ISSN 1443-850X

In this edition...
Invariably biotech companies change their business models, re-structure their asset base, replace old investors, change their place of business and ditch the CEO. Sometimes 'the change', whatever it is, is not picked up by the market, especially if the company has a low key approach to communications. This could well be the case with one of the sector's oldest companies, Circadian Technologies, which is more and more looking like a straight up and down drug developer, and not an investment company. The company's significant $21.5 million investment in, and ownership (67%) of Vegenics, is the reason why it might be time re-think Circadian.

The editors
Companies covered: BNO, BTC, CIR, CYT, NDL, NEU, PTD

	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)	2.2%
Cumulative Gain	**234%**
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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Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 218 (1 June 2007)
ISSN 1443-850X

Bioshares

1 June 2007
Edition 218

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

Time to Consider Vegenics as the 'Main Game' at Circadian

A year has passed since Circadian Technologies (CIR $1.45) co-founded Vegenics with the **Ludwig Institute of Cancer Research** (LICR) and **Licentia Ltd**, the technology transfer arm of the **University of Helsinki** in May 2006.

Vegenics has secured the global rights to the VEGF-C and VEGF-D patent estate including a receptor (VEGFR-3) and work associated with these growth factors, from the LICR and Licentia. In all, a total of 35 patent families gave been assigned to Vegenics. It has also been assigned licenses awarded by the LICR to **Ark Therapeutics**, **Imclone Systems** and **Lymphatix**.

Initially, Circadian held a 50% stake in Vegenics, after investing $4 million. Then in August last year Vegenics negotiated a deal with **CoGenesys** to gain access to that company's patents in the VEGF-C and VEGF-D space in exchange for an upfront milestone payment and royalties from sales of any products. Circadian has since invested an additional $17.5 million into Vegenics and now owns 67% of the company.

What is VEGF?

Vascular endothelial growth factors, of which there are six types (VEGF-A, VEGF-B, VEGF-C, VEGFD, VEGF-E and PIGF) are involved with the growth of new blood vessels (angiogenesis). Stimulating VEGF offers the potential to develop therapies for the treatment of heart disease amongst other uses.

Inhibiting VEGF (anti-angiogenesis) has been shown to play a crucial role in inhibiting cancer cell growth. **Genentech**'s Avastin, a VEGF-A inhibitor has arguably become one of the most successful and important drugs to be launched in the last three years.

'Frozen' IP...a nightmare

The intellectual property estate around VEGF- C & VEGF-D has been a nightmare to work through in the past because of locked positions that several competing groups had in this space which had been in patent litigation for over eight years with each other. What Circadian has been able to achieve is to negotiate with different commercial groups around the world to bring full rights to most, if not all of these assets into the one commercial vehicle. Circadian has in effect, acted as a circuit breaker to resolve a commercial impasse and this action may bring handsome rewards to not only Circadian but also to some of the originators of the IP estate.

The rights to this patent estate was divided between the Ludwig Institute for Cancer Research (in New York) and a spinout company from **Human Genome Sciences**, CoGenesys Inc. It also included the commercial arm of the University of Helsinki, Licentia Ltd, which had been collaborating with LICR.

Vegenics' Leading Asset

Ark Therapeutics Product

The leading asset for Vegenics is a gene therapy product being developed by **Ark Therapeutics** in the UK. Vegenics is now the assigned licensor of VEGF intellectual property licensed to Ark Therapeutics in return for a mid digit royalty stream from any future sales.

Cont'd over

The therapeutic being developed by Ark Therapeutics looks attractive. It is designed for use in patients who undergo regular kidney dialysis and have been surgically implanted with a shunt that allows easy access to veins for dialysis. These patients undergo dialysis twice a week, with two needles required to be injected, one to extract the blood and the other to return after filtering.

The problem with implanting shunts is that blood vessels fully grow over at the implant site within three months. This requires another shunt to be implanted. Patients could receive up to 40 shunts before the patient would require a kidney transplant because of a lack of access points for dialysis.

