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In this edition...
Global financial markets are doing it tough, so it comes as something of a surprise to see several local biotechs raise $150 million in the last month. However, capital has been raised because the funds are being directed towards later stage development goals.
Mesoblast will now move its cardiovascular product Revascor into Phase III trials, now that the full data from its Phase II trial has been released. Impedimed and Biota are two companies with important news to post in the next two weeks. We also discuss the range of opportunities being addressed by Benitec's gene silencing technology, with the company's freshly articulated development plan a pleasing step forward. And Mayne will look at improving efficiencies.
The Editors
Companies Covered: BLT, BTA, IPD, MSB, MYX

	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 - May '10)	49.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 now commenced	-24.5%
Cumulative Gain	**218%**
Av. annual gain (10 yrs)	**21.2%**

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Bioshares

25 November 2011
Edition 434

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

Capital Inflows Support Later Stage Biotechs

As high volatility dominates global financial markets, several later stage biotech companies in Australia are funding their programs with relative ease. In the last month, four companies have raised $151 million, including the $80 million to be raised by Pharmaxis which will now be fully underwritten by Wilson HTM.

It is positive to see financial execution risk, as discussed in *Bioshares* 432, being addressed, most importantly for Pharmaxis and Alchemia. Bell Potter, following its acquisition of Southern Cross Equities, has become the third dominant investment back active in the Australian life sciences sector, joining Wilson HTM and RBS Morgans.

For Pharmaxis, it allows the company to fund the launch of its cystic fibrosis drug in early 2012 in Europe. The company will now have around $110 million in funds. For Alchemia, it allows the company to start its long awaited Phase III trial with HA-Irinotecan in 390 patients with colorectal cancer. For both companies, it should be sufficient to bring them profitability. However, Alchemia has announced its intention to spin out its oncology assets into a separate company by the end of next year.

There was very strong interest in Starpharma's capital raising with a new investor from Asia taking a significant portion of the placement. The funds will be used to complete its Phase III studies in both the treatment and prevention of bacterial vaginosis, as well as advancing multiple other uses with its novel chemistry scaffold technology.

Both the Phosphagenics and Starpharma capital raisings have the trademark of the 2007 Acrux capital raising, where the funds were raised predominantly to progress a clinical candidate to the end of Phase III trials and ready for a new drug application submission. In 2007, Acrux raised $22.5 million to fund the Phase III development of Axiron at $1.60 per share, which has delivered an excellent return for those investors.

And for most of these companies, there is a good chance these capital raisings will place a floor under the respective share prices, particularly for Pharmaxis and Alchemia, where investors have been cogniscent of their weak financial positions.

Major capital raisings in the last month

Company	Method	Investment bank	Amount raised	Discount to closing price	Price	Additional
Pharmaxis	NRRI	Wilson HTM Corp.	$80 M	19%	$1.05	-
Starpharma	Placement	Bell Potter/Shaw	$32 M	0%	$1.075	$3M SPP
Phosphagenics	Placement	Bell Potter/RBS	$24.1 M	17.6%	14 cents	$3M SPP
Alchemia	Placement	RBS Morgans	$15 M	12.7%	24 cents	$3M SPP

total: $151 million

Benitec – Building Proof of Concept Data in Four Diseases

Benitec gave a clinical investigator group update recently on its gene silencing programs. As an emerging therapeutic drug class, RNAi has under-delivered, largely due to delivery issues. However Benitec believes its approach, using a DNA-directed RNAi, is superior and is advancing four core programs to prove its case and in the process, aiming to deliver substantial shareholder value.

Core Programs

Benitec's four core programs are in:

- Non-small cell lung cancer (NSCLC), which accounts for about 85% of all lung cancers
- Cancer-associated pain
- Hepatitis B
- Oculopharyngeal Muscular Dystrophy

Three Elements to RNAi Drug Development

There are three parts to the process of developing an RNAi drug candidate. The first is to know or find the target. The second is to fine the gene that you want to silence. And the third is to build the RNAi construct.

Lung Cancer

In the NSCLC program, the target, the BetaIII tubulin protein has been shown to be associated with chemotherapy drug resistance in NSCLC i.e. those patients with higher levels of the BetaIII tubulin protein had a worse response to chemotherapy and a lower overall survival.

Professor Maria Kavallaris and her team at the University of NSW believe they have found the right gene, that if 'knocked down' or suppressed, using Benitec's gene silencing, will better expose the cancer cells to chemotherapy.

