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Biosshares

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Edition 475

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

In this edition...
The global investment giant Fidelity Investment have been filling in the space in the Acrux share register vacated by Allan Gray, AMP and Paradice Investment Management. Movements on biotech share registers are worth noting, with Australian Ethical increasing its holding in Somnomed and Universal Biosensors. The less well known TDM Asset Management from Sydney's Hunter St has also taken a significant stake in Somnomed. These positions send a signal to other investors – take a good look!
Alchemia has had a slight hiccup in its Audeo Oncology demerger program with the ATO still to provide a tax relief ruling. The demerger is worth studying given that Alchemia is sitting on $79 million of tax losses.
Companies Covered: ACL,ACR, QRX, SRX, 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)	-14.7%
Cumulative Gain	**194%**
Av. annual gain (11 yrs)	**17.8%**

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Developments at Alchemia

Alchemia's (ACL:$0.55) proposed demerger of its oncology assets into Audeo Oncology (a US entity) was paused this week with the company adjourning its Scheme Meeting and General Meeting so that it could finalise a class ruling from the Australian Taxation Office that gives tax relief to Alchemia shareholders.

Alchemia does not expect the delay to materially affect the timetable of the merger and the capital raising that is to be undertaken by Audeo.

Under the demerger proposal, Alchemia share holders will receive 1 Audeo share for every 37 Alchemia shares they hold. After the de-merger, Alchemia shareholders will own approximately two-thirds of Audeo Oncology, which is to be listed on both the Nasdaq and the ASX.

The timetable for the demerger is somewhat complicated with the de-merger contingent on Audeo Oncology successfully completing a capital raising. Audeo Oncology has filed a registration statement with the US SEC in which a fund raising cap of US$60 million was fixed.

A next step in the Audeo Oncology fundraising round will be the release of its registration document which contains the pricing of the offer.

The idea of the demerger was first conceived in 2006 according CEO Pete Smith, the year in which he was appointed Director of Commercialisation at Alchemia (he was appointed CEO in May 2007).

The oncology assets that are being demerged into Audeo Oncology came into Alchemia by way of its merger with Meditech Research which also took place in 2006, but before the hiring of Smith. Alchemia acquired Meditech Research (which was renamed Alchemia Oncology) for $17.2 million. R&D spending on Alchemia's HyACT assets (Alchemia Oncology) totalled $38 million from May 29, 2006 to June 30, 2012, according to an Audeo SEC filing.

Tax Losses of $79 Million
A point worth noting is that a consolidation of accounts for Alchemia Oncology did not take place, which means that $79 million in tax losses (as of June 30, 2012) will be available to Alchemia to offset profits in the future.

Alchemia Oncology (Pty Ltd) has accumulated tax losses of $74 million. That entity has become a subsidiary of Audeo Oncology and in effect the potential benefits of the tax losses have now been lost. It would be most unlikely this Australian subsidiary would generate revenues and profits that the tax losses could be set against.

Cont'd over

Fondaparinux Revenues

Alchemia stated on September 24 that it expects to receive its first profit from sales of fondaparinux of $125,000. The profit relates to the quarter ending June 30, 2012.

Profit share income from Dr Reddy's from sales of fondaparinux has been less than expected to date because of inefficiencies in the manufacturing and finishing steps for producing the drug. The current fill and finish process is subject to a wastage loss which has been exacerbated by the use of smaller batch lots.

This has meant that, since launch in July 2011, the COGS of fondaparinux has been higher than expected and that in turn has meant it has taken longer for Dr Reddy's to recover fixed costs relating its launch and other costs of approximately $10 million.

Alchemia expects that the remainder of this more expensive active pharmaceutical ingredient (API) will have been used in final product batches that were made in the September quarter, with cheaper (on a COGS basis) API being used in bigger batch runs.

