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In this edition...
It has been a great week for Australian companies working in the cognitive function space. Prana Biotechnology posted positive results from its Phase II Alzheimer's trial and will now seek to find a development partner. And Cogstate and Neurodiscovery have seen a stepped increase in the need for their respective services.

We also include a private company profile on Xenome, again a company operating in the CNS space, which may be of further interest later this year as it builds momentum on the way to an IPO.

The editors
Companies covered: CGS, NDL, PBT, Xenome

	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)	-32%
Cumulative Gain	**121%**
Av Annual Gain (6 yrs)	**26.8%**

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

Prana Biotechnology PBT-2 Trial Results Continues Run Of Positive Phase II Studies

Australia has had an above average record in delivering success in Phase II clinical studies over the last two years. **Alchemia**, **Peplin**, **Pharmaxis**, **Chemgenex Pharmaceuticals**, **Clinuvel Pharmaceuticals**, **Progen Pharmaceuticals** (in liver cancer) and **Avexa** have all delivered positive Phase II trial results over this period with only **Biodiem**, **Metabolic Pharmaceuticals** (in two trials) and **Progen Pharmaceuticals** (in prostate and lung cancer trials with PI-88) having failed at the Phase II stage of development. This week another Australian biotech was added to the success list of companies: **Prana Biotechnology** (PBT: 50 cents), reported positive results in its Phase IIa trial of its small molecule compound PBT-2 in patients with early Alzheimer's disease.

The trial was designed to assess the drug in three main performance categories: safety, efficacy as measured by biomarkers in the blood stream and cerebral spinal fluid (CSF), and efficacy as measured through changes in cognitive performance.

PBT-2 Phase II Results

On all three measures, there was some indication that the drug candidate, PBT2, had a positive outcome. The compound was seen as being safe and tolerable, which was a major outcome given the safety concerns over the predecessor compound, PBT1, which was halted prior to conducting Phase II studies. There was a marked change in the amyloid-beta (Abeta) 42 levels in the CSF, being 12.8% lower than in the placebo group at the end of the trial, which was a statistically significant result (p=0.006). And in two measures of cognitive function there was an improvement in the patients on the highest dose (250mg) which was statistically significant (p=0.028 & 0.005).

There was a dose related effect on Abeta 42 levels in the CSF that was statistically significant (p=0.02) although the changes in the Abeta levels in the 50mg dose group were not reported.

Analysis

Overall it was an excellent result for Prana. But there are some points to consider. This was a small trial with only 78 patients divided into three patient subsets: placebo, 50mg dose and 250 mg dose. To get the drug approved, it is likely that this compound will need to be tested in several thousand patients.

Safety and Abeta CSF levels good

The safety result is good. The reduction in Abeta 42 levels in the CSF was impressive. It was a decisive approach by the company to measure changes in the CSF which surrounds the brain as it is the closest point to the brain where changes in biology can be accurately measured. Enrolling patients who agreed to endure a lumbar puncture twice in the trial would have been a very challenging task and the participation of the patients in this trial should be gratefully acknowledged by investors.

Cont'd over

That there was a dose dependency result between the two dosage groups was very positive although complete information would have been more beneficial to investors. There were no changes in Abeta levels in the blood stream which may require further explanation or investigation.

Selection of cognitive test parameters – a matter of contention

There was no beneficial change as measured by the ADAS-cog test. This has been the standard used historically by the FDA to measure the efficacy of Alzheimer's drugs for each of the four Alzheimer's drugs on the market. However the ADAS-cog test is a broader measure of cognitive function and a newer and more sensitive test, called the Neuropsychological Test Battery (NTB), is gaining popularity as a more helpful tool to measure drug efficacy in this disease, particularly where the onset of disease is less advanced. Prana used four of the nine measures that comprise the NTB test that was developed by **Elan Pharmaceuticals**. In two of those measures, the results showed that PBT2 delivered a statistically significant improvement in cognition. In the other two measures, there was not a statistically significant difference (and whether there was any difference over the placebo is unknown because of the lack of data reported).

The trial was run over a three month period. *Bioshares* view was that the trial was unlikely to achieve any measurable improvements in cognitive function. That there was a significant change in two parameters is encouraging.

The Elan Pharmaceuticals Alzheimer's program – why it's important

There are two reasons why the Elan Pharmaceuticals' lead Alzheimer's program is important to Prana. Firstly, the lead compound is an antibody drug that seeks to attack the same target as PBT2, that being Abeta levels. Elan Pharmaceuticals has recently moved into a Phase III study for Alzheimer's with its lead compound, bapineuzumab, which is delivered as an IV infusion. The company will conduct four Phase III trials in about 4,000 people with mild to moderate forms of the disease. That Prana's drug is orally available has significant advantages.

The second importance of this trial to Prana is that Elan is considering using the NTB platform it developed as the basis for primary endpoint outcomes for its Phase III trials. This is important because Prana's drug has been shown to be effective in improving two of the measures in the NTB test platform. If the NTB becomes an accepted testing regime for Alzheimer's disease, it will benefit Prana and other companies operating in this disease area.

