell-based therapies.

Mesenchymal Precursors (MPCs) Cell Themselves

MPCs are in multiple adult tissues...

One of the attractive features of MPCs is that they can be isolated from a number of different adult tissues including bone marrow, adipose tissue (fat), and epidermal tissues such as skin. Furthermore, MPCs can be grown (expanded) in cell culture without changing their characteristics or potential. Under the appropriate physiological circumstances however, MPCs will differentiate into specific types of body tissue such as bone, cartilage and muscle.

...and can be used from unrelated donors...

A second major advantage of MPCs is that they do not express cell surface antigens responsible for triggering an immune response (namely CD40, CD80 and CD46). This means that MPCs from an unrelated individual can be used without activating the patient's immune system which would normally eliminate the cells.

From a commercial perspective the ability to use allogeneic (unrelated cells) rather than autologous (from self) cells has a considerable impact on the economics of a cell therapy-based business model.

...which supports a compelling business model

Using autologous cells is a very expensive approach for providing therapeutic outcomes. Each preparation can only be used for the individual patient it was originally sourced from and there are high costs associated with both cell culture and also maintaining consistency and quality control. In addition, the time involved in preparing and expanding autologous cells means that they are not available for immediate use in a clinical setting.

By comparison, allogeneic cells, such as MPCs, support a commercially more attractive business model with the costs associated with preparation and quality control spread over a much greater sales base (hence generating higher margins) and instant access to a batch-controlled reagent. Tissue from a single donor can be purified and be expanded to treat hundreds of patients.

Advantages of MPCs:

- **non-immunogenic**:- allows universal donor providing:
 - significant cost advantage
 - immediate access in clinical setting
- **relatively easy to source** – isolation from adult tissue
- **relatively easy to expand** – established culturing conditions
- **partially 'matured'** – greater safety as low risk of forming tumours
- **free from ethical issues** currently surrounding embryonic stem cells

MPCs Provide Compelling Growth Business Model

While MPCs can only form certain tissues (bone, cartilage, fat, muscle and tendons) there are more than enough commercially attractive clinical applications for the regeneration of these tissue types.

MSB is focussed on orthopaedic applications

MSB is focused on orthopaedic applications such as healing fractures, fusion of spinal vertebrae and regenerating damaged cartilage (found in joints or between vertebrae in the spine). Angioblast, in which MSB has a 39.2% equity holding through investment, has the rights for all non-orthopaedic applications of MPCs and is currently focussed on various cardiovascular applications.

Business model will generate multiple products...

In addition to the attractive economics of a cell-therapy business based on allogeneic stem cells, their use for different applications allows the company to establish distinct products in the market. In all applications, the underlying technology is the delivery of MPCs to a site of tissue regeneration. However, as part of the development, each application will be optimised for the number of cells delivered and also packaged with the appropriate matrix or support. This will ensure that the company will be able to develop specific products which segment the market in relation to its technology. In turn, this provides multiple licensing opportunities with different partners for each application.

...and multiple partnering opportunities

MSB has also been active in establishing relationships with delivery companies for the development of cell-therapy applications. For example, with fractures, the company has used a Medtronic support matrix for the delivery of its cells. Angioblast's Phase-2 clinical trial will use the latest generation catheters from the Johnson & Johnson companies Cordis Corporation and Biosense Webster. While no formal commercial relationship has been established with these partners, the market potential of the combined product will be such that there would be good grounds for establishing a more formal commercial relationship in the future. From MSB's perspective, this will provide clear access to an established distribution channel and hence greater and more rapid market penetration.

MSB's Advantage With MPCs– Identification and Isolation

MSB has a competitive advantage from its IP

MSB's core IP relates to a combination of specific proteins (markers) present on the cell surface of MPCs. The company has granted patents for these cell surface markers that characterise their MPCs and provide protection until 2019. The company also has several application-specific patents and also patents relating to the isolation of MPCs from tissues other than bone marrow.

The combination of specific markers that characterise MSB's MPCs provides the company with two sources of competitive advantage:

- identification of MPCs
- isolation of MPCs

The IP on the cell surface markers (3G5 plus STRO-1 or VCAM-1) to identify MSB's MPCs prevents other parties from characterising their stem cell preparations using these markers. Thus, while other parties may find methods of enriching for MPC's, they will not be able to formally characterise their enriched population using these markers.

Can purify MPCs up to 1000x greater than competitors

The markers also provide a route for purifying the rare MPCs from adult tissues. By using antibodies to bind the cell surface markers, MSB has been able to magnetically extract the MPC's from a population of different cell types (such as a bone marrow aspirate). This generates a highly purified population with approximately 1000x greater number of MPCs than competitive technologies. Intuitively, the greater number of MPCs should result in a greater regenerative capacity in clinical applications.

