

Bioshares

Australia's biotech and pharmaceutical investment magazine

Number 9

March Quarter 2002

Australian companies covered in this edition

Peptech

Bionomics

Axon Instruments

Meditech Research

IPO season is back

latia

Benitec

Premier Bionics

Cryosite

International companies

Alza Corporation (US)

plus Our drug delivery special looks at what's hot in this sector and what's not

and Capturing profiles for the big league biotech markets

Bioshares

Bioshares is published by Blake Industry & Market Analysis Pty Ltd
 ACN 085 334 292
 Licensed Investment Adviser
 No.195083

The company was incorporated in 1998 and specialises in researching the biotechnology and healthcare sector in Australia.

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Subscriptions
 From JUNE 2003:

One Subscription Rate \$220 inc GST
48 issues a year (by email)

Edition Number 9 (March Quarter 2002)

ISSN 1443-850X

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Summary of Recommendations

Company	Recommendation
Eiffel Technologies	Speculative Buy Class B
Starpharma Pooled Development	Speculative Buy Class A
Sirtex Medical	Buy
Meditech Research	Speculative Buy Class B
pSiVida	Speculative Buy Class B
Occupational and Medical Innovations	Speculative Buy Class C
Norwood Abbey	Sell

Company	Recommendation
Axon Instruments	Strong Buy
Peptech	Lighten
Bionomics	Spec. Buy - Class B
Meditech Research	Spec. Buy - Class B

From the Editors

Long time readers of Bioshares will have noticed that we do more than appraise stocks. One of the first stated aims of Bioshares was to help you make better informed investment decisions. Note the use of the word informed. Well-informed biotech investors have to take a big-picture approach as well as the bottom-up, individual company analysis. Successful biotech investors know the value of reading widely, and are constantly analysing the drivers and issues in the sector.

To this end, we have invited contributions in the past from other stakeholders in the sector to comment on aspects of listing a company, clinical trials, risk reduction strategies, gene regulation and broad biotech investment trends. We have included features on signal transduction and carbohydrate drugs. And in this issue we have a major feature on drug delivery. Drug delivery is very much the focus of attention of a number of Australian companies, listed and unlisted, and the global sector is generating annual sales of US\$39 and billion growing at 15% a year.

Drug delivery is a major industry driver because it is a means by which large pharmaceutical companies can extend their franchised sales of high-margin best selling drugs, as patent expiry dates approach. New drug delivery technologies may also breathe life into drugs that looked good on the lab bench but failed because of a lack of a suitable delivery mechanism. But if you are really not convinced about the importance of drug delivery just look at **Biota**. Here was an Australian company that was set to take on the world with a novel flu drug. It didn't because a rival company developed a pill version of the drug in contrast to Biota's puffer delivery device. We provide mini-appraisals on the listed drug delivery companies but we also specifically revisit **Meditech Research**. This company has undergone a number of positive changes that herald a strengthening in the stock price.

It's been a difficult quarter for the sector with most biotech indices falling and falling heavily. A recent survey from the US asked seasoned biotech investors the secrets of their success and they gave the following advice: be patient, take profits when you can or trim winning holdings, don't believe hype, buy when everyone else is selling and sell when the herd is buying, and don't fall in love with a stock.

This issue looks at four IPOs to hit the market, with subscribers receiving two as advanced extracts. Whilst there have been some heavy falls in the sector, most of these stocks will rebound and the IPO pipeline continues to build. Stocks more than likely to hit the market later this year include **Arrow Pharmaceuticals**, **Biodiem** and **Pharmaxis**. Pharmaxis, which is profiled in this edition, plans to go all the way and become a stand alone pharmaceutical group. There are many more companies just waiting for the next IPO window and these include **Acrux**, covered in our drug delivery feature, and **Kinacia**, which is also profiled. Acrux is currently considering where it will list and interestingly its CEO says at the moment, Australia is looking like the most favourable market. Over the last five years venture capital firms have been investing heavily in biotech and their key exit strategy is through an IPO. So the message is expect the biotech IPOs to continue.

All the best with your investments.

The Editors

David Blake and Mark Pachacz

Market Movers

The Australian Healthcare & Biotech Sector Performance in 2001

Index	Change in Index on Q1 2002	Capitalisation	Index value
Bioshares Hospital Management Index	+8%	\$1.1b	149
Bioshares Health Services Index	-6%	\$2.1b	74
Bioshares Pharmaceutical Index	-13%	\$2.3b	118
Nasdaq Biotech Index	-15%	-	773
Bioshares Drug Discovery Index	-16%	\$2.2b	83
Bioshares Health Products Index	-17%	\$2.7b	105
ASX Healthcare & Biotech Index	-17%	-	4975
Bioshares Leaders Index*	-21%	\$16.9b	98
	total	\$27.3b	

* Bioshares Leaders Index contains only the five largest stocks in the sector – CSL, ResMed, Cochlear, Sonic Healthcare and Mayne. These stocks are not included in the other indices.

The first quarter has historically generated poor results for the biotech sector and this year was no different. The **Bioshares Drug Discovery Index** was down **16%** while the **Nasdaq Biotech Index** fell by a similar **15%**. From 1992 to 2001, the **Amex Biotech Index** has fallen by an average **9.4%** in the first quarter with much of this attributed to the lack of positive announcements over this period. The reason for this is that the schedule of major scientific meetings begins in April and with biotechs generally trading on the result of positive clinical data, the lack of clinical data released in the March quarter leaves little to inspire investors.

The fall in the overall **Healthcare and Biotech Index** by **17%** was largely due to the four largest stocks in the sector, which collectively fell by 21% over the period. Speculation of interest rate increases, which effects stocks such as **CSL** and **Cochlear** significantly because of their higher long term growth rates (see article on CSL in *Edition 5*), was partly responsible. In addition a profit downgrade by Cochlear and doubts over **ResMed's** competitive advantage, which *Bioshares* suggests is ill informed, has taken the gloss off these glamour stocks.

Outperformers

Of the 93 companies in the sector, almost two thirds experienced declines in their share price over the quarter. Going against this trend was **Chemeq**. The company is trialing a polymer version of an antimicrobial to replace antibiotics used in stock feed. It s, continued its strong run from 2001 (+300%) increasing by **80%** over the quarter. Antibiotics are added to animal feeds to prevent infection and to help promote weight gain. Chemeq received results from an independent trial showing its antimicrobial increased body weight in chickens by 20% against chickens not given the product. The company is expecting regulatory approval in Australia, New Zealand and South Africa by the end of the year and at the end of the quarter was capitalised at \$159 million.

Prana Biotechnology's share price increased by **66%** to capitalise the company at \$122 million. Investors bought the stock in anticipation of positive clinical trial results released in April relating to the company's Alzheimer's disease therapeutic. Investors were not disappointed. The company will now continue with further Phase II or III trials and results should be published in a peer-reviewed journal within three months.

Sigma also continued its strong run from last year (+195%) increasing a further **37%** in the first quarter with expected efficiency gains from a merger with API. The merger application was rejected by the competition watchdog, the ACCC, in April and the stock retraced some of this year's gains.

And **Agenix** increased by **34%** in the quarter with continued strong growth in sales across both the company's diagnostic business (+55%) and the **Milton Pharmaceuticals** business (+80%). Net profit was up for the last six months to \$1.7 million. The blue sky with the company is the **Thromboview** diagnostic technology. The antibody for **Thromboview** has now been successfully produced and clinical trials will begin in November.

Underperformers

Problems for laser vision correction group, **Q-Vis**, went from bad to worse. After the resignation of **Catherine Livingstone** from the board and difficulties raising sufficient cash to fund its R&D, the results reported from clinical trials in the US were disappointing. Three of 13 patients treated resulted in under-corrections which were linked to an engineering problem and was not connected to the effectiveness of the underlying solid state laser technology. However with funds running out and doubts about management of the company, Q-Vis is in a precarious position. The company raised only \$110,000 in a rights issue. Although it reduced expenditure, it has only \$5 million cash in the bank, perhaps enough to see the company out until the end of the year.

SSH Medical has developed a device to assist the Pap smear procedure. Although the market is potentially massive, the company has failed to generate substantial sales and signs for the company look ominous. In the last six months of last year, the company generated sales of only \$208,000 on an operating loss of \$2.2 million. The share price fell by **55%** in the first quarter.

Vita Life Sciences shares dropped **44%** for the quarter after net profit for the company fell by 84% because of lower sales in one of the company's divisions and changes to the company's account-

Continued – page 9

IPO Watch – Iatia Ltd

12 March – *Iatia Ltd* was formed in 1999 by Vincent Thiang to commercialise research emanating from the University of Melbourne. The company is developing two product families. One is a 'phase imaging' technology that can be attached to imaging equipment such as microscopes to enhance visual detail of objects. The second is a quite separate technology, which are precision optical headsets used primarily by surgeons and dentists. On a fully diluted basis, Thiang and related parties will own just under 80% of the company after listing.

Phase Imaging Technology

Images that are received by looking through a standard microscope give the viewer details of the intensity of the image only. That is the amount of light that passes through or is absorbed by that object. The other useful characteristic that can be helpful when viewing objects with the assistance of imaging equipment such as microscopes is details relating to the phase of the wave, and in the case of a microscope, the phase of the light wave. Where intensity/absorption relates to the amplitude of the light wave, the phase relates to the frequency of that wave.

By measuring phase changes of a wave passing through an object, specific details of the refractive index of the sample can be determined, which is a measure of the speed at which the wave travels through an object. Samples can have the same intensity but different phase characteristics. This technique is particularly useful in imaging objects that are weakly absorbing or non-absorbing, greatly enhancing the visibility of edges and boundaries compared to conventional imaging techniques.

The phase imaging technology is initially being applied to microscopes. The first product was released in November 2001 and in the six month period to 31 December 2001, the company generated sales of \$240,000. The product Iatia sells includes two parts: a phase imaging tube that bolts onto the microscope and automatically adjusts the lenses to take pictures slightly above and below the in-focus object, measuring the speed at which the wave travels through the sample (or the phase). The second part is the software program

to run the system. The product sells for \$14,000.

Share structure

Iatia is raising \$5 million by issuing 20 million ordinary shares. With each two shares issued investors will receive one 25 cent option. There are also close to 73 million 'Limited Deferred Shares'. The founding director's company, **Thiang Holdings Pty Ltd**, owns 70 million of these shares. A proportion of these shares (3/7ths) will convert to ordinary shares if the company generates a net profit of greater than \$3.5 million before June 30, 2003, and the remainder will be similarly converted if the company generates a profit of at least \$6.0 million by 31 December, 2004. This complicates the share structure and makes it more difficult to calculate the company's capitalisation at any time. However it is highly likely these shares will be converted and when calculating the values in the table on the next page, it is assumed they will be. This is not unreasonable. For instance, if the shares are trading at 25 cents, then by purchasing about \$6.0 million of software on 29 June 2003, Thiang Holdings will receive \$17.5 million.

Features of the phase imaging product

The technique allows the density or the refractive index of a sample to be measured. The system will be extremely useful for imaging biological samples for details of cells and cell nuclei. With an automatic, in-silico, staining or colouring feature built into the software, similar to desktop settings for personal computers, the technology could be simply used by pathology labs to quickly count cell numbers (by counting cell nuclei 'stained' a different colour to the remainder of the cell) rather than physically staining the samples and then using a microscope to examine the sample.

This is the first digital, quantitative phase imaging technology available in the world. The technique is digital as opposed to the existing, partial phase imaging techniques which are qualitative, based on relative optical strengths. The digital capacity allows the image samples to be stored, to be manipulated for staining as described above, and cross sections can be taken of samples to give exact thickness levels of

Listing price:	25 cents
Offer Opens:	22-Feb-02
Offer closes:	20-Mar-02
Expected date of listing:	5-Apr-02
Cash to be raised:	\$5 million
Underwriter:	Tolhurst Noall Ltd
	Ph: 03 9242 4000

the sample which leads to two future applications.

The first is measuring cell volume for biological analysis of samples. The second is use of the system to calibrate corneal distortion for prescription of corrective lenses. Currently ophthalmologists use an aberrometer to subjectively determine the extent of corneal distortion and selection of optical glasses through a trial and error approach. By digitally mapping the surface of the eye, an exact analysis and report of the eye may be achieved in future.

The software incorporates a suite of image analysis and manipulation tools that can add multiple applications to the technology that may not have even been considered.

The technique can be applied to measuring light waves using an attachment to a microscope, to electrons using an electron microscope, and even to x-rays. Currently another Melbourne based company, **X-Ray Technologies**, is using this technique to enhance x-ray images. In fact Iatia and X-Ray Technologies have an agreement not to dispute certain patent claims that may crossover between the companies' respective technology applications.

Weaknesses

- Iatia has yet to receive confirmation it has secured its intellectual property relating to its phase imaging technology. Patents have been lodged in all major regions but have not been granted.
- The company does not own the intellectual property, although it has entered into licensing arrangements with the **University of Melbourne**.
- Some of Iatia's software was created using a software program licensed from the **Massachusetts Institute of Technology (MIT)** at a royalty free rate. Accordingly, any technology that incorporates this program

Iatia share structure post IPO

Securities	Number
Ordinary shares following IPO	110,695,608
Limited deferred shares following IPO	72,787,852
25 cent options following IPO	99,916,150
<hr/>	
Share price	Capitalisation of company*
25 cents	\$45,870,865
50 cents	\$116,720,768
75 cents	\$187,570,670

*Assumes Limited Deferred Shares are converted

can be distributed by the MIT or any other US Government department, including education centres.

- The digital images generated by the phase imaging technique are not always in focus, although extremely useful information is generated by the technology as detailed above. Further development may advance the technology in this area.
- The share structure of the company is somewhat complicated by the inclusion of Limited Deferred Shares (see above). These arrangements are generally cleared up prior to IPO.
- The share structure is heavily weighted to one group owning just under 80% of the company if the Limited Deferred Shares are included. A more balanced share registry would be preferable.
- The majority of the founder’s and inventors’ shares will be under escrow for between 12 - 24 months. However a small proportion of the founder’s shares and some of the shares issued to private investors in recent capital

raisings will not be under escrow arrangements, meaning they can be traded once Iatia shares list.

- If the Limited Deferred Shares are included, the company will have a valuation of \$45 million, excluding any value of the 25 cent options. At 50 cents a share, the company would be valued at \$116 million (including the intrinsic value of the options).

Strengths

- The company is generating income from sales of its technology.
- The technology is widely applicable to not only the microscopy market, but also for use in electron microscopes and x-ray devices.
- The software system coupled with a simple bolt-on phase imaging tube provides the viewer with an advanced imaging system compared to existing equipment. Existing phase imaging techniques are not digital and resultingly are less flexible in receiving, storing and manipulating images. Iatia’s system appears well de-

signed and user friendly with multiple viewing and analysis options.

- The company has a strong Board which includes **Jim Short** (previously assistant Federal Treasurer), and **Geoff Lord**, who is closely involved with the successful pharmaceutical manufacturer **IDT Australia Ltd**.
- The product is affordably priced at \$14,000 compared to X-Ray Technologies’ systems which sell for \$250,000 and upgrades in the software and hardware will ensure repeat sales of the systems.
- Iatia has distribution agreements in place with no fewer than 10 companies in the US, Canada, Asia, Australia and New Zealand.

Summary

Iatia has both a number of positive and negative features to it as an investment consideration. The company is well structured in terms of its Board and Scientific Advisory Board. The share structure (i.e. Limited Deferred Shares) and possible improvements in the technology suggest the company may be listing prematurely however, given the company is generating sales and has distribution agreements in place, the offer to subscribe for shares with one option for every two shares allocated in this offer is worth considering. *Investors are required to fully read the company’s prospectus before subscribing to the offer. A copy of the prospectus can be obtained from www.iatia.com.au or by calling Tolhurst Noall stockbrokers.*

IPO Watch – Cryosite Ltd

15 April – *Cryosite Ltd, formerly named Australian Biologicals Registry Pty Ltd, was founded in 1999. The company applies cryopreservation and ultracold technology to the storage of biomaterials on a fee-for-service basis. Cryosite plans to build its business around the unique properties of cord blood taken from the umbilical cords of babies at birth.*

Business rationale

Cryostorage

Cryostorage is a well established method for storing biological materials and samples. It has achieved notoriety through the sensationalised efforts of wealthy individu-

als who have used the technology to preserve their remains (sometimes only the head) with a view to therapeutic resurrection in the millennia to come. It has now achieved more mundane acceptance through the application of the technology to the preservation of human eggs, embryos and sperm for use in in vitro fertilisation programs and embryonic stem cell research.

