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In this edition...
Peplin is moving quickly towards a market launch in 2011, with the bulk of its remaining clinical work in testing PEP005 as a treatment for sun spots to be wrapped up this year.
There remains not insignificant risks for Peplin at the hands of the FDA, but so far the clinical data has been strong. The competitive position for PEP005 is favourable – this is a compound that is far more patient friendly than rival treatments. Don't forget too that Peplin owns 100% of the global rights to PEP005 and will be setting itself up nicely when it wants to seek a European marketing partner.
Bionomics is now ready to begin a Phase I trial of BNC210, its anxiety drug, and Phylogica is on an improved footing with cash in the bank after raising funds.

The Editors
Companies Covered: BNO, PLI, PYC

	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 - Current)	9.8%
Cumulative Gain	**131%**
Av Annual Gain (8 yrs)	**14.7%**

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Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au
David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

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Bioshares

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

Positive Results for Peplin's Phase III Actinic Keratoses Trial

Peplin (PLI: $0.66) has announced the results of its Phase III study of PEP005 (ingenol mebutate) in patients with actinic keratoses (AK). Otherwise known as sun spots, AKs are dry, rough scaly lesions. The study was numbered PEP005-014.

The '014 Phase III trial enrolled 255 patients with between four to eight AK lesions within a 25 square centimetre area on non-head locations, including arms, back of hands, legs, shoulders, chest and back.

These patients received applications of PEP005 (0.05% concentration) on selected lesions over two consecutive days.

A total of 254 patients received the medication, however 20 subjects from one trial site were excluded from the analysis due to protocol violations. This left 234 patients completing the study.

Overall, there was a 67% median reduction in the number of lesions, a statistically significant result.

Only three of the six body regions assessed accumulated sufficient patients to generate meaningful results. These were arm, back of hand and chest. For these three regions complete clearance rates of 25%, 16% and 89% respectively were obtained. These results were also statistically significant.

The partial clearance rate for the arm was 48%, back of hand 24% and chest 89%. These results were statistically significant.

The median reduction in lesions on the arm was 73%, back of hand 50% and chest 100%, with the outcomes once more being statistically significant.

Comparison with PEP005-006 Study

The response rates in the earlier Phase II study (PEP005-006), which evaluated the application of PEP005 on the arms, shoulders, chest and back (but not back of hands and legs), were higher than in the PEP005-014 study.

For comparable regions, the complete response rate on the '006 study of 0.05% concentration was 45% compared to a 31% response in the '014 study. However, the vehicle (a gel with no active drug ingredient) clearance rate was also higher in the earlier study.

If the *difference* between the complete response rates for the 0.05% concentration and the vehicle rates are calculated for both studies, then a more consistent outcome is observed of 25% in the '014 study versus 31% in the '006 study.

Cont'd on page 3

Bionomics – Partnering Interest Grows for BNC105

Bionomics (BNC: $0.235) continues to progress well with its drug development programs. Its lead program with the anti-cancer compound BNC105, has almost completed Phase I studies. Phase II studies are expected to begin in the second half of 2009. The second most advanced program is with BNC210, a drug candidate for the treatment of anxiety, which is expected to move into Phase I trials in the next quarter.

BNC210 Phase I to Commence Q3

Bionomics expects to complete the Phase I study with BNC210 this year. In preclinical tests the drug candidate has shown to have a better drug profile than Valium and Prozac, and is obviously looking to deliver an improved pharmaceutical for a very large existing market (around US$15 billion a year).

Unlike Valium, BNC210 does not display any sedation or addiction effects and no impairment to memory. And unlike Prozac, BNC210 does not take four to six weeks to take effect and it has shown no drug-drug interaction complications. It has shown to be fast acting and effective in treating anxiety in preclinical studies with only a single daily dose.

BNC210 has shown to be extremely effective in a stress-related anxiety model, where Valium is not. BNC210 potentially has a 1000 times greater therapeutic window than Valium because of the low side effect profile displayed in preclinical studies.

The Phase I trial will deliver very important information on the safety profile of this drug. Being a drug candidate that will be taken by largely healthy people if approved, the safety level of this drug will need to be extremely high. The sedative effect of BNC210, the ECG profiles of the trial participants and the changes of liver enzyme levels will be monitored very closely and these results will deliver crucial information regarding the suitability of BNC210 as a future drug for the treatment of anxiety and depression.

BNC105 Phase I Trial Almost Completed

The Phase I trial of BNC105 in patients with a range of different solid tumours has almost been completed. Only 19 patients (from 30 originally estimated) were required to reach the maximum tolerable dose. Activity of the drug was seen in the third patient treated. The drug has been shown to cause a 98% tumour shut down within one hour of treatment and a 95% tumour shut down after two days, which is significantly higher than **Oxigene**'s Zybrestat, another vascular disrupting agent which is in Phase III development. (BNC105 has been designed as an improved version of this drug).

