

In this edition...

Neuren Pharmaceuticals has opened up again as an investment opportunity for several reasons. It has attracted a noteworthy investor onto its register, Lang Walker, who has been a successful investor in Acrux. The company has re-worked its enrolment strategy for its Phase II trial of NNZ-2566 and found a new clinical opportunity in an autism spectrum disorder known as Rett Syndrome.

Bionomics has begun to sketch out the kinds of terms it might be seeking as it looks to partner BNC210 and BNC105. Prima Biomed has received approval for CVac in Dubai.

Volatility in the Pharmaxis share price is presenting attractive buying opportunities following its EMA trend vote setback.

The Editors

Companies Covered: BNO, NEU, PRR, PXS

	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 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - May '10)	49.2%
Year 10 (May '10 - May '11)	45.4%
Year 11 now commenced	-4.2%
Cumulative Gain	303%
Av Annual Gain (10 yrs)	21.2%

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

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Individual Subscriptions (48 issues/year)

\$350 (Inc.GST)
Edition Number 410 (3 June 2011)
ISSN 1443-850X

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Bioshares

3 June 2011
Edition 410

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

Heightened Interest In Neuren

Neuren Pharmaceuticals (NEU: 2 cents) is emerging from a difficult period and is beginning to be a stock to watch for several reasons. Neuren is developing NNZ-2566 for traumatic brain injury (currently in Phase II) and Motiva for depression (Phase IIb) following stroke and brain injury.

What is noteworthy is that the company has taken on board new investors through a private placement which raised \$2 million. This group of placement investors included Sydney property developer Lang Walker, who made a significant investment in Acrux, holding an 8% stake as of September 30, 2010. Walker now holds a 13% stake in Neuren.

Coupled to this fundraising, the company also announced that it would wind up its convertible note arrangement with Springtree Special Opportunities Fund, ending a period of costly financing. Neuren had arranged to receive up to \$6.7 million in funds from SOF, but at the time of closing of the arrangement had accessed, we estimate, approximately \$2 million.

In December 2008, Neuren's Glypromate failed in a Phase III trial. The trial evaluated Glypromate's ability to reduce cognitive impairment in patients undergoing cardiac surgery with cardiopulmonary bypass. The trial failure resulted in an 80% fall in the company's share price, from 5 cents to 1.1 cents. However, it should also be noted that Neuren's share price had fallen steadily from a peak of 55 cents in February 2007. The Phase III trial commenced in May 2007.

Another reason that Neuren has survived a very difficult period is because it secured US Army funding of up to US\$22.8 million to support the development of NNZ-2566, which is an improved synthetic analogue of Glypromate.

NNZ-2566 (IV) Update – Phase II

Neuren is assessing NNZ-2566 in a Phase II trial in patients with moderate to severe brain injury, with the drug delivered intravenously. NNZ-2566 limits the effects of inflammatory cytokines that are released following brain injury.

The current Phase II trial is now into the stage where the second of three cohorts of patients are being dosed. All patients receive the same bolus of drug, however the rate at which the drug is administered by intravenous infusion changes. The first cohort (30 patients) was dosed at a rate of 1mg/kg per hour, the second (30 patients) at 3mg/kg/hour. The final 200 patients will be dosed at 6mg/kg/hour.

Recruitment for the trial has been a challenge due to the requirement to obtain consent from trauma patients' families. The company has lost approximately 40% of total potential enrollable subjects for this reason. The complicating factor is that the drug must be administered within 8 hours of the brain injury event and the delay of families to get to a hospital caused the drop-off in the rate of recruitment.

Cont'd on page 3

Conference Report

Southern Cross Equities Life Science Conference – Part II

Bionomics (BNO: 64 cents)

Why all the interest in Bionomics in recent months? Well there are two big ones according to the company.

Bionomics is developing two clinical drug candidates; one is a potential cancer drug, BNC105, that is being tested in Phase II clinical studies for the treatment of kidney cancer and also for the treatment of mesothelioma. The second program involves an anxiety and depression treatment, called BNC210.

At the Southern Cross Equities conference in Sydney (held last week), CEO Deborah Rathjen said that not only does the company potentially have an “Avastin” in development in BNC105, but may just have its hands on the next Prozac or Valium in development as well (BNC210).

Value Adds Coming Up

Bionomics has a number of value adds coming up said Rathjen. This month the company is due to report interim results on two Phase II cancer studies. Another major milestone for this year is securing a large licensing deal for its anti-anxiety drug, BNC210. The third key milestone which Rathjen brought to the attention of conference delegates was a potential milestone payment from its partner **Merck Serono** for its preclinical multiple sclerosis program (called Kv1.3).

