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**In this edition...**
Antisense Therapeutics has been patiently working in the antisense technology space for more than a decade. It suffered a setback when Teva handed back ATL's MS drug candidate ATL1102 in March 2010. Now the company is moving forward with the development of ATL1103 in the niche indication of acromegaly, with a key milestone expected before year's end.
In selected coverage of annual results announcements we report on Mesoblast, Acrux and Patrys. Wound healing company Tissue Therapies may be a beneficiary of the failure of Dermagraft in a pivotal venous leg ulcer trial. And Middleton's lawyer Andrew Gaffney commences a discussion on the pros and cons of cross border listings.
**The Editors**
**Companies Covered: ACR, ANP, MSB, PAB, 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) | 70.0% |
| 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 | -21.0% |
| **Cumulative Gain** | **232%** |
| **Av Annual Gain (10 yrs)** | **21.2%** |

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# Bioshares

**26 August 2011**
**Edition 422**

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

## *Antisense Therapeutics Moves Forward With Acromegaly Program*

Antisense Therapeutics (ANP: 0.8 cents) has placed itself in better position following the handback of its MS drug candidate from Teva Pharmaceutical Industries. Its current lead compound is currently in a Phase I study. However this study should progress into a multiple dose study that we expect to clearly show whether its lead drug candidate, ATL1103, has any effect of circulating IGF-1 levels. Those results should be out in early 2012.

Antisense Therapeutics (ATL) is currently capitalised at $7.6 million. A positive result early in the new year has the potential to deliver some very strong gains for investors over the next six months if this early clinical trial yields some positive results.

ATL1103 is now the most promising compound in ATL's suite of antisense programs. Antisense technology uses nucleotides, the chemical building blocks of DNA and RNA, to control protein expression from within a cell. ATL's partner, Isis Pharmaceuticals, is a pioneer of antisense technology and has built a second generation chemistry that improves the properties of oligonucleotides (chains of nucleotides between 12 and 30 nucleotides in length). ALT uses the Isis technology, with Isis synthesizing ATL1103 in exchange for a portion of any future income. (The exact percentage is undisclosed, but CEO Mark Diamond says it's much less than 33% obligation it has to Isis on the ATL1102 multiple sclerosis program.)

### Mode of Action

ATL1103 is designed to inhibit the production of the growth hormone receptor. When growth hormone in the body hits this receptor in the liver, it causes the production of IGF-1.

### Applications

There are a number of pharmaceutical applications for this type of therapy with ATL1103. The first one that ATL is targeting is in people who suffer from acromegaly, an orphan drug indication. In this disease, a benign tumour of the pituitary gland causes an over-production of human growth hormone. This causes an over production of IGF-1 (insulin-like growth factor). IGF-1 stimulates systemic body growth, promoting growth in just about every cell in the body.

People with acromegaly have severely enlarged organs, bones, hands and feet, with the condition often linked to gigantism. If untreated it can result in severe disfigurement, medical complications (such as diabetes) and premature death. In the US, there are about 25,000 people living with acromegaly.

Other potential applications for this drug candidate are in treating diabetic retinopathy, diabetic nephropathy and possibly even in the prevention of cancer (see cancer prevention application).

*Cont'd over*

### Reasons for Optimism with ATL1103

There are a number of reasons for optimism with this program. Firstly, ATL has put itself in a position that within the next six months it should have some clear data on what effect its drug candidate is having on circulating IGF-1 levels when given at what is expected to be a therapeutic dose.

Secondly, the biomarker used to measure effectiveness, IGF-1, is in fact the end point. It is easily measurable so results should deliver some clear outcomes, quickly, one way or the other.

Thirdly, this is an antisense drug and antisense drugs have shown to work well in the liver. This is not so surprising because this is where drugs accumulate with the liver's primary role being to filter the blood.

