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In this edition...
The first biotech IPO of the year will occur next month, and it's another US company listing here. Osprey Medical will list at 40 cents a share, raising $20 million in a fully underwritten offer. The pricing looks much more favourable for investors than previous US listings here and may do well.
Mesoblast is at full charge this year, with two very important studies about to commence and results due this year from two Phase II orthopaedic studies. And Phylogica has now signed four big pharma screening deals and is working on delivering two more by mid year.
The Editors
Companies Covered: IPO Preview – Osprey Medical, MSB, PYC

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - May '10)	49.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 now commenced	-23.1%
Cumulative Gain	**224%**
Av. annual gain (10 yrs)	**21.2%**

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IPO Profile - Osprey Medical Inc

Osprey Medical is seeking to raise $20 million through an IPO and listing on the ASX, issuing 50,000,000 Chess Depository Interests at 40 cents each. The ratio of CDI's to shares is 2:1. The indicative capitalisation of the company based on the offer price is $40.4 million. The IPO is underwritten by Shaw Corporate Finance.

History

Osprey Medical Inc was founded in 2007 as a spin out from the Baker Medical Research Institute, now the Baker IDI Heart and Diabetes Institute, in Melbourne. The inventor of Osprey's technology, Dr David Kaye, serves on Osprey's Medical Advisory board. He is the head of the Cardiology and Therapeutics Division of the Baker IDI. The Baker IDI holds an equity stake in Osprey.

The CINCOR System

Osprey Medical is commercialising a technology, termed the CINCOR system, which reduces the quantity of dye (contrast media) used in angiography, a routine cardiovascular imaging procedure that aids angioplasty and stenting procedures. The dye is used to aid the insertion of catheters. The problem with dyes is that they can cause kidney damage in a segment of at-risk patients. The current standard approach to reduce damage is hydration therapy. Hydration therapy requires the IV administration of fluids pre- and post-surgery and is only marginally effective.

A drawback with dyes is that it has proven to be difficult to make less toxic dyes and to use less dye, as reduced quantities of dye degrade the performance of the imaging process.

However, the main issue with the use of contrast media is that an estimated 25% of patients fall into an at-risk group who are likely to suffer kidney damage because they have chronic kidney disease. Patients who acquire contrast induced nephropathy (CIN) following a heart procedure have a 22% chance of dying in hospital, according to a study by Rihal in the journal *Circulation (2002).*

Osprey Medical describes the market opportunity for its CINCOR system based on at least 3.5 million angioplasty or stenting procedures occurring globally each year, with 2.2 million in the US and Western Europe. Osprey estimates that 400,000 of those patients are at risk of CIN because of pre-existing kidney disease.

How the CINCOR System Works

Prior to a cardiologist commencing a heart procedure, a CINCOR catheter is directed through the femoral vein to the heart and into the coronary sinus. A balloon is inflated that partially blocks blood flow, allowing a vacuum component of the catheter to remove contrast media that has been injected for imaging. A foot pedal is used to activate and deactivate the balloon and vacuum mechanisms according to the rate of injections of dye

Cont'd over

by the cardiologist. The method does not capture all contrast media but works to greatly reduce its circulation, especially through the kidneys.

US Business Location

Although Osprey Medical's technology has Australian origins, a US entity was established to hold the company's IP and to fulfil the commercialisation of the technology. Early on a decision was made to base Osprey in the heart of the US medical devices industry, in the St Paul-Minneapolis region of the US. The 'Twin Cities' are home to 3M, Medtronic, St Jude, Boston Scientific and a total of 600 medical device and related companies. More than 27,000 people are employed in medical device manufacturing in the area, more than double the next biggest area in the US of Chicago-Napierville-Joliet which has 12,500 people.

The rationale for locating the business in the Twin Cities area has to been to take advantage of specific manufacturing and medical device development skill sets.

Capital and Application of Funds/Technology Improvements

Since Osprey was founded lead investors CM Capital and Brandon Capital have invested US$19.9 million in Osprey Medical. As of October 2011, Osprey had spent US$6.9 million on R&D activities.

With the $20 million the company is seeking to raise, $8.4 million is allocated to clinical trial and regulatory activities, $4.2 million to CINCOR platform development, $2.5 million to sales and marketing, $2.3 million to quality and operations expense, $1.3 million towards working capital requirements and $1.3 million towards the cost of the offer.

Technology improvements include development of a syringe (Smart Syringe) that is designed to replace the foot pedal operation of the current system by detecting dye and automatically activating removal.

