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In this edition...
A number of features separate the quality biotech stocks from the not-so-good.

One key feature is experienced management, an element common to both Patrys and Impedimed, which are the focus of this edition.

Both companies have CEOs who have worked for major global device or pharma firms, and both have sourced key executives from well known US biotech and device firms.

Although commercial validation for both companies is still some time away, execution of each company's business plan can still be judged by investors.

The editors
Companies covered: IPD, PAB

	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)	-36.3%
Year 8 (May '08 - current)	-0.05%
Cumulative Gain	**107.0%**
Av Annual Gain (7 yrs)	**17.8%**

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Bioshares

9 May 2008
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Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies.

NIH Study Supports Impedimed's Diagnostic Technology

Impedimed (IPD: 80 cents) is developing a suite of diagnostic products that uses bio-impedance as the underlying technology. Bio-impedance is an electrical conductivity concept. In the context of human diagnostics, bio-impedance devices measure the degree of resistance (impedance) that fat and fluids impose on electrical current.

Impedimed has developed devices that make use of a single fixed electrical frequency for bio-impedance analysis (BIA) and others that measure impedance cross a broad range of frequencies (bio-impedance spectroscopy -BIS)

Bioimpedance measurement technologies have application in areas including analysing medical hydration and body composition and assessment and detection of lymphoedema.

Impedimed has selected the application of its technology in the area of early detection of lymphoedema in breast cancer patients as its priority program, with its major territorial focus in North America. The company is well advanced in pre-marketing its suite of devices, including its first approved product the Imp XCA, a single low frequency device approved for assessment of lymphoedema in the arm, which is aimed at the home care market. However, the company's major product focus is on the L-Dex U400, which will be marketed to surgeons, oncologist and physiotherapists. This is a more advanced BIS device. A marketing application concerning this model was filed with the FDA in April.

Latest developments

Impedimed announced recently that a journal article reporting on a study of the benefits of the early detection of lymphoedema had been published. The article 'Preoperative assessment enable the early diagnosis and successful treatment of lymphedema' was published online in the journal *Cancer*.

The study was sponsored by the US National Naval Medical Centre and the US National Institutes of Health (NIH).

The period of the study was from 2001 to 2006. The study involved 196 patients newly diagnosed with early stage breast cancer in one breast. Forty three (43) patients (22%) were diagnosed with lymphoedema, with the criteria for the diagnosis being a greater than 3% change in upper limb volume compared to a base line reading obtained prior to surgery.

The study found that the onset of lymphoedema occurred at an average of 6.9 months post-operatively. The context for this is that the highest risk of lymphoedema occurring is within three years post surgery. However, the precision available to clinicians to determine when this might be exactly has been poor. This study may support claims that the approach used in the study can mean that lymphoedema can be detected between 4 and 10 months before older technologies allow.

Cont'd over

(It should be understood that the study used opto-electronic perometry device supplied Pero-System Messgerate GmbH as the measurement technology and not one of Impedimed's bioimpedance based devices. While this may seem unrelated to Impedimed, in fact both methods are technologically more advanced than older less sensitive and less objective methods. The merits of both technologies are discussed below.)

Why is the study significant?

The study is significant for several reasons. Firstly, the study provided evidence that lymphoedema in breast cancer patients can be detected earlier when measured from a pre-operative base line using an appropriate method (e.g. opto-electronic or bio-impedance). Such methods are in contrast to less objective methods based on observation and measurement of volume and circumference of the limbs in which the oedema occurs (e.g. a tape measure and a bucket of water). According to another group of researchers, it is possible that build up of up to 150ml of fluid (in excess of normal) can occur before the visible symptoms of lymphoedema appear. A 200 ml change equates roughly to a 10% volume change, the point where it would appear that visible observation based definition of lymphoedema begins. The benefit from early detection is that treatment can be applied sooner and with greatly improved effectiveness.

The study broached the merits of a standardised approach for lymphoedema assessment in breast cancer patients, proposing that a new six grade scale for diagnoses be adopted. This proposed six grade scale includes a second grade that covers very early lymphoedema, currently referred to as sub-clinical lymphoedema, where a 3%-5% change in limb volume occurs.

What are the implications for Impedimed?

The publication of the journal article has some significant implications for Impedimed. The company can now refer oncologists, surgeons, physiotherapists and nurses to an independent study that provides evidence to support baseline testing to diagnose lymphoedema at a much earlier stage of the condition. The company can now use the study to build a convincing health economic and commercial argument for its diagnostic technology, with one device, Impedimed's Imp XCA, already approved by the FDA, for lymphoedema assessment.

Impedimed has targeted the early detection of lymphoedema as a primary market opportunity for a number of diagnostic products. This market is supported by oncologists and surgeons open to new and better treatment outcomes, who also act as technology adoption leaders. There are about 6,000 oncologists in the US and a similar number of breast cancer surgeons.

There are an estimated 2.4 million breast cancer survivors in the US, and between 10% and 40% of breast cancer patients are likely to develop lymphoedema.

Cont'd page 5

What is lymphoedema?