Disappointing disclosure

What has been disappointing with this trial is the lack of detail that was reported. Only whether the results were statistically significant were stated, with the changes in all levels measured not being released. In the conference call following the announcement, the company did reveal that change in only one measure, that of Abeta 42 in the CSF, being 12.8% lower than the placebo group in the highest dose group. It is expected that the full data will eventually be included in a scientific publication but the level of detail was clearly lower than that reported by other drug development companies.

Coincidentally, another biotech company, **Allon Therapeutics** in Canada, reported positive results from its Phase IIa study on the same day in a trial in patients with a precursor to Alzheimer's disease. Full details were provided by that company on the changes in levels of any indicators tested, how the tests were performed and their meaning, together with probability levels on whether the result was statistically significant or not.

If the presentation of full data is important to scientific peers, it should not be assumed that investors and analysts are less interested in gaining a fuller account of the trial data that is available, similar to that released by other listed biotech peers.

Summary

The results released by Prana Biotechnology this week suggests that the development of its lead drug candidate PBT2 merits further development. The data was positive in the three key areas of safety, improvement in cognition and reduction in an accepted biomarker. However, as with most Phase II trials, a number of questions have not been answered in this trial.

To bring this drug to market will take at least five years, hundreds of millions of dollars in funding and testing in several thousand patients. A major pharmaceutical partner will be required and the company is seeking to complete a licensing agreement this year, which should be the preferred option for the company.

Prana is capitalised at $91 million (excluding 56 million options and warrants over shares) and $9 million in cash at the end of last year.

Bioshares recommendation: **Speculative Buy Class B**

Private Company Profile – Xenome Ltd

Xenome is a Brisbane-based privately held company that was founded in 1998. The company is looking to conduct an IPO in the nest 12 months or so. Xenome is noted for its development of the therapeutic drug candidate Xen2174, a peptide compound derived from a toxin that is a chemistry used by the marine cone snail to stun and paralyse its prey.

After Prialt (ziconotide), a similar contoxin peptide to Xen2174, and marketed by **Elan Pharmaceutical**, Xen2174 is the most advanced compound in development based on this cono-toxin technology. Prialt is approved for treatment of severe chronic pain in patients who are intolerant to other treatments.

Others conotoxin class drug compounds known to Australian investors, such as **Amrad's** AM336 (to which Xenome had rights) and **Metabolic Pharmaceuticals**' ACV1 have been withdrawn from development.

Like Prialt, Xen2174 has been developed for the treatment of pain. Xenome has completed enrolment in a Phase II trial, in which the compound has been evaluated as a treatment for cancer patents suffering chronic pain. The results of this study will be released in mid-2008.

A Phase II in post-operative pain is scheduled to commence in Q3 2008 and another Phase II trial is planned for Q1 2009 in patients with chronic pain. The randomised post-operative pain study will evaluate a single dose in around 200 patients following orthopedic surgery. This indication is interesting because of the role played by the anaesthetist in selecting and delivering analgesics during surgery and the amenability for intrathecal drug administration for certain pain drugs during surgery.

While both Xen2174 and Prialt must be delivered intrathecally (i.e. into the central nervous system via the spinal column) there are some important differences. Xen2174 is a modified analogue of a conotoxin, whereas Prialt is not modified. The modifications made to Xen2174 have improved its stability and made for better drug-like qualities.

For example, Prialt requires titration (a controlled infusion over several days) and it can not be given as a bolus injection, whereas Xen2174 can be delivered as a bolus injection or by pump. Xen2174 is a 13 amino acid molecule, whereas Prialt is a 25 amino acid molecule, conferring a cost of goods advantage to Xen2174

IND filing

The clinical development of Xen2174 is supported by a US FDA IND filing (June 2004), and is, as far as *Bioshares* can ascertain, the first IND filing ever achieved by a private Australian biotech company.

Xenome has a second compound in development, XenKappa. This peptide targets the kappa opioid receptor, a receptor involved in pain signalling pathways which has proven difficult to develop as a druggable target, because of off-target side effects. A US FDA IND filing for Xen-kappa is planned for late 2009. XenKappa can be delivered subcutaneously or intravenously. This is a marked difference from the intrathecal delivery required for Xen2174 and Prialt.

Current Shareholders

The major shareholder of Xenome is the **Queensland Biocapital Fund** (QBF), an investment arm of **Queensland Investment Corporation** (QIC). QBF/QIC currently holds a 65% stake in Xenome, followed by **Amylin** (14.5%), a US peptide drug company that has launched two peptide drugs onto the market and **Innovis Investment Partners**, a US-based VC firm with 6.7%.

The Amylin Partnerhip

Amylin invested in Xenome to gain access to Xenome's peptide library, which totals 2,500 compounds, significantly more than Amylin's 1,500 compound library of peptides with a different chemical profile. Amylin's objective is to screen Xenome's library for compounds that have potential therapeutic benefits in diseases such as obesity and diabetes.

