ISSN 1443-850X

In this edition...
A bad week for equities in general makes for an even worse week in biotech. That said, market corrections throw up amazing bargains for investors with cash to invest.

Our top picks for the week are Pharmaxis, Cytopia, Peptech, Universal Biosensors, Peplin and Acrux. However, that is not to exclude another twenty stocks that offer great vallue at current prices.

We are confident that quality biotech stocks will rebound so long as expectations are met and the very strong drive by biotech companies to maximise value creation continues unbated.

The editors
Companies covered: CYT, PXS, MBP

	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 (from 4 May '07)	-14.5%
Cumulative Gain	**179%**
Av Annual Gain (6 yrs)	**26.8%**

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 228 (17 August 2007)
ISSN 1443-850X

Bioshares

17 August 2007
Edition 228

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

Market Correction Sees Biotech Stocks Heavily Oversold; Sector on Cusp of Golden Period

It's been a horrid and bloody week for stock market investors. The All Ordinaries 300 Index fell 4.6% over the week as the long anticipated sell-off moved into full swing, whether justified or not. Biotech investors have felt the full force of the sell down, with some biotech stocks falling more than 30% in one day. While there may be some argument for the broader market correction in Australian stocks, driven by asset repricing in US capital markets, there was arguably less justification for the more severe response to local biotech equities, where the sector has never been in such a fundamentally sound position in its 20 year Australian history.

A correction in equity markets offers opportunities for entry into quality stocks and at this point, it's perhaps appropriate to look at some of the strong fundamentals that underpin this industry.

$960 million in cash asstes

As mentioned in last week's edition, 18 of Australian listed biotech companies now collectively hold around $960 million in cash assets to fund their development programs. Peptech leads these companies with an estimated $170 million in cash and Progen has $100 million to fund its Phase III liver cancer program and other Phase II studies.

In the first six months of this year, Australian biotechs raised almost $500 million and we we expect to see approximately $700-800 million flowing into the sector this year to fund commercialisation programs, with the bulk of these inflows driven by the requirements of later stage clinical trials.

Eleven companies in Phase III/pivotal studies

Within six months, there will be 11 ASX listed biotech stocks with drugs in pivotal Phase III clinical trials, the final stage before registering these products with regulators and bringing them to market (see table next page). This includes the Trinan therapy under development by **Ark Therapeutics** to which **Vegenics** (**Circadian Technologies**) will receive a royalty stream from product sales (if approved for sale).

For a sector that is not known for its profitability, both locally and in the US, there are now four listed Australian biotech/drug development stocks with locally originated products or royalty entitlements to products on the market and contributing to profits. These are **CSL**, **Peptech**, **Biota Holdings** and **Sirtex Medical**. The CSL business was initially built on its vaccine products and its emphasis has more recently moved to the sale of blood fractionation products. Its royalty income stream from Gardasil, the HPV cervical cancer prevention vaccine, was released last year and is also now making an important contribution to that company's profitability.

Biota's Relenza (being sold by **GSK**), delivered Biota a royalty stream of $40 million in the last year. That figure may have further growth with competing product Tamiflu believed to

Phase III or registration trials underway or planned for next 6 months

Company	Product or Compound	Disease/Indication	Progress
Pharmaxis	Bronchitol	Bronchiectasis	Phase III EU awaiting results. Phase III US to start 2007
		Cystic fibrosis	Phase III EU underway. Phase III US to start 2007
Progen Pharmaceuticals	PI-88	Liver cancer	Phase III in planning
Clinuvel Pharmaceuticals	CUV1647	Light associated skin disorders	Phase III underway
		Erythropoietic Protoporphyria (EPP)	Phase III underway
Avexa	Apricitabine	HIV	Phase III in planning
Acrux	Testosterone MD lotion	Testosterone deficiency in males	Registration PK study to begin 2007
Chemgenex Pharmaceuticals	Ceflatonin	Gleevec resistant patients with CML	Registration trial underway
QRxPharma	Opioid combination	Chronic pain	Phase III trial to start 2007
Circadian Technologies (Vegenics)	Trinan (with licensee, Ark Therapeutics)	Prevent blockage of haemodialysis grafts	Phase III in planning
Neuren Pharmaceuticals	Glypromate	Neuroprotectant	Phase III underway
Halcygen	Super-generic of intraconazole	Antifungal	Registration PK study to begin 2007
Psivida	Medidur (with licensee, Alimera Sciences)	Diabetic Macular Oedema	Phase III underway

have generated sales of US$1.6 billion in the first six months of this year. Peptech generated a royalty income stream from the sale of anti-TNF drugs Remicade and Humira of $16 million last year.