One case in point is the drug acquired by Genzyme (Sanofi-Aventis), called Mipomersen (brand name Kynamro). This antisense drug has delivered stunning results, with a 36% reduction in LDL-C (cholesterol) levels. Four Phase III trials have now been successfully completed and the drug has been filed for approval in Europe and is expected to be filed for approval later this year in the US. Cholesterol is produced in the liver.

Genzyme licensed this drug candidate in 2008 from Isis for US$325 million in upfront and equity payments. Isis stands to receive a 50/50 profit split if sales achieve $2 billion a year. The compound has an application in people with a genetic disorder called familial hypercholesterolemia. These people have elevated cholesterol levels two to four times normal even when taking existing statin drugs.

Isis CEO Stanley Crooke has stated that this compound "lowers all estrogenic lipids and no negative effects on HDL", with no other drug having that same profile.

One point that could be an issue is the effect antisense drugs have on liver enzymes although that appears to be an acceptable side effect with Mipomersen with statins also having an effect on liver enzymes. Crooke said that "modest changes in liver enzymes" were seen in 8% of patients taking Mipomersen, although this is "reasonably monitored and should be easily manageable".

A fourth positive point is that ATL has successfully completed primate studies with ATL1103. In these studies, ATL1103 successfully reduced IGF-1 levels by 35%. That level of reduction in humans would be sufficient to normalize IGF-1 levels in 60% of people with acromegaly.

### Current Market

In about 60% of cases, acromegaly can be suitably treated with surgery, by removing the tumour in the pituitary gland. Radiotherapy is effective in about 30% of cases. And first line drug therapy (with somatostatin agonists such as Octreotide) work in around 60%-65% of cases and the therapy costs up to US$30,000 a year. It is delivered as a depot injection that lasts a number of months. This class of drugs generate sales of around $1 billion a year.

For the other 35%-40% of cases, a growth hormone receptor antagonist (affecting the same target as ATL1103) called Somavert, is used. This drug is effective in most cases but realistically only about 70% of patients maintain therapy because of delivery issues; Somavert needs to be injected daily. However, the real issue is that it comes in a lyophilized powder, requiring reconstitution and making it a complicated daily process to use.

The drug is also very costly, at $60,000 per year of treatment. Patients need to avoid taking insulin and a range of pain drugs including codeine, morphine, oxycodone and fentanyl. It also generates more than a two-fold increase in growth hormone levels,

Somavert generates sales of more than US$200 million a year.

### Market Opportunity

The market opportunity for ATL is in those 35%-40% of patients for whom the somatostatin agonists are not effective. That's somewhere between 15,000-20,000 patients. At $30,000 per year of treatment, it's a potential market of between $450-$600 million a year. This assumes that ATL1103 would largely replace the use of Somavert, which is expensive and has demanding daily delivery requirements, and would sell for $30,000 a year's treatment. ATL1103 would possibly be self administered once a week with a subcutaneously injection.

### Path to Market

The path to market for ATL with ATL1103 is not overly complex. The company is currently conducting Phase I studies which are due to be completed by the end of this year. The company is using Nucleus Network's clinical trial unit at the Austin Hospital in Melbourne.

Looking at the path taken for the development of the acromegaly drug Somavert by Pfizer, the company conducted a Phase II trial involving 112 patients. The trial looked at reductions in IGF-1 levels over 12 weeks. The Phase III registration trial enrolled 167 patients, who were treated for between six -18 months. Endpoints in this study were IGF-1 levels, growth hormone levels, and insulin and glucose levels.

### Current Phase I ATL1103 Trials

In June this year ATL started a Phase I trial in healthy volunteers with ATL1103. The first part of the trial in six people will look at four different doses of ATL1103, starting at 25mg, then 75mg, 250mg and 400mg. Each volunteer will receive one injection only. There will also be a placebo arm. This part of the trial we expect will be completed around October this year.

The second part of the trial will involve 12 people, with eight receiving ATL1103 and four receiving a placebo. These volunteers will receive six doses over three weeks, either at 250mg or 400mg. This dose should be sufficient to effect a change in IGF-1 levels if the drug works the way it has been designed to. The cholesterol lowering drug Mipomersen for instance has been filed for approval on a 200mg per week dosage level.

