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In this edition...
It is par for the course for competitive threats to emerge in early on in the drug business. Vertex Pharmaceuticals cystic fibrosis drug combo might appear to be a hot threat to Pharmaxis' Bronchitol but investors can note that Bronchitol has a market potential well beyond CF than has Vertex's gene mutation directed drugs. Somnomed's welcome news is that its next generation sleep apnea product, the smaller G2, has been cleared by the FDA. Universal Biosensors has successfully passed a key feasibility milestone for its second project with Siemens Healthcare Diagnostics. Allied Healthcare is progressing its CardioCel product towards a European CE mark. Phosphagenics is solving a technical hurdle encountered with its transdermal pain drug.
The Editor
Companies Covered: AHZ, POH, PXS, SOM, UBI

	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 - current)	-4.8%
Cumulative Gain	**229%**
Av. annual gain (11 yrs)	**17.8%**

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Bioshares

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

Pharmaxis Produces Like-For-Like CF Data with Vertex Drug Combo

Pharmaxis (PXS: $1.09) is officially launching its Bronchitol product in Europe, coinciding with the European Cystic Fibrosis Meeting taking place in Ireland. At the conference, Pharmaxis presented new analysis on data from its two Phase III trials with Bronchitol for the treatment of cystic fibrosis.

Vertex Pharmaceuticals had recently presented data from a small Phase II trial which was exceptionally well received by investors. That data overnight last month increased the market value of Vertex by $5 billion.

At this conference, Pharmaxis presented some data that allows a more like-for-like comparison of the two treatments. The data is remarkably similar.

On a relative basis (so an increase from say 40% function to 44% function is considered a 10% 'relative' improvement rather than a 4% 'absolute' improvement), 45% of patients taking Bronchitol achieved more than a 5% relative improvement in lung function, compared to 46% in patients taking the combined Vertex therapies. And 29% of patients taking Bronchitol achieved more than a 10% relative improvement, compared to 30% of patients taking the Vertex Therapies. Under this comparison, Bronchitol and the Vertex combination compare very favourably.

Reductions in Exacerbations

In April 2010, before the release of the second Phase III trial data, CEO Alan Robertson said that one important metric of performance would be exacerbations, or more specifically reductions in exacerbations. Exacerbations can be life threatening for people with CF, requiring high dose antibiotic treatment and for some, a two week stay in hospital. Exacerbations can be fatal. Robertson's target back then was to achieve more than a 20% reduction in exacerbations, which would be viewed as very significant by medical practitioners. The first trial showed a 26% reduction in exacerbation rate.

Combined data from the two Phase III studies showed that exacerbation rate was reduced by 29% in the overall population, with a 24% reduction in the adult population (indicating a higher reduction in exacerbations in children). That is very clinical meaningful result.

There are some other factors to consider:

Cont'd over

- The Vertex combination therapy has the appeal that it is a simple tablet taken twice a day. The Pharmaxis Bronchitol treatment requires inhalation of ten powdered capsules, twice daily.

- The Pharmaxis data is based on a 600+ patient Phase III trial, involving adults and children, where the Vertex data is based on a patient population of only 37 adults, in a Phase II study.

- The Bronchitol treatment can potentially be taken by all patients (although 7% show an intolerance to inhaling the powder), where the Vertex therapy only applies to people with CF who have two copies of the F508del mutation, which accounts for 46% of the CF population.

- The Bronchitol data was for a treatment period of six months, and the Vertex therapy only treated patients for 56 days.

Pharmaxis has now started to receive orders for its Bronchitol product in Germany. In a Pharmaxis announcement, Dr Moira Aitken, from the Division of Pulmonary and Critical Care Medicine at the University of Washington Medical Center, made the point that the Phase III study results with Bronchitol suggest it is a very useful drug. She also made the point that the patients in these Phase III studies were heavily treated, with 59% taking Pulmozyme and 56% taking inhaled antibiotics. There was also a high infection rate, with 60% having a bacterial lung infection with Pseudomonas aeruginosa, which is very representative of that seen in patients at CF clinics.

