ISSN 1443-850X

**In this edition...**
The reporting season for companies with a June 30 financial year is coming to a close. Mayne Pharma's earnings have bounced back from the hit it took last year in the lead up to anticipated generic competition for the acne drug Doryx. Although Doryx sales have fallen, they haven't followed the standard steep fall that usually follows the entry of generics. Nanosonics' jump in sales to $12 million for the year (up from $2.3 million) gave a hint as to what could be in store for company in the longer term. The good news for Bionomics this week was that its anxiety drug partner Ironwood Pharmaceuticals had its lead drug Linzess approved by the FDA thus ensuring Ironwood's continued focus on the IW2143 program. No doubt anxiety levels were observed to fall at both companies!
**Companies Covered: BCT, BNO, MYX, NAN**

| | 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) | -18.4% |
| **Cumulative Gain** | **182%** |
| **Av. annual gain (11 yrs)** | **17.8%** |

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

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Individual Subscriptions (48 issues/year)
**$375** (Inc.GST)
Edition Number 470 (31 August 2012)



# Bioshares

**31 August 2012**
**Edition 470**

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

## *Success for Bionomics' Partner Ironwood Pharmaceuticals*

Bionomics (BNO: $0.33) has indirectly received some very positive news; its development partner for its drug candidate IW2143 (previously BNC210) for the treatment of depression and anxiety, **Ironwood Pharmaceuticals**, has just received FDA approval for its lead drug, linaclotide, one month early. The drug has now been provided with the brand name Linzess.

Linzess is approved for the treatment of irritable bowel syndrome and also for the treatment of chronic idiopathic constipation (CIC). It will be co-marketed in the US by Ironwood and **Forest Laboratories**. Sales of the drug are estimated by some to exceed $1 billion by 2018. An estimated 13 million people suffer from irritable bowel syndrome with constipation and 35 million people live with CIC in in the US, according to Ironwood Pharmaceuticals.

The event is very positive for Bionomics because it ensures continued and undisturbed funding and attention from Ironwood for the Bionomics-Ironwood anxiety and depression drug program. Ironwood is expected to invest $60 million a year into IW2143 program.

### IW2143 Update

At the moment the anxiety program partnered by Bionomics with Ironwood is focused on reformulating the lead drug candidate, IW2143. The aim is to make minor modifications to the drug candidate in order to reduce the food effect associated with the compound. At the moment, the drug candidate needs to be taken after breakfast.

With Linzess, Ironwood had significant challenges to get the properties of that drug right, particularly in ensuring the stabilisation of an orally delivered peptide drug.

The companies are working on an IND submission with a plan to move the program into a Phase Ib trial. The companies are also planning a Phase IIa trial to follow the Phase Ib trial, which is expected to involve less than 120 people. Bionomics is eligible to receive a further US$10 million over the next 16 months from Ironwood, following an upfront payment of US$3 million in January this year, when the partnership was formed.

Ironwood is one of the leaders in using patient reported outcomes (PROs) as endpoints for assessing drug efficacy. In the Phase III trials of Linzess, there were 66 different endpoints, all PROs. It is very likely Ironwood will follow a similar tack with IW2143 for the treatment of anxiety and depression.

### Neurofit a Useful Asset for Bionomics

Bionomics has been getting a lot of use from its Neurofit preclinical testing business it purchased in France for €1.25 million in 2005. Over the last 12 months, 60% of the use of that business has been for Bionomics work. The Kv1.3 compounds (for the treatment of

*Cont'd over*

multiple sclerosis) were all tested by Neurofit, as were the IW2143 compounds, and hundreds of Bionomics' compounds for its latest program in Alzheimer's disease (alpha-7) have been tested through this facility said Bionomics CEO Deborah Rathjen.

Bionomics has 10 of its 45 staff based at this facility, which is a profitable business for Bionomics. The business conducts pre-clinical testing for other drug developers, including pharmaceutical companies.

### Alzheimer's Disease Program

Bionomics started its Alzheimer's disease program two years ago. Bionomics has been able to move additional resources into this program following the signing of the Ironwood deal in January. The company is seeking to modulate the alpha-7 nicotinic acetyl choline receptor found in the brain. Modulating this receptor may not only improve cognition, but also reduce inflammation in the brain, with both of these outcomes potentially having a beneficial effect in treating Alzheimer's disease.

