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In this edition...
Universal Biosensors continues to be a company to monitor very closely. The reason for the company's quiet optimism becomes more apparent each time we look into this company. It should be an eventful period over the next 18 months as its first product approaches the market.

Another company that looks set to succeed is Pharmaxis, as its Phase III trials in cystic fibrosis and bronchiectasis continue. We take a look at the competitive landscape for cystic fibrosis therapies.

And we update readers on Imugene which is progressing well.

The editors
Companies covered: IMU, PXS, UBI

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (from 4 May '07)	3.8%
Cumulative Gain	**239%**
Av Annual Gain (6 yrs)	**26.8%**

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Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9671 3633
Email: info@bioshares.com.au
David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

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Bioshares

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

Universal Biosensors – Will it Disrupt the IVD Industry?

Universal Biosensors (UBI: $1.25) may be on the cusp of causing a serious disruption to a major global industry, that of *in vitro* diagnostics (IVD). The company's lead product in development is a new glucose biosensor. Portable glucose monitors are not new and very profitable businesses have been created around these products. Confidence is quietly and quickly growing with this company as it approaches completion of its manufacturing facility and release of its first product next year into a multi-billion dollar market.

Universal Biosensors has developed a new monitor to measure glucose levels in diabetics. The first electrochemical digital monitor was released in 1986 by Medisense and while there have been minor changes since then, they remain largely unchanged. These followed on from optical earlier based-products. We have included a brief history on developments in the industry in the sidebar on page 2.

The glucose monitor is about the size of pocket calculator. People with diabetes take a sample of blood, place it on a strip, and place that strip into the monitor where through an electrochemical reaction, the level of glucose in the blood is analysed and displayed on the monitor.

Key advantages

What Universal Biosensors has done, and we have described this previously (see *Bioshares* editions 192 and 201), is to bring the two electrodes in the glucose monitor much closer and to face each other (opposing) rather than in a co-planar format (similar to two small coins placed flat side by side). This innovation allows manufacturing to be conducted in a completely different way. It also allows a lower volume of blood to be used for each diagnostic test and with a faster response time.

What we have come to understand more recently however is that there are other important advantages in this new test format. First and foremost is in ease of manufacture. The Universal Biosensor approach delivers orders of magnitude gains in manufacturing benefits, stemming from the development of a continuous throughput process. Existing sensors require five to six layers to be constructed for each sensor, a process that increases the labour involved substantially and contributes to a higher level of device defects. Universal Biosensors' devices should be substantially more profitable than existing devices because the factory space required has been reduced, the time to manufacture lessened and number of personnel required to manufacture the test strips also reduced.

But with a simpler manufacturing design, also comes other benefits, including more reliable and accurate devices (tests).

Cont'd over

Arrangements with Lifescan

The opposing electrode sensor technology, which had its origins at **Memtec**, was acquired by **Lifescan**, a **Johnson & Johnson** company, and then licensed to Universal Biosensors, which listed on the ASX last December. At this stage, Universal Biosensors has no commercialisation agreement with Lifescan.

Lifescan retains the rights to this technology for glucose level measurement and Universal Biosensors is free to commercialise it for all other applications. Since 2002, Universal Biosensors has had a product development agreement with Lifescan for developing the novel glucose monitor utilizing the opposing electrode technology.

The aim for Universal Biosensors is to negotiate a commercial manufacturing agreement with Lifescan for the glucose biosensor, and commercialise the technology independently for other tests. While this may appear as a significant hurdle or risk for the company that there is no commercialisation agreement, it's important to note that JJDC, (the internal venture capital arm of J&J) has participated in every capital raising undertaken by Universal Biosensors. This year, Universal Biosensors will complete the manufacturing plant for the disposable strips, which is where there is considerable value and competitive advantage to be derived from a unique maufacturing process. Manufacture of the glucose meter is being outsourced to third parties.

Commercialisation

Glucose level monitoring has a set reimbursable price in the US. In our judgement it's unlikely that Lifescan will compete on price, but with a significant share of the world market already, its lower costs from the new glucose monitor should provide significantly higher margins that should allow Lifescan to increase its global market share. With such a competitive advantage, we expect Universal Biosensors and Lifescan should be able to negotiate commercial agreement (for manufacture) easily palatable to both parties.

It is expected that the glucose test will be submitted for regulatory approval (510K in the US) this year or early next year and if so, should reach the market next year.

Universal Biosensors has working prototypes of the glucose monitoring device and also for some of the other tests it is developing, including its immunoassay C-reactive protein (inflammation measurement) and for its Prothombin time test (warfarin dosage).

Cont'd over

History of glucose monitor development

In 1986, Medisense released the first electrochemical cell glucose monitoring device. By 1996, the company was generating sales from the device and strips of US$166 million a year, when it was acquired by **Abbott Laboratories.** One of the researchers involved with the development of this device is one of the inventors behind the Universal Biosensors technology.

