ISSN 1443-850X

In this edition...
While distress confounds, value abounds at least in biotech markets. There are many very attractive investment propositions on offer for investors to build positions in. Not the least of these is Adelaide's Labtech Systems which is receiving milestone payments from its partner BioMerieux with royalties expected to flow next year. Drug development in the field of cancer is challenging, however Bionomics is beginning to gain important insights from its Phase I trial of BNC105.

Elsewhere we provide updates on Neurodiscovery, Alchemia, Peplin and take a fresh look at Anadis.

Companies covered: ACL, ANX, BNO, LBT, NDL, PLI

	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 - current)	-13.8%
Cumulative Gain	**79%**
Av Annual Gain (7 yrs)	**17.8%**

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

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

Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 282 (26 September 2008)
ISSN 1443-850X

Bioshares

26 September 2008
Edition 282

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

Labtech Systems – A Success Story

Labtech Systems is emerging as one of the smaller success stories in the Australian Life Sciences sector. Formed only four years ago and listing on the ASX in 2006, Labtech Systems has completed the development of its first product, which has been licensed to a major international laboratory equipment supplier, BioMerieux.

Labtech has built an automated agar plate streaking and handling system, named now the PREVI-Isola. It is due for commercial release this year and we estimate will sell for in excess of $100,000. It will be sold mainly to pathology laboratories, with the system having a capacity to process 1500 samples over eight hours.

Under the terms of the deal with **BioMerieux**, Labtech will receive $12 million in milestone payments and a royalty from sales of the main consumable used with this instrument, the Microstreak plastic applicator. To date Labtech has received around $7 million, with a further 2 million Euro to be paid next financial year (on the third anniversary of the deal) and a further 1 million Euro when a performance milestone is reached. The company generated a net profit of $0.7 million in the financial year just past.

Labtech Systems now has an estimated $5 million in cash with a revenue stream from consumable sales royalties expected to begin in April/May next year in quarterly payments. Labtech Systems is capitalised at $18 million.

There are two key questions with this company. The first is how large will the future royalty stream be to Labtech. The second is what direction will Labtech take. Will it become a holding company for the future royalty stream or will it reinvest part of that royalty into subsequent products?

Future royalty stream

It is difficult to estimate the future royalty stream to Labtech because the royalty rate from the applicators is unknown (other than being a double digit royalty), the price of the applicators is unknown, and the take-up by the market can only be estimated.

At an installed base of 1000 systems worldwide processing 500 agar plates a day, we estimate the royalty to Labtech Systems from the plastic applicators would be between $2 million - $5 million a year. It might take up to five years to reach this installed capacity, selling 200 instruments a year.

Royalty flow will continue for the life of the patent, which was filed in 2006 in the US, to 2026. A royalty fee of 3% of sales is payable to the Institute of Medical and Veterinary Science in Adelaide for the first three years, which then increases to 7%.

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Bionomics Hits Therapeutic Dose

Bionomics (34 cents) looks to have hit the therapeutic dose with its vascular disrupting agent (VDA) in a Phase I trial in patients with solid tumours. In a recent presentation lodged with the ASX the company shows its drug candidate BNC105 clearly disrupting tumour blood vessels in one patient with secondary liver cancer and in a second patient with mesothelioma, as seen in images taken with a DCE-MRI scan, within six hours of the drug being delivered. This early data appears very encouraging. What is also very encouraging is that so far, data obtained from pre-clinical mouse studies is correlating very closely with what is being seen with the early phase of human studies.

There are several clinical VDA programs underway by various companies, including by Cytopia, which now has two Phase II trials being conducted, one in patients with multiple myeloma and the second in patients with glioma. Aside from achieving effective disruption of tumours, the major issue with these types of drugs is their side effect profile, particularly potential cardiotoxicity effects, presumable because of unwanted vascular damage within the heart muscle. Limiting the destructive effects of VDAs in vital organs is one of the keys to success in developing this class of drug.

Value of pre-clinical testing

Bionomics' extensive preclinical testing with its drug candidate is proving very useful. Mice studies indicated that a therapeutic dose with BNC105 should be achieved at around a dosage level of 16mg/m^2. In this Phase I trial, the first vascular disrupting effect was noticed at a dose of 8.4mg/m^2. Being able to predict the effective dose in humans from mice that closely suggests the company has a very strong command of the drug design limits and capabilities of its candidate. This is crucial in the development of VDAs.

