ISSN 1443-850X

In this edition...
The risk that a regulator will slow down a new drug or device's journey to market is now well established in the minds of Australian life science investors. Tissue Therapies' has not only had to deal with a categorisation issue for its VitroGro wound healing product, but now faces another manufacturing review which means, in our estimate, that the product is now more likely to commence selling in 2013 Q4. However, the product has many merits, including convenience, and it should be adopted reasonably quickly.
Mesoblast investors can expect clarity on its relationship with Teva Pharmaceuticals, following Teva's Investor Meeting on December 11. Finally, we survey another group of stocks in our 5 Stock Wrap format.
Companies Covered: AJJ, CIR, CDY, CMP, ELX, MSB, TIS

	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 - current)	-12.3%
Cumulative Gain	**203%**
Av. annual gain (11 yrs)	**17.8%**

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

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) 9329 3350
Email: info@bioshares.com.au

David Blake - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph:(03) 9348 9317
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$400 (Inc.GST)
Edition Number 484 (7 December 2012)

Bioshares

7 December 2012
Edition 484

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

Tissue Therapies – EMA Clearance the Final Sticking Point

Tissue Therapies (TIS: $0.31) has just about everything it needs to start selling its wound treatment product, VitroGro, into Europe. It has manufacturing of the VitroGro protein scaffold set up (by Eurogentec), as well as the filling and production of the syringe and packaging (by Catalent). Quintiles will function as a contract sales force and Movianto will manage the distribution. There is already good awareness of the product, particularly in the UK. All the company needs now is to obtain clearance from EMA, which is the final sticking point for the company.

Device Categorisation

Tissue Therapies has finally been designated a specific device categorisation, with the VitroGro wound healing product essentially providing a scaffolding function. However, the notified body in the UK which has responsibility for assessing the company's application for regulatory approval, the MHRA, has asked that the manufacturing process (at Eurogentec) be reviewed by the EMA. We expect European approval will be received now at the earliest in August 2013 with a likely launch in Q4 2013.

Impact of Delay on US Clinical Trials

The delay is disappointing for Tissue Therapies and its shareholders. The problem for the company is that at the end of September, it was down to only $3.7 million in cash. Tissue Therapies has two options. The first is that it can slow down its spend until its product gets to market. Or, what is a more likely option, is that the company will raise more funds that will also allow it to commence a US trial in patients with venous ulcers.

The US venous ulcer trial will involve 320 patients and cost US$8 million. Patients will be treated for 10 weeks and the trial is expected to take 18 months to complete and receive results. The trial will be double blinded, which exceeds the FDA's requirements. It will be conducted primarily in the US as well as at three sites in France, three in the UK and three in Germany. It has selected the CRO to coordinate the trial (Amarex Clinical Research) and the Chief Clinical Investigator has also been chosen.

Accelerated Launch in Other Markets

While marketing approval in Europe has been delayed by at least nine months (we estimate), the company is revising its game plan to make up for lost time. In the fourth quarter of 2013, Tissue Therapies expects to launch in the UK, Benelux, Austria, Germany, Switzerland and northern Italy. It is now seeking to bring forward launches in Sweden, Denmark, Finland, Norway, Hungary, Czech Republic, Poland, Russia, Turkey and the Middle East to late 2013 or early 2014. The additional time the company now has will allow it to prepare for earlier launches in these territories.

Launch in Germany

Once the product is approved in Europe, the company will also launch a 550 patient reimbursement study in Germany, where it will receive payment for product used in the

– Tissue Therapies cont'd

trial. This is expected to generate $750,000 in revenue for the company. Tissue Therapies is seeking public reimbursement for its product in Germany in 2014. For 12 months it has been working with key opinion leaders in Germany, Austria and Switzerland.

UK Launch

In the UK, immediately after approval is received, the company will initiate a sampling program to gets its products in the hands of 72 wound care specialists who account for more than 80% of wound care expenditure in that region. The product will cost around £60 per week of treatment, with treatment lasting for around 10 weeks. It will be paid for through discretionary spending at speciality wound care clinics.

Additional Data – Reduction in Pain

Some very positive additional data has emerged from the company's European trial in 45 patients with venous leg ulcers. In this group of patients who were very difficult to treat with unhealed wounds for three years, not only did 42% of patients achieve more than 90% wound healing at 12 weeks, but there was also a severe reduction in pain associated with the wounds.