Cord Blood Bank

Cryosite anticipates that the major part of its revenues will emanate from the storage of cord blood. Cord blood is taken from the umbilical cord at birth. It

Listing price:	40 cents
Offer Opens:	27-Mar-02
Offer closes:	24-Apr-02
Expected date of listing:	14-May-02
Cash to be raised:	\$3.5 million
Underwriter:	Southern Cross Equities Ltd
	Ph: 02 9231 0880

is a rich source of haematopoietic stem cells, which in turn can be used to generate cells used in treatment, later in life, if the provider develops leukaemia or other cancers of the blood, or immune disorders.

The real selling point is that because a patient's own blood is used, the risk of rejection is significantly reduced, as is the risk of infection from blood-borne pathogens.

Australia has already developed a cord blood bank, the government supported **National Cord Blood Bank**. In the US, many commercial cord blood banks have been established, including **California Cryobank Inc, CORD Inc, Cryobanks International, StemCyte Inc** and **Newborn Blood Banking Inc**. These are in addition to more than twenty non-commercial cord blood programs.

Other service areas

However, there are many other sources of biomaterials that are likely to benefit from cryopreservation and archiving. These sources include forensic medicine, veterinary industry, biomedical research, agricultural research and environmental research. It is interesting to note that in Australia, researchers have been attempting to preserve unique animal and plant species using cryopreservation techniques.

Founders and directors

The directors of the company are Mr Theodore Onisforou, a Sydney lawyer, Prof. Ronald Penny, director of the St Vincents Centre for Immunology, Dr Peter French, manager of the St Vincents Centre for Immunology, and Mr Gordon Milliken, who contributes operational experience in various medical and animal fields. The company was founded by Dr French and Mr Milliken. Mr Onisforou plans to step down as chairman following the float. A new chairman will be sought, as will additional directors.

Capital structure

The company is issuing 8.5 million shares at 40 cents to raise \$3.4 million. The number of shares on listing will be 35 million. The capitalisation of the firm at this issue price is \$14 million. The offer is expected to close on 24 April, 2002, and the shares are expected to begin trading on 14 May.

The major shareholders, post-float, will be listed Pooled Development Fund, **Strategic Pooled Developments Ltd**, holding 18% of the stock and Theo Onisforou will hold 21% of the company. Of the existing

shares, 47% will be held in escrow for two years from the stock's listing date and 14% will be held in escrow for a year.

Strengths

- The first and foremost strength is that Cryosite has first mover advantage. As it markets its services it will generate brand and product recognition that should help build a modest competitive advantage.
- The demand for cryopreservation of unique plant, animal and human tissue samples and other bio-materials is unknown. However its lack of exploitation in a commercial sense may mean that new endeavours will uncover significant demand across a range of service areas.
- The company's emphasis on providing a cord blood cryopreservation service, with its potential for therapeutic benefit, is risky. However, it represents an alternative to many other stem cell and regenerative medicine strategies which are also unproven. It may be that cord blood could be stimulated to generate new blood vessels, muscle cells and brain cells.
- The company has several biological storage agreements in place that do not relate to its core business of umbilical cord blood storage. The agreements are with Proteome Systems, Sirtex Medical, Agen Biomedical and Fucell for the storage of material such as patient tissue samples. It has a distribution contract with American Type Culture Collection (ATCC), for the distribution of biological products used in research in Australia and New Zealand such as viruses, bacteria, fungi and oligonucleotides. And it has a contract with the contract research organisation, ICON Clinical Research, for the storage of clinical trial drugs.

Weaknesses

- The company has a pre-listing valuation of \$10.6 million. The offer document gives scant reasoning for this capitalisation. The company has net assets of only \$1.3 million with negligible sales in the previous six months and only one patent applica-

tion relating to the management of biological specimens. In the last 18 months the company has generated revenues of \$102,000 and accumulated a loss of \$1.6 million.

- The company has chosen to use some of the funds to be raised to pay accrued directors fees, totalling \$227,000. Of the \$3.5 million in funds to be raised under the prospectus, 25% of funds will go towards legal fees and listing costs. This is very high compared to a random sample of listing and legal costs as a percentage of gross funds raised for Biotron Ltd (9.2%), Panbio Ltd (10%), Peplin Biotech Ltd (9.3%) and Epitan Ltd (12%).
- Cryosite is in the invidious position of creating the market for its primary cord blood storage service from scratch. Unlike the US, this is a novel product for Australian healthcare consumers. The company has priced its product at \$2,000 for collection, processing and one year prepaid storage for one sample, to be followed up with a \$150 annual charge. In comparison, the US firm Newborn Blood Banking Inc charges a registration and processing fee of US\$500 and an annual storage fee of US\$100. Lazon BioTechnologies charges US\$700 and an annual storage fee of US\$120. The probability of using stored cord blood cells later in life is low, about one in 200,000, unless there is a familial risk potentially requiring stem cell transplant. Although Australian consumers may not be averse to the product concept and cost, it may take considerable time for numbers to build up to generate sizeable revenues for Cryosite. Its service will cater primarily to the wealthy with currently no reimbursement from Medicare or health insurers in Australia.
- The use of cord blood stem cells may be redundant in the future if therapeutic cloning technologies become available.
- The freezing of blood stem cells can cause stress damage and there is no guarantee of maintaining cell functionality for more than 15 years.

Summary

Although the underlying technology is well established, Cryosite is proposing to raise funds for a virtually untested business in an immature private industry sector in Australia. Businesses of the type that Cryosite is attempting to establish, at least in North America, are either operated in conjunction with public and private health provid-

ers, or are private businesses that are not listed on a stock exchange. With no significant sales and a limited corporate history, with the cord service launched in December 2001, the company appears to be listing prematurely and the question must be asked why the group has not been able to attract further venture capital funding.

Investors are required to read the company prospectus prior to subscribing the offer. The prospectus can be downloaded from the company website www.cryosite.com or by contacting the underwriter, Southern Cross Equities Ltd on (02) 9231 0880.

IPO Watch – Benitec Ltd (backdoor listing)

Overview

In May, Queensland biotech company Benitec plans to make a back door listing on the ASX by merging its assets with listing mining company **Queensland Opals**. Queensland Opals owns a small interest in Benitec and once the merger is complete, the mining company will have disposed of all other mining assets and will be renamed as Benitec Ltd. It will be a pure play biotech company.

Gene silencing

Benitec's initial research stems from work conducted at the **Queensland Agricultural Biotechnology Centre**, which is part of the **Department of Primary Industries**. Gene silencing is similar to antisense technology in that it works by arresting the function of genes in producing proteins, by cutting off the messenger RNA as soon as it leaves the nucleus. Messenger RNA is the single stranded copy of one of the DNA strands in the cell nucleus. The nucleotide sequence from messenger RNA is used as a blueprint to construct a protein. Proteins are the work engine of the body.

The principle difference between antisense and gene silencing is that where antisense uses only single stranded complementary RNA to bind with the messenger RNA inside the cell, gene silencing uses double stranded RNA. The difference between the two approaches some researchers believe is that gene silencing compounds may be 1000 times more powerful than antisense drugs. The theory behind the argument is that gene silencing triggers an enzymatic reaction that multiplies the effect on compounds.

Uses of the technology

Gene silencing may become a useful technology in four key areas:

1. Development of novel and very specific pharmaceutical compounds.
2. Production of new varieties of plants with enhanced characteristics.
3. A screening tool used in verifying drug and agricultural gene targets.
4. Production of livestock resistant to bacteria and viruses.

Share structure

The company will be raising up to \$6 million by issuing 12 million 50 cent shares. Queensland Opals will also issue shares to existing Benitec shareholders to acquire the interests of Benitec, particularly the gene silencing IP. The capital structure of the company will be as follows:

Existing Queensland Opal shares:	21 million
Shares issued to Benitec shareholders:	26 million
New shares issued:	12 million
Total	59 million

The company will have a capitalisation of \$29.5 million or pre-money valuation of \$23.5 million. By comparison, Antisense Therapeutics which listed in December last year and is commercialising its antisense compounds, now has a capitalisation of \$16 million (based on its current share price of 15 cents) if cash reserves are excluded.

Strengths

- Gene silencing may produce compounds that are thousands of times more potent than antisense drugs.
- The precise specificity associated with antisense drugs will be retained with gene silencing compounds.
- The company is developing intellec-

Listing price:	50 cents
Offer closes:	May-02
Expected date of listing:	May-02
Cash to be raised:	\$6.0 million
Contact:	Benitec Ltd
	Ph: 07 3371 8668

tual property in an area of research that is in a nascent stage of development.

- The use of gene silencing technology has been well established for use in agriculture and horticulture.
- The technology can be used for validating gene targets which may provide commercial use much earlier than in developing a novel therapeutic agent.
- Being a novel technology, Benitec may seek to out-license the technology to pharmaceutical or biotech companies that may generate revenues sooner.

Weaknesses

- The use of antisense drugs as therapeutic compounds has been commercially proven, with Isis Pharmaceuticals having received approval for its first antisense compound in 1998. This followed many years of failed attempts to develop the technology. Gene silencing is a technology that remains in the laboratory. The first clinical trials of gene silencing compounds as therapeutic agents are expected to occur no sooner than 2004, although use of the technology as target validation may occur sooner.
- One of the technical hurdles for the technology is the ability to deliver these compounds into individual cells.
- The company has yet to be granted patents in major jurisdictions over its technology.

- The company has yet to publish its technology in a peer reviewed journal for external validation of the technology.
- The company has yet to secure any commercial development partners.
- There may be a sell down by existing shareholders whose shares will not be escrowed once the company relists.
- One of Benitec's patent applications is currently being disputed by another party.

Summary

Benitec is developing a nascent technology that may prove to be more effective than the proven antisense approach. However gene silencing compounds have yet to be tested in people and the company has no development collaborators (**Antisense Therapeutics** has a collaboration with the world leader in antisense technology and also has a collaboration with the **Murdoch Children's Research Institute**). On a price comparison, Benitec will have a larger pre-money capitalisation \$23.5

million, more than Antisense Therapeutic's current capitalisation (less cash reserves) of \$16 million

Companies with earlier stage technologies have struggled to perform well on the local market. The lack of external validation of Benitec's technology will make it more difficult to gain investor support. For further details of this offer, contact Benitec on (07) 3371 8668. *Investors are required to fully read the company's prospectus before subscribing to the offer.*

IPO Watch – Premier Bionics

Another biotech company that will list on the ASX is Premier Bionics. Premier is more of a venture capital biotech fund, similar to **Biotech Capital** (BTC). It differs from BTC in that it will specialise in medical device and diagnostic companies. Premier Bionics will raise a modest sum of \$3 million.

Some may ask why bother to set up a com-

pany structure, list and raise only \$3 million. The company has raised the funds from some key professional investors. If it can generate some early success, it may have a ready access to further funds with early investors prepared to invest again once early gains have been generated.

The company has made its first investment in **Pulmosonix Pty Ltd**, a diagnostic de-

vice company that measures lung inflation. Premier Bionics is obviously an early stage investment vehicle. **Peregrine Corporate** and its directors have been involved in structuring this vehicle and have achieved impressive results with their previous biotech involvement with **Prana**

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Market Movers – from page 4

ing policy. **Biota Holdings** was down by 44% with little demand showing for the company's flu drug. **Peptech** fell by 42% (see analysis on page 20) after overshooting the mark. **Antisense Therapeutics** was down 40% after listing in December last year and **Axon Instruments** was down by 36%, falling to now very attractive levels for investors (see analysis on page 22).

Capital raisings

Companies raised \$267 million in the March quarter. The majority of this was sought to fund acquisitions by **Sonic Healthcare** and **Primary Health Care** of pathology and radiology clinics, and GP surgeries respectively. Among the biotechs, there were positive signs of emerging confidence in the sector from institutional investors with \$39 million raised, although there were disappointments. **Amrad Corporation** raised \$15.5 million just before announcing the failure of a Phase II clinical trial and just prior to two international pharmaceutical groups cancelling pre-clinical development programs with the company. The combination of events has since sent the share price into freefall, falling over 50%.

GroPep could raise only \$6.8 million to fund its acquisition of Biotech Australia's biopharmaceutical manufacturing plant. A likely shortfall in funds raised may have contributed to increased tensions between the board and CEO John Ballard, who has left the company.

MicroMedical Industries has taken advantage of the growing interest in its artificial heart program, raising \$11 million without much difficulty. **Eiffel Technologies** was forced to raise further funds to pay for refurbishment of its facility with the

company yet to receive full payment for its Pharmaction manufacturing business. However in what was a good sign for the company, it had little difficulty raising the funds.

Prima BioMed leveraged its solid share price gains by acquiring another technology to add to its suite of projects. The DCTag technology is potentially a powerful activator of the immune system for protection and treatment of diseases and illnesses such as malaria and breast, colon and prostate cancers.

The Brain Resource Company raised \$1 million from the **Queensland Investment Corporation** to expand its portfolio of brain analysis products. And as mentioned above, **Q-Vis** was only able to raise \$110,000 and will need to explore other funding options before the end of the year.

Capital raisings in 1st quarter 2002

Company	Amount raised	Security	Price
Sonic Healthcare	\$170 million	Ord. shares	\$8.10
Primary Health Care	\$58 million	Ord. shares	\$4.65
Amrad Corporation	\$15.5 million	Ord. shares	\$1.15
MicroMedical Industries	\$11.0 million	Ord. shares	80 cents
GroPep	\$6.8 million	Ord. shares	\$1.80
Eiffel Technologies	\$2.1 million	Ord. shares	15.5 cents
Prima BioMed	\$1.7 million	20 cent op.	-
Brain Resource Company	\$1.0 million	Ord. shares	25 cents
Prima BioMed	\$0.6 million	Ord. shares	42 cents
Virax Holdings	\$0.42 million	Ord. shares	60 cents
Innovax	\$185,000	Ord. shares	8.4 cents
Q-Vis	\$110,000	Rights issue	70 cents

total \$267 million

Drug delivery – Now a US\$39 billion industry and set for strong growth

Conference Report

Over the last 10 years, drug delivery technologies have proven to be a viable tool to provide what is called 'life cycle management' of valuable pharmaceutical products. There are now over 400 drug delivery system companies throughout the world with over a dozen Australian companies active in the sector. Mostly importantly, this year, US\$25 billion of drugs will come patent with US\$42 billion coming off patent by 2005. Below are some of the important points raised at the IIR 6th Annual Drug Delivery Partnerships conference held in Los Angeles earlier this year.

In 1982, **Pfizer** launched a new drug to treat hypertension, named **Procardia**. Its patent was set to expire in 1992 so in 1989 it launched a sustained release version of the product called **Procardia XL**, which included a semi permeable membrane in the tablet to ensure constant absorption by the body. The net result was that newer version added US\$9.1 billion in sales for Pfizer between 1989 and 2000.

In 1983, Swiss pharmaceutical group **Novartis**, launched an immunosuppressant, named **Sanimmune**, for transplant patients and people with severe arthritis and psoriasis. The drug was due to come off patent in 1995 and in that year the company released a microemulsion of the same drug, named **Neoral**, that increased bioavailability by 25 per cent and improved the absorption profile of that drug. In 1995, **Sandimmune** achieved sales of US\$1.2 billion. Where drugs can lose 80% of sales within three months when patents expire and generics become available, as was the case with **Prozac**, incredibly the newer product **Neoral** maintained sales in 2000 of US\$1.2 billion. Having a different bioavailability profile means patients can not easily swap over to the generic.

The business of today's drug delivery industry was paved by **Alza Corporation's** (see international profile on page 28) **Alejandro Zaffaroni** (see Edition 4 of *Bioshares* for profile) who started the industry by forming what is now the world's largest drug delivery company (and a stand alone subsidiary of **J&J**) in 1968. In 2000 the world drug delivery market was valued at US\$39 billion, and although well short of the world pharmaceutical market at US\$330 billion, the drug delivery industry is growing at twice the rate as the pharmaceutical industry, at 15%. It is expected to reach sales of US\$55 billion in 2005. And Stuart Arbuckle from **Celltech Pharmaceuticals** suggests that if inhaled insulin products make it to market then the interest in drug delivery technologies may increase even more.