Sirtex Medical generated sales of around $30 million in the last 12 months with its liver cancer treatment. The company should make a small profit (net operating cashflow of $1.2 million), which would have been substantially higher if not for $4.3 million in legal fees due to its current patent dispute with the University of Western Australia. **Acrux** will shortly be added to this list with its first product, Estradiol, a spray on HRT product, to go on sale in the US through **KV Pharmaceutical** in the next few months.

Eight new drugs to approach market in 2009

By mid-2009, we expect that eight more Australian biotechs are likely to have either drugs on the market or will be preparing to file their drugs for approval with regulators around the world (see table next page).

Sector delivering positive Phase II results overall

In contrast to several years ago when we saw a string of Phase II clinical failures or disappointments (see table on page 3), the last 18 months has delivered a series of largely positive Phase II trial data from at lease 14 Phase II. Its is of interest to note is that Australian biotech companies are delivering an unusually high success rate for Phase II trials. Where the success rate in the order of 50% would be more usual for Phase II studies, Australian biotechs over the last 18 months have had an 85% success rate.

Such success has enabled these companies to raise sufficient funds to bring their products closer to market. And while we have yet to see a major drug partnering deal with large pharmaceutical partners with a deal value greater than US$500 million or with a US$50 million up front payment, these deals may eventuate as biotech companies can now negotiate from a position of strength. With a ready access to capital, more companies can seek to complete Phase III trials independently, as is the case with **Progen**, **Clinuvel**, **Avexa**, **QRxPharma**, and **Halcygen**, or even take them to market alone in the US, which is the case with at least **Pharmaxis** and **Peplin** and possibly even **Acrux** and **Chemgenex Pharmaceuticals**.

Overseas funds continue to target Australian biotech

The increasing interest from US and European funds towards the Australian biotech sector confirms the strength and attractiveness of the local sector and even the biotech CEO churn rate has slowed abruptly, which is a sign that some biotech boards and some investors are content with the pace of progress being made.

Bioshares Current Top Picks

Acrux (ACR) – $1.17
Cytopia (CYT) – $0.60
Peplin (PEP) – $0.74.5
Universal Biosensors (UBI) – $1.30
Pharmaxis (PXS) – $3.18
Peptech (PTD) – $1.155

Drugs expected to reach market or ready to be filed for approval in next 24 months

Company	Product	Indication	Development event (as described by company)	Funds available ($M) (Est. or reported)
Pharmaxis	Bronchitol	Bronchiectasis	**Q4 2007:** file first marketing application	$76
ChemGenex Pharmaceuticals	Ceflatonin	Gleevec-resistant patients with CML		$25
Alchemia	Fondaparinux	Various anti-coagulation indications	**FY2009** US market launch	$25
Halcygen Pharmaceuticals	SUBA-itraconazole	Broad-spectrum anti-fungal	Filing for registration - **2008**	$11
Acrux	Testosterone MD-Lotion	Testosterone deficiency in men	Marketing applications targeted for **H2 2009**	$40
Peplin	PEP005	Actinic keratosis		$45
Clinuvel Pharmaceuticals	CUV1647	Light associated skin disorders		$60
Avexa	Apricitabine	HIV		$77
			Total	**$359**

