ISSN 1443-850X

Bioshares

19 September 2014
Edition 569

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

Companies covered: ACR, ALT, OCC

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - May '14)	26.6%
Year 14 (May '14 - current)	21.9%
Cumulative Gain	**449%**
Av. Annual gain (14 yrs)	**17.7%**

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

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Individual Subscriptions (48 issues/year)
$400 (Inc.GST)
Edition Number 569 (19 September 2014)

FDA Committee Reviews Testosterone Replacement Therapies

An FDA advisory panel, the joint Bone, Reproductive, and Urologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee has reviewed the current approved uses for testosterone and recommended that the label governing these two indications, of primary hypogonadism and of hypogonadotropic hypogonadism, be changed. The second of these two indications evolved in practice to include 'idiopathic hypogonadism', which is perhaps better known as 'age-related low testosterone'. This condition is representative of males with low levels of testosterone who seek to restore levels to enjoy a quality of life associated with normal levels, addressing for example, loss of libido and energy levels.

The advisory committee also recommended that the FDA require sponsors to conduct studies to further assess potential cardiovascular risks of testosterone therapy in certain indications.

The Basis Of The Review

The review of testosterone replacement therapy was stimulated by the publication of one observational (retrospective) study late in 2013 and another in early 2014, which purported to show that subjects receiving testosterone replacement therapy had significantly higher probabilities of experiencing adverse cardiovascular events.

The FDA reviewed these two studies as well as three other observational studies and it also reviewed a meta-analysis of completed placebo-controlled clinical trials.

The FDA said that because of substantial methodological limitations, the meta-analysis did not provide conclusive evidence of a causal relationship between testosterone therapy and cardiovascular events.

The FDA said that caution should be applied when interpreting the results of the five observational studies, because among other things these studies did not separate the effect of testosterone therapy on cardiovascular risk from the effect of serum testosterone risk.

The FDA also reviewed prescription data for testosterone therapies and discovered that in 2013, of the 2.3 million subjects receiving testosterone therapy, 1.3 million, or 57%, were receiving cardiovascular medication.

What Do The Proposed Changes Mean For Acrux?

Acrux (ACR: $1.30) is the originator of the topical testosterone therapy product, Axiron, which is marketed under an exclusive global license agreement by Eli Lilly.

Axiron has an approximate 14% share of the topical testosterone therapy market, alongside competitors such as Androgel, Testim, Androderm and Fortesta, which together make up 55% of the market with injectable products accounting for the rest. *Cont'd over*

Axiron received US$22.3 million in royalties on net sales of Axiron, which totaled US$181.4 million for FY2014. Acrux received royalties of US$14 million for FY2013. Acrux also received a US$25 million milestone payment in March 2014 relating to worldwide sales of Axiron reaching US$100 million in CY2013.

There are several things at stake for Acrux from changes to testosterone therapy labelling and the adding of testing requirements for testosterone therapy.

Acrux stands to receive an additional US$170 million in milestone payments relating to the sale of Axiron. The terms of these payments are not known.

If the overall testosterone therapy market declines, both for topical and injectables, as a consequence of the FDA introducing more specific labelling, requiring sponsors to gather more safety data and for doctors to properly test patients before prescribing testosterone therapy (currently 28% don't), then Axiron sales could fall in line with a weakening market.

While lower Axiron sales would translate to lower royalties, at greater risk is the future US$170 million in milestone payments, some of which may never be paid if, for example, a condition of payment is that annual sales reach or exceed an even high sales level, either globally or in the USA.

Investment Consideration

While Axiron may be one of the better testosterone replacement therapies on the market, it is likely that the overall market will weaken in the lead up to the release of guidance by the FDA on labelling and prescribing behavior.

We have placed a **Hold** recommendation on the stock pending the release of the FDA's specific guidance to testosterone therapy suppliers and prescribers, which should establish the cost and duration of any additional trials required, any interim measures that might be installed, and whether injectable dosage forms have harsher provisions placed on them, thus biasing the market to topical formulations.

One additional point for investors to keep in mind is that a depreciating Australia dollar against the US dollar has the potential to offset lower royalty income from Eli Lilly.

Acrux is capitalised at $206 million.

Bioshares recommendation: **Hold**

Scenarios

The worst case scenario is that any future randomised studies reveal that testosterone therapy does give rise to cardiovascular risk in patient groups who don't have existing cardiovascular or diabetic problems. That would severely restrict the use of testosterone therapy use except with the much, much smaller numbers of patients who have low testosterone due to the effects of chemotherapy or for reasons of physiological abnormality.

