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In this edition...
The approval of Tissue Therapies' VitroGro has been delayed by European regulatory bodies. The issue revolves around classification of VitroGro as a device, adding at least 30 days to the process. There is a consistent trend for ASX listed life science companies to experience delays or setbacks, and the lesson for investors is to factor in delays in the regulatory process from the earliest stages.
Universal Biosensors has posted encouraging half year results, with the blood glucose testing arm of its business now profitable.
What can investors deduce from two companies that share two directors? To this end we compare Genetic Technologies and Impedimed. Starpharma has closed yet another collaboration, this time with Nufarm, in the ag chemicals space.
Companies Covered: GTG, IPD, SPL, TIS, UBI

	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)	-20.3%
Cumulative Gain	**175%**
Av. annual gain (11 yrs)	**17.8%**

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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

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Bioshares

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

Delay in Europe for Tissue Therapies' VitroGro

Tissue Therapies (TIS: $0.395) has been informed that the approval of its wound healing therapy, VitroGro, in Europe will be delayed. This is because the British Standards Institute (BSI) needs to work out which device classification is appropriate for the therapy to be assessed under for marketing approval in Europe.

The BSI has referred the VitroGro classification assessment to the MHRA (Medicines and Healthcare products Regulatory Agency) in the UK to determine which medical device rule is appropriate. VitroGro will either be assessed under Device Rule 8 (a device which has the potential for implantation) or Device Rule 13 (a device which has the possibility of biologic action).

The important issue for investors is that there is no question whether VitroGro is a device or not. There should be no need to conduct any additional trials according to CEO Steven Mercer, with the therapy being assessed as a device and not a drug. However there will be at least a 30 day delay, plus the time it takes for Tissue Therapies to respond to questions.

The 8th Regulatory Set Back or Delay

Investors in biotech companies in Australia should now expect that the path through the regulatory approval process to be rarely linear. Tissue Therapies is the seventh ASX-listed company in the last three years from a group that has experienced commercial delays due to regulatory processes. Other companies that have experienced setbacks/delays are **ChemGenex Pharmaceuticals** (acquired by **Teva Pharmaceutical Industries**) with its cancer drug Omapro in the US, **Pharmaxis** with Aridol in the US and Bronchitol in Europe, **Mayne Pharma** with SUBACAP in Europe, **Alchemia** with fondaparinux in the US, **pSivida** (Alimera Sciences) with Iluvien in the US and QRxPharma in the US with MoxDuoIR. Only **Acrux**, which partnered with Eli Lilly, received approval on first pass through a regulator.

The point with all of these examples is that each company has persisted (in QRxPharma's case it will most likely persist) with gaining marketing clearance with regulators and in most cases the companies have or most likely will succeed in getting their products into major markets.

Omapro has recently being refiled for approval with the FDA. Alimera Sciences has indicated that it will re-file Iluvien in the US for patients with chronic DME, Pharmaxis was successful in getting Aridol approved in the US, albeit following a 10 month delay, and it was successful in having the European decision for Bronchitol, for the treatment of cystic fibrosis. reversed.

Mayne Pharma was also successful in having European regulators change their assessment, with the MHRA now viewing SUBACAP as approvable. Alchemia eventually ob-

Cont'd over

Universal Biosensors – Glucose Business Turns Profitable

Universal Biosensors' (UBI: 62.5 cents) glucose testing products business has just become profitable. In the first six months of this year, the business delivered a gross margin of just under $2.8 million, or 22% of its $12.5 million in revenue from making glucose strips, from its one cent per strip (approximately) it receives for each test strip its partner **Lifescan** makes, and from R&D work it is undertaking for Lifescan in making another glucose testing product.

Universal Biosensors' manufacturing revenue from the glucose strips was $9.5 million, up 69% from $5.6 million in the previous corresponding period (pcp). The acceleration in strip volume is a direct result of the US launch which occurred in January this year.

The newer OneTouch Verio IQ product in the US has also been launched in a number of European markets as well. The OneTouch Verio IQ is the third product iteration following the OneTouch Verio launched in 2010 in The Netherlands in 2010, and the OneTouch Verio Pro launched in Europe in 2011. The one cent per strip service fee was also up, to $1.0 million for the half year, compared to $0.2 million in the previous corresponding period.

