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In this edition...
First a negative opinion (in June), now a positive opinion from the European CHMP for Pharmaxis' Bronchitol. The caveat is that Bronchitol was recommended only for cystic fibrosis patients over the age of 18 and that the company must conduct a trial in 6-17 year olds. Mesoblast executive Graeme Kaufman reminded investors this week that mitigating execution risk by being sufficiently funded to get to market is a key to success. Elsewhere in the capital raising arena was Phosphagenics, which scaled back a $24 million placement in the face of very strond demand. QRxPharma is confident of signing a licensing partner before year's end, which should also de-risk that company's position further.
The Editors
Companies Covered: MSB, POH, PXS, 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)	70.0%
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	-27.0%
Cumulative Gain	**208%**
Av. annual gain (10 yrs)	**21.2%**

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Bioshares

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Edition 430

Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies.

Monday October 24 – Pharmaxis 9AM Conference Call Update

Pharmaxis – Bronchitol Success in Europe!

On Friday Pharmaxis received a positive recommendation from the Committee for Medicinal Products for Human Use in Europe for its cystic fibrosis drug Bronchitol. It is now highly likely the drug will be approved for use in Europe in January 2012.

There were two parts to the likely label that Pharmaxis will receive. The company will initially only be able to market the drug for use in people over the age of 18. This represents around two thirds of the target market. There are approximately 40,000 people living in Europe with CF.

The second part of the label is that it can be used as an add-on therapy to the best standard of care. CEO Alan Robertson said he was delighted to have this part of the label claim accepted

To market the drug for use in children (those between 6-17 years of age), Pharmaxis will be required to conduct a supplementary smaller study. Although the details of this study need to be determined with the European regulator, Robertson believed the likely cost will be less than $2 million, and the treatment period is not expected to be as long as the pivotal studies, potentially treatment for only one to two months rather than the six months treatment period in the major studies. Roberson said the company has substantial information on the way the drug works in children already.

Sales of Bronchitol are expected to begin at the end of March 2012 in Germany and the UK, where reimbursement is already available. In the other 25 member countries of the European Union, the company will need to arrange for reimbursement, which may take up to January 2013.

The next regulatory focus is on the US, where the company expects to file its NDA for Bronchitol in the first quarter of 2012. A decision then could be expected from the FDA in the first half of 2013. Robertson said two thirds of the material that will go into the NDA, toxicology data and CMC details, have already been assessed and cleared by the FDA through the approval of Aridol, which is the same active material. The regulatory process in the US may turn out to be less complicated than for Europe in our view.

We expect that significant sales of Bronchitol in Europe will not take effect to around mid 2013, which means the company has around a 20 month period for which it will need to fund operations. Pharmaxis said the company has a number of different options to fund growth. No doubt this will depend on the strength of the Pharmaxis share price in coming months.

With respect to pricing, Pharmaxis' COO Gary Phillips said pricing studies revealed that Bronchitol could be the priced up to the price of Pulmozyme, of US$12,000, with out decreasing demand. However the company has the option to select a lower price which

Cont'd over

QRxPharma Confident of Licensing Deal

QRxPharma (QRX:$1.45) is very confident that it can transact a deal to license out its lead program, MoxDuo IR, by year end. MoxDuo is a combination of two opioids, oxycodone and morphine. In August this year the company filed its completed NDA (new drug application) with the FDA. The FDA seeks give a final response at around 10 months for new drug applications (for generics the wait is around three years), which means QRxPharmna should get a final decision around the end of June next year.

By around 7 November, the FDA will respond to QRxPharma with any possible deficiencies that may be in its NDA or will indicate that the NDA application is in correct order and is assessable.

Possible deal terms

Our expectation is that the first license will be to a partner to market MoxDuo IR into the USA. An up-front payment could be expected, with then likely a larger milestone payment on approval from the FDA (similar to the Acrux-Eli Lilly deal), with further milestone payments and royalties from sales. An upfront payment of around $10-$20 million would be a good result for QRxPharma, depending on the way the deal is structured. QRxPharma at this stage expects to maintain manufacturing control.

