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In this edition...
The Australian biotech sector offers incredible diversity, ranging from the adult stem cell therapy company Mesoblast, to targeted small molecule drug developers such as Cytopia. And it includes companies such as Imugene that use genetic engineering to make novel therapies for the animal health industry. We provide a full update on Imugene inside, a company that has come through a difficult period remarkably well.

With many new biotech investors turning to the pages of Bioshares, we thought it timely to offer some tips (ten in fact!) of a quite general nature on biotech investing.

The editors
Companies covered: AVX, CXS, IMU, MBP, MSB, PGL, PRR

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (from 5 May '06)	17.7%
Cumulative Gain	**228%**
Average Annual Gain	**26.8%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd. The company also provides market and company analysis of the Australian pharmaceutical and biotech industries for local and international funds management institutions, venture capital funds and other related industry groups. For further details contact David Blake (see details below).

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Bioshares

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Edition 200

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

An Encouraging Start To 2007

It's been an encouragingly strong start to the year for biotech stocks in what has been anticipated to be a buoyant year for biotech stocks globally. The Bioshares 20 Index has increased 11.8% from its close at the end of 2006, and is up a convincing 41.2% from June 30, 2006.

The driver for Australian biotech stocks has been more locally driven, with the anticipation of pivotal clinical outcomes in the first half of 2007. **Progen Industries**, **Metabolic Pharmaceuticals**, **Avexa**, **Prima Biomed** and **Chemgenex Pharmaceuticals** are all expected to release data in this half from Phase II clinical studies and the anticipated run up in the respective company share prices has been in full swing.

Progen (Cap'n: $262 million) surprised the market late last year releasing positive interim results from a Phase II liver cancer study. Full results from this study are expected by mid year as are results from a Phase II lung cancer study with the same compound.

Metabolic Pharmaceuticals (Cap'n: $330 million) has seen its share price more than double since October last year with its Phase II obesity trail now completed and results expected in March. Our expectation is that the stock has further gains ahead although early investors should now consider locking in some profits (it remains in the Bioshares Model Portfolio).

Chemgenex Pharmaceuticals (Cap'n: $108 million) has seen its share price double since August last year. The company is due to report interim results from a Phase II/III study in patients with CML resistant to Gleevec treatment in the first half of this year. If the results provide sufficient clarity, then it may be sufficient for the company to seek FDA registration this year. We maintain a **Speculative Buy Class A** on this stock.

Prima Biomed (Cap'n: $11 million) is due to report the full results from its Phase II ovarian cancer vaccine trial this quarter. Further positive data will help support the company's share price ahead of a licensing deal or a possible acquisition of the company. Bioshares maintains a **Speculative Buy Class B** on the stock.

Avexa (Cap'n: $112 million) is due to report initial results from its Phase IIb HIV trial this quarter. Our expectation is that trial results will be positive, however recruitment for a larger Phase III trial will provide significant challenges for the company. A licensing deal could be expected if Phase IIb results are positive. The stock was removed from the Bioshares Model Portfolio early and we recommend investors consider beginning taking some profits with this stock.

Implications for the broader biotech sector

If results from the above companies are largely positive, then the positive sentiment is expected to filter through to earlier stage biotech stocks. Combined with an expected upswing in US biotech stocks this year, 2007 is shaping up to be a rewarding period for biotech investors.

Cont'd over

From previous page

Second round stocks that investors should be considering include **Acrux**, **Peplin**, **Cytopia**, **Neuren Pharmaceuticals**, **Prana Biotechnology**, **Bionomics**, and **Neurodiscovery**.

Half yearly results approaching

Three revenue generating companies in the Bioshares Model Portfolio - **Sirtex Medical**, **IDT** and **Cogstate** - will be reporting half yearly results next month with Sirtex and Cogstate reporting quarterly cash flow numbers in January. Our expectation is that strong growth will be recorded. For investors seeking less speculative investments, these stocks should be considered.

Stock Briefs

Mesoblast

Mesoblast's stock price has increased by more than 80% since October last year and is currently capitalised at $244 million. It is currently conducting adult stem cell trials to repair long bone fractures and also a cardiovascular trial to improve hear function through its investee company Angioblast Systems Inc, of which Mesoblast owns 39%.

These trials involve the use of autologous (patient's own) stem cells and the company is seeking to move into allogeneic (unrelated patient stem cells) in the US through an IND. Most recently, the company reached a major milestone in having its IND (investigational new drug) application cleared by the FDA for using its allogeneic stem cells in the treatment of spinal fusion in a Phase II clinical study in the US. This is expected to help pave the way for allogeneic clinical studies in the US in other orthopedic indications and cardiovascular applications.