The function of the lymphatic system is to transport excess interstitial fluid, which is the fluid in tissues that surrounds cells, back into the circulatory system. Interstitial fluid is similar to blood plasma and is comprised of water, amino acids, sugars, fatty acids, proteins, hormones and other messenger molecules, salts and other chemical waste from cells.

Another function of the lymphatic system is to absorb and transport fat and fat-soluble vitamins. The lymphatic system also has an important role defending the body when it is invaded by pathogens.

Lymph capillaries are one-way valve-controlled vessels for directing interstitial fluid into the venous system. These capillaries are found in nearly all parts of the body excluding bone marrow, the central nervous system and the other parts of the body that lacks blood vessels.

When interstitial fluid is within the lymph capillaries it is called lymph.

When interstitial fluid increases beyond a certain point and is not cleared away, pressure builds up and swelling, or oedema occurs, hence the term lymphoedema. Typically blood volume and blood pressure decreases as well, setting the scene for blood pressure related problems to eventuate.

The causes of lymphoedema are categorised into primary and secondary groups.

Primary lymphoedema occurs because of malformations (e.g. hypoplasia, or insufficient development of lymphatic organs) or of hardening of the lymph nodes or vessels.

Secondary lymphoedema occurs as a result of trauma, infection of lymphatic tissue by fungi, bacteria or parasites, radiation or surgery such as vein harvesting or vein stripping.

Another but very significant cause of secondary lymphoedema is that which occurs following surgery and/or radiotherapy for cancer, especially breast cancer. The removal of lymph tissue in breast cancer surgery reduces lymphatic transport capacity.

Radiotherapy is known to damage both networks of lymph capillaries and lymphatic collectors. The extent of damage is a function of the degree and extent of the treatment.

Early diagnosis

If diagnosed early, secondary lymphoedema can be simply and effectively treated with compression bandages. If diagnosis is delayed, intensive therapy followed by life long maintenance treatment is generally required.

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Thredbo Biotech Summit

July 25-26, 2008
Thredbo Village, NSW, AUSTRALIA
www.bioshares.com.au/thredbo2008.htm

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Speakers & Panelists

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Key Note Speaker
Dr Lester Crawford
Former FDA Commissioner

Dr Crawford's visit is supported by QRxPharma & Arana Therapeutics

QRx Pharma

Dr Crawford is an authorative and knowledgeable figure on US healthcare regulatory issues. Don't miss the chance to have a fire-side chat with Dr Crawford. Opportunities for Australian biotech companies to meet and mix with such experienced figures on Australian soil are rare and not to be missed.

Bioshares Model Portfolio (9 May 2008)

Company	Price (current)	Price added to portfolio	Date added
Cellestis	2.55	$2.27	April 2008
IDT	$2.16	$1.90	March 2008
Circadian Technologies	$1.03	$1.03	February 2008
Patrys	$0.30	$0.50	December 2007
NeuroDiscovery	$0.13	$0.16	December 2007
Bionomics	$0.33	$0.42	December 2007
Cogstate	$0.13	$0.13	November 2007
Sirtex Medical	$3.86	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.42	$0.66	September 2007
Starpharma Holdings	$0.34	$0.37	August 2007
Pharmaxis	$1.69	$3.15	August 2007
Universal Biosensors	$0.85	$1.23	June 2007
Biota Holdings	$1.02	$1.55	March 2007
Probiotec	$1.06	$1.12	February 2007
Peplin Inc	$0.47	$0.83	January 2007
Arana Therapeutics	$1.05	$1.31	October 2006
Chemgenex Pharma.	$0.94	$0.38	June 2006
Cytopia	$0.28	$0.46	June 2005
Optiscan Imaging	$0.28	$0.35	March 2005
Acrux	$1.02	$0.83	November 2004
Alchemia	$0.41	$0.67	May 2004

Portfolio Changes – 9 May 2008

IN:

No changes.

OUT:

No changes.

A Strong Team and Rich Pipeline make Patrys a Quality Pick

Patrys (PAB: 30 cents) is a company focused on the development of therapies using natural human antibodies. The company listed on the ASX last year at 50 cents a share. The antibodies developed by the company are isolated from human tissues and are being commercialised predominantly for the treatment of a range of cancers. The company has 12 lead candidates in development, including partnered antibodies, with clinical trials expected to begin in early 2009. The technology is potentially very valuable not only because of the drug candidates it has generated, but also because of the novel drug targets that many of these candidates hit.

Cancer cells are present in the body at all times but in very small quantities. The body's immune system controls these antibodies via 'natural human antibodies', the exact type that Patrys has isolated and is seeking to manufacture and commercialise.

The company has identified over 260 potential antibody leads and is seeking to commercialise 12 of these leads initially either independently or through partners.

It is the process of growing these antibodies outside of the body and ensuring that these antibodies are sufficiently resilient to be used as commercial biopharmaceutical products that is the major challenge for this company.

