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In this edition...
If the early sales figures for Acrux's Axiron are anything to go by, it looks like a very successful new product has been launched. Accordingly we have updated our valuation of Acrux, valuing its shares at least at $4.40 and more optimistically at $5.45. Pharmaxis has provided more detailed information on its Phase III CF bronchitol trials that reveal why European regulators did not recommend the drug for approval. The stock represents good value if you believe, as we do, that it will eventually get Bronchitol approved. Mayne Pharma has suffered a blow, with the FDA knocking back sales partner Warner Chilcott's submission for a new dose form of Doryx. One piece of good news is that Toyota is backing Cogstate's concussion management tool in football.
The Editors
Companies Covered: ACR, BTA, CGS, MYX, PXS

	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	-6.8%
Cumulative Gain	**293%**
Av Annual Gain (10 yrs)	**21.2%**

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Bioshares

8 July 2011
Edition 415

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

Impressive Start for Sales of Axiron

Sales of the Axiron transdermal testosterone product developed by Acrux (ACR: $3.74) and being marketed and sold by **Eli Lilly** have got off to a very impressive start. In a presentation by Eli Lilly, the company stated that in just the first three months of sales, Axiron is now by making up 29% of new prescriptions written by urologists and endocrinologists.

Since 18 March, the leading competitor **Abbott Laboratories**, which sells Androgen, has seen its product fall from around 57% of new scripts written by these specialists to just 34% (or to 39% if Androgen 1.6% is added which was launched in late May and is being prescribed in 5% of all new scripts from these specialist groups).

Another big drop has been in Testim, which fell from around 33% of new scripts to 21%. Fortesta and Androderm have been somewhat constant at around 5%-6% over the last three months.

With new scripts written by GPs, only 13% are for Axiron. This lower rate is because Eli Lilly has launched its marketing campaign with the specialists and marketing to GPs has not reached full force. The next stage for Eli Lilly will likely be a direct to patient marketing through common media channels.

Looking at these prescription rates, Axiron is well on its way to becoming at least a US$500 million product (per year). We can now see why there was such strong demand from many pharmaceutical companies that were seeking to license Axiron and why such a lucrative deal was able to be secured.

Acrux Valuation: $4.40 per share

We have updated our valuation on Acrux, with our estimate that sales of $800 million are achieved in three years time. Using a discount rate of 12.75%, and assigning no value to the US Evamist market at the moment, we calculate a value of $4.40 per share.

Applying more optimistic sales growth figures, that peak sales of US$1.2 billion are achieved in five years time, a fair value of $5.45 by our estimates is calculated.

Bioshares recommendation: **Speculative Buy Class A**

Pharmaxis – Still Good Buying

Investors have had a second opportunity to acquire Pharmaxis stock at around 80 cents, with the stock finishing today at 94.5 cents. Driven by tax loss selling and the expected news that European regulators would formally knock back the company's new drug application, the share price made a fast retreat from $1.20 to 80 cents. At the start of the new financial year the stock bounced back by 12% on July 1.

As expected, the reasons for the formal decline in the company's new drug application in Europe was two fold: firstly that there was insufficient improvement in patients' lung function observed to improve their condition; and that there was inconsistent improvement across age groups. Pharmaxis disagrees with this opinion and has appealed. The case it will go to a panel of experts to give their view. Two different member countries of the European Union will co-ordinate the process from thereon.

The company has released a detailed presentation, breaking up the data from its Phase III studies in patients with cystic fibrosis.

The two Phase III trials in 600 people with CF over the age of six were enrolled in the trials. The two trials delivered an 8.1% and 8.2% improvement in lung function from baseline, recording changes in the volume of expired air as measured in millilitres. The 8% improvement was sustained out to18 months.

Gain over Baseline

One of the issues the European regulator identified was the variation in this effect across age groups. In children between 6-11 years of age, there was a **13.2%** improvement in lung function over 26 weeks. In adolescents between the ages of 12-17, there was an **8.4%** improvement, and in adults over 18 years of age, there was only a **4.7%** improvement over baseline.

Compared to Control

Furthermore, against the control arm, there was only a **4.16%** improvement in children, only a **1.25%** improvement over the control in adolescents, but a similar result in adults, where a **4.9%** improvement over the control was observed. These figures include data from both trials. In summary, the data in adults was consistent, but in adolescents there was little difference observed against the control arm (the 1.25% figure).

Comparisons with other CF Therapies

Comparing improvements in volume of expired air with other therapies, Pharmaxis' Bronchitol delivered an average improvement of 114ml, compared to 120ml improvement with Pulmozyme (from its1994 Phase III trial) and 68ml improvement from challenge with hypertonic saline. The antibiotic Aztreonam delivered improvements of 74ml and 150ml in two separate studies, and the antibiotic Tobramycin delivered a 126ml and 97ml improvement in lung function in its Phase III studies.