*Cont'd over*

A very good result for ATL will be a 30% reduction in IGF-1 by week three which is the length of dosing. If this was achieved then it should correspond to around a 50%-60% reduction after three months if treatment was continued.

The second part of the trial should be completed by the end of this year with results out early in 2012.

### Other Potential Applications for ATL1103

There are some other interesting potential applications for ATL1103. There is evidence that reducing IGF-1 levels can have a beneficial effect in treating proliferative diabetic retinopathy which results in new and leaky blood vessels being formed in the eye.

There is evidence that reducing IGF-1 levels have a use as a breast cancer treatment. Somavert has shown positive results in animal models; and removal of the pituitary gland (which has the effect of reducing IGF-1) in some women with breast cancer has shown to be effective in improving survival outcomes.

Perhaps the most intriguing application is in the prevention of cancer, although this would obviously be a longer-term study. Science Translational Medicine published a paper in February this year which reported on a study in 99 people with dwarfism (called Laron syndrome), followed for 22 years.

These 99 people from Ecuador had a genetic mutation that lead to a severe deficiency in the growth hormone receptor (the receptor that ATL1103 reduces the formation of) and a severe deficiency in IGF-1. It was found that these 99 people experienced only one case of cancer, which was non-lethal, compared to a prevalence of 17% in these people's relatives who did not carry this genetic mutation. There were also no cases of diabetes seen in the group of 99 compared to a prevalence of 5% in relatives without the mutation.

As an additional investigation of the current Phase I study by ATL, one of the authors of the above paper will look at the serum of these volunteers for any anticancer properties they may have.

### Patents and Manufacturing

ATL1103 has been manufactured by Isis and ATL has sufficient quantities of the drug to conduct a Phase IIa trial should this Phase I trial be successful. A Phase IIa trial would cost at least $5 million and take around 18 months to complete.

ATL and Isis have patent applications in place and granted patents over the technology extending protection out to at least 2025, with two US granted patents and two under examination. It looks to be a very solid patent position.

### Funding

ATL had $2.3 million at the end of June. It will clearly need to raise more funds in 2012, although has sufficient funds to complete both parts of the current Phase I study.

### Board

On issue the company needs to tackle is the refreshment of its board of directors, with all five board members being on the board since the company listed 10 years ago. The board comprises of Bob Moses (chairman), Mark Diamond (CEO), Chris Belyea, Graham Mitchell, and George Werther.

### Summary

Antisense Therapeutics has a number of antisense drug candidate programs. One of those, ATL1102, has stalled following Teva Pharmaceutical Industries handing back the rights to ATL. ATL is looking to find another partner for this program.

ATL has granted a private Australian company, Afandin, founded by experienced cancer drug developer Ian Nisbet, an option to license ATL1101 to develop it for the treatment of prostate cancer.

Its lead program, ATL1103, is now in a position where some clear information about the drug's potential should become available in the next six months. The first milestone is for the company to complete its single ascending dose study, which if completed successfully, will indicate there are no initial safety concerns. At the end of this trial by year's end, the company will have completed the multiple dosing part. If no major adverse events have been reported by the end of the year and the trial has been completed, then that will also be a meaningful milestone for investors to look out for.

And in early 2012, information should be available about whether ATL1103 can have a meaningful impact on IGF-1 levels (a 30% reduction would be a very good result).

With a capitalisation of $7.6 million, Antisense Therapeutics is a stock that has the potential for significant gains over this period if ATL1103 shows safety and early efficacy.

*Bioshares* recommendation: **Speculative Buy Class C**

**Bioshares**

# *Results Round Up – Mesoblast, Acrux and Patrys*

## Mesoblast – Affirms Strategy and Direction

Mesoblast (MSB: $7.65) reported an accounting profit of $90.6 million for the year ending June 30, 2011. The company recorded revenue of $86 million. The revenue included the revaluation of its investment in Angioblast which followed its acquisition by Mesoblast, less the write-back of equity-based losses incurred in that same entity.