Pharmaxis is capitalised at $334 million with $91 million in cash at the end of March.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bronchitol and VX-809+KALYDECO - A Comparison of Relative Improvement

Company	Product/ Therapy	Patient population	Trial size	Length of study	Percentage patients with more than 5% relative improvement in FeV1	Percentage patients more than 10% relative improvement in FeV1
Pharmaxis	Bronchitol	All CF patients	Over 600 patients	6 months	45%	29%
Vertex Pharm.	VX-809 + KALYDECO	46% of CF patients (have 2 copies of F508del mutation)	37 adult patients	56 days	46%	30%

Universal Biosensors Passes Technical Feasibility Milestone for New Test Strip

Universal Biosensors (UBI: $0.64) has achieved technical feasibility in its second blood coagulation testing project, covering a new test strip which is expected to form the basis of a future product to be commercialised by **Siemens Healthcare Diagnostics**. Last year UBI signed a collaborative deal with Siemens to develop a number of blood coagulation tests.

The lead program with Siemens is a test used for titrating correct warfarin dosage, called the PT-INR test. This program is progressing well with a product launch expected in 2013.

UBI develops tests in four stages. Firstly it comes up with a product idea. It then seeks to show that product idea works (proof-of-concept). It then works to prove technical feasibility, which is what it has now achieved with the second coagulation test with Siemens. Then the programs move into a product development stage, which involves manufacture of the commercial product and testing.

UBI now has its glucose test being sold in most major global markets through Lifescan. And it has two coagulation tests with Siemens that are now in the product development stage. Once at this stage, CEO Paul Wright said the programs have been significantly de-risked.

The proof of technical feasibility is a great step according to Wright, with Siemens now believing it can take the new test strip and its associated reader also to market.

To date UBI has received US$4.5 million in project payments from Siemens, with a US$1.5 million payment due upon reaching this latest milestone. UBI and Siemens are working on an undisclosed number of coagulation tests that they are looking to bring to market.

This second coagulation product has now leap-frogged the C-reactive protein (CRP) diagnostic program, which is still in the technical feasibility stage.

UBI is capitalised at $102 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Phosphagenics Engages Labtec to Solve Patch Problem

Phosphagenics (POH: $0.155) has engaged **Labtec Gmbh** (Langenfeld, Germany) in recent months to develop a new adhesive for its TPM-Oxycodone patch, based on work conducted in-house by Phosphagenics. Oxycodone is an opioid class compound which is used to manage pain.

Labtec has been developing a number of transdermal patch products, having brought a generic fentanyl product to market (partnered with Ratiopharm). Phosphagenics also intends to employ Labtec in addition to 3M as a manufacturer of the patch.

The current version patch has been developed in conjunction with 3M and major advances in optimization of the patch have occurred to date. However, a crystallization problem occurred, which cannot be resolved while the 3M adhesive is used for the patch. Crystallization of active drug means that the drug is retained with the patch material and is not available for delivery as intended.

Phosphagenics alpha-tocopherol improves the delivery of active pharmaceutical ingredients across the skin. However, the design of a transdermal patch product, such as Phosphagenics TPM-Oxycodone patch, is extremely challenging. The developers must design a patch to release a desired quantity of API at a desired rate in a physical format which must be resistant to tampering or efforts by narcotic drug abusers to extract the API. A patch must also be robust enough to tolerate movement, temperature and moisture.

The FDA has approved 14 different patch products since 1984. While patch design varies, a patch might, generally speaking, comprise of a backing layer, which provides structural integrity and address wearability issues, and an adhesive layer which incorporates the API and other ingredients such as solvents and co-solvents.

Phosphagenics is planning to commence a Phase III trial in 2013 Q1. The company expects the current technical program with Labtec to not effect the commencement date of the trial.

While dealing with its technical problem, Phosphagenics is also collecting pharmaceutical market data to assist in the design of its pivotal Phase III trial. For companies such as Phosphagenics developing a drug using the 505(b)2 route, at the simplest level the challenge is merely to demonstrate equivalence with its reference drug. The greater challenge is to design a clinical trial which can demonstrate superior performance, by alleviating pain relief more quickly, or over a longer period with reduced side-effects, in order to deliver clear economic benefits over rival drugs.

Summary

Phosphagenics has encountered another technical challenge in the development of its TPM-Oxycodone product. However, the company is continuously improving its competencies and capabilities as a transdermal drug developer. The market opportunity for a transdermal oxycodone patch that is protected by high technical barriers to entry remains an attractive a goal for the firm and for investors.

Phosphagenics is capitalised at $158 million and held cash of $27 million at December 31, 2011.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

US Approval for Somnomed's Next Generation Product (the Somnodent G2)

Somnomed (SOM:$0.88) has received regulatory clearance in the US to sell its second generation Somnodent device, called the Somnodent G2. The Somnodent devices are oral splints consisting of two mouth guard-type devices that are worn during sleep. The concept is that the top guard prevents bottom guard (jaw) from moving backwards during sleep, helping keep the airways open during sleep.