Of the six patients with severe pain before the trial, all achieved a complete reduction in pain (to no pain). Five of the seven patients with moderate pain were reduced to no pain score after VitroGro treatment, and 10 of the 15 patients with mild pain were reduced to no pain after VitroGro treatment.

Summary

Tissue Therapies has a very large market potential for its wound healing product , VitroGro ECM. The 45 patient European trial has produced strong results. The company has generated health economic data that shows a 51% saving in healthcare costs by adopting the VitroGro therapy. Its low cost has the potential to support adoption through discretionary formulary spending in some regions. The therapy also has the advantage that it can be administered by nurses as opposed to doctors or specialists, providing substantial convenience and ease of use. This is an important competitive advantage

The company appears to have prepared its markets well by building awareness across key opinion leaders and specialists on progress with the company's technology. We view regulatory risk with this product to now be low. However, the company has funding requirements to address which should arguably include a 'Plan B' should commercialisation be delayed again, following several delays over recent years in the path to market.

Investors may be able to take advantage of price weakness in coming months to increase their holdings of Tissue Therapy stock.

Tissue Therapies is capitalised at $53 million.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Mesoblast AGM Report

At this year's Mesoblast (MSB: $5.64) AGM, an important symbolic presentation was made by Dr Ben-Zion Wiener, who is Teva's representative on the board of Mesoblast. Dr Wiener started at Teva in 1975 and at one stage managed 3,000 people as head of R&D at Teva. Dr Wiener retired from Teva last December and now is a special advisor to the CEO of Teva. Addressing the meeting by phone, Dr Wiener said that he was honoured to serve on the Mesoblast board. His address, albeit brief, was designed to demonstrate a commitment by Teva to the collaboration between the two companies given Teva's expected reshaping to be announced on Tuesday (see below).

Over that last year, Mesoblast has expanded its employee base considerably, from 29 staff in June 2011 to 69 to June this year. The company now employs 50 staff overseas, predominantly in the US.

The company spent $65 million on operations in 2012, and expects to spend around the same amount this year. Of that, $20 million was spent on clinical trials and $13 million on R&D.

Maintaining Manufacturing Control Key

CEO Silviu Itescu stressed the importance to the company of maintaining manufacturing control. It allows the company to control partnering risk, to control the cost of goods, as well co-ordinate different pricing for different therapies incorporating the company's adult stem cell technology.

Mesoblast anticipates 2013 to be a busy year. It expects to start the Phase III trial with Teva in patients with congestive heart failure. Phase II trial results are expected from its Type 2 diabetes, spinal fusion and invertebral disc repair.

The Phase III congestive heart failure trial is expected to recruit up to 1,700 patients. Teva and Mesoblast are seeking to conduct only the one trial and gain approval simultaneously in the US and Europe. The company's have already reached agreement with the FDA on how the ensure consistency of product (potency) is monitored for use in the Phase III study.

IV Franchise

The Phase II diabetes trial has a major significance to the company because it is an intravenous, systemic delivery of the stem cells. Following this trial, the company expects to expand the Phase II intravenous trials next year to reverse diabetic end stage kidney disease, to treat lung diseases (such as asthma) and to treat rheumatoid arthritis. With the stem cells potentially acting on multiple pathways, it may provide a more broadly effective therapeutic against complicated autoimmune diseases such as rheumatoid arthritis.

Mesoblast is also conducting a Phase III trial in bone marrow transplantation. A Phase II trial is also underway in Singapore investigating the use of the cells in treating the eye disease wet AMD.

Cont'd over

Bioshares Model Portfolio (7 December 2012)

Company	Price (current)	Price added to portfolio	Date added
Psivida	$1.26	$1.550	November 2012
Benitec	$0.014	$0.016	November 2012
Nanosonics	$0.475	$0.495	June 2012
Osprey Medical	$0.42	$0.40	April 2012
QRxPharma	$0.75	$1.66	October 2011
Somnomed	$0.84	$0.94	January 2011
Cogstate	$0.340	$0.13	November 2007
Sirtex Medical	$12.05	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.85	$6.60	September 2007
Pharmaxis	$1.20	$3.15	August 2007
Universal Biosensors	$0.90	$1.23	June 2007
Alchemia	$0.590	$0.67	May 2004

Portfolio Changes – 7 December 2012

IN:
No changes

OUT:
No changes

Short Positions – 13 ASX Life Science Stocks

For the last three years, equity markets have tracked sideways, with the All Ordinaries Index oscillating between 4000-5000 points. For the last 16 months, this trading range has been even tighter, trading between 4000-4600 points. Markets moving sideways means investors have shorter investment expectations. With there currently being a perceived cap on equity market gains, those market conditions can also encourage short selling of stocks, particularly growth stocks trading outside of standard investment metrics.