The manufacturing challenge

Human antibodies do not divide and have a short half-life outside the body. Patrys has developed 'human hybridomas' of its natural antibody leads, whereby it uses proprietary immortal fusion cells that combine with the human antibodies that can be grown/divided in a fermentation manufacturing process.

To date the company has manufactured its two lead drug candidates in five litre volumes. It is seeking to scale up the manufacture to 2500 litre production volumes (10 litres, 100 litres and 500 litres initially) through a commercial third party in the US. The first major milestone is expected around mid year 2008, when the company is hopeful to report on successful scale up of manufacture. It is this milestone that potential partners are most interested in first up.

Preclinical milestones

Patrys has given Japanese pharmaceutical group **Takeda** (which recently acquired **Millennium Pharmaceuticals** for US$8.8 billion) an option to evaluate five of its 12 natural antibody leads. Evaluation of those compounds in preclinical models is expected to be completed and reported by year's end. We do not view this as a major milestone. Positive preclinical data on other leads has already been generated. The current agreement is only an option for Takeda to evaluate the compounds. Of more significance will be whether a licensing or co-development agreement can be negotiated.

Clinical Milestones

The next major milestone after manufacturing scale up will entry into the clinic with Patrys's two lead compounds (PAT-LM1 and PAT-SM6). Phase I studies are expected to begin in the first quarter of 2009 with results in the third quarter 2009.

Partnering

The third major milestone over the next 12-18 months will be partnering deals. Patrys is looking to partner one of its leads prior to generating clinical data, and then partner another after clinical data has been received. The company sees itself as having an engine room for drug target and compound discovery. It aims to add four to six new targets every 12 months. As mentioned earlier, if the company can show it can scale up manufacture, then multiple licensing deals should be achievable on novel targets and human antibody leads. There is no reason that small molecules could also not be developed against the novel cancer targets identified.

The team

Patrys is spread across three locations in Australia, the USA and Europe. Australia is the headquarters where the CEO is based and where clinical development will occur (Melbourne). A research team is located in Wurzburg, Germany, where 11 of the companies scientists are based. And a business development and manufacturing team, made up of primarily ex-**Imclone Systems** employees is based in the USA. Imclone has built its success on the monoclonal antibody drug Erbitux, for the treatment metastatic colon cancer. Imclone is valued at just under US$4 billion.

Mike Connor is now head of manufacturing for Patrys. He was formerly Director of Clinical Manufacturing at Imclone. Kris Blader, also from Imclone, forms part of the business development team with the CEO Dan Devine. The head of R&D, Paul Andrews, also stems from the successful Imclone group. Prior to that he worked for the FDA and has represented Imclone at FDA meetings. Patrys looks to be well supported by a body of staff who have gained significant biopharmaceutical manufacturing and development experience at one of North America's most prominent biotech companies.

At the Board level, directors include **Pharmaxis** CEO, Alan Robertson.

Funding

On listing, the company raised $25 million and had $19 million at the end of March this year. This should be sufficient to fund the company until 2010, by which time Patrys should have reached a number of key value creation milestones.

Summary

Patrys presents the complete global R&D biotech package. Complete with a novel technology and strong management team spread across major regions throughout the world, it's a stock well worth considering. The company is capitalised at $45 million.

Bioshares recommendation: **Speculative Buy Class A**

– *Impedimed cont'd from page 2*

This market is backed by strong patient advocacy groups in the US. In about 20 US states and at the US Federal level, legislation exists that supports the reimbursement specifically of secondary lymphoedema diagnosis and treatment.

These factors may provide an important market pull for Impedimed's assessment and diagnostic products.

Comparison of objective lymphoedema detection systems

Several companies market perometers including **Juzo** (USA) and **Pero-System Messgerate Gmb**H (Germany). Perometers generate volumetric limb measurements using infrared. Perometers cost about US$50,000 and are not portable. Impedimed's bioimpedance diagnostic devices are portable and cheaper (US$14,500 - US$18,500). There is also the possibility that one of Impedimed's products may get to market as the predicate device for the early detection of lymphoedema in breast cancer.

Summary

Impedimed is emerging as a promising company. To date, Impedimed has kept a low profile, but the company looks to be very focused on securing a strong outcome in the early detection of lymphoedema in the breast cancer market in the US. To this end the company has been developing its US reimbursement strategy and building pre-marketing efforts in the US.

The company has excellent management and a strong board. The company is capitalised at $65 million, with $10.2 million in cash at March 31, 2008.

Milestones to monitor

FDA marketing clearance of L-Dex U400 – H2 2008
AMA coding submission – Oct 2008

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

***Corrections*:**
In Bioshares 261, incorrect cash figures in the '4.7B Reporting Companies Cash Balances Mar. 31, 2008' tables were stated for two companies.

The correct cash figure for Halcygen Pharmaceuticals at March 31 was $12. 1 million with a corresponding Survival Index of 4.8 .

The correct cash figure for Clinuvel Pharmceuticals at March 31 was $53 million with a corresponding Survival Index of 7.1.

Nanosonics was incorrectly referred to Nanomics.

We apologise to the companies concerned for these mistakes.

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

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