Sector driven by life cycle management

The growth in the drug delivery technologies industry has been driven by several factors, although no more important than protection of the billions of dollars in pharmaceutical sales of drugs that are coming off patent and prey to global generic pharmaceutical players. Drug delivery technologies offer a partial solution to pharmaceutical companies called life cycle management. Life cycle management works on three levels. It provides patent life extension (three years in the US based for a new strength version based on new clinical data or 10 years for a patented system with unique in vivo properties), it provides what

is known as line extension or variations of the same product, and controlled and sustained release formulations can improve efficacy, safety and compliance issues. Life cycle management is not just about extending patent life but achieving maximum sales of an approved product using several formulations earlier than 11 years from release.

Drug delivery technologies for New Chemical Entities (NCEs)

Pharmaceutical companies are also interested in using drug delivery technologies to solve delivery issues with NCEs yet to hit the market. Drug delivery has a role to play in early stage compounds that are poorly soluble, large compound drugs in development such as proteins and peptides which need to be administered by injection or by infusion, and with expensive active pharmaceutical ingredients that have shown low bioavailability characteristics. The demand for improved delivery methods of protein and peptide drugs is very high with more than 100 protein/peptide drugs having been approved by the FDA and with 350 in development. **Elan's** nanosystem technology is being used for the oral delivery of a protein for the first time.

Increased spend by pharma on R&D not paying off

Not only are a multitude of drugs coming off patent for big pharma, but the increased spending on R&D is not translating into more drug approvals from the FDA. In 1999, only 35 new drugs were approved by the FDA compared with 39 in 1997 and 53 in 1996. And if that wasn't bad enough news for the pharmaceutical giants, the period of market exclusivity for new drugs that are approved is falling dramatically. In 1965, when **Inderal** was approved in the US, its 'me-too' competitor drug, **Lopressor**, did not reach the market for 13 years. In 1977, when the drug **Tagamet** was released, its me-too counterpart, **Zantac**, reached the market six years later. This exclusivity period is shrinking so quickly that when **Celebrex** was approved in 1999, its competitor, **Vioxx**, followed it to market in just a matter of months. In Australia, local biotech company **Biota Holdings** felt the full effect of this when it released its flu drug, **Relenza**, in 1999 (marketed by **GlaxoSmithkline**). Not only did its competitor, **Tamiflu**, from **Gilead Sciences** make it to market the following year, but it now has 90% market share because of its preferred delivery method, a tablet form verses the inhaled **Relenza** product. The days of 100% market share are gone because there is more market sharing of information, due no doubt to the pervasive influence of the Internet.

Generic conversion more immediate

The news only gets worse for big pharma. When the big drug products are coming off patent, the people are converting to generic equivalents much more quickly, with the generic manufacturers more competitive and more organised. Typical conversion from branded to generic alternatives is 50% within six months. However when **Eli Lilly's Prozac** came off patent last year, there was an 80% conversion from Prozac to generic fluoxetine within three months.

In the US, the pressure to use generic alternatives is significantly greater than in Australia. Generic substitution was 47% in the US compared to only 12% in Australia, up from 18% in the US in 1984. The reason for the increase in the US is a blow out in health funding and the increasing control of the US government, Medicare and managed care organizations. Five years ago 60% of prescription costs were paid for by these groups. Now these groups pay for approximately 85% of all prescriptions in the US. Some managed care groups now require mandatory generic substitution and the percentage of HMOs requiring generic substitution increased to 72% in 1998 (from 63% in 1984).

To counter this, Arbuckle says drug delivery technologies are enhancing brand proposition. For patients, it improves ease of use, convenience and reduces embarrassment in taking medication. A clear example of the final point is the drug to treat ADHD, methylphenidate. When a once a day version was introduced (previously taken by children three times a day), sales increased by 45% over the next two years. According to Arbuckle, it provides differentiation and competitive advantage to the industry. It is also cheaper and quicker than NCE (new drug) development.

Higher return on investment

John Fraher from drug delivery group **Eurand** agrees and believes the return on investment is higher with developing novel formulations than with drug discovery. The discovery and developing process involved with new drugs increased to 14.9 years over the period 1990 - 1996, up from 11.6 years in the 1970s. Costs are increasing, up to \$600 million, with average sales of \$300 million - \$600 million. Drug delivery development takes seven years, costs up to \$20 million with average peak sales of \$250 million.

The take-home message from Keith Horspool at **Pfizer** is to make the most of reformulations of blockbuster drugs. Horspool says only 30% of drugs recover investment costs. Pfizer is now interested in every route of drug delivery and expects to be entering into more drug delivery collaborations citing it as relatively good value for money compared to the high development risk for discovery. On average, big pharma enters into five drug delivery collaborations a year and smaller pharmaceutical companies enter into just under two a year. Horspool says that between 1996 - 1998, the mean time before patent expiry that a new drug delivery system was considered was 3.2 years. This has now increased to six years.

In 2001, a third of all product launches included drug delivery technologies. From the top 50 pharmaceutical companies, only 15 drugs were approved that provided significant improvement

in disease; 15 drugs were approved that provided advantages over similar but existing compounds; and there were 10 me-too drugs approved.

Pharmas need more vigorous patenting

Mark Levy from **Thompson Hine** patent lawyers in the US not surprisingly believes that pharmaceutical companies need to patent more aggressively and observes short falls when compared with other industries. In 2001, **IBM** filed 3,400 patents, **Sony** filed 1,300 patents and **GE** filed 1,200 patents. By comparison, **Merck** filed only 325 patents in that year, **Pfizer** filed only 174 patents, **Glaxo** filed only 85 and **SmithKlineBeecham** filed 350 patents. Levy says Pharma could learn from other hi-tech industries in terms of adopting a more aggressive patent approach and the use of drug delivery technologies is a viable strategy.

New technologies on the block

Four companies were invited make presentations on emerging technologies in drug delivery systems. **Shearwater** discussed developments in its PEGylation technology with products now on the market. PEGylation involves the addition of non-toxic polymers to pharmaceuticals to reduce clearance rates from the body, providing sustained release, preventing unwanted immunogenicity and solubilizing hydrophobic drugs. Baxter healthcare outlined its nanosuspension platform, where by modifying the surface charge of the drug, a finer particle suspension can be achieved improving solubility and thereby increasing bioavailability.

What generated the most interest in emerging technologies however was the field of supercritical fluids (SCFs) with two presentations, once by **Ethypharm** from France and the other from **Lavipharm** in the US. Lavipharm explained that SCFs can be used for efficiently drying proteins with 100% recovery of monoclonal antibodies; coating of drugs for sustained drug release; producing drugs with a consistently fine particle size distribution down to 0.5 - 5 micron; and even the possibility of sub micron naked DNA delivery. SCF technology can be employed in a high throughput process and the stability and activity of the compounds can be maintained.

Ethypharm is currently using SCFs for the sustained release of therapeutic proteins. This can reduce EPO (recombinant human erythropoietin) dosage to once a month and the dosage of interferon alpha from once a week to twice a month. Because of their size, proteins such as insulin, need to be administered by injection or infusion. A reduction in dosage frequency can be a very attractive feature.

The advantage of using SCFs is they have properties of both gas and liquid. The gas properties include high molecular diffusion, low viscosity and very high compressibility. The beneficial liquid properties include high solvent power and high density.

Wall Street's view of the drug delivery sector

David Steinberg, a Wall Street analyst from **Deutsche Banc Alex Brown** has been covering the drug delivery sector for 11 years. He says the last 10 years has been a fabulous time for the sector

with 14 mergers in the last three years. Steinberg says that oral controlled release is the biggest market, followed by transdermal and then implant devices. The holy grail in drug delivery is the non-invasive delivery of proteins and peptides.

And while some consolidation has occurred within the pharmaceutical industry, it remains fragmented compared with other industries. In the oil industry, the top five companies have 63% market share and in the automotive industry the top five have 60%. In the pharmaceutical industry, the top five companies have only 37% market share.

Summary

Most drug delivery companies around the world don't have prod-

ucts on the market. There is a trend to become fully integrated pharmaceutical companies and David Steinberg suggests that the next big drug company may in fact be a drug delivery company. There have been some notable failures along the way, including **Powderject** in the UK, which has recently sold its drug delivery technology to concentrate on its vaccine business.

Drug delivery technologies are maturing and providing appropriate technologies to the pharmaceutical industry and they have demonstrated an ability to protect and increase product franchise. However to survive companies may need to adopt a fully integrated approach with products on the market because building a business on royalties alone is a difficult approach.

Australia's drug delivery system specialists

The Australian drug delivery players represent a diverse range of technologies and some of these companies are profiled in this edition of *Bioshares*. From safety syringe companies such as **Eastern Medical Systems** and **Occupational & Medical Innovations**, to transdermal enhancement specialists such as **Acrux** and **Soltec** (previously a part of **FH Faulding** and sold to US group Connetics Corporation), novel delivery system developers such as **Norwood Abbey**, bio-engineering/reformulation company **Eiffel Technologies**, novel dispersion and delivery technologies as those being developed by **Starpharma Pooled Development** and **pSiVida's** investment interest, inhalation specialists such as **Vapotronics** from Queensland (which has now relocated to the US), and cancer drug delivery specialists such as **Meditech Research** and **Sirtex Medical**.

Eiffel Technologies

Capitalisation: \$14 million

Recommendation: **Speculative Buy Class B**

Debra Bingham from Technology Catalysts International says that the number one technology pharmaceutical companies are looking for at the moment are ones that can solve solubility issues and provide bioavailability enhancement. The oral drug delivery market accounted for US\$22 billion in sales, or 56% of the overall drug delivery market. With some pharmaceutical companies declaring 80% of their interest in drug delivery technologies is in improving bioavailability, Eiffel Technologies is well placed to capitalize on a market demand with very few commercial players.

Eiffel was covered in depth in Edition 6 of *Bioshares*. It specialises in providing its expertise in supercritical fluid (SCF) technology to the pharmaceutical and biotech industry. The company is commercialising technology emanating from the chemical engineering faculty at the University of NSW. The company is at an early stage of development and this is reflected in its share

Norwood Abbey

Capitalisation: \$80 million

Recommendation: **Sell**

Norwood Abbey is developing a laser-based drug delivery system. The technology works on the principle of painlessly removing the outer layer of the skin with a hand-held laser. It combines a drug delivery system that allows pharmaceuticals to be delivered through the skin without a syringe.

price. It has yet to publish any of its trial data in improving bioavailability of pharmaceutical compounds. However Eiffel has two international research collaborations, one with Sheffield Pharmaceuticals and the other with BattellePharma, both located in the US. BattellePharma has partnerships with several pharmaceutical companies including Abbott Laboratories, GlaxoSmithkline and Pfizer. BattellePharma will use Eiffel's SCF capabilities to manufacture sub-micron protein particles to be used in BattellePharma's pulmonary device.

Eiffel is re-engineering drugs to allow alternative delivery of compounds such as cancer drugs or insulin. In total it is working in eight disease areas, including respiratory, neurological, cardiovascular and infectious diseases such as HIV. Eiffel is hopeful of announcing several further collaborations over the next 12 months as well as releasing details of SCF pilot studies. Refurbishment of its facilities is nearing completion.

Eiffel's few commercial competitors in the world specialising in SCF include Bradford Particle Design (acquired by Inhale Therapeutic Systems for US\$200 million), Ethypharm in France, and Lavipharm in the US.

Its first product is a local anaesthetic that it has now entered into a collaboration with Ferndale Laboratories in the US, a distributor of local anaesthetic products. Future applications may include laser-based vaccine delivery.

One of its competitors internationally in this market is Powderject Pharmaceuticals in the UK. Powderject was developing a drug delivery device that propels powdered drugs across the skin using a helium gas jet to accelerate the drug. It has experienced problems developing its technology and recently sold its drug delivery business to AlgoRx for only US\$10 million.

(Powderject will also receive royalties from the sale of any products and retains use of the technology for delivery of powdered vaccines). One of AlgoRx's first applications will also be needle-free delivery of local anaesthetics.

Needle-free drug delivery is a competitive field with products already on the market (see Edition 8 of Bioshares); Antares Pharma has a refillable device on the market that allows liquid insulin and human growth hormone to be fired across the skin (current capitalisation US\$27 million); Weston Medical has a disposable needle-free device that also fires liquid drugs through the skin (capitalisation US\$230 million); and Bioject is working on refillable devices to fire liquid drugs through the skin (capitalisation US\$42 million).

Acrux

Capitalisation: \$70 million (at the last capital raising)

Recommendation: **Unlisted**

Acrux is an unlisted company based in Melbourne and was formed in 1998. It is developing a transdermal drug delivery system that uses the same agents found in sunscreens to delivery drugs across the skin barrier and into the body. The device is in fact a spray that delivers a metered dose into the body and will compete with transdermal patches currently on the market.

The technology was invented at the Victorian College of Pharmacy and the patents have been assigned to Acrux. The invention relates to the identification of the key enhancers in sunscreens that facilitates transdermal transportation and the main patent has been granted in the US. Advantages of Acrux's technology over existing transdermal patches include lower production costs, dosage flexibility, negligible skin irritation and cosmetic acceptability.

Starpharma Pooled Development

Capitalisation: \$69 million

Recommendation: **Speculative Buy Class A**

Starpharma Pooled Development was covered recently in Edition 8 of *Bioshares*. The company is developing chemical scaffold structures called 'dendrimers'. Dendrimers are a platform technology where a precise three-dimensional structure can be constructed with multiple, active pharmaceutical groups located on the outside of the structure, or with active compounds located within this structure and released into the body when required.

The surface groups can have two functions; to target and attach to specific areas within the body for localised or more effective drug delivery; and the second involves adding active pharmaceutical groups that bind with cell receptors to effect the required cell response. The design of the surface groups can be so spe-

Norwood Abbey is at an early stage of development although perhaps this is not reflected in the company's share price. Perhaps similar to how Powderject changed its focus from drug delivery to vaccines, Norwood Abbey has begun to take on other research projects, primarily an immunology program for stimulation of T-cells in the treatment of prostate cancer and HIV/AIDS. With the market for needle-free injection systems making up only 0.5% of the total drug delivery market, and with this expected to rise to only 1.0% by 2005 according to *Scrip 2001*, the demand for Norwood Abbey's product may not be great.

The company recently entered into a collaboration with Pharmacia for its metered dose transdermal system to test and develop several of Pharmacia's compounds for use in Acrux's delivery device. Acrux has several compounds in development with some in clinical trials. Its lead product is estradiol used in hormone replacement therapy and is currently in Phase II trials.

The company's newly appointed CEO, Dr Igor Gonda, was previously with drug delivery group Aradigm Corporation in the US. The board of directors includes Dr James Foght, former managing director of Investment Banking for the Prudential Vector Healthcare Group and Ken Windle, previously the head of GlaxoWellcome's Asia Pacific Group. The company expects to list in the next six to 18 months depending on market conditions. At the moment, the Australian market looks the most favourable so it may be on the ASX, although AIM in the UK and the Nasdaq are also possibilities. Given the company is a pooled development fund, it may make more sense to list in Australia and let investors enjoy the advantages of no capital gains tax on the stock. It may also depend on where the company's commercial partners are located.

cific that it may be possible to mimic the function of naturally occurring proteins within the body that display multiple binding activity at various sites of the cell for increased drug efficacy.

One of the key features of dendrimer scaffolds is the degree of control and flexibility that can be achieved. As drug delivery vehicles, dendrimers could be designed to spontaneously swell and release their contents when the compounds come in contact with a particular organ or trigger molecule present in the body.

Starpharma will begin the first ever clinical trial of a dendrimer compound later this year when its vaginal microbicide begins testing. Starpharma has also formed a corporate vehicle, Dendritic Nanotechnologies Ltd, with the inventor of dendrimer scaffolds, Donald Tomalia. The company will explore the commercialisation of these compounds outside of the pharmaceutical industry.