Good Timing for QRxPharma

There are two changes to the way pain medicines are prescribed that will benefit QRxPharma. The first was the limit that the FDA placed on combining paracetamol with other pain drugs such as oxycodone (Percocet) and hydrocodone (Vicodin), restricting the amount of paracetamol that can be added to each tablet to 325mg, and the risk of overuse of paracetamol that can result in liver failure. Overdoses of paracetamol in combination with other drugs causes almost half of paracetamol related liver failure in the US, with many resulting in the need for a liver transplant or death. This acknowledgement of the dangers of using too much paracetamol should benefit QRxPharma's MoxDuo combination, which does not include paracetamol. This FDA restriction will be phased in over three years from January 2011.

The second change is one that is in process, and this is changes to the way the pain drug Vicodin (a combination of hydrocodone and paracetamol) is prescribed. There are 130 million prescriptions for Vicodin written each year in the US and it is currently a Schedule 3 drug. There is a Bill being proposed to Congress in the US to make this a Schedule 2 drug, which is more restrictive and would see it prescribed in the same manner as MoxDuo, which would also be Schedule 2 drug. This would even up the playing field for QRxPharma's MoxDuo. Changes to the way Vicodin is prescribed are expected to occur in the next 12 months.

Payors the Real Deciders

For QRxPharma, who it really needs to sell the benefits of MoxDuo to are the payors. MoxDuo IR reduces the side effects of taking morphine or oxycodone alone, which means patients can be discharged from hospital sooner. An additional $30,000 is spent in the US each year on each patient taking opioid drugs just to manage the opioid side effects, according to QRxPharma. So the cost savings of using MoxDuo will be one of the key selling points.

Licensing deal by end of 2011

QRxPharma CFO Chris Campbaell said the company is committed to delivering a licensing deal with discussions continuing on a number of fronts. The company has indicated that it is targeting the end of this year to complete a licensing deal, and if all goes well, anticipates MoxDuo being on the market in 2012.

Market Size and the Impact of Vicodin Rescheduling

QRxPharma is developing three different versions of MoxDuo. The lead is an immediate release version (IR), followed by a continued release pain therapy (CR) and an intravenous form (IV).

The IR product has the largest market application. Targeting just 50% of the market and assuming a 5% market share can be obtained, that translates to peak sales of $680 million a year. This assumes a sales price of $112 for two weeks of therapy. However, this has the potential to reach $2 billion of annual sales once the paracetamol restrictions are mandatory and Vicodin prescriptions are re-scheduled.

For the CR version, the company believes peak sales of $1.3 billion are achievable at 13.9% market share, and for the IV application, peak sales of $150 million are possible at a 13% market penetration. The IV version is currently at Phase II stage and the CR version at Phase I.

Summary

Clinical trials with MoxDuo have involved over 1600 people. The company has raised just under $150 million to get it this stage, with $32.4 million in cash at June 30, including its subsequent capital raising. It is now capitalised at $209 million.

The company is moving towards a number of value inflection points. It is confident of securing a licensing deal by the end of the year and has positioned its lead program well to start generating a return from the investment in its MoxDuo assets.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

– Pharmaxis cont'd

would increase penetration rates and help build early cash flow from the product.

In Europe the company receives a 10 year marketing exclusivity, and this may be increased to 11 years if a paediatric study is conducted, which is one positive benefit from conducting the additional paediatric study required by CHMP.

So far 2012 has been a very challenging year for the company. However Pharmaxis' position to commercialise its assets, not just Bronchitol in CF, has improved significantly. The company had $33.7 million in cash at the end of September.

Bioshares recommendation: **Speculative Accumulate Class A**

Bioshares

Phosphagenics Closes Heavily Oversubscribed Capital Raising

Phosphagenics (POH: $0.16) completed a $24 million placement this week, its largest and most significant capital raising since the company was founded in 1999 (as Tocovite). The capital raising was heavily oversubscribed. A $3 million share purchase plan was announced alongside the news of the placement.

The funds have been raised to support the later stage development of the company's TPM-Oxycodone patch, a pain relief drug, with a small proportion devoted to marketing activities for the Phosphagenics range of cosmetics products.

The raising is significant because the number of institutional investors in Phosphagenics has increased from two to 27. Phosphagenics' largest shareholder, Orbis Group, increased its stake in the firm from 14.6% to 16.1% with a $5.7 million follow-on investment in this round. A Singaporean investor made the single largest investment ($7 million).

