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Biosheres

27 March 2009
Edition 305

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

In this edition...
While the biotech sector remains in the doldrums, some companies in the diagnostic space are emerging as successful businesses. Why is this so? The reasons are that their products represent a significant improvement on current practise, they are taking responsibility for global marketing and they win acceptance through the publication of numerous clinical research papers. We also include our current top five stock picks, which include three companies with products close to market entry within the next 12-18 months and two companies, Sirtex Medical and Acrux, with products on the market already.
The Editors
Companies Covered: ACL, ACG, ACR, ACG, CST, CXS, FER, IPD, RHT, SRX, 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)	-25%
Cumulative Gain	**54%**
Av Annual Gain (7 yrs)	**17.8%**

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A Model Emerges on How to Build Successful Diagnostic Companies

At the forefront of biotech stocks on the verge of profitability, if not having already reached that business objective, are a handful diagnostic technology companies. Included in this group are **Cellestis** (which markets a test for latent TB), **Atcor Medical** (marketing the Sphygmocor product), **Cogstate** (selling cognitive function tests) and **Ferriscan** (marketing a non-invasive test for iron levels in the liver).

The list of development phase companies with an expressed focus on diagnostics or that have developed a diagnostic is quite extensive, and includes **Pharmaxis** (the Aridol lung function test), **Bionomics** (epilepsy gene diagnostics licensed to **LabCorp**), **Anteo Diagnostics** (a diagnostic chemistry platform company), **Tyrian Diagnostics** (developing a TB diagnostic, as well as commercialisation of the Wheatrite test), **Genera Biosystems** (developing the PapType HPV diagnostic), **Healthlinx** (rolling out an Ovarian cancer test), **Fermiscan** (commercialising a hair-based cancer detection test), **USCOM** (non-invasive measurement of cardiac function), **Circadian Technologies** (through their cancer of unknown primaries program at the Peter Macallum Cancer Institute which is now partnered with Healthscope) and **Impedimed** (developing and marketing a suite of products that can detect lymphoedema and body-mass conditions).

Broadening the set further, **Compumedics** manufactures EEG and ECG equipment used in sleep and neurological evaluation, **Optiscan Imaging** has developed various optical-based products based on its proprietary confocal imaging technology, and **Cyclopharm** markets the Technegas lung imaging product. (This company posted a profit for its full year that ended December 31, 2008 of $1.7 million, on sales of $10.8 million).

The outlook for diagnostics companies

The products created from diagnostic technologies have a healthy outlook. A key driver includes the search by governments and health-payors for information productivity tools that enable healthcare resources to be distributed more efficiently. Diagnostics are, at the end of the day, used as decision making tools by physicians, patients and others involved in managing healthcare.

In addition to using diagnostics to correctly ascertain a disease state or acute medical condition, diagnostics can yield information about patients who respond to drugs when others do not, and this can mean a drug may be more effectively administered. A recent example is the elucidation of the role KRAS mutation in colorectal cancer patients, which may mean more effective treatment is possible with the antibody drug Erbitux (cetuximab) for patients who test positive for the natural or un-mutated form of the KRAS protein. Expect to see more drugs developed with companion diagnostics that more clearly define a patient sub-set where strong clinical outcomes are observed.

Imaging technologies are also powerful health information productivity tools providing

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answers in increasing detail about the status of diseased tissue and organs both pre-intervention and post intervention. Improvements to cost, performance and portability are likely to occur in the medium term.

The search for powerful biomarkers, with strong predictive value is ongoing, with proteins such C-reactive protein an example of a protein that appears to correlate to inflammatory conditions and acute problems such as heart attack risk. The much-hyped promise of personalized medicine based on personalized gene-based information is arriving slowly, but in the mean time the discovery and validation of panels of protein based biomarkers is more likely to deliver meaningful diagnostic tools into the hands of healthcare professionals and in the hands of patients in their own homes.

