ISSN 1443-850X

In this edition...
A time honoured axiom of biotech is focus, which when added with persistence and an understanding of what the customer (either big pharma, prescriber or patient) wants, leads to commercial success. So it is with animal health company Imugene which signed up Merial in a deal that puts the company in a sweet spot. The company plans a capital return, a a rare thing in these times. Impedimed recently raised $2 million, and we explain why the company garnered support for the fresh funds. We also discuss Acrux's bumpy road but note the company's verstatility in compensating for setbacks.

The Editors
Companies Covered: ACL, ACR, IMU, IPD

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - current)	-36%
Cumulative Gain	**33%**
Av Annual Gain (7 yrs)	**17.8%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

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Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 298 (6 February2009)
ISSN 1443-850X

Bioshares

6 February 2009
Edition 298

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

Imugene – Another Success Story For Australian Biotech

The two different spheres of Australian biotech continue to pull apart, with successes being generated by a smaller section of what is, in the greater part, a very financially troubled speculative development sector. Imugene (IMU: 8.5 cents) is another company to add to that pool of biotechs that are shining through the haze brought about by the ongoing global financial crisis.

Late last year, Imugene somewhat quietly announced its most important news to date, which heralds the start of the final development stages for this small animal health biotech company. **Merial**, one of the world's largest animal healthcare companies, with products such as Frontline flea repellant, has signed a $30 million deal with Imugene for access to the company's technology platform.

Imugene will receive US$3 million a year over seven years as a license fee for Imugene's technology. Imugene will have an annual spend of less that $1.8 million moving forward, which makes Imugene Australia's next profitable biotech company. The company will also be entitled to a royalty from the sale of any products – a minimum of 5% and we estimate more for the key product – and additional payments if any other programs are added to Merial's list that will use the Imugene technology.

Capital return to shareholders planned

The decision of where to go from now for Imugene's Board and management, who own just under 20% of the company, is very clear. The company will now remain profitable, no new development projects with new technologies will be considered, and a capital return to the shareholders will be delivered.

The Imugene Technology

In edition 24 of Bioshares in 2003, we ran with the heading: "Imugene – A Promising Animal Vaccine Company With A Much Sought After Technology". We don't always get it right at *Bioshares*, but five years after we initiated coverage on Imugene, it looks like Imugene has reached success.

Imugene licensed technology from CSIRO that enables the delivery of vaccines and productivity enhancers (e.g. cytokines to improve the immune system) using an adenovirus vector delivery system for use in both chickens and pigs in the livestock industry. The benefit of this technology is that animals do not have to be injected, but rather the treatment is delivered via a spray or as feed additives. The adenovirus vaccine and cytokines are delivered through the mucosal glands in the nose which is thought to deliver an improved immune response, particularly as respiratory viruses are transmitted through these same glands.

It is also possible that a better immune response for vaccines is achieved if the antigen is produced in the body after delivery of genetic material in a virus, rather than chopped up

and injected into the blood stream. The use of needles to deliver vaccines and growth promotants in the livestock industry is not only time consuming but there is the issue of broken needles left in the animals.

The Merial deal

Merial has been evaluating the Imugene technology for the last seven years under technology evaluation agreements, from when Imugene was formed in 2002 after having licensed the technology from CSIRO.

Growth promotant vaccine

There are two initial applications that have been licensed. It includes the growth promotant in chickens that seeks to stimulate the immune system, which was first licensed in October 2005, which Merial first started evaluating in 2002.

PRRS vaccine

There is also a vaccine candidate already researched by Imugene, which is likely to be the vaccine against porcine reproductive and respiratory Syndrome (PRRS), which one of the most damaging diseases in the pork production industry. The disease causes losses of up to $1 billion a year worldwide. This vaccine has the potential to become the next blockbuster in the livestock industry. It is the largest animal pig disease in China. And given the difficulty in producing the master strain, copying this vaccine will be extremely difficult.