The merger with Angioblast was based on a valuation US$506 million, recorded in the FY2011 accounts at $504 million, the difference owing to exchange rate differences. Of the $504 million, $116 million was recognized as goodwill and $388 million was recognized as intellectual property acquired.

Just prior to the merger of Mesoblast with Angioblast, **Cephalon** acquired 26.5% of the shares of Angioblast from other shareholders for US$134 million. Mesoblast retained its 38.4% stake and other shareholders retained a 35.1% stake, until the merger took place. [Mesoblast has licensed CNS and cardiovascular product rights of its pre-cursor mesenchymal stem cell technology to Cephalon.]

Mesoblast has elected to amortise revenue of $130 million from its licensing transaction with Cephalon over the next 4 ½ years, with just $14 million accounted for in the reporting period ending June 30, 2011. This amortisation is aligned with the clinical-through-to-registration timeline of the programs licensed to Cephalon.

Mesoblast's retained a cash balance of $263 million at June 30, 2011 compared to $32 million at June 30, 2010. Payments to suppliers and employees were $22.5 million for the year ended June 30, 2011.

In discussing the Mesoblast's full year results CEO Silviu Itescu said its substantially improved cash resources are being used to add staff with clinical, regulatory and manufacturing expertise. Mesoblast has established new strategic business units.

The increased funding base will allow Mesoblast to move into new indications including Type 2 diabetes and immunologic conditions including lung diseases, inflammatory joint diseases and eye diseases.

One of Mesoblast's areas of strategic importance is that of manufacturing. The company intends to develop a state of the art facility via a strategic alliance, which will be cost neutral to Mesoblast. The facility will provide tax efficiencies and use the latest technology. Controlling manufacturing (albeit through a third party) will enable Mesoblast to more directly manage cost of goods and product margins, manage product differentiation for different partners, and optimize pricing.

Near term inflection points include the commencement of the Phase III heart failure trial, start of the Phase II intra-coronary heart attack trial, complete Phase II trials in spinal fusion and disc repair and initiate Phase II trials in diabetes and eye diseases. Mesoblast also is seeking to expand partnering arrangements.

***Comment***

Mesoblast is well placed to develop its adult stem cell technology and to do so across an ever broadening number of indications. Trials in diabetes and immune-based conditions will worth monitoring as details come to hand. It is worth noting that Mesoblast is now, generally speaking, moving into Phase II trials once preclinical studies are complete, saving time and money on the Phase I step in clinical development.

Although the publication of data from its Phase II heart failure trial at the American Heart Association conference in November will be worth monitoring closely, what may rank in importance is the company's securing of a strategic manufacturing partner. Mesoblast's goal of retaining rights over manufacturing is a crucial plank in the company's value creation strategy which cannot be underestimated.

Mesoblast is capitalised at $2.1 billion.

*Bioshares* recommendation: **Speculative Hold Class A**

## Acrux – No Dividend Until 2012 H2

Acrux (ACR: $3.73) reported a net profit after tax of $57 million from revenue of $93.5 million. The company held cash of $33 million at June 30, 2011. The company's estimated annual spending on operations is approximately $6 million.

Acrux's revenues were derived from income from its partnership with **Eli Lilly**, to which it has licensed Axiron (transdermally delivered testosterone for hypogonadal males.) The company said it anticipated Axiron royalties of US$7-8 million for FY2012 and approximately $US40 million in FY2013. Acrux anticipates its next dividend payment will be announced in August 2012.

At the company's annual results presentation this week, the Chief Marketing Officer of Eli Lilly, Rob Brown, discussed the significance of Axiron to Eli Lilly and provided information on the initial sales performance of Axiron.

Axiron is an important product to Eli Lilly because the product offers synergies with Cialis (for erectile dysfunction), with both drugs often being relevant to the same customer. The testosterone replacement market is also growing at a very fast rate, recording sales of US$1.5 billion in 2010, an increase of 26% from the previous year.

