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In this edition...
For the 250th edition of Bioshares, we would have liked to be delivering investment ideas to readers into a more favourable market about a sector that we'd had hope would have performed better over the last 12 months. The biotech sector has never been further advanced or better positioned from a funding perspective, at least in the upper end of the market. The next upswing in the sector is now overdue but market conditions look to be delaying that part of the cycle. In the meantime, Bioshares will continue to provide investment ideas on stocks that continue to offer appealing value propositions, albeit with likely longer term investment outcomes.
The editors

Companies covered: ACW, ACL, BIT, BTA, OMI, PGL, SLT, UCM

	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)	-30.0%
Cumulative Gain	**127%**
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).

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Bioshares

8 February 2008
Edition 250

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

So Few Acquisitions For Australian Biotech

Over the last five years, we've seen at least 16 listed Australian biotech companies make acquisitions with 11 of those being overseas. This week we added **Progen Pharmaceuticals** to that list after the company announced its intention to acquire oncology group, **Cellgate**, in the US. This is a surprisingly low number of acquisitions for a sector that houses over 130 listed companies. The low acquisition rate is also surprising given the success that some companies have enjoyed in accelerating their commercialisation timelines through acquisition.

A double-edged sword

Acquisitions can be a double-edged sword for companies. Acquisitions can allow companies to leapfrog the development path through the addition of later stage programs. **Chemgenex Pharmaceuticals** has been incredibly successful with its acquisition just four years ago of **Chemgenex Therapeutics Inc** and is now approaching a position to file its lead drug for regulatory approval in the US this year (through a rolling NDA submission).

– Cont'd over

Biotech company and asset portfolio acquisitions in last 5 years

Company	Acquisition target	Location of acquisition	Date announced
Progen Pharmaceuticals	CellGate	USA	February-08
Arana Therapeutics	Evogenix	Australia	May-07
Agenix	SHRG & YSY	China	February-07
Arana Therapeutics	Scancell*	UK	December-06
Starpharma Holdings	Dendritic Nanotechnologies	USA	October-06
CSL	Zenyth Therapeutics	Australia	July-06
Circadian Technologies	Vegenics**	USA and Finland assets	May-06
Arana Therapeutics	Promics	Australia	May-06
Alchemia	Meditech Research	Australia	March-06
pSivida	Control Delivery Systems	USA	October-05
Regenera	Advanced Ocular Systems	USA	October-05
Bionomics	Iliad Chemicals	Australia	May-05
Bionomics	Neurofit	France	December-04
Proteome Systems	Eukarion	USA	December-04
Chemgenex Pharm.	Chemgenex Therapeutics	USA	April-04
CSL	Aventis Behring	US, Austria & Germany	December-03

**Antibody assets* ***selected assets*

Bionomics has also been successful in getting into the clinic faster but has sought to become a more vertically integrated biotech company from its two acquisitions, **Neurofit** from France in 2004 and **Iliad Chemicals** in Melbourne in 2005. The company's lead compound, which was sourced from the Iliad pipeline, is now in Phase I clinical development for the treatment of solid tumours. Its second compound, BNC210, is expected to move into the clinic at the end of the year or in early 2009 for the treatment of anxiety. This compound has gone through extensive preclinical at the company's Neurofit facility in preparation for human trials. The acquisition by **CSL** of the **Aventis Behring** blood fractionation business helped propel CSL into a $19 billion company and one of the country's top 20 industrial companies.

But acquisitions, or the manner of, have contributed to disastrous results for **pSivida** and **Regenera** (now **Advanced Ocular Systems**) where there has been mixed approval from shareholders. The acquisition of **Evogenix** by **Arana Therapeutics** has also not reflected positively on the Arana share price, although the value of building a larger international antibody company has been lost on a number of investors. The combination of two like sized companies it would seem is more likely to receive an ambivalent response from shareholders where the perceived value and commercial prospects of the individual development programs can be difficult to agree upon.

An average of just over three acquisitions a year for a sector that should be expected to achieve value creation through the most efficient use assets is a disappointing metric for the sector. Filling the pipeline behind the current tranche of Phase III and Phase II programs is an essential requirement, either through acquisition or in-licensing, if the top-end of the sector is to continue the impressive performance that has been achieved over the last three years.

