ISSN 1443-850X

In this edition...
Stockmarkets around the globe 'corrected' this week. The All Ords fell 4% from a week ago. The Nasdaq Biotech Index fell 7.8% taking a far greater hit than the Bioshares 20 Index which fell 3.5%. The message is that smart investors appear to be picking up quality biotech stocks, a number of which make up the Bioshares 20 Index. In fact, this week's focus is on one of those quality stocks, Acrux, which announced its first deal with an international Big Pharma partner, Organon.
We also update readers on the cash positions of several biotechs, now that the half yearly reporting period has closed and consider some investment lessons regarding Metabolic and its failed drug trial.
The editors
Companies covered: ACR, CCE, IDT, MBP,SRX

	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 (from 5 May '06)	12.4%
Cumulative Gain	**213%**
Average Annual Gain	**26.0%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd. The company also provides market and company analysis of the Australian pharmaceutical and biotech industries for local and international funds management institutions, venture capital funds and other related industry groups. For further details contact David Blake (see details below).

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) 9671 3633
Email: info@bioshares.com.au
David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 206 (2 March 2007)
ISSN 1443-850X

Bioshares

2 March 2007
Edition 206

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

Acrux Signs With Organon (Akzo Nobel) – More Deals Expected

Acrux (ACR: $1.18) has secured arguably its most important commercial validation through a licensing deal with **Organon**, a division of **Akzo Nobel**. Akzo Nobel is a major global healthcare company with over 63,000 employees and a market value of US$17.6 billion. The deal relates to collaboration agreement between the two companies that will combine Organon's contraceptive products with Acrux's drug delivery technology.

The deal is important because it is the first time that a Big Pharma company has signed on to develop Acrux's drug delivery technology for human health applications. Previously, Acrux had signed a deal with **Eli Lilly** for animal health applications and with a medium sized biotech, **Vivus**, to develop the company's two leading products.

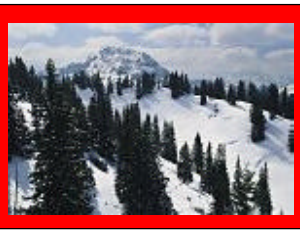
The contraceptive market is valued at US$6.7 billion a year. There are six main competitors in this market with Organon having currently secured a 13% market share. Organon has a number of contraceptive products on the market.

Details of agreement
This collaboration initially involves one compound and depending on the success of the first program, may extend to transdermal delivery of other combinations of contraceptive compounds. It is estimated that it will take Acrux six months to complete formulation and pre-clinical testing of the compound and that clinical trials could start in as early as 12 months. It took over eight months of discussions with Organon to secure the agreement which included intensive due diligence by Organon.

Acrux will receive a small upfront payment from Organon and future development and regulatory milestone payments of up to US$16 million. Acrux will also receive a royalty from sales of any products that reach the market, which we estimate to be between 3% - 5%.

Another important implication from this deal is that it may stimulate more interest from other major pharma for a product development collaboration/licensing deal. There is also a potential for Acrux to expand on this collaboration with Organon into other areas where Organon has a market presence, such as hormone replacement therapy (for Acrux's Evamist) outside of the US.

Cont'd over



Acrux is currently in discussions with potential partners for three other programs.

Female testosterone in Europe

Acrux has partnered with Vivus for its female testosterone product for the US markets. Currently Vivus and **Procter and Gamble,** which is developing a similar product, are in discussions in the US with the FDA relating to the design of Phase III trials.

In Europe however, Procter and Gamble has released its female testosterone product, Intrinsa, in three countries for the treatment of low libido. Acrux is in discussions with potential partners to complete development and sell its product, Testosterone MDTS for women, for in Europe. The company already has a distribution agreement with **CSL** to market and distribute the product in Australia and New Zealand.

Testosterone MD-Lotion for men

Acrux is also in global distribution partnering discussions for the testosterone lotion product for men. Clinical trials of this product will not require proof of efficacy, but only pharmacokinetic (PK) studies, which measures delivery of the drug into the blood stream. Acrux is currently completing a Phase II study in 40 men with results expected mid year. Acrux will also need to conduct a small compatibility study to see how the product interacts with deodorants (the testosterone product will be applied under the arm similar to a deodorant).