Currently nine cancer patients are receiving treatment, with some having completed their participation in the trial, which is seeking to find the maximum tolerable dose of the drug. The company has just started the fifth dose level at 25mg/m^2. No cardiac toxicity has been observed in the trial to date.

Looking ahead, it is expected that Phase II studies will begin in the third quarter of 2009, possibly in a 160 patient non-small cell lung cancer trial with two arms, including a combination therapy with an existing oncology drug. A second Phase II trial in 60 patients with head and neck cancer is also being considered.

BNC105 has been designed as an improved version of another VDA, Combrestatin A-4, which is currently in Phase III studies. Bionomics has reengineered the drug to deliver a wider therapeutic window with an increased cytotoxicity level. So far all is progressing to plan.

Bionomics is capitalised at $80 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Points to note about VDAs

VDAs are a new class of oncology drugs that remain at the development stage. Delivery of VDAs to the tumour site should generally not be difficult, given the target is the vasculature network itself (in the tumour) and the drugs are infused directly into the blood stream. VDAs are designed to be taken up more selectively within tumours which tend to have an increased vascular permeability.

Whilst VDAs have shown to be very effective in trials in destroying the centre of the tumour, the periphery of the tumour often remains in tact suggesting that a combination therapy approach with existing cytotoxic drugs will deliver the most favourable outcome.

The critical issue for VDAs is achieving an effective dose that can be administered safely. The main side effects with VDAs has shown to be cardiac toxicities (heart attacks) and motor neuropathy. According to an article in the *British Journal of Cancer* in March last year, the best way to view drug effect on tumours is with repeated imaging using DCE-MRI and PET analysis. However the role of these imaging techniques still requires further validation.

One of the leading VDAs in development is **Antisoma's** AS1404, which is in Phase III studies. Highlighting the potential of this class of drug, last year this compound was licensed to **Roche** in a deal which included an upfront payment of US$75 million!

The New Focus at Anadis

Anadis (8 cents) is, for an Australian biotech, quite long lived having listed in April 1999. *Bioshares* first covered Anadis in 2000 (*Bioshares* 4), but we have said little over the intervening years, with the company struggling to mount a case for investment.

Until February 2008, the company operated a contract manufacturing business, which has been divested. The company is now in a much stronger position to focus on therapeutic product development based around the hyper-immunised colostrum that is harvested from a special herd in one of Victoria's major dairy districts. The concept is that dairy cows are vaccinated with vaccine designed to produce antibodies with a therapeutic benefit to humans. The antibiodies are harvested from the colostrum that dairy cows produce for calves just after they born.

The company appointed a new CEO, Dr Zeil Rosenberg in April, 2007. Professor Colin Chapman (Pharmacy - Monash University) has joined the board this year.

Programs to monitor

Influenza

Anadis has developed anti-influenza antibody products suitable for passive immunisation and post exposure prophylaxis for seasonal and avain influenza. A number of pre-clinical studies have been completed. In January, the company stated that results from

Cont'd on page 5

Peplin's Pricey CEO

Peplin's new CEO, Thomas Wiggins, conducted a roadshow in Australia this week. Wiggins, who was the ninth employee at **Connectics** in the US and was CEO when it was sold to **Stiefel Laboratories** in 2006 for US$640 million, is highly suitable for the role at Peplin and remains committed to building a specialized dermatology business on the back of the company's core asset, PEP005.

The focus for the company is very much on the US market, where the opportunity for this topical treatment for skin cancers is the highest for commercial returns. The company is committed to building a distribution team once the product is approved, which could be as small as 60-80 staff and reach 80% of the market. The spate of acquisitions in the dermatology area in recent years (see table below) has provided a vacuum in the dermatology sector according to Wiggins, that will make building a dermatology sales team easier.