Overall, UBI generated sales for the half of $14.7 million (up from $6.3 million in the pcp). The company's net loss was also down, to $3.4 million (compared to a $7.9 million loss in the pcp).

UBI has had three strong quarters for manufacturing its glucose strips. The company has addressed its disappointing first quarter results in this calendar year, where the company made a loss from making the strips. UBI has worked on improving its manufacturing efficiencies, increasing its margins by 10%. It has also identified further improvements which should see better margins still in coming months.

In a conference call to investors, CEO Paul Wright said the company was now reinvesting its profits from its first product into its second product, the blood coagulation test PT/INR. This test has been partnered with Siemens and is expected to be launched by the end of September 2013.

UBI will retain exclusive manufacturing rights to this product. The profit will be used to help titrate correct warfarin dosage levels for patients. The test will compete against the market leading test, CoaguChek from **Roche**, will commands around a 75% market share.

UBI has achieved feasibility with two more undisclosed coagulation tests in June and July of this year as part of its Siemens partnership.

At the end of June UBI retained $14.7 million in cash. The company has a market capitalisation of $94 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

– Tissue Therapies cont'd

tained approval for its generic fondaparinux drug in the US although it took 20 months longer than expected. QRxPharma, which received a Complete Response Letter from the FDA in June, should, in our view, get its drug approved in the US, but there will be some more hurdles to cross before it does.

Mercer said that while gaining advice from key opinion leaders on VitroGro, there was very keen interest expressed by these clinicians in seeing VitroGro available on the market.

Tissue Therapies will not put any additional sales people onto its payroll until its wound healing device gains CE Mark clearance.

Tissue Therapies is capitalised at $71 million. It had $5.1 million in cash at the end of June.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Genetic Technologies and Impedimed: A Comparison

Genetic Technologies recently appointed to its board the former CEO of Impedimed, Greg Brown, joining fellow Impedimed board member, Mel Bridges on the same board. Brown was replaced as CEO of Impedimed by Richard Carreon on July, 10, 2012.

The appointment serves as a trigger for a comparison of the two companies.

Brown is well suited to serving on the Genetic Technologies board because he brings valuable experience gained from the selling of diagnostic products as well as recently, hard-won experience in the roll-out of Impedimed's L-Dex U400 device (a product used as an aid in the early detection of lymphoedema.) His knowledge of the women's healthcare market, coupled to his extensive links can be applied to the marketing of Genetic Technologies' Brevagen product, a test which combines a genetic risk score with a clinical measure known as the GAIL score. The test is used to determine susceptibility to breast cancer in women who have not inherited a harmful BRCA1 or BRCA2 mutation.

Sales in the US of both products have been at low levels and slow to build while both companies have worked to gain coverage from healthcare organisations that ultimately pay for the respective tests.

An Obvious Question

Given a shared focus on the US and on diagnostic/assessment tools applied initially in women's health, an obvious question for investors is what is the likelihood of the two companies merging?

The fact that the two companies now share two directors does not prove that a merger is in the works. However, the sharing of two directors would certainly allow for cross fertilisation of ideas and business strategies to occur.

What is more relevant is the extent to which both companies share customers, at least for the lead products they are commercialising in the US.

The fact that both companies have a major focus in the USA is an important point, all the more so since Impedimed has recently opted to wind back its commercialisation efforts in Europe, presumably as part of an attempt to preserve cash, and no doubt influenced by sustained, weak market conditions across Europe.