The Ark Therapeutics product, called Trinam, utilises a gene therapy approach, where a gene is delivered to a biodegradable cuff around the vein at the shunt site using an adenovirus vector. This allows the VEGF-D protein to be expressed and delay the overgrowth of the muscle cells in the wall of the blood vessel. This is a clever way of dealing with problems associated with gene therapy, as the gene delivery is localised to the tissue around the shunt, and does not enter the blood stream.

While there are no gene therapy products approved to our knowledge, this localised approach received quick clearance from the FDA Recombinant DNA Advisory Committee to proceed with trials. Interim results from the Phase II trials have shown an improvement in shunt survival of between five to 13 months. No systemic traces of the therapy have been detected in any of the patients, which is a positive result.

A Phase III trial is due to start in mid-2007 in over 200 patients and is expected to take 18 months to complete. Peak sales of US$270 million are being forecast for the therapy, which would result in an annual royalty stream of around $20 million, assuming a royalty stream of 6% to Vegenics.

This royalty stream assumes a 25% penetration of the market and could be higher as there are no competing products available. There is also a distinct possibility that if the technology works it could be applied to other uses, such as preventing restenosis in coronary stents.

Vegenics' patents for this technology expire between 2017-2019 although could be extended in the US and Europe by about three years.

Other Assets

Through the formation of Vegenics, the company has not only secured rights to the patent estate over VEGF-C and VEGF-D and VEGFR-3, and but has gained other commercial assets. These include a license agreement in addition to an option to develop an existing VEGF-C antibody developed by CoGenesys, which also brings with it (as we understand) access to proprietary antibody discovery and engineering technologies developed by **Cambridge Antibody Technologies** (CAT), inherited from Human Genome Sciences. With CAT now part of AstraZeneca, fresh access to CAT's antibody technologies is essentially no longer possible. The 'CoGenesys' antibody is in late stage preclinical development.

Cont'd over

Vegenics Assets Table (CIR has 67% interest in Vegenics)

Asset	Licensee/Licensor	Product	Indication or disease	Status	Terms (eg royalties)	License Scope
Context: There are six different forms of the VEGF growth factors; VEGF also known as VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E and PIGF. There are three known receptors, VEGFR-1, VEGFR-2 and VEGFR-3. Genentech has rights to certain inventions, including monoclonal antibodies, pertaining to VEGF-A and VEGF-E CSL, through its acquistion of Zenyth (ex Amrad) has gained cross-licensed rights with the LICR to VEGF-B IP Imclone Systems has rights to certain inventions, including monoclonal antibodies, pertaining to VEGF-R1 and VEGF-R2 Regeneron has rights to certain inventions, including a VEGF, PIGF fusion protein, and peptides Vegenics is the assignee to various inventions covering VEGF-C, VEGF-D and VEGFR-3 from the LICR, Licentia and CoGenesys						
VEGF-D gene	Ark Therapeutics (original license from LICR ass. to Vegenics)	Trinam (gene therapy product; VEGF-D gene in adenoviral vector)	To prevent blood vessels blocking in kidney dialysis patients who have undergone vascular access graft surgery.	Phase III (in USA)	6% (est.)	Non-exclusive
VEGF-R3 antibody	Imclone Systems (original license from LICR ass. to Vegenics)			Pre-clinical		Exclusive
Research antibodies (VEGF-C, VEGF-D)	Being sold by Chemicon, R&D Systems			Marketed		
Soluble receptor VEGF-R3	Not licensed					
Peptides to VEGF-C, VEGF-D	Not licensed					
VEGF-C antibody (from CoGenesys)	Vegenics has an option on this mab from CoGenesys (ex-Human Genome Sciences)			"Late stage pre-clinical" (completed pre-clinical safety and tox studies)	Vegenics paid an upfront fee, with milestones and royalties to follow on success	
VEGF-D antibody	Not licensed			Optimisation program with Evogenix		
VEGF-C antibody	Not licensed			To enter pre-clinical		

Another potentially important asset is an antibody that binds to the VEGFR-3 receptor, which is licensed to **Imclone Systems**. Imclone, which is well known for developing the monoclonal antibody Erbitux, has antibody programs in respect of VEGFR-1, VEGFR-2 as well as VEGFR-3. Imclone has produced a fully human antibody antagonist to VEGFR-3 termed hF4-3C5. This mab is in pre-clinical development, and if it is selected for clinical trials, then the Vegenics line-up of partnered programs in the clinic will be boosted. Vegenics' key assets are listed in the table on the previous page.

