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**In this edition...**
The 6th Bioshares Thredbo Biotech Summit was held on July 23 and 24. The program was broad in coverage and it included a review of sector events from the past twelve months, an outstanding take-over strategies workshop, an overview of developments in cardiology, a session devoted to new approaches in cancer and RNAi-based therapeutics, discussions on funding issues and the profiling of four private companies. For this edition, we report on three presentations, leading with Acrux's development of Axiron from Phase III through to licensing to Eli Lilly, an in-depth look at the application of Starpharma's dendrimers in the field of drug delivery, and a case study supplied by QRxPharma's Phil Magistro on drivers in the pain therapeutics market.
**The Editors**
**Companies Covered: Thredbo Summit Coverage – ACR, QRX, SPL**

| | 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 - Current) | -4.9% |
| **Cumulative Gain** | **175%** |
| **Av Annual Gain (9 yrs)** | **18.5%** |

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# Bioshares

**27 July 2010**
**Edition 369**

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

**The 6th Bioshares 2010 Thredbo Biotech Summit - Event Coverage**

## *Acrux and the Axiron Story – From Phase III to Licencing to Eli Lilly*

Earlier this year Acrux licensed the global rights to its Axiron product (transdermally delivered testosterone for males) to **Eli Lilly** in what is arguably a landmark deal for Australian biotech. Acrux executives Jon Pilcher (CFO) and Hugh Alsop (Director of Business Development) spoke to the 6th Bioshares Thredbo Biotech Summit audience on strategies, issues and processes that led to this outcome.

John Pilcher began by summarising what had been achieved to date. The deal, which took place in March 2010, followed the successful completion of a Phase III trial of Axiron. Manufacturing was set up with **Orion** in Finland, a task which Pilcher said was of the same difficulty and importance as managing and completing the Phase III trial.

Acrux submitted an NDA with the FDA in January with a review decision expected by Q1 2011. The company is being assisted by its licensee Lilly with this task.

### Deal Terms and Choice of Partner Both Important

Pilcher emphasised that it was not just the deal terms that were important for Acrux but certain characteristics of the licensee as well. Lilly is a top ten pharma, with distribution in 130 countries and strong in emerging markets. However, Pilcher said that biggest attraction for Acrux was that Lilly markets Cialis, an erectile dysfunction drug marketed to the same physicians to whom Axiron will be marketed. Lilly came to market with Cialis after **Pfizer** launched Viagra but "reeled Viagra in by clever marketing and a real commitment to mens health" and now Cialis is rivalling Viagra in sales. "Lilly was the perfect commercial partner - we couldn't have found anyone better" he said.

So far the company has received US$50 million as an upfront payment and stands to receive another US$3 million when manufacturing assets are transferred to Lilly. When Axiron is approved by the FDA, Acrux will receive US$87 million. Another US$195 million in payments is dependent on sales performance milestones being achieved, which Pilcher emphasised were not blue-sky milestones. Finally, the deal included a royalty component, which if modelled in net present value terms represents twice the milestone payments.

The deal had a great balance to it, said Pilcher, and the company was keen to get a substantial upfront on FDA approval. However, Pilcher said Acrux did not want to trade away upfront with "puny royalties". Acrux will start paying dividends, subject to FDA approval of Axiron, in 2011.

### Axiron Development History

Pilcher reviewed the development history of Axiron. In 2007 Acrux received a term sheet for Axiron, however the company rejected the offer and changed strategy for the product, electing to fund a Phase III program. The company raised $22.5 million for this purpose.

*– Cont'd over*

*– Axiron cont'd*

"When we looked at what was needed to complete development, we thought we had the capabilities to do that."

In 2008, the company set up the manufacturing agreement with Orion, commenced the Phase III trial, but also commissioned market research which meant that Acrux could validate its assumptions about Axiron.

Pilcher said that the partnering process did continue on from 2007, in that the company continued to build relationships with potential partners. However, these discussions did not include money terms until the partnering process kicked off at a higher level in 2009.

### Axiron Positioning and Market Opportunity

Hugh Alsop, Acrux's Director of Business Development, discussed the positioning of Axiron, using a product tag created for Axiron of 'letting patients get back to what is important'. In this case, the patient group is men who need to restore a sense of masculinity that is lost with low levels of testosterone. Symptoms include erectile function, decreased sexual desire, fatigue, loss of energy, mood depressions and osteoporosis.

The market opportunity is based on epidemiology studies that show that up to 39% of men over the age of 45 could have clinically diagnosed low testosterone. This gives an idea of the size of the market and estimates are that only 10% of that market are receiving treatment. Current treatments include injections, which are painful, and gels, which are messy and are subject to the risk of person-to-person transfer. In contrast, Axiron is applied to the armpit, is fast drying and is odourless.