For the week ending August 5, 2011, Brown said that Axiron had achieved a 22.3% share of the New-to-Brand prescriptions (NTBRx) and 6.1% of total prescriptions (TRx) in the US. The product was launched in April in the US in the specialist market and in June in the primary care market. Brown said the sales results were encouraging although they were early figures. "This product has surprised some Lilly folk", he said positively.

Brown defined the NTBRx category as the volume of prescriptions that are associated with a first-time use of a product. It included patients receiving their first prescription during a 12 month

period as well as patients who have switched to the product. Hence the category serves as a leading indicator of growth. Brown said Axiron was being sold in a 60:40 ratio of first-time prescriptions to patients switching to the product.

What surprised Eli Lilly was that half of the patients switching to Axiron were coming from the injectable administration category. These patients may have originally used the gel form of the drug but migrated to the injectable form out of dis-satisfaction with the gel product.

Axiron has yet to be widely covered by insurance payors in the US. Achieving coverage from about 80% of payors is expected to take 9-12 months. In the meantime, Lilly has introduced a co-pay card. The object of the co-pay card is to make the patient indifferent to the drug not being covered by the insurance company (in the interim). This is a short term strategy until the product receives coverage. However, for Acrux investors the co-pay is a marketing cost that plays against the net revenue figure from which royalty payments are calculated.

Although recent growth rates in the testosterone replacement therapy market have been strong, especially in the US, Brown was less sure about prospective growth rates, questioning whether growth will be sustained at current rates.

***Comment***
Axiron appears to be a product that has quickly gained a foothold in the US testosterone replacement therapy market. However, investors have now been given more clarity on revenues flowing to Acrux in the medium term, with expectations of a dividend paid in the 2012 H2.

*Bioshares* recommendation: **Hold**

### Patrys – Activity of PAT-SM6 Revealed at Low Starting Dose; Uncovers New Opportunity in Multiple Myeloma

Patrys (PAB: $0.075) reported a loss of $7.4 million for the year ending June 30, 2011. The company held cash of $6.2 million at June 30, 2011.

The company's lead product candidate is an IgM class antibody PAT-SM6, which is currently being evaluated in a nine patient Phase I trial in patients with transient melanoma. PAT-SM6 binds to a cell-surface protein termed GPR78, which is common in its mutant form in many cancers.

The company has announced that the antibody has been detected in biopsies taken from the melanomas of patients in the current trial, who were given the very low starting dose of 0.15mg/kg. In other words, the antibody has been detected binding to the mutant form of GPR78.

The activity of the drug at a low dose in melanoma is interesting in that it may mean that an effective dose may also be low, leading to lower cost of goods. By way of comparison the antibody drug Avastin is dosed at 5mg/kg when used in conjunction with IFL and 10mg/kg when used with FOLFOX.

If a low dose form of PAT-SM6 is possible, relative to other antibody drugs, less drug may be needed implying a lower treatment cost. However, the company must still evaluate the effects of higher doses (up to 9mg/kg) to discover safety and efficacy parameters of the drug candidate.

The company also announced the results of pre-clinical work conducted at the University Hospital of Wurzburg in Germany in the field of multiple myeloma (a bone marrow cancer). The study found that a Patrys antibody product bound to multiple myeloma cells from patients with a primary diagnosis to patients who had relapsing disease (after treatment for example current standard of care therapies).

The opportunity for new drug development in multiple myeloma is as patients are treated with drugs such as Velcade and Revlimid, resistance develops, instigating a need for new therapies.

This clinical insight is a potentially new line of opportunity for Patrys, since the therapeutic effect of agents used to treat blood-born cancers can be gauged quickly through blood tests.

Until now Patrys' focus has been on treating solid tumours. Patrys expects to complete its Phase I trial of nine patients this year, and commence an extension study in 18 patients in 2012 H1.