Continued over

pSiVida
 Capitalisation: \$17 million
 Recommendation: **Speculative Buy Class B**

pSiVida’s involvement with drug delivery systems is related to its investment in the UK biotech company pSiMedica. pSiVida is a 43% shareholder in the company with the other main shareholder being QinetiQ, or what was previously the UK’s Defence Evaluation and Research Agency (DERA).

pSiMedica is pioneering the commercial use of porous silicon or ‘biosilicon’ within the healthcare industry. The company’s

Sirtex Medical
 Capitalisation: \$80 million
 Recommendation: **Buy**

Sirtex Medical (covered in Edition 7 of *Bioshares*) specialises in the treatment of liver cancer through a localised delivery system. Its first treatment, the use of radioactive particles, has been approved for use by the FDA and the company is now training US specialists for use of its device. Sirtex’s treatment is currently being used in Australia, New Zealand and Asia.

SIR-Spheres are 30 - 40 micron biocompatible, resinous beads that are coated with radioactive yttrium-90. The radioactive particles destroy the cells they come into contact with and decay into a harmless by-product within a matter of days. The half-life of yttrium-90 is only 64 hours. What makes these particles an effective treatment for cancer is accurate delivery to the cancerous liver tissue without spreading to healthy parts of the liver.

Occupational and Medical Innovations
 Capitalisation: \$22 million
 Recommendation: **Speculative Buy Class C**

Occupational and Medical Innovations Ltd (OMI) falls under the broadest part of the drug delivery umbrella. It is the developer of a ‘mundane’ safety syringe product that forms the cornerstone of a line-up of mostly medically oriented safety products. OMI’s retractable safety syringe is the brainchild of company founder Bruce Kiehne. Needle stick injuries are a widespread problem and are not confined to personnel in the healthcare industry. One clear market message gained from examining OMI’s business objectives is that needles, as a delivery mechanism, are not about to be displaced in the near future by other devices. The company has successfully developed its retractable syringe beyond the prototype stage, as have many other companies. The major obstacle to the successful commercial exploitation of a retractable disposable needle is achieving volume production efficiencies that reduce the unit cost to several cents per device. As many as 24 billion disposable syringes are used globally each year.

The Queensland State Government jointly funded a study with OMI to ascertain the feasibility of building a \$100 million plant to manufacture OMI’s syringe. With that now completed, the company intends to raise \$15 million to build a pilot plant capable of producing 80 million units for the Australian market. Stud-

scientists discovered novel properties of silicon outside of the semi-conductor industry, namely that if silicon is made porous, it becomes biodegradable and as a result dissolvable within the body. It has also been shown to have a binding affinity to bones.

Biosilicon may become a useful drug delivery mechanism, where the silicon structure can be filled with pharmaceutical compounds that are released over a sustained period as the silicon structure dissolves. The binding and biodegradable properties of the porous silicon also opens up the possibility of using this material as bone splints that bind to the bone, provide the necessary support for healing damage and then simply dissolving once the bone strength and integrity has been restored.

This is achieved through a number of carefully designed parameters. The particle size is crucial as the particles can be delivered to the terminal arteries in the liver without passing through the liver and back into the blood stream, much like straining tea from tea leaves through a strainer.

Also because 99% of metastatic cancer (cancer that has spread from other cancers) is done so through the blood flow from the aorta (20% of flow supplying the liver), rather than from the gut (80% of flow supplying the liver), the treatment is directed into the blood from the aorta that flows into the liver. While some healthy liver tissue may be damaged in this treatment, this guided and selective delivery ensures the tumour receives 10 times more radiation than healthy tissue, which is regenerated quite quickly in any event.

Other follow up products include similar systems but where the radioactive particles are substituted with cytotoxic drugs and Thermo-Spheres that generate heat to kill the liver cancer cells from within.

ies of the retractable needle will be conducted in various hospitals in Queensland.

Although the company has developed a comprehensive portfolio of products, it still has many development milestones to pass. The company’s capital requirements in the future are likely to expand, well beyond the immediate capital raising for the pilot manufacturing plant. The company may benefit from a number of corporate adjustments to facilitate its path forward to a sustainable profit horizon. In its current incarnation OMI is an interesting technology company and warrants a Speculative Class C rating.

Bioshares Listed Drug Delivery Company Ranking
(based on investment potential)

	Company	Recommendation
1	Eiffel Technologies	Speculative Buy Class B
2	Starpharma Pooled Development	Speculative Buy Class A
3	Sirtex Medical	Buy
4	Meditech Research	Speculative Buy Class B
5	pSiVida	Speculative Buy Class B
6	Occupational and Medical Innovations	Speculative Buy Class C
7	Norwood Abbey	Sell
8	Eastern Medical Systems	-

Bioshares Biotech Portfolios

The first quarter of 2002 was a difficult period for the biotech sector across the board. The short-term *Bioshares* portfolio fell by 13.5% (in the three months to 3 May 2002), the **Nasdaq Biotech Index** fell by 15% over the first quarter and the **Australian Healthcare and Biotech Index** fell by 21% over the same period. There is a historical precedent for weakness in the March quarter. Between 1992 – 2001, the **Amex Biotech Index** fell on average by 9.2% in the first quarter, largely due to the lack of scientific reporting at conferences over that period.

Over the last 12 months, the *Bioshares* short-term portfolio increased by 22%, the long-term portfolio, selected on a set and forget basis, fell by 26%, the Nasdaq Biotech Index fell by 30% (to 617 points) and the Australian Healthcare and Biotech Index fell by 11% (to 4371 points). Even though it has been a tough time for the biotech sector, there is an argument here that suggests strong returns can be achieved even in a soft market by well-timed entry into well-researched stocks.

In the short term portfolio, most stocks fell in value except for **Ellex Medical Lasers** and **MicroMedical Industries**. Ellex continues to offer certainty and strong growth in a sector that is suffering because of its inability to sustain expected high growth rates. Although trading conditions continue to be difficult for Ellex, which manufactures ophthalmic lasers, it is successfully breaking into new markets. The company's photodisruptor was approved for sale in Japan and the company expects to sell over

100 lasers into that market this year. The lasers sell for \$50,000 each to the end user. The company also released its photocoagulator last year to treat retinal damage and similarly expects to sell over 100 this year. And to continue the expansion, Ellex has just signed an agreement with **Lumenis** in the US to manufacture lasers to treat glaucoma, and once again expects to make the magic number of 100 next year. At a valuation of \$1.86, the stock still has some upside.

MicroMedical Industries also offers some upside with the clinical trials (in people) of its artificial heart to commence later this year. The announcement of this alone will drive the company's share price.

Well that's all the good news! There have been some heavy falls in the portfolio, no more than **Axon Instruments**, which has fallen by 44% (see analysis on page 22). Sales in this half may not be impressive. However the company has five new products to release over the next 12 months and the stock has fallen to very attractive levels for investors. **Amrad Corporation** has almost matched that fall, down by 42%. The scoreboard was level for the company, announcing one positive result for **AM336** to treat chronic pain and with one negative result for **AM424** to treat nerve damage in cancer patient amongst other uses. The market has focused more on the negative result. The news that

Short-term biotech portfolio - previous

Company	Price (3/5/02)	Price change	Price at last quarter
Amrad	\$0.70	-42%	\$1.21
Axon Instruments	\$0.44	-44%	\$0.79
Eiffel Technologies	\$0.17	-8%	\$0.18
Ellex Medical Lasers	\$1.33	41%	\$0.94
Medica Holdings	\$1.07	-22%	\$1.38
MicroMedical Industries	\$0.85	8%	\$0.79
ResMed	\$5.40	-32%	\$7.98
Sirtex Medical	\$1.46	-22%	\$1.86
Starpharma	\$0.76	-3%	\$0.78

Q1'02 Av. (3 months) -13.5%
Portfolio gain (12 months) 21.6%

two pharmaceutical companies had pulled out of pre-clinical collaborations did not help either. Amrad recently sold the worldwide patent rights to **Chemicon** for a gene fusion technology. The negative news cascade triggered a call for new directors by minority shareholder **Circadian Technologies**. The meeting is scheduled for 22 May, and if successful, may impact positively on the share price.

Eiffel Technologies has yet to announce further collaborations for its super critical fluid technology for applications in drug delivery. However the stock continues to look very attractive at current prices given the lack of competitors and the demand from biotech and pharmaceutical companies (see drug delivery feature on page 10). Eiffel may well have more good news for investors.

Passive long term portfolio

Company	Price (3/05/02)	Price change	Price (4/5/01)
Amrad Corporation	\$0.70	-28%	\$0.97
Axon Instruments	\$0.44	-63%	\$1.20
Bresagen	\$0.96	-13%	\$1.10
GroPep	\$1.00	-68%	\$3.17
IDT	\$3.33	-15%	\$3.90
Medica Holdings	\$1.07	-14%	\$1.25
ResMed	\$5.40	-45%	\$9.78
Starpharma Pooled Development	\$0.76	36%	\$0.56

Av. (12 months) -26%

ResMed's share price began falling earlier this year amid news of a competitive nasal mask from Innomed Technologies. That threat proved to be unjustified but the stock continued to fall. Margins fell slightly and sales growth slowed to 24%. The fall in margins is of some concern (EBIT margin fell from 31% to 28% in the last result) and may be attributable to the company's acquisition in Germany and efforts to grow that market. The fall in sales growth and net profit growth (profit increased by 19% in the last nine months) is to be expected given the high sales of the company. ResMed is now generating sales of almost \$400 million a year and it is unreasonable for the company to continue to grow at 30%. If it did for the next 15 years, its share price would

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The Australian Healthcare & Biotech Sector

Capitalisation \$27.3 billion, 92 companies, updated for the close of the first quarter 2002

Drug Discovery Sub-Sector

Company	Code	Cap. \$m	Principal Activities	Price change Q1'02	Price 2/4/02
Peptech	PTD	355	Develops treatments for animal health care products using peptides. Holds patent relating to anti-inflammatory compound.	-41%	\$2.35
Novogen	NRT	270	Develops and produces naturally occurring phenolic hormones for treatment and prevention of cancer, and for estrogenic and cardiovascular functions. Sales in USA & Australasia.	-1%	\$2.83
Genetic Technologies	GTG	130	Previously Duketon Goldfields. Acquired Swiss group Gene Type. Provides DNA paternity testing services and holds broad patents relating to the use of Junk DNA.	0%	\$0.50
Prana Biotechnology	PBT	122	Research into Alzheimer's disease. Lead product in clinical trials. Research also into Alzheimer's diagnostic test.	66%	\$1.61
Metabolic Pharmaceuticals	MBP	120	Develops therapies for obesity based on technology purchased from Circadian & Monash Uni using anti-obesity drug. Listed in November 1998.	-2%	\$0.82
Amrad	AML	111	Seeks & develops innovative medicines with several clinical and preclinical programs.	-11%	\$0.85
Circadian	CIR	92	Management and funding of R&D projects with Australian and NZ universities. Exposure to other listed biotech companies Axon, Optiscan, Metabolic Pharmaceuticals and Antisense Therapeutics.	-23%	\$2.20
Sirtex Medical	SRX	92	The company has three core technologies relating predominantly to the treatment of liver cancer. The lead treatment uses radioactive particles to irradiate tumours in the liver.	-15%	\$1.70
Starpharma Pooled Development	SPL	85	An active Pooled Development Fund. It holds intellectual property relating to chemical scaffolds known as 'dendrimers'.	23%	\$0.95
GroPep	GRO	72	A biopharmaceutical company commercialising research from CSIRO & the University of Adelaide in the area of growth factors. Also sells cell cultures and reagents to the pharmaceutical industry.	-20%	\$1.85
Peplin Biotech	PEP	63	Developing plant based compounds for topical applications to treat skin cancers, and systemic compounds to treat solid tumours including prostate and breast cancer, and cervical pre-cancers.	-6%	\$0.95
Genesis Research & Development Corp.	GEN	59	A NZ genomics company co-listed on the ASX and the NZSE. Uses genomics to assist in development of human therapeutics and innovative products in the area of forestry and agriculture.	-10%	\$2.25
Provalis	PVL	53	UK based company involved in development and sales of diagnostic tests, R&D of vaccines for bacterial infections and sale of pharmaceuticals.	-42%	\$0.33
Bresagen	BGN	51	R&D into cell therapy, therapeutic proteins to treat breast cancer and asthma, human growth hormones, and production of horse growth hormones.	-18%	\$0.94
VRI Biomedical	VRI	44	Three project platforms based on mucosal dysfunction: the development of rapid diagnostic tests, oral vaccines and therapeutic probiotics (the use of harmless bacteria in fermented dairy foods).	-10%	\$0.76
Medica Holdings	MCA	44	An active Pooled Development Fund investing in biotech research SMEs. Gains are income and CGT exempt to investors. First 3 investments were in Alchemia, Cytopia and Xenome.	11%	\$1.26
Biota	BTA	38	Receives royalties from Relenza anti-flu drug and flu diagnostic kits, pharmaceutical R&D into anti-viral drugs.	-42%	\$0.50
Meditech Research	MTR	35	R&D of carbohydrate based drugs to treat AIDS, asthma, breast cancer and melanomas.	-6%	\$0.45
Antisense Therapeutics	ANP	32	Developing antisense compounds that block gene function with license from the Murdoch Children's Research Institute and collaboration with Isis Pharmaceuticals in the US.	-40%	\$0.15
Progen Industries	PGL	32	R&D of drugs to treat cancer and heart disease.	1%	\$1.32
Biotech Capital	BTC	31	A passive Pooled Development Fund investing in unlisted Australian biotech companies or in placements in public biotechs. The company raised \$40 million in August 2000.	-13%	\$0.39
Solbec Pharmaceuticals	SBP	30	Developing plant-based compounds for the treatment of melanomas and asbestos related lung cancers. JV with Lawley Pharmaceuticals for hormone replacement products. (Formerly Britannia Gold)	16%	\$0.19
Autogen	AGT	29	Genomics company with projects in obesity, diabetes and hypertension.	-15%	\$0.75
Anadis	ANX	26	Specialises in R&D of bovine colostrum (first milk from cows after giving birth) products for therapeutic use in animals and humans.	7%	\$0.32
Biotron	BIT	24	Commercialising early stage projects emanating from the John Curtin School of Medical Research	-18%	\$0.37
Bionomics	BNO	20	Identifying genetic targets for epilepsy and breast cancer.	-19%	\$0.60
pSiVida	PSD	19	Major investment in pSiMedica, UK, which is developing porous silicon for use as a drug delivery system and for use in orthopedics as self dissolving pins and screws. (Previously Sumich Group)	-12%	\$0.23
Prima Biomed	PRR	19	Commercialising research from the Austin Research Institute, Melbourne, relating to auto-immune diseases and cancer. Scientific advisors include Dr Peter Doherty. (Formerly Prima Resources)	25%	\$0.58
Epitan	EPT	17	Developing a natural tanning compound for cosmetic purposes that may also prevent the onset of skin cancers.	-28%	\$0.20
Virax	VHL	14	Bio-pharmaceutical R&D. Commenced clinical trial of HIV/AIDS vaccine in 1998.	-24%	\$0.50
Australian Cancer Technology	ACU	12	Commercialising research from Sydney's St Vincent's Hospital - p53 cancer vaccine program. Drug discovery collaboration with BioFocus in the UK. (Previously Exodus Minerals)	-23%	\$0.21
BioProspect	BPO	10	Has an exclusive license with the WA Government to access the state's abundant flora and fauna for natural product drug screening.	-3%	\$0.15

Drug Discovery Sub-Sector (Cont'd)

Company	Code	Cap. \$m	Principal Activities	Price change Q1'02	Price 2/4/02
Inovax	INX	9	Distribution of drugs in Australia & Indonesia. R&D of novel human & animal drugs & vaccines.	0%	\$0.08
Genesis Biomedical	GBL	8	Develops 'smart card' medical technology to replicate the biological signalling processing treatment of muscle disorders.	-4%	\$0.11
Pi2	PAI	7	Human Therapeutics has a majority interest in the company (72% at listing). Failed with treatment for psoriasis and leg ulcers and looking for new projects.	15%	\$0.06
Aust. Vaccine Technologies	AVT	4	Manufactures and markets a melanoma vaccine in Australia, NZ, and possibly Asia in the future.	-47%	\$0.04
Psiron	PSX	4	Manufactures and markets diagnostic blood test kits in locally and overseas. Develops novel therapeutics for psoriasis. (Formerly Medical Innovations)	-17%	\$0.06
NSL Health	NSL	3	Markets and develops allergy diagnostic test kits.	-13%	\$0.13