From there, the company will need to conduct a larger PK study, either alone or with a partner, before the drug can be approved. The global market for testosterone for men is estimated at US$600 million a year at present.

Nesterone MDTS for contraception

Acrux has another contraceptive program through its collaboration with **The Population Council**, trialing a new contraceptive product. The rights to this program have been excluded from Acrux's agreement with Organon. There is also a partnering opportunity in the medium term with this program.

Vivus partnership

Acrux has partnered its two leading products with a mid sized biotech company in the US, Vivus. In hindsight it was not the most optimal of partners as what is required to commercialise these products is a major pharmaceutical company with a large sales and marketing team. The expectation is now that Vivus will seek to sublicense the products for the US, which is the region covered by the collaboration.

To a large extent Acrux is restricted by the commitment of Vivus in commercialising these products in the US. There are set performance hurdles included in the contract with Vivus. Clinical data generated by Vivus remains the property of Vivus, which could restrict usage of the data for gaining regulatory approval in other regions such as Europe.

At present, Vivus looks to be focusing significant attention to its own lead product, Qnexa, for the treatment of obesity. This program has completed Phase II clinical studies with positive results.

Most biotech companies need to partner their programs to bring their products to market. There will always be a partnering risk and it should be expected that relationships will be tested as priorities within the respective groups change. The relationship between Vivus and Acrux became strained last year, with Acrux last November informing Vivus through its lawyers that it was in breach of their commercialisation agreement. However, Acrux management is now pro-actively managing the relationship.

Evamist, a transdermal hormone replacement product, was submitted for approval in the US in September last year by Vivus and should be on the market in early 2008 in the US.

Testosterone MDTS for women - delay

As mentioned, the other product licensed to Vivus, Testosterone MDTS for women, is waiting, and has been waiting since September 2005, to move into Phase III clinical studies in the US. The delay is due to expanded safety studies required by the FDA for the US market. The market in Europe has lower hurdles with a competing product from Procter and Gamble, Intrinsa, now selling for the treatment of low libido in women. Low libido has been linked to low testosterone levels in women, which is more pronounced in women who have undergone ovary removal surgery.

Fentanyl UDTS

Acrux is also continuing with development work on a transdermal fentanyl spray for pain relief. Fentanyl is a large market, estimated at over US$6 billion. This program has been delayed, with the company reformulating the product from a paste (UTDS) to a metered dose spray. An IND is expected to be filed by the end of April, with a Phase I clinical study expected to begin soon after. Being a narcotic, the commercialisation of transdermal fentanyl products is difficult because the potential for misuse and the importance of ensuring consistent dosage.

Summary

The deal with Organon represents the first big pharma alliance for Acrux in the area of transdermal human therapeutics. The results from the Phase III Evamist trail released last year stimulated interest in the potential of this technology and awareness of the Acrux technology has now certainly been further enhanced through the Organon agreement.

There may be more licensing agreements for Acrux announced in coming months. The company is capitalised at $168 million with $17 million in cash at the end of last year. The stock remains a quality investment opportunity.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Stock Briefs

Clinical Cell Culture in Trouble

Clinical Cell Culture (C3) (CCE: 7 cents) has revised its expectations of sales targets for FY2007. Previously the company had indicated sales of between $5-$7 million could be achieved. The management of Clinical Cell Culture now believes revenues will be more in line with 2006 (~$1 million).

The company said that failure to gain regulatory approvals for ReCell in Russia, China and Mexico were behind the downwards revision in sales forecasts. The company also expressed concern about the lack of sales of CellSpray since December and delays in patient recruitment in its US registration trial of ReCell.

The recent exit of specialist biotech investor **Biotech Capital** is sign that all is not well at C3. Signs are emerging that company's technology may take even longer to generate commercial success, if at all. The company held $16 million cash as of December 31, 2007. Regrettably, this may be insufficient to support the company beyond the end of this year, and the company's capacity to return to the market for funding is now severely diminished. It would now appear that a desirable strategy for C3 is to seek a merger with a firm with strengths in international marketing of wound care products, while it can do so from a firmer footing and not in a distressed condition.