Recent Dermatology Business Acquisitions

Company Acquired	Acquiror	Date completed	Price $US M
Barrier Therapeutics	Stiefel Laboratories	August 2008	$148
CollaGenex Pharmaceuticals	Galderma Laboratories	April 2008	$420
Bradley Pharmaceuticals	Nycomed	February 2008	$346
Connetics	Stiefel Laboratories	December 2006	$640

WhileWiggins has the credentials for the CEO role at Peplin, his appointment comes at a price. Details of Wiggins' employment contract are summarised below.

Base salary: US$350,000 p.a.
Annual bonus: Up to US$175,000
Change of company control payment: US$500,000
Peplin shares (ASX traded CDIs): 4.5 million (over 3 years)
Peplin options (over ASX traded CDIs): 4.5 million (over 2 years), exercisable at fair market value of Peplin shares when granted.

Should Peplin be sold in three years time at $2.00 a share, and assuming the option strike price averages at $0.80 and all performance bonuses are achieved, the new CEO will have been paid $17 million in cash, shares and options over shares over this three year period.

Summary

Peplin continues to be a significantly undervalued asset. Its technology risk is low with its asset in Phase III clinical studies. We estimate the drug candidate will reach the market in the US by mid 2011 for the treatment of actinic keratosis skin lesions.

Following the recently proposed placement and the acquisition of **Neosil**, which are pending shareholder approval, Peplin will have an estimated US$56 million in cash and will be capitalised at $130 million.
Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Alchemia Update

Alchemia shares are trading at record low levels offering very good value to investors. Its anti-coagulant drug, fondaparinux, the generic form of **GlaxoSmithKline**'s Arixtra, is expected to be filed for approval this year and be on the market by mid-2009 in the US. The company is currently capitalised at $35 million with $15 million in cash at mid year.

We estimate its profit share from FY2010 will range between $16 million - $23 million a year from fondaparinux sales (see assumptions below). The branded drug Arixtra is currently generating sales tracking at US$120 in the US. Alchemia's licensing partner Dr Reddy's should be able to gain 40% - 50% market share quickly at up to a 20% price discount in the US.

Profit share assumptions for fondaparinux

- Arixtra sales in the US: US$120 million
- Market share gained: 40% - 50%
- Price discounting: 10% - 20%
- Profit share with Dr Reddy's: 50% (min)
- AUD = 0.8 USD

Estimated net revenue to Alchemia: $16 million - $23 million p.a.

Other Phase III Arixtra trials

Arixtra is currently approved for five different indications by the US FDA (not including acute coronary syndromes) and five indication by the European Medicines Agency (including acute coronary syndromes). It is worth noting that GlaxoSmithKline is continuing with a busy Phase III schedule of trials for Arixtra, with seven trials planned or underway at present. Most trials look to be enrolling smaller numbers between 100 and 300 patients, with one trial enrolling 2,500 or so.

The number of trials is evidence that GSK sees fondaparinux as a potentially important revenue earner and obtaining approvals for niche indications is an important aspect to cementing the Arixtra franchise in the lucrative anti-coagulants drug market.

Trials (by Title):

"Extended Deep Venous Thrombosis Prophylaxis in Gynecologic Oncology Surgery With Intermittent Compression Devices (ICD) With or Without Postoperative Arixtra: A Randomized Controlled Trial" (280 patients)

"Fondaparinux to Prevent Thrombotic Complications and Graft Failure in Patients Undergoing Coronary Artery Bypass Graft Surgery: The Fonda CABG Study" (100 patients)

"Anticoagulation and Inferior Vena Cava Filters in Cancer Patients With a Venous Thromboembolism" (106 patients)

"Switching From Fondaparinux to Bivalirudin or Unfractionated Heparin in ACS Patients Undergoing PCI" (100 patients)

"Evaluation Of Fondaparinux (Also Called ARIXTRA) 2.5 mg Subcutaneously Once Daily For The Treatment Of Su-

perficial Thrombophlebitis (Also Known As Superficial Vein Thrombosis)" (2500 patients)

"Safety of Fondaparinux as Routine VTE Prophylaxis in Medical ICU Patients" (100 patients)

"The Use of Fondaparinux in Preventing Thromboembolism in High Risk Trauma Patients" (200 patients)

Developments with competitor drugs

Xarelto approved in Canada [September 16, 2008]

Bayer's Xarelto (rivaroxaban) was approved by Health Canada recently for the indication of prevention of venous thromboembolic events in patients that have undergone elective total hip or total knee replacement surgery. Xarelto is an orally available once-a-day Factor Xa inhibitor, which has been evaluated in several Phase III trials against Lovenox (enoxaparin), a low molecular weight heparin (delivered by sub-cutaneous injection).

