ISSN 1443-850X

In this edition...
Pharmaxis' Bronchitol will face an FDA Review Panel meeting on January 30. Such panels usually host one or two critics; however, the greater threshold for the company is the formal FDA decision scheduled for March.
Change is afoot at Alchemia following the sudden departure of CEO Pete Smith. The company must make some key decisions quickly to maintain investor confidence.
Good news has come the way of Perth-based Resonance Health, whose Ferriscan imaging diagnostic has received FDA approval. It will serve as a companion DX to Novartis' iron chelation drug, Exjade.
On the earnings front, sales receipts are on the up at UBI, flagging at last that income from One Touch Verio test strips is the real deal.
Companies Covered: ACL, ACG, CGS, PXS, RHT, 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)	-13.4%
Cumulative Gain	**199%**
Av. annual gain (11 yrs)	**17.8%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au

David Blake - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph:(03) 9348 9317
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$400 (Inc.GST)
Edition Number 488 (25 January 2013)

Bioshares

25 January 2013
Edition 488

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

Major Crossroads Ahead for Pharmaxis

Pharmaxis (PXS: $1.25) has recorded its second quarter of sales for Bronchitol for the treatment of cystic fibrosis. December sales figures increased to $455,000, up 92% on the previous quarter (or tracking at a rate of $1.8 million a year). It is now more clear that product take-up will be gradual rather than rapid, subject to the rate at which physicians become familiar with the treatment. In the meantime, Pharmaxis has some major events approaching in the next three months, so investors can expect increased volatility in the stock.

US FDA Scientific Advisory Committee Meeting

This coming week (on Wednesday 30 January), the FDA's scientific advisory committee will meet to assess Pharmaxis' new drug application (NDA) for Bronchitol for the treatment of cystic fibrosis in the US. Whilst the panel's decision (vote) will not bind the FDA to its decision on the NDA on March 18, the decision will represent the likely final outcome.

Pharmaxis has found the regulatory assessment paths for its products to be less than straightforward. It's application for Aridol as an asthma diagnostic test took 10 months longer than expected, and approval of Bronchitol in Europe took 18 months longer than expected, with setbacks occurring with regulatory submissions for both products.

Our assessment is that the company should eventually succeed in gaining FDA approval of Bronchitol for the treatment of CF. However, how many passes through the regulator will be required and whether label claims will need to be adjusted (as they were in Europe where it is approved for those aged 18 years and over) are the unknowns.

Why should the drug get approved in the US? The ansswer is that it has shown clear efficacy in improving lung function in people living with CF, including those already taking the CF drug Pulmozyme. What makes the decision less certain is one number from the company's second Phase III trial.

The results from the first Phase III trial in 324 patients were very positive. At six months lung function was improved 6.6%. The all-important p-value (probability that the result was a random outcome), needs to be less that 0.05. In this case it was 0.001. In patients taking Pulmozyme as well, lung function still improved by 5.2%, with a p-value of 0.002, well within requirements. Of the patients evauated, 7% could not tolerate the treatment, which involves inhaling 400mg of powder into the lungs twice a day.

In the second Phase III trial in 318 people with CF, patients experienced an impressive 8.2% improvement in lung function at six months. The only shortfall was that the p-value narrowly missed the less than 0.05 target, being 0.059. This second trial had a higher patient usage of Pulmozyme, 75% compared to 55% in the first trial which would have contributed to the difference in results.

Cont'd over

Status of Bronchitol in Europe

In Europe, Bronchitol is approved for the treatment of people with CF aged 18 and over. This is because the European regulator dissected the data and found less efficacy in younger patients (which is what would be expected in healthier/younger people).

In the UK, the National Institute for Health and Clinical Excellence (NICE) has recommended use for those people who have failed Pulmozyme treatment.

In Germany, the CF physicians are working out for themselves which adults will benefit most from treatment with Bronchitol (presumably those with the most deteriorating lung function and those experiencing frequent lung infections and hospitalisations).