Investment Considerations

Circadian has been categorised to date by *Bioshares* as an investment company, that acted both as an incubator of very early stage projects and investor in more mature assets, such as the **Amrad Corporation** (which later changed its name to Zenyth Therapeutics). With a much more significant holding in Vegenics, it now may be time to treat Circadian as a fully-fledged drug developer with the potential to develop and outlicense a suite of its core VEGF technologies. Unlike many previous investments (although Amrad is an exception), Circadian has invested a relatively large sum in Vegenics, a cumulative total of $21.5 million. On that basis alone, Vegenics represents a major change of strategy for Circadian. In addition, Circadian, also holds a number of investments that it can liquidate at opportune moments to fund its main focus in Vegenics. At 16 April, Circadian had cash assets and assets in marketable securities (in Avexa, Antisense Therapeutics, Metabolic Pharmaceuticals and Optiscan Imaging) of $56 million.

When compared with other Australian listed or soon-to-list biotech companies with Phase III programs (see table below), Circadian, with its significant interest in Vegenics, is ranked relatively low by capitalisation. The majority of these companies are capitalised at greater than a $100 million, with exception of Neuren Pharmaceuticals which is probably being marked down because of its current weak funding position, and Halcygen, which its capitalisation is an indicative figure based on its IPO price. And while the top four companies by capitalisation (Pharmaxis, Progen, Clinuvel and Avexa) are all well funded, they all are managing unpartnered programs. In other words they are bearing significant program risk on their own behalf. In contrast, for two companies with partnered programs (Circadian/Vegenics with Ark Therapeutics and Acrux with KV Pharmaceuticals), that project risk and its related funding risk has been off loaded to a third party.

The assets that Vegenics has under its direct management are high quality with substantial potential. There exists the potential to develop at least three antibodies and a soluble receptor, with some of these probably to be developed as cancer therapeutics. There is also a market opportunity in the area of lymphodema, a disease in which VEGF-C is implicated. While it may be a small disease by market size, it may be an ideal disease to initially develop and launch an antibody drug into, and then progressively find new indications. Vegenics' immediate focus is to develop peptide and antibody antagonists to VEGF-C and VEGF-D. Other possible applications for the technology include the areas of eye diseases, inflammation, heart disease and wound healing. There is substantial potential to leverage the IP estate through out-licensing.

What also makes Circadian an attractive investment proposition is the company's capacity to raise funds. Should Vegenics require additional development capital beyond the current $18 million it has at present, then the pedigree and positive reputation of Circadian Technologies would be likely to see any necessary funds raised expeditiously and effortlessly.

Circadian is capitalised at $58 million. It had cash assets of $26 million in April, $30 million in listed investments (note 30% capital gains tax for these investments is payable on sale of securities) and has invested $21.5 million in Vegenics.

Bioshares recommendation: **Speculative Buy Class A**
(Circadian has been added to the Bioshares Model Portfolio.)

Australian biotechs planning, conducting or have completed Phase III clinical trials, including partnered programs

