ISSN 1443-850X

In this edition...
It appears that state of biotech financial health in Australia is on par with that recorded for the US, with about one-third holding less than six months cash. And the battle for cash assets, as observed in the Cytopia-led engagement with Progen, also mirrors events in the US, where disgruntled shareholders are asking for the cash to be returned.

We update readers on the FDA panel recommendation on the anti-clotting drug Xarelto and its implications for Alchemia, and gauge the state of play with the US biotech market from Edward and Stephen Nash from Merriman Curhan Ford.

The Editors
Companies Covered: ACL, UBI

	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)	-28%
Cumulative Gain	**49%**
Av Annual Gain (7 yrs)	**17.8%**

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

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AFS Licence
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Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 304 (20 March 2009)
ISSN 1443-850X

Bioshares

20 March 2009
Edition 304

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

Battle for Cash Assets in Non-Performing Biotechs not Exclusive to Australia

The dispute over control of **Progen Pharmaceuticals** and its sizeable $70 million of funds continues between the current Progen board and a **Cytopia**-led Progen shareholder group. Following the decision to cancel merger plans with Avexa after 74% of Progen shareholders who voted, voted against the merger, the Progen board continues its desire to maintain control of the company.

The Progen board has now decided to conduct a $40 million share buy-back, doubling the previous $20 million proposed buy-back if the Avexa merger was successful. With the remaining $30 million in cash, Progen will continue with development programs, which includes the possibility of conducting further trials of PI-88 in Taiwan to have that product approved in that market.

Progen shareholders will have the opportunity to vote in on Friday March 27 to decide whether the current board should be removed and to install three directors proposed by Cytopia. If elected, the directors will have a mandate to conduct an uncapped share buy-back, as much as remaining funds will allow, and then to explore a merger with Cytopia in the interests of remaining Progen shareholders.

The battle for existing scarce funds in the biotech sector such as that being conducted by Progen and Cytopia is not exclusive to Australia. In the US the battle for existing cash held by biotech companies that have failed to deliver is becoming a regular occurrence. A recent article in *The New York Times* has focused on this emerging theme.
(see http://www.nytimes.com/2009/0310business10biocash.html?scp=2&sq=biotechnology&st=cse)

The fight for the cash from under-performing biotechs is being driven by major shareholders, who argue that "the remaining cash belongs to them and that they - not a losing company's executives - should decide how to invest it". Arbitraguers are also helping force the issue, investing in companies trading at over 50% below their cash assets.

It is a fair enough argument for companies that have had in some cases several program failures. The NYT article phrases it a little more colorfully. "..there have been countless zombies - companies that lurch from product to product, surviving years or even decades without ever achieving success". Progen could arguably be now placed into this category.

An investment concern with Progen is that funds will be whittled away, as has occurred in other biotechs, with Cytopia estimating that at least $1.2 million has been spent on the failed merger with Avexa. The NYT article quotes a portfolio manager at the **Biotechnology Value Fund**, Oleg Nodelman, who argues that investors need to become more active. "Someone's got to police the space. We're making sure the last $50 million in the company don't go to the bankers and the consultants and the golden parachutes".

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Bioshares Survival Index similar to US figures

The comparison with US biotechs is not limited to battles over cash assets in under-performing biotechs. Burrill & Co. in the US has released its latest annual state of the biotech industry report for 2009. It reveals some surprising statistics, including that 120 of the 360 listed biotechs in the US have less than six months cash. In Australia, the data is similar with 27 of the 89 biotechs that report quarterly cash flow statements having less than six months cash. The report estimates that the US sector will lose 100 of its 360 listed biotech companies this year.

In Australia the numbers are expected, as a percentage, to be similar, with at least 10 companies exiting the sector since November last year (three through acquisition or acquisition of assets –**Arana Therapeutics**, **Heartware** and **Stem Cell Sciences**), and by our estimates, another 20 by year's end.

According to Steve Burrill, "The implicit assumptions that we've built our industry off for 30 or 40 years have changed". Burrill also stated that "If you had to give up 50% of your company for five or 10 or $20 million, a year ago, you probably have to give away up to 90% today to get the same amount of money". (The report can be purchased from www.burrillandco.com)

Government support?

The US biotech industry is also seeking increased government assistance to get through the global financial crisis, including matching funding from the NIH for funds contributed from charity research organisations according to the Burrill report.

