ISSN 1443-850X

In this edition...
After several months of waiting, biotech investors have finally been shown a deal worth talking about. Acrux has licensed its testosterone gel product to Eli Lilly in a deal worth up to US$335 million on a milestone payments basis, with undisclosed royalties we estimate in the high teens/low twenties. This is a landmark deal for Australian biotech which shows in a transparent way what can be achieved if focus and discipline are applied to a sound technology that has clear relevance to patients. The deal also illustrates the need that exists in Big Pharma for quality products that can help them address the vexing problem of drugs coming off patent.

The Editors
Companies Covered: ACR

	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 - May '09)	-7.3%
Year 9 (May '09 - Current)	70.8%
Cumulative Gain	**232%**
Av Annual Gain (9 yrs)	**20.9%**

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

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Individual Subscriptions (48 issues/year)
$350 (Inc.GST)
Edition Number 352 (19 March 2010)
ISSN 1443-850X

Bioshares

19 March 2010
Edition 352

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

Acrux Signs Eli Lilly in Landmark Licensing Deal for Australian Biotech

This week the drug developer Acrux (ACR: $2.48) signed the biggest drug licensing deal in Australia's biotech history. Acrux licensed global rights to its proprietary testosterone gel product, called Axiron, to **Eli Lilly** in a deal worth US$335 million. It is a landmark deal for Australian biotech, one for which previous deals do not even come close (see table next page).

Acrux is set to receive US$50 million as an up-front payment and another $3 million on the transfer of manufacturing assets (from Orion, a third party manufacturer based in Finland.) Another US$87 million will follow if the FDA approves Axiron. A further US$195 million in sales related milestones is also anticipated and which we believe will be received. Royalties on net sales are also included in the deal but are not disclosed. We estimate the royalty rates, including stepped royalties, to range from the high teens and the low twenties.

The CEO of Acrux, Richard Treagus, said that the royalty stream comprises approximately two-thirds of the deal value. He described the deal as "one that takes Acrux forward into a new era, completely transforming the company's financial position". The deal has been done with "a great partner on great terms".

The deal was negotiated within the time frames expected by the company, which was to complete the deal by the end of Q1 2010. Acrux management noted that Eli Lilly worked within the time lines and "saw the opportunity very clearly". Acrux was attracted to Eli Lilly's articulation of a clear vision (for Axiron) within a growing men's health market, in which its erectile dysfunction drug Cialis is a strong and successful product. Acrux was also attracted to the Eli Lilly strong global reach, with that company operating in 143 countries.

Acrux CEO Treagus described the management team as having performed an "exceptional job" with the deal process. He said that the Acrux had a long standing relationship with Eli Lilly going back to 2004 and would consider this relationship to have been fostered by Acrux's management team.

While Acrux remains committed and focused on progressing Axiron through its FDA review process, the company believes it can now look to advance other programs, including the female testosterone product, which it has partnered with Vivus. Acrux believes this product has significant potential. And although Acrux will continue to maintain a running brief on business and technology acquisitions, it believes its primary focus is on securing the Axiron registration.

Acrux is a company that is managed with the immediate interests of its shareholders taking priority. This will see the company likely to begin distributing dividends to its shareholders in FY2011 from its attractive licensing deal with Eli Lilly.

A Turning Point For Australian Biotech

The Eli Lilly deal should herald a turning point for Australian biotech. Fund raising efforts for biotech companies and biotech investment funds should become considerably easier, perhaps not immediately but over the next 12 months.

Specialist biotech investment group, **IB Manager**s, has just announced plans to form its second biotech fund, this time looking to raise up to $200 million. Its first fund has generated a return of over 80% since inception in July 2008, including a very helpful three-fold gain in Acrux when QIC decided to sell out at 45 cents a share.

This licensing deal also shows that transparency that is achievable with investment in drug development, a sector where performance returns and project outcomes have often been difficult to characterise. In 2007 Acrux raised $23 million (at $1.60 per share) to take the Axiron commercialisation further. The upside was clear if all went well; a multi-million dollar licensing deal for a product that had clear competitive distinction over existing products and a growing billion dollar market. It has done exactly that.

Other Australian biotechs are now adopting the same approach, where funds are raised to complete a distinct commercial objective with a set medium term outcome. **Starpharma**'s capital raising last year to fund the Phase II and Phase III clinical program with Vivagel for the treatment of bacterial vaginosis is a recent example. This is also potentially a major market worth hundreds of millions of dollars a year.

What's Next for Acrux?

We expect a large portion of the company's revenue will be distributed to shareholders. Acrux will continue to extract value from its technology platform however it has been shown that this can be achieved for a relatively modest outlay.