C3 is capitalised at $30 million.

Bioshares recommendation: **Sell**

Sirtex Medical - Reports 1st half results

Sirtex Medical (SRX: $3.38) generated a net profit of $887,000 for the first six months of this financial year. Sales increased by 34% for its liver cancer treatment product, SIR-Spheres. The result was affected significantly by legal costs of $1.7 million for the period. The **University of Western Australia** currently has a legal action proceeding against the company's founder and against Sirtex relating to ownership of the underlying technology.

If legal costs (which may recur for the next two years only) are excluded, then Sirtex generated a net profit before tax of $3.34 million for the period, and after tax this equates to an after tax profit of $2.34 million. Annualised, it equates to a net profit of $4.68 million. With Sirtex currently valued at $188 million, it represents a PE ratio of 40 times for the company.

Sales of the product in the US had slowed in the last half to 24% growth. With overall sales growth of 34%, it does not currently justify the high price-earnings ration of 40 that the company is trading at. This company deserves to be monitored closely. At this point we place a **Lighten** recommendation on the stock.

IDT - Reports 1st half results

IDT (IDT: $1.91) reported a net profit for the first six months of this financial year of $2.16 million. Whilst it was a large increase over the previous corresponding period ($0.65 million profit), it is only a marginal increase over the corresponding period two years earlier when a net profit of $1.96 million was recorded.

The result is disappointing in light of the strong result returned in the second half of FY2006, when $2.87 million profit was returned and forecasts of strong growth made.

Whilst this latest result suggests the revenue for IDT may be seasonal, it's been a turbulent time for the company over the last two years suggesting a higher risk premium should be attributed to this stock. IDT is currently capitalised at $82 million and is trading on a PE ratio of 16 times. This appears appropriate. The company had $1.0 million in cash and is paying a fully franked dividend of 4.7%.

Bioshares recommendation: **Hold**

Bioshares Model Portfolio (2 March 2007)

Company	Price (current)	Price added to portfolio
Acrux	$1.18	$0.83
Alchemia	$1.11	$0.67
Bionomics	$0.27	$0.21
Cogstate	$0.18	$0.18
Cytopia	$0.62	$0.46
Chemgenex Pharma.	$0.70	$0.38
Optiscan Imaging	$0.48	$0.35
Neuren Pharmaceuticals	$0.47	$0.70
Peplin	$0.78	$0.83
Peptech	$1.65	$1.31
Phylogica	$0.35	$0.42
Probiotec	$1.07	$1.12
Progen Industries	$6.23	$3.40
Sunshine Heart	$0.22	$0.19
Tissue Therapies	$0.60	$0.58
Ventracor	$0.92	$0.92

The Bioshares 20 Index

Change from June 30, 2006	**41.2%**
Change from Dec 31, 2006	**11.9%**
Change - week ago	**-3.5%**

Nasdaq Biotech Index

Change from June 30, 2006	**2.6%**
Change from Dec 31, 2006	**-4.6%**
Change - week ago	**-7.8%**

Some Lessons from Metabolic Pharmaceuticals' Failed Obesity Drug Trial

The development of Metabolic Pharmaceuticals' obesity drug candidate AOD9604 has been terminated following the unblinding of data from the company second Phase IIb trial. The company announced that AOD9604 did not deliver a statistically significant loss of weight at any of three doses evaluated in the 502 patient study.

What happened after the trial result was announced?
Shares in Metabolic fell 71% to close at 22.5 cents on the day of the announcement. Since then they have a fallen a further 27% and closed on Friday at 16.5 cents. At this price the company is capitalised at $49.6 million. It holds cash assets of $24 million, which equates to 8 cents per share.

What also happened on the day of the announcement was that 95 million MBP shares exchanged hands. This compares to 20 million shares exchanged in the twelve trading days in February, 32 million in January 2007, 12 million in December 2006, 34 million in November and 24 million in October. In the seven trading days after the day of the announcement, 71 million shares have exchanged hands.

