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In this edition...
Sentiment to the biotech sector in the US appears to be improving with 11 life science companies announcing their intensions to list in the last month.
In the meantime, an increasing number of local biotech CEOs are beginning to look more comfortable as their businesses are taking shape. In particular Bionomics and Chemgenex Pharmaceuticals have done exceptionally well to move from being genomics companies to product-focused companies over the last five years.
Not so for Biodiem's CEO who was replaced this week with an interim CEO with an investment banking background, suggesting perhaps a new direction for that company.

The editors
Companies covered: AVX, BDM, BNO, CXS

	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)	-5.5%
Cumulative Gain	**209%**
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

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

Positive Signs for US Biotech IPO Market

Signs of life are emerging in the US biotech market. In 2006 there were 19 biotech IPOs according to **Burrill & Co**, raising an average US$50 million. These stocks gained on average 40% after listing last year. Over the last month, 11 life science companies have filed registration statements with the SEC for proposed IPOs.

One of these companies, **Reliant Pharmaceuticals**, a pharmaceutical firm, is looking to raise around US$400 million. Three medical device companies have indicated their intention to list – **Reliant Technologie**s, **Concentric Medical** and **Bioform Medical**. And seven biotech companies have filed to IPO, with four drug development companies in the list, including Australia drug developer Peplin Inc.

Biolex Inc is looking to raise around US$70 million. This company is commercialising its expertise in the manufacture of difficult to make proteins, including monoclonal antibodies, in the Lemna aquatic plant system. Its expetise also extends to glycosolated proteins, for which manufacture has been difficult to achieve in plant systems. **BG Medicine** is a biomarker discovery company. **Precision Therapeutics** is an interesting oncology services company that uses a cell-based test to predict the likelihood that a patient's tumour will respond to existing or new chemotherapy combinations.

Over the last 12 months the Nasdaq Biotech Index has increased by 12%, although it has been largely tracking sideways over the last three years. The recent increased activity in IPO filings is a positive sign for the sector and warrants close monitoring as a leading indicator of sentiment towards the US biotech market.

Of interest also is that Australian companies are now approaching the capital raising levels of their US counterparts. This year has seen three Australian biotechs - **Plantic Technologies**, **QRx Pharma** and **Hexima** - list on the back of large capital raisings. Plantic raised $47 million on the AIM stock market, and on the ASX, QRxPharma and Hexima

Cont'd over

US Life Science Company IPO Registrations Filed in Last Month

Registration Date	Company	Indicative Capital Raising (US $M)	Products in development/Technology
August 6	BG Medicine	$80	Biomarker discovery
August 9	Peplin Inc	$75	Entering Phase III trials for AK
August 10	Reliant Pharmaceuticals	$400	Branded cardiovascular drug sales
August 14	Biolex Inc	$70	Protein drug synthesis in Lemna aquatic plant
August 16	Reliant Technologies	$95	Laser medicine devices
August 17	Concentric Medical	$69	Catheters for stroke
August 21	Bioform Medical	$115	Implants for plastic surgery
August 22	Adnexus Therapeutics	$86	Adnectin protein drug development
August 24	Precision Therapeutics	$80	Personalised oncology treatments
August 31	ARYx Therapeutics	$86	Drug development
September 3	Anacor Pharmaceuticals	$57	Drug dev. 3 Phase II trials underway

Strong Growth Ahead for Sirtex

Sirtex Medical (SRX: $3.90) has delivered for the second year in succession strong growth in sales of its liver cancer radiation therapy product. Once again sales have grown by $10 million over the previous corresponding period, to $33.3 million, up 48% on the previous year. The Sir-Spheres treatment incorporates radioactive resin microsheres that are injected into the liver via the hepatic artery. The spheres have a short half-life, although long enough to disrupt cancer cells in the liver.

The product is approved for sale in most major markets in the world, including the US and Europe, and most recently Sirtex has been forming marketing alliances in Asia, including South Korea, India and Taiwan, where the incidence of liver cancer is considerably higher.

Current regions where the product is sold include the US (sales of $25.3 million, up 35%), Europe (sales of $5.5 million, up 140%) and Australia, New Zealand, Hong Kong, Malaysia, Singapore and Thailand. The treatment is now available in over 160 medical centers worldwide.