Improving cognition and reducing inflammation in the brain however is not limited to Alzheimer's disease, but such an effective therapy may also have a therapeutic benefit in Parkinson's disease, multiple sclerosis, schizophrenia and ADHD according to the company.

There are two ways to effect the alpha-7 receptor for these disease indications. One is to stimulate and turn on that receptor using an agonist. A private US biotech **EnVivo Pharmaceuticals** has generated statistically positive Phase IIb results using an agonist approach. That trial involved 409 patients with Alzheimer's disease and is now moving into Phase III trials. Another biotech, **Targacept**, is awaiting results from its Phase II study with its alpha-7 agonist.

The alternative approach is to modulate this receptor, not completely switching the receptor on. This is called a positive allosteric modulator (PAM) approach and is the approach selected by Bionomics. The benefit of using this approach over the agonist approach is that the receptor is not constantly activated regardless of need. Constant activation can lead to receptor desensitisation, tolerance to drug therapy and potentially increased risk of gastrointestinal and cardiac side effects. PAMs can also offer selectivity over other nicotinic receptors.

Bionomics is not without competitors in the PAM approach against the alpha-7 receptor. Bionomics is close to selecting its lead candidate and will look to move the program into the clinic in 2013. It has identified several compounds that can modulate this receptor and that have shown to restore memory in mice.

### Milestones Ahead

Bionomics is conducting a Phase II trial with its oncology drug candidate, BNC105, in 134 patients with renal cancer. The trial is on track to be fully enrolled this year. The primary endpoint in this trial will be the percentage of patients with progression free survival at six months, compared to those taking Afinitor without BNC105. Results should be out in mid 2013.

Bionomics has also started a Phase I/II trial with BNC105 in women with ovarian cancer. The safety aspect of this trial (combining BNC105 with other ovarian cancer treatment drugs) is expected to be completed by mid 2013.

Bionomics is also looking to form additional licensing and partnering deals. The company will seek to partner its Kv1.3 program in multiple sclerosis over the next nine months. This program was returned to Bionomics from **Merck Serono**. The company will also look to out-license BNC105 if results from its renal cancer study are positive in 2013.

Additional interest has also emerged in the stock, with a US-based biotech fund now investing in the company.

### Additions to the Executive Leadership

In coming weeks, Bionomics expects to announce the appointment of a VP of Clinical Development and a Chief Medical Officer. These appointments signal a move by Bionomics to become a more comprehensive and integrated clinical stage biotech company.

### Summary

Bionomics is capitalised at $114 million with $17.3 million in cash at the end of June. Bionomics expects to benefit from the Federal Government's Tax Incentive, which will see the company receive at least $3.1 million for FY2012 R&D expenditure. With the Ironwood deal completed in January and with clinical programs underway but no results expected this year, CEO Deborah Rathjen does not agree with some analysts that the remainder of 2012 will be a quiet year for Bionomics.

*Bioshares* recommendation: **Speculative Buy Class A**

**Bioshares**

## *Bluechiip Update*

Bluechiip (BCT: $0.24) has formed a strategic relationship with another service provider in the US. **Gentris Corporation** provides a biorepository service for companies conducting clinical trials and genomic analysis programs. The alliance will see both companies share their expertise and will allow Gentris to also offer temperature tracking of samples.

Bluechiip's tracking systems use acoustic technology to code and identify samples. In contrast to bar coding and RFID, which have issues with extreme temperatures, the Bluechiip tracking system can be used at all temperatures and can include continuous temperature sensing.

Gentris has purchased some trial product from Bluechiip, and is at least Bluechiip's second customer. ATCC, which stores around 10 million biologic samples, started using the Bluechiip system in June this year.

Bluechiip is capitalised at $21 million and had cash of $0.5 million at the end of June. The company expects to receive an R&D rebate of $1 million. Pending receipt of the rebate we place a Hold on the stock.

Bioshares recommendation: **Speculative Hold Class B**

# *Mayne Pharma Advances Two New Products*

Mayne Pharma (MYX: $0.38) posted a net profit after tax of $6.1 million, an increase of 264.7% from the previous year. Sales revenue increased by 10.4% for the year to $51.9 million.

Gross margins increased from $20.1 million for FY2011 to $22.6 million for FY2012.