We rate this with a very low probability because the usage of testosterone in vast population numbers has not been shown to be related to any major cardiovascular events and the usage to date has been muddied by the 57% of patients who are on medications for cardiovascular or diabetic conditions.

What can be expected is that each drug sponsor will be required to provide evidence of their drug's cardiovascular safety from a randomized clinical trial designed to assess the difference between endogenous levels and administered levels and potentially whether the route of administration plays a role in safety.

Such trials will also likely be asked to provide documented evidence of a testosterone therapy's ability to address specific symptoms of age-related testosterone deficiency, such as low libido and erectile dysfunction.

An Advantage for Axiron?

In this regard, Acrux's partner Eli Lilly is scheduled to complete in October a 600 patient Phase III trial of Axiron on its effect on total testosterone levels, sex drive and energy. A 24-week open label follow-on component has been included to assess long term safety of Axiron. This may prove to be very advantageous to Lilly and Acrux.

It is possible that the FDA's revised guidelines will target the injectable testosterone sector more than the topical market because of the strong growth in number of males aged 0-39 taking injections, whose share of that cohort increased from 46% in 2010 to 58% in 2013. In the 40-64 age group, the share of patients receiving injected testosterone increased from 33% in 2010 to 41% in 2013.

Injected testosterone is noted for delivering an energy rush, which might explain the appeal of the therapy to younger men. It is not clear if this route of administration is a source of unique safety issues.

Bioshares Model Portfolio (19 Sept 2014)

Company	Code	Price (current)	Price added to portfolio	Date added
Actinogen	ACW	$0.045	$0.050	September 14
Benitec Biopharma	BLT	$1.030	$1.025	September 14
LBT Innovations	LBT	$0.130	$0.130	July 14
pSivida	PVA	$4.570	$3.800	May 14
Invion	IVX	$0.078	$0.089	February 14
Impedimed	IPD	$0.450	$0.245	December 13
Analytica	ALT	$0.036	$0.025	December 13
Imugene	IMU	$0.016	$0.022	November 13
Oncosil Medical	OSL	$0.125	$0.155	September 13
IDT Australia	IDT	$0.240	$0.260	August 13
Viralytics	VLA	$0.270	$0.300	August 13
Tissue Therapies	TIS	$0.400	$0.255	March 2013
Somnomed	SOM	$2.05	$0.94	January 2011
Cogstate	CGS	$0.310	$0.13	November 2007

Portfolio Changes – 19 September 2014

IN:
No changes

OUT:
No changes

IPO Funds Boost Orthocell's Drive to Market

Regenerative medicine company Orthocell (OCC: $0.345) has now been listed for more than a month, with its share price easing from its offer price of 40 cents. The company, which was founded in Perth in 2006, raised $8 million.

The capital obtained through the IPO will among other things, allow the company to improve and develop the communications side of its business, with Orthocell to invest in more sophisticated digital marketing materials that will help surgeons educate patients about Orthocell's novel cell therapy technologies, which include its lead product Ortho ATI (a tendon stem cell product), Ortho ACI (a chondrocyte product) and CelGro, a scaffold product sourced from porcine collagen.

The new funds will also support the company's regulatory efforts and clinical trial programs, including the appointment of a clinical trials co-ordinator. Orthocell has plans to initiate clinical trials for its Ortho ATI product in the areas of tennis elbow, rotator cuff, knee and gluteal tendinopathies over the next nine months.

Long Term Results From Tennis Elbow Trial

Orthocell recently released results from a 20 patient long term study of Ortho ATI for the treatment of tennis elbow. The study showed that grip strength improved by 84% after one year and by 207% at an average of 4.5 years after the treatment took place. The study also found an 83% improvement in mean pain score, a 87.3% improvement in mean DASH(Disabilities of the Arm, Shoulder and Hand) score and a 64.3% improvement in mean UEFS (Upper Extremity Functional Scale) score.

Orthocell now holds the longest data on treating tendons with autologous stem cells and which it claims is disease modifying.

In the not too distant future data is expected to become available from a 90 patient randomised, blinded study conducted at Erasmus University in Rotterdam, The Netherlands, in patients requiring treatment of chronic Achilles teninopathies.

This is a key trial because it is a randomised, double-blind placebo trial which is evaluating the efficacy of Ortho ATI at 24 weeks post treatment.

Summary

Orthocell is now well positioned to work towards achieving a number of clinical and commercial goals for Ortho ATI and CelGro.

The release of data from the Rotterdam trial data could be a trigger for stronger investment interest as will the registration of Ortho ATI on the TGA's register of therapeutic goods. (The company currently holds a manufacturing licence from the TGA.)