Sirtex - Financial Results & Forecasts

	2004	2005	2006	2007	2008E	2009E
Revenue from sale of goods ($M)	9.5	11.8	22.6	33.3	47	65
- growth ($M)		2.3	10.8	10.7	13	19
-growth rate		24%	92%	47%	40%	40%
Cost of sales ($M)	2.6	3.0	4.7	6.9	10	14
Gross profit ($M)	6.9	8.8	17.9	26.4	37	52
Gross margin	73%	75%	79%	79%	79%	79%
Pre-tax Profit ($M)	**-0.6**	**-1.4**	**5.5**	**4.3**	18*	30*

** Exlcudes FX losses and legal costs*

Strong growth anticipated

Continued strong growth is anticipated. As the sales and distribution network has been largely established, the company should see an increasing percentage of sales flow through to the bottom line. Pre-tax profit for this year was $4.3 million. (Excluding FX losses and legal expenses for the last financial year equates to a profit before tax of $11.1 million). If we exclude foreign exchange losses and legal costs going forward, then we forecast pretax profit for the next two years of $18 million and $30 million, which includes an estimated increase in clinical trial costs going forward.

Litigation - Judgment pending

Sirtex is currently involved in legal action together with the founder of Sirtex, Dr Bruce Gray, initiated by the **University of Western Australia**. Final submissions have been submitted and all parties are now awaiting judgment. The action relates to ownership of the intellectual property that underpins the Sirtex technology. In our view, Sirtex has added enormous value to the commercialisation of this technology, having conducted clinical trials, registered the product in major regions throughout the world and gained good penetration into global markets. Sirtex has filed a cross-claim against Dr Gray, regardless of the outcome of the University. Without knowing the outcome of the trial, at most risk is Dr Gray's 30% stake in Sirtex. Sirtex denies the claims made by the University and has made a counter claim for damages.

With the Federal Court judgment pending, a resolution to the dispute is approaching, notwithstanding any appeals. The University does not seek to put Sirtex into administration as would it jeopardise a valuable income stream from the very successful business that Sirtex has built.

Summary

Sirtex has become a very successful business. Its product generates gross sales margins of almost 80% and sales have shown strong growth over the last two years. This solid performance is expected to continue, with more of the gross profit to flow through to the bottom line. The legal proceedings with the University of Western Australia are nearing an end. When completed there should be improved clarity regarding the business and management will be able to focus more closely on growing the business. However, the litigation remains a risk for the company.

Sirtex is capitalised at $218 million with $10.6 million in cash assets. Excluding any further legal costs or foreign exchange losses, the company is trading at a prospective PE for 2008 of 17, or at 4.6 times forecast 2008 sales. These are attractive multiples given the strong outlook and that the company is moving through a profit inflexion point.

Bioshares recommendation: **Buy**

Bioshares

– from page 1

raised $50 million and $40 million respectively. The last two years has shown that through follow-on capital raisings, companies have been able to raise between $70 - $90 million to advance later stage programs.

There is also good news for earlier stage companies, with local venture capital groups expected over the next two years to reach similar sizes to some of their US counterparts. Access to a larger pool of capital will place Australian companies on a more equal footing with US biotechs and that should help deliver superior commercialisation outcomes than has previously been the case in Australia.

Bioshares

ChemGenex – Milestones to Watch

ChemGenex Pharmaceuticals (CXS: 96 cents) has seen its share price bounce back this week following a roadshow to Australian investment audiences by the company's CEO Greg Collier. The share price rose 8% from the previous week.

ChemGenex's lead drug in development is the semi-synthetic compound ceflatonin (CGX-635). This drug candidate is currently in three Phase II trials, with the CGX-635-CML-202 trial set to complete enrolment this year.

Chemgenex is developing ceflatonin as a drug to treat chronic myeloid leukemia in patients who have failed Gleevec treatment, or have failed Sprycel treatment, or have also tested positive for the T315i point mutation on the BCR-ABL protein.

The company has flagged the following milestones for investors to monitor in the last quarter (Q4 2007) of this year.

- Presentation on mechanism of action data of ceflatonin
- FDA guidance meeting on ceflatonin
- Presentations at the American Society of Hematology meeting
- Commencement of rolling submission for ceflatonin with the FDA
- Completion of enrollment for ceflatonin CML T315i study (CGX-635-CML-202).