Underlying EBITDA (allowing for adjustments) was $11.5 million , up 2.3% from the previous year.

The company expended $4 million on R&D during the year, down from $6 million in FY2011. Cash at the end of the financial year was $11.6 million compared to $5.8 million at the same time a year ago.

The company carried at June 30, 2012, an earn-out liability of $9.3. A year ago the earn-out liability stood at $15.1 million. The earn-out liability stems from the company's acquisition in October 2009 of the then Mayne Pharma by the then Halcygen Pharmaceuticals from **Hospira**. The earn-out is calculated on sales but is capped on an annual basis and runs for a six year period ending in 2015.

## Doryx Sales Surprise

Mayne's results for FY2012 come as a surprise given that the company's revenues from its biggest earner Doryx had become subject to competition from generic companies in the US in May of this year. The effect of anticipated competition appeared in the company FY2011 accounts when Doryx sales recorded for that year fell 46% to $20.9 million. [Sales for FY2012 were $20.5 million.]

**Warner Chilcott**, the company which sells Doryx in the US (and buys the manufactured product from Mayne Pharma) chose to run down stocks of older dose forms while it waited to bring out a new dose form with which to fight off generic competitors. However by May 2012 Mayne was unable to defend its '161 patent (which covered the 150mg formulation of Doryx) from claims that **Mylan Pharmaceuticals** and **Impax Pharmaceuticals** had infringed that patent. Mylan has since begun marketing an AB-rated version of Doryx. (An AB generic means that bioequivalence has been demonstrated.)

Mayne has lodged an appeal with the US Court of Appeals regarding the decision.

Weekly prescription volumes of Doryx have fallen from just under the 14,000 level when Mylan introduced its product, to stabilise around the 8000 mark, a fall of about 35-40%. Typically when generic competition is introduced, sales of the monopoly branded drug fall by as much as 70-80% in a short space of time. Sales of Doryx prescriptions have run counter to expectations. Why that is the case is discussed in the box on the next page.

## New Products in Development

Mayne has revealed two products it intends to develop as part of its plan to build revenues that have been weakened by generic competition for Doryx and to also balance its investment in SUBACAP, a patent-protected formulation of itraconazole used to treat fungal infections, including infections of the toenail.

***Extended release pain capsule***

The first product Mayne intends to develop is an extended release pain capsule with a target ANDA filing date of 2013 H2. Sales in the existing market that this product will address are worth US$270 million. Mayne will collaborate with a US drug delivery company to develop this product.

***Extended release anti-hypertensive***

The second product is an extended release anti-hypertensive tablet with a target ANDA filing date set for 2014. Sales in the existing market that this product will address are worth US$1.1 billion. This product will make use of Mayne's pellet-in-a-tablet technology.

A key criteria for selecting these products is that they can filed for approval simply based on demonstrating bio-equivalence as opposed to *clinical* equivalence and superiority, a set of issues that has made the development of SUBACAP a more difficult and more expensive program. Additionally, patents for both of the targeted existing products have expired with negligible patent risk attached to the programs. Finally, the development time lines for both products are relatively short.

An equally important consideration is that the two products are less subject to new competition because they are complex oral formulations. Mayne Pharma intends to apply its expertise in developing complex oral release drugs to these two new projects. 'What we good at is developing generic equivalents of complex oral released products particularly in the US. We have a heritage of doing that,' said Mayne Pharma CEO Scott Richards in discussion with *Bioshares*.

'The pain and hypertension products are products where we have a leg up in terms of the delivery of technology outcome. We are not starting at ground zero. We have picked products that we thought we had a practical advantage in (developing) and where we saw there was a market today, where competition is limited and that by the time we come to market there will still be viable market to take a share of. We have picked products where we have a reduced-to-practice history of full or partial success that we will replicate. We have picked generic products because the pathway is extremely defined,' he said.

## SUBACAP Update

SUBACAP was approved by the UK's MHRA in June, having been initially not approved in December 2011. Mayne presented additional data and arguments to the MHRA based on more relevant approaches to the measuring the bioequivalence of antibiotic drugs, including the minimum amount of drug required to kill a pathogen.