The capital raising was priced at 14 cents, a 10% discount to the 30-day VWAP. It follows a $7.5 million private placement completed in March this year at 9 cents and an $7 million underwritten SPP completed in October 2009 at 9.2 cents.

Why Did the Capital Raising Receive Such Solid Support?

The key to understanding Phosphagenics success in raising $24 million rests on the fact that funds are primarily being directed towards a product opportunity where no current product exists (trans-dermal oxycodone) and where the time needed to complete registration studies is within a three year time frame. It also rests, quite crucially, on the fact that manufacturing scale-up and optimisation of the patch has been reached with Phosphagenic's manufacturing partner, 3M, which improved the performance of the patch by 500%.

A further point is that the registration pathway, at least through the US, is under the 505(b)2 avenue, which means that drug sponsor does not need to reproduce expensive toxicology and safety studies, with the main requirement to simply to demonstrate bioequivalence (levels in the blood) to the reference molecule.

Looking more widely, the success of Acrux's Axiron would have provided an investment road map for Phosphagenics. In July 2007, Acrux raised $22.5 million to fund the Phase III development of its transdermal testosterone product, Axiron. Acrux successfully completed this trial program in 2009, and filed an NDA with the FDA in January 2010. Acrux signed a global licensing deal with Eli Lilly in March 2010 and FDA approval followed in November 2010. Under the licensing agreement, Acrux has so far received more than $140 million and has returned $100 million in dividends. In June 2007, Acrux was capitalised at $219 million. Today Acrux is capitalised at $556 million.

TPM-Oxycodone Development Plan

Phosphagenics has evaluated a number of drugs that could be improved using its alpha-tocopherol technology. These include systemically delivered insulin, morphine and oxydocone, and localised topical delivery of lidocaine, diclofenac and tretinoin. Several of these product opportunities have been targeted for outlicensing by Phosphagenics.

TPM-Oxycdodone has advanced to the Phosphagenics lead internal human health program for several reasons. Firstly, there is no transdermally available oxycodone on the market. Duragesic is a patch developed by Johnson & Johnson, which delivers fentanyl across the skin. Although fentanyl is a much more potent opioid than morphine (100 times more) and oxycodone (roughly twice as potent as morphine), the patch has been a target of illicit abuse and associated with deaths from respiratory depression.

Phosphagenics intends to complete a Phase II/III PK profiling study in 80 healthy male volunteers of its now optimised TPM-Oxycodone patch in 2012 and then to commence a registration study towards the end of that year. A regulatory submission would follow in 2013 with an approval expected to follow in 2014.

The patch is now being designed for a two-to-three day application rather than for a seven day period. This usage re-configuration is based on physician feedback from market surveys, in which it was found that physicians prefer to attend to patients every 2-3 days.

Among potential indications, Phosphagenics is considering use of the TPM-Oxycodone patch in the field of cancer pain therapy. In a Phase Ib trial completed in February 2010, the company showed that its patch could potentially address the problem of break through pain. The patch did this by increasing plasma concentrations of oxycodone with daily repeat application over ten days of the matrix version of its patch.

Risk with Opioid Medicines

The greatest risk with the product is whether the FDA (and other agencies) are satisfied with the risk management strategy (REMS) that Phosphagenics (and potential partner/s) will be implementing to deal with compliance failure or potential for abuse of the product by patients and other persons.

Summary

Phosphagenics has now transformed its register, which has been biased towards founders and retail investors. With the company's recent placement program scaled back considerably we anticipate that demand for Phosphagenic stock to remain firm and liquidity to improve. Apart from clinical progress of TPM-Oxycodone, what can be also be expected to draw investors to the stock is progress the company makes in generating sales of it cosmetics products, which have generated sales of $2 million since the launch of the Elixia skin care products in April.

Phosphagenics is capitalised at $160 million (on completion of the placement).

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Life Science Investment Summit Report

The third Australasian Life Science Investment Summit (ALSIS) was held in Adelaide this week, running in parallel with the final day of **Ausbiotech 2011**, the annual conference organised by Ausbiotech.