However, the customers served by both compa-

Cont'd over

A Comparison of Genetic Technologies and Impedimed

	Genetic Technologies (GTG)	Impedimed (IPD)
CMP ($)	$0.11	$0.19
Capitalisation ($M)	$51.1	$34.4
Latest Cash	**$8.9**	**$15.5**
Date Listed (ASX)	29/08/2000 [Duketon Goldfields acq. Genetype AG]	24/10/2007
Listings	ASX; NASDAQ (from 2005)	ASX
Business Locations	Melbourne, VIC	Brisbane, QLD
	Charlotte, NC	San Diego, CA; Rochester, NY
Staff [EFT}	61	29 (down from 42)
CEO	Dr Paul MacLeman	Richard Carreon (from 10/7/12)
Chair	Mel Bridges	Cherrel Hirst
Board	**Mel Bridges**	**Mel Bridges**
	Greg Brown	**Greg Brown**
	Huw Jones	Michael Pannacio
	Malcolm Brandon	Jim Hazel
	Mervyn Cass	Martin Kriewaldt
	Tom Bonvino	Cherrel Hirst
Shares (M)	464.8	181.2
Top Shareholder	Mervyn Jacobsen (29.36%) [Resigned as director 12-12-2008]	Starfish Ventures (13.4%)
Receipts (Cash Flow) ($M)		
FY2009	$9.76	$3.38
FY2010	$9.68	$3.67
FY2011	$18.94	$3.82
FY2012	$6.30	$2.90
NOCF (Cash Flow) ($M)		
FY2009	-$5.03	-$11.79
FY2010	-$4.22	-$10.39
FY2011	$2.24	-$11.30
FY2012	-$7.72	-$11.80
Current Lead Product	**Brevagen [Acq. 2010]**	**L-Dex U-400**
Form of Technology	Genetic risk score combined with clinical score (GAIL score)	Bioimpedance spectroscopy
Use	To determine susceptibility to breast cancer in women who have not inherited a harmful BRCA1 or BRCA2 mutation	An aid to the detection of sub-clinical lymphoedema
Approvals - USA	CLIA-wavered lab test; Authorised in 48 US states; NY and Florida pending	FDA approved [arm in women, Oct 2008; legs, men and women, Nov 2011]
Reimbursement Status	Updated CPT Code Stack	CPT Category III
Credentialling/ Coverage	13 million covered lives	23.4 million covered lives
Marketed to:	High Value MD/OBGYNs, women's health clinics, also DTC awareness	Surgeons (breast and other cancers), radiation oncologists, therapists
Other Assets	Non-coding DNA patents (IP assertion program)	Technology is applicable to lymphoedema that arises from the treatment of other cancers
	Medical Testing and Profiling Services (Sales $4.6 M - FY11)	

nies for Brevagen (GTG) and L-Dex (IPD) are not the exactly same. Brevagen is marketed to women's health clinics; L-Dex is marketed to breast surgeons, radiation oncologists and therapists. What they do share is a focus on preventative care within the broader area of breast cancer. There were an estimated 230,00 new cases of breast cancer diagnosed in the US in 2011, suggesting that breast cancer is a source of sizeable outlays within the US healthcare system.

A major synergy is possible where a merged entity can build strong marketing messages that link several preventative women's health care products and which are directed to women or through women's health advocacy to the healthcare organisations which ultimately pay for such tests.

Another area in which synergies could be obtained is in the back office where interactions are managed with US health care organisations and insurance bodies (i.e. preferred provider organisations, health management ogranisations, for-profit and not-for-profit health insurers). In the US, medical product companies must often establish call centres to assist with coding and payment enquiries from clinics and surgeries.

A standard saving generated by mergers is from where corporate overheads can be trimmed, with board fees, office and accommodation costs are typical expenses that can be reduced. A general argument in favour of mergers is where savings from corporate overheads can be achieved and then re-directed towards sales activities. In a sales establishment phase, investment in marketing is crucial to future success.

Nasdaq Listing

Genetic Technologies is a dual-listed entity, being listed on the ASX and the NASDAQ. A merger of two US-focused businesses into an already ASX and Nasdaq listed entity may increase the appeal of a merged entity to investors who prefer to trade on the Nasdaq.

Other Points to Note

– Mergers are subject to shareholder approval which make the views of the largest shareholders relevant. The largest shareholder of Genetic Technologies is Mervyn Jacobsen, who holds a 29.36% stake, as of 4/4/2012. His holding decreased from a 42.13% stake as of 22/3/2005, the date of his previous Substantial Holder notice. The largest shareholder in Impedimed is Starfish Ventures, a venture capital firm, with a 13.4% stake. How these investors might view a proposed merger is an unknown.

– The likelihood of both companies raising capital in the medium term is high. The companies share the same Survival Index measure of 1.2, meaning that they have cash sufficient to support 1.2 years of operations based spending and receipted income for the latest financial year.

– Both Genetic Technologies and Impedimed continue to seek data to validate or expand the validation of their respective preventitive health care diagnosic or aid to diagnostic tools.