Confidence is certainly building at Bionomics. In Rathjen’s presentation she indicated the company is now working on the next cancer and CNS disease compounds that it hopes will follow BNC105 and BNC210 into the clinic in coming years.

The company is also getting very specific about the types of licensing deals it expects to negotiate, perhaps part of the process in spelling out to potential partners the size of the deals it believes are appropriate for access to its clinical drug candidates.

What a BNC105 Deal Might Look like

For BNC105, Rathjen referred to the deal between Novartis and Antisoma for Antisoma’s VDA (vascular disrupting agent). Bionomics’ cancer drug candidate is also a VDA. In that transaction, Antisoma received an upfront payment of US\$75 million, potential milestone payments of up to US\$890 million, and a double digit royalty from any future sales (which are now unlikely given the program was stopped after showing insufficient efficacy in a Phase III trial last year). The deal was signed after positive Phase II results in non-small cell lung cancer.

What a BNC210 Deal Might Look Like

For BNC210, Rathjen listed a deal between **Amgen** and **Johnson & Johnson** for AMG403, which included a US\$50 million upfront fee and milestone payments of up to US\$385 million. Royalties were not disclosed but for BNC210, we expect a high single digit royalty is a likely outcome.

What has generated so much interest in BNC210 from potential partners is that the company included efficacy measures in the Phase I trials that are normally included in the Phase II setting, and

with excellent results, said Rathjen. What is also promising about this compound is that animal data was translated very predictably in human Phase I trials.

Three Blockbuster Market Opportunities

Another feature of Bionomics is that each of its three leading programs (cancer, anxiety and multiple sclerosis) all represent multibillion dollar market opportunities. Avastin – which is the first-in-class cancer drug that works differently to VDAs by starving tumour blood supply as opposed to destroying the vasculature network from the inside which is the way VDAs work – last year generated sales in excess of \$6.5 billion; the anxiety-depression market is worth US\$26 billion a year; and current MS drugs generate annual sales in excess of \$9 billion a year according to Rathjen.

Rathjen said the company’s goal was to be best and first-in-class. With BNC201, the company is first-in-class and with BNC105 the company believes it has the best-in-class drug (in the VDA space).

Partnering

With respect to partnering, Rathjen said it is all about partnering at the appropriate point. With BNC210, that is early in the piece (now), and with BNC105 the company will be partnering for Phase III development.

With BNC210, the company is down to 13 potential partners with each having signed data confidentiality agreements. Rathjen said the BNC210 results generated a lot of interest on the partnering front.

BNC210 Phase I Trials Results

The Phase I BNC210 studies were both two-way crossover study (where patients move from the active group to the placebo group midway through or vice-versa) which made the data extremely robust said Rathjen. BNC210 was simply taken as a tablet every morning with breakfast.

First Trial

In the first trial in 59 volunteers, the subjects were chemically induced to display panic symptoms, with 15 people successfully achieving a state of panic. People taking BNC210 who showed panic symptoms were stabilised within 10 minutes. With drugs such as Valium or Xanax, patients would not have been stabilised so quickly.

Second Trial

In the second trial, there were 21 evaluable volunteers in what was also a two-way crossover study. The effect of the drug on the brain was compared to an existing anxiety drug, Lorazepam, which is in the same drug class as Valium.

The trial showed a decrease in brain signalling in patients taking BNC210, which is an indicator of drug efficacy said Rathjen. This is the first time this has been shown with BNC210. There was no

Cont’d over

– *Bionomics cont'd*

effect of sedation seen with BNC210, no attention deficit, and no negative effect on motor coordination or memory.

The brain activity showed clear differentiation to the control arm, in which patients taking Lorazepam were adversely effected with sedation, co-ordination and memory.

In the study, the effect of sedation was also tested using another measure called the Karolinska Sleepiness Scale, where Lorazepam caused sedation and BNC210 did not in this trial. BNC210 also showed no effects of addiction measured by a standard test (ARCI49) where Lorazepam did show signs of addiction in the study.

Interim Phase II Cancer Trial Results Due This Month

With respect to the mesothelioma trial underway, Rathjen said a very high bar has been set, being a difficult cancer to treat. Our view is the company may surprise the market in this trial with some early signs of efficacy given its confidence approaching the reporting of this trial. The study is a single arm study only and images of lung cancer tumours and changes will be of interest. If BNC105 shows positive signs of treating mesothelioma, it will indeed be an exciting indicator of the potential of this drug candidate.

