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Biosharesv

15 June 2012
Edition 459

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

In this edition...
European political stresses and troubles abound and the shock waves have pounded local equity markets. Many biotech stocks have suffered, but not all. We have studied the performance of 13 leading biotech stocks for the past six months. The question is why the outperformers have done well and the losers have suffered. The take home message is that stock picking still works in the toughest of markets, especially with stocks with safe-haven properties. Merck Serono has terminated its involvement with Bionomics' Kv1.3 program, However, Bionomics may have a fresh chance to generate much more value from the program going forward. Management changes at Impedimed have seen CEO Greg Brown move to an executive director role, with a US-based CEO taking over the reigns.
Companies Covered: BNO, IPD

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - current)	-7.0%
Cumulative Gain	**221%**
Av. annual gain (11 yrs)	**17.8%**

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Biotech Investment Strategies for Handling European Financial Volatility

Investors in biotech stocks, along with other equity investors, face a difficult period for as long as the European financial crisis remains an unresolved issue. This crisis has been responsible for a decline in biotech stocks over the last two months, and the broader equity market has also been troubled with the ASX All Ordinaries Index declining by 9% since the beginning of May. In contrast, the US biotech sector is moving to 12 year highs. What does this mean for Australian biotech investors? Furthermore, what stocks should ASX focused biotech investors be looking at during this time of global financial volatility?

US Biotech Sector Approaches 12 Year High

The US appears to be successfully battling through its own financial maelstrom, with the US housing market, the root cause of the global financial crisis, looking to have bottomed and now turning the corner. The US in now a recovery phase, albeit a slow one, and notwithstanding the high national debt levels that still need to be addressed.

The US biotech sector, as reflected by the performance of the Nasdaq Biotech Index (NBI), continues to perform remarkably well.

In the US, the Nasdaq Biotech Index is a weighted measure of market performance 118 listed biotech and pharmaceutical companies with a market capitalisation in excess of $200 million. The NBI is approaching a 12-year high at 1300 points. It has been steadily climbing for the last three years , up 111% in this time. It has risen rapidly since November last year, up 35%, following the US$11 billion purchase of Pharmasset by Gilead Sciences for that company's end of Phase II hepatitis C drug program assets. This has led to a buying spree in the hepatitis C space.

Leading Biotechs get their Financial Base in Order

The leader board of ASX biotech stocks, what we call the Tier-1 biotechs in Australia, continue with their charge to market with new products, product approvals, market launches, and now building sales for these products. The interest in Australia is supported by the robust US biotech sector performance. For the earlier stage biotechs however, the Global Financial Crisis (GFC) has taken and continues to take its toll, whether in Australia, the US or any other country.

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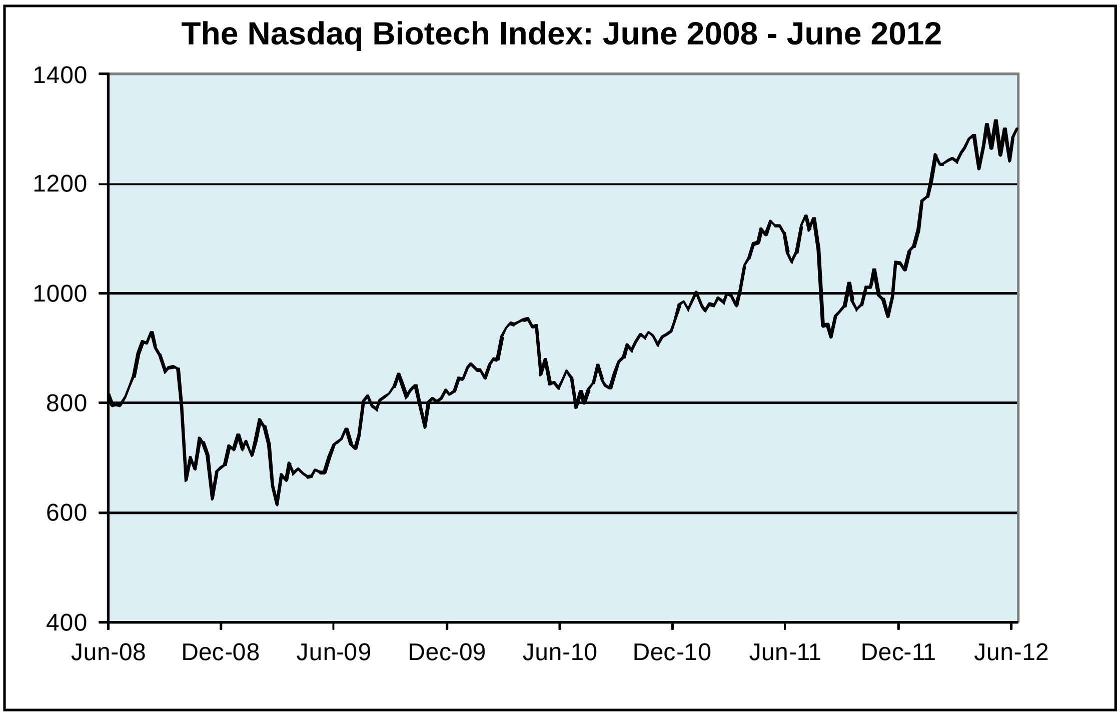