Phase II studies will look at evaluating BNC105 both as a single agent and as a combination therapy. One school of thought is that VDA's will achieve the most effective result when used in combination with another mode of therapy. Disrupting the tumour is likely to see the tumour grow through another pathway that might be predictably inhibited with either existing or new oncology drugs. A Phase II study will start in the second half of 2009 and will take two years to complete enrolment. Interim data should become available after 12 months.

Stable disease in the Phase I study was achieved in a small number of patients with mesothelioma and renal cancer, suggesting cancer types the company may look at treating in Phase II studies. There is no treatment for mesothelioma, so that is a logical solo drug trial with BNC105. A combination Phase II trial with **Novartis**' drug Afinitor, (everolimus) which was approved for the treatment of renal cell cancer as a second line therapy in March this year, may be considered by Bionomics in combination with BNC105.

Partnering Interest

Potential partners for the BNC210 program are companies with existing products franchises in the psychiatric and neurological drug markets. Bringing this compound to market will require large Phase II studies and extremely large Phase III trials. It is unlikely Bionomics would move into Phase II studies without the financial assistance of a partner. A licensing deal for such a program may be more front-loaded, with a $10-$20 million upfront payment a very good result for the company.

To date, Bionomics has around 20 companies formally interested in the BNC105 program and 13 companies to date have signed CDAs for BNC210, which is indicative of the partnering potential for the BNC210 program. Having completed a licensing agreement with **Merck Serono** for its preclinical program last year in multiple sclerosis, an aggressive objective for the company would be to complete a Phase I partnering deal with BNC210 in 2009 or in early 2010, and a Phase II partnering deal for BNC105 in 2010 on the back of interim Phase II cancer trial data.

The patent lives on both BNC210 and BNC105 are long, going out to 2026.

Summary

Bionomics continues to make consistent and measurable progress with its leading programs. The company has moved a long way from being an early stage genomics company, to now a biotech drug discovery and development engine room. We place a strong expectation that at least one or potentially two further licensing deals could be completed on the lead programs over the next 18 months if good data can be generated. Bionomics has positioned itself through clever structuring of its clinical trials to give the likelihood of this event a reasonable chance.

Bionomics is capitalised at $60 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

From page 1

Similarly for the partial clearance rates, the differences between the active gel and the placebo of 43% ('014 study) and 45% ('006 study).

It should be noted too that the '006 study was about half the size in terms of patient numbers in the 0.05% concentration group and in the vehicle (placebo) group.

Implications

The PEP005-014 Phase III study is the first clinical study to show a statistically significant benefit of an active drug over the vehicle in treating 'hard to treat' non-head and neck regions.

This should provide the company with a clear marketing benefit over rival treatments, such as Solaraze, when it eventually obtains a marketing clearance. Following the '006 study, dermatology key opinion leaders indicated that if Peplin evaluated PEP005 for treating back of hand and back of leg, then it would increase the company's chances of dominating those two areas if significant data was generated. (Back of hand represents about 20% of the non-head AK market.)

Milestones

Following the recent completion of Peplin's Phase II trial for PEP005 (the '015 trial) to treat AK lesions on the scalp and face, the company now anticipates holding an end-of Phase II meeting with the FDA in June. These discussions will help the company formulate plans for what may be two Phase III trials, depending on what the FDA prefers.

Peplin will also be designing a Phase III trial for PEP005 to treat non-head regions, but only one trial will be required if enough patients are enrolled that confer the equivalent power from two studies.

The company's final study to be conducted before a New Drug Application is to be submitted is a 200 patient open label safety study of PEP005 at the 0.05% concentration, that test PEP005 on non-head areas.

If all goes well, Peplin will be in a position to hold a pre-NDA meeting in 2010 Q1 and file an NDA in mid-2010.

Summary

Although Peplin still has up to four major studies to design, enrol and complete, the key investment point is that these should all be completed by the end of this year, or with some creep into 2010. This is very rapid in terms of drug development. The activity and benefit of PEP005 is emerging with even stronger clarity. Peplin remains as we have described previously "a core long term holding" (*Bioshares* 189) and is a very attractive opportunity while Big Pharma is extremely hungry for late stage assets. It will be an acquisition target over the next 12 months.

Peplin is capitalised at $203 million.

Bioshares recommendation: **Speculative Buy Class A**

Phylogica Boosts Cash Resources

Phylogica (PYC: $0.075) has done what only a handful of biotechs in Australia have done this year and that is to raise a reasonable tranche of funds to support its commercialisation activities. Phylogica has raised $3.8 million through a placement and a convertible note. Existing shareholders, including listed venture capital group **Biotech Capital**, together with new investors contributed the funds.

