ISSN 1443-850X

Companies covered: ACR, IIL, Minomic, 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)	70.6%
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 - May '13)	3.1%
Year 13 (May '13 - Current)	65.4%
Cumulative Gain	**489%**
Av. annual gain (13 yrs)	**20.3%**

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 - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph: 0403 850 425
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$400 (Inc.GST)
Edition Number 538 (7 February 2014)

Bioshares

7 February 2014
Edition 538

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

Innate Immunotherapeutics – Preclinical Studies Validate Clinical Mechanism of Action

Innate Immunotherapeutics (IIL: $0.22) listed on the ASX in December last year at 20 cents a share. The company is commercialising a treatment, MIS416, for a form of multiple sclerosis, called secondary progressive MS (SPMS). There are no approved treatments for this form of the disease, and the market size is estimated by the company at $3 billion a year.

This week the company discussed some important mouse studies which had been published last month in the science journal PLOS ONE. Innate has already shown that its therapy achieves 'significant' improvements in patients from a Phase I study and from an ongoing compassionate use program. There are currently 17 patients in New Zealand with SPMS continuing on the compassionate use program.

The mouse study results showed that in an animal model for MS, interferon gamma was up-regulated. Interferon gamma is generally linked to promoting inflammation. However there is a 'good' and 'bad' interferon gamma, and when treated with Innate's drug candidate, MIS416, it was found that the right form of interferon gamma was up-regulated reducing inflammation. When the company checked the blood samples of patients who had been treated with MIS416, it found the same elevated levels of interferon gamma. The correlation here between the mouse and human data supports the scientific mechanism of action of this drug candidate.

Dr Larry Steinman from Stanford University called this 'an exceptionally important manuscript' and that 'the unmet need for SPMS might be filled with MIS416.' Dr Steinman is Professor of Neurology and Neurological Sciences at Stanford University. He has received multiple awards for his research in MS and led the development of the MS drug Tysabri. Dr Steinman will now collaborate with Innate.

For Innate potentially, this finding could lead to, in *Bioshares* view, an application in the treatment of other neurological inflammatory-based diseases. Dr Steinman also has an interest in Alzheimer's disease, although there is no stated intention to explore other diseases.

Phase II Trial on Track to Start in June

Innate raised $10 million from its IPO to fund a 90 patient Phase II study in SPMS in Australia. That trial is due to commence enrolment in June. The company expects to be 50% enrolled by August. The reason it is so confident of rapid enrolment is that it already has one clinician with 30 patients with SPMS keen to participate.

This trial will include a placebo arm (30 patients). Patients will receive a double baseline test which will be averaged. All patients in the trial after 12 months will be given the option to receive MIS416 on an extended basis.

Cont'd over

– Innate cont'd

JP Morgan Meeting Feedback

At the JP Morgan meeting in January in the US, the company confirmed interest from six pharmaceutical companies following Innate's progress, as well as having been requested to meet with two new companies, Abbvie and Amgen.

Innate expects to start a formal partnering process in June next year, six months before results are released from the Phase IIb study. What potential partners want to see is the activity of MIS416 against placebo. There have been no placebo-controlled studies with MIS416.

Second Compassionate Use Program

Next month, Innate intends to expand its compassionate use program with a second group of patients with SPMS to start treatment. The company anticipates releasing quarterly data on the progress of these patients, with this being an open (not blinded) study. Continued data is also expected to be released from the existing compassionate use program.

The compassionate use program is providing the company with evidence of efficacy. Importantly, it is also proving long term safety information. Given that patients will be on therapy for the rest of their lives, safety is a big factor. To date the safety profile has been excellent. The longest a patient has been on therapy is five years and three months(124 doses) with therapy ongoing.

FDA Comments on Improved MS Trials

The challenge for Innate will be in selecting the appropriate endpoints for the Phase III studies. Last month the FDA gave some guidance of how to improve MS studies, stating that a disability endpoint for MS was required. This could involve (a) patient-reported outcome measures (b) a physical function analysis and (c) a biomarker. Innate believes its Phase IIb trial is on the right track with a number of patient-reported outcomes in its trial protocol, a number of neuromuscular function tests, and MRI imaging measuring brain atrophy.

Effectiveness in Primary Progressive MS?