This is evidenced by two smaller cap companies recently, **Circadian Technologies** and **Atcor Medical**. Both companies raised funds however each was only able to raise $1 million, with Atcor's raising also coming from directors and senior management. And other biotechs such **Patrys**, have found capital raising very difficult.

Most of the leading biotechs in Australia have addressed their funding issues. The most recent was **Nanosonics**, which raised $15.5 million with somewhat ease, the raising being conducted by Shaw Corporate Finance. Shaw was also the underwriter of the **Osprey Medical** float ($20 million), and the joint lead manager of the **Starpharma** placement ($32 million) last year with Bell Potter. The other leaders that have comfortably addressed their funding requirements in the last year include **Pharmaxis** which raised $80 million (underwritten by Wilson HTM and Merrill Lynch), **QRxPharma** which raised $35 million (through RBS Morgans and Bell Potter Securities as lead managers), **Phosphagenics** which raised $24 million (through RBS Morgans and Bell Potter Secturities as lead managers), and **Alchemia** which raised $15 million (through RBS Morgans).

Acrux has no further need to raise capital and is now returning excess funds to shareholders through dividend payments. **Sirtex Medical** is a profitable business. **Mesoblast** had $226 million in funds at the end of March, **Bionomics** has indicated it has sufficient funds for the time being with $18.8 million at the end of March, Universal Biosensors is similarly comfortable with its cash position. It had $15.7 million at the end of March with revenue expected to increase from collaborative deals and increased glucose test strip sales.

Last month **Impedimed** announced it intended to raise $13.5 million under a rights issue, however was only able to raise $8.7 million (the capital raising was led by Wilson HTM Corporate Finance and RBS Morgans Corporate). This increased Impedimed's bank balance to $17.4 million at the end of May. The raising was conducted at a substantial 18.6% discount to its closing price.

Biota had $51 million in funds at the end of March. It merger with US biotech Nabi Biopharmaceuticals in the US will strengthen its balance sheet and deliver the merged entity around $100 million in funds.

Still to Address Funding Requirements

One company with programs at an advanced stage that still needs to address its funding requirements is Clinuvel Pharmaceuticals. It had only $9.2 million at the end of March, which represents 10 months of spending, based on its last nine months burn rate.

IPOs

The opportunity for IPOs, whether in Australia or in the US, remains difficult. In recent weeks a sleep therapy technology company from the US, Ventus Medical, was seeking to list on the ASX and raise $40 million. The listing has now been stopped, with the only successful biotech listing in Australia this year being from **Osprey Medical**.

In the US, 20 biotechs have announced intentions to IPO this year. Of those three companies have listed, four companies have postponed or withdrawn their listing plans (all since the start on May), and 12 companies have filed to list.