The Federal Government in Australia this week announced an $83 million Innovation Investment Follow-on Fund of which **Ausbiotech** estimates only one quarter will go towards the biotech sector. The axing of the Commercial Ready Grant system together with a near complete cessation of private funding opportunities for small biotech companies, as a result of the global economic crisis, is set to see up to 30 companies fail over the next 12 months.

Norwegian Government shows the way

Arguably an example to follow is that of Norway which has a small emerging biotech industry, perhaps similar to Australia's. In January this year, the Norwegian Government announced a US$418 million stimulus package to prevent half of its fragile biotech industry going bankrupt. A government run fund will receive US$279 million to invest in biotech and IT, and loans to biotech companies would increase to around US$140 million a year. The Norwegian biotech industry is heavily focused (80%) in oncology with 50 cancer drug candidates in clinical trials. It was estimated that half of the biotechs in Norway would go out of business in 12 -18 months if additional government support was not received.

Australia – 50% of companies have less than 18 months cash

In Australia, as of the end of last year, at 60 companies (50%) had less than 18 months cash remaining (46 (38%) had less than 12 months cash) from the remaining 120 listed life science companies in Australia (excludes those businesses being acquired). Those statistics are almost identical to that of Norway.

Administrators appointed at Ventracor

This week Ventracor was the latest victim of the GFC in the sector with Steven Sherman and John Gothard of Ferrier Hodgson appointed as administrators. More than $200 million was invested in Ventracor since its float in 1993. However the company ran out of funds at a time when entry into the profitable US market was only about a year away. Its demise can be attributed to the inability of the company to raise sufficent funding when it was still available. That its competitor Heartware raised $30 million in mid 2008 indicates that fundraising in 2008 was not an impossible task. It is emerging that funding was available to the company last year - over $50 million - but the board rejected the discount price of that investment.

A rule of business in biotech is to take money when it's available. Other companies that have ignored this rule are believed to be **Neuren Pharmaceuticals**, which was offered cash at about 40 cents a share but rejected it, and Phylogica, which was stymied in its attempt to raise cash at higher prices, by some influential shareholders. The pressure from shareholders concerned about dilution is the reason for the rejection of such offers, with even some Pharmaxis shareholders not in favour of its last $50 million capital raising at $3.90 a share in 2007. That $50 million has proven to be incredibly important. Pharmaxis is now trading at $1.46 but has $94 million in cash as of December 31, 2008

Bioshares

Universal Biosensors – Update

Results from the landmark JUPITER (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin) study last year looks like it will change the way cardiovascular risk is managed in the healthcare setting. The JUPITER study showed that statin use in people with low cholesterol (LDL) but high hsCRP (high-sensitive C-Reactive protein) delivered an extreme statistical benefit in healthcare.

The trial compared Rosuvastatin against a placebo in 17,802 people with not high levels of cholesterol who would not normally be prescribed statin treatment. However the results were so alarmingly positive that the trial had to be stopped early in fairness to those people in the placebo arm. The results showed that Rosuvastatin reduced the occurrence of heart attacks by 54% compared to placebo, strokes were reduced by 48%, unstable angina down by 47% and total morbidity by 20%!

Statistical analysis of the data from the JUPITER study indicates that hsCRP screening in the US followed by statin therapy for five years could prevent 250,000 heart attacks in the US.

The impact from this study is expected to be so profound that last month the journal Clinical Chemistry dedicated an entire edition to the emergence of CRP as important biomarker and predictor of future cardiovascular events.

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Invited Contribution

US Markets Show Vital Signs of Life for Biotech Investors

By Edward Nash, Managing Director and Senior Biotech Analyst and Stephen Nash, Managing Director and Head of OTCQX Advisory at Merriman Curhan Ford

After a long run of volatility and recessionary market conditions the U.S. stock markets produced their best performance since November 2008 over the past week, sparking speculation that perhaps soon, we might hit the bottom of the market.

The bumpy ride may not be over yet for the U.S. markets, which have been hard hit during the global financial crisis, but the snippets of good news send an important signal to Australian companies looking to the U.S. for capital and investors - now is not the time to be turning your back on the U.S. In fact quite the contrary, now is an opportune time to begin engaging the U.S. market which remains one of the deepest pools of capital in the world and is home to many seasoned biotech investors.