Short selling means gaining access to stocks from owners (generally fund managers), selling the stock (first), then buying the stock back, at a lower price if all goes well, where a profit is made. The stock is then returned to the owner (fund manager), with a fee paid to the fund manager for borrowing the stock.

There are currently 13 listed life science stocks being shorted on the ASX. From a perspective of total shares on issue, Acrux has the most of its shares being shorted at 6.3% on shares on issue, fuelled by the failure to meet expectations for growth in market penetration of Axiron in the US in this calendar year.

Short Positions in ASX Life Science Stocks
3 December 2012

Company	Shares being shorted	Percentage of total shares on issue
Acrux	10,531,907	6.30%
Mesoblast	10,088,856	3.51%
Pharmaxis	7,408,081	2.40%
Starpharma	5,660,905	2.00%
Prima Biomed	6,288,810	0.59%
Sigma	6,898,552	0.59%
CSL	2,727,912	0.54%
Cochlear	3,791,160	0.50%
Genetic Technologies	967,290	0.20%
ResMed	3,154,158	0.20%
QRxPharma	130,762	0.09%
Sirtex Medical	110,566	0.02%
Allied Healthcare Group	109,920	0.01%

Mesoblast, which has a market capitalisation of $1.6 billion, has been an obvious target for short sellers. However on the flip side, it is arguably the company with the single most potential for growth of any ASX listed biotechs. A recent rumour circulated through equity markets resulted in an intra-day 18% drop in the company's share price, which was fully retraced that day. This allowed three million short positions to be covered in one day. Such trading activities deserve to be thoroughly investigated by regulators.

Two other companies with noticeable levels of short positions are Pharmaxis, with 2.4% of its shares being shorted, and Starpharma, which has 2.0% of its stock in short positions by hedge funds.

– Mesoblast cont'd

Upcoming Results

The 12 month spinal fusion results are expected shortly. Results from the Phase II 100 patient trial in invertebral disc repair are expected in mid 2013. This market is potentially 10 times greater than that for spinal fusion. Phase II results in the Type 2 diabetes trial are also due next year.

Teva Investor Meeting Tuesday 11 December

Mesoblast's partner, Teva Pharmaceutical Industries, will hold its 2012 Investor Meeting on Tuesday 11 December, 2012. The briefing is expected to detail plans for reshaping the company. Under the new CEO, Jeremy Levin, Teva plans to streamline its operations and cut costs, with a focus on targeted acquisitions to improve profitability. The company is under some pressure with sales of its leading drug Copaxone set to fall in 2013 due to increased competition.

Mesoblast is capitalised at $1.6 billion.

Bioshares recommendation: **Lighten (Take Profits)**

Five Stock Wrap

Company	Asian Ctre for Liver Dis. & Trans	**Code**	AJJ	**CMP**	$0.16	**Cap'n ($M)**	$30.2	**Cash ($M)**	$3.4	**PE**	**15.1**

- AJJ is an Australian medical business based in Singapore which listed in 2009; also operates clinics in Malaysia and Viet Nam
- Attracts liver transplant patients from the Mid East and Nth Asia, as well as locally/regionally; has performed 200 living donor transplants
- Conducted 15 transplants in FY12 (prev yr - 21); however overall patient transactions increased 4.4% to 15,685
- Posted revenue of S$24 M for FY2012 (ending Aug 31), up 15.8% and NPAT of S$2.5 M, up 56.2%
- Revenues for 14 months ended Aug 31 2010 were S$25 M
- Decline in transplants revenues in FY2012 was offset by longer patient stays for dialysis; drug sales were 15% of total revenues
- Is setting up a centre to treat blood diseases and for bone marrow transplantation (commencing H1 2013)
- Recently signed agreement with Uni Pittsburgh Med Ctre whereby UPMC will supply services to new centre

Comment: Expansion of medical services via UPMC agreement should strengthen AJJ revenue base over the long term

Bioshares recommendation: **Hold** Timing -

Company	Cellmid	**Code**	CDY	**CMP**	$0.015	**Cap'n ($M)**	$8.2	**Cash ($M)**	$1.750	**SI**	**1.3**

