

In this edition...

We provide coverage of the Pharmaxis Investor Day held in Sydney, where a summary of clinical data recently presented at the US Cystic Fibrosis conference was made available. With Pharmaxis edging to a pivotal registration point in the commercialisation path of Bronchitol in Europe, it's a stock that will be watched very closely by investors.

We also provide coverage of Bionomics' AGM, with that company also approaching a transformational year in 2011. And we provide more coverage from the recent Ausbiotech 2010 conference held earlier this month.

The Editors

Companies Covered: BNO, 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 - Current)	8.8%
Cumulative Gain	215%
Av Annual Gain (9 yrs)	18.5%

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

Extract from *Bioshares* –

Bionomics AGM Coverage

Confidence was riding high at this year's Bionomics AGM, held on 15 October. The chairman, Chris Fullerton, suggested that the year ahead as the most critical year in the company's history. CEO Deborah Rathjen described 2011 as being a transformational year for Bionomics. This is because the company will have crucial data emerging from three clinical programs.

BNC105 Update

The first flagged data release will be from the company's cancer drug candidate, BNC105, in the treatment of patients with kidney cancer in a Phase II study. The first stage of the trial, for which interim results should become available in the first quarter of 2011, will be from use of BNC105 used in combination with the **Novartis** drug Afinitor, in patients who are no longer responding to Afinitor.

This first part of the trial will initially look at whether combining the two drugs in patients is safe. After the first patient is treated for 21 days, more patients will be treated with the combination therapy. There will be no efficacy comparison between BNC105 and Afinitor. That will occur in the second stage of the trial, once safety of the combination of the two drugs is established. In preclinical studies, Bionomics has shown that there is a synergistic effect from combining the two drugs.

Efficacy data should also be available in this interim analysis from images of changes to the solid tumours, and the company will also be able to monitor the blood levels of tubulin which will act as a marker of tumour destruction.

The Phase II Mesothelioma Trial

The Phase II mesothelioma trial is recruiting well. This is a very difficult disease to treat and in *Bioshares* view, the expectations that BNC105 will be effective should be lower than in kidney cancer. However there is a high unmet clinical need for treating mesothelioma. It is a solid tumour and one patient in the Phase I trial with mesothelioma (and one with kidney cancer) showed signs of stabilized disease following treatment with BNC105.

There is no staggered start to the mesothelioma trial, with the safety of BNC105 delivered on its own already established. The interim results, which should be available in the first half of 2011, should give sufficient detail on efficacy of the drug to either (a) stop the trial if there is no evidence of efficacy or (b) continue the trial if the drug is showing to be effective and seek a licensing arrangement.

Data from the interim results from the kidney cancer study should also be sufficient to enter into licensing discussions if the drug is showing to be effective.

– *Cont'd over*

BNC105 is a variation of the drug candidate Combrestatin A4 (CA4) which was discovered at the NCI in the US in the 1980s as a natural compound. Scientist Bernard Flynn, founder of **Iliad Chemicals**, synthesised BNC105 using his Multicore chemistry platform. Iliad was acquired by Bionomics in 2005 and its Multicore chemistry is behind Bionomics' three lead programs.

BNC105, a tubulin polymerisation inhibitor, has a dual effect, stopping the blood flow to tumours and thereby rapid tumour destruction from the inside out. The drug candidate also inhibits cell mitosis (cell division) similar to the alkaloid drugs such as Taxol which target tubulin, and starts apoptosis (cell death). This is believed to be because the compound interrupts with the microtubulin assembly. However, unlike the alkaloid cancer drugs, BNC105 is believed to be not subject to resistance mechanisms.

The issue with CA4, according to Flynn, was that its half-life in the body is too short, being around 40 minutes, which is too short a time to elicit tumour growth inhibition. BNC105 has a half-life of three hours in the body.

BNC105 is also 10 times as potent as CA4 (as measured by IC50 - inhibition concentration, being the concentration of drug required to inhibit disease by 50%), and has 10 times the amount of free drug concentration in the body, because it binds to albumin much less than CA4 (10% free drug function for BNC105 versus 1% for CA4). Presumably that would give BNC105 a 100-fold increased potency over CA4 and a much greater therapeutic window in which to operate.

Antisoma Development - ASA404 On Hold

During the year, a VDA drug program (ASA404) that had been developed by **Antisoma** and licensed to **Novartis** was halted due to poor trial progress. The chairman commented at the AGM that with ASA404 now on hold, BNC105 has become the global front runner in the VDA space and that the interest in the VDA space remained strong according to Rathjen. BNC105 is far superior to ASA404, believes Rathjen, with BNC105 having a dual mechanism of action (compared to a single action with ASA404) and the mechanism of action was known for BNC105 unlike for ASA404.

