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In this edition...
FY2013 was a quiet year for Mesoblast but also a busy year for the world's premier stem cell company. Important progress was made on the manufacturing front with manufacturing equivalence across sites in Singapore and the US being addressed as well as improvement to COGS made. Look out for Mesoblast to do a Japan deal sometime soon. Allied Healthcare's Cardiocel product gained its CE Mark this week, which is an outstanding achievement for people who put in the hard yards to get it there. The upside is the label claim which covers the repair of heart defects, not simply those discovered in very young children. QRxPharma faces a tough few months following another delay with the FDA
Companies covered: AHZ, MSB, POH, QRX

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - Current)	56.5%
Cumulative Gain	**457%**
Av. annual gain (12 yrs)	**16.6%**

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Mesoblast Updates Market on Phase III CHF Trial

Stem cell company Mesoblast (MSB: $5.48) provided the market with updates this week on several of its programs during the course of a conference call organised to discuss the company's full year results.

Of great interest to analysts was the status of the company's Phase III trial of its allogeneic (off-the-shelf) mesenchymal pre-cursor (MPC) stem cell product in subjects with congestive heart failure. The program, co-managed with its partner Teva Pharmaceuticals, has been slow to get off the ground. Mesoblast CEO Silviu Itescu discussed some of the reasons for the apparent slowness in initiating this trial.

Mesoblast in conjunction with its manufacturing partner Lonza has made 'herculean' efforts to meet the regulatory standards for producing its cell therapy products from two different sites; one in the US and one in Singapore. The company wanted to construct two manufacturing sites to build in redundancy and because Mesoblast has an exclusive arrangement with Lonza at its Singapore site for the manufacture of stem cell products.

A challenge that Mesoblast/Lonza had to satisfy the FDA was that batches of product made at both sites were equivalent from a manufacturing perspective. Another manufacturing issue resolved in the last 12 months was achievement of scaled-up production of Mesoblast's stem cell product, together with cost of goods reductions, and product delineation. Mesoblast also stated in its Annual Report that it had focused on the development of 'second generation production methods'.

The use of two manufacturing sites also means that Mesoblast can meet the requirements for all its clinical trial needs and potentially even for the early stages of commercial supply.

With manufacturing issues now largely resolved, Mesoblast is in the final stages of preparation of the Phase III trial documentation for final submission to the FDA .

This 1,700 patient trial is expected to begin before the end of the year (CY2013 H2). The trial has been designed for several analyses to be made during its progress. The first interim analysis (a futility analysis) will occur about 18 months from the commencement, or when approximately 60% of patients have been recruited and 40% of events (as defined in the protocol) have occurred. Depending on the interim results, Mesoblast may or may not need to expand the number of patients being recruited into the trial.

One challenge for the trial identified by Mesoblast is that the physicians from sites included in the trial must be skilled at using the special catheter used to deliver the stem cells to the heart. This might mean, for example, that a core number of ~40 'expert' sites are fed by cardiologists who refer patients to the more skilled centres.

Cont'd over

Itescu also noted that in the three years since the 60 patient Phase II trial in heart failure was initiated, that there have been no hospitalisations for decompensated heart failure or any cardiac-related deaths in patients who received the highest dose. Patients not treated with Mesoblast's MPC's have experienced a 30% event rate.

Spine Franchise

Mesoblast has two clinical programs underway in the area of spinal treatments. In January, the company released positive 12 month data from its lumbar spinal fusion trial and in April it released positive interim, six month results from its disc repair trial.

The company is currently in discussions with the FDA about the design of a Phase III trial for posterior lumbar fusion. Based on precedent, it is likely that a single, randomised trial would be sufficient, in which MPCs are evaluated alongside an autologous bone graft. The endpoints would be similar to the Phase II trial, demonstrating non-inferiority to bone graft, pain reduction and need for additional surgery. Mesoblast would like to commence a Phase III trial in first half of 2014.