Clinical trials performance history

Date	Company	Event
Phase II clinical failures and disappointments in 2004 & 2005		
June 2004	Amrad	Serono stops Phase II trial with Emfilermin for infertility treatment
October 2004	Peplin	Allergan hands back PEP005, which was about to begin Phase II trials
December 2004	Metabolic Pharmaceuticals	Obesity drug fails for first time in Phase II
March 2005	Antisense Therapeutics	Phase II trial halted due to deaths related to competing drug Tysabri
April 2005	Prana Biotechnology	Halts Phase II Alzheimer's trial
Phase II & Phase III clinical successes in 2006 & 2007		
May 2006	Peplin	Positive Phase IIa trial results in actinic keratosis
May 2006	Acrux	Positive Phase III results with transermal HRT
May 2006	Prima Biomed	Positive Phase II results from ovarian cancer trial
June 2006	Clinuvel Pharmaceuticals	Positive Phase II results with CUV1647 as a photpprotectant agent
August 2006	Clinuvel Pharmaceuticals	Positive Phase II results with CUV1647 in patients with polymorphous light eruptiuon
December 2006	Progen	Positive Phase II trial in liver cancer
December 2006	Chemgenex Pharmaceuticals	Positive Phase II data for Ceflatonin in Gleevec resistant patients with CML
February 2007	Clinuvel Pharmaceuticals	Positive Phase II results with CUV1647 in patients with Erythropoietic Protoporphyria
March 2007	Avexa	Positive Phase IIb results from HIV trial
May 2007	Alchemia	Positive Phase II results from HyCAMP metastatic colorectal cancer study
June 2006	Chemgenex Pharmaceuticals	Positive Phase I/Iia study with Quinamed in patients with soliud tumours
July 2007	Peplin	Positive Phase IIb results in AK study
2006 & 2007 trial failures		
February 2007	Metabolic Pharmaceuticals	Obesity treatment drug candidate fails second Phase II trial
August 2007	Metabolic Pharmaceuticals	Phase II trial with ACV1 for neuropathic pain

Cytopia Set for New Phase in Corporate Development

Cytopia (CYT: 60 cents) is set to begin a new phase in its corporate development following acceptance by the Federal Government's Pooled Development Funds Registration Board of Cytopia's request that its Pooled Development Fund (PDF) status be revoked.

The rules and regulations supporting PDFs were established in 1992. The PDF scheme was designed to attract capital towards early stage investment opportunities. The PDF scheme was closed to new entrants on June 21, 2007. Cytopia follows Starpharma's lead in relinquishing its PDF status in 2004. Other current registered publicly listed PDFs in the biotech space include listed investment fund **Biotech Capita**l and **Acrux**.

Revocation of PDF registration has the consequence of setting the deemed acquisition price of Cytopia shares for existing Cytopia shareholders at 67.5 cents per share. It also means that Cytopia shareholders will be able to offset capital losses from selling Cytopia stock against capital gains. Going forward, Cytopia will be free to act as any other 'ordinary' public company, in terms of ability to acquire other businesses or invest in companies, with assets greater than $50 million.

Lead drug program – CYT-997

Cytopia recently completed a Phase I trial of its anti-cancer drug CYT-997, delivered intravenously (IV), that works by disrupting the blood vessels that feed tumours (a vascular disruption agent - VDA). A goal of the trial was to discover the maximum tolerated dose (MTD). The trial, which involved 31 patients and began in Q3 2005 was expected to take 9-12 months to complete. However, the task of finding the MTD took twelve months longer than expected. The MTD was found to be at least five-fold greater than doses tolerated in pre-clinical toxicology studies. If, as is suggested by this finding, that CYT-997 has a reasonably wide therapeutic window, then the compound may offer oncologists more flexibility in treating patients.

Concurrently, the company has been conducting a Phase I trial of an oral formulation of CYT997. The benefits of an oral formulation are significant, potentially allowing patients to administer the drug in the home care setting. For many aged cancer patients this is an important consideration.

The company plans to commence a Phase II clinical trial of CYT-997 (IV) before the end of this year. The company is still to determine the specific details of this Phase II trial, but melanoma and brain and liver cancers are being considered as treatment targets.

Investment View

Cytopia is an extremely attractive investment proposition. Cytopia is capitalised at $44 million and as of June 30, 2007 retained cash assets of $14 million. In terms of comparative valuations it is trading at a 30% discount to a close Australian comparator company, **Bionomics**. Bionomics is also developing a vascular disrupting agent, which has not yet entered the clinic. By reasonable metrics, Cytopia should trade well in excess of Bionomics' capitalisation, and progress of a drug candidate into Phase II warrants an even higher market re-rating. With the PDF status now rescinded, the company should have fresh appeal to investors and companies looking to fill their pipelines through acquisition.

Bioshares recommendation: **Speculative Buy Class A**

Pharmaxis – Phase III Results Expected

Pharmaxis (PXS: $3.18) is due to report the results from a Phase III study completed in patients with bronchiectasis before the end of next month. The trial has involved 363 patients in a 12 week placebo controlled, double blinded trial followed by 12 months in an open label extension study. Results may come out as early as next week. It will be a critical milestone point for the company. Given the strong interest in patients requesting to continue treatment under the Special Access Scheme, we believe there is a ver good chance the results will be positive.