Multiple Applications Under Development

Good progress since listing

Since listing on the ASX in December 2004, the company has made significant progress towards the development of multiple clinical applications for its MPC technology. The key elements of this progress are:

- scale up manufacturing of MPCs under GMP (Good Manufacturing Practice)
- demonstration of both safety and efficacy of allogeneic (unrelated donor) MPCs in large animal (sheep) trial
- demonstration of efficacy of autologous (own) MPCs in human clinical testing for both orthopaedic and cardiovascular applications (trials still in progress)

The company has just commenced the final, critical demonstration of the technology for their business model; using allogeneic cells in human clinical trials. In December 2006, the FDA approved an Investigational New Drug (IND) application for a Phase-2 clinical trial using allogeneic MPCs for spinal fusion (joining up two vertebrae following extensive damage to the intervertebral disc). In May 2007, the FDA approved a second IND application from Angioblast for a Phase-2 clinical study using allogeneic MPCs delivered via a cardiac

Two INDs approved by FDA in record time

catheter to repair damage of heart muscle following a heart attack. The fact that both of these IND applications were granted within 30 days of submission indicates that the FDA is comfortable with MSB's cell-therapy approach and the quality of the preclinical and manufacturing data that was part of the submission.

MSB currently has programs for 4 orthopaedic programs in progress and Angioblast has progressed its cardiovascular program to Phase-2 clinical testing.

ALLOGENEIC PHASE-2 CLINICAL TESTING

Spinal Fusion (Mesoblast)

MPCs can eliminate second operation for spinal fusion

Approximately 300,000 procedures are currently undertaken each year in US for the fusion of vertebrae after irreparable damage has occurred to the cartilaginous disc that separates them. The standard treatment involves two surgical procedures with the second operation involving taking bone tissue taken from the patients pelvis.

MSB's approach will eliminate the second surgical procedure, which often leads to long term complications, such as chronic pain and infection, by applying MPCs to the region during the first operation.

Phase-2 clinical trial has commenced

In April 2006, MSB announced interim results from a 34 sheep trial for spinal fusion using allogeneic (unrelated) MPCs. On the basis of the safety and efficacy data from this study, the company submitted an Investigational New Drug (IND) application to the FDA for a human clinical trial using allogeneic stem cells. The FDA approved the IND in December 2006 (30 days after submission). The company has now commenced its Phase-2 clinical program for this application which will be undertaken at the Hospital for Special Surgery in New York. The Phase-2 program is likely to involve two trials with the first trial focussed on clinical safety as its primary endpoint and is likely to involve around 40 patients. However, while this first trial will not be statistically powered to demonstrate efficacy, it should provide an indication of the MPC approach for facilitating effective fusion of vertebrae.

With over 300,000 procedures each year, recruitment for the Phase-2 program should be straightforward. We expect interim results from this trial will be available in early CY08. Furthermore, the cost savings associated with elimination of the second surgical procedure will more than offset the additional cost from incorporating MPCs in the treatment.

Heart Muscle Repair Following Heart Attack (Angioblast)

In the US, around 1.1m people suffer from heart attacks each year. In addition over 5m Americans have congestive heart failure with 550,000 new cases reported each year.

During a heart attack, the cells in muscles of the heart are deprived of oxygen and die leaving areas of the heart that are unable to function properly. MSB is developing a technique to repair the damaged heart tissue by delivering MPCs to the affected region using a cardiac catheter.

Good results from animal models of heart attacks

Angioblast has already run two trials in sheep using allogeneic cells which showed improvements in heart function of up to 50% following artificially induced heart attacks. The company also has a 10 patient clinical trial in progress for this application at the John Hunter Hospital using autologous MPCs. Enrolment for this trial should be near completion. With a 6-month follow-up period, we would expect the final results to be announced in February 2008. Interim data released for the first 3 patients have indicated that the autologous MPCs have provided a significant improvement in heart function.

Phase-2 IND application approved in May 2007

On the basis of the animal trial data and the interim data from the autologous clinical trial, in May 2007, the FDA granted approval for an IND application for a Phase-2 clinical trial using allogeneic MPCs delivered using a cardiac catheter in heart attack patients. As with the spinal fusion Phase-2 program, we expect this will comprise of two trials with the first trial primarily focused on safety but providing indicative data on efficacy.

AUTOLOGOUS CLINICAL TESTING**Long Bone Fractures (Mesoblast)**

Around 6m fractures occur in the US with 10% resulting in delayed healing or non-union (failure to join up) and require bone grafts or implantation of additional tissue to promote healing.