ALSIS is a genuine Australasian affair, including not only New Zealand companies, but for the first time a wound and bone healing company, CIMTECH, that is aiming to develop natural products from the Cook Islands.

ASX listed companies which presented included Acrux, Alchemia, Benitec, Bionomics, Biotron, Calzada, Cellmid, Genetic Technologies, Mayne Pharma, Nanosonics, Neuren Pharmaceuticals, Phosphagenics, Phylogica, Prana Biotechnology, QRxPharma, and Sunshine Heart.

Other private companies that presented were Atomic Diagnostics, Minomic International, Biosceptre International, Broadvector, Elastagen, EnGeneic, Global Kinetics Corporation, GlycoSyn IRL, Hunter Immunology, Innate Therapeutics, Lipotek, Meat and Livestock Australia, Mesynthes, Nemgenix, Neural Diagnostics Orthocell, Photonz and PolyActiva.

A Surprise ! – 'Allara Therapeutics'

Although 37 companies were scheduled to present in tight six-minute slots, the surprise of the day was the 38th, which was the last minute inclusion of Allara Therapeutics, a company still being formed. Allara is seeking to raise $30 million to fund the development of a suite of drugs no longer deemed relevant to the **Teva Pharmaceutical Industries** portfolio following its recently approved acquisition of **Cephalon**. In fact, some of these assets were previously in the hands of **Arana Therapeutics**, which was acquired by Cephalon in 2009. Stefan Nock, currently General Manager of Cephalon Biologics, and formerly Acting CEO of Arana Therapeutics, said the proposition could be described as a "Series A investment in a Series C company".

Allara is being structured as trans-Pacific antibody drug development company, locating product development in Sydney and business development in San Francisco. A key attraction of establishing an Australian entity is the recently passed R&D tax credit legislation, which offers a 45% cash back on R&D expenditures. At this stage, the company is not contemplating an ASX listing.

Allara has packaged four antibodies alongside several other targets. CEP-37250, which is being developed jointly with **KyowaKirin**, is a humanised monoclonal antibody which targets a novel colorectal cancer surface antigen. It has been re-engineered using **BioWa**'s Potelligent technology, which removes fucose sugars to enhance its antibody dependent cellular cytotoxicity. However, what may make it commercially interesting is that it is effective in the presence of both wild-type and KRAS-mutated cancers, filling the gap where Erbitux and Vectibix have no effect. An IND for CEP-37250 was filed in 2011 Q3.

Its next in line antibody is CEP-37248, an anti-IL-12/23 humanized antibody which may have potential in treating Crohn's disease and Primary Biliary Cirrhosis. An IND filing is anticipated for 2012 Q2.

Two programs at the lead or validation stage are an anti-CD1d antibody, with the disease target being steroid-refractory asthma, and an anti-myeloma antibody.

The Allara business model is based on spending $10-$15 million per asset over a three year period and then moving to sell the asset at the clinical proof-of-concept stage. With more and more large pharmaceutical companies moving out of this earlier stage of product development, it may be that Allara represents an exciting opportunity structured by a group of seasoned biotech executives with an impeccable sense of timing.

Hunter Immunology

One company of interest to investors is Hunter Immunology, which is undertaking a backdoor listing through **Probiomics** (ASX:PCC), with the re-listing scheduled to be finalised by 2012 Q1.

Hunter Immunology has been developing HI-1640V, an oral immunotherapeutic for treating Chronic Obstructive Pulmonary Disease (COPD). In a Phase IIa trial, HI-1640V reduced exacerbations or flare-ups by 60%, hospitalisations by 90% and anti-biotic use by 56%. This data is one explanantion of why the company has gained the attention of many pharmaceutical companies, signing confidentiallty agreements with 10.

HI-164OV is an enteric-coated tablet which contains 45 mg of inactivated, whole cells of non-typeable *Haemophilus influenza* (isolate 164). (The cause of most flare ups is *Haemophilus influenza*)

The company enrolled 320 patients in a Phase IIb study across 21 Australian centres before winter. Results of the randomised, double-blind, placebo controlled trial are expected in March or April 2012. The primary endpoint of the trial is the rate of exacerbations that require corticosteroid treatment or hospitalisation.

