ISSN 1443-850X

In this edition...
It's not exactly been a good news week for biotech this week. Tissue Therapies continues with its waiting game with the UK's MHRA as to whether VitroGro fits under Device Rule 8 or Device Rule 13. But patience is a virtue and the company is not sitting on its thumbs, with planning for trials in the US well under way as well as eyeing opportunities in Turkey, the Middle East and Latin America.
Impedimed has struggled to commercialise its early stage lymphoedema assessment tool. While clearly an improvement on the bucket of water and tape method approaches, the evidence of superiority has never been quite enough to satisfy US health insurance companies.
Bioniche improved sales in FY2012 but its efforts commercialise is E.coli cattle vaccine have slowed considerably.
Companies Covered: BNC, IPD, 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)	-16.2%
Cumulative Gain	**190%**
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)
$375 (Inc.GST)
Edition Number 472 (14 September 2012)

Bioshares

14 September 2012
Edition 472

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

Tissue Therapies – A Matter of Patience

Tissue Therapies (TIS: $0.42) continues to wait on the UK's MHRA to decide which rule (either Device Rule 8 or Device Rule 13) applies to its wound healing product, VitroGro ECM. This waiting continues despite a 30 day period allowed for the assessment to take place. The ruling is required before a final CE Mark approval can be given.

VitroGro ECM is a synthetic protein scaffold that on application to venous ulcers or diabetic ulcers (two very common chronic wounds), supports or mobilises the growth and proliferation of cells necessary to form the extracellular matrix. The technology was invented at the Queensland University of Technology, which is entitled to a 4% royalty total income from sale of Tissue Therapies' products relating to its patents (in the territories where the patents have issued).

Ready for Sales

Tissue Therapies is set to immediately begin selling VitroGro ECM, with many of the necessary warehousing, logistics, inventory and sales systems ready and in place for a staged European roll-out.

However, the company will use internal resources for its beachhead sales effort, prior to the hiring of sales staff.

The company has prioritised the UK and Germany to be its primary launch territories in Europe once it has a received a CE Mark for Vitro Gro ECM. The UK accounts for 5% of the global wound care market with Germany accounting for 10%.

UK Strategy

In the UK, Tissue Therapies plans to begin sales of VitroGro ECM by targeting 72 specialist wound care clinics which account for 80% of NHS spending on chronic wounds. The company senses that wound care clinicians in the UK are keen to access a product that has the potential to make a marked difference in treating leg and foot ulcers.

The NHS calculated that greater than £1 billion was spent on wound care in 2009. The problem with current treatment approaches is that they are not supported by health economic data with either none or poor clinical evidence.

As a rule of thumb, 40-50% of ulcers are healed using current standard of care by 20 weeks. VitroGro ECM is capable of lowering that time to 12 weeks.

In a 44 patient study, Tissue Therapies showed that VitroGro ECM achieved complete healing in 34% of patients and more than 90% healing in 43% of patients at 12 weeks of treatment, in a group of relatively older patients with venous ulcers.

Tissue Therapies will be relying on the discretionary spending powers of specialist wound care clinics to pay for VitroGro ECM product, in addition to presenting economic

Cont'd over

arguments to Primary Care Trusts (the bodies which manage hospital and health care organisations in the UK).

German Strategy

Tissue Therapies will target the top ten wound care clinics during its launch phase in Germany but not on a reimbursed basis.

The company will prepare guideline documentation for gaining reimbursement by German private health insurers by the 2013 Q3. German private health insurers cover 10% of the population.

Tissue Therapies is working to gain reimbursement from public health insurers of VitroGro ECM in Germany under a new regulatory mechanism (137E), a process designed to accelerate the introduction of new technologies. The public health insurers cover 90% of the population.

The application will follow a 550 patient reimbursement study and will be reviewed by the Gemeinsamer Bundesauschuss (GBA). Tissue Therapies is anticipating reimbursement acceptance in 2014 from this agency.

A benefit to Tissue Therapies is that it will be paid by the German agency for the VitroGro ECM product used in the reimbursement study.

US Strategy

Tissue Therapies' commercialisation plans for North America have lagged European efforts, but planning is well under way to commence two key trials in 2013. A venous ulcer trial in 320 patients is budgeted to cost US$8 million and take 18 months to complete. A diabetic ulcer trial enrolling 380 patients is budgeted to cost US$9 million and is expected to also take 18 months to complete.

The trials will be randomised and double-blinded, with a saline placebo administered. Tissue Therapies has decided to add the double-blind parameter despite not being required by the FDA to do so. This should strengthen the evidentiary power of the results.

Tissue Therapies is anticipating a 12 month regulatory review period, followed by a three month reimbursement assessment by CMS, ultimately positioning the company to begin product sales in 2015. Somewhat advantageously, the single reimbursement assessment with the CMS also means that complex and lengthy coverage decisions with private insurers will not be required.

VitroGro ECM is categorised by the FDA as a biologic product. One very important advantage to having a biologics classification in the US, is that unlike devices, the FDA does not place a limit on the number of sites a product sponsor can recruit from.