What lessons can be gained from this Phase II clinical trial event?

Lock in profits
One of the very first lessons the Metabolic AOD9604 trial failure provides is of the value of locking in profits from a stock that has had a strong run in the lead up to an announcement of make-or-break significance for the company. This may be a difficult task to execute when a stock shows incredible buoyancy and is supported by wide-spread enthusiasm. And it may seem even more difficult to tolerate if the stock appreciates further. However, when a stock run-up is connected to clinical trial outcome the statistics are weighted against successful results.

Concede failure, losses can and will occur
A second lesson is the necessity to concede before investing in speculative biotech stocks that the entire capital invested could be lost. This ties in with desirability of investing in biotech stocks on a portfolio basis, where speculative investment allocations are made on the basis of an investor's appetite for risk.

Understand the investment proposition
Investors do get 'burnt' by losses incurred from biotech investments. Successful biotech investors also incur losses but they expect them and wear these losses when they occur. They also understand why they have made an investment in a stock and clearly understand the investment proposition.

The investment proposition is likely to focus on how much capital a biotech company will consume over a period of time to answer certain questions or generate data regarding medical technology, balanced against other technology, competition and corporate risks.

If the answer to these questions is low relative to the net returns from potential product sales and if the time to the potential yield from an investment crystalisation point (eg the sale or license of the technology to another firm) is relatively short, then an investor may balance such investment positives against other investment negatives, for example, some uncertainties regarding 'freedom to operate' or future reimbursement status.

We estimate that Metabolic has expended to date about $35 million developing AOD9604 as an obesity treatment, supported by a government grant of $2.1 million. Had AOD9604 demonstrated clinical benefit, then perhaps another $50-$100 million may have been required to complete further clinical trials and bring the product to market around the globe. The upside for a safe, even moderately beneficial obesity treatment is huge, with possibility of billions in revenues achievable. In other words, the cost to payoff ratio is very high.

Could the trial outcome have been predicted - was it doomed to failure?
For any medical technology in development there will be proponents and detractors. Within the Australian investment community there were views circulated over the years that held AOD9604 as an almost certain failure. A key point regarding the two Phase II trials of AOD9604 was that they were pivotal studies conducted in humans, although what was disappointing about the first study was the inconclusive nature of the trial and management's attempt at the time to paint the trial as a "success". No amount of pre-clinical studies of a drug or technology can compare to the actual verification of that drug or technology in human patients. Animal studies are not infallible guides to how a drug may work in humans, although animal models and cell based assays are very valuable in filtering drug candidates that have undesirable properties.

No drug developer, or the board of a biotech company, can know with complete certainty that a drug candidate will succeed. Boards have to make reasoned judgments to commit to the development of a drug based on indicative and preliminary data and a medical hypothesis. Years of relevant experience in drug development and extensive knowledge of a disease can be tremendously helpful, but are still no guarantee of clinical success or commercial success. High profile failures of drugs such as the marketed COX-2 inhibitors celecoxib (Celebrex; **Pfizer**) and rofecoxib (Vioxx; **Merck**) and more recently the Phase III candidate torcetrapib (Pfizer) are evidence that even the most well endowed and resource rich companies are not immune to product failures.

Metabolic is investigating the application of AOD9604 as a potential treatment for osteoporosis. What is the likelihood that the technology will fail again?
There is always the likelihood that a drug or associated technology can fail again when tested as a treatment for other diseases. For example, **Amrad** unsuccessfully evaluated emfilermin

Cont'd over

(leukemia inhibitory growth factor) first for chemotherapy induced peripheral neuropathy (results announced March 2002) and then again unsuccessfully, in partnership with Serono, as an infertility treatment (results announced June 2004)

Why did AOD9604 fail?

We do not know why AOD9604 failed to deliver statistically significant weight loss, compared to placebo, in this latest trial. The real reason may never be known, even by parties privy to all the data. However, some factors to be considered in the event of a review of the project include selection of the wrong doses, formulation issues, drug administration including factors affecting absorption of the drug (a peptide) through the gut, genetic variability and patient selection and trial design.