One of the appeals of BNC105 is that it has shown to be a very safe drug. The drug is removed from organs very quickly with no drug in the blood stream the day after delivery. The company has also built a new model that shows that BNC105 also has an effect on renal metastases to the lung. It also has the potential to treat all solid tumour types according to Rathjen. (In 2008 the company indicated that BNC105 had caused almost complete destruction of tumour blood vessels in all six tumour types investigated to date.)

Prospective Licensing Deals

At this year's AGM, there was a commercial focus on comparator companies and comparable licensing deals that Bionomics could potentially achieve. The licensing deal between Antisoma and Novartis for ASA404 generated a \$75 million upfront fee in 2007. In 2009 and 2010, the chairman pointed to four relevant licensing deals, presumably setting the scene for what is achievable for Bionomics in the year ahead.

Oncogenix signed a Phase II deal on a prostate cancer compound which included a \$20 million upfront payment plus a \$10 million equity investment. **Array Biopharma** signed a Phase I deal with Novartis with a \$45 million up front payment. **Exelixis** and **Sanofi-Aventis** signed a Phase I/II cancer drug deal with a US\$140 million upfront payment and \$21 million in research payments. And **TopoTarget** signed a Phase II/III cancer drug development deal with **Spectrum Pharma** which included a \$30 million upfront payment.

Bionomics' Phase II kidney cancer trial was started in January this year and the mesothelioma trial was started in March. Both trials are running according to schedule with the recruitment rate into the mesothelioma trial particularly pleasing. Rathjen believes either program could be fast tracked to Phase III if the Phase II data looks good.

BNC210 Update

Bionomics' third trial is with BNC210 for the treatment of anxiety and now depression. In fact these will be two Phase Ib trials in the same indication. The first trial will look at the effects of BNC210 on 22 volunteers who are induced to develop short-term anxiety and panic-like symptoms (using a peptide CCK-4). Part of the group will be given a placebo and the second group BNC210.

The second trial will compare BNC210 with a valium-like drug (Lorazepam) in 24 health volunteers. The aim will be to compare the side effects of the two drugs such as memory impairment and sedation.

Results from both trials are expected in the first quarter of 2011. If the results are positive, Bionomics intends to partner the program.

Whilst licensing discussions are pending completion of the above trials, relationships have already been formed with the key groups potentially interested in Bionomics' two lead drug candidates and those groups are believed to be watching the progress of these trials.

BNC210 also utilises the company's Multicore platform and was initiated after the Iliad acquisition. The concept came from work published in scientific literature to which the Multicore technology was put to work. The preclinical models for anxiety are well established and transfer well into the clinic. The same pre-clinical models Bionomics has used have all generated consistent data with 10 anti-anxiety drugs currently on the market. In a variety of preclinical models, Bionomics has shown that BNC210 reduces anxiety and depression without the effects to memory or sedation.

There is a strong sense of confidence at Bionomics that BNC210 will also deliver positive clinical trial results that will position the program for a major partnering deal.

KV1.3 – MS program with Merck Serono

The preclinical partnership in multiple sclerosis with Merck Serono was recently extended for another year, presumably so that the first milestone of selecting a lead drug candidate could be achieved.

– *Cont'd over*

Non-executive director and scientific advisor, Dr Errol De Souza, commented that the level of interest from key opinion leaders on the BNC105 and BNC210 was extremely high. Commenting also on the relationship with Merck Serono, De Souza said that the pharmaceutical company viewed its collaboration with Bionomics as one of its best.

Summary

In its two lead programs, Bionomics is seeking to treat diseases or disorders where the current disease is not effectively managed with existing treatment (kidney cancer and mesothelioma) and a disorder where there has been very little progress over the last 10 years to improve existing therapies (anxiety and depression). There is significant unmet need for both cancer indications. In kidney cancer, the five-year survival rate for advanced disease is only 2%. For patients with mesothelioma, the life expectancy after first line chemotherapy is only one year.

Bionomics' lead programs are both tackling very large markets. Avastin, an anti-angiogenic antibody drug now generates sales of over \$5 billion a year. The anxiety and depression market is worth \$26 billion a year with one prescription issued each second for the popular anxiety drug Xanax.

Bionomics is very confident that it will be successful in the transformational year of 2011. Deborah Rathjen commented that a decade of work at Bionomics has produced two very exciting drug candidates. The quality of data that emerges from the current trials will dictate the interest from potential partners.

Bioshares recommendation: **Speculative Buy Class A**

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

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