The Role of Specialists

Whichever way regulators want to slice and dice the official approval label, in the end the specialists will ultimately decide how the drug should best be used in practice. Because the specialists are the ones at the coal face, and they will be the ones talking to the patients, monitoring changes in lung function, and monitoring episodes of infection and hospitalisation. And because the specialists have very few tools to treat the underlying disease, an additional tool such as Bronchitol should be made available.

The company could argue (with the FDA) that given that therapy with Bronchitol is safe, that its use will be closely monitored by physicians, and that effectiveness will be easily assessed both by the patient and the specialist on an ongoing basis, then some latitude should be given to the new drug application where the company has marginally missed its primary endpoint in its second Phase III trial.

Briefing documents from the FDA for the advisory panel should be released by Tuesday morning AEST. This document will list any concerns the regulator has about the NDA and what issues it wants the expert panel to assess.

Bronchitol Sales

Currently 96% of Bronchitol sales are made in Germany (67%) and Australia (29%). At a conference call this week, management indicated that in Germany, 10% of the population with CF (presumably adult population) has completed its first initiation test. The company is starting to see a return on its investment in Germany, where there are no pricing or reimbursement hurdles.

After conducting an in-depth survey, the company now expects that sales in Germany will reach 50% of Pulmozyme sales in the near future. Between 33%-40% of people with CF in Germany use Pulmozyme. In Germany, there are around 7,500 people living with CF. The company expects to eventually reach the same level as Pulmozyme sales.

In the UK, the company indicated that sales were being hampered by getting Bronchitol onto formularies. All centres covered by the NICE guidance are required to have Bronchitol on their formularies next month. The NICE recommendation is for people over 18 with CF who can not use or have failed Pulmozyme use, whose lung function is deteriorating by more than 2% a year, and where other osmotic agents (presumably hypertonic saline) are not appropriate.

Bronchitol is also now being sold into Austria and Denmark. In Denmark, there are 500 people living with CF and supported at two CF clinics. First sales were recorded in October.

In this weeks's conference call, CEO Alan Robertson indicated that logistics were working extremely well. France will be the next country launch, at the completion of price discussions. Bronchitol is expected to be launched in the second quarter of 2013 in Italy, then in Spain.

In Australia, the process of reimbursement through the PBS is cumbersome, a process which the company is looking to streamline. While all but one centre has made the product available, physicians are selective of patients to use the therapy, making product uptake slower than expected.

European Youth Trial

Pharmaxis has agreed with European regulators on the structure of a trial of Bronchitol in people aged six to 17 years. That trial will enrol 150 subjects who will be treated for eight weeks. That trial is expected to start in coming months and to complete in 2014. The trial should cost around $3 million.

Bronchiectasis Phase III Trial Results

A second major event approaching for Pharmaxis is the outcome of the second Phase III trial in people with bronchiectasis. This trial enrolled 485 people almost 12 months ago. The trial will close this quarter with results out in the second quarter. In the US there are around 195,000 people with bronchiectasis, with the addressable market being about 100,000 people.

Summary

Pharmaxis has a number of major hurdles ahead. The market expectation for Pharmaxis is that the path through the FDA will not be straightforward. However, in our view the product should eventually gain approval in the US.

A positive result from the Phase III bronchiectasis trial is not being factored into the company's share price. And market penetration of Bronchitol into all markets will take time as physicians become comfortable with the product. However, positive changes to any of the above current assumptions has the potential to drive strong growth in the Pharmaxis share price.

Pharmaxis will be a volatile stock over the next three months as the FDA assesses Bronchitol and as Phase III trial results in bronchiectasis are released. More risk averse investors with a short term time investment horizon should consider reducing their exposure and wait until the FDA's decision on Bronchitol is made in March. Slow rates of revenue growth are also an additional risk factor with this stock

Pharmaxis is capitalised at $385 million.

Bioshares recommendation: **Reduce Exposure**

Alchemia – CEO Pete Smith Resigns

The leadership of Alchemia (ACL: $0.31) is set for further change following the resignation of CEO Pete Smith today. The chairman of Alchemia, Mel Bridges, has assumed the role of executive chairman. He will 'move quickly to appoint a replacement CEO'. The company described the resignation of Pete Smith as occurring by 'mutual agreement'. Pete Smith also stepped down from the company's subsidiary Audeo Oncology.