– *Neuren cont'd*

To address this issue the company has submitted a further IND with the FDA, which allows for emergency room physicians to enrol patients without consent if no family members are present. Neuren is also expanding the number of the trials sites from 10 to 18 and will begin recruiting female patients into the trial and has also expanded the age inclusion criteria from 18-70 years of age to 16-75 years of age.

To date, Neuren has filed three INDs for NNZ-2566; two under the IV dosing specification, including the recent 'without consent' provision, and a third covering oral administration.

NNZ-2566 (Oral) Update

Neuren has completed the formulation of an oral form of NNZ-2566 which it will advance into a Phase I trial in 2011 Q4 followed by a Phase II in 2012 in mild traumatic brain injury.

The results of its formulation studies were that the compound was best solubilised in water, and that the solution has a natural lemony taste. This may prove to offer a benefit in aiding compliance if the drug is used for chronic dosing, which as emerged as a possibility in a condition known as Rett Syndrome.

New Opportunity in Rett Syndrome

Neuren has embarked on a new discovery and development program, applying NNZ-2556 to the treatment of Rett Syndrome, which is an autism spectrum disorder. Children with Rett Syndrome have an IGF-1 deficiency, but disease is caused more fundamentally by a mutation in the MECP2 gene. The syndrome is characterised by too few connections being formed between brain cells.

We do not expect the interim results from the Phase II kidney cancer study to deliver too much information on drug efficacy, with the first part of the trial designed to show the drug is safe to be taken with Afinitor.

New Discovery Programs

Bionomics has new CNS programs in discovery stages in the areas of Alzheimer's disease, schizophrenia and epilepsy. It also has discovery programs underway in oncology.

Summary

June should be a big month for Bionomics with the interim results from two Phase II cancer studies with BNC105. With a major licensing deal around the corner (in the next three to six months), there is good reason to keep buying this stock.

Bionomics is capitalised at \$220 million.

Bioshares recommendation: **Speculative Buy Class A (upgraded)**

Bioshares

Three years ago researchers were studying Rett Syndrome in a MECP2 knockout mouse model they had developed. The researchers administered Glypromate (the pre-cursor peptide to NNZ-2566) to animal research subjects and observed a dramatic reduction in the pathology of the condition.

The researchers switched to NNZ-2556 when they became aware of its availability but also because there is no composition patents covering Glypromate and because it could not be developed as an oral drug. Neuren formed a collaboration with the Rett Syndrome Research Trust which paid for the studies of NNZ-2566 in the MECP2 mouse model. In a mouse model NNZ-2566 was shown to increase the average length of dendrites in the hippocampus section of the brain.

Neuren hopes to commence a Phase II proof of concept trial in 2012. The company will file a protocol for this trial under the NNZ-2566 (Oral) IND.

NNZ-2566 is, in the case of Rett Syndrome, a disease modifying agent. It addresses the neuro-pathology of the disease which is caused by excessive cytokine activity. NNZ-2566 blocks this over-expression.

Rett Syndrome is one of a number of chronic rare diseases. NNZ-2566 would possibly be administered on a twice daily basis for the duration of a patient's life. Chronic dosing would mean that long term toxicology studies would be required to better under the drug's long term toxicology profile. Neuren CEO Larry Glass suggests that at this stage, all that the company may need to complete

– *Cont'd over*

Bioshares Model Portfolio (3 June 2011)			
Company	Price (current)	Price added to portfolio	Date added
Psvida	\$4.14	\$3.95	May 2011
Bioniche	\$1.12	\$1.35	March 2011
Somnomed	\$1.30	\$0.94	January 2011
Phylogica	\$0.067	\$0.053	September 2010
Sunshine Heart	\$0.051	\$0.036	June 2010
Biota Holdings	\$1.18	\$1.09	May 2010
Tissue Therapies	\$0.48	\$0.21	January 2010
Hexima	\$0.32	\$0.60	October 2008
Atcor Medical	\$0.13	\$0.10	October 2008
Impedimed	\$0.66	\$0.70	August 2008
Patrys	\$0.13	\$0.50	December 2007
Bionomics	\$0.64	\$0.42	December 2007
Cogstate	\$0.22	\$0.13	November 2007
Sirtex Medical	\$5.00	\$3.90	October 2007
Clinuvel Pharmaceuticals	\$1.90	\$6.60	September 2007
Starpharma Holdings	\$1.51	\$0.37	August 2007
Pharmaxis	\$1.13	\$3.15	August 2007
Universal Biosensors	\$1.05	\$1.23	June 2007
Alchemia	\$0.69	\$0.67	May 2004

Portfolio Changes – 3 June 2011

IN:
No changes.