Progress of the company's spray-on hormone replacement product (Evamist and Ellavie) has yet to see the full potential realized, which partner issues in the US and European approval pending. The female testosterone product, Luramist, which is currently licensed to **Vivus Inc**, has a 1 April deadline to start Phase III trials.

The first animal health product partnered with Elanco (Eli Lilly) is due for FDA approval shortly and is expected to reach the market this year (there are very few details currently about these products). The company also has a number of earlier stage programs in the transdermal delivery of compounds such as NSAIDs, contraceptives and nicotine.

Manufacturing

The only disappointing aspect from the Eli Lilly deal was that Acrux will transfer manufacturing control to Eli Lilly, however it is understandable the Acrux's partner wants full control of this program given it will be investing around US$500 million to commercialise Axiron (including upfront payments, approval milestone payment and market launch).

Market Potential for Axiron

In our model for the Acrux valuation, we ascribe peak sales achieved for Axiron of US$600 million. As of March 2009, the global market for testosterone products was worth US$1.0 billion with gels making up 72% of all prescriptions. The market is growing at 20% a year, yet most of that growth is in gels, and it is being driven by GPs not specialists.

The leading product is Androgel, which generated sales of just over US$550 million in the 12 months to March 2009. In our view, the Acrux/Eli Lilly product is far superior, with half of the drying time, and a much smaller application area, under the arm, versus on the torso for Androgen. In a sample patient survey, two thirds indicated they would switch to the Axiron product if given the choice. Transmission to others, particularly children has become a concern with the FDA and the Axiron product conceivably will greatly reduce that risk.

Given the 20% growth in the market, and the entry of a superior product with a major marketing partner that will be investing up to US$500 million in this product, and that only 5-10% of the potential market has been captured in the USA, we estimate the global market has a very good opportunity to exceed US$2 billion over the next three to five years. We view our US$600 million sales forecast as achievable and could be exceeded if the strong market growth continues.

– Cont'd on page 4

Australian Biotech Licensing/ Partnering Deals

Biotech	Partner	Date	Upfront	Deal Terms
Acrux	Eli Lilly	March 2010	US$50 M	Up to **US$335 M** plus royalties
Chemgenex Pharmaceuticals	Hospira	December 2009	$18.8 M	Plus up to **$119 M** and royalties
Universal Biosensors	LifeScan	2002-2009	N/A	>**US$20 M** received
Phylogica	Roche	December 2009	CHF400,000	Undisclosed
Bionomics	Merck Serono	June 2008	US$2 M	Up to **US$49 M** total plus royalties
Antisense Therapeutics	Teva	February 2008	US$2 M	Up to **US$100 M** plus royalties
Biota Holdings	Boehringer Ingleheim	November 2006	Undisclosed	Up to **US$102 M** plus royalties
Cytopia	Novartis	June 2006	$5M est.	**$13 M** over 3 years
G2 Therapies	Novo Nordisk	February 2006	US$6 M	Up to **US$102 M** plus royalties
Biota Holdings	MedImmune (AstraZeneca)	December 2005	US$5 M	**$35 M** received
Biodiem	Organon	November 2004	-	**US$8 M** plus royalties

Eli Lilly – What Kind of Partner?

While Eli Lilly has cemented a deal of significance with Acrux it is not the first deal the company has signed with an Australian company nor with Acrux. In 2003, Lilly signed a deal to develop a product using Acrux's transdermal delivery technology for the animal health arena. This product is currently under review by the FDA. Lilly has twice licensed dendrimer technology for drug delivery from **Starpharma Holdings** in human health and animal health respectively. However very little detail has been revealed regarding these collaborations. **Circadian Technologies**, has courtesy of Eli Lilly's 2008 acquisition for US$6.5 billion of **Imclone Systems**, a licensing relationship covering the VEGFR3 antibody, IMC-3C5. Lilly anticipates filing an IND for IMC-3C5 in 2010. Circadian Technologies holds a proprietary position over VEGFR3 through its **Vegenics** investee company, which is now a 100% owned subsidiary.

What Kind of Company is Eli Lilly?

Eil Lilly is the tenth largest pharmaceuticals firm in the world, employing approximately 40,000 people around the world. EIi Lilly was founded in 1876. The company reported revenues of US$21.8 billion for CY2009, an increase of 7% from the previous year.

Lilly specialises in developing and marketing products in the areas of neuroscience (depression, anxiety and ADHD), endocrinology (diabetes and osteoporosis), oncology, cardiovascular and also in animal health. Sales of human pharmaceuticals were US$19.9 billion in 2009, supported by animal health sales of US$1.2 billion.