Partnering of the fusion product and the disc repair product is complicated by the fact that device companies would be more likely to partner the fusion product but pharmaceutical companies with a focus on pain could as equally be interested in the disc repair product. The disc repair product is an early intervention product which can be delivered as a short day procedure. The driver for device companies is that it could 'pull through' sales of medical hardware. Partnering discussions are ongoing and Mesoblast's objective is to find a partner with the appropriate reach and depth within their networks.

Eye Diseases – Wet and Dry AMD

Mesoblast is conducting an 18 patient Phase II trial of its stem cell therapy at the Singapore National Eye Centre in subjects with 'wet' age-related macular degeneration. The trial is comparing two different doses of MPCs, co-administered with Lucentis (an anti-VEGF-a antibody fragment) which targets vascularisation, against Lucentis alone. The primary endpoint of the trial is safety at the end of 12 months with secondary endpoints evaluating efficacy in terms of synergy with Lucentis to improve visual acuity and potential to decrease the dosing frequency of Lucentis.

The trial has completed dosing on a lower dose and has now moved to the second, higher dose. Mesoblast expects to complete this study by the end of this year and release results in 2014.

Interest in this trial in 'wet' AMD stems from the potential to evaluate MPC's in 'dry' AMD, a market which is ten times larger and to do this on the back of safety data generated from the Phase II trial. Depending on the outcome of the trial, Mesoblast will consider partnering the program in order to support Phase III programs.

An interesting market opportunity exists in Asia in AMD because of the incidence of a genetic variation which means that 50% of the population do not respond to anti-VEGF therapy. This adds another layer of interest to the commercial discussions that Mesoblast can have with potential partners.

Partnering – Japan Deal Approaching

A recurring theme from the Mesoblast conference call was that of partnering. CEO Itescu flagged that the company is approaching a deal with a Japanese pharmaceutical company (or conglomerate) in respect of its MPC products. This timing of this deal has related to the recent grant of a key Mesoblast patent in Japan (expiring in 2025) and the prospect that the Japanese government may eliminate the requirement for Phase III trials for stem cell products.

Another factor weighing on partnering activities is the importance attached to the clearance by the FDA of the Phase III heart failure trial. The value here is that with the trial design clarified and with manufacturing requirements accepted by the FDA the greater the certainty that can be applied to forming partnerships for applications of MPCs in other diseases and conditions.

Finally, the company's strong cash position has changed the dynamic of conversations that Mesoblast has with potential partners. For example, discussions now can include questions such as what aspects can be funded by Mesoblast (within a partnership) and how returns can be shared. And because Mesoblast has funds that it could potentially apply to sales, it has been able to change discussions with potential partners about their sales and marketing efforts.

Spending Commitments

For FY2014, Mesoblast's spending on activities will be in roughly the same proportion as for FY2013, which was 52% for R&D ($43.1 million), manufacturing commercialisation 25% ($21 million) and management and overheads (excluding share-based payments) 37% ($31 million). Total expenses excluding share-based payments for FY2013 were $82.5 million.

Summary

Mesoblast is capitalised at $1.7 billion and retained cash of $315 million, with its cash position having been boosted by a $170 million capital raising in March.

Mesoblast is a busy company. It has a Phase III trial underway in cord blood expansion, four Phase II trials ongoing in acute myocardial infarct patients, macular degeneration, rheumatoid arthritis and diabetic nepthropathy and also has Phase III trials for lumber fusion and for congestive heart failure set to commence later this year or early in 2014.

The risk with an investment in Mesoblast is that as it partnerships grow, its programs expand in number and grow in complexity, the likelihood of execution failure increases considerably.

Investors should also bear in mind that the company is still some years away from delivering the type of Phase III results that could put substance into the company's current share price.

Bioshares recommendation: **Sell**

Further Six Month Delay for QRxPharma

QRxPharma (QRX: $0.82) narrowly missed its deadline to resubmit all of the data required for its amended New Drug Application (NDA) of its new pain therapeutic, MoxDuo IR. The company expects to refile its NDA in coming weeks, which should see a six month review. QRxPharma now expects a decision in Q2 2014.