In the RECORD I study, involving 4,591 patients undergoing hip arthroplasty (3,153 actually treated), major blood clots occurred in 0.3% of the rivaroxaban group and in 0.5% of the enoxaparin group. The dose of rivaroxaban administered was 10 mg per day whereas the dose if enoxaparin administered was 40mg subcutaneously once a day.

However, rivaroxaban was associated 0.3% major bleeding events versus 0.1% major bleeding events for enoxaparin. (In the RECORD III trial major blood clots occurred in 0.6% of the rivaroxaban group and in 0.5% of the enoxaparin group.)

[By way of some additional comparison, when fondaparinux was evaluated against enoxaparin in acute coronary syndrome patients, there were 2.2% major bleeding events for fondaparinux versus 4.1% for enoxaparin.]

Xarelto is partnered with **Johnson & Johnson (Ortho-McNeil)** for the US market and a NDA has been submitted to the FDA.

Xarelto is a drug to watch because several major studies would seem to suggest that is at least as good as enoxaparin, perhaps superior, with advantage of being an orally administered drug that can be taken at home.

Apixaban misses endpoint [August 26, 2008]

Apixiban is an oral direct Factor Xa inhibitor. This anticoagulant, being developed by **Bristol Myers Squibb** and **Pfizer**, was studied in a head to head Phase III trial for prevention of VTE with enoxaparin (2.5 mg twice daily v 30mg twice daily respectively) in patients undergoing total knee replacement. However, Apixiban did not meet the endpoint of demonstrating non-inferiority compared to enoxaparin.

Daiichi Sankyo's Du-176b [September 8, 2008]

Daiichi Sankyo is developing an oral anticoagulant, DU-176b, a direct Factor Xa inhibitor. The company announced results from a head-to-head trial with dalteparin, a low molecular weight heparin. The study evaluated four doses, each given once a day, in 903 patients undergoing total hip replacement surgery.

The four doses of dalteparin were 15mg, 30mg, 60mg and 90mg.

A finding of the study was that the highest dose (90mg) was associated with the lowest rate of blood clots (venous thrombus embolism - VTE) of 10.6% compared with 43.8% for dalteparin. There were no major bleeding events related to dalteparin. In contrast, the highest dose of DU-176b recorded the highest rate of major bleeding of 2.3%. There was a positive dose related effect of VTE incidence and a negative dose related effect on major bleeding events.

Daiichi Sankyo anticipates commencing Phase III studies of DU-167b before the end of 2008 in patients with atrial fibrillation.

Although Daiichi Sankyo is better known to Australian investors through its drug co-development of the next generation long acting influenza drug CS-8958 in partnership with **Biota**, one of the company's major strengths is cardiovascular drug development. It is also worth noting that the company acquired Belgium company **U3 Pharma** in May for US$235 million. With this move it broadened its oncology portfolio. In June Daiichi Sankyo took a majority position in Indian generics firm **Ranbaxy**, with an intention to acquire outstanding shares. The transaction valued Ranbaxy at US$8.5 billion. These acquisitions make Daiichi Sankyo a wild card consideration in local M&A scenarios, noting that Alchemia has partnered with India's **Dr Reddy's Laboratories** for the manufacturing and marketing of fondaparinux.

Summary

Xarelto (an oral drug) should provide strong competition to Lovenox (an injectable), which has the majority of the anticoagulant market. It has shown to be more effective than Lovenox with a similar safety profile. Bayer recently filed Xarelto for approval with the FDA. This drug, and other oral anticoagulants, as they emerge and where they generate strong data, are the main threat to the success of Alchemia's fondaparinux (delivered by sub-cutaneous injection), although Arixtra has demonstrated superiority to Lovenox.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Labtech Systems – from Page 1

Subsequent products

Based on this range, Labtech looks set to provide a healthy and growing royalty stream to investors. An important aspect going forward is whether the company will look to develop additional products. It is likely that some of the shareholder base will want the company to distribute the royalty stream to shareholders as a dividend stream.