Company	Compound	Disease	Progress	Partner/licencee	Cap'n	Est. royalty rate
Pharmaxis	Bronchitol mannitol powder	Cystic fibrosis, bronchiectasis	Both trials underway. Bronchiectasis fully recruited.	None	$607 M	n/a
Progen Pharmaceuticals	PI-88	Liver cancer	1000 patient trial to begin this year	None	$337 M	n/a
Clinuvel Pharmaceuticals	CUV1647	Light associated skin disorders	250 patient PLE trial started. 70 patient trial in EPP due to start.	None	$302 M	n/a
Avexa	Apricitabine	HIV	1000 patient trial to begin this year	None	$250 M	n/a
Acrux	Evamist	Transdermal HRT, supergeneric	Completed. Positive results. FDA approval due 2H 2007	**KV Pharmaceutical**	$199 M	10%**
ChemGenex Pharmaceutricals	Ceflatonin	CML	Undergoing 81 patient Phase I/II registration trial	None	$175 M	n/a
QRxPharma	Opiod combination	Chronic pain	2 x 660 person trials to begin	None	$143 M	n/a
Circadian Technologies (Vegenics - 67% int.)	Trinan	Prevent blockage of haemodialysis grafts	200+ trial to begin 2H 2007	**Ark Therapeutics**	$58 M	6%**
Neuren Pharmaceuticals	Glypromate	Neuroprotectant	Commenced 600 patient trial this week.	None	$57 M	n/a
Halcygen*	Super generic of intraconazole	Antifungal	120 patient PK study only	None	$38 M*	n/a

** Upon listing next month ; ** estimated*

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Registration is now open. Full conference details are available on our website
http://www.bioshares.com.au/thredbo2007.htm

Demand for Biologic Drugs and Technologies is the Key to Understanding Peptech's Bid for Evogenix

Peptech (Ptd: $1.55) has received a cold response from investors following the announcement of its proposed merger with **Evogenix** (EGX: 90 cents). Peptech is an antibody development company with a swag of cash ($188 million) and a further US$75 million in royalty income expected over the next few years. Evogenix is an antibody optimisation and humanisation company and its share price has increased three-fold since listing at 25 cents a share in August 2005.

The merger is a great fit for both companies. For Peptech, it delivers the company a number of antibody development programs and a synergistic humanisation technology to its own Synhumanisation technology. It also contributes to creating a fully integrated antibody development group.

For Evogenix, it allows the company (as absorbed) to take its in-house development programs further into the clinic. And through continuing to assist smaller biotechs with their antibody drug lead requirements, it potentially brings in a steady stream of development programs from those companies into Evogenix that the merged entity could fund.

Ever since it was discovered that Peptech was sitting on a valuable royalty income stream from its TNF patents, there have been arguments about what the company should do with the excess cash. There are groups that treat the company as a standard industrial company and this mindset doesn't belong in biotech. When Peptech invested $10.7 million into **Domantis** in December 2005, it was criticised for not returning funds to shareholders and for making an irresponsible investment in a speculative investment. When it was announced that Domantis was to be sold to **GlaxoSmithKline**, Peptech was then criticised for losing a valuable drug development asset, although the company made a gain of $138.2 million from a $40.2 million investment.

The Peptech board and management has earned the credit of being an astute manager of its drug development and cash assets. The proposed merger with Evogenix will make the merged entity an attractive takeover acquisition over the next two years in a sector that has stunning investment appeal for very clear reasons.

Antibody Drugs - Very Successful Products!

The first is that antibody drugs have become exceptionally successful commercial products over the last five years earning tens of billions of dollars in revenue a year. Almost half of all drugs being approved by the FDA are protein-based drugs. But even more importantly, these attractive investment considerations are amplified by the fact that antibody drugs are currently not subject to generic competition. Where small molecule drugs might offer patent protection for 10 years, antibody drugs are safe from generic competition giving the companies indefinite market protection, or at least until an improved version comes along or other companies complete Phase I, II and III trials once the drugs are off patent. And while debates ensue about biogenerics and biosimilars, the issue remains at that level, a debate.

These are the reasons we have seen a tide of antibody company acquisitions over the last three years as traditional small molecule pharmaceutical companies, that are losing massive sales in proprietary small molecule drugs coming off patent, scramble to get exposure to this hot area.

The Acquisition Trail...