Sales of Leading Products

Lilly's biggest selling product is Zyprexa, a treatment for schizophrenia, which netted sales of US$4.9 billion in 2009, up 5% from 2008. Next in line is Cymbalta, a product indicated for depression, diabetic neuropathic pain and generalised anxiety disorder, which took in sales of $3 billion in 2008, an increase of 14% from the previous year. The company's third most important product is terms of sales is Humalog (insulin for diabetes) (US$2 billion) followed by Alimta (various cancers) (US$ 1.7 billion) and Cialis (erectile dysfunction) ($1.6 billion).

Drugs Coming Off Patent

An issue for Ely Lilly is that 75% of its 2009 revenues will face loss of patent protection between 2011 and 2017, led by Zyprexa ($4.9 billion; 23% of revenues), for which patent protection lapses in 2011. Cymbalta ($US3 billion, 14% of revenues) follows in 2013.

R&D and Pipeline

Lilly expended US$4.3 billion on R&D in 2009 and employs 7,600 people in research and development activities.

The company has recently received FDA approval for Livalo, a lipidemia drug which is expected to prescribed for patients who don't respond to treatment with statins. Another drug, Arxxant is ready for market launch.

The company is also progressing new indications for Cymbalta for chronic pain, diabetes drug Exanatide for once weekly administration, Cialis for benign prostatic hyperplasia, Alimta for head and neck cancer and locally advanced NSCLC, and Erbitux in esophageal, pancreatic, bladder, rectal, brain and prostate cancers.

Forteo, currently approved for osteoporisus is being investigated as a treatment for back pain. Of some interest to Acrux investors is that Lilly is also running a Phase II trial of Forteo delivered transdermally. Given than the less than patient friendly pen injection device the company developed for Forteo, the investigation of a transdermal system is no surprise, and it would also be no surprise if Lilly looks for ways it can translate any success it experiences with Axiron into products such as Forteo.

In Phase III sit two Alzheimers drugs, solanezumab, and semagacestat, each in two Phase III trials, which are complementary approaches for controlling the deposition of beta-amlyoid. However, it will take some time before results from these trials are known, let alone submitted for registration. In Phase III but from the Imclone stable come IMC-11F8 (non small cell lung cancer) which targets the VEGFR1 receptor and IMC-1121B (breast and gastric cancer), which targets the VEGFR2 receptor.

Pressure

The company, no doubt under pressure by a looming patent cliff, has attempted to make its drug development process more efficient. It has established a process called Chorus, with which it claims has reduced the average cost of achieving proof of concept from US$21 million to US$6 million per new molecular entity and increased its Phase II success rate from 30% to near 50%. This has been achieved by spending more on target validation and moving the 'first human efficacy dose' into the development process much earlier in the process, effectively at the Phase I stage.

Lilly claims to have tripled the number of NMEs it has in clinical development from 2004 to 2009 and doubled the number of Phase I commencements over that period.

Conclusion

This brief survey of Eli Lilly suggests a number of reasons why it has licensed Axiron from Acrux. The product looks to fit well with in its men's health portfolio, especially alongside Cialis, its erectile dysfunction drug. It also may fit well in its endocrinology portfolio, if possible uses in obesity, metabolic syndrome and type 2 diabetes can be established for testosterone treatment.

There is appeal in understanding the relevance of the Acrux drug delivery technology with products such as Forteo. However, Axiron's greatest appeal may be that it can deliver revenues from 2011 onwards, a year in which Eli Lilly is expected to experience a significant loss of income when Zyprexa comes off patent.

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Patents

Acrux's core patent - for transdermal delivery of therapeutic drugs with a dermal penetration enhancer (a type of skin tolerant ester sunscreen) - has been granted in most major regions including the USA, Europe and Japan. This patent expires in 2017. It has granted patents over its metered dose delivery system (for spray-on products such as Evamist but not Axiron) out to 2021. For its Axiron product, it has pending patents covering the delivery of drugs with its penetration enhancers to the armpit region. If granted, this patent family would give protection out to 2026. According to an RBS Morgans report, it is believed the term of the contract with Eli Lilly is for the life of the product, not the life of the patents.

Acrux Valuation

Using the assumptions below, we place a currency valuation of Acrux shares at **$3.95**. The majority of the value (**$3.45 a share**) we place on the male testosterone product, Axiron. For other programs and assets the company has under development or on the market, we ascribe a value of 50 cents a share (or around $80 million).

This includes a modest royalty stream attributed to the hormone replacement product outside of the USA, to be marketed as Ellavie, and to the animal health products being developed with Elanco (Eli Lilly).

We currently ascribe little value to the Evamist product in the USA until further clarity emerges on the commercialisation of that product.