Performance of the PRRS vaccine

In results released by Imugene in August last year, Imugene the spectacular results were apparently considered too good to be true by some of the company's potential licensing partners. Over a two week post-challenge period, animals given an oral vaccine delivered a 10% weight improvement over pigs that were challenged with the live virus and unprotected. The group given an injected form of the vaccine yielded a 16.9% improvement in weight over the untreated. This was the first time an orally delivered vaccine was shown to be effective against this virus, according to the company, with the commercial advantages of a non-injectable vaccine being "huge".

If Merial wishes to add other vaccine programs using the Imugene technology, which there is a good chance it will, the company will need to pay an additional license fee to Imugene. This deal includes full and exclusive access to Imugene's adenovirus delivery vectors for use in the animal health industry.

There are two very important factors to be understood here. Merial has been working with the Imugene technology since 2002. It has also brought to market a number of its own vector-based vaccines, including a viral vector vaccine for Newcastle disease in chickens (fowlpox virus), distemper in dogs (Canarypox virus), rabies for various animals (Canarypox virus), equine flu (Canarypox virus), and feline leukemia (Canarypox virus).

Advantages of the adenovirus vector

The adenovirus vector brings with it several advantages over other vectors in use which is likely what has spiked Merial's interest. The adenovirus has the ability to carry most genetic material, it can be manufactured cheaply, can be delivered orally, is stable, doesn't mutate and doesn't lose its gene inserted and has good storage properties as a vaccine product.

For Imugene, it has been able to negotiate the contract from a position of strength. It is not a typical milestone based partnering deal. Rather Imugene will receive an annual license fee that will make it profitable, payments from moving additional compounds into product development, milestone payments from registration of products, and the future uplift from product royalties. If Merial decides to not progress the technology, all of the IP is passed over to Imugene. In total, there may be between 8-10 applications for the Imugene technology.

By granting a full license to one party, it can streamline product development. Whilst it may take two to four years to bring the first product to market, once the system is in place, subsequent products could be released every six months, being developed in parallel. Imugene will continue to be involved in making the seed vaccine, which requires considerable expertise and in-house know-how, for additional products.

Of the US$3 million to be received annually, US$2 million was received at the end of January last month. Imugene does not anticipate further capital raisings, new product development or M&A activity.

Summary

What has helped make Imugene successful is a dogged determination and steady management to keep the company on track, limit expenditure, and wait out for the right deal on the right terms. It held on the successful strategy that the company's technology should be commercialised by one group and was not willing to slice and dice the commercial opportunities. The ability to understand the company's place and purpose has not been clearer than when the company signaled that on completion of this deal, new product development (with other technologies) or acquisitions would not be considered. The purpose of Imugene has been to successfully commercialise the adenovirus vector platform. The profits from this technology will now start to flow through to shareholders (we anticipate within 12 - 18 months).

The risk with Imugene now lies with the potential termination of the Merial agreement. However, Merial has been evaluating this technology since 2002, which gives some comfort to investors that Merial knows this technology very well.

Imugene adds to the growing list of successful biotechs in Australia, successful because it has secured a licensing deal that should make it profitable over the next six years with a very good chance of accelerated profit growth once product sales commence.

Bioshares recommendation: **Speculative Buy Class A**

Impedimed Update

In the midst of the global capital crisis, Impedimed (IPD: 73.5 cents), quite remarkably, has raised funds, and even more remarkably not incurred a savage discount in the process. Impedimed secured $2 million from **Orbis Investment Management**, a fund manager that has made its mark as a significant investor in several Australian life science firms. Orbis lifted its stake from 12% to 14.8%. Orbis also holds stakes in **Acrux** (19.2%), **Pharmaxis** (18.9%), **Phosphagenics** (19.2%), **Alchemia** (16.3%) and **Peplin** (9.1%). The placement was made at 70 cents, slightly under its October 2007 IPO price of 72 cents.

Impedimed has developed a range of detection devices that use bio-impedance spectroscopy as a means to evaluate lymphoedema and also other muscle and body mass conditions. Bioimpedance measures the opposition to the flow of small currents of electricity through the body. Lymphoedema describes the accumulation of excess lymphatic fluid and tissue. Lymphoedema can be detected with bioimpedance spectroscopy because the impedance decreases when the lymphatic fluid builds up.