We removed stock from our model portfolio last week to lock in some short term profits (the stock was added at $1.20 a share) although our long term view remains positive for this company and we maintain a **Speculative Buy Class A** on the stock.

Bioshares Model Portfolio (19 Jan 2007)

Company	Price (current)	Price added to portfolio
Acrux	$0.78	$0.83
Alchemia	$0.89	$0.67
Bionomics	$0.27	$0.210
Cogstate	$0.21	$0.18
Cytopia	$0.67	$0.46
Chemgenex Pharma.	$0.71	$0.38
Evogenix	$0.75	$0.47
IDT Australia	$2.01	$1.80
Optiscan Imaging	$0.44	$0.35
Metabolic Pharmaceuticals	$1.10	$0.53
Neuren Pharmaceuticals	$0.52	$0.70
Peplin	$0.86	$0.83
Peptech	$1.58	$1.31
Phylogica	$0.50	$0.42
Prima Biomed	$0.054	$0.09
Progen Industries	$5.84	$3.40
Sirtex Medical	$2.94	$1.95
Sunshine Heart	$0.23	$0.19
Ventracor	$1.07	$0.92

The Bioshares 20 Index

The Bioshares 20 Index

Change from June 30, 2006	**41.2%**
Change from Dec 31, 2006	**11.8%**
Change - week ago	**-1.8%**

Nasdaq Biotech Index

Change from June 30, 2006	**11.8%**
Change from Dec 31, 2006	**4.0%**
Change - week ago	**-0.1%**

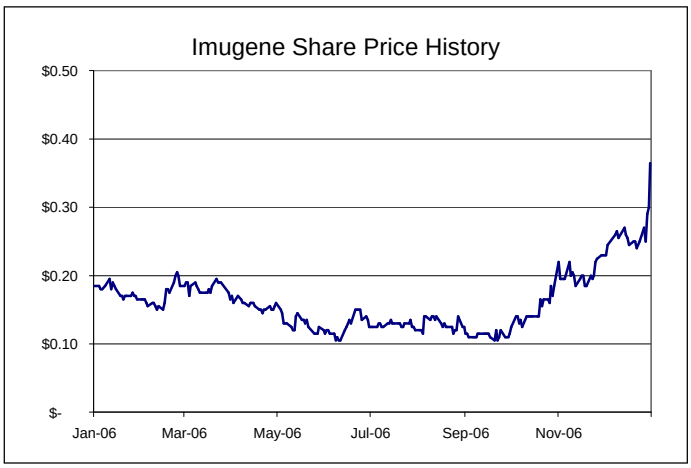
Imugene's Avian Flu Vaccine Trial Drives Price Gains

Imugene (IMU: 36.5 cents) is an animal health technology company with its principal market focus on the poultry and pig production markets. Imugene has been commercialising viral vector technologies that were originally developed by the **CSIRO**. Imugene is in fact a classic biotechnology company, in that its core technology depends on the principles of genetic engineering established in the 1970s.

What is a viral vector?

In the world of biology a vector is a mechanism for transmitting or transporting an infectious organism or particle. The classic example is the mosquito, which as a vector, transports the parasite plasmodium falciparum. Viruses are highly infectious organisms and some are well suited to the job of transporting the genetic material that is later converted into agents (specific functional proteins or antigens) that can be used to fight diseases or build immunity in the host organism.

The viral vectors developed by the CSIRO and Imugene are built on adenoviruses. The advantage of using this family of virus stem from the fact that it is a widely distributed but generally benign virus, with most forms of the virus causing not much more than mild upper respiratory tract infections. Most humans will have been infected by adenoviruses by the age of ten. Likewise most pigs and chickens after a certain age will have been infected by one of more strains of the virus. Importantly, adenoviruses that infect pigs only infect pigs and adenoviruses that infect poultry only infect poultry.



Adenoviruses target cells in the lungs and gastro-intestinal tracts. This offers the advantage that adenovirus vectors can be delivered cheaply through feed or water or by aerosols, which is significant feature when applied to production animal markets, where productivity technology costs must be kept low, relative to the cost of producing a finished product.

Another advantage of adenovirus vectors is that they have enough 'logistics' capacity to carry the genetic information relevant to treating several different diseases at the same time.

Adenoviruses also have a limited capacity to share (or combine) DNA from foreign organisms. (see http://www.ogtr.gov.au/pdf/ir/dir046finalrarmp.pdf ,p19) This implies that adenovirus-based vectors should be relatively safer compared to viruses such as the influenza virus that has the potential mix DNA from different species specific influenza viruses.