OUT:
No changes.

Prima Biomed to Launch Product in Dubai this Year

Prima Biomed (PRR: 30 cents) has announced that its cancer vaccine, CVac, has been granted approval to be sold in Dubai, subject to completing final regulatory steps. The company anticipates sales into Dubai later this year.

A price similar to that of Provenge of \$93,000 for a year's treatment will be sought, and there is also the possibility that the product will become available this year in Australia, as an autologous cell therapy treatment. Prima indicated that it may also extend the application of CVac to other mucin-1 positive cancers (such as breast cancer).

The go ahead in Dubai comes on the back of a capital raising that has brought in \$21 million from 15 new institutional investors that have come onto the register. The interest no doubt is driven also by Dendreon's cancer vaccine, Provenge, where sales are expected to accelerate later this year once manufacturing bottlenecks are cleared.

Prima is also seeking to raise \$20 million through a rights issue. Its Phase II trial results are due out in September and an 800 person Phase III trial is due to start later this year.

Following its rights issue, Prima will be in a position to commence its Phase III study. Its new shareholder base will also potentially give it access to further funding when required to bring its novel ovarian cancer therapy to major markets around the world.

One of the most important aspects of a successful biotech venture is the ability to fund its commercialisation. This is something Prima has now shown it certainly has the capacity to do. Prima is capitalised \$296 million, excluding any shares raised through the rights issue.

Bioshares recommendation: **Speculative Hold Class B**

– Neuren cont'd

is a bridging study that examines toxicology issues out at 90 days, compared to the 28 days set down in its current IND filings.

The main issue with developing NNZ-2556 for the Rett Syndrome opportunity is funding. Neuren expects to make an announcement regarding funding in the near future.

Investment Consideration

Neuren has 181 million options outstanding with exercise prices ranging from 1.4 cents to 4.4 cents with the majority of these options issued through the convertible note arrangement. Neuren has 509 million ordinary shares issued. The potential overhang created by these options, assuming the option holders sell their shares if share price rises sufficiently is a factor investors should be aware of in coming months.

However, as clinical trial results emerge in 2012 and the data meets or exceeds expectations then the stock price is likely to respond accordingly.

The emergence of a new treatment opportunity in Rett Syndrome is a positive development for Neuren as is the introduction of new investors onto the share register.

The key patent covering NNZ-2566 expires in 2022.

On a fully diluted basis Neuren is capitalised at \$13.8 million. The company will be conducting a rights issue following its recent \$2 million private placement in May.

Bioshares recommendation: **Speculative Buy Class C**

Bioshares

Pharmaxis Stock Remains Volatile & Oversold

Pharmaxis' (PXS: \$1.125) share price has become very volatile as investors continue to dispute the fair value of the stock following the regulatory setback in Europe in the previous week.

We maintain the view that there is a reasonably good chance the company's drug, Bronchitol for the treatment of cystic fibrosis, will still gain approval this year following an appeal process, which is in our view the likely path forward. Under this process an expert panel will be convened by the regulator and regulatory representatives from two different countries (not the UK which was the rapporteur for the initial assessment) will be selected to co-ordinate the process – one country which votes in favour of approval and one country that votes against approval in the forthcoming formal vote, at which Pharmaxis has been informed it is unlikely to be approved.

The share price sell off still remains overdone. Two recent comparisons are **ChemGenex Pharmaceuticals** and **pSivida**. When these companies received a regulatory setback/delay, their respective share prices fell by 50% and around 35%. A similar decline for Pharmaxis would suggest a trading range for the stock of between

\$1.45-\$1.90. Pharmaxis is still down 62% from the last traded price before notice from European regulators.

Our view is that Bronchitol will eventually gain approval in major markets. It has shown to be both safe and effective in not only improving lung function, but also arresting the rate of lung function decline that characterises cystic fibrosis. This should have the longer term effect of extending life for people living with cystic fibrosis, for whom the available treatments are few and time demanding.

The issue for the company will be the cost of this delay, particularly if additional funds need to be raised. The company at the end of March still had a healthy \$56 million in cash.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

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. For both groups, the rating “Take Profits” means that investors may re-weight their holding by selling between 25%-75% of a stock.

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: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Mayne Pharma Group, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Mesoblast, Atcor Medical, BioMD, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida

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