The U.S. biotech sector indices have held up relatively well when compared with the broader market indices. During 2008, while the broader market has fallen by 30 to 40 percent, the biotech indices show that while the sector has incurred losses, they have not been as large as the general market. The BTK, AMEX Biotechnology Index, which tracks the larger biotech companies, fell by 15 percent during 2008, while the index which tracks the small cap biotechs, the NASDAQ Biotechnology Index, or NBI, fell by 16 percent.

Having observed several cycles that have seen the fortunes of biotech companies both in the U.S. and globally rise and fall, the research analysts' view at Merriman Curhan Ford is that there is a lot of pent-up value in the sector that represents a good buying opportunity and a chance for investors to stock up on the large-cap biotechs such as **Gilead**, **Genzyme** and **Amgen**.

The right therapeutic area

While the larger, established names in biotech and life sciences can trade on expected value-add, specifically with regard to earnings, for the smaller companies it's all about being in the right therapeutic space. In this high risk environment, which has seen an unprecedented amount of M&A, reverse mergers and even bankruptcies, being in the right therapeutic arena can be key in determining whether a biotech lives or dies.

Hepatitis C is one of the treatment areas attracting a great deal of interest recently. It is a global disease, with the number of new cases each year, or incidence, growing in the Western world. There have been no new treatments in over a decade and the current treatment regimens are sub-optimal, at best.

One of the standouts in this area is Nasdaq listed **Anadys Pharmaceuticals** (NASDAQ:ANDS), which during 2009 has seen its market capitalisation grow from around US$50 million to around US$157 million on the back of promising Phase 1 data for ANA598, the company's oral non-nucleoside polymerase inhibitor for chronic Hepatitis C virus (HCV) infection.

Vertex Pharmaceuticals (NASDAQ:VRTX), which is also developing an oral hepatitis C protease inhibitor, has been able to raise over US$500 million in the last six months. This has allowed it to acquire a private company from Canada, **ViroChem**, which has increased their Hepatitis C clinical portfolio.

Other 'hot-spots' in biotech are interference RNA; stem cell research, will certainly benefit from the easing of regulation under the Obama administration; and cardiovascular disease which is always of interest but due to the size of trials is often difficult to fund. The key for companies in this space will be to secure partners early on or run trials through Phase II development and then be acquired.

Vaccines, particularly for cancer, are also attracting a lot of interest, although this is a highly competitive field, with many companies working on a range of technologies. A strategic consideration for biotechs in the current market will be to examine whether they can create opportunities to diversify their pipeline through partnerships in other treatment areas with greater commercial opportunities or less competition.

Take the example of **Ardea Biosciences**, which is developing RDEA594 for the treatment of gout. As this is an orphan disease it has the potential to garner large market share as there have been no new therapeutics on the market for gout, except for the recent approval of Urosil from **Takeda**, which has only a 51 percent response rate. Ardea also has RDEA806 in development for the treatment of HIV. It is a non-nucleoside reverse transcriptase inhibitor. (NNRTI). Data to date show that is could be the best-in-class NNRTI and possibly supplant Sustiva as the class leader, which currently has over $1 billion in annual sales. RDEA806 has completed Phase II testing and Ardea is looking to partner the drug, for a sizable up-front payment, milestones and back-end royalty on eventual sales, if commercialised.

Innovative approaches to financing

We're also seeing more innovative approaches to financing within the biotech sector. There have been deals that have provided advances in royalty streams, more reverse mergers, and pharma taking larger equity positions in finalised deals. In addition, M&A has increased to levels not seen before in biotech and stretch from the small-cap arena up to big pharma.

Australian companies with products in development for any of these 'hot' treatment areas have a great opportunity in the U.S. If they have strong proof-of-concept data in one of the aforementioned therapeutic areas, they have a good chance of capturing the support of U.S. investors.

Having said that, Australian companies need to be mindful that there are barriers for foreign companies in the U.S., the obvious time zone differences, lack of access to research and live trading is an ongoing challenge, even for companies in nearby locations such as Canada.

Cont'd on page 5

Xarelto Gets Green Light From FDA Advisory Panel – Implications For Alchemia

Bayer and **Johnson & Johnson's** (J&J) anticoagulant Xarelto (rivaroxaban) was reviewed by an FDA advisory panel this week. Xarelto is sold outside of the US by Bayer, having been approved in Europe and Canada last year, and will be marketed in the US by J&J. The relevance of the progress of this drug to Alchemia is that it will compete strongly against Alchemia's fondaparinux, which should reach the market early next year.