What's next for Metabolic?

Following major setbacks such as a clinical trial failure, it is not uncommon for board and management changes to take place, usually in an incremental fashion. This may occur at Metabolic, and if so the company may then embark on a fresh strategy to communicate the potential of the company's current assets to investors. Investor sentiment towards Metabolic is likely to be pessimistic for some time until the company re-groups and presents a clearer picture of the company's future plans, as well as explanations of past events.

The historical levels of high investor interest in the stock are also unlikely to repeated going forward and sentiment towards the company may be very weak as the company progress its ACVI pain compound through a Phase II trial.

Another important element to the MBP stock price is the large volume of shares bought at the $0.19 - $0.22 range. This represents a substantial overhang in the stock and any positive price drivers for the stock may be defused by the sellers looking to exit at a 30%-50% premium to that $0.19 - $0.22 entry point, or at between $0.25 - $0.33.

Metabolic is capitalised at $49.6 million.

Bioshares recommendation: **Speculative Hold Class B**

Cash Balances – Selected Companies

	Code	Company	Cash End 31/12/06 ($M)	Survival Index
1	CIR	Circadian	$42.3	5.8
2	BTA	Biota	$41.9	5.4
3	PGL	Progen Industries	$30.0	3.2
4	NRT	Novogen	$46.3	3.0
5	CYT	Cytopia	$18.3	2.6
6	OIL	Optiscan Imaging	$5.0	2.0
7	POH	Phosphagenics*	$14.4	1.8
8	MBP	Metabolic	$25.7	1.6
9	VCR	Ventracor	$35.2	1.1
10	CXS	Chemgenex	$9.9	0.8
11	AGX	Agenix	$5.0	0.7
12	EIF	Eiffel Technologies	$0.4	0.5
13	ANX	Anadis	$1.1	0.4
14	VHL	Virax	$1.4	0.2
15	PLT	Polartechnics	$0.9	0.2

* POH figures are for FY CAL 2006

In edition 202 of Bioshares we published the cash balances as of December 31, 2007 of 88 companies that report under ASX's 4.7B rule. With the half yearly reporting period now concluded, we can add to the analysis with the reporting of cash balances for a number of other biotech firms that sit outside the 4.7B rule.

Once again we have calculated a Survival Index figure for each company, which divides a company's annualised net operational cash flow into the company's cash balance at the end of the December 31, 2006. A Survival Index of 0.5 means a company has about 6 months of cash to fund operations. A Survival Index of less than one is likely to mean a company will be looking to raise funds in the near future.

This approach is not the most accurate measure of a company's financial viability as it does not take into account future increased spending, recently raised funds or recently reduced spending patterns. We have excluded several companies from this analysis because they generate positive operational cash flows and are more appropriately assessed by standard financial measures.

The Survival Index figures presented above indicate that three companies in particular are weak financially, including **Polartechnics** (SI = 0.2), **Virax** (0.2) and **Anadis** (0.4). However, Polartechnics has raised $6 million through a convertible notes program and Anadis expects to gain $1.2 million from the sale of property. **Eiffel Technologies** has been cited by its auditors as having 'Material Uncertainty Regarding Continuation as a Going Concern' if it is not able to effect a corporate transaction such as a merger with another firm.

Chemgenex Pharmaceuticals has subsequent to December 31 secured $10 million through a placement and expects to raise a further $10 million through a rights issue. Also since December 31, Circadian has invested $8 million in **Vegenics**, reducing its proforma cash balance to $34.3 million

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.

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: Phylogica, Neuren Pharmaceuticals, Pharmaxis, NeuroDiscovery, Prima Biomed, Biotech Capital, Cygenics, Cytopia, Biodiem, Peptech, Starpharma Holdings, Cogstate, Xceed Biotechnology, Healthlinx, Incitive, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Medical Therapies

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$320**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$520	2-3 email addresses
	$620	4-5 email addresses
	$750	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: 61 3 9671 3633

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 _____

_____

_____