Existing Shareholders

Current significant shareholders of Osprey include CM Capital (33%), Brandon Capital (14.5%), the Medical Research Commercialisation Fund (8.6%) and the Baker IDI (2.2%).

Regulatory Strategy

Osprey has already received CE mark approval for CINCOR. The approval was based on a 41 patient trial in which access to the heart was achieved through the jugular vein in the neck. A more recent study confirmed the viability of the procedure via the femoral vein. The study achieved a 50% reduction in CIN, with no serious adverse events reported.

The company will follow a 510(k) approval pathway in the US, which should see a decision made 90 days following submission.

In support of its US regulatory application, Osprey will conduct a 600 patient pivotal trial, recruiting subjects with Stage 3-5 kidney disease undergoing stenting or angioplasty, across 30 sites. The trial will randomise patients on a 2:1 basis. The trial will evaluate safety and aim to demonstrate efficacy on the basis of the reduction in serum creatinine levels (marker of kidney function) 24 hours and 96 hours post surgery. Ultimately, the company would hope to demonstrate a 50% reduction in CIN, as achieved in its pilot trial.

Commercial Strategy

Osprey intends to launch CINCOR in Europe this year, employing two sales staff in Germany and the Netherlands, but will also use a distributor to support European product sales. The European launch has been described as a 'controlled commercial launch', reflecting the company's desire to engage key opinion leaders with whom they can develop 'centres of excellence'. In this phase of commercialisation, the company expects that improvements and refinements will be made to the way in which the CINCOR system is used by cardiologists, before it is launched into other territories.

Osprey is also initiating a 45 patient post-approval study in Europe in order to build medical awareness through the involvement of key opinion leaders and the eventual publication of study results. This is an important activity for the company, given that publications are vital marketing tools for all drug and device companies.

Once US marketing clearance has been obtained, Osprey intends to recruit a sales force of 20-25 personnel to cover the majority of the US market. Osprey believes management of a US sales force is viable because many of the patients within the company's target market are funnelled to the larger hospital systems in the US.

Pricing and Reimbursement

In the US, Osprey will be able to take advantage of an existing billing code for use of CINCOR. However, it will also initiate a separate process with the CMS, the largest public health insurer in the US, to obtain a speciality code. Osprey intends to undertake economic modelling to support this application.

The company argues that an incentive exists for hospitals to adopt the CINCOR system because CIN is categorised as a hospital related event, which means hospitals must cover the costs of hospitalisation. Therefore, any measures that can clearly reduce CIN hospitalisation costs are likely to be examined with interest.

Business Risks

Osprey Medical faces several risks in taking the CINCOR system into a commercial setting, with several of these identified by the company itself. Amongst these is the well known problem of adoption, which has clinical practise, work flow and equipment integration and payment considerations attached to it.

For commercial success to take place, contrast induced nephropathy as a clinical problem must be more widely understood, especially amongst high risk groups. It is possible that the CINCOR system will elevate the status of the problem because it offers a solution to a previously intractable problem.

Assuming it achieves the necessary recognition, the integration of CINCOR into the cardiologists workflow and equipment set

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must take place. The risk that unforeseen workflow integration factors will inhibit CINCOR's adoption remain until is it used by a broader mass of cardiologists, not simply the highly expert and very skilled pioneering key opinion leaders.

Investment Considerations

For investors, one risk to bear in mind stems from ongoing capital requirements. There is a pattern in the medical devices sector for small companies to be acquired by large companies. There is a tendency for small companies to rely on an acquisition as 'the end game', which can see companies ignore the true capital requirements of the business. Acquisitions which see a company 'flipped' cannot be guaranteed, and one could argue not even be implied. A company's commercial plans should be built on the basis of an independent future even if certain components rely on obtaining manufacturing, distribution and marketing partners. However, Osprey has articulated a commercial strategy that is based on generating investment returns managing, for the most part, direct sales of CINCOR.

A second issue for investors is that the timetable of key commercialisation events is spread out with one major key valuation inflection point, the US launch of CINCOR, not expected to be achieved until 2014, following the completion of the 600 patient trial and the receipt of an FDA approval. Although there are significant milestones to monitor, more meaningful sales data may not appear for several years post launch in the US. Sales in the US will also hinge on payment and reimbursement actions, which can take many months to secure.

Information on European pricing and reimbursement, expected to flow through in 2012, will be important for investors both from a timing point of view and a factual point of view. Pricing and payment with European territories has come under increasing stress as economic pressures have worsened over the last few years.