Imugene's Pipeline

Program	Partner	Status	Next Milestone	Notes
Poultry (Fowl Adenovirus Vector system - FAV)				
Poultry Productivity Enhancer (PPE)	Merial (Licd. Oct 2005)	Merial now managing development	Commercial release	
Avian Infuenza	Not partnered	Trial underway with benchmark Biolabs USA	Complete trial towards end of January 2007	Two vaccines being tested (broilers chickens; breeder and egg layer chickens
Coccidiosis	Has research contract with Abic (a subsidiary of TEVA)	Ready for trials early 2007	To sign a license agreement with ABIC if trials are successful	Utilises genetic material owned by ABIC
Pigs (Porcine Adenovirus Vector system - PAV)				
PRRS (Porcine Reproductive and Respiratory Syndrome)	Not partnered	Completed proof of concept trial	To license for further trials, product dev. and sales	
Pig Respiratory Disease	Merial	Optimisation of vaccine candidates	Testing of constructs	Utilises genetic material owned by Merial

Progress over the last 12 months

1. Poultry Productivity Enhancer

In January 2006, Imugene received a licence from the Office of the Gene Technology Regulator (OGTR) to enable it to commence a field trial of its fowl adenovirus type 8a vector (FAV), which had been modified with the gene for the chicken interferon-gamma gene.

The hypothesis behind the application of the interferon-gamma protein is that induced over expression of this immune system protein will aid in combating infection, decrease or eliminate the requirement for antibiotic drugs and improve the health and consequent finished weight of the production animals.

All aspects of the trial were completed by October 2006. The trial met all safety endpoints. These included demonstrating that the vector (vaccine) did not spread from treated to untreated chickens in the same pen. It also showed that infection did not occur in pigeons, spar-

– Imugene cont'd

rows or starling when representatives of these species were treated with a dose of the vaccine, nor to the same birds that were untreated but housed with the chickens. Pigeons, sparrows and starlings are birds that often live in close proximity to chickens and could be at potentially greater risk from receiving and transmitting the viral vector. The trial also confirmed that no vaccine was found in floor litter material or was detectable on surfaces after normal shed clearing, or in other words was not passed into the environment.

The successful completion of this trial represents a major and significant achievement for Imugene because it establishes the safety of the technology according to Australian law, which came into effect in 2001, governing genetically modified organisms. It was the first of only two submissions to the OGTR (to date) concerning animal applications of a GMO (specifically vaccine) from a set of 64 submissions, with 62 of these concerning plant applications.

However, it should be noted that although Imugene has satisfactorily completed the trial, it has yet to receive approval by a regulatory authority for application of the technology in Australia. This remains an outstanding risk for the company in Australia and in markets where the decision of the Australian gene technology regulator is perceived as important.

Current status of the PPE

Imugene licensed the PPE to Merial in October 2005. The product is now being developed for international and Australian commercial release and according to Imugene's management is well on track. Imugene stands to receive milestone payments as the PPE progresses through Merial's development schedule. Should the PPE reach the market, Imugene is likely to receive a standard industry royalty on net sales of between 4% and 8%.

2. Avian Influenza Vaccine (Poultry)

Imugene is currently evaluating a vaccine that is designed to protect chickens from the H5N1 avian influenza virus and it represents an important new potential product for Imugene. The vaccine uses the same fowl adenovirus vector technology that is used in the PPE. However, Imugene's H5N1 influenza vaccine includes the genetic code for a part of the influenza virus, specifically the haemagglutinin. Because the vaccine uses only part of the virus, and because of the adenovirus' limited capability to 'mix' or re-assort genes, the probability that influenza virus recombination from the genes used in FAV construct is probably negligible.

Imugene's avian influenza vaccine offers several advantages over other existing vaccines. For example, it does not need to be injected and can be administered in feed or water or by aerosol.

Imugene's FAV technology allows vaccines to be constructed very quickly, in as little as 14 weeks, which gives countries looking to manage outbreaks of new strains of avian flu a possible line of defence that had been previously unavailable.

A third advantage claimed by Imugene is that it is possible to detect vaccinated poultry versus infected birds. This has economic implications for companies that export poultry and need to satisfy export or import controls over influenza infected poultry.

The company expects to announce results of its avian influenza vaccine trials towards the end of January or sooner. The birds in the trial have received an initial vaccine dose, which was followed by a booster at 14 days. On January 17, all birds were challenged with a live flu virus and seven days from that that date, the trial endpoint of the number of birds still alive will be assessed. A rule of thumb measure for the industry is that a good vaccine should have a 90% success rate.