Progen Pharmaceuticals

Progen Pharmaceuticals has made an acquisition of a small US-based biotech company called Cellgate. The company has two discovery platforms in the areas of epigenetics (silencing the expression of cancer causing genes) and in targeting polyamines inside cancer cells. The acquisition comes with a number of preclinical compounds and a clinical compound that will move into Phase I studies in the second quarter of this year.

Progen will pay approximately US$1.5 million in shares for the company, together with accepting liabilities for the target company of up to US$1.0 million. Further milestone payments in cash or shares up to US$19.5 million are payable, which will start when any Cellgate compounds move into the second stage of clinical development.

Cellgate employed close to 20 people last year with many laid off in late 2007, presumably due to insufficient funding. Progen will take on Cellgate's CSO and house a team of up to eight people in San Francisco. The acquisition comes with industry standard royalty obligations to the founders. As part of the acquisition, Progen has negotiated the restructure of key agreements underlying the Cellgate technologies.

The lead Cellgate compound, 11047, had previously been in a Phase II prostate cancer trial, although an incorrect dose was used. It is expected this compound will move into two Phase I dose escalation studies in the second quarter of this year with results expected around mid 2009. An IND for a second compound is expected to be filed in early 2010.

The success of depleting the polyamine concentration in cells in cancer clinical trials has been very limited due to either toxicity issues or insufficient depletion of polyamines. It is thought that polyamine inhibitors used in conjunction with existing chemotherapy drugs may prove more successful. Progen will investigate the use of 11047 both as a single agent in its Phase I study and in combination with other cytotoxic drugs.

The Cellgate acquisition is a necessary move to broaden Progen's clinical stage pipeline. The acquisition was structured such that no cash outlay was required with the company gaining access to a clinical candidate, preclinical drug candidates, and drug development expertise. Further additions to the Progen pipeline would be welcomed to reduce the risk dependency on the company's lead drug candidate, PI-88.

Progen had $91 million in cash at the end of last year, which will be sufficient funding for the company for the next two years.

Bioshares recommendation: **Speculative Buy Class A**
(suits longer term investors)

Bioshares

Five Stock Wrap

Company	Actinogen	**Code**	ACW	**CMP**	$0.185	**Cap'n ($M)**	$7.4	**Cash ($M)**	$3.00	**SI**	**8.2**
• ACW listed in Dec 2007, raising $3.8M. Perth-based ACW was founded in 1999 as Australian Biogen Ltd.											
• ACW is discovering novel antibiotics and antifungals sourced from micro-organisms found in soil (actinomycetes)											
• Main opportunity exists to isolate and develop compounds that can treat MRSA and VRE strains of bacteria											
• ACW has filed one provisional patent to date (Nov 1 2006), titled "Bacterium and antibiotic produced thereby"											
• Company board comprises majority of scientists or medical doctors; no pharmaceutical industry expertise evident											
• Milestones: Confirmation of molecules for more advanced pre-clinical stidues											
Comment: ACW is an early-stage research company that lacks resources to fully exploit its discovery base											
Bioshares recommendation: **Better opportunities elsewhere**						Timing Considerations - Revisit in 12 months					

Company	USCOM	**Code**	UCM	**CMP**	$0.40	**Cap'n ($M)**	$15.2	**Cash ($M)**	$3.0	**SI**	**1.2**
• UCM markets an ultra-sound based non-invasive cardiac output monitor. The monitor has Aust., US, EU & some Asian approvals											
• UCM listed Dec 2003; SP peaked at $3.85 in May 2004 but has progressively weakened because sales expectation have not been met											
• Product sales FY07: **$0.875M**; FY06: **$1.12M**; FY05: **$0.480M**; FY04: **$0.384M;** Cash receipts for FY08H1 were **$0.345M**											
• UCM has increased medical publications to support sales but has lacked the financial and sales strength to drive sales in key markets											
• New CEO Paul Butler was appointed Jan 2007; Butler has relocated to US to push alliance development											
• Milestone - forming of a strategic marketing alliance with a medical device group to access the US market											
Comment: securing a US marketing partner will generate a new set of risks that UCM must recognise and mitigate											
Bioshares recommendation: **Speculative Hold Class C**						Timing Considerations - wait for signing of US partner					