The following assumptions are made in are valuation:

– Discount factor: 12.6%
(This will reduce towards 10% once the market has been accessed for Axiron).
– Probability that Axiron will reach the market: 90%
– Corporate tax rate: 30%
– Royalty rate: 20%
– Peak sales of US$600 million achieved in 2014
– 3.5% royalty payment to Monash University from Acrux earnings
– Patent protection out to 2026
(Note that the core penetration enhancer patent expires in 2017 with patents filed to give protection potentially out to 2026)
– Calculation is on a fully diluted basis, with 166.5 million shares
(Assumes all options will be exercised and raising approximately $8 million.)

PDF Tax Benefits

Acrux is a Pooled Development Fund (PDF). This valuation does not take into account any financial benefit from the tax exemption of any dividends received by shareholders coming from a PDF. Dividends are exempt from tax. Tax payers on a marginal tax rate above the company rate do not have to pay additional tax on dividends. Australian residents can opt to recognise any tax franking credits if their marginal tax is lower than the company tax rate, although they need to hold the shares for more than 45 days.

– Cont'd over

Acrux Commercial History

March 2010	US$335 licensing deal signed with Eli Lilly
January 2010	Axiron filed for approval with FDA
September 2009	Phase III results success with Axiron
December 2008	First animal health product submitted for approval with FDA
June 2008	Phase III trial with Axiron commenced
July 2007	Raises $22.5 million to fund Phase III trial for Axiron at $1.60 per share
July 2007	Positive Phase II results for Axiron
July 2007	Evamist (transdermal HRT) approved by FDA
October 2006	Expands animal health agreement with Elanco (Eli Lilly)
May 2006	Richard Treagus appointed CEO
October 2005	Orbis Mutual Funds acquires 12.5% at 60 cents per share; seller includes founder Tim Morgan
September 2004	IPO, raises $30M at $1.00 per share
June 2004	Core ownership of technology assigned to Acrux from Monash University
September 2003	Forms collaboration with Elanco (Eli Lilly) for animal health applications
June 2002	Raised $9.8M at $1.00 per share
2002	Igor Gonda appointed director and later CEO
May 2001	Raised $11.3M at 83 cents per share
August 1999	Raised $5M at 17 cents per share
June 1999	Licence granted from Victorian College of Pharmacy (Monash University) for core technology
1998	Company founded by Ross Dobinson, and co-inventor of technology Tim Morgan

Bioshares Model Portfolio (19 March 2010)

Company	Price (current)	Price added to portfolio	Date added
Tissue Therapies	$0.24	$0.21	January 2010
Biodiem	$0.18	$0.15	October 2009
QRxPharma	$0.87	$0.25	December 2008
Hexima	$0.40	$0.60	October 2008
Atcor Medical	$0.15	$0.10	October 2008
CathRx	$0.22	$0.70	October 2008
Impedimed	$0.87	$0.70	August 2008
Mesoblast	$2.07	$1.25	August 2008
Circadian Technologies	$0.72	$1.03	February 2008
Patrys	$0.16	$0.50	December 2007
Bionomics	$0.33	$0.42	December 2007
Cogstate	$0.29	$0.13	November 2007
Sirtex Medical	$6.20	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.26	$0.66	September 2007
Starpharma Holdings	$0.70	$0.37	August 2007
Pharmaxis	$2.64	$3.15	August 2007
Universal Biosensors	$1.65	$1.23	June 2007
Probiotec	$1.75	$1.12	February 2007
Acrux	$2.48	$0.83	November 2004
Alchemia	$0.67	$0.67	May 2004

Portfolio Changes – 19 March 2010

IN:
No changes.

OUT:
No changes.

Summary

What is there to be learnt from the Axiron licensing deal? One thing we observe is that Acrux made a licensable product. It did this by taking on Phase III development and eliminating clinical risk that a prospective partner would otherwise have to bear. Acrux also conducted important market studies, that identified the quantitative and qualitative potential for Axiron. Such studies have rarely been commissioned by Australian biotech companies.

Acrux also turned around a $22.5 million capital raise in a timely manner, approximately 2½ years, in the process, doubling the investment payback to at least that of a bankable $50 million upfront milestone. Focus, clarity of purpose and a belief that execution matters are the features that characterise Acrux's management. These attributes are now allowing the company to move up to a next phase of corporate growth and development and generate further returns for shareholders.

The last 13 months has delivered the most tangible signs of success for the Australian biotech sector seen in its 25 year history. There have now been three $300 million plus transactions in the sector, including the acquisitions of **Arana Therapeutics** and **Peplin** last year. The Axiron deal is the most impressive of the three and one from which investors can enjoy a continued benefit.

Bioshares recommendation: **Speculative Buy Class A**

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

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