These acquisitions include: **Cambridge Antibody Technology**, which was acquired by **AstraZeneca** for US$1.3 billion in May last year. AstraZeneca has since made a bid for **MedImmune** for US$15.2 billion for access to that company's antibody drug Synagis, which had sales last year of US$1.1 billion (the acquisition of the Flumist vaccine was also an important asset for the company giving it access to the accelerating interest in vaccine products); **Amgen** acquired antibody specialty company **Abgenix** for US$2.2 billion in late 2005 and then protein technology company **Avidia** last year for US$290 million; **Merck** acquired two antibody companies last year, **Glycofi** for US$400 million and **Abmaxis** for US$80 million; **GlaxoSmithKline** acquired single domain antibody group **Domantis**, as mentioned above, for US$470 million last year.

And not to be looked over, **CSL** last year acquired **Zenyth Therapeutics** to broaden its biopharmaceutical assets and skills base. We suspect CSL will look to significantly expand its biopharmaceutical focus, with a major acquisition in the next 12 – 18 months of a biologic therapeutic business, potentially as large as $5 billion. There are also two Australian antibody therapeutic companies expected to list this year, including one whose listing will be managed by one of the leading biotech broking firms.

AstraZeneca's '25%' goal

AstraZeneca has stated that its goal is for 25% of its new drug candidates to be biological therapeutics by 2010 and it continues to look for more biopharmaceutical acquisitions. By 2009, Peptech plans to have one Phase III antibody program underway (with PNO621 recently commencing Phase I trials), one Phase II antibody program, and two Phase I antibody clinical programs which, together with its antibody engineering platforms, should make it a very attractive asset as major pharmaceutical groups continue to buy into this sector.

If the merger proceeds, the combined entity will have a capitalisation of $361 million with $175 million in cash and up to a further $100 million in royalty income from the TNF patents.

Bioshares recommendations**:**
Peptech: **Buy**
Evogenix: **Speculative Buy Class A**

Alchemia – Sufficient data to Progress with HyCAMP program?

Alchemia released full results from its Phase II study of HyCAMP in 80 patients with metastatic colorectal cancer who had failed 5-FU chemotherapy. Specifically, the trial was comparing use of the chemotherapy drug irinotecan against HyCAMP, which is a combination of Alchemia's hyaluronic acid with irinotecan. The use of hyaluronic acid is thought to help target chemotherapeutics such as irinotecan to cancer cells, thereby reducing side effects and improving treatment outcomes.

In our view it was a mixed result for Alchemia. The primary endpoint was to achieve a reduction in diarrhoea in patients undergoing treatment. The overall incidence of diarrhoea was much lower than expected, which prevented a statistically significant result being achieved. However, what was confusing was that more patients on HyCAMP experienced grade 3 or 4 diarrhoea during cycles 1 and 2 (19.5%) than in the irinotecan arm (5.7%).

There was some positive data relating to disease control. This is measured by complete response (there was none in either arm), partial response and stable disease. In the HyCAMP arm, 75% of patients achieved disease control versus 45% in the control (irinotecan) arm. The trial indicates that HyCAMP does allow patients to handle more treatment cycles, with 34% of patients on HyCAMP able to complete the full eight cycles compared to 14% in the control arm. The mean progression free survival benefit was statistically significant, 2.8 months extra, from 2.4 months in the control to 5.2 months in the HyCAMP arm. The median overall survival estimated was only an additional 1.8 months, from 8.4 months in the control to 10.2 months in the HyCamp arm. And there was conflicting data from measurement of the CEA (carcinoembryonic antigen) biomarker, with the highest reduction seen in the control arm. HyCAMP was found to generate a statistically significant benefit as measured by time to treatment failure.

The HyCAMP technology was acquired by Alchemia from Meditech Research in 2006. The former CEO of Meditech Research, Ian Nisbet, who can be considered an experienced oncology drug developer, has previously indicated that in oncology as a rule of thumb, Phase I results are not significant, and you take the Phase II results and halve the effect seen which should give you a rough estimate of what you might see in a larger Phase III study.

HyCAMP is obviously helpful in enabling patients to undergo more rounds of chemotherapy with irinotecan but the added benefit as measured in progression free survival was only 2.8 months and a median survival benefit of 1.8 months.