Company	Occup. & Med. Innov.	**Code**	OMI	**CMP**	$0.40	**Cap'n ($M)**	$15.9	**Cash ($M)**	$0.9	**SI**	**0.3**
• OMI develops and markets safety products including auto retractable syringes, disposable scalpel blades and an IV access valve											
• OMI listed in 2000; from around $1.00, SP rocketed to over $5.50 in late '02 then fell steadily to $0.50 in '05. Volatile recent 12 months.											
• Register is dominated by founder/inventor and exec. director Bruce Keihne ~ 19.8% stake (inc. spouse)											
• Retractable syringe(s) received FDA approval in Nov '06											
• Cardinal Health appointed as a US non-exclusive distributor in Sept '07											
• Received US$4.3M order for the distributor's private label syringes for CY2008; OMI expects to book half the revenue in FY2008.											
• Risks: The quality of the share register is a risk with OMI											
• Litigation has been an issue for the company in the past; one dispute was found in OMI's favour but is ongoing to some degree.											
Comment: On a risk adjusted basis, OMI is attractive at current prices, with a significant commercial achievement in sight											
Bioshares recommendation: **Speculative Buy Class C**						Timing Considerations - None					

Implications of GlaxoSmithKline's CY2007 and Q42007 sales reported 7 Feb 2008

Company	Biota	**Code**	BTA	**CMP**	$1.19	**Cap'n ($M)**	$217.3	**Cash ($M)**	$60+	**S.I**	**N.A**
• Sales of Relenza reported by GSK for the Q4 2007 were US$152M (AU$171.4M). BTA receives a 7% royalty on Relenza sales											
• BTA's expected royalties for the quarter are $12M and cumulative 6 month royalties run to $16.5M. (FY07 royalties were $40M)											
• BTA expects GSK to sell all of its installed capacity for current year (implied capacity H207 was 26 million courses)											
• We estimate Biota's cash position to lie between $60-$65 million assuming similar spending on legal costs to FY07											
• BTA also announced that the amended timetable for its litigation with GSK: mediation now to commence by 31/7; trial to start 4/8 this year											
• Other developments: Long acting neuraminidase compound, CS8958, which is co-owned with Daiichi Sankyo, is now in Ph. II trials											
Comment: We regard BTA as a core quality biotech holding and is excellent buying at current prices											
Bioshares recommendation: **Buy**						Timing Considerations - None					

Company	Alchemia	**Code**	ACL	**CMP**	$0.50	**Cap'n ($M)**	$79.9	**Cash ($M)**	$20.35	**SI**	**2.6**
• Alchemia is developing, with marketing partner Dr Reddys, potentially the only generic version of GSK's anti-coagulant drug Arixtra											
• For the US, GSK recorded full-year (CY07) Arixra sales of US$109M, and final quarter sales of $32 million											
• The latest annualised quarterly figures translate to estimated profit share return for ACL of $16 M if gains 40% market in US											
• key development for Arixtra and generic fondaparinx is the gaining of more indications for the drug, eg acute coronary syndrome											
• An ANDA (generic drug application) we expect to be submitted to the FDA this half by Dr Reddys											
• Other developments: ACL recently held a pre-IND meeting concerning HA-irinotecan with the FDA, with very positive results											
• Progression free survival was agreed as an endpoint and only one pivotal trial will be required (400 pts, metastatic colorectal cancer)											
Comment: ACL is trading on a Technology Value of $60M and is good buying at current prices											
Bioshares recommendation: **Speculative Buy Class A**						Timing cons. - ANDA filing in US significant milestone					

Notes: SI - Survival Index - refer to Bioshares 249 for explanations

The Hepatitis C Challenge

Developing therapies or vaccines against hepatitis C (HCV) is extremely challenging. According to *Nature Biotechnology*, at lease eight HCV antiviral programs were cancelled or suspended in 2007. The existing standard therapy takes to years to treat patients, has many side effects, and only works in about half of the patients. So why the delay in developing new HCV therapies or vaccines?