***Comment***
The company has funds to complete the current nine patient trial and commence the extension study. However, it will be seeking funds to commence Phase I/IIa multidose solid tumour trial for PAT-SM6 in 2012 and to also complete pre-clinical toxicology, commence large scale manufacturing of PAT-LM1 in readiness for a Phase I/IIa trial.

The company's challenge is to build wider investment support for its drug candidates and clinical development plans.

Patrys is capitalised at $18 million.

*Bioshares* recommendation: **Speculative Hold Class B**

**Bioshares**

## Contributed Discussion

# *The US Invasion*

The last three years has seen significant changes both in volatility and market valuations of listed companies - which have directly impacted on capital raising strategies, takeover opportunities and returns to shareholders. In such uncertain markets, companies have to be more innovative in their strategic plans.

One result of these changes has been that the ASX has become more attractive to overseas companies and likewise there has been a decline in capital raising interest / IPOs in other foreign stock markets. So competition has increased from foreign companies for the Australian investment dollars and biotechnology has not been immune from such competition.

However this has not been one way traffic with only foreign companies raising capital in Australia – some Australian companies have also been able to tap into the same foreign markets (presumably where the relevant Australian companies bring different valuations and risk parameters than their counterparts in those foreign markets).

In the previous 18 months, my firm Middletons has acted on a number of transactions with US entities, with the transactions possibly driven by this uncertainty. In this series, we will discuss:

(a) US entrance into Australian markets with IPO listings on the ASX by foreign entities (either directly or via an interposed company) - the alternative structures, differences in investor considerations and market perceptions

(b) Australian entities raising foreign investment dollars in reverse – top hat schemes, ADR listings, private placements

(c) Other possible strategic returns to shareholders (takeovers, strategic relationships, licensing) with or by foreign entities

### Entrance into the Australian Market

We have observed three approaches or structures commonly used for an entrance into the Australian markets by US companies.

***Direct ASX Listing as a Foreign Company***

US Co may seek an ASX listing in its own right if it becomes registered in Australia with ASIC as a foreign corporation and appoints a local agent.

The US Co would still prepare a prospectus in compliance with the Australian Corporations Act, lodge that prospectus for registration with ASIC and at the same time lodge an application for admission to the ASX Official List. After expiry of the standard exposure period, the US Co is able to undertake its capital raise on the terms of that prospectus much in the same way as an Australian company would undertake.

However, in a direct foreign listing, to enable foreign companies to have their securities cleared and settled electronically through CHESS, depositary interests called "CDIs" are issued by a licensed "Depository Agent" and trading in the US Co's securities occurs via trading of the CDIs on the ASX (rather than trading in the shares in US Co). This has similarities with the US ADR program for non US entities trading their securities in the United States.

Two of the main differences between holding CDIs compared to holding shares in an Australian company, is that first, the holder's rights and entitlements are governed primarily by the law of the foreign company (for example the Delaware General Corporation Law "DGCL" in the case of a foreign company incorporated in Delaware) and secondly the holder of the CDIs has a beneficial interest in the equivalent number of shares, but not the legal title to those shares. The legal title to the underlying shares is instead held by an Australian Depositary Agent (the primary one being a wholly owned subsidiary of the ASX). Holders of CDIs are entitled to all of the economic benefits of the underlying shares (such as dividends, if any) as though they were the holders of legal title.

It is important to note that ASX Listing Rule 15.15 provides that a listed foreign company's constitution must NOT include provisions relating to takeovers or substantial shareholding notices - so unless a modification is obtained from the ASX, takeovers and like provisions (such as substantial shareholder notices) that Australian shareholders normally expect in an Australian listed company are not necessarily present in a foreign listed entity with trading in its CDIs.

Examples of direct foreign ASX listings include **Reva Medical Inc**, **Boniche Life Inc**, **Resmed Inc**, **Alcoa Inc**, **Viterra Inc**, **Olympus Pacific Minerals Inc.**

***Restructure with New Australian Entity Seeking ASX Listing***

An alternative to a direct foreign ASX listing discussed above, is for an Australian entity to be established which then enters into a share swap agreement to acquire all of the issued shares in the US Co. This is commonly referred to as a "top hat" arrangement and effectively interposes a new Australian holding company as the ultimate 100% holding entity of the foreign entity US Co.