This data appears to deliver a marginal end benefit to the patients. At least one additional trial will be required to be conducted in the US, with a greater number of patients, which reflects a greater number of patient sub-types, to gain FDA approval. Whether a potential partner is willing to take on this project on is unknown. With the full results now available, it is unlikely Alchemia will continue development of the HyCAMP in-house unless it can raise further funds. Whether it builds an in-house oncology clinical drug development team is another issue. The program may be attractive to **Pfizer**, which currently sells irinotecan, with that drug due to go off-patent in 2008.

Summary

There was some positive data to emerge from this trial although it could have been better and more consistent. Further trials will be required before this drug gets to a favourable position in front of the US FDA. Whether the data gives Alchemia or a potential partner the confidence to progress the compound further remains to be decided.

Alchemia is capitalised $151 million with $13.6 million in cash at March 31 this year.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Biotech Capital Alters Strategy with Neurodiscovery Investment

Biotech Capital (BTC: 40 cents) has continued its foray into the listed biotech investment space by taking a stake in **NeuroDiscovery** (NDL: 20 cents). Biotech Capital is a listed biotech venture capital fund with $40 million in assets. Biotech Capital will invest $1.5 million in NDL as part of a $3.25 million capital raising by NDL at 17 cents per share.

To Biotech Capital, NDL represents an investment with potentially significant upside from its portfolio of pain treatment drug candidates and with the downside protection of a profitable service business in NDL, **NeuroSolutions**, that arguably could support the current valuation of NDL on its own.

NeuroDiscovery's Subsidiary

NDL has 100% ownership of NeuroSolutions, which conducts electrophysiology testing. NeuroSolutions is a profitably standalone business that this financial year should generate sales of around $2 million. The business is based in Warwick, just outside of London.

Following this capital raising, NDL will be capitalised $11.6 million (at 20 cents per share) with an estimated $4.5 million in cash.

Drug Development Assets

NDL's lead drug candidate, NSL-043, is being developed for the treatment of neuropathic pain. The rights to this compound are shared equally with **Sosei Group Corporation**, a Japanese biopharmaceutical company. This compound had previously progressed to a Phase III clinical trial in inflammation although failed because of poor efficacy.

NeuroSolutions has tested the compound in several preclinical models and found the drug to be very effective in those models.

Phase I Trial Commences of NSL-043

This week, Sosei Corporation commenced a 40 person Phase I safety study with the compound, which is required to be conducted even through its safety profile has been well documented in over 500 people to date. The drug candidate is dosed orally. The Phase I trial is being conducted in the UK with Sosei's development group for this program is based in Cambridge, UK.

The rewards for an effective neuropathic pain drug are very high, with the market estimated at over US$1 billion. There are few effective drugs for this indication, with the leading drug, gabapentin (used also for treatment of epilepsy) being the drug of choice, although only effective in between 30% - 50% of people suffering neuropathic pain.

A second Phase I trial (multiple escalating dose) should be completed this year ahead of a key Phase II trial in 2008. Critical results from the Phase II trial are due, at the earliest, in the first half of 2009.

Other Assets

NDL has three other drug discovery and development programs and assets in the area of pain. The company uses the expertise of its drug screening team at NeuroSolutions in Warwick to help select and optimize drug leads. Its second program is testing a natural product from Peru (NSL-101) that should have a high probability of showing efficacy in clinical trials later this year.

A Phase II trial in up to 50 patients undergoing wisdom teeth extraction is expected to begin in the next three months. NSL-101 is a topical drug candidate and has a history of indigenous use in Peru. If this trial delivers a successful result, NDL will seek to out license the product.

Summary

Biotech Capital is an experienced investor in the biotech sector. Its latest investment is Neurodiscovery supports that fund's move to invest in companies in the sector that either have a revenue generating business or are moving through the clinical development of drug candidates. In this case, Biotech Capital gets both which makes it a very appropriate decision for that company. It's also a solid validation for NeuroDiscovery, attracting Biotech Capital to its register, and strengthens its funding position. At a capitalization of $11.6 million, Neurodiscovery presents an appealing, speculative investment consideration.