Total 2,186

Health Products Sub-Sector

Resmed Inc.	RMD	2377	Manufactures diagnostic and treatment equipment for sleeping disordered breathing.	-28%	\$7.45
Cochlear	COH	2221	Manufactures cochlear hearing implants (for people that don't benefit from hearing aids).	-7%	\$42.30
Fisher & Paykel Healthcare	FPH	836	A New Zealand based company which manufactures humidifiers and CPAPs to treat sleeping disorders. The company segregated its healthcare division from appliance and finance business in 2001.	-40%	\$8.20
OPSM Protector	OPS	462	Manufactures & markets products & services for optical health and personal safety internationally.	-15%	\$3.45
Axon Instruments Inc.	AXN	295	Manufactures confocal microscopes to scan gene chips, and the software interface. Manufactures neuroscience medical equipment.	-36%	\$0.63
Micromedical Industries	MMD	125	Develops and manufactures cardiac technologies such as ECG machines and defibrillators. Developing artificial heart technology.	26%	\$0.83
Cellestis	CST	121	Marketing a diagnostic for latent tuberculosis.	-25%	\$1.41
Polartechnics	PLT	113	Develops and commercialises medical instruments to diagnose pre-cancer and cancer, in particular cervical cancer and melanomas.	-20%	\$2.70
Gradipore	GDP	104	R&D of industrial and research grade protein, DNA and viral separation equipment.	-21%	\$2.22
Compumedics	CMP	87	Develops, manufactures and markets sleep diagnostic and monitoring equipment.	-23%	\$0.62
Norwood Abbey	NAL	83	A drug delivery company that uses laser technology as an adjunct or alternative to injections.	-32%	\$0.79
PanBio	PBO	80	Develops and markets a range of over 60 diagnostic products.	10%	\$1.59
Optiscan Imaging	OIL	75	R&D of portable microscopes for clinical diagnosis. Sales of microscope system in Australia.	15%	\$1.16
Agenix	AGX	72	Sales of medical diagnostic products and pharmaceuticals, R&D into enzymes in pulp and paper industry and blood clotting diagnosis. (Formerly Biotech International)	34%	\$0.47
Ellex Medical Lasers	ELX	67	Develops, manufactures and markets solid state ophthalmic lasers used to treat secondary cataracts and retinal disorders. (Listed through shell company Gemstone)	23%	\$1.16
Southern Dental Industries	SDI	46	Manufacture & distribution of amalgam (fillings) & other dental materials and product R&D.	28%	\$1.99
Occupational & Medical Innovations	OMI	28	Developing safety devices used in the healthcare industry, including safety syringes.	34%	\$1.10
Q-Vis	QVL	18	Has developed laser technology for application in vision correction. Consolidated held 20% of the stock at time of listing.	-68%	\$0.38
SSH Medical	SSH	17	A medical device company developing disposable speculums and a Veda-Scope for application in humans and animals, used in gynecological examinations.	-51%	\$0.23
Eiffel Technologies	EIF	15	Developing Super Critical Fluid technology to improve the extraction process of compounds from raw materials and for improved drug delivery mechanisms. Previously (Pharmaction Holdings)	-16%	\$0.16
Eastland Medical Systems	EMS	15	Developing retractable syringes. Listed in January 2002.	-10%	\$0.18
Brain Resource Corp	BRC	14	Developing brain analysis centres in Sydney, New York and London.	9%	\$0.25
Medical Monitors	MDM	13	Develops and manufactures cardiac monitoring and diagnostic devices. (Listed through shell company Defiance Mining).	5%	\$0.09
Xcell Diagnostics (Fimiston Resources)	XEL	7	Collaboration with Skin Cancer Analysis Technology emanating from the University of WA, applying diffuse reflectance spectroscopy to skin cancer detection.	-18%	\$0.09

Total 7,291

Pharmaceuticals Sub-Sector (includes natural health products)

Company	Code	Cap. \$m	Principal Activities	Price change Q1'02	Price 2/4/02
CSL	CSL	6636	R&D and manufacture of pharmaceutical products including vaccines and human plasma fractions.	-19%	\$42.19
API	API	768	Provides goods & services to pharmacies.	15%	\$3.90
Sigma	SIG	684	Pharmaceutical manufacturing and wholesaling.	37%	\$4.96
Pan Pharmaceuticals	PPH	340	Manufactures over-the-counter health products for Australia and exports to over 40 countries. No branded shelf presence, selling only to corporations.	-12%	\$1.98
Chemeq	CMQ	159	A research-based company that manufactures and markets antimicrobials (to kill the growth of microbes/germs)	80%	\$2.45
Institute of Drug Technology	IDT	157	Manufacturer of pharmaceutical ingredients to international standards for major pharmaceutical groups.	-11%	\$3.65
Blackmores	BKL	97	Manufactures vitamin, mineral and herbal supplements and skin & hair products in Australia and N.Z.	-4%	\$6.45
Vita Life Sciences	VLS	61	Previously a property developer called Macarthur International. Its two divisions manufacture lung imaging equipment and vitamin supplements to food manufacturers predominantly in Asia.	-44%	\$1.18
Clovercorp	CLV	29	Development and production of natural oils (Tuna Fish Oil, Evening Primrose Oil & Borage Oil) which contribute towards improved human health.	-17%	\$0.19
Aquacarotene	AQL	4	Growth, harvesting, refinement and marketing of natural betaCarotene.	25%	\$0.05
Pharmanet Online	PNO	2	Production and sales of patented pharmaceutical products and point of sale software to the pharmaceutical and healthcare industry.	-22%	\$0.04

Total 8,937

Health Services Sub-Sector

Sonic Healthcare	SHL	1536	Provision of pathology services.	-24%	\$6.01
Medical Imaging Australasia	MIA	931	Provides diagnostic imaging services in Australia.	0%	\$1.41
Primary Healthcare	PRY	445	Owns medical and dental centres and eye clinics, providing services to doctors and health care providers who operate within these clinics.	-9%	\$4.54
The Gribbles Group	GGL	344	Formerly Revesco. Owns Gribbles Pathology Group.	-23%	\$0.82
Promedicus	PME	136	Provides IT services and systems to the healthcare industry, including the electronic distribution of radiology results from radiologists to GPs.	5%	\$1.36
Foundation Health Care	FNC	69	Previously Formulab Neuronetics Corporation. The company provides services including rental properties to GPs and health services providers.	0%	\$0.43
IBA HealthCare	IBA	34	Provides software products and support programs to the healthcare industry to streamline administration and assist in decision making.	27%	\$0.21
Health Comm. Network	HCN	33	Provides online databases, books and journals (The Lancet, MIMS etc...) to health care institutions, and clinical practice software to health practitioners.	0%	\$0.58
Lifecare Health	LCH	10	Physiotherapy and healthcare business.	0%	\$0.10
Global Doctor	GOD	10	Formerly Terrex Resources. Manages dental and medical centres throughout Australia and Asia.	0%	\$0.02
Healthpoint Technologies	HLT	9	Sells counselling information products to pharmacies and health groups on over 3000 different items. Formerly Sustainable Technologies. CEO is George Savvides, previously Sigma CEO.	-32%	\$0.07
ICS Global	ICS	8	Provides IT system to hospitals and insurers to electronically monitor private health insurance eligibility and healthcare claims.	-6%	\$0.17
Work Systems	WSS	5	Owns, distributes and supports electronic commerce and software for use in health and aged care units in the Asia-Pacific region.	-22%	\$0.07
Australian Healthcare Technology	AUH	3	Providing e-business solutions to the health services, pharmaceutical industry and to large and medium sized businesses. Formerly BTB.net	-41%	\$0.03

Total 2,037

Hospital Management Sub-Sector

Mayne Group	MAY	4080	Owns and operates private hospitals, and provides security (Armaguard) and courier services in Australia, Europe and USA. Acquired FH Faulding pharmaceuticals business	-27%	\$5.05
Ramsay Healthcare	RHC	630	Owns & operates 13 hospitals throughout Australia.	9%	\$4.92
DCA Group	DVC	221	Owns aged care facilities and manages radiology clinics.	-2%	\$1.87
Healthscope	HSP	196	Ownership & management of hospitals & clinics.	16%	\$2.65
Medical Corporation Aust.	MOD	41	Investing in medical & healthcare projects in Australia, Vietnam & China (pharmaceutical business in China, hospital in Vietnam).	0%	\$0.44

Total 1088

Capturing profile for big league biotechs

David Van – SDA Biotechnology



SDA Biotechnology

Australian companies are failing to capture opportunities in the global, big league biotechnology market in North America because of a shortfall in basic communications and promotion. The consequent lack of profile is costing them access to capital, prospective partners and the world market for bioscience developments and products.

While Australia provides a good incubator base for innovation and has a reputation for scientific excellence, the Australian market does not offer the critical mass necessary for an individual company to elevate itself to global status.

Nevertheless, many companies make the mistake of heading overseas with marketable intellectual property, licences and products in the belief that a simple presence in the big league will have the world knocking on their door. But it can prove an expensive and sometimes terminal mistake if a company omits to go equipped without a communications strategy capable of creating a profile in an extremely competitive and selective environment.

That need not be a costly option provided the company plans ahead and factors into its development strategy what might be termed the Australian advantage. The Australian dollar's low exchange rate and the choice of a home-grown partner offering the combination of local industry knowledge and international links can provide the necessary edge in communications on comparatively, very favourable terms.

Large American biotech companies, by Australian standards, are hungry for new ideas and products, and showing increased readiness to partner and provide expertise, management support and capital to start-ups and small operators with products ready to go into the lengthy, expensive testing pipeline. They are selective, but have an eye for a commercial idea and the patience to see it through the development phase to market.

The value of the Australian dollar – about half that of America's – is an important factor that will help drive a company's growth potential. On this score, companies that opt to stay at home will be significantly under-capitalised against those that extend their base globally.

Profile is the key to the success of the venture. American executives, bankers, and VC's rely heavily on the trade media to keep abreast of developments as well as the analyst community that follow their specialist areas. Traditionally this has been extremely difficult to do from 'down under' due to many factors including cost, time differences, enormous cultural differences, and a vast, ever-changing media environment. To achieve a useful profile requires implementation of an effective

communications strategy targeting the scientific community, industry, capital market, investors and the media.

For this task, there are significant competitive and practical benefits in taking on an Australian communications partner that is able to provide the added qualification of international experience and connections.

Companies that fail to build a communications strategy and a detailed implementation plan into their American venture will find themselves paying out American dollars if they subsequently are put in the position of having to engage an American-based firm to undertake the communications task. The same high-cost situation applies in the event they do apply some foresight to communications planning, but then engage the local arm of one of the big multinational PR/marketing firms.

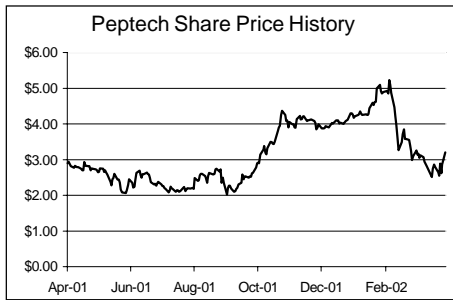
Companies should also bear in mind the caution that the American PR firm will have little appreciation of the specific positioning requirements of a comparatively small Australian biotech in its endeavour to gain profile and attention in the exponentially larger and more complex American market.

Many if not most companies will invest money to attend or even display at a trade show without leveraging this opportunity to meet with relevant media. "We are not ready to be in the media" is the oft-heard rationale, yet they are clearly trying to lift their profile in attending the show. Not all media relations needs to be about 'getting ink' – most trade media are incredibly interested in industry trends and will store away information for when it is appropriate.

Profile in the American biotech sector itself and among the capital markets and investors, analysts and specialist industry media is important, but it is equally essential to get the attention of the mainstream daily media and American magazines that circulate globally. This, in turn, feeds back into Australia. The global recognition substantially enhances the company's status in its home market.

David Van has recently joined SDA Biotech as director of client services after returning from working in the US and U.K. for the past three years. David consulted to large publicly listed companies as well as early-stage startups and their VC backers providing strategic communications planning, profile building, issue management and IP protection litigation support. If you have any queries about the issues raised in this article, please contact David on +61 3 9629 9777 or at davidvan@dignum.com.au

Future earnings revision downgrade amid increased uncertainties causes concern for Peptech



Peptech (PTD)	
Current price (15 April 2002)	\$3.20
Capitalisation	\$483 million
Valuation	\$2.90
Cash (31/9/01)	\$25 million
Profit (12 mths to 30/9/01)	\$31 million
Recommendation	Lighten

April 15 – After receiving the news everyone was waiting for last month, that the US Patent Office issued Peptech a 'Notice of Allowance' for its TNF antibody patent in the US, Peptech's shares launched into freefall, falling by as much as 60% in the last eight weeks. With the company now set to receive massive ongoing royalties, why have investors dumped the stock?

To some degree, the company's share price movement has been a victim of the old share market adage, buy on rumour, sell on fact. However claims from the **Australian Shareholders' Association** of excessive bonuses to board members, the planned resignation of the company's CEO, **Stephen Kwik**, amid rumours he was ousted by the board, and uncertainty of where and whether the company will invest future royalties wisely has unsettled many investors. This was exacerbated by the resignation from the board of the **Tweddel** ticket although in recent days investors have become more comfortable with this arrangement and the share price has firmed.

The value of a company is often calculated using the discounted cash flow method, which estimates future income and discounts that income by an appropriate discount factor which reflects the risk in that investment. The current uncertainty facing the company, more related to company structure and investment policy rather than future income streams, has caused investors to feel very anxious about their investment in Peptech.

In January this year, Ed Tweddel (director of **NAB**, chairman of **Pacific Dunlop**), was elected as chairman of Peptech. On the Tweddel ticket, was fellow NAB board member and lawyer **Catherine Walter**, and also fellow South Australian **Graham Walters**, who was a former chairman of

KPMG. Other existing directors include **Dr Greg Winter** and **Till Medinger**, both based in the UK. The selection of Tweddel, Walter and Walters, was a surprising one given that directors with wider biotech experience would have been more suitable. So concerned were shareholders that a handful of private investors with large holdings in Peptech were successful in voicing their concerns over the recent additions to the Peptech board. Overall the board was substantially lacking in local directors with drug discovery and development experience. If Peptech is to become a dynamic and important flagship for Australian biotech, then it needs appropriate board representation with the necessary industry experience and associations.

Peptech's share registry consists largely of retail investors and the sell down after news of the patent allowance may be partially attributable to speculators taking profits. Margin calls to leveraged investors may have accelerated that fall. However the notice of allowance should have lowered the risk to this investment. Peptech has already settled with **Centocor (J&J)** in Europe and once the patent has been printed, which may take up to six months from allowance, Peptech will aim to convince Centocor to pay royalties on US sales. Peptech has already settled with **Abbott Laboratories** in Europe for its antibody drug, which is expected to be on the market within 12 months. It will also need to settle with Abbott in the US once the claims on its US patent are made public. And the much talked about potential royalties from sales of these drugs will be substantial according to indicative royalty rates supplied by the company.

The claims allowed in the divisional pat-

ent that has been allowed in the US have yet to be made public. However drugs that bind to the TNF receptor (not the antibody binding site) such as **Immunex's** drug **Enbrel** are not expected to be included in this patent and there is very little chance Peptech will widen its patent claim in the US to incorporate this drug.

However sales of TNF antibody drugs are in the billions and are expected to grow strongly. Remicade is expected to generate US\$1 billion in sales this year and this is expected to increase to US\$2 billion by 2005. Abbott is also forecasting billion dollar sales for its drug and Peptech is expected to receive just under 2% in royalties from both of these groups from sales of these drugs. That's in the order of \$30 million next year, or \$100 million by 2005.

Market upside

And there is upside in the TNF drug market. The market is worth over US\$2 billion a year at present based on current sales however supply is unable to cope with demand. There is also an expanding application of these drugs. Centocor and Immunex's drugs are currently used to treat rheumatoid arthritis. Abbott's compound will treat Crohn's disease if approved. Earlier this year Immunex's drug was approved for use in treating psoriatic arthritis and the company is now finding its drug is effective in treating psoriasis as well. By 2007, it is estimated that 37 per cent of the market for TNF drugs will be for novel therapeutic applications, and most of these applications should fall under Peptech's patent, if they bind to the antibody site in the TNF protein.

TNF drugs are one of the most commercially successful therapeutics to come on the market in the last four years. The drugs

are so successful that in December last year, one of the largest biotech companies in the world, Amgen, announced it would acquire Immunex for an astounding US\$16 billion – all for access to its TNF drug Enbrel.