A share swap is undertaken such that the US Co's shareholders become shareholders in the Australian entity in the same respective proportions. The share swap can be structured so that it is only effective on listing to preserve flexibility for US Co and its shareholders.

The newly established Australian entity then undertakes the same steps of preparing a prospectus for the capital raising, lodging with ASIC and also preparing its ASX application for admission to the ASX official list. As indicated above, once the capital raising is successfully completed and the Australian company listed, trading occurs in its shares (as distinct from CDIs) in the normal course. The benefit of this approach is that, from a retail investor viewpoint, they are simply buying shares in an Australian holding company (subject to the Australian Corporations Act) which, on admission to the ASX, will wholly own the foreign US Co. The US Co is simply a wholly owned subsidiary and the rights of shareholders derive from their direct shareholding in the newly listed Australian holding company.

*Cont'd over*

It is a structure the retail investor is well used to for the majority of their investments and they have the benefit of the usual provisions under the Australian Corporations Act which a shareholder would have in any Australian public company (such as the regulation of related party transactions involving directors and also importantly takeovers).

Examples of such top hat arrangements include **Cordlife Ltd**, **EvoGenix Ltd**, **Patrys Ltd**, and **QRXParma Ltd**.

***Backdoor Listing – Reverse Takeover / Merger***

An existing Australian ASX listed company may "acquire" a US Co in what is referred to as a "backdoor listing".

While many see a backdoor listing as an easier path to the ASX, in fact there is greater regulatory scrutiny and requirements than a direct IPO. Generally depending on the size of the existing listed entity and the merger target (US Co), it may trigger (due to the proposed change to the nature or scale of activities of the existing listed entity) a requirement for "requalification" by that existing listed entity - which results in significantly more work / expense than a direct IPO.

In these circumstances the existing listed entity will need to convene a shareholders meeting to approve the transaction (being the "acquisition" of US Co), the restructure of the listed entity's share capital (usually as a condition of the acquisition) and where any shareholder will trigger the takeover threshold of 20% as a result of the acquisition (and the issue of new shares by the existing listed entity), obtain an independent expert report as to whether the transaction is "fair and reasonable" to non associated shareholders - in addition to complying with all of the requirements of a standard direct ASX IPO listing.

Unlike Australian companies where it is difficult to implement a merger with a larger number of shareholders in the private company, under DGCL the "acquisition" process as regards the US shareholders is a lesser hurdle, with the requirement under DGCL only to obtain 51% shareholder approval to deliver 100% acquisition (however the US dissenting shareholders do have certain appraisal rights to dispute valuations but not to prevent the transaction or acquisition from taking place).

Also importantly where the backdoor proposal brings with it an existing Australian listed entity which itself has significant synergistic assets / activities, the transaction may not trigger the requirement for a requalification post merger and the merged group may be more attractive to investors than the individual parts (pre merger / acquisition).

***Choice of Structure***

The choice of structure will primarily reflect tax considerations (including the tax profile of the existing pre IPO shareholders in US Co) and also commercial considerations (such as will the market presently support an IPO as compared to a backdoor listing). While direct foreign ASX listings (where CDIs are traded) are not as common as a direct listing of an Australian company (where its shares are traded), generally broker sentiment seems to be that investors (particularly wholesale or sophisticated investors) do not draw any significant distinction between the two forms of listing structure.

In either case (whether a CDI listing or a share listing), there has been some discussion by commentators as to whether there needs to be some "Australian" connection to justify or attract investor interest. The contrary view is that if the ASX is to be a player in the greater Asian Pacific region (and attract greater foreign investor interest in the stocks quoted on the ASX), then we should position the ASX as an exchange attracting listings irrespective of their association or connection with Australia.