Benitec has made one of its gene silencing constructs, called shRNAi (short hair pinned RNAi) to block this gene. In initial studies in mice, the team has shown it can knock down the gene in human lung cancer cells grafted onto mice.

The beta-III tubulin protein is also expressed in other cancers, including breast and prostate cancer, and glioblastoma.

The next step is to more mice studies, and then more mouse preclinical studies in combination with chemotherapy to see whether chemosensitivity has been improved.

Cancer-associated Pain

Benitec is making good progress on a potential RNAi therapy for the treatment of chronic pain, particular that associated with cancer. It has looking at two possible targets, and has selected an enzyme called PKCgamma which it believes is an excellent target. In a rat model of neuropathic pain, it has achieved an 86% hit rate to block pain by turning off the PKCgamma enzyme. Turning this off has also shown to overcome morphine tolerance. The PKCgamma enzyme is increased in the spinal cord when patients are experiencing cancer associated pain.

In this program, Benitec has identified the target, identified the best gene, and has also developed the right sequence to block this gene. The target is patented in China and it has freedom to operate in the rest of the world. It owns IP around its gene silencing approach, but also around the DNA sequence it has found to best block this target.

The company will use a lentivurs to deliver its DNA (that will produce the RNAi in the cell), which works well against non-dividing cells.

Cont'd over

Benitec's Technology

Benitec's approach to gene silencing has some distinct advantages over the short double stranded RNA interference (siRNA) approach, which is the approach used by all of its competitors. What Benitec has secured is the intellectual property and freedom to operate around the use of DNA directed RNA interference (ddRNAi).

The powerful discovery, only 13 years ago, was that if you can introduce double stranded RNA into the cell cytoplasm, then it is processed by the cell machinery. The cell machinery separates the two strands and produces a very powerful silencing tool that binds to the messenger RNA which is about to signal specific protein production. Using RNAi, the concept is to stop the production of unwanted proteins responsible for disease.

The common approach is to introduce the double stranded RNA into the cell, usually by incorporating it with liposomes. But this delivery issue remains a major hurdle.

Benitec's approach is to use DNA that is introduced into the cell (nucleus) with a benign virus, such as the lentivirus or the adeno-associated virus (AAV8). Delivering a specific code into the DNA of a person's cell this way, the cell nucleus can be programed to produce the RNA of choice using Benitec's approach. The problem is that the nucleus only makes a single stranded RNA. And this is where it gets even more complicated.

To turn the single strand into a double strand of RNA (remember the discovery 13 years ago was for the use of double stranded RNA), Benitec uses a 'hair pin' which allows the single stranded RNA to fold back on itself and thereby cleverly form a double stranded RNA, the same that competitors have difficulty getting into cells. Because the DNA is now part of the cell, the double stranded RNA is continuously produced, continuously blocking the messenger RNA. This achieves a very strong and everlasting effect.

For Benitec's competitors, they cant's use viruses to deliver the RNA, because only DNA, not RNA, can be incorporated into the virus. That's why delivery for them remains a major stumbling block.

On the risk side, because it is a sustained effect, the issue then becomes ensuring long term safety, with it difficult to reverse or neutralize the action.

Hepatitis B Program

Benitec is working on the proof-of-concept for its hepatitis B program with a Chinese company, Biomics Biotechnologies.

The challenge here is to deliver the therapy to the liver, however the company's technology has had success through its hepatitis C program through its spinout company, Tacere Therapeutics. (Tacere had a major collaboration with Pfizer in this area.) Benitec's partner in China has shown it can achieve close to 100% transfection of all liver cells using this technology.

Its researchers have found the best gene sequence and then Benitec built 14 short hair-pinned RNAi constructs with the best three to make up a triple cassette. The constructs work, says the company.

This is potentially a curative therapy for hepatitis B. It uses the AAV8 virus, the same as Tacere's hepatitis C program. Benitec has leverage a lot from its hepatitis C work, saving it many years, believes CEO Peter French.

The next steps for this program are to build the triple cassette, conduct preclinical studies, and then prepare for clinical studies. The risk with this program, and what the company will be wary of, is if it produces too much of a therapeutic effect then it can lead to toxicity.

Muscular Dystrophy

Benitec is working with scientists in London and Paris to develop a gene silencing approach for the treatment of oculopharyngeal Muscular Dystrophy, one of the nine types of MD. This is a disorder that occurs in people between the ages of 40-70. The condition often leads to swallowing difficulty and choking.