Lymphoedema is of special concern to patients who undergo surgery for breast cancer and have breast tissue and lymph nodes removed. Studies indicate at least one in four patients develop lymphoedema following surgery. The early detection and therefore early treatment of lymphoedema can have a major bearing of the progression and management of the disease. Treatment is usually effected with the application of pressure bandages. A five year study conducted by the NIH showed that lymphoedema, where a baseline reading is made before surgery, can be detected four to 10 months before it presents in its generally observed clinical form. The NIH study has been a major breakthrough study, although the study was conducted with a alternative technology known as perometry. Perometry devices are expensive and cumbersome and are not approved for the detection of lymphoedema in breast cancer patients.

Adoption Strategy

Impedimed has launched its L-Dex U400 device into the US market, following clearance from the FDA in October, 2008. The L-Dex U400 is cleared for the assessment of unilateral lymphoedema in female breast cancer patients. This model is being marketed to breast surgeons, oncologists and physical therapists. Following FDA approval, Impedimed has written 28 L-Dex agreements. Revenue from these agreements is expected to increase in a cumulative fashion, as patients return for regular monitoring.

While there are approximately 4,000 oncologists, 5,000 breast surgeons and 5,000 general surgeons that constitute an addressable core market for Impedimed in the US, marketing efforts are constrained by the company's very small sales force of 6 personnel, which is capable of closing and implementing about two agreements per month per representative. Numerous visits are required to achieve a successful sign-on and a related constraint is that is training is required for surgeons and their staff to effectively incorporate the L-Dex U400 into their workflow.

Impedimed has developed a parallel strategy for boosting the take up of L-Dex agreements. The company intends to support the establishment of a patient registry, following interest received from a professional surgeon organisation. Such a registry would be independent of the company and would be managed by a professional surgeon organisation. If clinical data from the registry can be found to provide further evidence of benefits of Impedimed's detection technology, then it is possible that the professional body will write recommendations that support the use of the technology. In this way is it possible that wider adoption could be achieved beyond what even a large sales force could achieve and sooner. It would appear that part of the Orbis placement was linked to the goal of initiating and developing a registry.

Impedimed is also developing a more advanced device, the U500 model, which is designed as a unilateral or bilateral detection device for both lower and upper limbs. This capability should expand Impedimed's opportunities in other areas of surgical intervention, for example, prostate cancer. Significantly, the U500 uses proprietary electrodes, a feature that which will strengthen the company's competitive position.

There is an important reason for Impedimed to increase the number of users of its technology in the form of L-Dex U400 placements and agreements. At present, the use of the device is only covered by some private insurers (under an existing miscellaneous reimbursement code) and not by the public insurers such as CMS. Wider coverage could occur if the company was in receipt of a specific Category 1 code (CPT1) from the American Medical Association (AMA). The AMA reviews code submissions three times a year, in April, July and November, but publishes the resulting codes in December of the following year. If Impedimed had by the time it submitted to the AMA a submission that included that fact that more than several hundred surgeons were using the L-Dex product, the less likely they might be to allocate a far less attractive CPT category 3 code and far more likely to allocate a far more favourable CPT category 1 code.

Risks

One of the current risks for Impedimed is an inability to secure several hundred L-Dex agreements or certified users prior to the November AMA submission, which is the last submission date for 2009. And certainly the establishment by a professional society to support a registry is outside the control of Impedimed and outcomes favourable to Impedimed are not guaranteed.

Summary

Investors should take note of the Orbis top-up investment in Impedimed and the price at which it was conducted. The company has a strong register, and like **ChemGenex Pharmaceutical**s in September 2008, has been able to benefit from the support of committed shareholders. Impedimed has a clear understanding of how it must prosecute its US marketing strategy. Impedimed is capitalised at $63 million and holds cash assets of $6.7 million.