The company has reached a Special Protocol Assessment agreement with the FDA to progress SUBACAP towards registration in the US. The clinical program includes only the one Phase III study. However, Mayne has been successful scheduling a meeting with the FDA in November to discuss the necessity of conducting a Phase III study at all and it will use arguments presented to the MHRA at this meeting. The company sees the agree-

### Why Doryx Sales Have Not Fallen as Expected

Sales of Doryx in response to the introduction of generic competition have *not* followed the standard substitution curve because of a strategy adopted by **Warner Chilcott** to target only a small number of US dermatologists with a focus on acne with a high priced drug, supported by a loyalty card and rebate program and by also offering product samples. Warner Chilcott's strategy has been to create a very brand-loyal niche customer base, using a 75 strong sales force which calls on 25 dermatologists each or 1,875 in total. However, that figure represents just 11% of dermatologists in the US.

Prior to the introduction of generic competition in the US, Doryx only held a 3% market share of the oral tetracycline prescription market in the US (including doxycycline and minocycline formulations). According to Mayne Pharma, about 8-10% of tetracyclines used for acne have been branded, with the remaining 90% comprising generic products. In other words Doryx has been selling in a sense against broader generic competition for quite some time, and doing so with a very large price differentials. The ex-wholesale price of one 150mg tablet of Doryx is US$12-$14; in contrast, by way of example, a prescription of 30 doxycycline tablets or capsules costs as little as US$4. However, it should be remembered that Doryx is an extended release formulation. In the FDA's Orange Book there are 76 approved formulations (by drug sponsor) of doxycycline, covering oral, tablet and injectable routes of administration and including 20mg, 25mg, 40mg, 50g, 75mg, 100mg,150mg and 200mg dose forms. There are 12 delayed release doxycycline formulations listed in the Orange Book

Despite Mylan's ability to introduce a fully AB rated 150mg generic and delayed release version of Doryx onto the market, it has only been able to secure a 35% market share and by applying a 20% discount to the Doryx price. What has stymied Mylan's attempt to capture greater market share is that dermatologists loyal to the Doryx brand have continued to write 'dispense as written' on prescriptions and to not authorise substitution by a generic. Warner Chilcott has also used its customer loyalty program to also minimise the effect of Mylan's 20% price discount.

Warner Chilcott has maintained its Doryx sales force, which in usual circumstances would be reallocated to other products or let go, because it is continuing, and expects to continue to compete with Mylan's generic product.

Looking ahead, sales of acne treatments generally begin to increase as teenagers go back to school in the US in the Autumn term. Doryx prescriptions are seasonal with falls in summer partly related to sun sensitivity side effects of the drug. So the volume of Doryx prescriptions should rise in the next few months

Mayne Pharma CEO Scott Richards suggested that once the destocking has run its course through Warner Chilcott's inventory, coupled to a new market equilibration coming into play that 'our 2014 financials will be a growth story for Doryx.'

'Having being involved in the generics business for years, this result has been the exception. Usually if you lose a patent case and the generic goes to market and for whatever reason you fail to prevent generic competition, it's sayonara. But in this case several reasons make it a somewhat unique product because the prescribers are small in number and are very brand loyal. It's not like Lipitor. You can't get around to every GP and get them to write "dispense as written" – they are not going to do that because they are not that loyal. Warner Chilcott has played a high cost niche approach,' said Richards.

ment by the FDA to hold the meeting as positive but at the same time is not prejudging the outcome.

Now that an approval for SUBACAP has been achieved in the UK, Mayne will follow a decentralised approach in gaining approvals in other European territories.

Previously, partnering discussions for SUBACAP in Europe had been put on hold. Now Mayne Pharma is gearing up to partner the product, with a preference to sign on more than one partner across Europe. The company has been developing a partnering prospectus which has been informed by $250,000 invested in primary market research in the US and Europe to validate the target product profile of SUBACAP with physicians, key opinion leaders and payors. Mayne intends to put in front of potential partners a sound understanding of SUBACAP pricing options rather than leave such decision making entirely to prospective partners. However, the company also expects the discussions to inform the company on how the product could best be positioned in different drug markets across Europe.