Improved Production Yields for Fondaparinux

Alchemia also announced that, along with Dr Reddy's Laboratories, would make investments to improve the manufacturing process for fondaparinux. The two companies agreed to split additional costs of $10 million, with Alchemia's share to be deducted from the fondaparinux revenue stream.

The steps required to manufacture fondaparinux are many, with upwards of 50 steps required. The process is very difficult when compared to those required for many other synthetic chemistry derived drugs products, which may for example require five or six steps.

The two companies have been in fact working on the efficiency improvements for some time and have been able to increase yields of drug product by 60%. A 100% improvement is not out the question by the time the yield improvement project is completed.

There are important commercial implications to the achievement of improved yields. The first of these is that with a lower cost of production obtained, Dr Reddy's can compete more competitively (on a price basis) in the hospital drug market, a market in which it currently has a 6% share (up from 2%). The hospital fondaparinux market is worth an estimated US$100 million in gross terms and US$50 million in net terms.

HA-Irinotecan Phase III Trial Update

Alchemia's Phase III trial of HA-Irinotecan in 390 patients with metastatic colorectal cancer continues to recruit 'really well' according to CEO Pete Smith, with no unexpected toxicities observed to date.

More than 215 patients have been enrolled and 82 patients have received 10 cycles of chemotherapy or more. Half the patients are dosed with Alchemia's unique formulation of hyaluronic acid and irinotecan along side a cancer drug regime known as FOLFORI. Patients in the other arm of the trial receive irinotecan and FOLFORI.

HA-Irinotecan binds to CD44 receptors, which are over expressed on many cancer cells, thus providing a degree of selectivity for the drug compound. The exclusive binding allows for more drug to enter the cancer cell and to increase the killing power of irinotecan (a topoisomerase inhibitor).

The endpoint of the trial is when 350 patients have experienced disease progression or survival, an event which is expected to occur in the second half of 2013. This will result in the production of a progression free survival measure, which if it is sufficiently robust, will be the basis of a new drug submission to the FDA.

Alchemia's management estimate that $15.5 million will be required to complete the company's current Phase III trial of HA-Irinotecan in patients with metastatic colorectal cancer and $0.3 million to complete a Phase II trial in patients with small cell lung cancer. The budget for the Phase III trial has been in the order of $30 million.

The Audeo Investment Thesis

The investment thesis for Audeo Oncology is that investors can invest in a multiple product opportunity company where only one Phase III trial would be required per indication, and taking a 505(b)2 approval pathway. The development cost per indication should be low enough to warrant investment in indication opportunities where end product affordability is a driver in reimbursement discussions.

The CD44 target is highly expressed on many cancer cells but has received little attention to date with the exception of Roche which is developing RO5429083 as a monoclonal antibody to that receptor.

The Alchemia Investment Thesis

The Alchemia investment thesis is that the company will revert post-merger to being a company more akin to that of a royalty flow cash box, somewhat similar to that adopted by Acrux, although both companies, either currently or in future, invest in servicing the relationships they hold with pharmaceutical partners.

What is also more clear now is the potential benefit from accumulated tax losses that resides with Alchemia. As and when fondaparinux profit share revenues grow, then the benefit of these tax losses should become apparent.

Summary

Investors have been given in effect a free option with the Audeo demerger which has been made all the more attractive by the proposed dual listing of Audeo, with Audeo shares expected to trade as CDIs on the ASX. The CEO of Alchemia, Pete Smith said that 'having CDIs is the right thing to do for our shareholders'.

Alchemia is capitalised at $154 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Register Movements & Stock Updates: ACR, SRX, SOM, QRX, UBI

Acrux Register Changes

Acrux (ACR: $3.36) has seen its share price fall by around 20% since the company announced on August 23 that it would not meet its profit guidance for FY2013.

Acrux had been expecting revenue from its Axiron product, being marketed by Eli Lilly, of $40 million in this financial year, however that is likely to be around $15 million. The reason being that net sales of Axiron in 2012 will not exceed $100 million. Once they pass this level in any year, Acrux can expect to receive a milestone payment of $25 million. The $100 million of net sales is now expected to be passed in 2013, which means Acrux will receive the $25 million milestone payment in FY2014.