Cancer stem cell company **Verastem** listed in January raising US$55 million. It is capitalised at $214 million. Drug developer **ChemoCentryx** listed in February raising US$51 million. It has a market value of $438 million. Antibiotic drug developer Cempra Pharmaceuticals also listed in February, raising US$50 million. It is valued now at US$166 million. In March Merrimack Pharmaceuticals listed in the US raising US$100 million. It is currently valued at US$675 million.

All four companies are above their issue prices; Verastem is up 2%, ChemoCentryx is up 20%, Cempra is the best performer up 32% and Merrimack is up 5%.

Cont'd over

Six Month Performance

In the chart on the next page, we look at the performance of 13 leader board biotechs in Australia over the last six months (from Dec 31, 2011).

Bionomics [Change from Dec 31, 2012: -43%]

Bionomics' share price was down around 20% for the first four months of this year. An on-market sell down by Start-Up Australia of its remaining stake in Bionomics saw that decline increase to over 40% over the first half. The lack of major milestones over the next six months, other than completion of recruitment in its Phase II renal cancer study, has also contributed to the decline. There may also be a shift by investors into less risky biotechs, given the level of global financial uncertainty and volatility.

Impedimed [-49%]

Impedimed has also seen its share price fall by over 49% this year. A capital raising at a heavy discount has been part of that reason. The other part is that sales of the company's diagnostic test (for lymphedema in patients following breast cancer surgery) have failed to grow, with receipts from customers in the nine months to the end of March being only $2.2 million, less than the $2.8 million received in the previous corresponding period.

Phosphagenics [-33%]

Phosphagenics has seen its share price fall 33% with the company indicating it will need to work with an additional transdermal patch supplier, following drug crystallisation issues with the existing patch.

Universal Biosensors [-20%]

Universal Biosensors share price has declined by 20% since the end of 2011 due to a disinterested register.

Nanosonics [-19%]

Nanosonics has seen its share price fall by 19%, even though its placement was conducted at a 3 cent a share premium (at 53 cents) to its closing price. Its receipts from customers increased from $1.4 million for the nine months ending 31 March 2011, to $7.9 million for the same corresponding period this year. The stock was recently been added to the Bioshares Model Portfolio.

Mesoblast [-20%]

Mesoblast has seen its share price fall away 23% in the last four weeks, possibly a result of the continued global financial uncertainty also triggering some investors to take profits.

Biota Holding [-7%]

Biota Holdings had seen its share price increase by 25% over the 12 months, although the share price has fallen by 7% from the end of 2011. Investors are possibly exiting ahead of a planned merger and delisting from the ASX.

Pharmaxis [+4%]

Pharmaxis has lost most of the gains it has made during the year, up now only 4%. Results from a competing cystic fibrosis therapy from Vertex Pharmaceuticals contributed to that retracement. However Pharmaxis has shown its results are just as good and are not restricted to 46% of the population as with the Vertex therapy. Pharmaxis has since launched Bronchitol in Europe. Pharmaxis is an attractive investment opportunity.

QRxPharma [+9%]

QRxPharma has lost most of its gains of the six months, as some less risk investors sell down prior to the FDA decision on the company's new drug application for MoxDuo IR this month.

We expect the decision to be generally positive but the chance of a qualified decision must always be factored in. However in the current market, investors should not expect the stock to deliver wild gains if the company gets the green light. There may be an opportunity to buy the stock de-risked at a slight premium following the FDA decision.

Starpharma [+17%]

Starpharma was up 60% at one stage in the first half. However that gain is now only at 17%. Similar to Mesoblast, the current market conditions may be seeing some investors taking profits in that stock.

Sirtex Medical [+37%]

Sirtex Medical is offering stronger certainty of earnings. Its share price is up 37% for the year, with unit sales of its liver cancer therapy up 34% in the March quarter of the previous corresponding period.

Alchemia [+45%]

Alchemia is still up 45% over the year, with fondaparinux sales now firmly entrenched in the US and the company due to receive around $25 million a year in profits. It is also moving towards spinning out its oncology business, which may crystallize more value within the company.