Some Features Common to Three Australian Diagnostic Technology Companies

Cellestis with its novel and now profitable tuberculosis diagnostic, Impedimed with its lymphoedema diagnostic products, and Atcor Medical are all building proprietary positions with novel diagnostic tests. What's similar about all of them is that each has and continues to invest in continued clinical validation in changing the way preventative healthcare is perceived and practised. Each has decided to invest in a direct distribution system with or without distributors. Furthermore, each technology represents a stepwise improvement on existing methods of detection, diagnosis or clinical practise. And the case of Cellestis and Atcor Medical, publication of hundreds of papers by researchers on these companies' respective technologies has also been instrumental in achieving commercial success.

Atcor Medical Starts To Capitalise On Global Monopoly Position

Atcor Medical (ACG: 17.5 cents), through pioneering its non-invasive central blood pressure test has put itself in a monopoly position to capitalise from an improved approach to the measurement of progressive cardiovascular disease. The standard blood pressure measurement (cuff pressure) only provides some of the information of progressive cardiovascular disease. Measuring *central* blood pressure with cuff pressure has contributed to the provision of high quality information on the stiffness of the arteries and therefore more in depth information on a patient's cardiac health.

The problem with this in the past is that central blood pressure has had to be measured through an invasive procedure. Atcor Medical invented the first reliable system for measuring central blood pressure non-invasively, through a procedure as straightforward as measuring central blood pressure. However, being the first mover, Atcor Medical's test (SphygmoCor) has enabled it to become the gold standard.

And to defend its position, the SphygmoCor device is patented with a proprietary internal mathematical transfer function that can not be reverse engineered.

It has been a significant task for the company to commercialise its product, but positive commercial outcomes are now beginning. In the first half of this financial year Atcor delivered a maiden profit of $180,000. Sales increased by 76% (64% in constant currency) to $5.3 million, with strong growth anticipated to continue for the full year with the company forecasting sales in excess of $10 million.

New FDA guideline for stricter CV risk control with diabetes drugs

The strong growth is being driven by sales of the company's SphygmoCor unit (with service agreements) to major pharmaceutical and biotech companies. Not only is the test being used in later stage cardiovascular drug studies, but is now moving to earlier Phase I studies as drug developers are understanding the value of this test in picking up cardiovascular issues early in the drug development process.

In December last year the FDA released a guidance document relating to the development of drugs to treat Type 2 diabetes and specifically the requirement to show that new diabetes drugs do not increase cardiovascular risk. The first victim to this guideline may have been **Takeda**'s potential blockbuster, Alogliptin, which earlier this month was delayed from gaining FDA approval with the FDA requesting further cardiovascular safety data.

Potential market for central blood pressure test continues to increase

The larger cardiovascular testing market for pharmaceutical trials has increased the potential market for this test to around US$300 million (from US$216 million as estimated by Atcor) for pharmaceutical and research purposes. This is the first application for the SphygmoCor test. Based on forcecast sales of $10 million, only about 2% of this market has been captured.

The next and larger application Atcor has started working on is for use of the test by specialists, specifically cardiologists and nephrologists. This market has been estimated at US$500 million. Atcor is targeting the top 200 leading hypertension practises in the US.

The third and largest market for Atcor is in primary care. This market is valued at around US$1.3 billion and is obviously a longer term objective to make inroads into this market, being dependent on adoption in clinical trials and through specialist networks.

Validated technology

To date over 400 scientific publications featuring Atcor's central blood pressure test have validate the technology with data continuing to emerge.

Financials

Atcor Medical is capitalised at $17 million. It had $2.9 million in cash (with $1.2 million more in directors' loans due to be received in November this year) and we do not the expect the company will need to raise additional funds. Sales are expected to increase by at least 55% in this financial year to$10 million of sales. The company is trading at 1.7 times sales, where arguably a multiple of 3-5 times sales could be applied. The company is tightly managed and represents good value to investors, trading at a discount to our

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estimated fair value range and with considerable future growth upside from wider adoption of the SphygmoCor test.

Bioshares recommendation: **Speculative Buy Class A**

Cellestis – Another Global Gold Standard

Cellestis (CST: $2.03) has developed the first and only commercial test for latent tuberculosis using a blood-based immune response (interferon-gamma release) test. It is more accurate than the 100 year old skin-scratch test and does not require a second visit to the doctor/nurse. The company has a monopoly position on this blood-based test with 255 scientific papers covering the technology, with 26 alone in the first three months of 2009!