The change follows the failure of Alchemia to list Audeo Oncology in the US.

The objective of the spin-out and de-list plan was to improve recognition of the hyaluronic acid (HA) drug formulation assets held in Audeo Oncology. Foremost of these assets is HA-Irinotecan, a formulation of hyaluronic acid and irinotecan which is currently part way through a Phase III trial in a 390 patients with metastatic colorectal cancer.

The company closed the quarter with $6.2 million in cash at hand, with $2 million expected to eventuate from tax refunds.

The company recently stated it had sufficient funds to meet its short and medium term requirements. However, the company is likely to be concerned about its longer term financial situation.

One likely explanation for Smith's departure is that the company may now be seeking to wind down its investment in Audeo Oncology, seeking only to fulfil its obligations to conclude the Phase III trial. Half of the funds that were to be raised by Audeo Oncology (~US$22-$25 million) were allocated for the completion of the trial, in support of filing with the FDA and for reserve purposes. The funds required for the completion of the trial itself would be less than US$22-$25 million.

Receipts from customers for the December quarter, 2012 were $1.5 million, much lower than our anticipated $3.75 million. It is assumed that these receipts relate primarily to its share of income from the sale of fondaparinux in the US by Dr Reddy's Laboratories.

The company would do well to promptly advise its shareholders of its financial obligations and the status of its relationship with Dr Reddy's. Executive Chairman Bridges 'stressed that he will keep shareholders and the market informed as to the revised plans for the Audeo Oncology assets.

Alchemia is capitalised at $87 million.

Bioshares recommendation: **Under Review**

Bioshares

FDA OKs Ferriscan as Companion Diagnostic to Novartis' Exjade

The FDA has authorised Resonance Health's (RHT: $0.017) Ferriscan as a companion imaging diagnostic in support of the safe and effective use of Exjade in patients with non-transfusion dependent thalassemia.

Ferriscan is a non-invasive imaging technology that can be used to assess liver iron concentration (LIC).

Thalassemia is a genetic blood disorder which results in the decreased product on red blood cells and hemoglobin.

Exjade is an iron chelator that is used to reduce excess iron in the blood (and which becomes concentrated in the liver). Exjade is marketed by Novartis.

Non-transfusion dependent thalassemia is a milder form of thalassemia in which frequent blood transfusions are not required.

However, the risk of iron overload is still present, hence the benefit of Ferriscan which can be used as a tool by physicians to improve the management of this patient group.

The implications for Resonance Health are significant. The FDA approved the Ferriscan diagnostic under a de novo approval path (meaning that no comparable product was available). Ferriscan now becomes a predicate device that any similar future products will need to be measured against.

The FDA approved Ferriscan on the basis of data obtained from Exjade clinical studies, including one study that found that Ferriscan was as accurate as liver biopsy when measuring LIC.

This data, along with the FDA approval, has the potential to expand the use of Ferriscan in identifying and managing patients with iron overload. It should also aid in Resonance Health's efforts to gain coverage for the test from US health insurers. This has been a major challenge for the company to date.

What is yet to be determined is the frequency at which the test will be applied to non-transfusion dependent thalassemia patients.

Summary

The FD's approval of Ferriscan is a very positive event for Resonance Health. The approval ties the use of a drug, Exjade, to a diagnostic, for the management of a serious genetic disorder. We suspect that the non-invasive aspect of the test was an important supporting factor in the FDA's decision making. Liver biopsies are painful and risky procedures.

Resonance Health shares warrant an upwards re-rating on the back of the FDA approval.