Bioshares recommendation: **Speculative Buy Class A**

Acrux Moves Through A Rough Patch

It has been a rough six months for pharmaceutical company Acrux (ACR: 44 cents). Over this period, its two development programs with partner **Organon** have been stopped, sales of its transdermal HRT product Evamist are tracking at around 50% of expectations, its marketing partner for Evamist, **KV Pharmaceutical,** has been challenged with several major issues, including a closure of its manufacturing facility, and last month Acrux progressed into arbitration proceedings with Vivus relating to the company's testosterone spray for women, Luramist.

Organon partnership ends

In March 2007, Acrux signed two preclinical development programs with Organon to use the Acux transdermal delivery technology to produce contraceptive sprays and an undisclosed transdermal drug. Organon was acquired by Schering-Plough soon after these deals were announced and in August last year, the programs were cancelled by Schering-Plough, with a re-prioritization of programs by Schering-Plough the likely driver. Acrux successfully completed the first stage of this program, receiving payments of US$1 million, and is hopeful of forming new partnerships for these programs in the firs half of this year.

Evamist sales running at 50%

In April last year, KV Pharmaceutical released first product developed by Acrux, Evamist, onto the market in the US. In August the company was selling 4000 prescriptions a month, and this doubled by November. By September the product was getting 3% of the new prescription market for transdermal HRT products (and 12% of the new and all patients switching between brands). However, the current penetration is still running at around 50% of expectations. Acrux receives a tiered royalty that increases up to an estimated 12%-13% if sales of around US$125 million are achieved.

Major problems at KV Pharmaceutical

In December last year, KV Pharmaceutical announced it sacked its CEO and Chairman, Marc Hermelin, although Hermelin will stay on the board and maintains he resigned from his position before he was sacked. Obviously all was not well at KV pharmaceutical, which became more apparent when late last month it suspended all manufacturing following dozens of product recalls.

Fortunately for Acrux, Evamist is manufactured by a third party in Texas and KV will continue to sell the product. If there is a positive aspect to KV's position, it's that it may have additional sales staff available to market the Evamist product. However the instability at KV is concerning for Acrux. Aside from Evamist, in August last year Acrux signed a major development collaboration with KV covering six products. The progression of these programs is now in some doubt. KV Pharmaceutical is now capitalized at only US$28 million. At the end of September, it had US$159 million in cash and US$268 million in total debt.

Legal action against Vivus progresses

In November 2006 Acrux initiated legal action against **Vivus** in relation to the development of Luramist, a testosterone spray for women with low libido. Acrux is seeking a reversion of all rights to this program and monetary damages. Last month this action proceeded to an arbitration hearing.

Fentanyl MDTS development stopped

Late last month Acrux indicated it would not pursue the development of a spray-on fentanyl product. Acrux has cited the onerous level of development, including technical challenges and costs. This is not surprising. Commercialisation of transdermal fentanyl products, whilst potentially very lucrative, have been extremely challenging, given the potency of this pharmaceutical and potential for abuse or misuse. Conversely, the development of NSAIDs, which are significantly milder analgesics, is more straightforward with lower risks for adverse patient outcomes.

Commentary

The problems at Acrux highlight the partnering risks that always exist when new collaborations are formed. Our expectation is that Evamist will become a successful commercial product although there is some uncertainty ahead. The problematic nature with collaborations may sway Acrux into keeping the development rights for its Male Testosterone product as long as possible, with the company expected to complete Phase III trials in the second half of 2009.

The portfolio approach Acrux has taken with its technology platform means that the impact of setbacks with individual products or programs can be absorbed as other programs continue to progress.

The first Acrux developed product for animal health has been filed for approval with the FDA by **Eli Lilly**. A development milestone with this program is expected in the second half of this year with royalties expected to begin next year. Acrux has filed Ellavie (the Evamist product name in Europe) for approval with European regulators and we expect licensing deals to be announced this year.

Two major applications of its technology are the Male Testosterone gel and the recently announced topical NSAID product applications. Acrux has achieved positive proof-of-concept results using its technology with delivering the NSAIDs diclofenac, ketoprofen and ibuprofen. Major deals (between US$60 million - US$100 million) have been completed in the last two years for transdermal patches and gels applying diclofenac and ketoprofen, where the products were in Phase III development or approved (see addition #292). Acrux's delivery system was able to achieve a five to nine times higher delivery of these drugs compared to existing topicals. The company is seeking partners for its NSAID program.