Part of the reason is that pivotal knowledge about this virus has only been gained in the last 20 years. The virus was only isolated in 1989. The three dimensional structure was the HCV protease was described in 1996. And the virus was not able to be grown in cell culture until 1999 when the replicon system was developed, which has led to a wave of new therapeutics in development against the virus. According to *Signals Magazine*, in 2006 more than US$3 billion of deals were signed for HCV programs in 2006 alone. Another problem for drug developers is that there is only one established animal model for the virus, the chimpanzee, which is expensive to use.

Rapid mutation rate of the virus

Another obstacle in developing effective therapeutics is the rapid mutation rate of the virus. The HCV replication rate and viral load is even higher than that of HIV with at least 100 known strains of the virus. And for therapies to be effective, reducing viral load in the blood does not produce effective patient outcomes as in HIV, but the virus needs to be removed from tissues through a T-cell mediated immune response as well as an antibody response to attack the virus in the blood.

Despite the challenges of HCV drug development, the commercial rewards are significant. Existing drugs such as ribavirin and interferon-alpha generate sales estimated in excess of US$2 billion for the treatment of HCV. Over 170 million people worldwide are infected with the virus with four million in the US. HCV infection untreated can lead to cirrhosis of the liver and liver cancer. Chronic infection of HCV is also the largest reason for liver transplants in the west. The virus is transmitted mainly through the use of share needles and to a lesser degree through sexual contact.

In Australia there are at least three listed companies with HCV therapeutic programs underway. A summary is included below.

Biotron - p7 HCV target

Biotron (BIT: 17 cents) is moving into two Phase II studies this year with its lead antiviral compound, BIT225, for the treatment of HIV and HCV. BIT225 has been selected because of its capacity to inhibit ion channels in viroporins involved in the replication of viruses such as HIV and HCV. The two trials are expected to involve around 30 patients each infected with HIV or HCV. The HCV trial is due to start soon with results from this trial in mid 2008. The HIV trial is expected to begin around mid year.

The HCV program represents the largest commercial potential for Biotron. This is because of the lack of effective compounds available to treat HCV infection, as discussed above. Conversely for HIV, there are least 20 effective antiviral drugs on the market that work particularly well in controlling HIV infection. However, the Biotron approach to the treatment of HIV is new, targeting the Viral Protein U, which acts as a virus reservoir. Successful inhibition of this protein is thought to reduce the infectability of cells infected by the virus, which might be a worthy avenue to pursue. A challenge ahead for the company before the next trial begins is to develop an assay to measure effectiveness of this treatment approach, with changes in viral lead not being a suitable marker.

In HCV, BIT225 targets the p7 protein on the virus which creates an ion channel necessary for viral replication. To measure the effectiveness of the compound, the company cannot use the replication assays developed in recent years for testing protease inhibitors, but must use surrogate markers to establish drug efficacy.

In *in-vitro* studies, Biotron has shown that when BIT225 was used in conjunction with the existing drugs ribavirin and interferon, it was more effective (100%) at preventing viral replication and with even a lower dose of the existing drugs, compared to use of the existing treatment regime alone (70% effective).
Bioshares recommendation: **Speculative Buy Class C**

Biota Holdings - Nucleoside analogues against HCV

In November 2006, **Biota Holdings** (BTA $1.185) entered into a research collaboration and licensing arrangement with Boehringer Ingelheim to commercialise Biota's nucleoside analogues for the treatment of HCV. Boehringer has been a leading player in the HCV field. This program was previously partnered with GlaxoSmithKline and emanates from Biota's acquisition of Numax Pharmaceuticals in the US in 2001.

The nucleoside compounds seek to inhibit elongation of the virus RNA chain by inhibiting the NSB5 polymerase. Nucleoside inhibitors are unlikely to see viral resistance because binding is at the more conserved part of NSB5, although they have a greater risk of toxicity issues.