The condition is a good one for Benitec to apply its technology for a number of reasons. The genetic mutation is small and located on a small gene (called PABPN1). The condition is also localized around the throat which makes it more accessible for delivery.

The company will use either the AAV8 virus as a vector to deliver the DNA or stem cells in combination with the lentivirus.

HIV Program

Perhaps one of the most encouraging signs for this technology is from a trial in four patients with HIV. This trial has shown, using a combination of three technologies including Benitec's ddRNAi, that after three years, three of the four patients continue to carry the inserted gene in their immune system, and one patient continues to express the shRNAi developed by Benitec.

A long term expression of this gene silencing could lead to a cure for HIV the company believes. However how the delivery of this therapy is very difficult and remains one of the core challenges in this application. Work is being progressed at the City of Hope National Medical Center in California under grant funding. The head researcher with this program has described the results as spectacular. However likely due to the level of difficulty with this program, Benitec is not funding it further. Importantly, the trial is the first clinical evidence that Benitec's RNI interference approach can actually work in people.

Summary

Benitec's technology has the potential to achieve curative therapies for a number of diseases, however its technology risk is very high.

Over the next year the main goals for the company are to build its proof-of-concept data in its four disease programs (cancer pain, hepatitis B, lung cancer and muscular dystrophy) and to form licensing/collaborative agreements around its technologies.

Benitec is capitalised at $13 million and had $5.6 million in cash at the end of September. Last year it generated a loss of $3.5 million.

Bioshares recommendation: **Speculative Buy Class C**

Bioshares

Mayne Pharma Looks to Deliver Efficiency Gains

Roger Aston gave his last address as CEO of Mayne Pharma at the company's AGM this week. Aston is stepping aside with the new CEO to be based at the company's manufacturing facility in Adelaide. This is an indication that the company will now focus on more on delivering efficiencies from its under utilised drug manufacturing facility, with the yet to be appointed new CEO is very likely to have a strong pharmaceutical manufacturing background.

Aston's skills have been more in drug development. The company's leading development program is an improved version of the antifungal drug Itraconazole, which Mayne calls SUBACAP. The global market for this drug is around $500 million a year. The drug can have some bad side effects, and Mayne has shown that patients need only to take half the amount of drug to get the same levels of active drug into the blood stream, which reduces the side effects associated with the drug.

Improving the profile of the drug means it may also expand the market for the drug and take share from other classes of antifungal drugs. The appeal of Itraconazole is its broad level of activity against different fungal infections.

SUBACAP has been submitted to the European regulator for approval. Aston said he would be disappointed if the drug was not approved by mid 2012. To get the drug into the US will take a further 18-24 months. In many other regions such as Asia, the company should be able to start selling the drug once European approval is achieved.

Doryx

Forty percent of the company's sales now come from the manufacture of the drug Doryx for its customer Warner Chilcott. The company appears increasingly confident that it and Warner Chilcott will hold generic competitors at bay. It has settled with three of the six generics players developing generics for Doryx. The 30 month

Cont'd over

stay ordered by the FDA, which prevented generic competitors coming to market, ended at 30 September however there have been no generics come to market yet.

One of those competitors, Mylan, is challenging Mayne's patent around Doryx, which extends protection out to 2022. The court case is expected to take place around January/February next year. If Mylan settles out of court before hand, then it's game over believes Aston.

Doryx has been a very successful drug for Warner Chilcott (and for Mayne which makes the drug) generating sales of over $1 billion. Whilst there were some disruptions last year in this market, with Warner Chilcott unsuccessful in bringing a 200mg dose to market, Aston said this current year will a lot better than the last for Doryx manufacturing orders.

Switching Focus

The last year has been one of transition and growth to a more sustainable and less risky business. The transition is expected to continue. Previously, 60% of the company's sales were from Doryx manufacturing orders. In the last year, this has fallen to only 40%. However in the process, the company's remaining business increased its sales by 18%.

It appears there are more efficiencies and growth that can come from its existing business outside of Doryx orders, and this explains the change in management. Another gain for shareholders may come from sale of one third of its land in Adelaide (10 acres) with the company recently looking into a possible sale of this excess land.

The company has indicated that it will continue to develop new products using its drug delivery expertise, with current products in development, and with in-licensing new products.