Xarelto is an *oral* anticoagulant that has delivery advantages over existing anticoagulants Lovenox and Arixtra (fondaparinux), which are both *injectable*. Earlier in the week news from some FDA staff was suggesting there were safety concerns over this drug. Bayer's share price fell by 11% over the week. However on Friday an FDA advisory committee recommended the drug for approval (19 versus 2) and Bayer's share price has recovered almost all of that ground.

The drug is expected to be a blockbuster, taking market share away from Lovenox, which generated sales last year of US$3.9 billion for **Sanofi-Aventis**. Lovenox is also under attack from generics, with **Momenta/Sandoz**, **Amphastar/Watson Pharma** and **Teva Pharma** all having filed ANDAs with the FDA. However, the issue is whether the emerging generics can be established as being identical to Lovenox, given Lovenox is a complex drug extracted from pig intestines. (It is a mixture of linear polysaccharides but without folding or immunogenicity issues associated with proteins drugs.)

Sales of Xarelto globally could reach as high as US$2 - 4 billion. However, this will not happen quickly and there are a number of hurdles to cross. At the moment it is approved for short term use (in Canada and Europe) for use in patients undergoing knee and hip replacement to prevent blood clotting as DVTs to avoid pulmonary embolism.

However, approval for use in the treatment of Acute Coronary Syndrome (heart attack or unstable angina) for Xarelto is not expected until at least 2011. Lovenox is approved for post surgery applications and the treatment of DVTs in Europe and the US and for ACS in Europe. Arixtra is approved only for post surgery (orthopedic and abdominal) with the FDA requesting further information before it is approved in ACS.

An analyst from **Wachovia Capital Markets** estimates initial sales for Xarelto/ rivaroxaban of US$300 million in the US for J&J increasing up to US$1.6 billion by 2013 as other indications, including prevention of stroke, are approved.

FDA to decide on rivaroxaban in May

Whether Xarelto/rivaroxaban will receive approval in late May this year is still uncertain. Questions remain over the safety of the drug in longer term use with some concerned about off-label longer term use. An analyst from **Credit Suisse** noted that the FDA may want to see data from a recently completed Atlas study, which may mean approval may not come until 2010 in the US. On one chat site, a concerned surgeon wrote that he or she would not use Xarelto/rivaroxaban because of the greater risk of bleeding and the (potential) liver damage. Xarelto/rivaroxaban not only prevents clotting but also has an effect on existing clots which explains the increased bleeding associated with the drug. Ongoing studies with the drug in over 60,000 people are continuing!

The implications of the above are that Xarelto/rivaroxaban adoption rates will likely be moderate rather than rapid. Orthopedic surgeons are not known to be rapid adopters of technologies. The entrenched position of Lovenox will be difficult to change, but it should change over the next five to seven years. Arixtra has now also formed a strong position in this market with sales expected to reach US$500 million this year.

It has been a long road for Alchemia to bring its technology enabled generic to market. Arixtra was originally developed by **Sanofi-Synthelabo** (now Sanofi-Aventis) and it took Sanofi 10 years to work out how to manufacture the drug. There are considerable technology and funding barriers for other companies to work on bringing another generic fondaparinux to market without the carbohydrate drug manufacturing tools Alchemia holds. It is not impossible, just unlikely, while the US market (clearly the most profitable market for fondaparinux) is only worth US$200 million. The work and investment Alchemia has made over most of this decade will act as a barrier to other competitors.

An unknown – What will GSK do?

While the fondaparinux market continues to grow, thanks to the continued marketing effort of GSK, one unknown is whether GSK will continue to market the drug with a generic competitor on the market. However, there are currently 16 trials registered with the NIH that are recruiting patients into trials with fondaparinux. Nine of these are being sponsored by GSK and seven are being sponsored independently, and in total are seeking to enrol over 9,000 patients.

GSK is awaiting for approval of Arixtra for the treatment of Acute Coronary Syndrome (such as heart attack patients). An ACS trial started last month looking to recruit up to 4000 patients. Of interest to note is that most of the US sites, 40 out of 51, have been withdrawn from this trial, with the remaining 11 sites not yet recruiting, suggesting that GSK is concentrating its marketing efforts in Europe, where GSK's market exclusivity for fondaparinux/ Arixtra lasts until 2012. (Only a small number of sites in Spain (7) have started recruiting patients.) However it's also worth noting that Lovenox is also not approved for ACS in the US.