Acrux [+53%]

Acrux remains a star performer, up 53%, with a new set of institutional investors coming on to the register, as the global market for testosterone continues to show strong growth and the company's Axiron product continuing to increase its market share in the US, where it is sold by Eli Lilly. The product was also recently granted marketing approval in Australia.

Investment Considerations

Those stocks offering more certainty, such as Acrux and Sirtex Medical, are experiencing higher demand, in preference to early stage drug development assets, such as Bionomics, that can expect to trade at increasingly higher discounts to fair value in the current investment climate.

Stocks where certainty of future earnings should increase over the remainder of 2012, and thereby market value we expect to also rise, include Alchemia (from fondaparinux earnings), Nanosonics (from building sales), QRxPharma (from MoxDuo IR approval and launch) and Pharmaxis (following market launch).

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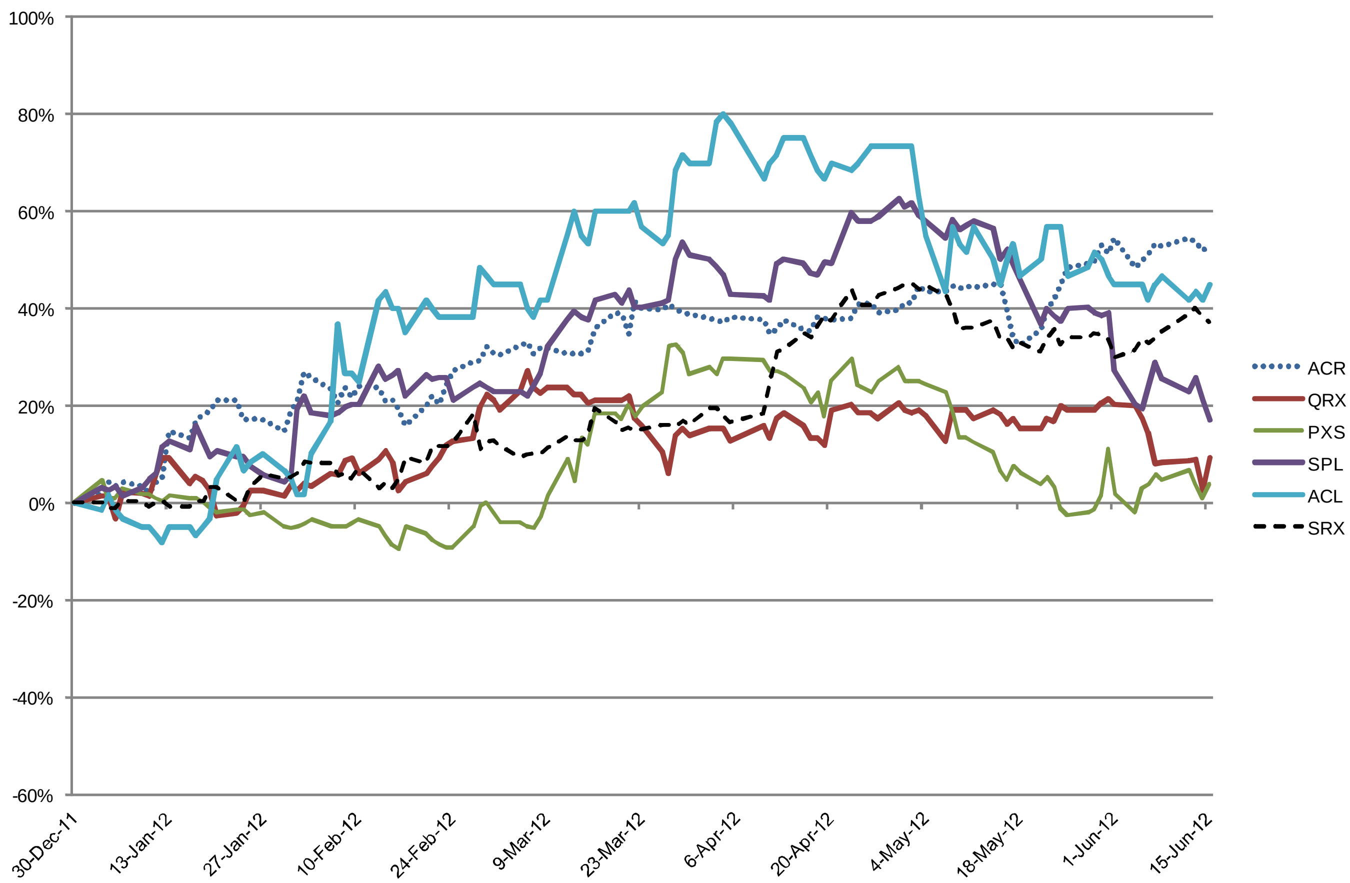
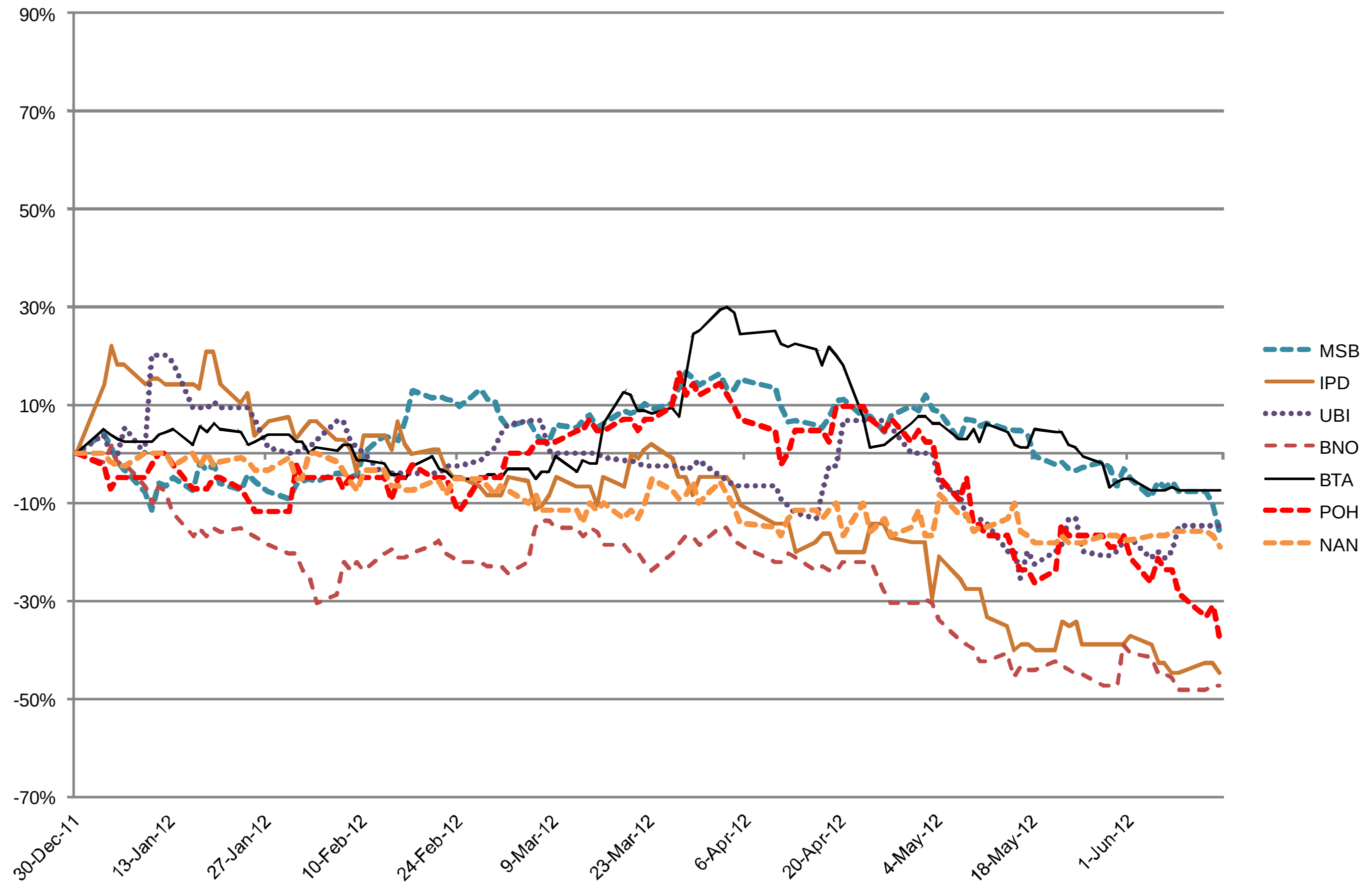
Biotech Leader Board Stocks (13) – Stocks with Price Gains Over Six Months