Imugene may be one of a handful of companies to successfully develop a H5NI avian flu vaccine for poultry. **Vaxin** has also developed an adenovirus vector based H5N1 injected into chicken eggs. However, the influenza virus genetic material in the vector is derived from the H5N9 virus sub-type. The Vaxin vector showed a 68% protection against a H5N1 strain.

3. Coccidiosis

Imugene is developing a FAV coccidiosis vaccine for **Abic Biological Laboratories**, the animal health business owned by **Teva Pharmaceuticals**. Abic is supplying its proprietary genes for use in the vaccine. Abic has developed CoxAbic, an oil emulsion, inactivated, sub-unit vaccine, that contains a complex of proteins of different sizes derived from the Coccidia parasite. However, this vaccine is expensive and Imugene's FAV technology provides economic benefits. Coccidiosis parasites infect different parts of the gut and apart from causing the deaths of chicks, also impact on the ability of a bird to convert feed into body mass.

Vaccine candidates are now ready for animal trials.

4. Porcine Adenovirus Vector (PAV)

Imugene is developing two different vaccines for pig diseases using its porcine adenovirus vector (PAV). The first of these has been developed to treat porcine reproductive and respiratory syndrome and the company has successfully completed a proof of concept trial. An improved version of the vaccine has also been developed. However, partnering activities were slowed in 2005 due to a patent challenge.

The company's second PAV program targets pig respiratory disease and is being conducted in collaboration with Merial, but using Merial's proprietary genes. PAV constructs using an improved promotor (a piece of DNA that controls gene expression) are being optimised and tested.

Analysis and Comment

Imugene has been slowed down on two fronts in its commercialisation activities. Firstly, the company's license submission to the OGTR was filed in 2003. A follow-up submission was made in September 2005, with a license awarded in January, 2006. Overall the process with the OGTR took at least 24 months, if not longer, and was certainly longer than that anticipated by the company.

– Imugene cont'd

Secondly, the company's US patent application covering the porcine application of adenovirus vector technology was challenged in the USA. This has now been resolved in Imugene's favour, with a rival granted patent now considered part of Imugene's IP estate. However, while the dispute was unresolved, partnering and development activities were put on hold.

Imugene has travelled through the latest downturn in the biotech sector remarkably well. This is because the company raised funds in a timely manner in early 2005, and unlike a number of cash strapped biotechs, it has not been forced to raise capital on a significant discount to a weak share price. In its favour the company has also cancelled programs, including the Receptor Mimic Technology project and the flea vaccine project and concentrated its focus on its adenovirus vector programs. The company has been the recipient of several Commonwealth Government grants, including a $882,000 Commercial Ready grant for its avian influenza vaccine program. Imugene has maintained a very low cash burn and this also has enabled the company to progress through difficult market conditions.

Imugene's business model is to generate contract research income from potential licensees and sign-on and milestone payments and royalty income from licensees, who take on manufacturing and sales responsibilities. This approach is more sensible and carries less risk than the wholly owned manufacturing and marketing approach. Imugenes' business model makes sense because its technology can be adapted for multiple applications, and hence potentially out-licensed multiple times. Ultimately, Imugene is a royalty income business.

The advent of the conclusion of the avian influenza vaccine trial is providing some short term momentum for the stock, with the stock up 43% from its close on December 29, 2006. Other drivers for the stock include the licensing of the Porcine Adenovirus Vector (PAV) system for treating Porcine Reproductive and Respiratory Syndrome and the signing of a Coccidiosis vaccine license with Abic.

Imugene is capitalised at $48 million and its estimated cash position as of December 31 was $1.9 million.

Bioshares recommendation: **Speculative Buy Class A**

Ten Tips for New Biotech Investors

With interest in biotech investing on the rise it is timely that Bioshares offers new (and not so new) biotech investors some pointers about investing in biotech stocks.

1. Don't just look at the price, calculate the company's capitalisation

Biotech companies are bought and sold on a weekly basis around the globe. In fact many are set up with the express purpose of being acquired. The price tag of a biotech firm is not its share price per se, but its enterprise value. What is the market saying the firm is worth as a whole is what matters. Therefore, investors need to check the shares, options and warrants on issue, taking note of any shares that are not listed (eg held in escrow), as well as any convertible notes outstanding. Investors also need to regularly check the shares on issue as the number of shares can change considerably in a twelve month period.

Calculating an enterprise value is the starting point for comparing the company with similar companies, locally and also internationally.