In 2000, **Therasense** released its improved glucose biosensor that required smaller blood samples and was touted to deliver rapid tests 'virtually pain free', presumably because of the small volume required. By 2004, this product was generating annual sales of US$210 million and was then acquired, also by **Abbott Laboratories**, for a staggering US$1.2 billion.

Today over 10 billion glucose test strips are sold annually (for a price of approximately 50 cents each) as part of a point-of-care glucose monitoring market valued in excess of US$8 billion per year world wide. The monitors and strips are sold through chemists and supermarket chains such as **Wal-Mart** and **Walgreens** in the US. The incidence of diabetes is escalating worldwide ensuring no lack of market growth in this sector, which is expected to reach US$11 billion by 2011.

When Medisense was acquired in 1996, some of the researchers came to Australia to work for **Memtec**, where the opposing sensor technology that underpins Universal Biosensors' capabilities, began development. Another part of the research team from Medisense went on to **Inverness Medical**, to develop other glucose biosensors. In 2001, Inverness Medical was sold to Johnson & Johnson for US$1.3 billion, and became part of J&J's subsidiary LifeScan, which focuses on development and sales of glucose monitoring equipment.

There are now four key players in the glucose diagnostic market – **Roche**, **Lifescan**, **Bayer**, **Abbott Laboratories** – that control 80% of the global market. Lifescan is currently positioned as the second largest player in this sector.

Bioshares Model Portfolio (15 June 2007)

Company	Price (current)	Price added to portfolio
Acrux	$1.52	$0.83
Alchemia	$1.04	$0.67
Biodiem	$0.30	$0.29
Biota Holdings	$1.69	$1.55
Circadian Technologies	$1.40	$1.45
Cytopia	$0.64	$0.46
Chemgenex Pharma.	$1.05	$0.38
Optiscan Imaging	$0.44	$0.35
Peplin	$0.86	$0.83
Peptech	$1.52	$1.31
Phylogica	$0.39	$0.42
Probiotec	$1.18	$1.12
Starpharma Holdings	$0.43	$0.37
Sunshine Heart	$0.20	$0.19
Tissue Therapies	$0.58	$0.58
Universal Biosensors	$1.25	$1.23

Recent plant tour

What has been impressive with Universal Biosensors is that it looks set to be commissioning its manufacturing plant within about 18 months from final design. *Bioshares* recently toured the new facility, which has three of the six major equipment items (custom built in the US and Germany) in place, and the entire plant due to be finished and operating in the second half of this year. Since the company listed in December, 2006, it has increased its employee count from 27 to 38 staff.

And if things go really well….

We believe there is a high probability that Universal Biosensors will sign a commercial manufacturing and supply agreement with Lifescan, which should deliver Universal Biosensors a reasonable income stream. Universal Biosensors is developing at least two other tests for which it has developed working prototypes and these tests stand a good chance of being successful, although it will need to find marketing partners.

Where the real blue sky is with this stock is if Universal Biosensors can play a significant role with its biosensor technology in the decentralisation of multiple existing laboratory (pathology) tests to the point-of-care setting.

Summary

Universal Biosensors is developing and commercialising a new biosensor technology that has been in development for over 10 years. It potentially represents a step change in biosensor technology that may deliver a robustness and cost efficiency that could lead a decentralisation of IVD testing.

Universal Biosensors is capitalised at $160 million with $25 million in cash at 30 April, 2007. An apparent premium is being applied to its share price not because of what it has achieved but because of what it can potentially achieve. And if it's successful, acquisitions of biosensor technology companies have shown that there may be still be strong upside for this stock.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Correction

In last weeks edition of Bioshares (219) in the analysis of Amgen's recent acquisitions, in paragraph two on page 4, it was incorrectly stated that:

"Amgen sells Neulasta, a drug that is approved to treat patients suffering from anemia associated with chronic renal failure and also for the treatment of chemotherapy-induced anemia in patients with non-myeloid malignancies."

The paragraph should read:

"Amgen sells Aranesp, a drug that is approved to treat patients suffering from anemia associated with chronic renal failure and also for the treatment of chemotherapy-induced anemia in patients with non-myeloid malignancies.

Stock Update

Imugene's PRRS Vaccine for Pigs to be Trialed

Imugene (IMU: 30 cents) is a developer of vaccines to treat production animals including chickens and pigs. To date, the company has outlicensed one vaccine product to **Merial**, and has several more in development. Thse include an avian influenza vaccine and a cocciodiosis vaccine (both for poultry), and two vaccines to treat pig diseases.