It is not an obstacle to an ASX listing that an entity does not conduct business activities in Australia. However, ASX requires that the entity has an Australian resident representative to accept responsibility for communications with the ASX for the purpose of ongoing compliance with the Listing Rules.

A very brief comparison, set out in a table of some of the key differences for a foreign company incorporated in Delaware (which has a CDI listing on the ASX) and a listed Australian company (as alternative listing structures) is available at the following weblink *www.bioshares.com.au/australiavdelawarecorplaw.pdf.* This table highlights some of the key considerations under the Australian Corporations Act and the Delaware Law (picking Delaware as a common jurisdiction for establishing companies in the US with its lower state taxes).

In the coming articles we will look at Australian entities raising foreign investment dollars in reverse and other possible strategic returns to shareholders from foreign companies.

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**Bioshares**

**Bioshares Model Portfolio (26 August 2011)**

| Company | Price (current) | Price added to portfolio | Date added |
|---|---|---|---|
| Genetic Technologies | $0.16 | $0.18 | August 2011 |
| Acrux | $3.73 | $3.37 | June 2011 |
| Psivida | $4.20 | $3.95 | May 2011 |
| Bioniche | $0.78 | $1.35 | March 2011 |
| Somnomed | $1.21 | $0.94 | January 2011 |
| Phylogica | $0.064 | $0.053 | September 2010 |
| Sunshine Heart | $0.046 | $0.036 | June 2010 |
| Biota Holdings | $0.90 | $1.09 | May 2010 |
| Tissue Therapies | $0.47 | $0.21 | January 2010 |
| Atcor Medical | $0.08 | $0.10 | October 2008 |
| Impedimed | $0.52 | $0.70 | August 2008 |
| Bionomics | $0.48 | $0.42 | December 2007 |
| Cogstate | $0.17 | $0.13 | November 2007 |
| Sirtex Medical | $5.00 | $3.90 | October 2007 |
| Clinuvel Pharmaceuticals | $1.54 | $6.60 | September 2007 |
| Pharmaxis | $0.99 | $3.15 | August 2007 |
| Universal Biosensors | $0.90 | $1.23 | June 2007 |
| Alchemia | $0.34 | $0.67 | May 2004 |

### *Portfolio Changes – 26 August 2011*

**IN:**
No changes

**OUT:**
No changes

## *Tissue Therapies – Update*

Tissue Therapies (TIS: $0.47), the developer of the VitroGro wound healing product, may have gained an important commercial advantage this week when **Shire Pharmaceuticals** announced the failure of Dermagraft, a wound healing product, in a 500 patient pivotal trial in venous leg ulcer patients.

Dermagraft did not meet its endpoint of achieving complete healing, defined as 100% re-epithelialization with no presence of scab of drainage, at 16 weeks. Dermagraft showed a higher rate of closure *when combined with compression therapy*. However, the product also needed to show a minimum level of absolute superiority over compression therapy.

Shire Pharmaceuticals acquired **Advanced Biohealing**, the developer of Dermagraft, in May for US$750 million. Dermagraft is approved for the treatment of full-thickness diabetic foot ulcers of greater than six weeks duration.

The Dermagraft venous leg ulcer trial failure is relevant to Tissue Therapies, because it is conducting a trial in venous ulcer patients. Interim data in its trial showed complete healing in eight of 24 evaluated patients, with Vitrogro administered once or twice weekly for 12 weeks in patients *who did not respond to compression therapy*.

With competition now freed up in the venous ulcer market, a refreshed opportunity exists for Tissue Therapies, or more likely with a commercial partner, to tackle the broader venous ulcer market. We would expect a clinical development program similar to the randomised 500 patient Dermagraft pivotal trial to be adopted. However, the key point for Tissue Therapy investors is that the broader venous ulcer market is up for grabs again for new technologies.

Tissue Therapies is capitalised at $79 million and held cash of $15 million at June 30, 2011.

*Bioshares* recommendation: **Speculative Hold Class A** (pending completion of licensing deal)

**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***

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