A key element of ChemGenex's commercialisation strategy is the initiation of the rolling submission with the FDA. This means that as data becomes available for various treated sub-sets of patients, and it meets the requirements for submission to the regulatory authority, then conditional (and accelerated) approval could be be obtained. Then as more data comes to hand it would be attached to the submission. The company's key milestone in Q1 2008 will be a prefiling meeting with the FDA.

ChemGenex is an increasingly well managed company and continues to represent very attractive buying with major registration milestones looming on the short term horizon. ChemGenex is capitalised at $187 million and retains an estimated $23 million in cash.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bionomics' BNC105 Edges Towards the Clinic

Bionomics (29 cents) is progressing steadily towards classification as a clinical stage drug development company, with the filing of an Investigational New Drug (IND) application for BNC105 expected to be filed with the US Food and Drug Administration in October 2007. Once approved, Bionomics would then be in a position to commences a Phase I/II trial early in 2008.

How BNC105 works

BNC105 is a potential cancer treatment that works by disrupting tumour blood vessels. BNC105 can be placed within the tubulin binding class of cancer drugs.

Tubulin is a protein that forms together (polymerises) with other tubulin proteins into microtubules. These microtubules are a key component of a cell's skeleton (cytoskeleton). However, microtubules have a number of other functions including controlling the formation of mitotic spindles, which are a machinery used in the process of cell division.

Drugs such as paclitaxel, docetaxel and vincristine stop polymerisation, which leads to changes in the numbers of microtubules. Vascular disruption agents (VDAs) such as BNC105 interfere with the dynamics of tubulin. When these compounds target the endothelium cells that line the blood vessels that feed tumours, the effect is to cause the cells to change shape from thin, flat and plate-like, to large and more rounded. As they balloon out, they restrict blood flow in the tumour, resulting in necrosis or cell death, and then tumour decrease or elimination.

Merits of BNC105

What makes BNC105 a potentially attractive cancer drug is that it can offer, as a recently designed molecule, a fresher patent life, and from the basis of pre-clinical animal studies conducted by Bionomics, an improved side effect profile. In the field of VDA drugs there are small number of competitors, with the BNC105 appearing to offer a much wider therapeutic treatment window (20 times) than the most advanced drug in the class, CA4P. BNC105 was derived from CA4P by original inventive modification. One issue with CA4P is a dose limiting toxicity relating to atrial fibrillation. CA4P is currently in a Phase III trial.

From a manufacturing point of view, BNC105 is also reasonably simple to make requiring six manufacturing steps, with the final two under GMP.

BNC105 Trial Design

Bionomics has outlined what a Phase I/II trial of BNC105 *might* look like. The trial will be run as an open label study, selecting end-stage patients with low life expectancy who have imagible tumours. The company anticipates enrolling up enrol up to 35 patients over twelve months from three sites in Melbourne.

To more effectively gauge an appropriate dose, the trial is likely to start with a one patient cohort, to whom escalating doses are administered when efficacy is noticed. This approach should allow the clinical investigators to switch all cohorts to an effective dose sooner, with a larger number of patients providing relevant safety (and possibly some efficacy) data more rapidly.

This trial design is similar to a steadily emerging approach in clinical trials called adaptive clinical trial design. It is an approach in which the data is assessed during the trial and is used to change the direction of the trial. The approach is sometimes called 'play the winner' trials or response-adaptive trials. However, in the case of the proposed BNC105 trial, it is more a case of being an adaptive dose finding study.

BNC105 Program Cost

To date, Bionomics has spent approximately $4 million on the BNC105 program. This has included manufacturing costs, GLP toxicology and non-GLP toxicology studies. The company holds $12.8 million cash, which should be sufficient for the company to progress through the Phase I/II study, which it estimates will cost $2 million.

Corporate Evolution

Bionomics commenced a transformation from a gene discovery company into a broader based drug discovery and development business in July 2005 when it acquired **Iliad Chemicals,** a drug discovery company that originated from the **Australian National University**. Bionomics paid an initial $9 million for Iliad, and must pay another $3 million (through the issue of another 13.6 million bonus shares at 22 cents each) when a drug candidate from the Iliad asset base commences a Phase I trial. Should the bonus shares be issued (for which there is a strong likelihood), then the merger between the two firms will have been effected on an almost 1:1 basis.