Innate has previously thought its drug candidate would not have much effect in patients with primary progressive MS, which is where patients skip the relapsing-remitting MS stage. However, in recent reporting, some improvement is being seen in those patients with the primary progressive form. Potentially MIS416 may also have an effect on patients with this form of disease. However,those patients may just need to stay on therapy for longer.

Competition

There are nine drugs approved for the treatment of relapsing-remitting MS (patients progress from this form to SPMS) that generate sales of US$11 billion a year. Two of these drugs, Tysabri and Siponimod, are in Phase III studies for the treatment of SPMS. The problem for these two drugs is that both can have serious side effects with Tysabri having a black box warning.

Post IPO Trading

Prior to (and after) listing, Innate had a large shareholder base of over 1700 shareholders. One of the risks with this stock was that that the early shareholders would use the opportunity to sell down their holdings in the open market. However shareholders have shown to be very committed, with many investing at higher prices prior to the IPO. There is now only small amounts of stock being offered at current prices.

Innate is capitalised at $38 million. It had $8.4 million in cash at the end of last year.

Milestones

- Second compassionate use program to start in NZ (March 2014)
- Trial sites in Australia to be announced (April 2014)
- Phase IIb enrolment to start (June 2014)
- 50% trial enrolment (August 2014)
- 6 month compassionate use update (September 2014)
- 100% trial enrolment (Nov 2014)
- 9 month compassionate use update (December 2014)

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

FDA Review Causes Acrux Share Price Slump

Acrux shares (ACR: $2.06) have fallen from a high this year of $2.71 by 37% to a low this year of $1.98. The price fall can be related to an announcement by the FDA that it is investigating the risk of stroke, heart attack and death in men taking FDA-approved testosterone products.

Acrux is the orginator of Axiron, a unique trans-dermally delivered testosterone product, which is market globally by Eli Lilly.

The FDA stated that it has not concluded that FDA-approved testosterone treatment increases the risk of stroke, heart attack or death.

A study published in the *Journal of the American Medical Association (JAMA)* in November 2013 reported that men in a coronary artery disease imaging study had a 30% increased risk of stroke, heart attack and death if they had been prescribed testosterone. The study included 8,709 males with low testosterone levels, who received a coronary angiography between 2005 and 2011. Out of the 8,709 males, 1,223 were on testosterone replacement therapy.

A second observational study in young and old men with pre-existing heart disease reported an increased risk of heart attack in the first 90 days following the prescription of testosterone. The risk was two fold greater for men older than 65 years and two to three fold higher for younger men.

Comments

The FDA frequently investigates and reviews approved medicines and devices. As new and better information comes to hand concerning safety and the benefit profile of a medicine or device, it often imposes new conditions of use if new safety concerns arise.

Current prescribing information for Axiron includes a black box warning to avoid secondary exposure to testosterone. Warnings and precautions also exist for men with enlarged prostates (benign prostatic hyperplasia), and that serum testosterone, prostate specific antigen (PSA), liver function, lipid concentrations, hematocrit and hemoglobin should be monitored periodically.

The study reported by *JAMA* took place between 2005 and 2011. Axiron, which delivers testosterone from an applicator onto the skin (under the armpit), would not have been included in the study, because sales did not commence until April, 2011. Other routes of administration and formulations would have been involved, including topical gels and injections.

A line of enquiry that the FDA may consider in its investigation is whether it is different formulations and different routes of administration e.g. by injection, which are related to increased cardiovascular risk.

Testosterone therapy was first approved by the FDA in 1953.

The sell off in Acrux shares has created a very favourable buying opportunity for a stock which *Bioshares* expects will be paying a tax-free special dividend of 10 cents after it receives a $25 million milestone payment from its partner Eli Lilly in early March. Another $50 million milestone payment for 2014/15 has also been flagged, based on the sustaining of Axiron's current sales performance throughout 2014.

One other factor that investors should keep in mind are sales of Axiron outside of the USA. Lilly has been progessively obtaining marketing authorisations in countries such as Canada, Germany and Brazil, and sales in ex-USA regions are at a low base compared to prescription levels in the USA.

Acux is capitalised at $343 million.

Bioshares recommendation: **Buy**

Bioshares

Will Things Turn For UBI in 2014?

Universal Biosensors had a torrid year in 2013. After raising $13.1 million at the end of 2012 at 90 cents a share, its share price halved, finishing last year at 46 cents.