Resonance Health is capitalised at $6.1 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Bioshares Model Portfolio (25 January 2013)

Company	Price (current)	Price added to portfolio	Date added
Psivida	$1.40	$1.550	November 2012
Benitec	$0.016	$0.016	November 2012
Nanosonics	$0.525	$0.495	June 2012
Osprey Medical	$0.65	$0.40	April 2012
QRxPharma	$1.00	$1.66	October 2011
Somnomed	$1.07	$0.94	January 2011
Cogstate	$0.350	$0.13	November 2007
Clinuvel Pharmaceuticals	$2.15	$6.60	September 2007
Universal Biosensors	$0.88	$1.23	June 2007
Alchemia	$0.310	$0.67	May 2004

Portfolio Changes – 25 January 2013

IN:
No changes

OUT:
With some high volatility ahead associated with the passage of Bronchitol through the FDA's review and approval process, we have removed Pharmaxis from the Model Portfolio.

Cash Flow Updates: Atcor Medical, Cogstate and Universal Biosensors

Atcor Medical (ACG: $0.07)

Atcor Medical's net operational cash position was boosted by a $0.7 million R&D Tax Concession refund. The company recorded cash receipts of $1.7 million compared to $2.6 million in the previous quarter.

The company's next generation version of its central blood pressure measurement technology, the Sphygmocor XCEL, was approved by the FDA in November 2011. The device uses a cuff rather then electrodes to sense blood flow, thus making the system simpler to use.

The company expects the new system to open up access of the Sphygmocor technology into the the clinical practise market, as opposed to the clinical trials market, the area which has been the major source of revenues for the company to date.

Bioshares recommendation: **Speculative Hold Class B**

Cogstate(CGS: $0.35)

Cogstate's cash receipts for the December quarter increased to $3.4 million, up from $2.6 million in the previous quarter. The company expects to report sales revenues of $6.1 for the half year ending December 31, 2012. It has adjusted its guidance for the half year from an expected half yearly loss of $1.0-$1.2 million to $0.5 million.

Cogstate has $4.75 million in contracted revenues expected be to recognised by June 30, 2013.

Cogstate increased its holdings of cash to $4.26 million from $3.45 million at the same time a year ago.

Bioshares recommendation: **Speculative Buy Class A**

Universal Biosensors (UBI: $0.88)

Universal Biosystems posted cash receipts of $8.1 million for the December quarter, compared to $8.3 million for the previous quarter. Cash receipts for the six months ending December 31, 2012 were $16.4 million compared to $9 million for the previous corresponding period.

Quarterly service fees that accrue to UBI from test strips used in the One Touch Verio System increased 288% in the December quarter from the same quarter a year ago, providing a quarterly income of $666,000. UBI receives 1 cent per strip regardless of where the strip is manufactured. This is a key figure because it indicates a quarterly crude usage rate of 66 million strips, which in coming quarters will be subject to a trend analysis. Annualised, it indicates a test strip usage figure of 264 million. However, Lifescan sells an estimated 4 billion strips a year which suggests that that there is still considerable growth prospects in front for One Touch Verio blood glucose systems as they replace older systems.

UBI closed the quarter with cash at hand of $24 million. The company raised $12.7 million during the December quarter.

Bioshares recommendation:
Speculative Buy Class A

Selected Cash Flow Statement Data

Quarter	09/2011	12/2011	03/2012	06/2012	09/2012	12/2012	Cash End ($M)
Atcor Medical [Capitalisation: $10.5 M]							
Cash Receipts ($M)	$1.89	$2.15	$1.79	$1.24	$2.56	$1.69	
NOCF ($M)	-$0.32	-$0.07	-$0.20	-$0.70	$0.26	$0.84	$2.14
Cogstate [Capitalisation: $26.7 M]							
Cash Receipts ($M)	$2.05	$2.46	$4.45	$2.14	$2.14	$3.41	
NOCF ($M)	-$0.20	$0.33	$2.12	-$0.83	-$1.02	$0.51	$4.26
Universal Biosensors [Capitalisation: $153 M]							
Cash Receipts ($M)	$5.52	$3.45	$6.61	$7.25	$8.28	$8.11	
NOCF ($M)	$1.39	-$3.50	$0.07	-$0.42	-$0.42	-$2.52	$23.65

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, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$400**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$630	2-3 email addresses
	$855	4-5 email addresses
	$1090	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____