AMP Sells Down in Acrux

One of Acrux's largest shareholders has been selling down. AMP at one stage this year owned more than $50 million in Acrux. It started selling down (from 7.4% to 6.35%) in June of this year.

After the profit downgrade, AMP reduced its share holding from around 6.35% to less than 5% and is believed to have continued its sell down.

Paradice Investment Management was also not happy about the profit downgrade, selling $6.6 million of shares in the days after the profit downgrade. Paradice had taken a substantial position in Acrux in May with 6.28% of the company.

Prior to the profit downgrade, Ellerston Capital increased its stake in Acrux from 5.4% to 6.58%.

In the year to May, Allan Gray Australia announced it had decreased its stake in Acrux from 12.31% to 4.86%. Allan Gray (formerly Orbis) has been a long time investor in Acrux.

Fidelity Increases Holding

About $8 million of recent stock sales have gone to the major global investment group, Fidelity Investment, which has increased its stake to 5.19% after Acrux's profit downgrade.

Company Update

The US transdermal testosterone therapy market has grown 30% in the first half of 2012 according to the company and is on track to reach US$1.9 billion by the end of 2012. The most likely reason for such strong growth is that marketing by the major players, Abbott Laboratories and Eli Lilly, has intensified. In 2013 Eli Lilly will launch a TV marketing campaign to help drive sales.

It was last reported that Eli Lilly had a 12.5% market share with Axiron. That should continue to grow, with the majority of Axiron prescriptions coming from new patients. Eli Lilly is increasing manufacturing capacity by 50% at the Orion manufacturing facility in Finland. The upgrade is expected to be completed in the first quarter of 2013 and we expect further expansion at that facility to continue. Lack of supply has hampered marketing efforts. It is expected the products will be launched in Australia and Canada once the manufacturing upgrade is completed.

In the US market, one of the major health insurers will be reimbursing Axiron and another recent entrant, Fortesta, from January 2013 over the incumbent product and market leader Androgel. That insurer covers 22 million people.

Abbott Laboratories has been moving its patients across from its 1% Androgel dose to its 1.6% Androgel version. The reason behind this is not only that the higher dose is presumably easier to apply, but also that competitor Watson Pharmaceuticals is able to enter the market with a 1% generic version of Androgel from 2015.

Discounting to Fall in December Quarter

Currently Axiron is discounted by as much as 65% until it gets onto the reimbursement lists of insurers in the US. There is expected to be a significant reduction in rebating in the December quarter. We expect the net discount to factory sales will end up around 20% for Axiron. Acrux receives royalties based on nett sales, not gross sales.

Based on a US market size of US$2.2 billion by the end of 2013, a 20% market share for Axiron, a 20% royalty to Acrux and a 20% discounting, Acrux, we estimate, will be receiving royalties at an annualised rate of US$70 million by the end next year.

Summary

Acrux has been sold down in recent weeks because its $25 million milestone will not accrue this year but should accrue in 2013. The transdermal testosterone market continues to grow at a rapid rate in the US. We expect this to continue in 2013 with an Eli Lilly TV marketing campaign. Rebating by Eli Lilly is also expected to fall away significantly this year.

We expect Axiron to move to a 20% market share position by the end of 2013, which should see Acrux receiving royalties of US$70 million a year. In 2014 the company should receive a US$25 million milestone payment and a US$50 million payment in 2015. (A further US$120 million is expected after 2019.)

Acrux is capitalised at $559 million

Bioshares recommendation: **Speculative Buy Class A**

Sirtex Medical Sales Surge By 37%

Sirtex Medical (SRX: $9.92) has seen dose sales of its liver cancer therapy Sir-Spheres surge by a whopping 37% in the September quarter over the previous corresponding period (pcp). All regions performed exceptionally well, led by the USA which delivered a 42% growth (up from 19% growth in the 2011 September quarter over the PCP), and Europe (and the Middle East and Africa) which grew unit sales by 26% (turning around the 7% decline in the 2011 September quarter).