Biotech Leader Board Stocks (13) – Stocks with Price Declines Over Six Months



Merck Serono Hands Back Kv1.3 Program to Bionomics

Bionomics (BNO: $0.335) has been handed back its Kv1.3 program by **Merck Serono**. The Kv1.3 program is named after a potassium voltage channel which has been shown to play a role in various immune-related conditions such as multiple sclerosis, psoriasis and arthritis. Voltage channels are electrical gradients which cross cell walls.

Why Has Merck Serono Discontinued the Partnership?

Bionomics did not state why Merck Serono handed the program back Bionomics. The R&D program commenced in June 2008 when Merck Serono and Bionomics signed a development and licensing agreement. Merck Serono paid Bionomics an up-front payment of US$2 million and agreed to pay Bionomics total potential payments of up to US$47 million in addition undisclosed royalties. To date, Bionomics has received $9-$10 million in payments from Merck Serono.

Under the arrangement Bionomics was actively managing the chemistry or compound aspect of the program with Merck managing pre-clinical activities such as toxicology and ADMET studies.

There are several possible reasons why Merck Serono handed the program back. The first is that it is a casualty of Merck Serono's downsizing of its operations in Geneva (where the Serono part of the business has been located). **Merck KGaA** and **Serono** merged in 2006. A second consideration is that several new MS drugs – e.g. Panaclar (BG12), Aubagio (teriflunomide) and Lemtrada (alemtuzumab) – are passing through the regulatory approval phase, causing a re-adjustment of the commercial landscape for MS drug developers. A third reason is that Merck Serono has identified issues with specific compounds, chemical scaffolds, or the disease biology that have caused it to reject the program.

Going Forward/Implications

Bionomics intends to accelerate the Kv1.3 program and will expand the program into other immune related conditions, which had not been a focus of Merck Serono. Some program cessations or handbacks of drugs initially developed by Australian biotechs have been because of technical or clinical failure, as was the case with Amrad's emfilermin (partnered with **Serono**) and quite likely Cytopia's Jak3 program (partnered with **Novartis**). However in 2004, **Allergan** abruptly terminated its arrangement with Peplin for

Cont'd over

Selected Drug Development Handbacks

Program/Assets [Stage of program]	Therapeutic Area	Company	Partner/ licensee	Date of Agreement	Date of Handback	Comments*
Emfilermin [Clinical]	Assisted Reproduction (Fertility)	**Amrad**	Serono	May-03	Jun-04	Proof of concept study failed. Option first granted in 2000; full license in May 2003; deal values not disclosed.
PEP005 [Pre-clinical]	Non-melanoma skin cancers	**Peplin**	Allergan	Nov-02	Oct-04	Up-front of US$1 M; potential payments US$22 M (Americas territories only). Peplin was acquired by Leo Pharma in 2009 for $328 M.
Transdermal Spray [Pre-clinical]	Contraception	**Acrux**	Organon	Mar-07	Aug-08	Two agreements for two products; Up-front of US$1 M; Potential payments of US$12 M to US$16 M per product. Acrux intended to re-partner the programs but this did not occur.
Jak3 [Discovery]	Immuno-supression	**Cytopia**	Novartis	Jun-06	Jun-09	Joint early stage discovery - 'all in' basis. Payments of $13 M over three years. Total potential deal value - $274 M. Program appeared to have been left in the hands of Novartis for further development but there is no evidence of this occurring. Program most likely discontinued because of evidence suggesting that inhibition of Jak3 is insufficient to stop signalling.
Kv1.3 [Discovery]	MS/autoimmune conditions	**Bionomics**	Merck Serono	Jun-08	Jun-12	Up-front of US$2 M; potential payments US$47 M. Also received ~$7-8 M in program payments.