The raising comes at a time when interest from major pharmaceuticals companies is building and follows a change in business model at the company. Phylogica is focusing on being a more traditional drug discovery partner for drug developers.

Previously Phylogica had wanted to bring its products into the clinic and generate clinical data (the first clinical program was to be in wound healing) then partner them out. The company will now stick to its main capability in generating drug leads from its library of peptides derived from bacterial genomes, which through millions of years of evolution have developed significant chemical diversity.

To increase the interest from larger partners, Phylogica has reorganised its library to generate peptides with more drug-like properties and generated data to highlight the appeal of its peptides. This includes improving the half-life of its peptides, showing its peptides can be delivered into cells and also act as drug transporters, and the ability to deliver the peptides across the blood-brain barrier.

The company has also teamed up with **Aegis Therapeutics** to work on nasal delivery of Phylogica's peptides (called Phylomers) using the proprietary Aegis drug delivery system. The two companies will work collaboratively to seek commercial partnerships and licensing deals for the combined technologies.

According to the company, the most meaningful advance that is spiking the interest of larger players is the outcome from a research collaboration with the **MRC Hutchison Institute** in Cambridge. Using the Phylomer libraries, the groups were able to get a 0.1% hit rate in phenotypic screens on human cancer cells. This is a high hit rate from a random Phylomer library and it showed that a biological pathway involved in cancer cell growth could be blocked (thereby stopping uncontrolled cell growth). The structural diversity and natural world origins of the Phylogica's peptide libraries, unlike other peptide libraries, greatly increases the chances of phenotypic outcomes (i.e. biological evidence of disease modification) being achieved.

This will be a decisive year for Phylogica, with the event to monitor being the signing of a research collaboration with a major partner. According to the company, the interest from potential large partners is accelerating. Major preclinical partnering collaborations for small biotechs with drug discovery engine rooms are continuing to occur.

Cont'd over

Phylogica cont'd

A case in point is **Forma Therapeutics**, which signed a deal in January worth up to US$200 million to develop inhibitors of protein-protein interactions. Forma's technology also seeks to utilise the structural diversity found in natural products with traditional small molecule chemistry. Phylogica is using structurally diverse peptides from ancient genomes to deliver novel drug candidates, but also potentially as pathfinders to prove biological effect. Phylogica will be looking form such a collaboration this year as a major validation for the company's technology.

Phylogica is capitalised at $16 million.

Bioshares recommendation: **Speculative Hold Class B**

Bioshares

Corrections and clarifications

Bioshares 311
In the text relating to Starpharma on page 4:
The following sentence should read:

"While the details of the deal were not specified, Starpharma's dendrimer chemistry is likely to used to improve the dosing characteristics of certain animal pharmaceuticals, for example, to provide controlled release formulations which may *increase* the intervals between doses.",

with the word 'increase' replacing the word 'reduce'.

Bioshares Model Portfolio (22 May 2009)

Company	Price (current)	Price added to portfolio	Date added
ASDM	$0.33	$0.30	December 2008
QRxPharma	$0.50	$0.25	December 2008
Hexima	$0.47	$0.60	October 2008
Atcor Medical	$0.22	$0.10	October 2008
CathRx	$0.62	$0.70	October 2008
Impedimed	$0.76	$0.70	August 2008
Mesoblast	$0.79	$1.25	August 2008
Cellestis	$2.96	$2.27	April 2008
IDT	$1.60	$1.90	March 2008
Circadian Technologies	$0.77	$1.03	February 2008
Patrys	$0.06	$0.50	December 2007
Bionomics	$0.24	$0.42	December 2007
Cogstate	$0.24	$0.13	November 2007
Sirtex Medical	$3.00	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.40	$0.66	September 2007
Starpharma Holdings	$0.32	$0.37	August 2007
Pharmaxis	$2.72	$3.15	August 2007
Universal Biosensors	$1.20	$1.23	June 2007
Biota Holdings	$1.24	$1.55	March 2007
Probiotec	$1.69	$1.12	February 2007
Peplin Inc	$0.67	$0.83	January 2007
Arana Therapeutics	$1.37	$1.31	October 2006
Chemgenex Pharma.	$0.49	$0.38	June 2006
Cytopia	$0.09	$0.46	June 2005
Acrux	$1.13	$0.83	November 2004
Alchemia	$0.38	$0.67	May 2004

Portfolio Changes – 22 May 2009

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, Cytopia, Arana Therapeutics, Starpharma Holdings, Cogstate, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical

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