One key investment point for Orthocell is that it is developing two different but related technologies – Ortho ATI and CelGro – both of which have the potential for significant revenue generation. The presence of two technologies that can form the basis for multiple products de-risks the company considerably.

The company's third product, Ortho ACI, has been out-licensed to a Chinese company for development in China. Orthocell does not plan to develop the product for other markets outside Australia.

Orthocell is capitalised at $28 million.

Bioshares recommendation: **Speculative Buy Class A**

Orthocell Milestones

2014 Q3	Commence Tennis elbow trial
2014 Q4	Randomised data from Dutch trial
2014 Q4	Commence patella tendon trial
2014 Q4	Commence gluteal tendon trial
2015 Q2	Commence rotator cuff trial
2015 Q2	ARTG submission for collagen scaffold
2015	Sign collagen scaffold deal (EU)

Analytica Readies Pericoach for Full Commercial Launch Next Month

Analytica (ALT: $0.038) is on track for the commercial launch of its PeriCoach system, which is expected to occur in the second half of October. The PeriCoach has been developed to assist in the treatment of urinary incontinence in women. The system will be sold for around $300 and already 400 clinicians have expressed an interest in the product.

Controlled Release Precedes Full Launch

In June, the company sensibly conducted a controlled market release of the product with a version that is compatible with Android phones and tablets. On commercial release, the device will be compatible with both android and Apple operating systems.

In Australia there are about 1,000 clinicians that specialise in the urinary incontinence field. Of the 400 who have now signed up to be trained and notified of the full market release of the product, around 60 have now been trained under the controlled market release.

Analytica CEO, Geoff Daly, said a controlled market release was "absolutely the right way to go'" with about six issues that surfaced around the use of the product. These items, which have now been resolved, included some production issues, purchasing problems and an issues with inadequate blue tooth capabilities.

Presence at Cairns Meeting

Last week Analytica had a booth set up at the Continence Foundation of Australia meeting in Cairns, at which Daly said it was a fantastic outing for the company with delegates literally waiting three-deep at times to obtain information about the PeriCoach system (see photo from latest company update).

With the interest obtained from that event, the company has scheduled six training sessions around the country and it expects around 30 clinicians to attend each of the training sessions. "Acceptance is just phenomenal," said Daly. Analytica is now receiving calls from clinicians requesting meetings to learn more about the product.

Analytica is using a top down and a bottom up approach to selling the device, marketing both to the clinicians and to the patients. The product has featured recently in *The Australian Women's Weekly* as well as *Australian Doctor*, and presence at Australian and international industry meetings. The company is also seeking to develop partnerships with continence foundation groups in each of the states in Australia from which Daly indicated there is strong interest.

Competitor Product

Analytica has one main competitor, that being the InTone device which received FDA approval in 2012. However Daly says the advantages of Analytica's device is that it is smaller, is less than half its price, and Daly believes the PeriCoach appears less threatening to the patient.

Clinical Trial to Start in November

The company has put in place notable Clinical Advisory Boards in Australia and the US. Analytica expects to start a clinical trial in around 100 women in November which is will run for 20 weeks. The company has successfully completed smaller usability trials.

The company expects to file its regulatory submissions before year's end in Europe and the US. At this stage, the company will start to market and sell directly into specific areas in the US and may consider the use of distributors at some point.

Analytica has around 15 staff, including a full time regulatory person. The company has hired three sales people for Australia, with a fourth to be hired to sell into South Australia and Western Australia. The company also has a sales manager for the US and will be building a US sales team in the next six months.

Sales Model

Analytica will supply clinicians interested in its product a complimentary system to trial. They may also be given a demonstrational model for desk to show patients what the device will look like. The patients can then either buy the units themselves direct from the company, or preferably the clinicians will hold stock of the units which will be sold to the patients.

Risks

A key risk for investors is that product take-up will be slow and that the company will need to continue to raise money to fund the marketing of the product. A challenge for the company will also be to manage the launch of the product into Europe and the US, with or without the assistance of distributors.

Summary

While Analytica has had a relatively quiet period with respect to commercial progress as it has moved through the controlled release phase of its PeriCoach system, the stock should receive greater attention in the last quarter of this year, as it enters the full commercial launch phase of its lead product.

Analytica is capitalised at $31 million. The company generated a net loss of $3.2 million last year and held cash of just under $2.0 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Analytica Milestones

2014 Oct	Full commercial launch of PeriCoach in Australia
2014 Q3-Q4	Clinician training sessions in Australia
2014 Q4	File for US approval
2014 Q4	File for EU approval

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. For both groups, the rating "Take Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

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: Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Tissue Therapies, Viralytics, Phylogica, pSivida, Benitec BioPharma, Admedus, Calzada, Invion, Imugene, Analytica

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