In the first six months of this financial year, the company doubled sales almost to $14.4 million and generated a strong growth in net profit to $2.8 million (from $0.3 million in pcp) for the half year. The company also even paid its first dividend to shareholders (1.0 cents per share, unfranked).

Untapped market potential

Cellestis is generating sales of around $30 million a year although has penetrated only around 2.5% of the market according to the company. In the last six months the company has generated strong growth in all regions of between 84% - 100%.

Cellestis has opted to sell its TB tests direct, using its own distribution network in the USA, UK, France Germany, Switzerland, Austria and Poland, and uses distributors in other regions including Asia, Scandinavia, Southern and remaining parts of Eastern Europe, Canada, and Latin America.

Its gross margins are higher where it sells direct however these regions have taken longer to become profitable. From now, a greater proportion of the revenue starts to flow through to the bottom line, which in combination with strong sales growth expected, makes the company an attractive investment to consider.

Global acceptance as gold standard

The Cellestis Quantiferon TB test continues to be included in government healthcare authorities as an accurate and even reference test for latent TB. Last year it was listed in the US Army and Navy TB control guidelines.

Financials

Cellestis is capitalised at $191 million and is trading on a PE of 33. The company had $17.9 million in cash at the end of last year. Within the next 12 months, we expect Cellestis' price-earnings multiples will fall below 20 and will start to receive interest from more standard investment funds.

Bioshares recommendation: **Hold**

Impedimed – Specific Reimbursement Code the Goal

Impedimed (IPD: 70 cents) is developing a suite of devices that use bio-impedance technology to aid in the clinical assessment of lymphoedema and other body composition related conditions. A major market opportunity exists in the USA where a large pool of breast cancer patients who have gone through treatment an surgery are at risk of developing lymphoedema. Lymphoedema is the build-up of excessive fluid and protein accumulation in space between cells in tissue mass. About one quarter of breast cancer patients who have radiation therapy, mastectomies and lymph nodes removed could develop lymphoedema, which if left untreated can result in disfigurement, chronic pain and fatigue and a loss of quality of life.

Early detection can allow for early treatment to take place, which is generally involves the application of compression bandages.

The L-Dex U400

Impedimed's lead product in the US is the L-Dex U400 device. It was approved by the FDA in October 2008 for the assessment of unilateral lymphoedema in female breast cancer patients. This model is being marketed to breast surgeons, oncologists and physical therapists and is sold through LDEX user agreements.

The company is targeting an addressable market of 4,000 oncologists, 5,000 breast surgeons and 5,000 general surgeons through a small sales force but is also working in conjunction with professional surgeon bodies to build interest.

Coverage

At present, the use of the L-Dex U400 is only covered by some private insurers (under an existing miscellaneous reimbursement code) and not by the public insurers such as CMS. Wider coverage could occur if the company was in receipt of a specific Category 1 code (CPT1) from the American Medical Association (AMA), which the company is working towards.

Impedimed's main challenge is to secure this CPT1 code. Its chances of receiving this code will be improved by the numbers of surgeons it has signed up to L-DEX agreements and by the number of studies published on the Impedimed technology or on the benefits of the early detection of lymphoedema. Several papers have recently been published that add weight to Impedimed's argument for a CPT1 code. In particular a study by Shih et al in the *Journal of Clinical Oncology* quantified the additional costs born by breast cancer patients who develop lymphoedema – US$22,150 greater than the medical costs for non-lymphoedema sufferers of US$64,550 over a two year period after the initiation of breast cancer treatment. Of that, lymphoedema breast cancer patients spent US$9,400 or 60% more than non-lymphoedema patients on out-patient costs. The authors recommend that "further efforts should be made to elucidate reduction and prevention strategies for breast cancer related lymphedema".

Financials

Impedimed holds an estimated $6 million in cash and is capitalised at $63 million. The company is backed by a solid investment register, with Orbis Investment Management holding 14.8%.