(However, it should be noted that antibiotics work down stream in treating/preventing infection build-up in the lungs. Pulmozyme works further up the line by breaking up the mucous that builds up in the lungs. Hypertonic saline and Bronchitol arguably work even further up the line, by hydrating the lungs – the core issue with CF – and thereby assisting with maintaining proper lung function and hygiene.)

Another point that needs to be considered is that in the Bronchitol studies, 55% of patients in the first trial and 75% of patients in the second trial were already taking Pulmozume. Also between 80%-90% of patients were taking antibiotics during the trials.

Reduction in Exacerbations

In the combined studies, there was a 29% reduction in exacerbations (which is a very meaningful measure that normally results in the patient requiring hospital treatment) and a 46% reduction in exacerbations in patients who stayed the course of treatment.

The safety profile of Bronchitol was shown to be very good.

Regulatory Timelines

The company indicated that the reaxamination will be completed in the fourth quarter of this year. The company will launch almost immediately in Germany and the UK if it is successful.

In the US, the company will file its NDA in the first half of 2012. Under its orphan drug status, the company will have seven years market exclusivity in the US and 11 years exclusivity in Europe.

Bronchiectasis

The company's second Phase III bronchiectasis trial with Bronchitol will be completed this year with results in 2012.

Summary

Our view is that is that Bronchtol retains a reasonable chance of gaining EMA approval later this year via the appeal process.

Pharmaxis is capitalised at $215 million. It had $56 million in cash at the end of March.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Corrections and Clarifications: Capital Raisings

In *Bioshares* 414 we stated that Bluechiip raised $2.6 million through its IPO when in fact it raised $3 million. Prima Biomed raised $21 million through a placement, not $20 million, bringing its total capital raised to $41.3 million.

The Tissue Therapies rights issue was underwritten by RBS Morgans.

Cogstate – Toyota to Fund Rollout of Concussion Management Tool to 130 Football Clubs

The take up of the Cogstate (CGS: $0.17) concussion management tool, designated by **Axon Sports** as the Computerized Cognitive Assessment Tool (CCAT), continues with Toyota funding the use of the test to 130 football clubs.

Toyota is a major sponsor of the AFL and it also formed a 'Toyota Good for Footy'' program. Providing the Axon Sports test to football clubs continues Toyota's commitment to improving safety in football.

Under this program over 25,000 footballers in Australia will have access to the Axon Sports test at no cost. Footballers will receive a baseline test, and the test will be used to monitor their brain function to judge whether they have recovered sufficiently to return to play following concussion.

Despite not being a major contract for Axon Sports, it does build brand awareness for the Axon Sports brand, and helps confirm the need and utility of such a product in contact sports, not just in Australia but globally. As part of the contract, Toyota will also invest in promoting the rollout of the test. Already all AFL clubs and all ARL clubs use the Cogstate/Axon Sports test.

The Axon Sports business is making good progress on many fronts. This newly created business has the potential to deliver a very high margin and significant revenue stream to Cogstate. This blue sky for the company is edging closer to a reality.

In the US, the Mayo Clinic has chosen Axon Sports as the cognitive test it will use as part of the roll-out of a concussion management service to the entire state of Arizona. Under the Mayo funded initiative, every high school athlete in the state, which is over100,000 athletes, will have access to the Axon Sports test free of charge. Details of this program can be seen at www.mayoclinic.org/concussion-testing/arizona.html.

New Product Range – Axon Potential

Earlier this year Axon Sports released a new product range, called Axon Potential. This suite of products comprises of athlete training tools, such as training to pick baseball pitches, teaching soccer awareness and anticipation skills, and learning grid iron blitz schemes. For any new products that come into Axon Sports, Cogstate maintains its 50% ownership in the joint venture.

CEO Brad O'Connor recently returned from the US where he observed focus groups with athletes in Portland who provided feedback on the new products. O'Connor said the new products were very well received.

Cogstate has an underlying business that generates sales in the order of $8-$9 million a year from providing its test for use in pharmaceutical trials, particularly in measuring cognition in testing potential new drugs for Alzheimer's disease and schizophrenia. Recent cost cutting by the company should make the company profitable (around $0.5 million) moving forward on that level of revenue. What has made it difficult for that business in the last two years is the appreciating Australian dollar against the US dollar.

Cogstate is capitalised at $11 million with $2.9 million in cash at the end of March. It is an excellent investment consideration. However with very poor liquidity in the stock, it suits longer term investors.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Biota Holdings – More Prophylactic Studies Needed for Inavir in Japan

Biota's (BTA: $0.995) partner **Daiichi Sankyo** released results from a prohylactic study with Inavir (called CS-8958 outside of the US and also laninamivir octanoate), a flu drug that is now selling in Japan. The study failed to achieve the company's preset goal of risk reduction rate of 70% that other family members would get the flu, with only a reduction rate of 43% achieved.

The study was done in the midst of the swine flu pandemic, where family members were almost certainly more cautious than normal in catching the flu from another family members. It is reasonable that judging the relative benefit of taking Inavir as a prophylactic over the placebo group in this study is not an accurate reflection of the benefit of the drug. Other prophylactic flu drug trials have been successfully conducted in more closed environments, such as prisons. More prophylactic studies will likely be required in Japan.