A report from **ICCI Securities** this week on Dr Reddy's cites fondaparinux and a generic version of Prilosec as "the two candidates with the potential to offer significant upsides", with expectations that generic fondaparinux will be launched in April 2010 and potential profit upside for Dr Reddy's of US$22 million during the first year.

Even if GSK reduces its marketing of Arixtra in the US from next

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Nash & Nash - from page 3

If Australian companies are serious about courting U.S. investors they need to spend time engaging U.S. investors and ensure they have the right support to be able to address Street expectations. An OTCQX listing is beneficial in providing live trading data for U.S. investors, but having a sponsor that provides research coverage and introductions to U.S.-based investors is critical as well. It's also essential that companies speak the same financial language as U.S. investors. These investors are used to seeing GAAP estimates and quarterly reports which include an income statement, balance sheet and cash-flow statement.

There are many good opportunities for biotechs, and that includes Australian biotechs, in the U.S. at the moment. It is essential for Australian biotechs to hit the ground running in this current economic environment and educate investors as to the strong technology and undervalued nature of Australian biotech.

For enquiries regarding this article contact Stephen Nash: nash@mcfco.com

Alchemia - from page 4

year, the US fondaparinux market should have been built up well to around US$300 million a year at the time of launch. From early next year, we estimate Alchemia will receive a profit share in excess of $30 million a year.

Alchemia is capitalised at $46 million with $11 million in cash at the end of last year.

Bioshares recommendation: **Speculative Buy Class A** (However expect some price volatility early this week following the positive decision from the FDA advisory panel on Xarelto/rivaroxaban.)

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UBI - from page 2

The relevance of this to Universal Biosensors (UBI: $0.46) is that one of the diagnostic products the company has been working on for the last few years is a point-of-care diagnostic for CRP. The company has produced a proof of concept prototype using its diagnostic platform technology that is producing some very good results. If this is the case and if CRP becomes a test as widely adopted as cholesterol, then the company's test will be in high demand from major diagnostic test manufacturers looking to secure global marketing rights.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Avexa Reports Further Positive Data

Avexa has reported data from 39 patients continuing on from its Phase IIb trial with its lead drug candidate, ATC, for the treatment of HIV patients with the M184V mutation. The data looks very good with more than 85% of patients having a HIV count below detectable levels. The CD4 levels in the patients after 96 weeks also continued to rise confirming the continued action of the drug candidate.

The challenge at this point for the company is to secure a partnering deal for ATC. With the constraints in funding due to the global financial crisis, it is a buyers market at the moment with an increasing number of biotechs with Phase II and III programs seeking to complete partnering or licensing deals. At 31 December last year, Avexa had cash assets of $20.5 million.

Bioshares recommendation: **Wait for partnering deal before investing**

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Bioshares Model Portfolio (20 March 2009)

Company	Price (current)	Price added to portfolio	Date added
ASDM	$0.35	$0.30	December 2008
QRxPharma	$0.28	$0.25	December 2008
Hexima	$0.34	$0.60	October 2008
Atcor Medical	$0.17	$0.10	October 2008
CathRx	$0.32	$0.70	October 2008
Impedimed	$0.73	$0.70	August 2008
Mesoblast	$0.76	$1.25	August 2008
Cellestis	$1.95	$2.27	April 2008
IDT	$1.50	$1.90	March 2008
Circadian Technologies	$0.71	$1.03	February 2008
Patrys	$0.06	$0.50	December 2007
Bionomics	$0.21	$0.42	December 2007
Cogstate	$0.23	$0.13	November 2007
Sirtex Medical	$2.19	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.22	$0.66	September 2007
Starpharma Holdings	$0.19	$0.37	August 2007
Pharmaxis	$1.46	$3.15	August 2007
Universal Biosensors	$0.46	$1.23	June 2007
Biota Holdings	$0.58	$1.55	March 2007
Probiotec	$1.45	$1.12	February 2007
Peplin Inc	$0.55	$0.83	January 2007
Arana Therapeutics	$1.44	$1.31	October 2006
Chemgenex Pharma.	$0.50	$0.38	June 2006
Cytopia	$0.12	$0.46	June 2005
Acrux	$0.46	$0.83	November 2004
Alchemia	$0.29	$0.67	May 2004

Portfolio Changes – 20 March 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: Pharmaxis, 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, Tyrian Diagnostics, Mesoblast, Atcor Medical