The core issue with this NDA is Study 022, and specifically the changes in oxygen saturation levels, which is the most significant safety aspect surrounding the use of opioid drugs. When oxygen levels drop below 90% it becomes a medical concern. In Study 022, two patients *not* taking MoxDuo IR had their blood oxygen levels fall dangerously low to 30%. MoxDuo IR, which is a combination of morphine and oxycodone was compared to equivalent opioid levels of morphine and oxycodone separately.

While QRxPharma had completed its own reassessment of Study 022, it is still waiting for the completion of third party quality control of the data. The data involved in this study is very large, involving more than 30 million data points. Some concern about the integrity of the data emerged when it was found that one site did not adjust its time readings for day-light-savings time.

QRxPharma was given a Complete Response Letter (CRL) from the FDA relating to its amended NDA. The FDA had previously requested more information about the movements in oxygen saturation levels in the blood as this is proving to be the core safety issue/benefit surrounding the MoxDuo therapy. On August 14 the company submitted this additional data, however, not the quality control assessment and as such has since missed its deadline. So the process starts once again with just over a six month delay likely.

Chief Operating Officer Ed Rudnic referred to the previous FDA terminology to clarify the CRL. Previously companies were either given (a) a letter that their drug was approved, (b) a non-approvable letter that a drug would not be approved, or (c) an approvable letter that a company would need to complete certain tasks to have a drug approved. QRxPharma falls into this third category said Rudnic.

CEO John Holaday said that the use of prescription opioids has become a political issue, with these drugs coming under increased scrutiny. Of the seven opioid drugs submitted for approval recently, only one got through at first pass, with others requiring 18 months further regulatory review on average before approval, and some not being approved due to formulation issues.

For its resubmission in coming weeks, QRxPharma will not need to resubmit the whole data package, but only the quality control assessment around Study 022 time points and the final report.

Funding

QRxPharma had $12 million at the end of June. Its cash burn is $1 million per month. The company will need to review its capital requirements, as the company does not have funds outside the other side of the anticipated product launch in H2 2014.

Timing Summary

- Resumbit NDA in coming weeks
- Six month review expected to start in Q4 2013
- FDA Advisory Committee meeting 1H 2014
- FDA re-assessment H1 2014
- Market launch H2 2014

QRxPharma is capitalised at $119 million.

Bioshares recommendation: **Sell**

Bioshares

Allied Healthcare Receives CE Mark Clearance for Cardiocel

Allied Healthcare Group (AHZ: 9.5 cents) has received CE Mark clearance to start selling its heart tissue repair product Cardiocel in Europe. The company will initially be selling the product for the treatment of congenital heart disease and also for the repair of heart valves in adults and children.

Allied Healthcare is commercialising a proprietary tissue reprocessing technology which is applied to bovine tissue. Unlike rival products, this tissue is much less likely to calcify, with calcification yet to appear in recipients. It also facilitates the rejuvenation of tissue with blood vessels and other growth factors.

The product has been used in Australia under a special access scheme with around 50 children having been implanted with the Cardiocel product. In Australia, the progress of these patients is being monitored and will provide Allied Healthcare with data that will further support the use of this product through publication.

The Cardiocel sheets, which are 4cm by 4cm in size, will sell for $1500 each although there may be the ability to increase pricing as the product gains wider acceptance. Allied Healthcare has been stockpiling the product at its facility in Perth. Sales to Europe are expected to start in Q4 of this year. The company will also seek to gain approval in Australia and then in the US in 2014.

Chief Operating Officer Julian Chick says that a trend emerging over the last two years towards repairing heart valves rather than replacing the valves will work in Allied's favour. The market for valve repair is three to four times larger than that for correcting heart defects in children. In the US each year there are 785,000 cardiac interventions with a good proportion of those linked to heart valve issues said Chick.