The growth is evidence that the treatment is becoming accepted as part of the treatment regiment for liver cancer globally.

There have been few changes in substantial holdings in Sirtex this

Cont'd over

Bioshares Model Portfolio (8 Oct 2012)

Company	Price (current)	Price added to portfolio	Date added
Nanosonics	$0.485	$0.495	June 2012
Osprey Medical	$0.32	$0.40	April 2012
QRxPharma	$0.68	$1.66	October 2011
Somnomed	$0.83	$0.94	January 2011
Phylogica	$0.026	$0.053	September 2010
Biota Holdings	$0.73	$1.09	May 2010
Tissue Therapies	$0.43	$0.21	January 2010
Bionomics	$0.33	$0.42	December 2007
Cogstate	$0.340	$0.13	November 2007
Sirtex Medical	$9.85	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.56	$6.60	September 2007
Pharmaxis	$1.27	$3.15	August 2007
Universal Biosensors	$0.77	$1.23	June 2007
Alchemia	$0.570	$0.67	May 2004

*Portfolio Changes – 8 October 2012**

IN:
No changes

OUT:
We haved removed Mayne Pharma (MYX) pending our review of the company's acquisition of the private US pharmacuetical firm, Metric.

*The date for the prices in the Model Portfolio in this edition are taken from the date of mailing rather than the masterhead publication date.

year. In August, long time holder Hunter Hall lowered its position slightly from 27.86% to 26.86%. And last month, Perpetual reduced its stake from 8.89% to 6.61%. Sirtex is now capitalised at $553 million.

Bioshares Recommendation: **Buy**

Somnomed – Substantial Investor Changes

Sleep therapy company Somnomed (SOM:$0.81) has seen two investment groups take up substantial holdings this year. In May, Australian Ethical acquired a 5.05% stake in the business. And more recently, Sydney-based fund TDM Asset Management gained a 6.95% shareholding in Somnomed.

Somnomed's CEO stepped down earlier this year. Executive Chairman Peter Neustadt will now oversee the management of the company. A global CEO will be installed in FY2014. Somnomed recently appointed a VP of Managed Care, to manage reimbursement with US health care providers. It has also appointed a new manager to head up the US operations, Kien Nguyen, who has the title of President of Somnomed Inc.

The company is seeking to accelerate sales growth to between 30-35%. Somnomed is capitalised at $33 million.

Bioshares recommendation: **Speculative Buy Class A**

QRxPharma – Allan Gray Increases Stake

The Complete Response Letter from the FDA in June this year saw Westpac (including BT Investment Management) reduce their stake in QRxPharma (QRX: 66.5 cents), ceasing to be substantial shareholders. Lang Walker's group however took the opposite view and increased its position from 8.33% to 9.63% in July.

More recently, Allan Gray increased its stake in QRxPharma last month from 8.99% to 10.23%.

The market is still waiting for further details with respect to how much information the FDA will find acceptable before it can approve the company's drug, MoxDuoIR for the treatment of acute pain, including minutes from the company's FDA meeting.

QRxPharma is capitalised at $96 million.

Bioshares recommendation: **Speculative Hold Class A**

UBI – J&J Investment Arm Exits

As reported in *Bioshares* 473, Johnson & Johnson's investment arm, which held a 9.4% stake in Universal Biosensors (UBI: 78.5 cents), has exited its investment in UBI. The stake has been taken up by Australian Ethical, which now owns 5.33% of the company, and New Zealand investment group Fisher Funds Management, which owns 6.25% in UBI.

UBI is capitalised at $ 125 million.

Bioshares recommendation: **Speculative Buy Class A**

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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