– Genetic Technologies, while focused on the roll-out of Brevagen, manages an IP assertion program that continues to yield income for the company. It manages a DNA profiling and DNA services business and also sells other medical tests. It is looking to expand its offerings across a spectrum of cancer diagnosis and treatment modalities. Genetic Technologies recently received a CE Mark for Brevagen, permitting the company to sell the test in Europe.

Summary

A comparison of Genetic Technologies and Impedimed reveals that the two companies share a focus on preventive health and women's health as well as a territorial focus on the US. Both companies have advanced to the stage of achieving a degree of coverage from US healthcare payors but have yet to see their investments in sales and marketing for their lead products to date generate significant sales or profits.

Investors can note that the CEO of Genetic Technologies, Paul MacLeman, said in the company's Annual Report for 2011 that "... we remain on an acquisition footing and are actively assessing new products that fit with our sales force call patterns and strategic fit."

Mergers are more likely to succeed where a solid business case can be made for changes to the management of assets or allocation of resources which increase the prospects for positive shareholder returns.

A merger between Genetic Technologies and Impedimed is in our view, an event that is very likely to be considered by both companies because a merger could be founded on strong commercial arguments.

Bioshares recommendations:
GTG – Spec Buy Class A
IPD – Spec Buy Class A

Bioshares

Bioshares Model Portfolio (10 August 2012)

Company	Price (current)	Price added to portfolio	Date added
Nanosonics	$0.480	$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	$0.69	$1.09	May 2010
Tissue Therapies	$0.40	$0.21	January 2010
Bionomics	$0.27	$0.42	December 2007
Cogstate	$0.250	$0.13	November 2007
Sirtex Medical	$7.30	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.65	$6.60	September 2007
Pharmaxis	$1.13	$3.15	August 2007
Universal Biosensors	$0.63	$1.23	June 2007
Alchemia	$0.555	$0.67	May 2004

Portfolio Changes – 10 August 2012

IN:
No changes

OUT:
No changes

Starpharma Expands Collaboration with Nufarm

Starpharma Holdings (SPL: $1.46) has signed a commercial collaboration with **Nufarm**. Nufarm makes and sells a range of crop protection chemicals. The companies will be using Starpharma's dendrimer chemistry to deliver agrochemicals with improved properties.

Starpharma has partnerships with other industry players in the crop protection area and it also has its own internal programs. Its lead internal program is with the Roundup herbicide, which is now off patent, and Starpharma has already achieved successful improvements to that product.

The types of properties that can be potentially improved using Starpharma's dendrimer chemistry include greater solubility of crop chemicals, which have included up to 70% hydrocarbon solvents. The addition of Starpharma's chemistry may improve the handing safety and volumes of the chemicals, reduce solvent residues, increases activity, potentially improve adhesion properties of the chemicals to the plants, and may change soil penetration properties.

Vivagel BV Trials

Starpharma's lead clinical program is its Phase III trials underway with Vivagel for the treatment of bacterial vaginosis (BV). The company is conducting two Phase III trials with around 220 women in each trial.

There are some important aspects to these trials. The first is that recruitment has been very quick, with the first trial fully recruited and the second trial more than 70% recruited. This is an important factor which reflects commercial demand for a product.

The second point is that results from the Phase II trial in 132 women delivered a very clear and effective result. At the end of treatment, 74% of patients achieved a clinical cure, and 46% at two to three weeks post treatment were clinically cured. The results were clearly significant and there should be a high likelihood of positive results from the current Phase III trials, given the therapy will be unchanged from the Phase II arm.

Special Protocol Assessment

The third positive aspect for Starpharma is that it has received a Special Protocol Assessment from the FDA, which is a legally binding document that states Starpharma's product will be approvable if it achieves the targeted clinical outcomes.

The likely reason for the strong demand to participate in the BV trial is that existing systemic antibiotics have some poor side effects, including secondary infections such as candida, and stomach toxicity, and cannot be taken with alcohol.

Starpharma has the commercial scale manufacture of Vivagel secured with a third party manufacturer. Results from the current Phase III trials are expected by year's end. If successful, the company will file a New Drug Application with the FDA, and it will then seek and negotiate a sales, marketing and distribution deal.

Starpharma is capitalised at $406 million. It had $42.8 million in cash at the end of June.

Bioshares recommendation: **Speculative Hold 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. 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