Earn Out Payments

Mayne has paid off its remaining debt from its acquisition of the Mayne Pharma business. It has five years to run on its payout to Hospira, with $6.6 million paid in February this year. A maximum payout in any year occurs when sales reach $65 million, and no payout is applicable if sales fall below $40 million. The maximum payout for subsequent years will be $6.5 million. The current future earn out liability has been calculated at $15.1 million.

In the last financial year Mayne generated sales of $50.1 million, with an underlying EBITDA of $9.2 million and a net profit of $1.7 million. The company has a market capitalisation of $71 million. It has total assets of $53.7 million and cash of $5.8 million. No final dividend will be paid this year.

Bioshares

Bioshares recommendation: **Buy**

US Hedge Fund, East Hill, Increases State in Biota to 10.25%

Biota Holding's ts second largest shareholder, East Hill Holding Company, continues to increase its stake in the company, while its share price languishes. Earlier this month East Hill announced it had increased its ownership in Biota to 10.25%.

East Hill came onto the register as a substantial shareholder in December last year when it increased its stake to 5.06%. Most of its buying since then has been between 76 cents and $1.16 a share, with one trade at $1.49 a share.

What is driving the interest from East Hill in Biota? It appears to be a well informed buyer. One of its scientific advisors, Jeremy Knowles, also sits on the scientific advisory boards of Vertex Pharmaceuticals, one of the top tier small molecule drug discovery and development companies. Vertex has a market capitalisation of US$6 billion.

The commonality between Vertex and Biota Holdings is that both companies are working on Hepatitis C programs focused on inhibiting the same target, the HCV NS5B polymerase. Biota's hepatitis program with Boehringer Ingelheim in HCV ended last year.

Vertex has not been active in M&A. Its last acquisition was in 2009, when it acquired private company ViroChem, for US$100 million. ViroChem had two clinical candidates for the treatment of hepatitis C. In June this year it licensed nucleotide analogues against the same target, NS5B, from Alios Biopharma.

Biota remains a takeover target and this is perhaps one of the reasons behind management's more aggressive plan to improve shareholder value by listing in the US, either through a listing or through a merger.

Biota is capitalised at $136 million with $70 million in cash at the end of June.

Bioshares recommendation: **Speculative Buy Class A**

East Hill Holding Company Shares in Biota Holdings

Date of notice	Increase in BTA holding to:	Purchase price
November 2011	10.25%	76-84 cps
September 2011	9.23%	80-104 cps
June 2011	8.19%	96-116 cps
March 2011	6.14%	90-149 cps
December 2010	5.06%	99-1.02 cps

Bioshares

Mesoblast – Phase II Full Heart Failure Trial Results

A clinical investigator associated with Mesoblast (MSB: $6.80) recently presented the full results of the company's Phase II dose escalation trial of Revescor (allogeneic mesenchymal precursot stem cells) in patients diagnosed with heart failure at the Scientific Session of the American Heart Association's annual meeting Orlando, Florida.

Results released to date include data from the 18 month follow-up point in the trial, including the observations that there was a 50% decrease in serious adverse cardiac events and an 80% reduction in major adverse cardiac events (MACE). There was a 13% cardiac-related mortality in the control group compared to 0% in the treatment arm.

New data presented at the AHA meeting included immunologic monitoring results, changes in left ventricle ejection fraction (LVEF), changes in left ventricle end systolic volume, change in the 6-minute walk and longer term data for MACE and cardiac death free survival.

At the 22 month follow-up point, one patient (out of 45) who received Revesor had died of cardiac related causes compared to three (out of 15) in the control group.

Immunologic Effect

The trial reported that an anti-HLA antibody response occurred in six out 45 patients, but that response only lasted for greater than 1 month in two patients. Anti-HLA antibodies are associated with the rejection of donor organs or tissues or cells. However, the trial reported that antibody response did not exhibit any clinical symptoms and had no effect on the outcomes of the trial.

LVEF

The Cleveland Clinic defines the normal range for a left ventricle ejection fraction as lying between 50% and 70%. Heart failure is often diagnosed when the LVEF fall below 40%.

The administration of Revascor did not have a meaningful effect on LVEF on the combined treatment group, nor in almost all the three different dose groups at the 3 month, 6 month or 12 month time points. However, a statistically significant effect was observed in the 25 million cell dose group at 3 months, where a 7% gain occurred.

Cardiac Remodeling

The trial reported that the highest dose of Revescor (150 M cells) had a statistically significant effect at 6 months on cardiac remodeling as indicated by change in systolic volume, which fell by 7.3 ml. At 12 months the fall was 7.9 ml (not stat. sig.).