In 2013, UBI's partner, Lifescan, issued a voluntary recall of its glucose meters which sent strip sales backwards. Lifescan built its own manufacturing line for the strips and as a result, the volume of orders to UBI fell considerably. UBI has since reached an agreement with Lifescan to transfer complete manufacture to Lifescan as the manufacturing orders were not profitable at low volumes.

And to cap off a bad year, UBI's second partner Siemens announced that the product launch of the PT-INR test for checking warfarin levels would be delayed by six months, with a product launch now expected around mid year. At the end of last year UBI also surprised investors by announcing a $25 million debt facility with the company drawing down $15 million up front.

Will it be a better year for UBI and has the stock been oversold? As the company accurately emphasises, the key metric to measure with UBI is the quarterly service fees the company receives from Lifescan for all of the UBI-designed strips it sells, regardless of who makes them. After falling in the second quarter last year from $840,000 to $760,000 due to the product recall, strip sales have rebounded over the last two quarters, increasing in the December quarter to $972,000 from $833,000 the previous quarter. In US dollars, this increased by about US$90,000 over the quarter.

One way to look at UBI is the yield the quarterly service fee offers. Based on the company's market value of $85 million, the annualised latest service fee represents a gross yield 4.6%. This yield can be

Cont'd on page 5

Private Company Report

Minomic Builds a Better Prostate Cancer Diagnostic

Minomic International is a privately-held public company based in Sydney. It is currently seeking to raise $5 million, with the capital raising managed by Veritas Securities. To date the company has raised $9 million. We provide the following report for readers of Bioshares who are interested in and capable of, investing in private companies, and in advance of any future possible IPO of the company.

Minomic International, founded in 2007, is developing Mi-Stat, a diagnostic and post-prostectomy assessment tool for prostate cancer. This is a non-invasive test for detecting a protein (the Mil-38 antigen) that is present only on cancerous prostate cancer cells but not present on normal prostate cells.

The Mi-State test aims to overcome a major weakness with the existing and widely available prostate-specific antigen (PSA) test, which was first commercialised in the 1990's. The PSA test detects the PSA protein about 80% of the time but is only effective in determining that prostate cancer is actually present 40% of the time.

The problem is that PSA levels can be elevated in males for a variety of reasons, not simply because of cancer. Other causes of elevated PSA can be inflammation or bike riding or more commonly a condition called benign prostatic hyperplasia (BPH), which is the enlargement of the prostate. As men age, the incidence of BPH increases.

The economic driver for an improved prostate cancer diagnostic stems from the cost of managing the three out of every five patients who yield a false positive test result. Typically after a positive test result, a patient is sent for a biopsy. This is unnecessary in three out of five patients who test positive for PSA.

Reducing the need for confirmatory biopsies, which cost about $2,000 as a day procedure according to Minomic, would save health payors significant sums of money when compared to the $25 cost of the basic test. Taking a biopsy from the prostate also increases the chance of infection because the route used is trans-rectal. A small percentage of biopsied patients will experience infection problems which require further treatment and expense.

According to Minomic's proof of concept study of Mi-Stat, the test was 71% accurate in detecting the presence of prostate cancer and was correct in determining prostate cancer 73% of the time.

The company established recently that it could increase the accuracy of its test to 90% if it included the PSA test. It also established that it could detect its prostate cancer marker in blood, thus expanding its application into multiplex blood test systems. This places it on par with the PSA test, which is a blood test.

Investment Points

The commercialisation of diagnostic products is often very challenging, especially if the test provides information that is new to the world of clinical practice and the analyte in question requires new instruments or formats to be acquired by testing laboratories.

An Iterative Technology

What makes Minomic's Mi-Stat test attractive for investors is that it is less a disruptive technology but more an iterative technology. This means the risks and costs associated with commercialisation are decreased. It is, in common with many of the current commercially available PSA tests an immuno-chemistry or antibody-based test. While the test is being developed in a kit form, it could be easily developed for use with more sophisticated instruments used in testing labs.

Existing Reimbursement Codes (USA)

What is much more important in terms of commercialisation in the USA is that the test would slot into the existing coding and payment structures established for the PSA test. In fact, in the USA, the PSA test is recommended by the American Cancer Society (and others) for screening for all men over age 50 and at age 45 for men at higher risk. However, how and when the Mi-Stat test would be accepted as a medical policy by health insurers is an unknown. One could expect that Minomic's planned 1,200 patient prospective study will be necessary in gaining coverage from insurers as well as principally satisfying the FDA of the test's robustness.