Allied will initially focus on selling the product into eight to10 leading centres in Europe. It has one person based in Germany and one in the UK at this stage. Allied has been holding Key Opinion Leader meetings since October last year.

Allied Healthcare is capitalised at $98.5 million.

Bioshares recommendation: **Sell**

Bioshares

Biotech Short Positions

There are five biotech stocks that have considerable short positions against their stock (as of 21 August 2013). Taking a short position in a stock means that you sell the stock first (having borrowed that stock from the owner for a fee) and that you are expecting or hoping that the share price will fall, at which point you will close out your position and buy the stock.

The five stocks are Cochlear, Starpharma Holdings, Acrux, Mesoblast and Pharmaxis. How have these short positions changed over the last 12 months? To answer this question, we have tracked the short positions of these stocks and put the data into the chart below.

The stock most heavily shorted in the sector, as a percentage of its total shares on issue, is Cochlear, with 10.35% of its shares being short sold. This had increased considerably from 1 July when 7.3% of its stock was short sold.

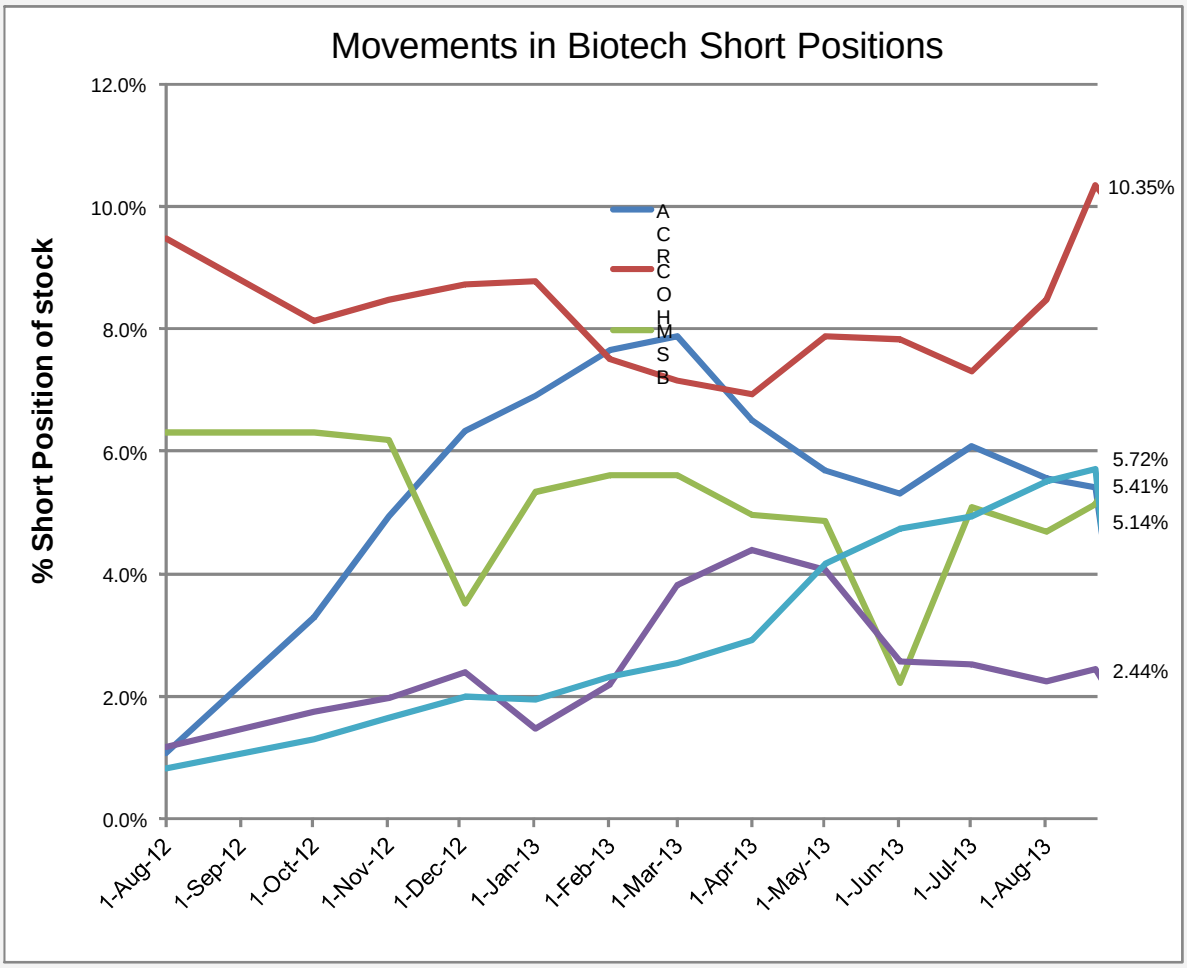
Three stocks have around 5% of their shares being shorted. These are Starpharma (5.72%), Acrux (5.41%) and Mesoblast (5.14%). It's been a tug of war between Mesoblast and the short sellers. A year ago, over 6% of the stock was in short positions, falling to 3.5% at the end of last year, then falling to 2.2% in June this year, and now back just over 5%. That equates to $89 million in short positions currently.