* note, in all cases royalties were included in deal terms but not disclosed

Bioshares Model Portfolio (15 June 2012)

Company	Price (current)	Price added to portfolio	Date added
Nanosonics	$0.485	$0.495	June 2011
Osprey Medical	$0.39	$0.40	April 2012
QRxPharma	$1.65	$1.66	October 2011
Mayne Pharma Group	$0.320	$0.435	September 2011
Somnomed	$0.82	$0.94	January 2011
Phylogica	$0.048	$0.053	September 2010
Biota Holdings	$0.75	$1.09	May 2010
Tissue Therapies	$0.48	$0.21	January 2010
Atcor Medical	$0.08	$0.10	October 2008
Bionomics	$0.34	$0.42	December 2007
Cogstate	$0.270	$0.13	November 2007
Sirtex Medical	$6.15	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.60	$6.60	September 2007
Pharmaxis	$1.08	$3.15	August 2007
Universal Biosensors	$0.60	$1.23	June 2007
Alchemia	$0.440	$0.67	May 2004

Portfolio Changes – 15 June 2012

IN:
No changes

OUT:
No changes

– Bionomics cont'd

PEP005, a topical product for treating non-melanoma skin cancers. However, Peplin committed to further development of PEP005 under its own management, raising close to $100 million to advance PEP005 through late stage clinical development. In 2009, Peplin was acquired by **Leo Pharma AS** for $328 million. PEP005, now known as Picato, was approved by the FDA in January 2012.

If the Kv1.3 program has been handed back by Merck Serono for reasons of technical failure, Bionomics' obvious course of action (apart from stating the reason) is to cancel the program or possibly commission a review of the data. However, given that Bionomics has been actively involved with the program via joint quarterly steering committee meetings, that would seem unlikely.

What Bionomics may now wish to give serious thought to is the costs and benefits of taking a Kv1.3 lead molecule through to Phase II in multiple sclerosis and a proof-of-concept study in rheumatoid arthritis, and then contemplating a license deal.

Summary

On balance it is more likely that the handback is casualty of larger human resource problems currently besetting Merck Serono. Bionomics looks to have found itself in full possession and control of a potentially valuable asset over which it had retained ajoint oversite of since the collaboration began in 2008. If work undertaken by Merck Serono is crudely estimated at $10 million, the Kv1.3 program is an asset which has had at around $20 million spent on it, none of which has come from shareholders pockets.

Bionomics is capitalised at $116 million and held cash of $18.8 million at March 31, 2011.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Management Changes at Impedimed

Impedimed (IPD: $0.27) has announced changes to its management, appointing a US based CEO, Richard Carreon, with former CEO Greg Brown moving to an Executive Director role. The move has practical elements for the company given that it has been directing much of its energy towards the securing of agreements with US health insurers to provide coverage of the use of its LDex U400 device as an aid to lymphoedema assessment.

Brisbane-based Brown spent long periods of time out of Australia working on Impedimed's commercialisation objectives and one can assume that a personal factor was involved in the decision to move out of the CEO role. The fact the he is continuing as an executive director indicates his ongoing commitment to the firm.

However, a primary reason for the share price weakness is that Impedimed has found it difficult to persuade insurers to write medical policy covering its technology because of a lack of clinical evidence gained from using the LDex 400 product. Impedimed has been relying on clinical data obtained from rival technologies that support its arguments for pre-emptive assessment of lymphoedema.

Impedimed has also run a high net cash burn since it listed in 2007, with cumulative net operational cash flows from FY2008 to March 2012 now totalling $50.3 million. After completing a weakly supported rights issue, the company is holding an estimated $17.4 million in cash.

Impedimed should benefit from a new CEO at the helm who can refresh the LDex proposition to insurance companies.

Impedimed is capitalised $49 million.

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

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Circadian Technologies, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Atcor Medical, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Genetic Technologies, Calzada, Bioniche

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