However the company has shown it has a track record in successful instrument development and there is the possibility of subsequent product development, although that decision has not been made.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Anadis – from page 2

human trials could be available by mid-2009.

HIV – Bioguard

Anadis has developed an anti-lipopolysaccharide (LPS) or endotoxin antibody formulation, Bioguard. Anadis' Bioguard 'medical food' standard product may offer benefits to HIV patients on anti-retroviral therapy because it may work to restore immunological function in the gut. LPS is known as a potent stimulant of the immune system and in certain diseases such as HIV, immune systems can exist in a constant state of over activation.The Bioguard product may be an attractive licensing opportunity to companies marketing HIVdrugs. Anadis plans to test Bioguard in a randomized clinical trial to measure its effect with combination HIV drug therapy on CD4+ cell counts in HIV patients with sub-optimal CD4+ levels.

Summary

The major risk attached to Anadis is in regards to finance. The company has net assets of a little over $1 million at June 30, which may be sufficient for at best 12 months operations. The company could see income from sales of the Travelan product occur again when local and international distribuors, who may be appointed in the near future. However, Anadis has access to a three year $5 million equity line of credit with Fortrend Small Cap Investors and has tapped approximately $100,000 of that LOC up to 30 June 2008. Anadis is capitalised at $10 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Change of CEO at NeuroDiscovery

Neurodiscovery's (NDL: 9 cents) CEO, Dr Ian Chessell, will step down after only seven months in the job. Chessell was a high level appointment for the company, having previously been the Global Head of Pain Research for **GlaxoSmithKline**. Chessell will stay on as a non-executive director. He will be replaced by board member Chris Moyses. Moyses was previously Chief Medical Director and Development Director at **Oxford GlycoSciences**.

It is disappointing for the company to lose someone with Chessell's exceptional experience from the role of CEO although he will continue to assist the company from a board position. Possibly Chessell had received a better offer from a larger group, with the constraints of working for a small biotech company in the current investment climate not suiting the former big pharma research head.

The focus for NeuroDiscovery is to ensure it has sufficient funding to progress its lead candidate, NSL-043, into a Phase II trial in neuropathic pain with its partner, **Sosei**. Chessell's previous and ongoing input into the Phase II clinical trial design and licensing opportunities will remain a valuable resource for the company.

Capitalisation: $5 million
Cash (30/6/08): $1.75 million

Bioshares recommendation: **Speculative Hold Class B**

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Bioshares Model Portfolio (26 September 2008)

Company	Price (current)	Price added to portfolio	Date added
Impedimed	$0.72	$0.70	Aug-08
Antisense Therapeutics	$0.06	$0.07	Aug-08
Mesoblast	$1.25	$1.25	Aug-08
Avexa	$0.17	$0.32	Jun-08
Cellestis	$2.02	$2.27	April 2008
IDT	$2.00	$1.90	March 2008
Circadian Technologies	$0.92	$1.03	February 2008
Patrys	$0.24	$0.50	December 2007
NeuroDiscovery	$0.09	$0.16	December 2007
Bionomics	$0.34	$0.42	December 2007
Cogstate	$0.14	$0.13	November 2007
Sirtex Medical	$2.25	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.22	$0.66	September 2007
Starpharma Holdings	$0.31	$0.37	August 2007
Pharmaxis	$2.18	$3.15	August 2007
Universal Biosensors	$0.75	$1.23	June 2007
Biota Holdings	$0.69	$1.55	March 2007
Probiotec	$1.35	$1.12	February 2007
Peplin Inc	$0.43	$0.83	January 2007
Arana Therapeutics	$0.88	$1.31	October 2006
Chemgenex Pharma.	$0.82	$0.38	June 2006
Cytopia	$0.18	$0.46	June 2005
Optiscan Imaging	$0.20	$0.35	March 2005
Acrux	$0.93	$0.83	November 2004
Alchemia	$0.22	$0.67	May 2004

Portfolio Changes – 26 Sept 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,Arana Therapeutics, Starpharma Holdings, Cogstate, Xceed Biotechnology, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Proteome Systems