Starpharma stock has seen short positions increase from 2% at the end of last year to now 5.72%. And Acrux short positions peaked in March at close to 8% and have since been falling towards 5%. That peak in short positions coincided with the peak share price for the year of around $4.00.

Short positions in Pharmaxis were increasing up until April, peaking at around 4.4% when the company announced the Phase III bronchiectasis results that did not meet expectations. Its short positions have since been in decline, steadying at around 2.5% over the last two months.

Other biotech/healthcare stocks for which there are short positions outstanding but represent less than 1% of issued stock are Allied Healthcare Group, CSL, Genetic Technologies, Novogen, Prima Biomed, QRxPharma, ResMed, Sigma Pharmaceuticals, Sirtex Medical and Virtus Health.

Short positions can be monitored at the following site: http://www.asic.gov.au/asic/asic.nsf/byheadline/Short+position+reports+table



Bioshares Model Portfolio (30 August 2013)

Company	Price (current)	Price added to portfolio	Date added
Invion	$0.077	$0.060	August 13
IDT Australia	$0.370	$0.260	August 13
Viralytics	$0.340	$0.300	August 13
Circadian Technologies	$0.270	$0.270	March 2013
Tissue Therapies	$0.360	$0.255	March 2013
Benitec Biopharma	$0.300	$0.40	November 2012
Somnomed	$1.23	$0.94	January 2011
Cogstate	$0.480	$0.13	November 2007
Universal Biosensors	$0.68	$1.23	June 2007

Portfolio Changes – 30 August 2013

IN:
No changes.

OUT:
No changes.

Phosphagenics Update

Phosphagenics (POH: 8.5 cents) is pursuing a number of parties whom it has alleged defrauded the company of $5.7 million, including former CEO Esra Ogru.

In speaking to *Bioshares*, Phosphagenics' now sole CEO Harry Rosen said the company has not gone to the police, in order to press charges, because it has wanted to focus on recovering the lost funds.

The company has been in dialogue with ASIC about the fraud matter.

Rosen agreed that a comprehensive review of the company's operations over the last eight years should be performed.

While Rosen agreed that some board changes should take place, he did not agree that the entire board should be replaced, rather that some continuity should be kept.

Comment

Phosphagenics faces serious governance and management issues which can only be properly addressed by the installation of a board that has no association with the events that have taken place.

Why charges have not been laid is a matter that shareholders may well wish to see better explained. Other instances of corporate malfeasance at Australian biotechs, such as the theft of $5.5 million at Agenix, saw that company's CEO Neil Leggett prosecuted and jailed for nine years.

Bioshares recommendation: **Sell**

How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A

These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B

These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C

These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion, Circadian Technologies

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