The Osprey Medical IPO offering of shares is inherently speculative given the stage of the company's corporate life. However, there are several features of the offering that have strong appeal.

The company has a singular and clear focus on developing its CINCOR system, reducing the problems of distraction that multiple product and platform technology companies face. The company's CEO, Mike McCormick, is highly experienced in the medical devices industry, previously being President of Centerpulse Spine Tech and CEO and President of Anulex Technologies.

One positive feature of the CINCOR system is that efficacy can be demonstrated using a simple blood test for creatinine levels, within hours of surgery taking place. The use of unambiguous, easily collected, simple data should benefit Osprey's passage in both the regulatory and commercial arenas.

The pricing of the offering looks appealing, with the pre-money valuation similar to the level of investment that has previously been made into the company.

Another positive aspect is that the Osprey technology solves a problem in a contemporary industrial setting. It is not a disruptive technology. It is an improvement to a process which should increase the chances of wider adoption. However, the ultimate attraction of the CINCOR system is that it is fundamentally a system designed to make other medical interventions safer. Safety is often the primary consideration of regulatory authorities. In the case of Osprey's CINCOR its efficacy goal is in fact a safety goal.

Key Dates
Offer Opens - March 8, 2012
Offer Closes – April 2, 2012
CDIs Trade – April 16, 2012

A copy of the prospectus can be downloaded from http://www.ospreymed.com/pdf/OSP_Prospectus.pdf Investors are required to read the prospectus prior to subscribing to the offer.

Bioshares

Mesoblast Update – Forthcoming Type 2 Diabetes Trial a Major Driver

Mesoblast (MSB: $7.29) provided investors with a half year result briefing. What has been attracting the most attention for the company is the potential to use the company's stem cell technology for the treatment of congestive heart failure, following positive Phase II trial results and the major license deal, largely on the back of this progress.

An emerging focus for the company however is the potential use of the technology as an intravenous therapy for a range of disorders, the most significant being Type 2 diabetes. The briefing looked at the preclinical results which appear to strongly support clinical evaluation in this area.

Type 2 Diabetes Application

Adult stem cells when delivered in to the body are able to restore normal tissue and physiological function. Whilst the method of action remains somewhat unclear, Mesoblast believes its adult stem cells can be used to restore normal pancreas function, both the sensing of high glucose levels in the blood and also restoring insulin secretion function.

In mice studies where the islet cell population had been purposely damaged, the introduction of adult stem cells was shown to increase islet density and increase insulin levels after three weeks. The results were statistically significant against a control.

There is no good large animal model for Type 2 diabetes. However there is an appropriate model in non-human primates, in obese cynomolgous monkeys. In just a single IV injection of stem cells, there was a dose-dependent reduction in glucose levels which was sustained for six months. The trial involved 17 monkeys. The higher doses all delivered a statistically significant result. There was also a statistically significant reduction in C-reactive protein (CRP) levels at all but the lowest dose. CRP is a measure of inflam-

Cont'd over

– *Mesoblast cont'd*

mation in the body and high levels indicate patients with Type 2 diabetes are in a high risk heart attack group.

Single IV Dose Phase II Diabetes Trial

It is these results which gives the company confidence to launch a Phase II trial in Type 2 diabetes. This trial will be similar in numbers to its recent Phase II heart failure trial, enrolling 60 subjects with early Type II diabetes, 15 in the control group and 15 in each of the ascending dose groups of the active arms. Patients will be followed for three months and it will involve just the one IV injection of the stem cells. It will be a very interesting trial, and one that should deliver some clear outcomes.

The potential market for Mesoblast is very large, with an estimated 25 million people in the US having Type II diabetes. However, the opportunity does not lie in diabetes alone. A safe and effective IV stem cell product could also help restore normal body function in other diseases, including rheumatoid arthritis, asthma, and even in stroke and multiple sclerosis.

Interim results from the trial are expected this year. The rights to the stem cells for use in the treatment of diabetes and other anti-inflammatory disorders are outside of the Cephalon (Teva Pharmaceutical Industries) deal.

Other Milestones

Mesoblast has $241 million available for the simultaneous development of multiple products said CEO Silviu Itescu. The company is ensuring there is product delineation that allows pricing differentiation. By controlling the manufacture, the company is in a position to 'slice and dice' the many potentially commercial applications of the technology.

Three other major milestones this year are the commencement of the Phase III congestive heart failure trial, and also results from the company's Phase II trials in spinal fusion and disc repair.

The application for the therapy in expansion of cells in bone marrow transplant is continuing however the importance of this application is dwarfed by the potential in cardiovascular disease and diabetes.