Progress with the avian influenza vaccine has been positive, with direct injection into chicken eggs generating a 100% protection if followed by a booster seven days later. A single dose into the egg achieves an 82% coverage or response. The company hopes that with some modest 'tweaking' it can increase the benefit from single dose direct injection into the egg. The company is also stepping up development so that it can offer vaccines to treat H5, H7 and H9 variants of the influenza strains.

(Vaccination by direct injection into the egg is a commercially significant enough technology for **Pfizer** to buy **Embrex**, a developer of egg vaccination technology, earlier this year for US$155 million.)

The company's PRRS (porcine respiratory and reproductive syndrome) vaccine is set to commence trials in June in the US. Two doses will be evaluated in this study and the vaccine will be given by injection. There is no vaccine available for this disease, which means the company does have to acheive 100% efficacy, with 55% – 60% a favorable outcome. Vaccines for pigs command higher prices relative to poultry industry vaccines so this vaccine trial should be watched closely. According to the company, this disease costs the industry US$600 million a year in lost production.

Imugune is capitalised at $39 million and held $1.4 million in cash as of March 31, 2007. The company has 4.2 million 22 cent October 2007 options outstanding, which gives the company a useful funding option if its shares stay in the money.

Imugene is a company that investors should monitor because success with at least one animal health vaccine may see the company become an attractive acuisition target by one of the large global animal health firms, such as **Pfizer**, **Schering** or **Merial**.

Bioshares recommendations: – **Speculative Buy Class A**

Bioshares

How Important is the Cystic Fibrosis Indication for Pharmaxis' Bronchitol?

Pharmaxis (PXS: $3.29) is developing Bronchitol, a dry powder formulation of mannitol, as a treatment that can aid in the clearance of mucous that accumulates in the lungs of people with cystic fibrosis.

The medical condition of cystic fibrosis

Cystic fibrosis is a debilitating and life-shortening disease that occurs because of a genetic abnormality. A defect in the CFTR gene means the correct CFTR protein is not produced. Aproperly functioning CFTR protein aids the flow of water in tissues and maintains the fluidity of mucus and other secretions. Mucus clogs the lungs of cystic fibrosis sufferers, making breathing difficult and also increasing the rate of bacterial infections in the lungs. Perhaps as many 75,000 patients suffer from cystic fibrosis in the world's leading pharmaceutical markets, including 30,000 sufferers in the US.

The market opportunity

The principle competitor for Bronchitol in the cystic fibrosis market is Pulmozyme. Pulmozyme was first approved in the US in 1993. It is otherwise known as dornase alfa or rhDNase (recombinant human deoxyribonuclease). The job of this protein is two cleave, or to put it more crudely cut up DNA, specifically the DNA in the cells that comprise the mucous in the lungs of cystic fibrosis patients.

Pulmozyme is a drug marketed by **Genentech** in the United States and by **Roche** outside of the US. Genentech recorded sales for 2006 of Pulmozyme in the US of $199 million. Global sales (including the US) were approximately US$360 million in 2006. At least for the US market, perhaps only a third of cystic fibrosis patients receive Pulmozyme. This is based on the assumption that the annual cost of Pulmozyme treatment is in the order of US$20,000.

The opportunity available to Pharmaxis stems from the observation that Pulmozyme is a treatment that has not been adopted by the majority (~70%) of cystic fibrosis patients. Cost of treatment may be a factor, but other reasons could include inconvenience relating to its method of delivery but also quite possibly because of a lack of benefit received. Pulmozyme must be delivered by a nebulizer and be prepared before use.

The outcome is that Pharmaxis can target an unmet need in a market that may be worth as much $200 million per annum in the US alone. Pharmaxis could still generate similar sales levels at a competitive lower price by capturing market share from Pulmozyme as well as gaining new sales. Pharmaxis, as a manufacturer and marketer ,could expect to garner significant and sustainable net revenues from the sale of Bronchitol to cystic fibrosis patients in the US alone.

Success in the cystic fibrosis market would allow Pharmaxis to have a base from which to support sales of Bronchitol in other indications, including bronchiectasis, for which there no approved mucous clearing treatment.

Lack of competition

Most importantly for Pharmaxis is that it would appear there are few other mucous clearance drugs in development for cystic fibrosis. One compound, Lomucin (talniflumate), is being developed by **Geneara Corp** as a mucous clearing agent. Lomucin is a small molecule drug that inhibits the hCLCA1 chloride (salt) channel, and which is thought to be involved in the production of mucous. Geneara Corp commenced a Phase II trial of Lomucin in September 2005 in 200 patients. However, since then the company has reduced the number of patients in the study to 80. The trial is being supported by the US Cystic Fibrosis Foundation.

The obvious risk for Bronchitol in the cystic fibrosis market comes from compounds or therapies in development that aim to treat the underlying causes of the disease by assisting or repairing the defective CFTR protein that prevents chloride to move properly in the cells that line the lungs and elsewhere in the body. Two compounds in this category include **PTC Therapeutics** PTC124 (Phase II completed) and **Vertex Pharmaceuticals** VX-770 (Phase IIa commenced).