Tissue Therapies has identified for 30 clinics in the US (plus 10 more for the diabetic ulcer trial) for the trials. It will also include three in the UK, three in Germany and three in France. The three French sites will also be used for the French reimbursement purposes, which require studies on French subjects for reimbursement.

The company has yet to make decisions on where it will have VitroGro ECM packaged (fill and finished), where product will be warehoused and how it will structure its sales and marketing capability in North America.

Other Regions/Countries

In addition to strategies for commercialising VitroGro ECM in Europe and the USA, Tissue Therapies is currently conducting scoping studies on selling the product in Turkey, South America (Chile, Brazil and Mexico) and the Middle East, with a CE Mark receipt underscoring prospective efforts in those regions.

A strategy for the Japanese market, at 11% of the global wound care market, is in place. However, the time it will take to access the market is subject to an expensive and lengthy regulatory review process.

The company has, through existing manufacturing and logistics providers, the ability to ship product anywhere in the world. However, it is considering whether if some countries, a fill and finish facility will be necessary.

Summary

Tissue Therapies' goal is to be cash flow neutral by the end of CY2013. Clearly, that position is contingent on receiving CE Mark approval and securing sales and growing sales in the UK. Revenues of note will not begin from Germany until 2014, once reimbursement from the statutory health insurers, which cover 90% of the German population, is secured.

Tissue Therapies is very close to moving from being a R&D stage company to a revenue generating global bio-medical business. Although its initial revenues will in all likelihood be very modest for the first few quarters, the evidence that VitroGro ECM will be a clinically sought after product should become apparent one way or another in its first year of sales.

Tissue Therapies held cash of $5.1 million at June 30, 2011. However, it also completed a private placement in August, raising $1.1 million from an un-named South American investor. This capital raising is, in our view, an indicator of future potential support for the company.

The key investment point for Tissue Therapies investors is that the company is on the cusp of selling a medical product with typically attractive margins into markets where the current standard of care is poor.

Tissue Therapies is capitalised at $72 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Impedimed – Changes Underway With New CEO

Impedimed's (IPD: $0.15) new CEO, Richard Carreon, started with the company in July. As with many CEO changes, the new CEO often makes many changes, particularly if success has been elusive, which is the case for Impedimed.

Carreon is no different and was in Australia this week explaining a number of changes for the company, discussing issues confronting the company but also describing some of the attractive features of the company's bioimpedance assessment technology.

Carreon has substantial experience in commercialising medical devices. He spent just under 12 years at **Medtronic**, taking FDA approved products through the market launch path. He also has considerable experience in reimbursement, which is a vital aspect to the success of Impedimed.

Carreon first turned down the job of CEO at Impedimed but soon changed his mind after visiting an oncology clinic in the US and seeing the impact lymphedema has in women who have undergone breast cancer surgery.

Particularly important is that lymphedema is fully preventable in women following a mastectomy. The current "gold" standard is using a tape measure, followed in second place by placing your arm in a container of water and measuring how much water is displaced. The problem with these methods is that they pick up the swelling in the arms too late. Impedimed is seeking to make its more sensitive bioimpedance assessment tool the new standard of care.

Another one of the appeals of Impedimed to Carreon is the opportunity to sell to numerous different classes of physicians. Each woman with breast cancer sees between eight to 11 different doctors over the first five years. This is a key point for Carreon as it offers multiple selling points. A women diagnosed with breast cancer now has a 90% survival chance at five years.

Major Effort to Slow Cash Burn

A major change that has taken place at Impedimed is that the company has reduced its burn rate by 31%. By the start of August Impedimed had reduced its staff count from 42 to 29, with an expansion into Germany and Japan now delayed.

Change to Selling Model

In February 2011, Impedimed decided to start offering its device to its customers at no charge, but selling consumables. This was to get around the capital acquisition decision process within hospital groups.

Targeting ACOs – An Excellent Fit?

Impedimed is targeting Accountable Care Organisations (ACO), of which there are around 160 now in the USA. Guidelines for the ACO model were released in 2011. The ACO model seeks to tie payments to improved quality of care and can be based around a set fee for a particular therapy.

Impedimed's product is potentially an excellent fit for ACOs, where better patient outcomes and cost savings to the payor can be achieved through earlier detection and prevention of lymphedema using the Impedimed technology.

Quality not Quantity

Impedimed under Carreon will be targeting quality not quantity. It is looking to train key centres as reference sites. An example of this is the ACO **Kaiser Permanente** which is now evaluating Impedimed's L-Dex system at two of its 42 hospitals.

The oncology specialist group **21st Century Oncology** is also evaluating L-Dex. This group operates 94 centres in the US and six centres are using the L-Dex product. At these centres, all patients will be baselined with L-Dex prior to breast cancer surgery.

The evaluation will look at the most effective way to utilise the product, looking at whether high risk patients need to be monitored more closely than those at low risk of lymphedema.

Impedimed will receive feedback from these two groups on a quarterly basis.