The fields of cystic fibrosis and bronchiectasis may appear to be a niche market. However it has attracted some of the best biotech companies in the business. The lead product on the market for clearing mucous in patients with cystic fibrosis is a product called Pulmozyme, marketed by **Genentech** (cap US$77 billion). Last year the product generated sales of US$360 million for Genentech and **Roche**, the licencee outside of the US. **Vertex Pharmaceuticals**, one of the top tier smaller biotechs in the US (Cap. US$4.7 billion) has its own cystic fibrosis therapeutic program, now in Phase IIa trials. The company's approach is to repair the defective CFTR ion channel in patients with cystic fibrosis, which prevents the transport of chloride ions across the respiratory cells membranes.

And this week arguably one of the most dynamic biotechs in the US, **Gilead Sciences** (Cap. US$34 billion) decided to in-license a cystic fibrosis and bronchiectasis program from **Parion Sciences** in France, which will look at developing sodium channel blockers to treat these disorders. Gilead built its business on the antiviral market, developing drugs such as Tamiflu, the competitor to Relenza, and a suite of HIV drugs which underpins its business. It is is a very positive sign for Pharmaxis that this market is attracting some of the most impressive biotechs in the world to a therapeutic area that remains poorly serviced.

Bioshares recommendation: **Speculative Buy Class A**

Metabolic Pharmaceuticals Fails Again

Three Phase II failures in three years is not a good track record for the team at Metabolic Pharmaceuticals (MBP: 5.1 cents). The company had previously conducted two Phase II obesity drug trials that failed. This week the company cancelled a Phase II program in treating neuropathic pain before it released the Phase II results, after laboratory studies showed the program was unlikely to be economically viable.

Metabolic now has three core remaining assets. The first is a potential drug delivery platform. Through one of its earlier programs, the company has found that an amino acid sequence attached to peptide drugs may make these compounds orally available, rather than delivered via injection. The company has generated some positive preclinical data although it is still some way off from bringing this discovery into the clinic. An obvious peptide target for the company is insulin, a 51 amino acid peptide that in 2005 generated sales of US$7.3 billion. Remarkably, sales of this drug are expected to almost double that figure by 2010.

The company's second remaining asset is its estimated $20 million cash reserve (the company had $25 million in cash at the end of last year). Metabolic is currently capitalised at $15 million, a 25% discount to its estimated cash reserves. The third asset the company has is its trading losses, which currently relate to about $22 million in potential tax benefits from over $74 million in accumulated losses.

The Metabolic management and board has substantial work ahead to convince its shareholders it is an appropriate manager of the company's assets. Although the company has an experienced and capable CEO at the helm, it has become apparent the company is already in the sights of other biotech companies who could use Metabolic's cash and might argue there are more attractive or more achievable commercial prospects that could be supported. Given the company's current discount to cash, we place a **Speculative Buy Class C** on the stock.

Bioshares Model Portfolio (17 August 2007)

Company	Price (current)	Price added to portfolio
Acrux	$1.18	$0.83
Alchemia	$0.71	$0.67
Biodiem	$0.29	$0.29
Biota Holdings	$1.64	$1.55
Circadian Technologies	$1.22	$1.45
Cytopia	$0.60	$0.46
Chemgenex Pharma.	$0.75	$0.38
Optiscan Imaging	$0.38	$0.35
Peplin	$0.72	$0.83
Peptech	$1.16	$1.31
Pharmaxis	$3.18	$3.18
Phylogica	$0.27	$0.42
Probiotec	$1.09	$1.12
Starpharma Holdings	$0.33	$0.37
Sunshine Heart	$0.15	$0.19
Tissue Therapies	$0.45	$0.58
Universal Biosensors	$1.30	$1.23

Portfolio Changes – 17 August 2007

IN:

Pharmaxis has been added to the portfolio. The company is due to report a Phase III study with its lead compound Bronchitol this quarter. Positive results will be a major milestone for this company.

OUT:

Neuren Pharmaceuticals has been taken out of the portfolio. With a need to raise further funds over the next six months, we believe there may be more weakness with this stock.

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, Incitive, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Medical Therapies, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin

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:	$550	2-3 email addresses
	$750	4-5 email addresses
	$950	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 _____

_____

_____