The principal investigator Dr Robert Perrin indicated that the150 M cell dose may be the preferred dose to adopt in future studies because it has an effect on remodeling and also because none the patients in that group were hospitalised.

The SCIPIO Trial

At the same AHA meeting investigator Dr Robert Bolli from the University of Louisville presented interim results from a Phase I

Summary of Trial Results - Two Stem Cell Heart Failure Trials

Sponsor	Mesoblast	U.Louisville/NIH
Investigator	Emerson Perin	Roberto Bolli
Phase	Phase II, Dose escalation	Phase I, open label, safety
Status of Results	Final Results	Interim Results
Trial Short Name	Revascor Heart Failure	SCIPIO
Stem Cell Type (1)	Mesenchymal Pre-cursor	Cardiac
Stem Cell Type (2)	Allogeneic	Autologous
Class of Heart Failure	NYHA Class II-IV	
Surgical Status		CABG surgery
LVEF Criteria	<40%	<40%
Delivery Method	NOGA-guided transendocardial injection	Intracoronary Infusion - 4 months after CABG surgery
Dose/s	25,75,150 million cells	NA
Patients		
Enrolled	60	24
Treatment	45	17
Control	15	7
Results		
Safety	No cell related adverse events	None reported
	Safe and well tolerated	
Antibody response	13% of MPC treated patients developed donor specific Anti-HLA Antibody response	NA
	2 out of 45 pts had antibodies persisting for > 1 month, both from the highest dose group (150 M cells)	NA
Efficacy	At 12 months 40% reverted (improved) to NYHA Class I; 14% of control group improved	
	Overall risk of MACE reduced by 78%	
	Overall risk of cardiac mortality reduced by 89%	
	Overall risk of HF hospitalization reduced by 43%	
Ejection fraction	In treatment groups at 3 months, 1.5% increase; at 6 months, 1.7% increase; at 12 months 1.2%	At 4 months LVEF in 14 pts increased from 30.3% to 38.5%; control group no change
	In the 25 M cell dose treatment group at 3 months, 7% increase (stat. sig.); at 6 months, 3.7% increase; at 12 months, 5.2%	At 12 months LVEF in 8pts, increased by 12.3% points to 40.6% compared to baseline
Cardiac remodeling	In the 150 M cell dose treatment group, systolic volume fell by 7.3 ml at 6 months (stat. sig.), and 7.9 ml at 12 months. (n.s.s.)	

Bioshares Model Portfolio (25 November 2011)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.57	$1.66	October 2011
Mayne Pharma Group	$0.470	$0.435	September 2011
Genetic Technologies	$0.12	$0.18	August 2011
Acrux	$2.83	$3.37	June 2011
Bioniche	$0.69	$1.35	March 2011
Somnomed	$1.09	$0.94	January 2011
Phylogica	$0.055	$0.053	September 2010
Biota Holdings	$0.75	$1.09	May 2010
Tissue Therapies	$0.57	$0.21	January 2010
Atcor Medical	$0.08	$0.10	October 2008
Impedimed	$0.55	$0.70	August 2008
Bionomics	$0.44	$0.42	December 2007
Cogstate	$0.26	$0.13	November 2007
Sirtex Medical	$4.55	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.41	$6.60	September 2007
Pharmaxis	$1.04	$3.15	August 2007
Universal Biosensors	$0.75	$1.23	June 2007
Alchemia	$0.325	$0.67	May 2004

Portfolio Changes – 25 November 2011

IN:
No changes

OUT:
No Changes

– *Mesoblast cont'd*

trial of autologous (patient's own) cardiac stem cells administered to patients who had undergone coronary artery bypass graft surgery. This trial showed that LVEF was increased from 30.3% to to 38.5% at four months and to 40.6% at 12 months.

Commentary

The presentation of results from the SCIPIO trial at the AHA conference may be beneficial to Mesoblast despite the fact that the SCIPIO trial reported compelling results in change in LVEF at 12 months (of 34%), compared to a best result for Mesoblast in the smallest dose group at 3 months of 7%.

The benefit is that another, unrelated clinical trial has demonstrated the feasibility of adult stem cells as a treatment modality in heart failure. The weakness of this alternative approach is that as an autologous therapy it is a more complicated and arguably expensive approach, and is certainly not applicable in where an immediately available product is required.