Richards is confident that SUBACAP is a very good product. In his view, SUBACAP has a number of unique selling points: SUBACAP can be taken with out food whereas the reference and competitor product Sporanox must be taken with or after food; SUBACAP can be taken without regard to any gastric acid modifiers, which means anyone on a proton pump inhibitor or H2 receptor blocker, whereas Sporanox contraindicated in these circumstances; SUBACAP is pH independent whereas Sporanox isn't; SUBACAP is also superior to Sporanox on measures of patient inter- and intra- variability; and SUBACAP achieves the same therapeutic response as Sporanox but with half the amount of drug.

### Summary

Mayne Pharma is demonstrating a strong sense of clarity and purpose under the recently installed leadership of Scott Richards. The company does have a number of key challenges ahead but a sense that the company intends to be a much more focused and disciplined pharmaceutical company has emerged.

The company is capitalised $58 million and employs approximately 150 people.

*Bioshares* recommendation: **Speculative Buy Class A**

**Bioshares Model Portfolio (31 August 2012)**

| Company | Price (current) | Price added to portfolio | Date added |
|---|---|---|---|
| Nanosonics | $0.490 | $0.495 | June 2012 |
| Osprey Medical | $0.37 | $0.40 | April 2012 |
| QRxPharma | $0.68 | $1.66 | October 2011 |
| Mayne Pharma Group | $0.380 | $0.435 | September 2011 |
| Somnomed | $0.77 | $0.94 | January 2011 |
| Phylogica | $0.027 | $0.053 | September 2010 |
| Biota Holdings | $0.67 | $1.09 | May 2010 |
| Tissue Therapies | $0.44 | $0.21 | January 2010 |
| Bionomics | $0.33 | $0.42 | December 2007 |
| Cogstate | $0.290 | $0.13 | November 2007 |
| Sirtex Medical | $7.70 | $3.90 | October 2007 |
| Clinuvel Pharmaceuticals | $1.56 | $6.60 | September 2007 |
| Pharmaxis | $1.08 | $3.15 | August 2007 |
| Universal Biosensors | $0.59 | $1.23 | June 2007 |
| Alchemia | $0.565 | $0.67 | May 2004 |

### *Portfolio Changes – 31 August 2012*

**IN:**
No changes

**OUT:**
No changes

# *Nanosonics Grabs $12 Million in Annual Sales*

Disinfection technology company Nanosonics (NAN: $0.49) achieved a substantial lift in sales for the year ended June 30, 2012. Sales of $12.3 million were 447% higher from the previous years figure of $2.3 million.

The loss for the year fell to $4.7 million, compared to a loss of $11.2 million for FY2011.

The full year figures mean that a clearer grasp of the company's gross margin has come into view, with a gross margin of 61% applying for FY2012.

North America contributed $10.2 million in sales, Australia and New Zealand, $1.6 million in sales and Europe and elsewhere $0.4 million.

Nanosonics closed the 2012 fiscal year with cash resources of $29 million at hand, sourced from a placement which took in $15 million and a convertible notes financing from Nanosonics' North American distributor **GE Healthcare** of $7.5 million.

Nanosonics manufactures and markets the Trophon EPR product, a system which is used to disinfect ultrasound cavity probes.

Nanosonics anticipates launching new products in FY2013 that complement the Trophon EPR product. The products include a printer and software ( the Traceability Solutions pack) to aid in the auditing of the use of the Trophon EPR system. Offering a traceability and printing function will assist Nanosonics customers when they seek reimbursement for use of the device and for accreditation of hospital facilities.

Nanosonics CEO Dr Ron Weinberger warned that sales figures for the coming quarter 'may be inconsistent' but that over a 12 month period was confident of sustaining growth.

The reason behind a softer anticipated result for 2012 Q3 is that there current inventory levels (presumably already in the hands of GE Healthcare) are sufficient to meet supply in North America.

A weakness in Nanosonics sales figures were sales in Europe, which amounted to $0.4 million. Nanosonics will be increasing its resources in Europe to support the distributors it has appointed there. Nanosonics will also be working more closely with GE Healthcare in the sales process in the US to grow sales by contributing its knowledge of expertise in infection prevention and infection control, especially at the point of sales closure.

Nanosonics currently has an annual manufacturing capacity of 6,000 units on a single shift. In two to three years the company is looking to increase capacity to 15,000 units and in the longer term to 30,000 units.

Nanosonics is capitalised at $132 million (assuming conversion of convertible notes) and employs 84 people.

*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, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Genetic Technologies, Calzada, Bioniche, Atcor Medical