The devices are effective at treating both obstructive sleep apnea and also snoring. To date the company has sold over 70,000 of the first generation products, and is current selling around 30,000 a year. The devices sell for between $500-$600, although the end user pays an additional $1200 or so to have the device fitted by a Somnomed qualified dentist.

Somnomed is generating sales in the order of $14 million a year while running the business at a cash neutral position. In the first half of this year, Somnomed unit sales increased by 26% over the previous corresponding period, selling 14,443 devices, which translates to an average selling price of $470.

The second generation product is 20% smaller than the first generation product, making the product more comfortable to the user. This is a very important product iteration. The first generation product is effective but is somewhat bulky and comfort has been a product attribute requiring improvement.

The commercial advantages of releasing a second generation product are numerous. The company has sold over 70,000 units to date, and a percentage of these users will look to change over to the smaller and more comfortable next generation product. It may allow the company to increase pricing. It also helps Somnomed maintain its position as the leading global supplier of oral splints for the treatment of sleep related disorders.

There is also upside to come in Somnomed sales from users replacing their existing devices due to wear, with the expected life for these devices being three to five years. As the overall user base expands, there should be a compounding in sales from replacement of existing systems. From this perspective, the business model is very sound.

Somnomed is capitalised at $37 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bioshares Model Portfolio (8June 2012)

Company	Price (current)	Price added to portfolio	Date added
Nanosonics	$0.505	$0.495	June 2012
Osprey Medical	$0.38	$0.40	April 2012
QRxPharma	$1.64	$1.66	October 2011
Mayne Pharma Group	$0.350	$0.435	September 2011
Somnomed	$0.88	$0.94	January 2011
Phylogica	$0.049	$0.053	September 2010
Biota Holdings	$0.74	$1.09	May 2010
Tissue Therapies	$0.48	$0.21	January 2010
Atcor Medical	$0.09	$0.10	October 2008
Bionomics	$0.31	$0.42	December 2007
Cogstate	$0.280	$0.13	November 2007
Sirtex Medical	$6.06	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.72	$6.60	September 2007
Pharmaxis	$1.09	$3.15	August 2007
Universal Biosensors	$0.64	$1.23	June 2007
Alchemia	$0.440	$0.67	May 2004

Portfolio Changes – 8 June 2012

IN:
No changes

OUT:
No changes

Allied's CardioCel Heads for CE Mark

Allied Medical Group's (AHZ: 1.9 cents) regenerative medicine subsidiary Celxcel is moving its CardioCel cardiovascular patch product towards gaining a CE mark, a certification required for use in European territories.

The advantages of Celxcel's tissue treatment technology to current treatment processes include reduced cytotoxicity and reduction to the extent and rate of calcification in the patch. Patches are sourced from bovine pericardium supplied by **Maverick Biosciences** in Dubbo. Maverick supplies animal derived tissue materials to a number of leading medical product companies around the world.

In the first stage towards gaining CE Mark approval, the company will initially be working with the British Standards Institute (a notified body) which will review Celxcel's design dossier. The dossier will then be submitted to the UK's Medicine and Healthcare Regulatory Agency for a formal review process which will take about 12 weeks to complete.

The Cardiocel product may be eventually be used to repair a wide variety of cardiovascular problems including ventricular septal defects, atrial septal defect, atrioventricular septal defect, right ventricular outflow tract repair, aortic root enlargement, outflow tract reconstruction, valvular reconstruction and replacement (heart valves), and for vascular repair in general.

In addition to gaining certifications for cardiovascular repair, the company will also seek to achieve certifications for its tissue patch or repair technology to cover hernia repair and pelvic floor reconstruction (GyneCel).

The pelvic floor reconstruction market is dominated by surgical mesh products, which have recently been placed on notice by the FDA as a modality in need of major improvements to risk management. Celxcel had previously commenced a trial of GyneCel in pelvic floor repair but aborted the trial due to infection problems related to the surgical procedure. However, the application area continues as a key area of focus with the company working with researchers in Belgium to improve surgical and operating procedures and to also initiate animal studies in hernia repair.

Allied also expects to file for US marketing approval for CardioCel later in 2012.

Allied Medical is a diversified medical business, operating a medical devices sales and distribution business and has a 44.4% stake in Coridon, in addition to its regenerative medicine activities.

Allied Medical is capitalised at $15 million. It held cash of $1.6 million at the end of the March quarter, subsequently raising $1.9 million through a rights issue and $0.28 million through shortfall issue.

Bioshares recommendation: **Speculative Buy Class B**

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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