Revaluation

With new information now at hand, *Bioshares* has updated the valuation on Peptech based on the company's anticipated future income stream. *Bioshares* is now of the understanding Peptech's key TNF patent will expire in 2010, three years sooner than previously indicated. This has a significant impact on the overall expected royalties the company will receive from its global TNF patent.

Uncertainty also remains over the company's patent being granted in the US. Peptech has received one notice of allowance over a divisional patent in the US. (A divisional patent allows a company to divide out more than one of the inventions from a parent patent application into a new patent application without losing priority

rights. It is required in the US if the patent examiner says a patent application claims more than one invention).

However Peptech has a further five divisional patents that may be approved, and it is possible the company may need to receive a further one or two divisional patents before Centocor (and Abbott) agree to pay royalties on US sales. With the printing of the divisional patent up to six months away and with the possible need for further divisional patents to be granted (these are currently being assessed) before it can be shown that Centocor is infringing, there remain some hurdles before Peptech begins to receive royalties from US sales. *Bioshares* currently has a value of **\$2.90** a share for Peptech with a 12-month price target of \$3.60.

Future upside

Upside in this company will come from commercial development of Peptech's interest in **Diversys** which as previously covered in this magazine, is an excellent investment. Diversys is expected to list on

the Nasdaq within the next two years and Peptech's initial investment will appreciate significantly if that occurs. Peptech is also developing more effective single domain TNF antibody drugs that may supersede the existing TNF drugs.

However with the existing uncertainties associated with this company, the stock will trade primarily on the value of expected royalties rather than the blue sky associated with future projects. Peptech is currently trading above our estimated fair value of the stock. With a current share market capitalisation of \$483 million, upside is limited to our 12-month price target of \$3.60. There is the possibility of significant downside if key patents are not granted in the US. *Bioshares* recommends investors to lighten their exposure to this stock and to take advantage of any selling opportunities in a firming of the share price.

Companies covered in Bioshares

Company	Ed.	Company	Ed.	Company	Ed.
Acrux	9	Cryosite	9	Norwood Abbey	4,9
Affymetrix (US)	1	CSL	1,5	Novogen	1
Agenix	8	Eiffel Technologies	6,9	Optiscan Imaging	2
Alza Corporation	9	Elan Pharmaceuticals (IRE)	2	Oxford Glycoscience (UK)	2
Amrad	3	Ellex Medical Lasers	8	PanBio	6
Anadis	4	Faulding	1	Peplin Biotech	5
Aust. Cancer Tech.	8	Genaissance Pharm. (US)	6	Peptech	4,6,9
Autogen	2	Genzyme Transgenics (US)	5	Polartech	1
Axon Instruments	3,9	Gradipore	2	Prana Biotechnology	3
Benitec	9	GroPep	3	Praxis Pharmaceuticals	9
Biacore Int. AB (Sweden)	7	Iatia	9	Premier Bionics	9
Bionomics	9	IDT	4	Psiron	3
BioPure Inc	7	Invitrogen (US)	8	Psivida	7,9
Biota Holdings	6	Isis Pharmaceuticals (US)	3	Q-Vis	5
Biotech Capital	4	Kinacia	9	ResMed	1,2
Bresagen	2,3,7	Maxygen (US)	4	Sage Global Fund	4
Cambridge AB Tech. (UK)	3	Medica Holdings	1,2,4	Sirtex Medical	5,7,9
Cellestis	6	Meditech Research	3, 9	SSH Medical	7
Chiron Corporation (US)	6	Metabolic Pharmaceuticals	2	Starpharma	1,4,8,9
Circadian Technologies	7	MicroMedical Industries	5	Vertex Pharm. (US)	5
Cochlear	2	Millennium Pharm. (US)	4	Weston Medical (UK)	8
Compumedics	8	Myriad Genetics (US)	1		

Premier Bionics – from page 9

Biotechnology and Prima BioMed. The structure looks reasonable, and although early stage, the offer is worth considering by investors. The offer closes 17 May.

A prospectus can be downloaded from www.premierbionics.com.au or from Peregrine Corporate (ph 03 9824 8166). *Investors are required to fully read the company's prospectus before subscribing to the offer.*

Correction

In Edition 8 of Bioshares we stated IEM was a shareholder in Biodiem. IEM has never been a shareholder in Biodiem.

Axon Instruments stock now offering excellent entry point



In the last few years, Axon Instruments made its mark as a high calibre equipment manufacturer for the life sciences industry. From its formation 18 years ago, designing and manufacturing equipment for neurosurgery, to the production of gene chip scanners at the height of the genomics movement, Axon has consistently reinvested funds for the expansion of R&D products whilst maintaining a positive bottom line. Growth in sales and product range has been the business focus of the group with sales increasing at a compounded growth rate of 32% over the last five years. This is an impressive performance.

A slow down in the microarray (gene chip) market in the second half of 2001 saw sales growth of the DNA scanner market soften, from a 75% growth in sales in 2000 to only a 23% growth in sales in 2001. However, the company recently introduced two additional products and with another four products to be released in the coming 12 months, the company is positioning itself for sustained profit and sales growth.

The gene chip (microarray) market has not lived up to expectations. Failure of the price of gene chips to fall from current prices of US\$500 each to what is believed to be the critical level of US\$100 has made gene chips unaffordable to many researchers. And no gene chips means no scanners.

Excellent entry point opportunity

Following the heady levels reached by the stock after listing in 2000 at the height of genomics fervour (reaching a high of \$2.50), the stock has now reached levels where traditional valuation markers can be applied. Excluding the company's cash reserves, the stock is now trading at a

Axon Instruments (AXN)	
Current price (3 May 2002)	44 cents
Capitalisation	\$206 million
Cash and securities (31/12/01)	\$65 million
Cap. less cash	\$141 million
Sales (CY2001)	\$65 million (+23%)
Price/(Sales-cash)	2.2
Profit (CY2001)	\$1.5 million
Sales growth over last four years	32% p.a.
Recommendation	Strong Buy

All figures in AUD @AUD/USD=0.54

Instrument	Approx. selling price	Sales estimate	Release
Acuity software program	US\$4,000	US\$0.6 million p.a.	Avail.
GenePix 4100 personal scanner	US\$30,000	n/a	Jun-02
OpusXpress ion channel meas.	US\$250,000	US\$5 million p.a.	Jun-02
ImageXpress cell imaging	US\$250,000	US\$10 million p.a.	Sep-02
PatchXpress ion channel meas.	US\$150,000	>US\$10 million p.a.	Early 2003
Protein chip scanner	US\$50,000	n/a	2003

price-to-sales ratio of only 2.2 times. By comparison, diagnostic group **PanBio**, which has grown sales over the same period at a compound annual growth rate of 30%, trades on a price-to-sales (less cash) multiple of 4.3. **Blackmores**, a consumer products business that does not re-invest a greater proportion of its earnings, has grown sales by 3.6% a year over the same period and trades at a price to sales multiple of 1.3 times. In 2001, Axon invested substantial funds into R&D, totalling \$23 million, to ensure it can sustain its high growth rates.

With a softening in the gene chip scanner market and with significant sales of new product lines not expected to kick in until the second half of 2002, the turn around in this stock may not come around until the end of the year. *Bioshares* suggests that current situation is offering a very attractive entry points into a high quality stock. If sales numbers for the June half are not impressive, the stock may fall further and an investment strategy may incorporate a further investment if this occurs.

The upside in the gene chip scanner market is in the wider use of genetic analysis in pathology markets and in the personalised medicines of the future. Interest is now building in Taiwan, China and Korea for using DNA analysis in pathology for

identification of infectious diseases. Companies such as **Genaissance Pharmaceuticals** and **Variagenics** in the US and **GeneMatrix** in Korea are building databases to link therapeutic effect with genetic make-up of patient populations. The use of genetic profiling for selecting cancer therapeutics is now being applied although there are further advances to be made. *Bioshares* recommends Axon as a **Strong Buy**.

What are the products Axon has just released but also expects to release over the next 12 months?

OpusXpress ion channel screening instrument (US\$250,000)

This instrument has now been completed and the first unit will come off the production lines in June this year. This instrument will be used to screen drug candidates by measuring real time changes to ion channel responses. The membranes which surround cells in the body do not allow current to pass through. However these cells are embedded with ion channels which specifically let ions such as potassium or calcium to pass through thereby stimulating or inhibiting cell function. Drugs such as calcium blockers to treat pain relief work by restricting ion channels. This product may contribute to as much as US\$5 million

a year to Axon sales.

The device is named after the frog *Xenopus laevis*. Ion channel research is widely conducted on the oocytes – the unfertilised egg cells – from these frogs. The genetic sequence for a particular ion channel is introduced into the frog oocyte which immediately starts acting as a protein manufacturing factory to express the ion channel protein in the oocyte. This particular frog is used for a number of reasons. These include the large size of the oocytes (greater than 1mm in diameter), the cells can survive for many days in the test tube, the cells are available readily in large numbers, they have few existing ion channels to interfere with the measurement of electrical activity across ion channels, and the oocytes reliably express foreign DNA.

There are existing machines that measure ion channel characteristics in the frog oocytes. Axon's instrument however allows measurement of eight different oocytes at the same time, a capability not currently available. Researchers will use the device in drug screening, by introducing drug candidates into the cells and measuring the effect on standard, human ion channels that have been cloned into the cells. The system allows the testing of 192 drugs in approximately two hours without operator intervention.

ImageXpress cell imaging instrument (US\$250,000 per instrument)

This device is a robotic microscope that moves from mini test tubes (called wells) taking fluorescent images of the cells and their contents and storing and analysing those pictures. The device works on industry standard 96 well and 384 well plates. The screening process

will take about half an hour for a 96 well plate. It will measure cell characteristics such as relative nucleus to cytoplasm diameters, and migration of proteins from the cytoplasm to the nucleus. The instrument will be used for drug screening by researchers at pharmaceutical and biotech companies and at research institutions. Researchers will add novel drug candidates to a well containing a cell and observe the impact that compound has on a particular cell. This system allows up to 2000 compounds to be screened in one day. The advantage of cell based screening to biochemical screening is that it can more efficiently eliminate compounds from a screening base that are unlikely to have potential therapeutic benefits.

Cell based screening such as this has only been introduced on a high throughput level such as this in the last two years. Companies such as **Cellomics** and **Universal Imaging** have similar products on the market and it is estimated that Cellomics has sold approximately 50 of these devices in the last two years. If Axon does well, it will generate annual sales of US\$10 million a year from this instrument. The instrument has been essentially completed and will be on the market by September this year.

PatchXpress ion channel screening instrument (US\$150,000 per instrument)

This is the second generation ion channel drug screening instrument for Axon. It is quite different from the first product and Axon's CEO, Alan Finkel, refers to it as the 'holy grail' of (ion channel) drug discovery.

The instrument works not by holding in place a frog oocyte and measuring the charge across the ion channels in that cell (in response to the addition of drug can-

didates). Rather, this system is built on an array of well plates (16, 96, 384), similar in some degree to the cell imaging device. The design of these multiwell plates, which will be Axon's first consumable product, is the key technical challenge.

Each well will contain a substrate onto which the cells will be placed using a robotic arm. The cells used will be mammalian cells with specific ion channel proteins expressed in this cell. The cells in fact are prepared by others and are commercially available. A fine aperture in the substrate will measure the electrical charge across the cell after a drug candidate is placed in the well. The software with the system will record the charge across the ion channel and analyse the overall data.

If successful, this may become a blockbuster product for Axon similar to its microarray scanners. Technical challenges remain for this project and the completion date for the product is early 2003. There are currently no automated ion channel screening instruments available that work on mammalian cell lines but the competition is expected to be intense.

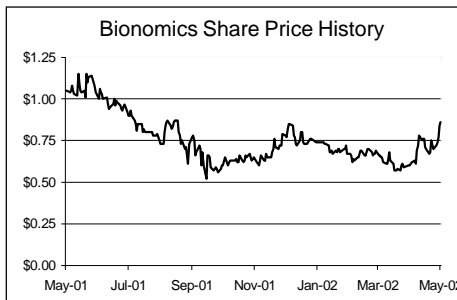
Protein chip scanner (US\$50,000 per instrument)

Axon is also working on a protein chip scanner. In conjunction with **Zyomyx**, which is developing the protein chip, Axon's scanner will record and analyse the data on the protein chip, similar to what is achieved with its gene chip (microarray) scanner. This is now in the customer test stage and production will begin in 2003, although the release will be determined by Zyomyx.

Biotech unlock dates

Company	Code	Shares in escrow ('000s)	% of total shares	Unlock date
Ambri	ABI	3674	9%	16-Jun-02
Medical Monitors	MDM	15057	11%	Jul-02
Q-Vis	QVL	12768	30%	14-Jul-02
Pi2	PAI	70078	64%	28-Jul-02
Norwood Abbey	NAL	45224	40%	2-Aug-02
Sirtex Medical	SRX	34393	65%	24-Aug-02

Bionomics: a steady, credible transition from genomics to drug discovery



Bionomics (BNO)

Current price (3 May 2002)	86 cents
Capitalisation	\$34 million
Cash (31/12/01)	\$10 million
Loss (6 mths to 31/12/01)	\$1.7 million
Recommendation	Speculative Buy Class B

Overview

Bionomics is a genomics company with research focused on discovering and validating genes and other druggable targets in the areas of epilepsy, breast cancer and angiogenesis. The company is transitioning from the 'virtual' contract/out-sourced research biotech model to an in-house integrated target and discovery model. It has secured two important international collaborations in the last twelve months, and in a major step forward leased newly constructed, purpose-built facilities in Thebarton, Adelaide.

History

Bionomics exists because of the vision of Adelaide researcher Dr Mathew Vadas, director of the **Hanson Centre for Cancer Research**, and the involvement of Professor Grant Sutherland, recently retired head of the Department of Cytogenetics and Molecular Genetics at the **Women's and Children's Hospital** in Adelaide. Bionomics as a concept dates back to 1995, and was incorporated in 1996, well before the genomics explosion in 2000, when the draft sequence of the human genome was completed.

With benefit of hindsight, a number features stand out concerning the company's creation and growth as a publicly listed company. What is unusual in Bionomics is the absence of an inventor-founder. Although the company was built around intellectual property obtained from the WCH and the **University of Melbourne**, its origins make it unique amongst Australian biotechs. Some biotechs exist as a result of venture capitalists funding start-ups. Others exist as investee companies of biotech portfolio companies. Some biotech companies exist initially as projects funded by mature companies, or even as technology created in CRCs.

Bionomics listed at a time when the market for biotechs was favourable, so favourable that the company had not even installed a CEO. CEO Dr Deborah Rathjen was appointed in May 2000, five months after the company's listing in December 1999. Understanding this history is important for investors because it can aid in seeing the investment drivers and motiva-

tors within the firm. Typically founder/inventor firms that are coupled to VC firms will be driven by strong incentives towards profitability or the gaining of substantial investment returns. The company has no substantial shareholders, ie those holding greater than 5%, amongst the company's 2,500 shareholders. Directors owned at June 30, 2001 less than 1 million ordinary shares out of total of 32 million shares.

Although the company has made strong progress since listing more than two years ago it has weakened as an object of investment interest, due in part to the tapering of interest globally in genomics firms, but also because of increased competitive intensity amongst ASX listed biotechs for market interest. Since it listed in 1999, Bionomics has to date raised a nett \$18 million, leaving a cash balance of approximately \$10 million. It now has access to an effective full-time staff of 35, has three drug discovery partnerships with two companies. However, progress over the last six months, especially the Genmab and Hybrigen collaborations confirm it has a serious aim to maximise future potential returns for shareholders.

Board and management

The board of Bionomics is chaired by Adelaide businessman Fraser Ainsworth, who had an extensive career in CSR, prior to establishing Potential Energy Pty Ltd. Other members include Peter Maddern, who acted as a transition executive officer for Bionomics. Rathjen has proved to be a successful appointment based on the company's solid progress to date. What is

particularly relevant for investors is the presence of Dr George Morstyn and Dr Chris Henney. Morstyn recently retired as Chief Medical Officer of Amgen, the largest independent biotechnology company in the world. He has returned to live in Australia. Henney is a microbiologist who founded Immunex, recently acquired by Amgen for US\$16 billion. The potential of their contribution should not be underestimated, in terms of advice of research direction, path to market and links to financial markets and opinion leaders in North America.