- CDY launched OTC product, Evolis, for promoting hair growth in June 2012; product sells for $89; now selling in 700 chemists
- CDY obtained the ex-Japan and ex-China distribution rights for Evolis (the Australian brand name) from Advangen Inc (Japan) in 2010
- Evolis competes with minoxidil, a drug originally developed as a vasodilator (for treating heart failure) and finasteride
- Evolis' advantages over minoxidil are that it is fragrant and residue free, doesn't cause initial shedding and has no reported side effects
- Progress with midkine antibody progams has been slow and constrained by funding
- CAMI103 a potential treatment for heart muscle damages; program remains at pre-clinical stage of development
- The manufacturing process for CAMI103 was refined prior to commencing large animal studies
- CAB101 completed humanisation engineering in Oct 2011; animal studies now in progress to identify key therapeutic indication

Comment: Midkine antibody program will struggle unless substantial funding is obtained; company may need to consider rationalising business to focus on OTC business

Bioshares recommendation: **Sell** Timing -

Company	Circadian	**Code**	CIR	**CMP**	$0.350	**Cap'n ($M)**	$17.0	**Cash ($M)**	$13.0	**SI**	**1.8**

- Investment holdings in Vegenics (for VEGF IP), Ceres Oncology, Opthea, Precision Diagnostics, Polychip Pharm & Syngene
- Errol Malta recently resigned from CIR board; now chairs board of Ceres Oncology
- Appointed Megan Baldwin as CEO of Opthea, which is commercialising eye disease therapeutics
- Last enrolment in (up to) 40pt Phase I study of VGX-100 (VEGF-C monoclonal antibody) expected 2013 Q1
- Phase I study is a two arm dose escalation study, in combination with Avastin (VEGF-A mab); subjects - pts with solid tumours
- Phase I safety component results expected 2013 Q1; cohort progression in mono arm up to 20mg/kg indicates safety has been good
- VGX-100 development costs have been est $3-4M manufact., IND prep $4-5M, trial, $1.5-2M
- Company estimates ongoing cash burn at $6M pa

Comment: CIR is close to a significant inflexion point for VGX-100 program; key result would be that no additive tox with Avastin is observed

Bioshares recommendation: **Speculative Buy Class B** Timing -

Company	Compumedics	**Code**	CMP	**CMP**	$0.062	**Cap'n ($M)**	$10.0	**Cash ($M)**	-$0.3	**PE**	**9.6**

- CMP manufactures and markets sleep and brain diagnostic and monitoring equipment
- Company posted loss of $2.8M for FY2012, following small profit of $0.081 M in FY2011
- Revenues fell 10% to $27.9M for FY2012
- Company cited shipment delay for weaker FY2012 performance (held sales orders of $6.4M at June 30, 2012)
- Bank debt reduced by 40% to $2M at June 30; operating cash at June 30 as $1.4M compared to -$0.26M a year ago
- AUD exchange rates have been a negative for CMP in recent years
- CEO and founder David Burton owns 61% of CMP; this holding sits as an investment negative

Comment: CMP's major challenge is to grow earnings (profits), something at which it has struggled to do for many years

Bioshares recommendation: **Sell** Timing -

Company	Ellex Medical Lasers	**Code**	ELX	**CMP**	$0.195	**Cap'n ($M)**	$16.6	**Cash ($M)**	$1.20	**PE**	**15.8**

- Ellex manufactures and markets lasers used for treating and diagnosis of cataract, glaucoma, refractive and retinal conditions
- FY2012 sales increased by 10% to $47M; Australian sales rose 85% to $11.3M; NPAT rose 250% to $1.05M; Gearing ratio is 25%
- 72% sales are direct (FY2011 - 73%); balance through distributors
- Seeking to grow sales with new super-fast Ellex 2RT laser for treating early age-related macular degeneration (retinal rejuvenation)
- Completed a 50 pt pilot study in early age-related macular degeneration (AMD) in 2011; results to be published soon
- Conducting randomised trial in early AMD in Sydney and Melb. Intends to open two more sites
- Drug therapies target later stage AMD; lack of treatment options in early AMD offer market opportunity for ELX
- ELX will apply a per-procedure fee model to retinal rejuvenation market; 2RT laser is made without dependence on third parties

Comment: Ellex's return to profitability and longer term growth plans using recurring income model are positive

Bioshares recommendation: **Hold** Timing -

Notes: PE - Price/Equity ratio SI - Survival Index (refer to Bioshares 480 for explanation)

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: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$400**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$630	2-3 email addresses
	$855	4-5 email addresses
	$1090	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____