The company has also rebuilt itself at the board level, with none of the company's board members from its IPO in 1999 remaining (although CEO Deborah Rathjen was appointed Managing Director in June 2000).

The company also has three other projects underway, with its BNC210 anxiety drug moving out of the pre-clinical stage and being made ready for the clinic. This drug candidate came about through the application of drug design technology developed by Iliad Chemicals.

Assessment

Bionomics is capitalised at $69 million. At its current price, Bionomics looks to be fairly valued given that it has no drug candidates in the clinic.

Bioshares recommendation: **Speculative Hold Class A**

Management Changes at BioDiem

Biodiem (BDM: 25 cents) made some management changes this week, with its long serving CEO, Tom Williams, moving to the position of Chief Operating Officer and its young board member, Andrew O'Brien, installed as an interim CEO. It's a surprising move given O'Brien's lack of management experience. O'Brien has an investment banking background and most recently was brought in to attract funding to another biotech, Prima Biomed, as a consultant, without success.

Biodiem has around six months funding available. Results from its Phase II study, in 188 patients with diabetic macular odema, are due to be released in November. The current management changes are surprising not only because of the candidate, but also that the change was not effected with a permanent CEO installed who has direct biotech commercialisation experience.

Biodiem is capitalised at only $13 million with two attractive development programs underway, one with **Akzo Nobel** for a live attenuated influenza vaccine, and the second with BDM-E, a peptide for the treatment of eye diseases. However, similar to Prima Biomed, if the company does not have the capacity to commercialise those projects, then the technologies may need to find another home, which may well be O'Brien's mandate.

Bioshares recommendation: **Reduce exposure**

Avexa Reports 24-week Data

Avexa (AVX: 62 cents) delivered some very positive 24 week data from its Phase IIb trial with its lead compound apricitabine. At 24 weeks, HIV levels in the blood had been reduced to undetectable levels in 80% of patients. There was also a proportional increase in CD4 cells in patients over the control arm in the two different dose arms receiving Avexa's apricitabine.

Avexa is in the process of planning a Phase III trial. The company should have a high probability of success in this trial given the success of recent HIV drugs that have entered Phase III trials although the difficulty in completing such a trial on time should not be underestimated.

The company is currently capitalised at $252 million with $76 million in cash at June 30. Based on our estimated peak sales of US$300 - US$350 million, and with a gross royalty estimated at 30% if the compound were licensed out at the end of successful Phase III trials, our valuation for the technology is between 55 - 60 cents per share.

Avexa is well positioned to leverage from its strong position to strengthen its clinical pipeline in an area where it has developed considerable expertise, that of HIV therapeutics. While the chance of success is high with the lead program, the majority of the value attributed to this company is for its lead program, which we suggest has an 80% chance of bringing the product to market from this point.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares Model Portfolio (7 September 2007)

Company	Price (current)	Price added to portfolio
Acrux	$1.40	$0.83
Alchemia	$0.84	$0.67
Biota Holdings	$1.74	$1.55
Circadian Technologies	$1.22	$1.45
Clinuvel Pharmaceuticals	$0.75	$0.66
Cytopia	$0.57	$0.46
Chemgenex Pharma.	$0.96	$0.38
Optiscan Imaging	$0.40	$0.35
Peplin	$0.89	$0.83
Peptech	$1.27	$1.31
Pharmaxis	$4.18	$3.15
Phylogica	$0.30	$0.42
Probiotec	$1.22	$1.12
Progen Pharmaceuticals	$3.80	$3.52
Sirtex Medical	$3.90	$3.90
Starpharma Holdings	$0.36	$0.37
Sunshine Heart	$0.17	$0.19
Tissue Therapies	$0.45	$0.58
Universal Biosensors	$1.30	$1.23

Portfolio Changes – 7 September2007

IN:
Sirtex Medical has been added. See article om page 2.

OUT:
Biodiem has been removed from the portfolio, in line with our recommendation to Reduce exposure to the stock. See article above.

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, BioMD

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	$950	6-10 email addresses

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