The Biota/Boehringer program has yet to reach the clinic. There are at least three other competing companies in the clinic with NSB5 polymerase inhibitors. These are Roche (in Phase II trials), Pharmasset/Roche (in Phase I/II) and Astrazeneca (in Phase I trials). However last year there were four NSB5 inhibitors that failed in the clinic suggesting confirming the difficulty of working in HCV and the NSB5 target.
Bioshares recommendation: **Buy**

Select Vaccines - Virus like particle HCV vaccine

Select Vaccines (SLT: 1.7 cents) is developing a number of vaccines using its virus-like-particle platform. The platform uses proteins from the hepatitis B duck virus as a scaffold to generate both an antibody and T-cell immune response. The company's HCV vaccine is in preclinical development. Other programs under development include virus-like-particle vaccines against influenza to give broader protection, including against the pandemic H5N1 strain.
Bioshares recommendation: **Speculative Buy Class C**

Stock Briefs

Pharmaxis

Pharmaxis (PXS: $3.20)updated investors this week with a quarterly conference call and release of its quarterly newsletter. Some key points were as follows:

CF301 - Aust. /EU CF Phase III trial

The company expects to complete recruitment for the Aust/EU Phase III cystic fibrosis trial, CF301, in Q2 2008, with about half of the 250 patients recruited to date across 43 sites. Headline data is expected in early 2009. Results of a UK investigator sponsored study comparing bronchitol with pulmozyme for the treatment of CF are expected to be reported in this quarter.

US BX Phase III trial

The US bronchiectasis Phase III trial protocol, which was submitted under a special protocol assessment, will have 'degree of antibiotic use' as a primary endpoint and 'quality of life' as a secondary endpoint, different to the completed Phase III trial that had quality of life and mucous clearance as the primary endpoints.

PXS25 Phase I trial

Pharmaxis also announced that it will commence a Phase I study of PXS25 this year. PXS25 is small molecule compound that inhibits its immune cell trafficking. Following from finding that PXS25 suppresses neutrophil concentration in the lung, the company will seek to progress PXS25 in asthma related indications and not as previously planned, multiple sclerosis.

Pharmaxis is capitalised at $622 million.
Bioshares recommendation: **Speculative Buy Class A**

Sirtex Medical

Following receipt of correspondence with the company, *Bioshares* can provide readers with a further update on Sirtex Medical (SRX:$4.05). The company's sales in the most recent quarter were affected due to supply issues related to quality control. These supply issues have now been resolved. Supply was interrupted in December last year and in the early part of January.

US manufacturing facility on-line this month

The company's US manufacturing facility in Wilmington will begin supplying product towards the end of this month. Production will be ramped up over the next three months, by which stage it is expected that the facility will supply the full demands of the US market. This is all very positive news.

Regarding the judgment from litigation action brought about by the University of Western Australia, the company had no further information on the timing of this event. A decision in Sirtex's favour should impact materially on the company's share price. We expect an outcome from this action should not be far away, given the proceedings concluded in August last year.

We have upgraded our recommendation to a **Buy** following clarification of supply issues.

Sirtex Medical is capitalised at $226 million.

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Bioshares Model Portfolio (8 February 2008)

Company	Price (current)	Price added to portfolio	Date added
Patrys	$0.40	$0.50	December 2007
NeuroDiscovery	$0.18	$0.16	December 2007
Bionomics	$0.32	$0.42	December 2007
Cogstate	$0.13	$0.13	November 2007
Ventracor	$0.46	$0.625	October 2007
Sirtex Medical	$4.05	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.36	$0.66	September 2007
Progen Pharmaceuticals	$1.90	$3.52	September 2007
Starpharma Holdings	$0.37	$0.37	August 2007
Pharmaxis	$3.20	$3.15	August 2007
Universal Biosensors	$1.02	$1.23	June 2007
Biota Holdings	$1.19	$1.55	March 2007
Tissue Therapies	$0.20	$0.58	February 2007
Probiotec	$1.16	$1.12	February 2007
Phylogica	$0.15	$0.42	January 2007
Peplin Inc	$0.75	$0.83	January 2007
Arana Therapeutics	$0.97	$1.31	October 2006
Chemgenex Pharma.	$0.75	$0.38	June 2006
Cytopia	$0.45	$0.46	June 2005
Optiscan Imaging	$0.25	$0.35	March 2005
Acrux	$1.01	$0.83	November 2004
Alchemia	$0.50	$0.67	May 2004

Portfolio Changes – 8 Feb 2008

IN:

No Changes

OUT:

No Changes

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, Pharmaxis, NeuroDiscovery, Biotech Capital, Cytopia, Biodiem, Arana Therapeutics, Starpharma Holdings, Cogstate, Xceed Biotechnology, Incitive, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys

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