The failure to lift LVEF performance by a large percentage improvement is in fact not relevant to development of Revascor in heart failure. This is because it demonstrated a potential to stabilise and greatly reduce the risk of patients with heart failure experiencing further major cardiac events as well as reducing hospitalisations. These outcomes are associated with economic benefits. Furthermore, as Mesoblast CEO Silviu Itescu stated at the Mesoblast AGM, the FDA's guidance is that Phase III trials should use mortality and cardiovascular or heart failure hospitalisation, with endpoints such as ejection fraction to not be used because they have not been validated as surrogates for clinical outcomes. What is clear from the Phase II heart failure trial is that Revescor has a decisive impact on cardiac mortality and hospitalisations nearly two years after a single treatment.

One aspect revealed post hoc of the Revascor Phase II heart failure trial was that the patients in the control group were somewhat healthier than patients in the treatment arms, having for example, far fewer numbers, on a proportional basis, who had a previous history of a heart attack. This may have influenced some of the results of the trial.

Mesoblast now has a solid data set with which to design its FDA-focused Phase III cardiovascular programs, with a Phase III trial expected to commence in the first half of 2012.

Mesoblast is capitalised at $1.9 billion and retained cash of $260 million at September 30, 2011.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Long Term Data to Support Impedimed's Reimbursement Campaign?

Impedimed (IPD: $0.55), which markets the L-Dex bio-impedance device for aiding the assessment of very early stage lymphedema, continues to press ahead towards its objective of securing its 20 million covered lives from US health insurers, originally set as a target for 2011 H1.

Although the number currently stands at 12.5 million the company remains confident that a major step towards that target will occur in the not too distant future, noting that a least one US insurer, Cigna, will release a new medical policy in January 2012.

This figure of 12.5 million covered lives comprises 9 million US Federal employees, 3 million Federal employees under workers compensation legislation and 175,000 with Group & Pension Administrators. The company's objective was to reach 20 million covered lives in 2011, increasing that to 50 million in 2012.

In the US, private health insurance schemes cover an estimated 152 million people through employer programs, with another 25 million through other schemes. The US government provides insurance through its Medicaid and CHIP programs to 37 million people and covers 47 million people over the age of 65 through Medicare. The balance of 50-55 million are uninsured.

Amongst the major private health insurance companies are Aetna (18.2 million covered lives), Wellpoint (34 million), Kaiser Permanente (8.7 million), United Healthcare (18 million), Humana (10 million) and Cigna (9 million).

Impedimed has been stymied in its attempts to reach its 20 million target by some insurers who have been looking for evidence of longer term benefits of its L-Dex test where used to diagnose lymphedema in women who have breast cancer surgery.

Forthcoming Long Term Data

Impedimed expects to have the five year follow up results of the Stout Gergich early stage lymphedema detection study at its disposal after presentation at the San Antonio Breast Cancer Symposium in early December. It can then take this data to insurance companies and, it is anticipated, provide evidence that L-Dex testing can deliver positive long term benefits to women at risk of developing lymphedema following breast cancer surgery, by returning them to baseline.

Impedimed is of the view that if the trial shows a greater than 70% success in preventing progression to irreversible forms, then payers would be better able to validate the cost savings made by using the L-Dex system for pre-emptive care and monitoring.

What can be expected is that when one or two major private insurers release a medical policy supporting the reimbursement of Impedimed's L-Dex device, then others will follow.

A primary driver for L-Dex use is that it is now a medical standard, in other words, has the legal backing from the American College of Surgeons, which administers the NAPBC 2011 clinical standard 2.15, which calls for pre-emptive care of lymphodema and recommends L-Dex (or periometry) for reducing false positives and false negatives with existing technologies.

In the meantime, some insurers, for example Aetna, are reimbursing L-Dex use at the regional level despite national medical policies not being published. Impedimed can gain payment in these circumstances by using its managed care team to argue on a case by case basis that L-Dex use is reimbursable because its passes the test of medical necessity.

Impedimed has commissioned market researchers to better understand which payers are in fact covering the test at a local level.

Summary

Impedimed is moving closer to gaining national medical policy support for the reimbursement of its L-Dex device. Although slowed than expected, progress is expected to move ahead more quickly once a major private US health insurer recognises, through medical policy publication, the benefits of the device in managing lymphedema.

Impedimed is capitalised at $85 million and held $15.4 million in cash as of September 30, 2011.

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. 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, Patrys, LBT Innovations, Mesoblast, Atcor Medical, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec, Allied Healthcare Group