Large Global Market

The global market for PSA testing (or screening) is very large, with 223 million tests conducted world-wide in 2011 according to VPG Publications.

Investment Horizon - 2015

Minomic is aiming to receive a 510(k) clearance from the US FDA in 2015. Such a clearance may pave the way for a trade sale or licensing of the product, the company's preferred exit mechanism. However, an IPO may also be an option.

Two Key Studies Planned for 2014

Minomic intends to complete a pilot retrospective study using samples from 350 patients from urology practice groups in the US. This will be followed by a larger 1,200 patient prospective study, the results of which will form part of the company's FDA 510(k)

Cont'd over

Bioshares Model Portfolio (7 February 2013)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$0.815	$0.620	December 13
Impedimed	$0.220	$0.245	December 13
Analytica	$0.023	$0.025	December 13
Imugene	$0.016	$0.022	November 13
Oncosil Medical	$0.130	$0.155	September 13
IDT Australia	$0.380	$0.260	August 13
Viralytics	$0.340	$0.300	August 13
Tissue Therapies	$0.340	$0.255	March 2013
Somnomed	$1.50	$0.94	January 2011
Cogstate	$0.380	$0.13	November 2007
Universal Biosensors	$0.48	$1.23	June 2007

Portfolio Changes – 7 February 2014

IN:
No changes

Recommendations:

OUT:
No changes

Recommendations:

– Minomic cont'd

submission. Data from the pilot study is expected to be available in July.

Results from the 1,200 patient study are more likely to become available in January 2015, although the study itself is expected to be completed around October.

Patents

Minomic has recently begun refreshing its intellectual property covering the Mi-Stat test. Its foundation patent expires in 2017 (US Patent 5,622,836). It will file patents with new claims about the antibody it uses in its test as well as claims covering the increased sensitivity of the test gained by the inclusion of the functional components of the PSA test. These patents would, if granted, extend the company's patents out to 2034 and also correct some of the historical weakness with the company's IP position.

Risks

The main risks ahead for Minomic relate to delays in completing its clinical program and with manufacturing of clinical trial materials. Another risk ahead relates to the guidance the company is yet to receive from the FDA. The FDA could, for example, suggest changes to the clinical program or to manufacturing requirements which could delay the time to approval even further.

Summary

The Mi-Stat test is emerging as a diagnostic with the potential to be markedly better than the entrenched PSA test. However, Minomic's challenge is to 'execute to perfection' throughout its clinical validation program and build a rock solid dossier for its 510(k) submission.

Bioshares

– UBI cont'd

expected to increase every quarter as Lifescan converts its customer base from the older Ultra series of glucose meters to the UBI-designed Verio meters. On the current growth rate, this yield can be expected to double in around two years, and should double sooner if uptake can be accelerated, possibly within 12-18 months. UBI is not returning this service fee to shareholders, but it is a worst case scenario at looking at this stock.

UBI's R&D costs have been high over the last 18 months because of the investment the company is making in the next products, which are being developed in collaboration with Siemens. UBI is sharing more of the upside but also more of the costs. Once product development has been completed, UBI's costs should reduce (in FY2015). UBI has also reduced its cost base recently from restructuring as a result of ending its commercial manufacture of the glucose strips.

UBI had $23 million in the bank at the end of December. It has access to a further $10 million through the debt facility. The company expects these funds will give it time to move into profitability. The term of the loan is five years. The interest payments will be funded from the quarterly service fees.

Looking forward, UBI can expect revenue from glucose strip service fees, from milestone payments from Siemens (a further $6 million, $1.5 million for each of the four products), and from an R&D tax rebate, in the order of $6 million.

Over the next two quarters, drivers for this stock will be increases in the glucose strip service fee (to an estimated $1.2 million a quarter by June) and launch of the first diagnostic test (PT-INR) with Siemens.

The stock appears to have bottomed and at its current value looks appealing.

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: Starpharma Holdings, Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Tissue Therapies, Viralytics, Phylogica, pSivida, Antisense Therapeutics, Benitec BioPharma, Admedus, Calzada, Invion, Circadian Technologies, Imugene, Analytica