In the next financial year Acrux expects to receive 'significant royalties' from sales of Evamist, Ellavie and the animal health products to be sold by Eli Lilly's Elanco division, although the KV debacle may impact on Evamist sales over the next 12 months. Acrux is well funded with $25 million in cash at the end of last year. Any further weakness in the Acrux share price will be an opportunity to increase exposure to this stock.

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Alchemia – Fondaparinux No Longer A Niche Product

Perhaps another company that will be added to the biotech success stories in 12 months time will be Alchemia (ACL: 14 cents). We anticipate Alchemia's manufacturing and marketing partner **Dr Reddy's** will file Alchemia's generic fondaparinux (sold by **GlaxoSmithKline** as Arixtra) for approval with the FDA in the next six weeks. It may be very good timing with the branded drug Arixtra showing strong sales growth.

Global Arixtra sales are now tracking at US$360 million a year, having grown 62% over the last 12 months based on the most recent quarter figures. Alchemia is the only known company that has developed a generic version of what Alchemia's CEO Pete Smith has said is the *most* difficult pharmaceutical product to manufacture. However, Alchemia has developed a process that reduces the number of manufacturing steps by about half.

The expectation is that Alchemia's product will be on the market about this time next year, when the size of the global market should be about US$500 million, based on current growth rates.

Events look to finally be moving in Alchemia's favour. Arixtra sales are now strong. There is still some uncertainty in the heparin market with new products being approved which may deter other generic manufacturers from making the investment needed to produce generic fondaparinux. The heparin market is valued in excess of US$4 billion a year. It has still yet to become fragmented, with Lovenox maintaining the majority of this market. However, it looks like fondaprinux is securing a firm footing.

The key figures to monitor for Alchemia are sales in the US, which is where Dr Reddy's will market the generic first. Europe will remain closed to generic competition until 2012. US sales are tracking at US$208 million based on the most recent numbers and should be approaching US$300 million in 12 months time.

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Bioshares Model Portfolio (6 February 2009)

Company	Price (current)	Price added to portfolio	Date added
ASDM	$0.35	$0.30	December 2008
QRxPharma	$0.30	$0.25	December 2008
Hexima	$0.32	$0.60	October 2008
Atcor Medical	$0.17	$0.10	October 2008
CathRx	$0.54	$0.70	October 2008
Impedimed	$0.74	$0.70	August 2008
Mesoblast	$0.79	$1.25	August 2008
Cellestis	$1.54	$2.27	April 2008
IDT	$1.60	$1.90	March 2008
Circadian Technologies	$0.67	$1.03	February 2008
Patrys	$0.06	$0.50	December 2007
Bionomics	$0.18	$0.42	December 2007
Cogstate	$0.21	$0.13	November 2007
Sirtex Medical	$2.23	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.22	$0.66	September 2007
Starpharma Holdings	$0.19	$0.37	August 2007
Pharmaxis	$1.15	$3.15	August 2007
Universal Biosensors	$0.55	$1.23	June 2007
Biota Holdings	$0.42	$1.55	March 2007
Probiotec	$1.35	$1.12	February 2007
Peplin Inc	$0.60	$0.83	January 2007
Arana Therapeutics	$0.81	$1.31	October 2006
Chemgenex Pharma.	$0.36	$0.38	June 2006
Cytopia	$0.11	$0.46	June 2005
Acrux	$0.44	$0.83	November 2004
Alchemia	$0.14	$0.67	May 2004

Portfolio Changes – 6 Feb2009

IN:
No changes

OUT:
No changes

How Bioshares Rates Stocks

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

Group A

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

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

(CMP–Current Market Price)

Group B

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

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

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

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

Speculative Hold – Class A or B or C
Sell

Corporate Subscribers: Pharmaxis, Cytopia, Arana Therapeutics, Starpharma Holdings, Cogstate, Xceed Biotechnology, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical

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