COPD is medical condition that imposes costs through hospitalisations. An estimated 54,000 people were hospitalised in Australia in 2010 due to COPD exacerbations. It is expected that Hunter Immunology's immunotherapy would be taken each year prior to the onset of winter, thus providing an annuity income from the product. Hunter Immunology is focusing on moderare to severe COPD. About 10% of the overall COPD group, 10 million people, are estimated to suffer from moderare to severe COPD globally.

Once Hunter Immunology successfully lists on the ASX it anticipates that it will raise funds to support clinical studies in asthmatic patients. Hunter Immunology also plans to re-build sales of the Probiomics probiotics products.

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Bioshares Model Portfolio (21 October 2011)

Company	Price (current)	Price added to portfolio	Date added
Mayne Pharma Group	$0.360	$0.435	September 2011
Genetic Technologies	$0.15	$0.18	August 2011
Acrux	$3.34	$3.37	June 2011
Psivida	$4.00	$3.95	May 2011
Bioniche	$0.70	$1.35	March 2011
Somnomed	$1.10	$0.94	January 2011
Phylogica	$0.059	$0.053	September 2010
Biota Holdings	$0.79	$1.09	May 2010
Tissue Therapies	$0.47	$0.21	January 2010
Atcor Medical	$0.07	$0.10	October 2008
Impedimed	$0.50	$0.70	August 2008
Bionomics	$0.42	$0.42	December 2007
Cogstate	$0.17	$0.13	November 2007
Sirtex Medical	$4.60	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.51	$6.60	September 2007
Pharmaxis	$0.94	$3.15	August 2007
Universal Biosensors	$0.86	$1.23	June 2007
Alchemia	$0.29	$0.67	May 2004

Portfolio Changes – 21 October 2011

IN:
No changes.

OUT:
No changes

Mesoblast – Eliminating Execution Risk the Key to Success

Mesoblast (MSB:$9.67) and its partner **Cephalon** (**Teva Pharmaceutical Industries**) were this week awarded the Licensing Executives Society, for the USA and Canada, *The Life Science Deal of Distinction Award* for the licensing deal announced last December for access to Mesoblast's stem cell technology.

That deal included a $130 million upfront payment, a $240 million equity investment in Mesoblast by Cephalon, and potential future milestone payments worth up to $1.7 billion.

That deal was done largely based on results from Mesoblast's Phase II heart failure study in 60 patients. Those stunning results in only 60 patients with heart failure (45 in the control group receiving three different doses of stem cells) and a placebo group (15 patients) delivered statistically significant improvements (80% reduction) in outcomes for patients, as measured by reductions in major cardiac events.

In this patient population, it's expected that 20% of patients will not be alive at two years. In the placebo group this was just the case, with now three patients having died at two years (20%), compared to no cardiac related deaths in the stem cell treated group.

Graeme Kaufman from Mesoblast gave a presentation this week on Mesoblast. Kaufman said the sum market of all stem cell companies in the work was around $1.5 billion, less than that of Mesoblast, which is valued at $2.7 billion. Why many biotechs are valued at only around $50 million is because execution risk is a major risk, that being the ability of the company to raise all the funds it requires to bring its product or products to market.

Kaufman said that the market is implicitly pricing in execution risk. Most companies won't make it because they can't access the funds. For Mesoblast, the deal with Cephalon largely removed that execution risk, with now only technical risk remaining, he said.

Mesoblast intends to keep a healthy bank balance, of between $300 - $400 million, have multiple distribution partners and it has secured a manufacturing partner in Lonza that will build the company's manufacturing facilities. Kaufman said Lonza was a huge validation for Mesoblast. They manufacture for all of Mesoblast's competitors and have an exclusivity arrangement for the whole of Singapore.

About 20% of the company's owners are based in the UK, with one fund owning 11% now. Kaufman said getting the company's register right was crucial, enabling it to raise cash when required.

Mesoblast had cash of $263 million at June 30. While the company has a high valuation, of $2.7 billion, we expect its share price to continue to improve with many positive clinical milestones expected in the next 18 months. In mid November, the full two year Phase II heart failure results are expected to be released, providing more detail on what has been to date a stunning clinical trial.

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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