Commercial Strategy

Bionomics' commercial strategy has clearly evolved in the last two years. It has shifted from mere gene discovery and validation to the extraction of more value from R&D through partnerships with complementary businesses and the establishment of in-house proteomic and protein drug target validation capabilities.

The company originally aimed in 2000 to be a leading biotech company in the business of developing validated drug targets. In 2001 it expanded its ambition to one of exploiting broadly based gene technologies to discover, develop and sell gene-based products in the global market place. It also stated an ambition "to partner (its) research programs at an early stage and participate in the success of the resulting products... and ...leverage management experience in the biotechnology commercialisation process". *Bioshares* expects that Bionomics may incorporate, at an appropriate time, a drug design team and medicinal chemistry capability if the commer-

cial opportunities are best maximised with those resources at hand.

One of Bionomics commercial strategies has been to partner development tasks. The company has set up drug discovery collaborations for angiogenesis targets identified through its gene research program. There is an advantage in viewing the two collaborations through the one lens. Firstly, the partnerships with Hybrigen and Genmab are both built around angiogenesis gene discoveries. The Hybrigen component will deliver the requisite protein target information whereas the Genmab component will deliver the therapeutic agents (humanised monoclonal antibodies) that will target the angiogenesis proteins.

Originally, Bionomics commenced a partnership with Hybrigen in September 2001 to investigate protein targets for a breast cancer gene. In January 2002, Hybrigen and Bionomics established a joint venture to capture and share in any IP, such as novel drug targets, stemming from the angiogenesis program. Hybrigen's role is in protein discovery and protein target validation. Hybrigen has developed an improved system for protein interaction studies that applies a continuously adjustable level of detection. The time-saving upside in the Hybrigen technology is a significant reduction in false-positive leads. This technology should speed up drug target discovery and validation, reducing time taken from 12-18 months to 2-3 months.

In March 2002, Bionomics initiated a collaboration, with Danish antibody company Genmab AS, to develop fully human antibodies for Bionomic's angiogenesis targets. Bioshares expects these targets will result from the Hybrigen joint venture.

The angiogenesis and breast cancer projects offer relative (to the epilepsy program) lesser prospects for investment returns. Both areas are relatively congested in terms of the global pipeline of drugs in development. Angiogenesis drug research is often divided into two regimes, tumour angiogenesis and cardiovascular related angiogenesis. Control of tumour angiogenesis is proving a difficult area for drug development, despite its fundamental attraction as a 'host derived process'. Recently, Pharmacia subsidiary Sugem withdrew SU416, a kinase inhibitor, from Phase III

trials for colorectal cancer. However, this is not to say that Bionomics' programs are not without merit and not worth pursuing.

The company also established an alliance with Perth-based **Ozgene** in June 2000 to facilitate functional genomics research for breast cancer.

The epilepsy program

Epilepsy is the gene and drug discovery area for which Bionomics has not yet developed collaborations. This disease area is the one that most likely offers the greatest opportunity for investment returns. A number of features about the nature of epilepsy drug treatments and the relative lack of interest in the field, means that Bionomics has relatively better prospects.

Drugs have been available to treat epilepsy since the 1930's, with the introduction of Dilantin, which was still generating sales of US\$250 million in 2000. The market for anti-epileptic and anticonvulsant drugs was more than US\$4 billion in 2000. The dominant drug in this class was gabapentin, drawing US\$1.3 billion in sales in that year.

Barbiturate anti-epileptic drugs such as methylphenobarbitone, primidone, and phenobarbitone were commonly prescribed in the fifties and sixties. Some commonly prescribed drugs, such as sodium valproate and gabapentin, which modulate the neurotransmitter gamma-aminobutyric acid (GABA), represent a third technology iteration. However, the study of the molecular and genetic basis of the disease, as undertaken by Bionomics but by not many other companies, is what will lead to a fourth generation of treatments.

Compared to other drug and disease classes, epilepsy is a less intense area of drug research and development. This is due to partially effective drugs being developed many years ago. However, a market opportunity exists because several subsets of epilepsy are poorly treated and the overall suite of contemporary treatments is not perfect either, limited by side effects and degree of seizure modulation. Seizure control is effective in about 60% of patients, with remaining 40% suffering from intractable pharmaco-resistant epilepsy.

Significantly, most medications are unable

to generate significant seizure-free rates. According to one study of four drugs, the best outcome for achieving no seizures over a one-year period was 6%, for patients who took topiramate. The equivalent success rate for gabapentin was 1%, lamotrigine, 3% and vigabatrin, 3%. In other words, at best, 96% patients were not able to live for a period of 12 months without having a seizure, illustrating the fundamentally poor level of performance of these drugs. There is also marginal benefit from combination therapy. What is fairly clear about epilepsy treatments is that there is a need to discover new molecular targets, especially targets that can provide the basis for halting epilepsy rather than treating the condition. This is where Bionomics research is directed.

There are roughly ten drugs in clinical development for epilepsy, with some of these drugs also seeking other CNS indication approvals.

Bionomics' target area is idiopathic generalised epilepsy, which constitutes 40% per cent of inherited epilepsies. Other epilepsies include cryptogenic partial, symptomatic partial, extratemporal, temporal lobe, dysgenesis and epilepsy resulting from head injury.

The most important patent filing Bionomics has made in regard to epilepsy does not relate to specific ion channels, but is the patent covering a new paradigm of epilepsy. Bionomics' research has identified more than 30 changes in voltage gated and ligand gated ion channel genes that may be associated with epilepsy.

The next step for Bionomics' epilepsy program will be the development of a drug discovery partnership or joint venture. Two possible candidates are the conopeptide companies **Xenome** (Queensland) and **Cognetix** (Utah), or even specialist CNS chemistry units such as those found with Monash University.

Patents

Bionomics' patent position demonstrates one of the clear strengths of the company. The table (on page 31) lists 21 patents either granted in Australia, in application internationally or filed on a provisional ba-

Is Meditech Research set to partner ?



Meditech Research (MTR)

Current price (3 May 2002)	36 cents
Capitalisation	\$28 million
Cash (31/12/01)	\$3 million
Loss (12 mths to 31/12/01)	\$1.6 million
Recommendation	Speculative Buy Class B

Overview

Meditech Research is a drug development company that is commercialising a drug delivery technology based on a naturally occurring carbohydrate called hyaluron. Hyaluron is a porous matrix that can accommodate other active pharmaceutical ingredients. It also investigating carbohydrates called glycosaminoglycans (GAGs) in a project at the University of Western Australia. Meditech Research intends to change its name in the near future to better reflect recent changes in the company and stem confusion from similar named companies.

Bioshares first covered Meditech Research in the September Quarter Edition 2000 (Number 3). While the company has not experienced any negative setbacks for its lead anti-cancer formulations of the HyACT drugs, HyDOX and HyFIVE, the company has struggled to gain stock market acceptance.

One reason for this concerns the market's limited understanding of companies like Meditech Research and **Sirtex Medical** that have been developing therapeutics based on contemporary cytotoxic therapies. Market sentiment is often more 'inspired' by newer forms of drugs such as monoclonal antibodies, small molecule drugs and analogues of naturally derived compounds.

There is good reason for this – these new drugs may be potentially safer and more effective. However, the risk/return profile of these investment propositions is much, much greater because proof of principle usually has to be achieved in Phase II studies, many more years away, and many more investment dollars away.

The value proposition in companies such as Sirtex is that they take existing documented and approved drugs or therapies, with non-optimal but understood side effect profiles and work to increase the effectiveness of those compounds and try to reduce side effects. Targeting and delivery technology companies such as Meditech Research in fact have much more upside than what is first apparent. Their technologies are not limited to existing off-patent pharmaceutical agents. Proprietary regis-

tered compounds may also be incorporated into delivery and targeting technologies thus expanding scope and opportunity and investment returns.

The second reason the company has struggled as a corporate entity is that it lacked a full-time CEO for at least nine months, and possibly lacked the effective value of a CEO for even longer. The company rectified its primary management weakness with the appointment of Chris Carter as CEO in February 2002, although he didn't commence full-time duties until April. Chris Carter was previously group managing director for Muller Phipps, a subsidiary of **Pharmanova Ltd** in Southern Africa. Importantly, he brings relevant experience in the areas of pharmaceutical product registration, production and formulation, negotiation and project management, to which is added educational qualifications in pharmacy and an MBA from Henley Management College (UK).

Impact of consultancy

The vacuum that was eclipsing Meditech was attacked through the hiring of Robert Moses as a consultant business analyst in 2001. Moses is emerging as a highly regarded and sought after Melbourne-based independent biotech and pharma director following his retirement as **CSL's** Corporate Vice-President. Moses is the only candidate acceptable to both sides in the current Amrad/Circadian board struggles. (He also chairs **Antisense Therapeutics Ltd.**) The end result of Moses's consultancy was to take up a position on the Meditech board in October

and increase his involvement with the company.

Progress update

HyACT

The company's lead technology, **HyACT**, is built on the formulation of chemotherapies such as doxorubicin (HyDOX), and 5-FU (HyFIVE) with hyaluron. Hyaluron not only transports the cytotoxic agents in vastly reduced quantities to tumour cells, but the hyaluron increases the receptivity of the cancer cell to the 'drug package'. An observed feature of hyaluron gained from in vitro studies is that the CD44 receptors internalise as much as 1200 times more of the drug when combined with hyaluron. This attribute has a significant implication for dosage regimes. It may mean that vastly reduced quantities of a cytotoxic agent need be administered to achieve an equivalent effective outcome in terms tumour regression, which achieves much better toxicity outcomes. It is also thought that the HyACT may block metastasis of tumours.

The company has completed two Phase I clinical trials of HyACT, although results of the second have yet to be released. The first with was for HyDOX applied to metastatic cancer, with no adverse effects reported. The second trial applied HyFIVE as a treatment for colorectal cancer.

Other formulations, such as HyCAMP are being evaluated by Meditech Research. It is the prospect of many more formulations, especially in conjunction with owners of proprietary compounds that merits investors' attention.

Fungicide and bacteriacide

Meditech filed a patent which covers the preventative treatment for toxic side-effects caused by chemotherapeutic agents in August 2001. This patent relates to an aspect of a new broad-based technology the company has termed **HyAPE**, short for Hyaluronic Acid Procarotytic Elimination technology. It uses similar principles on which HyACT is based, where the hyaluron binds to several receptors over expressed on cancer cells. Presumably, Meditech has discovered that hyaluron has binding affinities, or can be engineered to bind to various fungi and bacteria that infect patients whose immune systems are compromised when undergoing radio- or chemo- therapy.

GAGs

The disease focus of the GAGs project includes asthma and allergy, HIV and melanoma. To date half-a-dozen anti-inflammatory compounds have been identified. An exciting spin-off from the GAGs project was the development of a process that increases the stability and sensitivity of the widely used ELISA diagnostic platform. This discovery was the subject of a patent filed in August 2001.

Solerase

A minor sideline to Meditech's operations is that it has been restored selected rights to a skin care product called Solerase. The product is a formulation of hyaluron and diclofenac sodium and is applied to the treatment of actinic keratoses. The company is seeking a partner to register and market the product in Australasia, New Zealand, Singapore and Malaysia. The product may generate useful license revenues.

Financials and capital raising

Meditech Research at its last reporting date had a cash balance of \$3 million, qualified by liabilities of \$500,000. Its annual cash burn has been in the vicinity of \$3 million per annum. As part of the Solerase rights restoration, the company gained \$1.2 million in 2001. This was a considerable boost

to the company's financial position. However, the company will shortly undertake a capital raising, primarily to fund the Phase II cancer trials. It has obtained shareholder approval to issue 10 million shares.

Patent position

Meditech Research's key patents have yet to be granted in key jurisdictions. One patent covering the gene therapy uses of hyaluron has been granted in Australia and South Africa. A key aspect and investment plus of the patents is that the outstanding life of the patents is 18 years.

Risks and Weaknesses

Although Meditech's hyaluron-based targeting technology offers potential value, it is limited by the binding preferences of hyaluron to CD44 and RHAMM receptors. One implication is that it is less likely to be first line treatment in oncology, or a blockbuster drug. There is a greater probability that it would achieve status as an adjunct treatment or combination therapy treatment. Its clinical and hence commercial value is contingent on the various evolutions of treatment regimes for the status and type of each cancer, as oncology practitioners blend in the application of new chemical entities, new formulations of existing drugs, protein based drugs and immunotherapies.

Biotech companies are more likely to be poorly resourced rather than well resourced and they usually have a genuine difficulty balancing the application of scarce resources between technology and development areas and commercialisation and marketing areas. One area that Meditech may need to consider applying resources to is in the area of clinical and regulatory management. This is a key skill area for biotechs, even when the role is mostly project management. The value in a full time staff member taking on these duties is that the time of the CEO,

Chief Scientist or Chief Technology Officer is better spent on their respective core duties.

Recommendation

Bioshares' initial appraisal of Meditech Research shares was that they warranted a Speculative Buy Class C rating. At this point in time the company offers evidence that its stock deserves a re-rating to **Speculative Buy Class B**. The quality and depth of the company's management has improved considerably with the board members and management now offering convincing yet complementary skill sets. The company has added to its patent portfolio and also discovered a new application for hyaluron in the treatment of fungal infections. Offsetting these positive features has been an unfortunate set of corporate events that contributed to the weak (current) cash position and requirement to seek funds at a time that is less than opportune. To counteract future funding challenges the company needs to build a reputation as an efficient and diligent drug developer and delivery technology company. However, future funding requirements may ease dramatically if commercial arrangements with pharmaceutical partners come into place over the next 12 months, which is a distinct possibility.

Events to monitor

- *Complete capital raising before end-July*
- *Finalise a more comprehensive agreement with the Lions Eye Institute*
- *Re-locate head office to Melbourne*
- *Commence Phase II trials for colon and breast cancer (3-4 months)*
- *Generate Phase II study results (9-12 months)*
- *Undertake negotiations with potential pharmaceutical partners.*

Biotech listed option expiry dates

Company	Option Code	Exercise price	In/Out-of-the-money	Expiry date
Ellex Medical lasers	ELXO	\$1.00	In	31-May-02
Healthpoint	HLTO	\$0.20	Out	28-Jun-02
Biotron	BITO	\$0.60	Out	30-Jun-02
SSH Medical	SSHO	\$0.40	Out	30-Jun-02
Global Doctor	GODOA	\$0.10	Out	1-Jul-02

International Company Profile (US)

Alza Corporation – a world leader in drug delivery systems

History

Alza Corporation was founded by biotech visionary **Alejandro Zaffaroni**, who later founded a number of other biotechs including **Affymetrix**, **Maxygen** and **Durect**. Its first osmotic, sustained release tablet was released in 1974 and its first transdermal product was released in 1981. By 1990 it had over 2000 patents issued worldwide. From sales of US\$150 million in 1984, last year the company generated sales in excess of US\$1 billion. In 1999 it merged with SEQUUS Pharmaceuticals for access to the company's liposome technology and in 2001 the company was acquired by Johnson & Johnson for US\$10.5 billion, on a PE multiple of 46 times or 9 times annualised sales.

Alza's technologies

Oros oral drug delivery

The Oros technology platform was first developed in the early 1970s and has become the backbone of the company's subsequent drug delivery technologies. The technology involves covering a tablet in a semi-permeable membrane that uses the natural phenomenon of osmosis to fill the tablet with water. This action has two effects: the first is the dissolving of the active drug within the tablet; the second is as the membrane swells from the increasing water volume, the active drug is slowly dispersed from the tablet through a small orifice in the tablet. The first Oros product was released in 1983 and marketed by pharmaceutical group **Novartis**. The company now has 12 products on the market.

D-Trans transdermal patches

These were first released by Alza in 1981 and are now commonly used by many companies as nicotine patches or for hormone replacement therapy (HRT). The company currently has seven patch products on the market.

Macroflux transdermal delivery patches

The Macroflux patch consists of an array of tens to hundreds of microneedles attached to an adhesive patch. The microneedles pass through the dead skin and release drugs into the active tissue and into the blood stream. The technology is still under development and there are no products like this on the market. It will be applied to the delivery of proteins, peptides and vaccines.