Bioshares recommendations
Biotech Capital: **Speculative Buy Class A**
NeuroDiscovery: **Speculative Buy Class B**

Bioshares

Bioshares Model Portfolio (1 June 2007)

Company	Price (current)	Price added to portfolio
Acrux	$1.39	$0.83
Alchemia	$1.07	$0.67
Biodiem	$0.32	$0.29
Biota Holdings	$1.72	$1.55
Circadian Technologies	$1.45	$1.45
Cytopia	$0.67	$0.46
Chemgenex Pharma.	$0.94	$0.38
Optiscan Imaging	$0.44	$0.35
Neuren Pharmaceuticals	$0.44	$0.70
Peplin	$0.83	$0.83
Peptech	$1.55	$1.31
Phylogica	$0.39	$0.42
Probiotec	$1.15	$1.12
Sunshine Heart	$0.19	$0.19
Tissue Therapies	$0.61	$0.58
Universal Biosensors	$1.23	$1.23

Portfolio changes

Circadian Technologies and Universal Biosensors have been added to the portfolio.

Stock Briefs

Bionomics (BNO: 29 cents) Selects Anxiety Drug Candidate

Bionomics has selected a compound, BNC210, that it will submit to a pre-clinical development program, with a goal of developing a drug to treat anxiety. The company is attempting to develop a compound that is non-sedating, fast-acting, is administered orally once a day, does not impair motor function, and has a minimum set of interactions with other drugs. Bionomics' intent is to target a class of drugs that are limited in their benefit because they impair memory, cause nausea, drowsiness, sexual dysfunction, have addictive properties and take a long time to act. The company filed a provisional patent over BNC210 in October 2006.

The company's next steps will be to commence scale-up manufacturing studies, and commence formal pre-clinical studies. On a parallel track the company will commence partnering activities as a strategy to support the further clinical development of BNC210. Given the company's limited cash resources – it held cash assets of $5.4 million at March 31, 2007 – this would appear to be a prudent strategy.

Bionomics is a capitalised at $55 million.

Bioshares recommendation: **Speculative Buy Class A**

Cytopia (CYT: 66.5 cents) Appoints CYT997 Clinical Advisory Board

Cytopia has announced the appointment of a four person clinical advisory board to support the Phase II development of CYT997, a cancer drug candidate that works by disrupting cancer blood vessels. Members of a clinical advisory board should be well placed to advise on the discussions with the FDA, design of trial protocols and the selection of clinical trial sites. They may also be able to stimulate interest in a candidate drug amongst oncologists or other specialty physicians. Several of the clinical advisory panel also emanate from clinical research organisations.

There are only a few other Australian listed companies that have established advisory boards that have a clinical, rather than scientific orientation, including **ChemGenex** and **Peplin**. The appointment of a clinical advisory board could be interpreted as positive and clear signal of the confidence the company has in CYT997. It should also be seen in the context of another recent announcement by Cytopia, in which it said that two patients who participated in a Phase I trial of CYT997, were continuing to receive CYT997 under the Commonwealth Government's Special Access Scheme. The scheme allows unapproved medicines to be supplied on a special needs basis.

Cytopia is a capitalised at $49 million and holds estimated cash assets of $15 million.

Bioshares recommendation: **Speculative Buy Class A**

Neuren Pharmaceuticals (NEU: 43.5 cents) Commences Phase III Trial

Neuren Pharmaceuticals has reached an important milestone with the commencement of its Phase III study of Glypromate. This is marked by the first dosing of Glypromate, a compound that is being evaluated for its ability to reduce cognitive impairment in patients that have undergone coronary artery bypass graft surgery or cardio-pulmonary bypass surgery. The trial will enrol up to 600 patients across 24 sites, with the trial expected to conclude at the end of 2008. The primary endpoint of the trial will be the change in baseline in a composite cognitive score and the change in the comparative levels in the activities of a daily living composite score.

Neuren is a capitalised at $57 million and held cash assets of approximately $6.4 million at March 31, 2007. The company's cash position is of some concern.

Bioshares recommendation: **Speculative Hold Class A**

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

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