Category I Challenge

The L-Dex product, used to aid in the detection of lymphedema, currently has Category III reimbursement status. However payment is not guaranteed and often does not occur under this reimbursement code. Impedimed will encourage physicians to continue to seek reimbursement, even if it is rejected, because having a growing list of rebuttals will help the company argue its case to move to a Category I code. Impedimed needs to receive a decision on its Category I classification by 1 July 2015, otherwise it will lose its Category III code, which is a temporary code for experimental devices. The company will also look to get reimbursement at local and regional levels.

Carreon said Impedimed has a great intellectual property position with 28 patent families and has the first mover advantage. In *Bioshares* view the issue for Impedimed is that it needs to build the market for its product.

Clinical Evidence Challenge

According to Carreon, Impedimed does not have clinical evidence of its technology in the right areas. To rectify this it is getting high quality groups to act as reference sites, as indicated above. In the short term it will leverage existing data.

In the medium term it will expand its data to fill the gaps that payors have. And in the long term it will conduct trials to build the evidence on clinical efficacy and cost savings to payors.

At the moment the company can still not accurately state the incidence of lymphedema following surgery, only saying it is somewhere between 13%-47%, which are figures based on a paucity of data collected by other researchers over the years.

Comments

The change in Impedimed's selling model, from selling through operating leases to supplying the product at no charge under a

Cont'd over

Bioshares Model Portfolio (14 September 2012)

Company	Price (current)	Price added to portfolio	Date added
Nanosonics	$0.490	$0.495	June 2012
Osprey Medical	$0.37	$0.40	April 2012
QRxPharma	$0.69	$1.66	October 2011
Mayne Pharma Group	$0.350	$0.435	September 2011
Somnomed	$0.81	$0.94	January 2011
Phylogica	$0.028	$0.053	September 2010
Biota Holdings	$0.72	$1.09	May 2010
Tissue Therapies	$0.42	$0.21	January 2010
Bionomics	$0.32	$0.42	December 2007
Cogstate	$0.300	$0.13	November 2007
Sirtex Medical	$8.07	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.63	$6.60	September 2007
Pharmaxis	$1.09	$3.15	August 2007
Universal Biosensors	$0.73	$1.23	June 2007
Alchemia	$0.565	$0.67	May 2004

Portfolio Changes – 14 September 2012

IN:
No changes

OUT:
No changes

Bioniche Reports FY2012 Results

Canada-based Bioniche (BNC: $0.52) registered an 8.9% lift in sales for the year ended June 30, 2012, from the previous year. Sales for FY2012 were C$29.8 million, compared to $27.3 million for FY2011. Sales in FY2010 were C$27 million, indicating the latest year's results to be a welcome upturn for the Bioniche's largely veterinary focused commercial operations.

Bioniche recorded a loss for the year of C$24.2 million, a 93% change from the C$12.5 million loss recorded in FY2011. The worsening in the company's net result can be attributed in part to a decline in licensing and research collaboration income and the incurring of financial expenses of C$3 million.

The company's commercialisation plans for it *E.coli* cattle vaccine, Econiche, have been stalled, both in Canada and in the US. The company cited a lack of mandatory vaccination in Canada as an impediment. The US Department of Agriculture has also sought additional requirements for the vaccine, which Bioniche has considered as not being 'justifiable in terms of cost and time for a conditional license.'

Bioniche did receive a Special Treatment Certification for Importation of Econiche into the UK in August, 2012. However, the company's Animal Health and Food Safety Vaccine manufacturing facility is currently undergoing validation to meet GMP requirements. The company expects this process to take another 12-18 months to complete, as stated in its August announcement. However, Bioniche's CEO Graeme McCrae said validation would take 6-12 months to complete in the company's annual results announcement.

Bioniche is capitalised at $54 million.

Bioshares recommendation: **Sell**

– Impedimed cont'd from page 3

Product Supply Agreement has resulted in sales falling by 27% from $3.7 million in 2011 to $2.7 million in FY012.

The company has a reasonable level of cash resources at this stage, with $14.5 million in cash at the end of June, although it has a high spend rate. The loss for FY2012 was down to $12.3 million, from $14.8 million in 2011.

Impedimed's performance to date illustrates that it is a long, hard and expensive road to introduce a new diagnostic product into a major market and to change healthcare practices. Impedimed has many challenges ahead, including gaining further data to argue the benefits of its technology. It has only 185 of its devices placed in the US, with only 43 devices placed in the last year. Regrettably, there are no signs of any acceleration in uptake of its product.

Summary

We have changed our recommendation on Impedimed to Speculative Hold Class B, recognising that challenges in front of the company are significant, which coupled to the company's longer term cash requirements, may see the company struggle to raise new funds.

The company's share price will respond to two things: either revenues increase and demonstrate a trend increase or another company solicits a bid for Impedimed.

Caution should be adopted with Impedimed shares while demand for the stock is weak and sentiment towards the company is negative, with further price weakness not out of the question.

Impedimed is capitalised at $27 million.

Bioshares recommendation: **Speculative Hold Class B**

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, Circadian Technologies, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Genetic Technologies, Calzada, Bioniche, Atcor Medical, Invion