2. Download a copy of …

…the ASX and Ausbiotech Code of Best Practice for Reporting by Life Science Firms (http://www.asx.com.au/investor/pdf/biotech_best_practice.pdf). This document provides guidance to life science firms on how and when a range of different issues should be reported to the ASX.

Some firms, including some biotech companies, would prefer it that investors remained meek and mild and ignorant of the business they have invested in. This document is a positive step in bridging the 'disclosure' gap that exists between investors and biotech company managers.

3. Detail matters!

A hint about a company that knows its business is when it provides detailed and comprehensive technical and business information about its activities. You may wish to give a wide berth to companies that gloss over the complexities of bringing a medical product or service to market.

4. Who is running the show?

While there is no perfect CEO and no perfect biotech board, investors in Australia have learned (painfully) that it matters that a biotech firm is managed with a very strong commercial focus. And that means the company has a product focus, not a research focus. Be cautionary about biotech firms that fund research activities in university departments. While there are often many valid reasons for using university facilities and staff, the company that operates outside of a university and employs its own staff and is not run by a scientist is probably going to be run in the manner of a serious business and not as a grant project for a university researcher. That said, there are a handful of biotech CEOs who know how to get bang from their buck when they do work with university researchers.

Cont'd over

5. Unfamiliar with a word or idea?
Try these online dictionaries:
http://www.merck.com/mmpe/index.html
http://www.cancer.gov/dictionary/
http://www.bio.org/speeches/pubs/er/glossary.asp

6. Learn this question (and ask it):
Do you have 'freedom to operate'? This term relates to the ability of biotech firm to exploit its invention or property. This is bedrock stuff for biotech companies and simply holding a patent that enables an inventor or assignee to exclusively exploit their invention is not always sufficient for a company to sell its product with the 'monopoly' protection of patent. Sometimes additional licences to other companies' technologies must be sought

And also persistently ask: When do the granted patents supporting your IP expire in key markets? Biotech companies of all sizes and persuasions will willingly tell you they hold certain patents, but become a little more unsettled when asked to provide expiration details.

7. Know your co-investor!
As much as you possibly can, find out who else has invested in the company you are interested in. Although annual reports will provide a list of the Top Twenty investors and significant shareholders, paying attention to changes to the register over the course of a year, by looking at change of shareholding notices can pay off. For example, a major investor continuing to increase their stake can be a positive sign in favour of a smaller investor similarly increasing exposure to a stock.

Find out about venture capital (VC) backed biotech companies. While VCs are amongst the most experienced biotech business builders in the country, they too make mistakes and do not always leave the best for the rest. Quantify their holding in a firm and estimate the point in time at which they may aim to exit their investment.

Also, some of your co-investors may be concerned about the perplexing issue of dilution and loss of control. Dilution is a matter of fact in biotech investing, and in 98% of cases there are usually no sales of significance that can be used to support development tasks. This means fund raisings must take place at regular intervals, with the consequent dilution for shareholders. Avoiding capital raisings out of fear of dilution will only make it worse later on.

8. Grunt
So the biotech firm you have fallen in love with has grand plans to capture a huge share of massive market for an unproven technology. And they want to do this with a management team of three people. Skilled personnel are what make the biotech world go round, and quality companies will employ as many of the right people as they can afford to do the job properly. Where you can, find out how many staff are employed by the biotech firm you are interested in and how big the company's executive team is.

9. Another question…
So what's the regulatory pathway? Its one thing to develop a drug or device or diagnostic, its another thing again to get it approved by a regulatory authority, and what goes with one regulatory authority may not suit another across the pond. A key point to consider is if the regulatory pathway being travelled by a company is well trodden. Being first does not always mean plain sailing.

10. Competitor Research
Although smart biotech firms will disclose their competitor firms, many will not. (Some don't out of ignorance!) So make an effort to find out yourself. Regular reading of biotech news sites such as http://www.biospace.com is one way to build knowledge.

Sometimes it is simply useful to identify the number of actual or potentially competitive products and where they sit in the development cycle, without necessarily fully attempting to always understand every element of a competitor's technology or product. As it is, competition analysis in the world of drug and device development is fiendishly difficult and not at all straightforward, but the efforts you make on your own behalf will not go in vain.

Bioshares

How Bioshares Rates Stocks

For the purpose of valuation, *Bioshares* divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, *Bioshares* grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Phylogica, Neuren Pharmaceuticals, Pharmaxis, NeuroDiscovery, Prima Biomed, Biotech Capital, Cygenics, Psivida, Cytopia, Biodiem, Peptech, Starpharma Holdings, Cogstate, Xceed Biotechnology, Healthlinx, Incitive, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals

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