MSB is developing a clinical approach that combines MPC's with a carrier to promote new bone growth to assist with the healing of these fractures.

Spectacular results in preclinical studies

In the initial preclinical studies, a 5cm piece of bone was removed from the femur (leg bone) of sheep. Sheep that received an implant containing allogeneic MPCs had much better rates of bone regeneration (80% v 42%) demonstrating that allogeneic stem cells are able to promote bone growth. Furthermore, analysis of the new tissue showed that the bone was of high quality and the region of joining was superior.

Patient regains mobility in initial clinical trial

In April 2006, MSB initiated a 10 patient trial using autologous MPCs for non-healing long-bone fractures. Enrolment of this trial was completed in June 2007 and, to date, there have been no adverse events reported in the 8 patients that have been implanted. The first five patients for whom data is available for analysis have shown strong bone regeneration and high quality union of the fractures. The result from the first patient treated in this trial was spectacular with a 5cm gap in his femur healing which allowed the patient to walk unaided for the first time since his motorcycle accident.

With positive preclinical data and good results from the autologous clinical trial, MSB should be able to commence a Phase-2 trial for bone fractures in the very near future. While the company is likely to select a specific application for its clinical trial, a clear demonstration of improved healing in a clinical setting is likely to result in significant off-label use for a range of applications.

PRECLINICAL TESTING**Osteoarthritis & Knee Cartilage (Mesoblast)**

Expect data from preclinical study soon

In the US, 800,000 arthroscopic knee surgical procedures are undertaken each year. These are usually due to deterioration of cartilage meniscus that acts as a cushion between the large leg bones at the knee joint. These operations usually consist of removal of the debris accumulated in the joint from deteriorating cartilage or the injection of different agents in an attempt to replace the cushioning. Unfortunately, both of these procedures usually only provide temporary relief and neither assist with rectifying the damage which has occurred to the cartilage.

In December 2005, MSB was awarded a \$2.7m Commercial Ready grant to undertake a preclinical study in sheep for the use of MPCs in cartilage repair and reconstruction. The results of this study will open up further applications for both the treatment of osteoarthritis of the knee and also damage to the meniscus from sports injuries.

As most of the funds from the grant have been used, we expect that this trial is very close to completion. A positive result would provide access to a large and growing market due to the ageing of the population. Furthermore, the lack of efficacy from the Osiris trial with Chondrogen means that the competition in this area is currently very limited.

Intervertebral Disc Cartilage Repair (Mesoblast)

Preclinical animal trial commenced

Lower back pain is very common affecting up to 15-20% of the population. One of the most common causes of lower back pain is deterioration of cartilaginous discs that separate the individual vertebrae in the spine. If this is left untreated, deterioration can continue and ultimately require spinal fusion of the discs (see above).

In July 2007, MSB announced the commencement of a preclinical trial in sheep which will use MPCs to repair and regenerate damaged disc cartilage. This trial will be undertaken at the Institute of Medical and Veterinary Sciences (Adelaide, SA) and preliminary results should be available in 1Q CY08. If these results are positive, we envisage that they could support an additional IND application in 2008.

Expect other programs in the future

The above list only reflects the development programs that Mesoblast and Angioblast currently have in place. As these progress, we envisage the company will continue to expand the therapeutic applications for its MPCs including other cardiovascular applications (congestive heart failure, peripheral arterial disease). Furthermore, as these trials progress, the regulatory hurdles for approval will decrease, particularly given the safety data will have relevance to all of the companies products. In addition to its MPC programs, Angioblast has R&D programs looking at stromal-derived factor-1 (SDF-1) for stem cell migration and angiogenesis and plasminogen inhibitor type-1 (PAI-1)

Competitors

While there are several companies developing stem cell technologies, many of these are using embryonic stem cells and/or are focused on different applications (eg: nerve regeneration in degenerative disorders). Many of the companies which are focussed on adult stems cells are developing products based on haematopoietic stem cells for cancer, blood disorders and post-radiation bone marrow rejuvenation.

Less competition in orthopaedic areas

A number of companies are developing mesenchymal stems cells for different therapeutic applications. However, MSB's intellectual property for cell surface markers which identify the cells and the utilisation of those markers to isolate highly purified MPC's provide the company with a unique competitive advantage. In terms of applications, many of the competitors are primarily focussing on the use of stems cells (including embryonic stem cells) for cardiovascular applications (competing with Angioblast). Fewer companies are currently developing orthopaedic applications.