Another benefit

Amylin made an equity investment (instead of a library access payment) in Xenome to ensure the company's viability while it continued through a difficult period. Xenome had struggled for a period under the management team that was in place following the departure of two well known investors, **Medica Holdings** (now **Cytopia**) and **Biotech Capital**, and the former CEO Tony Evans.

New CEO

The company recently appointed the well regarded Ian Nisbet to the position of CEO, which heralds a major step forward for the company, as Nisbet brings extensive small biotech and large biotech company experience to the firm. In addition to Nisbet, the company has appointed Wendy Martin as a US based Chief Medical Officer (CMO). Martin has had hands-on experience in developing ziconotide, while working at Elan Pharmaceuticals.

Comments

Xenome has had several challenges over the years, including management and funding issues, but with the flagging of an IPO to occur sometime in the next twelve months and the appointment of a new CEO, the real progress made by the company in developing a drug from a new class of pain medicines stands a greater chance of being recognised positively by a wider set of investors.

While intrathecal delivery is not the most common route of administration for pain drugs, the prospects for Xenomes's Xen2174 to compete with an improved set of attributes to those possessed by Prialt is an attractive investment feature.

Finally, the company's re-defining of itself as a peptide company (as opposed to a pain company), will broaden its investment appeal, although it must be said that the company has an important challenge in convincing Australian investors of the merits of peptide drug development.

Stock Briefs

Cogstate

Cogstate (CGS: 13 cents) has enjoyed buoyant conditions in its service sector this month. The company reported this week that it had quoted for $2.7 million of business in February alone and $5.8 million of quotes in this financial year to date. Given that the company generated revenue of $1.6 million only for the first half of this financial year, there may considerably better times ahead for the company. The level of business interest in the cognitive testing has certainly picked up for Cogstate although the quieter months on November and December last year explain some of the added volume in quoting this month.

However, the company is making ground towards becoming a more established player in this field. It is being seen more and more as a company with a very good product with some advantages over its competitors. The increased level of activity also suggests there is a growing interest in computerised cognitive testing as opposed to the traditional pencil and paper tests.

The existing quotes are likely to take two to four months to secure the contracts and the company may, as an estimate, win about half of the work it bids for. Of the nine companies it received interest from this month, five are new potential customers.

Receipts from customers to date for this quarter are $1 million, suggesting the company should deliver a cash flow positive quarter. The company requires in excess of $4 million a year in sales, by our estimates, to record a positive cash flow. The company appears to be on the cusp of profitability moving forward.

Cogstate's business is beginning to develop a level of robustness that should see more consistent results for the group moving forward. The company is capitalised at $7 million. The business is well managed and offers an appealing investment proposition into a company that should not be seen as a speculative investment for very much longer.

Bioshares recommendation: **Speculative Buy Class B**

Neurodiscovery

Another company that offers contract service business to biotech and pharmaceutical companies, Neurodiscovery (NDL: 17.5 cents), also had some good news to deliver this week. The company signed a deal with a US pharmaceutical company worth up to $1 million in revenue for the next 12 months. The company generated sales of $1.1 million for the first half of this financial year.

Neurodiscovery offers the appeal of contract services business that is profitable and arguably underpins the current market value of the company alone, and a drug development arm with considerable blue sky potential.

The company's incoming CEO is currently GlaxoSmithKline's global head of pain research. His focus will be to accelerate growth in the contract services business and to deliver on some major therapeutic milestones in the company's two clinical programs.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares Model Portfolio (29 February 2008)

Company	Price (current)	Price added to portfolio	Date added
Circadian Technologies	$1.10	1.025	February 2008
Patrys	$0.35	$0.50	December 2007
NeuroDiscovery	$0.18	$0.16	December 2007
Bionomics	$0.38	$0.42	December 2007
Cogstate	$0.13	$0.13	November 2007
Ventracor	$0.39	$0.625	October 2007
Sirtex Medical	$3.79	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.34	$0.66	September 2007
Starpharma Holdings	$0.40	$0.37	August 2007
Pharmaxis	$2.60	$3.15	August 2007
Universal Biosensors	$0.92	$1.23	June 2007
Biota Holdings	$1.28	$1.55	March 2007
Tissue Therapies	$0.22	$0.58	February 2007
Probiotec	$1.28	$1.12	February 2007
Phylogica	$0.12	$0.42	January 2007
Peplin Inc	$0.72	$0.83	January 2007
Arana Therapeutics	$1.02	$1.31	October 2006
Chemgenex Pharma.	$0.81	$0.38	June 2006
Cytopia	$0.36	$0.46	June 2005
Optiscan Imaging	$0.24	$0.35	March 2005
Acrux	$1.00	$0.83	November 2004
Alchemia	$0.58	$0.67	May 2004

Portfolio Changes – 29 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, Labtech Systems

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