Baxter Enters The Stem Cell Arena

Baxter, a global blood products company whose main rival is CSL, announced in late February that it was commencing a 450 patient Phase III trial of an autologous stem cell therapy for treating chronic myocardial ischemia. While the choice of autologous cells is diametrically opposite to the more commercially viable single donor (allogenic) approach taken by Mesoblast, that Baxter is willingly to evaluate a stem cell approach in heart disease is one of the first forms of endorsement to come from a large biopharmaceutical firm. It sends an important validating signal of Mesoblast's approach at a broader level.

Mesoblast is capitalised at $2.1 billion.

Bioshares recommendation: **Speculative Buy Class A**

Phylogica Update

Phylogica's (PYC: 5.0 cents) share price should see some recovery in the weeks ahead. One of its major shareholders has sold out of the stock on market this year which has placed a lot of downward pressure on the share price. The company held an investor briefing this week, stating that after completing four discovery deals with major pharmaceutical companies, it was seeking to complete another two this financial year.

The company briefing was very well attended indicating strong interest in this biotech. The main reason for that is that since December 2009, the company has signed drug discovery deals with Roche, Astrazeneca (MedImmune), Pfizer and then most recently with Johnson and Johnson. These companies make up four of the world's top 10 pharmaceutical companies. And according to the company, the deals are getting bigger and bigger.

Johnson and Johnson Deal

The first deal signed with Roche was the least commercial, with no up front fee. It was an option deal worth only $400,000 to the company. Its latest deal signed with Johnson and Johnson, signed on 31 December last year, has already brought in US$1.2 million with a further 18 months of research payments. It is the largest deal the company has completed to date.

The J&J deal is looking at using Phylogica's peptides (called Phylomers) to deliver between five to 15 drugs into specific cell types. Cell delivery was the basis of the Roche deal and this aspect of the drug properties of its Phylomer libraries is obviously generating healthy interest from major drug developers.

The company said that so far it has delivered each time with its partnerships. Its deal with Astrazeneca is based on developing a new antibiotic against Pseudomonas aeruginosa infection which the company says it is close to successfully completing. Under that deal, the company has received $2 million from its $100 million deal. If one of its peptides gets to market, the company will receive a total of $100 million.

The types of deals the company is now signing are structured as follows. They generally involve around a $2 million fee to conduct the screening work for a particular target, which can take 12-18 months. If the company decides to license a peptide or peptides, there is around a $2 million sign-on fee, then there are milestone payments of up to $150 million which the company will receive if any compounds make it to market. This can include around $10 million when a Phase II trial commences and around $20 million at the start of a Phase III trial. The company will also receive somewhere between 3%-5% royalties from any future sales of products.

Revenue Growth

Two years ago the company introduced a new business model, whereby it would seek to generate early stage revenue with a view to build a profitable business in the medium term, rather than long term, which is more traditional for biotech companies. In financial year 2010, the company had $433,000 of revenue. In 2011 it gener-

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Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.87	$1.66	October 2011
Mayne Pharma Group	$0.285	$0.435	September 2011
Acrux	$3.78	$3.37	June 2011
Bioniche	$0.65	$1.35	March 2011
Somnomed	$0.90	$0.94	January 2011
Phylogica	$0.050	$0.053	September 2010
Biota Holdings	$0.80	$1.09	May 2010
Tissue Therapies	$0.36	$0.21	January 2010
Atcor Medical	$0.08	$0.10	October 2008
Impedimed	$0.50	$0.70	August 2008
Bionomics	$0.50	$0.42	December 2007
Cogstate	$0.26	$0.13	November 2007
Sirtex Medical	$4.99	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.73	$6.60	September 2007
Pharmaxis	$1.06	$3.15	August 2007
Universal Biosensors	$0.75	$1.23	June 2007
Alchemia	$0.425	$0.67	May 2004

Portfolio Changes – 9 March 2011

IN:
No changes

OUT:
No changes

– *Phylogica cont'd*

ated $2.2 million in revenue. This year it is aiming for $4-$6 million in revenue, and then to double that in 2012.

If the partners from the four deals signed to date elect to license any compounds, a reasonable license fee in the order of $2 million will eventuate. Its first three partnerships are all now being evaluated for a potential license.

As interest builds in the Phylogica discovery platform, equity positions in the company from big pharmaceutical venture funds may also eventuate.

Phylogica is capitalised at $22 million. It had $3.9 million in cash at the end of last year.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

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

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