Osteocel on market but commercially difficult**Osiris (NASDAQ: OSIR, MCap US\$345m)**

Of all the competitors, OSIR is probably the closest to MSB. OSIR has one product in the market called **Osteocel** for spinal procedures and other orthopaedic surgical procedures. The sales of this product have been limited by supply as the product is an unexpanded preparation from bone matrix. Not only does this mean that a continual supply of donor tissue is required to generate the product, but also the proportion of progenitor cells in preparation is likely to be low. In the 12 months to 31 March 2007, sale of Osteocel were US\$9.1m. From the company's accounts, we estimate the average selling price for Osteocel was US\$2,000 with a gross margin of 55%.

OSIR's other products (Prochymal for graft-versus-host disease, Chondrogen for cartilage applications and Provecel for cardiac applications) are based on enriched and expanded mesenchymal stems cells (MSC's) from bone marrow aspirate. OSIR's enrichment process relies on the adhesion of MSC's to plastic surfaces which will still result in a large proportion of non-MSC cells in the initial preparation. Intuitively, we would expect the regenerative capacity of any preparation will be proportional to the number of MSC or MPC cells present.

Prochymal is currently in a pivotal Phase-3 trial for steroid refractory graft-vs-host disease with both Orphan Drug and Fast-track status. Neither MSB nor Angioblast are currently developing products for this application.

Other products will not be as pure as MSBs

Chondrogen for the regeneration of meniscus (a type of cartilage that cushions the knee joint) announced results from a 55 patient Phase-1/2 trial in February 2007. While the trial met its primary endpoint (product safety), the product did not demonstrate a statistically significant increase in the volume of meniscus. At this stage, OSIR have not stated their intentions regarding taking this program forward which provides a clear opportunity for MSB should their current preclinical testing provide positive results.

OSIR announced positive safety and efficacy results from its 53-patient Phase-1 trial for the intravenous administration of **Provacel** to patients who have suffered a heart attack. Angioblast's trial for this indication involves the implantation of cells directly into the heart of patients using a cardiac catheter.

Aastrom (NASDAQ:ASTM, MCap US\$150m)

Aastrom only providing autologous cell therapies

Aastrom is using bone marrow aspirates as a source of adult stem cells for bone, vascular, cardiac and neural regeneration. Unlike MSB and Osiris, ASTM does not attempt to enrich for MPCs and, due to the nature of the expanded cell population, it can only be used for the patient the initial sample was taken from (ie: autologous only with no allogeneic applications).

The company is in a pivotal Phase-3 clinical trial for osteonecrosis of femoral head (deterioration of the top of the thigh bone) and is commencing a Phase-2b clinical trial for peripheral arterial disease (PAD).

While some of the applications that ASTM is developing overlap with MSB/Angioblast, the greater expense of autologous cells (plus the lower number of stems cells) will provide MSB with a significant advantage (both from a cost and effectiveness prospective) in the areas where they do compete directly.

Arthersys (BVIC.OB, MCap US\$52m)

Arthersys early stage in development

In addition to early stage drug discovery programs, Arthersys has acquired rights to MultiStem technology based on Multipotent Adult Progenitor Cells (MPACs) developed at the University of Minnesota. The company appears to be at a very early stage in terms of progressing this technology towards clear clinical applications.

Cytori Therapeutics (NASDAQ:CYTX, MCap US\$145m)

Cytori has rapid isolation but still only autologous

CYTX is isolating adult stem cells from adipose tissues. As with ASTM, this is primarily for autologous applications however, unlike ASTM, the cells are used directly following isolation from the tissue (using their Celution System) rather than requiring an intermediate expansion step through cell culturing. CYTX has a 36-patient safety and feasibility trial in progress in Europe for chronic ischaemia and is looking to initiate a clinical trial in reconstructive surgery during the second half of 2007.

Neuronyx. (Private)

Neuronyx focussed on cardiovascular

Neuronyx is using what they call adult bone marrow-derived somatic cells (hABM-SCs) to repair damage to cardiac tissue following heart attack. The cells that they are using are allogeneic and the company claim to have a GMP compliant process that allows them to significantly expand the cells. The company has a Phase-1 clinical trial in progress for repair to cardiac tissue following heart attack/acute myocardial infarction.

Company Structure.

MSB shareprice has increased four-fold since listing

MSB was listed on the ASX on 14 December 2004 raising \$21m at \$0.50 with an implied market capitalisation of \$46.8m on listing. At the time of listing, founder Prof. Silviu Itescu retained 46.1% of the company. Since listing, the company raised \$17.1m at \$1.25 in July 2006 via an institutional placement and share purchase plan (SPP). Following the sale of 6m shares in February 2007, Prof. Itescu still holds 37m shares (34.5%) which are in voluntary escrow until February 2008. There are no other shares in escrow and the remaining ordinary shares are held through the ASX. Approximately 8m options are on issue with expiry dates up to 2009. Most of these options are in the money and thus likely to be exercised prior to expiry.