Bioshares recommendation: **Speculative Buy Class A**

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Bioshares Top Five

With the stock market having entered a rally in the last three weeks and the Dow Jones Industrial Average up 19%, it's timely to release our current top five picks in the sector. What is common with each of these companies is the proximity of their products to market (with the exception of Sirtex Medical which is already very profitable and Acrux which has released its first product) with the potential for multiple fold gains over the next 12-18 months.

Acrux

Acrux (ACR: 53.5 cents) has a portfolio of products that are starting to bear fruit. Its first, Evamist, is selling in the US, with approval pending in Europe. Initial sales have been running at around 50% of expectations but should pick up. The animal health products partnered with Eli Lilly and the first filed for approval last year, may be a surprise earner for the company, and Axiron, a male testosterone gel, is due to be filed for approval with the FDA later this year. It could be a very big earner for Acrux, either as a trade sale or in upfronts and royalties. Acrux is capitalised at only $85 million and is a standout investment opportunity both for value, upside potential and product diversity.

Bioshares recommendation: **Speculative Buy Class A**

Alchemia

Alchemia's (ACL: 29 cents) generic anti-coagulant product, fondaparinux, is due to be on the market in the US by early next year. The branded product, Arixtra (**GlaxoSmithKline**), is currently selling US$208 million a year, with this expected to approach US$250 million - US$300 million next year.

We estimate it will generate a profit share for Alchemia of at least $30 million a year. The product should gain at least 40% market share very quickly with only minimal price erosion (up to 20%), being the only generic. The product is currently being assessed by the FDA. Alchemia is capitalised at $47 million.

Bioshares recommendation: **Speculative Buy Class A**

Chemgenex Pharmaceuticals

Chemgenex Pharmaceuticals (CXS: 59 cents) expects to complete the filing of its lead drug candidate, omacetaxine, with the FDA by mid-year. From there the drug could be on the market in the US in early to mid 2010.

Data from a preclinical study in mice reported this week also highlighted that omacetaxine was also effective at killing the leukemic stem cells that generate the cancer cells in the body as well. In this trial omacetaxine killed 90% of the stem cells in a mouse model, compared to 9% and 25% for the existing drugs Gleevec and Sprycel respectively, which are on the market. Such data if reproduced in human trials may help boost the application and use of omacetaxine considerably.

Chemgenex Pharmaceuticals' share price has fallen over 50% from its 12 month high. It is capitalised at $141 million with $13.7 million in cash at the end of last year.
Bioshares recommendation: **Speculative Buy Class A**

Sirtex Medical

Sirtex Medical (SRX: $2.30) generated a net profit of just under $11 million in the first half of this financial year for its liver cancer treatment. The therapy uses radioactive ceramic spheres, SirSpheres, with a short half-life, to irradiate tumours in the liver. What has slowed adoption has been familiarity with delivery of this treatment, which are delivered via a catheter through an artery in the groin region.

However in the last six months of last year, there were 1706 treatments with the SirSpheres up from 1237 (+38%), suggesting this is now becoming an increasingly accepted (and effective) treatment.

Sirtex is capitalised at $128 million. It generated revenue of $29.5 million for the first half with an additional $9.8 million in foreign exchange gains. Stripping out unrealised FX gains, which takes into gains from currencies held in overseas accounts (and including the benefit from realised FX gains which will be mostly recurring in future years if the currency remains at current levels), Sirtex made a net profit of around $7 million for the half, which equates to a PE ratio of 8.5 times. Either on a sales multiple (2.0 times) or PE basis, this stock looks very attractive. Upward movements of the Australian dollar will reduce its profitability.

Bioshares recommendation: **Strong Buy**

Universal Biosensors (UBI)

UBI (UBI: 53 cents) has developed a novel diagnostic meter. The first application is for use by diabetics to monitor glucose levels. The advantage over existing products comes from manufacturing the test strips, which with the UBI process can be conducted at a fraction of the cost. The meter should also be more accurate and require less sample blood.

UBI needs to negotiate a new contract with **Lifescan (Johnson & Johnson)** for the second generation device, which will supersede the first generation system even before it is released. The second generation system was only six to nine months behind the first generation system and the decision was recently made to concentrate on the second generation system which will bring with it some likely cost and enhancement features.