E-Trans electrical transdermal delivery

The system uses a small battery and an electrical circuit which includes the skin to drive ionic species of drugs into the body. The system has the ability to provide delivery of drugs on demand without assistance, continuous delivery, delivery according to a programmed scheduled or in conjunction with a feedback controller after being signalled by the body to do so. The patient can simply press a button to deliver the drug from the electronic patch being worn as quickly as an infusion pump or an intravenous drip. This project is still in development. (*A feedback diagnostic and delivery system is also a possibility of pSiVida's biosilicon technology*).

Stealth liposome technology

This technology was added to the company's product range through the acquisition of **SEQUUS Pharmaceuticals** in 1999. This technology was first applied to the delivery of oncology drug, doxorubicin, and is now on the market. By encapsulating the drug with a liposome coating, and in this case a further polymer coating, the circulation half-life of the drug in the body can be increased. The size of the particles is critical (similar to with **Sirtex Medical's** Sir-Spheres) which allows the small drugs to pass through vascular imperfections in cancer tumours. Over time the drug is released increasing duration of effect. The outer polymer layer provides the added benefit of not activating the immune system. Alza claims the technology can incorporate targeting compounds on the outside of the drug to bind to a specific site in the body and even gain entry into a cell to release the drug in a Trojan horse style. (*Sound familiar? – see **Starpharma** in drug delivery feature*)

Alzamer Depot injection technology

This involves the injection of a thick gel into the body for prolonged drug release, up to one month according to Alza. This project is still in development.

Duros implant technology

These implants are the size of a matchstick and work as follows. After being inserted beneath the skin, the same osmosis phenomenon absorbs water in from one end of a titanium rod. This increases the pressure within the implant moving a piston along the titanium rod forcing out the active drug from the other end for up to 14 months. (*Once again, pSiVida's biosilicon technology could be used in a similar implant whereby the silicon would dissolve over time and release the active drug in a controlled manner.*) The technology may be used for the delivery of proteins, peptides and other macromolecules and the company currently has one product on the market. DURECT has an exclusive license from Alza to develop and market this technology.

Merger with J&J

The merger with J&J was a good fit for both companies. Although Alza is now a subsidiary of the pharmaceutical group, it is run as a stand-alone company free to collaborate with other pharmaceutical or biotech companies. Since the merger, Alza has formed collaborations with two other pharmaceutical groups.

The immediate benefits to J&J are three-fold: it has ready access to a variety of drug delivery technologies; there are no legal or contractual issues to be formalised before development work begins; and J&J is prompted to think how it can use this technology, not whether it should or not. The structure allows Alza to maintain the flexibility of a smaller biotech group without the bureaucracy of a large pharmaceutical organization. Collaborations between big pharma and drug delivery companies need to flourish and in the past this has shown to be a problem. In 1999, there were 58 drug delivery deals with pharmaceutical

companies and in the same year 50 collaborations were terminated.

Summary

The process of drug discovery and development is an expensive and time consuming process. The continued failure rate of Phase III trials is expected to see average drug development costs blow

out to an astounding US\$1.35 billion. Companies such as J&J have become aware of the less risky approach in enhancing an existing drug compound. Drug development systems are far from mature and companies with novel technologies and importantly results on the board will continue to attract the attention of big pharma.

The perfect biotech CEO

There are many facets to biotech investing. A novice investor soon learns about the importance of patents. They might soon learn that cancer is not one disease but several hundred. They will learn that the letters 'FDA' stand for the US Food and Drug Administration, an omnipotent regulator that one does not try to force the hand of. (Is erbitux Latin for 'submit proper data'?). Another early lesson will be that drug and therapeutic product development takes time and is prone to optimistic milestone forecasting. Take any estimate offered by a biotech company about anticipated milestones, add six months, and you might end up being much more closer to the actual date than you realise.

A key educational achievement is to discover why there are many investment opportunities in biotech. In biotech investment markets there are relatively more information disparities coupled to relatively fewer 'super-attuned' investment opinion leaders who work to set prices of securities. The situation could roughly be likened to a unique code of football, played over a boundary-less kilometres wide field, in which some rules seem to change frequently, with no restrictions on the number of players, or balls, in contrast to any of the standard forms of site-limited football. Some biotech investment winners will discern the new rules, know when and where the new players will come from and the balls they will play with.

The biotech investor who has grappled with some of these salutary points will have also quickly realised the importance of the CEO to the prospects of the biotech company they have invested in. The position of Chief Executive Officer is important in every company. In a biotech company there are some major differences, and it is worth discussing some of the attributes of a good biotech CEO. A caveat – there is no perfect biotech CEO. Even moderately good biotech CEOs are very hard to find, not just here in Australia, but in every country with an active listed biotech sector.

A sign of a good biotech CEO is that if they haven't already started the process, then they are probably not far off commencing the search for their replacement. They may be grooming an internal candidate, or building links through and with other companies. Recognition of dispensability and the limitations of tenure is a sign of professional maturity and good leadership. Succession planning matters in a biotech because it is a lengthy, complicated business that perpetually unveils new opportunities. Unfortunately succession planning is not generally a matter for the public record. However, when attending company presentations, note if sections have been delegated to younger members of the management team.

What is the main task for a biotech CEO? Given that biotechs are high-powered vacuum cleaners specially designed suck up

cash, there is a very strong argument that a biotech CEO's primary role is to raise cash, manage at a general level the optimal disbursement of that cash and ultimately get the best returns for shareholders.

Is it important that they have a PhD? It is very helpful that biotech CEOs have scientific, medical or technology education. Commercial experience is also very desirable. What is more important is a demonstrated capacity to learn and assimilate new ideas. They also need to practise the art of delegation. What is essential, even obligatory, is that they possess and exercise communication skills at the highest levels. A biotech CEO needs to persuade staff that they are engaged in a worthwhile commercial endeavour. They need to convince existing and prospective shareholders to supply funds, not once but many times over the commercialisation life of a technology. They need to be able to explain what their company does, why it exists, why it is different. They need to know the difference between hype and justifiable excitement. And to a great degree they will recognise their role is educative, knowing how to continually grow shareholders' appreciation of the scientific aspects of their business or drug or device or diagnostic, despite some investors protests to 'not bother them with that technical stuff'. A good biotech CEO will speak intelligently on behalf of the entire biotech sector.

There is a knowledge aspect to the attributes of good biotech CEOs. It helps if they have a context for their company in the Australian biotech sector, both from an investment point of view and from a technology development point of view. They should know what most other companies in the sector do. The differences between most biotechs are simply not obvious to many people and need to be explained. Good biotech CEOs will identify and easily discuss their competitors. They will be aware of key current events in the international biotech scene.

Should the CEO be one of the company founders or inventors of the technology underpinning the company. Answer – only when the company founder or inventor also has requisite communication skills or learns them quickly. More likely, however, a smart inventor hires a CEO, and gets the best person for the job.

If you are travelling overseas and see an Aussie biotech CEO in airport lounge, be very happy. If they are on the road, at a conference in Boston, or cutting a deal in Cambridge (UK), that's good news. Hopefully, when they trip over as they rush to greet you, the business cards of the Licensing Vice-Presidents of the major North American pharmaceutical firms will fall from a coat pocket. Another excellent sign!

The IPO Pipeline – Pharmaxis & Kinacia

Many biotech stock market investors like to get a feel for the IPO flow through of companies in the sector. In this issue we profile two companies that may seek a listing on the ASX. It is important to note that the companies featured here may not list at all as they merge from venture capital stables. However, some advance information about prospective listings is useful. It means that investors can get a head start so that when a prospectus eventuates a more timely and considered evaluation can take place.

Kinacia

Kinacia originates from the **Australian Centre for Blood Diseases** at **Box Hill Hospital** and its corporate headquarters are in Box Hill Melbourne. Kinacia, formerly Thrombogenix, was founded in 1997 by Professor Hatem Salem and Dr Shaun Jackson. Their studies into the formation and character of blood clots ("thrombo" genesis) have provided the medical and scientific basis for the company.

Following its last capital raising Kinacia was capitalised at \$32 million. Five venture capital groups have funded the company: **Australian Technology Group, Momentum Ventures, Australian Bioscience Trust, Thorney Investments** and three entities from the **Macquarie** stable of companies. It has received \$11.3 million in three rounds of financing and has also received two R&D Start grants worth \$1 million and \$2.5 million. Should it list it will do so with track record of solid venture capital backing and the well recognised validation as a Start grant recipient.

Kinacia's lead compound is an anti-platelet drug with potential use in conjunction with angioplasty surgery and as an adjunct treatment for heart attack. It is developing a range of follow-up compounds, and is optimising lead compounds with potential applications in oncology, inflammation, and restenosis. The company now holds a library of more than 230 novel proprietary compounds.

Kinacia moved forward in 2001 with the appointment of a new CEO, Dr Ross Murdoch, previously Global Head of Clinical Projects for **AstraZeneca**. The firm employs 27 full-time and part-time researchers.

Lead anti-platelet compound

Kinacia recently completed a Phase I trial of its lead anti-platelet compound to treat clotting that frequently occurs following percutaneous coronary angioplasty. This surgical procedure usually sees clotting re-occur in 24 hours in 30% of cases. It is a major market opportunity, despite the presence of one drug ReoPro (abciximab), a monoclonal antibody treatment being available, and representing the current gold standard.

Antiplatelet compounds work quite differently to anti-coagulants such as heparin. Anticoagulants break down the fibrin mesh in blood clots, whereas antiplatelets attack the 'solid supports', the platelet cells within clots. Clots have different characteristics depending on location or circumstance. Clots in arteries can have high numbers of platelets but lowers levels of fibrin. In clots found in the condition known as Deep Vein Thrombosis there are lower numbers of platelets and increased concentrations of fibrin. Kinacia believes it is well in the lead with its compounds for clotting associated with angioplasty by at least a year.

Pharmaxis

The second of our pipeline profiles is Pharmaxis, which has also been the subject of a name change. Previously the company was known as Praxis Pharmaceuticals Australia Pty Ltd.

Pharmaxis has several things in common with Kinacia, including the presence of the Australian Bioscience Trust (ABT) as a key venture capital investor. ABT has supplied funding of \$2.0 million in two rounds, since December 1999. The other shareholder is Praxis Pharmaceuticals Inc, headquartered in Vancouver, Canada but incorporated in Utah.

There are several elements to the Pharmaxis that mark it out as a more than noteworthy potential stockmarket listing.

Pipeline

Pharmaxis holds a comprehensive and well-staged drug pipeline. If listed it would immediately move to the front ranks of listed Australian drug developers. The most advanced product is an asthma monitoring device in Phase III trials. It is trialing a drug, pulmitol in separate Phase II studies for cystic fibrosis and chronic obstructive pulmonary disease (COPD). Another compound PXS23 is in preclinical studies as a potential treatment for multiple sclerosis. It is also being studied for relevance in treating other inflammatory disorders such as rheumatoid arthritis, psoriasis and irritable bowel syndrome.

Chairman

Pharmaxis has recruited a suitable chairman to the board, Denis Hanley. Hanley was a founder and CEO of **Memtec Ltd**, a membrane and filtration technology company that listed on the ASX the Nasdaq and finally the New York Stock Exchange. (Memtec was bought out by **US Filter**.) In earlier days he worked for **Baxter Labs**. The Baxter group is known as a training ground for many Australian healthcare sector leaders, including Peter Farrell (**Resmed**), John Woodard (**MicroMedical**) and Mel Bridges (**Panbio**).

Acquisitions

One of the most attractive aspects of Pharmaxis' current business plan centres on its intention to enhance the company's value and capabilities through acquisitions. The company describes the inflammation drugs research industry in Australia as fragmented and believes it is in a position to consolidate aspects of this drug development sub-sector.

Ownership of technology

A final point worth observing about Pharmaxis is that the company intends to retain, as much as possible, ownership of the drugs and products it develops, which might include taking on the cost of and responsibility for registration and marketing.

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sis. Only one patent has issued locally although none have been granted in the all important jurisdiction of the USA. The patent portfolio covers at least 230 novel genes. Nevertheless, this patent table is one of Bionomics’ key performance measures, and shows what investors have gained from the \$9 million expensed in the last two years. It is also a reflection of the skills and capability of CEO Rathjen, who brings first hand patent and IP knowledge from her days as business and licensing manager for Peptech, where she was involved with the now lucrative anti-TNF patents.

Risks

Firstly, despite Bionomics progress in identifying a number of disease genes there is the risk that these discoveries will not translate into any profitable outcomes, either as saleable IP, saleable validated drug targets or at some stage contribute to a pharmaceutical product.

Secondly, Bionomics is subject to the vagaries of financing risk, common to all biotechs, but nevertheless a risk that must be stated. Bionomics is at this stage (until or unless it enters an alliance with a cash-endowed pharma partner) dependent on the market for cash to fund its projects. Bionomics’ capacity to raise cash is a function of market sentiment, the success of meeting development milestones and corporate capabilities, among other factors. A reminder of the dilutive aspects of capital raisings for companies whose only recourse is the issue of more stock is warranted.

Finally, personnel risk is a critical issue for Bionomics, but this is a typical risk for biotech companies. Although the company’s expansion at senior management level offsets development risk, loss of these key personnel may retard company progress. What is welcoming about the company’s establishment of a senior staff team is that it creates a pool of expertise from which the company could draw on for future management succession needs.

Recommendation

Bioshares ascribes a **Speculative Buy Class B** rating to Bionomics. Bionomics has made considerable progress since it listed in November 1999. It would be fair to say that the company chose to list at a

very early stage of its corporate and technology development. Indeed, listing without an appropriate CEO was a risky move, although the subsequent appointment of Dr Rathjen was positive. The company has matured to the point where investors can be confident that the company has increased its IP and human resource asset base, and is now focused on creating more value for shareholders.

Events to monitor

- *Establishment of a small molecule drug discovery partnership*
- *Establishment of an internal small molecule drug discovery program*
- *Further drug target validation collaborations (epilepsy)*

Bionomics Patent Portfolio		
	PCT or Prov. No.	Invention Title
Epilepsy		
1	PCT/AU01/00541	Mutation in the beta2 nicotinic acetylcholine receptor subunit associated with nocturnal frontal lobe epilepsy [AU-B-56247/96 - granted in Australia]
2	PCT/AU01/00729	Mutation associated with epilepsy
3	PCT/AU01/00872	Identification of two principal mutations in ion channels associated with idiopathic generalised epilepsies
4	PCT/AU01/01648	New epilepsy mutations
5	PR4922	Novel mutation
6	PR6452	Mutations in ion channels
7	PS0910	Mutations in ion channels
Breast Cancer		
1	PCT/AU00/01329	Identification of a novel breast cancer tumour suppressor gene (TSG16)
2	PCT/AU01/01097	Tumour suppressor gene (BNO64)
3	PCT/AU01/01623	A novel gene (TSG18)
4	PCT/AU02/00096	A novel gene (BNO1)
5	PCT/AU02/00136	Dna sequences differentially expressed in tumour cell lines
6	PCT/AU02/00137	Identification of genes involved in the tumourigenic process
7	PCT/AU02/00138	Dna sequences for human tumour suppressor genes
Angiogenesis		
1	PR7973	DNA sequences for human angiogenesis genes I
2	PR7974	DNA sequences for human angiogenesis genes II
3	PR8210	DNA sequences for human angiogenesis gene IV
4	PR8532	Dna sequences for human angiogenesis genes VI
5	PR8590	DNA sequences for human angiogenesis genes III
6	PR8838	DNA sequences for human angiogenesis genes V
7	PR9095	A novel homeobox gene

Biotech Portfolios – from page 15

trade at \$100, not \$5. The stock is significantly undervalued. Selling by institutions has created an excellent entry opportunity into a one of the highest quality companies in the sector.

Starpharma fell marginally after rising as high as \$1.00. The two pooled development funds, **Starpharma** and **Medica Holdings**, offer good value at current prices.

One of the keys to successful investing is to go against the trend. There are many biotech companies now that offer exceptional value. When the next wave

of biotech fervour arrives, these stocks are likely to have increased substantially and hopefully have produced solid gains before then. The short term portfolio remains unchanged.

Not all price downturns are a consequence of market sentiment. Aspects of **GroPep’s** acquisition of biopharmaceutical manufacturing assets appear to have contributed to the fallout between former CEO **John Ballard** and the GroPep Board. The company needs to regain the faith with the market and this may occur through selecting a well suited CEO, relieving any short term funding issues and even a restructured business model.

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