Angioblast established in US to focus on all non-orthopaedic applications

While MSB was established and listed on the ASX to focus on MPC technology for orthopaedic applications, the rights for all other applications of the technology reside with the US-based company Angioblast which was also established by Prof. Itescu. At the time of listing, MSB invested \$10m into Angioblast in exchange for a 33% equity position (implying a pre-investment valuation of A\$20m). At the time of the second raising (July 2006), MSB shareholders approved a second investment of A\$8.5m which would bring their holding to 39.2% (implying a pre-investment valuation of A\$87.5m). Following completion of this investment, Prof. Itescu will hold 50.3% of the shares in Angioblast.

Company structure has raised some issues

This structure, with the two related companies Mesoblast and Angioblast, has raised issues from a number of actual and potential investors, namely:

- the ownership of the key IP is held by Angioblast with a license granted to MSB only for orthopaedic applications
- funds raised by MSB are used to support all of the R&D in Angioblast however the returns to MSB shareholders only come in proportion to their equity holding
- while various checks and balances are in place, MSB still remains a minority shareholder in Angioblast which limits its control on future decisions
- some investors view the Angioblast applications as commercially more attractive however their exposure is indirect and diluted through MSB's holding.

We would have preferred a more standard structure for MSB which provided investors with a more direct investment in the IP and the benefits from all the clinical development programs as they progress.

However, despite our reservations, it is possible that the current structure may actually end up providing the greatest benefit for MSB shareholders in the long run because:

- as a separate legal entity, there are fewer barriers to Angioblast eventually listing in the US market.
- the valuations achieved by US listed companies are typically higher than the Australian market
- a favourable valuation for Angioblast will have a significant impact on MSB by:
 - placing a firm value on MSB's 39.2% equity stake
 - supporting a re-rating of MSB itself on a comparable basis

However, may end up delivering most value to MSB shareholders

Thus, at some stage, we envisage that there may be an event that can crystallize the value of Angioblast, either through a listing or from investment by external parties. There is a good chance that such an event would be at higher valuation than is currently factored into the MSB share price and may end up being in the favour of MSB shareholders.

Thus, while the separation of IP and therapeutic applications into two separate companies does cause some issues, it may prove effective for maximising the value for all shareholders in both companies. Until that time, however, we still harbour some reservations on the structure as it does not provide MSB investors with complete and direct ownership of the technology they are investing in.

Management and Board**Experienced Board and management team**

Both MSB and Angioblast were founded by Prof. Silviu Itescu who is on the Board of both companies. Prof Itescu is on the medical faculties of Columbia University (New York) and the University of Melbourne. In addition to Mesoblast and Angioblast, Prof. Itescu has been a director on two Australian biotechnology companies (Amrad Corporation and Ambri Ltd) and has been an advisor to biotechnology and healthcare investment groups.

Michael Spooner has been Executive Chairman of MSB since August 2005. The company has recently announced Michael Spooner's resignation from that role, however he will remain in the role until a Non-Executive Chairman is appointed and the will continue on the Board as a non-executive director. We believe that the company will look to appoint a new Chairman that can assist with the next stage of the company's development that will involve both additional financing and establishment of strong corporate partnerships.

MSB also has two other non-executive directors on the Board, Donal O'Dwyer and Byron McAllister. Mr O'Dwyer has extensive experience in cardiovascular and medical devices is represents MSB on the Angioblast Board. Mr McAllister has experience in product development and regulatory experience, particularly in the area of biologics. He has worked for a number of international life science companies including Amersham, Abbott Laboratories and Coulter Electronics.

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Recommendations are assessments of each Lodge Partners Analyst's view of potential total returns over a 1 year period.

Expected total Return is measured as (capital gain (or loss) + dividend)/purchase price

We have divided our recommendations into three main categories:

Buy: Expected Total Return in excess of 15% over a 1 year period.

Hold: Expected Total Return between 0% and 15% over a 1 year period.

Sell: Expected Total Return less than 0% over a 1 year period.

Analyst Verification

I verify that I Matthijs Smith, have prepared this research report accurately and that any financial forecasts and recommendations that are expressed are solely my own personal opinions. In addition, I certify that no part of my compensation is or will be directly or indirectly tied to the specific recommendation or financial forecasts expressed in this report.

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