In the first six months, Inavir was very successful, generating sales of $77 million in Japan, from which Biota received a royalty of just under $2.8 million (equating to a royalty rate of around 3.5%.)

Earlier this year Biota was awarded a US$231 million contract from BARDA in the US, to commercialise CS-8958 in the US, and thereby make it available to the US population. Currently the manufacturing process of CS-8958 is being set up in the US, based on the Japanese process. Following that, clinical studies will begin to bring that drug to market in the US. The contract with BARDA is for five years.

Biota Holdings is capitalised at $178 million with $77.5 million in cash at the end of last year. If receives a 7% royalty from sales of Relenza in most markets out to 2014 and in Japan to 2019. Biota's other core program is a HRV (human rhinovirus) and this is midway through a Phase IIb trial in 400 patients with asthma in 46 sites in the US. The trial is expected to be completed in March next year.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bioshares Model Portfolio (8 July 2011)

Company	Price (current)	Price added to portfolio	Date added
Acrux	$3.74	$3.37	June 2011
Psivida	$4.35	$3.95	May 2011
Bioniche	$0.90	$1.35	March 2011
Somnomed	$1.30	$0.94	January 2011
Phylogica	$0.080	$0.053	September 2010
Sunshine Heart	$0.053	$0.036	June 2010
Biota Holdings	$1.00	$1.09	May 2010
Tissue Therapies	$0.58	$0.21	January 2010
Atcor Medical	$0.14	$0.10	October 2008
Impedimed	$0.59	$0.70	August 2008
Patrys	$0.10	$0.50	December 2007
Bionomics	$0.64	$0.42	December 2007
Cogstate	$0.17	$0.13	November 2007
Sirtex Medical	$5.16	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.80	$6.60	September 2007
Starpharma Holdings	$1.61	$0.37	August 2007
Pharmaxis	$0.95	$3.15	August 2007
Universal Biosensors	$1.10	$1.23	June 2007
Alchemia	$0.61	$0.67	May 2004

Portfolio Changes – 8 July 2011

IN:
No changes.

OUT:
No changes.

Setback for Mayne Pharma's Doryx Interest

Mayne Pharma (MYX: $0.40) has been dealt a setback by the refusal of the FDA to approve **Warner Chilcott's** submission for a new dosage form of Doryx. Mayne Pharma holds the patent over Doryx and Warner Chilcott markets three Doryx dosage formulations in the US, with the delayed release 150mg formulation accounting for 95% of sales of the three formulations. The other formulations are at strengths of 100mg and 75mg .

Warner Chilcott had completed a Phase III 480 patient study (see www.clinicaltrials.gov – NCT01113931) in patients with chlamydia infection of Doryx in a 200mg formulation (doxycyline hyclate 200 mg tablet), comparing that dosage form to Vibramycin (doxycycline hyclate 100 mg) taken twice a day.

The submission was rejected we understand because the study was perceived to be insufficiently powered.

The rejection of the submission places uncertainty over the new Doryx formulation, which was designed to maintain the brand profile of the product range as generic competitors for other strengths come on market.

A meeting between Warner Chilcott and the FDA could possibly take place by September, in which an approval pathway is discussed. At best the FDA, could ask Warner Chilcott to conduct a supplemental study that adds more patients to the current study. At worst, Warner Chilcott could be asked to re-do the entire study, which could put back the market entry of Doryx 200mg by twelve months or more. One point at least in favour of the clinical program is that recruitment is relatively easy to address with morethan 2.8 million chlamydia infections occurring each year in the USA.

Earnings Guidance

Mayne Pharma has now provided guidance that its full year revenue will be in the range of $49-$51 million and that EBITDA will be in the range of $8-$10 million. The EBITDA for the half year ended December 31, 2011 was $5.1 million. Sales of Doryx fell 47% for the year according to Mayne Pharma CEO Roger Aston, a consequence of the FDA's delay in dealing with the 200mg Doryx submission and contraction in stocking of old dosage forms of Doryx (in anticipation of the approval of the 200mg version.) Doryx has in the past accounted for roughly half of Mayne's sales

Until Warner Chilcott is able to ascertain from the FDA a pathway for Doryx 200mg, Mayne Pharma's revenue prospects from that product line are in limbo. We place a Hold on the stock, pending receipt of FDA advice possibly in September, or other information that introduces greater certainty regarding Mayne's revenue outlook.

Positive news for Mayne may emerge towards the end of the year as a marketing authorisation submission for Mayne's antifungal drug is considered by the European medicines regulator.

Mayne Pharma is capitalised at $60 million. The company's cash balance at June 30, 2011 was $5.6 million.

Bioshares recommendation: **Hold**

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

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Circadian Technologies, Biota Holdings, Mayne Pharma Group, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Mesoblast, Atcor Medical, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida

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