We expect the new contract will be signed in the coming weeks with manufacturing sales beginning as early as this year and the company we estimate will be profitable in 2010. (UBI has a manufacturing service agreement with Lifescan which will need to be renegotiated for the new product.)

UBI is also making strong headway on its two subsequent products having developed working prototypes for; a point of care test for C-reactive protein (CRP), and a prothrombin time test for warfarin users. Demand for CRP tests is set to escalate following last year's JUPITER study (see last week's Bioshares).

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Selected Profiles – Other Diagnostic Companies

Resonance Health

Resonance Health (RHT: 0.1 cents) has built a small profitable business from developing a novel non-invasive method of measuring liver iron levels, called Ferriscan. Rather than taking a liver biopsy, this method uses a mathematical algorithm to analyse MRI scans. The scans can be taken on the other side of the world with the images sent to Perth for processing.

In the first half of this financial year the company increased revenue to $1.2 million with a net profit of $0.3 million. The company had $2.7 million in cash at the end of last year and has now generated five consecutive quarters of positive cash flow. The liver test is the only non-invasive test available and has received regulatory approval in Europe, the US and Australia. The company is also developed a non-invasive test for measuring liver fibrosis.

Bioshares recommendation: **Not Formally Covered**

Fermiscan

Fermiscan (FER: 17 cents) has developed a novel breast cancer screening test that analyses hair samples from women to detect the disease. It's a very surprising way to detect the disease, with the theory behind the test that breast cancers secrete cytokines that cause a very subtle diffraction in the hair fibre that can be detected using a high powered synchrotron, with Fermiscan utilising beam line resources at the Melbourne synchrotron.

In a 2000 person study completed last year, the diagnostic test detected 64% of breast cancers. By way of comparison mammography plus ultrasound picks up 78% of breast cancers. Of interest would be whether the Fermiscan test picks up a different subset of breast cancers that traditional methods do not, which the company believes may be the case.

The test is being released in coming months in Sydney and will cost $249. To its advantage the test does not require any unpleasant testing procedures and can be used on all women, although has been shown to be more accurate in women under the age of 70 (74% accurate). Going against the test is that it has a high false positive rate (23.1%) compared with standard methods (11%) i.e. roughly one in four positive readings are false.

A recent independent Italian study confirmed the accuracy of the test (sensitivity 83% and specificity 76%). The report stated that "It (the diagnostic) appears to recognise systemic change and therefore enables management of the disease at even an early change." Fermiscan has previously shown that patients with breast cancer who were positive with the test became negative after a mastectomy procedure. The Italian report recommended further evaluation of the test in a multi-centre study in Europe.

Bioshares recommendation: **Under Consideration**

Bioshares

Bioshares Model Portfolio (27 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	$0.18	$0.10	October 2008
CathRx	$0.31	$0.70	October 2008
Impedimed	$0.70	$0.70	August 2008
Mesoblast	$0.80	$1.25	August 2008
Cellestis	$2.03	$2.27	April 2008
IDT	$1.52	$1.90	March 2008
Circadian Technologies	$0.69	$1.03	February 2008
Patrys	$0.05	$0.50	December 2007
Bionomics	$0.22	$0.42	December 2007
Cogstate	$0.25	$0.13	November 2007
Sirtex Medical	$2.30	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.20	$0.66	September 2007
Starpharma Holdings	$0.28	$0.37	August 2007
Pharmaxis	$1.48	$3.15	August 2007
Universal Biosensors	$0.53	$1.23	June 2007
Biota Holdings	$0.54	$1.55	March 2007
Probiotec	$1.48	$1.12	February 2007
Peplin Inc	$0.60	$0.83	January 2007
Arana Therapeutics	$1.40	$1.31	October 2006
Chemgenex Pharma.	$0.59	$0.38	June 2006
Cytopia	$0.13	$0.46	June 2005
Acrux	$0.54	$0.83	November 2004
Alchemia	$0.29	$0.67	May 2004

Portfolio Changes – 27 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

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