Competitive pressure can also arise from companies developing approaches that aim to hydrate the mucous in the lungs. **Inspire Pharmaceuticals** is developing Denufosol, a compound that is designed to improve mucosal hydration and mucous clearance by modulating the P2Y2 receptor. This compound in previous studies has been delivered through a nebulizer, three times a day. Inspire commenced a Phase III study of Denufosal in July 2006, enrolling 350 patients, with an expected enrolment completion date of Q4 2007.

Other compounds in development that aim to restore salt transport include **Sucampo Pharmaceuticals** SPI-8811 Moli1901 (Phase II underway), **Parion Sciences** 552-02 Moli1901 (Phase II planned) and **Lantibio**'s Moli1901 (Phase II underway).

Orphan drug designation

In terms of total patient numbers, cystic fibrosis is small. Candidate drugs to treat cystic fibrosis can qualify for orphan drug designations from the FDA, a status that confers seven years exclusivity if and from when it is approved. The 'orphan drug' mechanism is generally designed to attract drug development for where the number of patients suffering a particular disease in the US is less than 200,000. Pulmozyme received FDA orphan drug designation and approval. Pharmaxis' Bronchitol received orphan drug designation in August 2005 from the FDA and from the European Medicines Agency in November 2005.

Bronchitol's orphan drug status may be beneficial in extending market protection that would be covered by patents in the US and other key markets until 2015. For example, if Bronchitol received US FDA approval in 2010, then Pharmaxis would gain an 'extra' two years of market exclusivity until 2017.

Cont'd over

– Pharmaxis cont'd

Clinical Trials - Cystic Fibrosis

Pharmaxis is currently conducting one Phase III trial of Bronchitol in cystic fibrosis, is planning to commence a Phase III study in the USA, has completed enrolment in a Phase II dose finding study, and another Phase II trial in pediatric patients is being conducted by a UK based investigator.

CF301

The Phase III study, CF301, enrolled its first patient in April. This trial will enrol up to 250 patients, and will be conducted in Australia, Ireland and the United Kingdom. The trial will be double-blinded for 26 weeks, and then proceed to open label for 26 weeks. The company expects to complete enrolment in Q4 2008 and announce the results in Q3 2009. The primary endpoint of the trial is the degree to which Bronchitol improves lung function.

CF302

The trial design for Pharmaxis' US Phase III trial is still the subject of discussions with the US FDA. The company expects to commence this trial in Q4 2007.

Summary

Pharmaxis' development of Bronchitol as a mucous clearing agent for cystic fibrosis patients and other patients with a similar problem of mucous congestion in the lungs (bronchiectasis) is built with solid commercial outcomes in mind. The market for mucous clearing agents is thin, and in the case of cystic fibrosis, the company has received both fast track and orphan drug designations.

By targeting the niche cystic fibrosis market, and for which control of global marketing is manageable by an Australian company, the company should stand a better chance of building on the revenues that can be applied to market development and opportunities in indications such as bronchiectasis, for which the global market opportunity may be eight times the size of the cystic fibrosis market. This is why Pharmaxis's cystic fibrosis Bronchitol program is very important for Pharmaxis.

Pharmaxis is capitalised at $584 million and held cash assets of $80 million as of March 31, 2007.

Bioshares recommendation: **Speculative Hold Class A**

Pharmaxis' Bronchitol Clinical Program for Cystic Fibrosis

Code / Name of Trial	Qtr first patient dosed	Qtr last patient dosed	Qtr results announced	Dosage levels	Duration of treatment	Blinding Status	Trial Locations	Total Planned Patient Enrolment	Pts. Enrolled to date	Study Endpoints	Secondary Endpoints
Phase II [Compares Bronchitol with Pulmozyme; not related to the registration pathway]											
CF203 - Investigator Intiated Pediatric Study	Q4 05	Q1 07	Q4 07	400mg	3 months	Not blinded	UK	41	25 (closed)	Lung Function	Quality of Life
Phase II											
CF202	Q1 06	Q2 07	Q4 07	400mg, 240mg, 120mg, 50mg	2 weeks	Not blinded	Canada Argentina	35	30	Lung function	
Phase III											
CF301	Q2 07	Q4 08	Q3 09	400mg	6 months, followed by 6 months unblinded	Double blinded placebo controlled	Aust UK Ireland	250	Commenced in April	Lung function	Quality of Life
Phase III											
CF302	Q4 07	Q4 08	Q3 09	400mg	6 months	Double blinded placebo controlled	USA	200	0	Lung Function	Exacerbation/quality of life

For all trials:
Route of adminstration is by inhalation
Frequency of administration is twice daily

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

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