Axiron has been shown to restore testosterone consistently to normal ranges and has been clinically proven to improve libido and sexual function said Alsop. This means men can feel more confident and have real vitality in their lives.

The global market for testosterone products has now reached US$1.2 billion as measured by sales, of which 83% is in the US. The market has shown strong growth for a number of years with a compound annual growth rate from 2004 to 2009 of 17%.

### Phase III Results

The primary endpoint was the restoration of testosterone within the normal range at the end of four months, for 75% of trial subjects. The Phase III endpoint was exceeded with 84% of trial subjects registering testosterone levels in the normal range after four months. In fact, after only two weeks of treatment, 76% of trial subjects were recording testosterone restored to the normal range.

### "Execute to Perfect"

The philosophy that drove the development of Axiron was contained in a phrase 'Execute to Perfect' that was introduced early on by the CEO of Acrux, Richard Treagus. The phrase was used to create a mindset that ensured that all the elements of the development program were covered.

Alsop said that the Axiron development program was "not just about the clinical trial, not just about meeting the primary endpoint. It was about completing a package that the marketing partner had very little to do to finish off. They (the partner) didn't have set up manufacturing, they didn't have to worry about IP, do further work on containment closure, or scale up the applicator."

"When we put the board proposal together in 2007 we made sure we had every element, clinical, IP, containment closure, supply chain, brand funding, all in that board presentation, all were addressed and were a fundamental part of the project plan," said Alsop.

Alsop said the reason Acrux opted for a comprehensive development plan was that "We did not want to be sitting opposite a licensing partner who said 'You have great clinical data, but we need to spend another 'x' million dollars on the supply chain, or fix up IP, or you still have scale up work to do on your applicator. We did not want to be in that position."

### Catching the Big Fish

The partnering process was driven with five objectives in mind, the first of which was to have an outcome that maximised value by Q1 2010. Acrux had publicly stated an objective to be profitable for FY2010, so a deal had to delivered in H1 2010.

The second objective was to control the entire process. "We had a process in place that drove the timeline, the information sharing requirements, when offers needed to be submitted, what structures they needed to be in," said Alsop.

The third objective was to maximise the number of possible partners.

The fourth objective was to carefully manage the information sharing process from two perspectives, one of which was confidentiality. Alsop said that Acrux put in a confidentiality process specific to the partnering process that was very onerous and set the bar higher than what many pharma companies were used to. This was done to protect the eventual licensee of the product in terms of the information that was being shared but also used to qualify interest in the product. The second element of information sharing process was the management of the confidentiality of the data access. This was achieved using an online data room.

The fifth objective was to establish competitive tension. "In every discussion we had, we emphasised it was a competitive process by using deadlines and using language to emphasise it was a competitive process, in terms of deadlines, dates, the provision of information in specific formats. We wanted to convey to every person that they weren't the only person we were talking to."

### Insights from Interactions with Potential Partners.

Alsop discussed some of the insights they learned from their interactions with potential partners. One early sign stemmed from how a potential partner responded to the stringent CDA requirement. "One particular company was still negotiating the CDA six weeks after receiving it. If they are taking that long to do that, then how could they be expected to get through the product licensing negotiations? That was a very telling step".

*– Cont'd over*

*– Axiron cont'd*

### Navigating within Big Pharma

Another challenge faced by Acrux was the need to determine if the person they were talking to had a mandate or possessed influence in the organisation or were a champion for the opportunity. "We needed to understand this early on because we did not want to waste our time with people that weren't serious".

A further challenge for Acrux was to understand a potential partner's process of evaluation and approval. "We needed to know what information they needed and when they need such information to make a decision."

### Looking for Genuine Interest

Another factor that Acrux had to deal with in the process was dealing with the parties wanting to gather competitive intelligence versus real interest. To address this, if the interested party asked for specific Phase III data, Acrux stipulated that had they had to put an offer on the table before they saw the data. This meant that companies fishing for information quickly walked away. This put a hurdle in place to sort out the genuine from the non-genuine potential partners.

Another insight gained was from analysing the type of questions received, for example, if the questions came across as 'poking holes in our product'. "Were they putting up every reason why the clinical trial was designed wrongly, every reason why it wouldn't get approved, every reason why the COGS wouldn't satisfy their requirements?" The opposite was whether they were objectively evaluating the product and pitching the product in the business and understanding what they need to finish the product and get it to market. These were a good indicator of the level of interest and the seriousness of interest in our product.

### Travel !

Another facet of the process was discovering whether or not a potential partner was willing to travel to Australia. Although Australians are willing to travel long distances, the reverse can be the case for international companies. "When six weeks after we released our Phase III results a team of six people from a Big Pharma company turned up on our doorstep, we knew we had some serious interest," exclaimed Alsop.

### Tools Used in the Process

Alsop described some of the information and information management tools used in the licensing process. Acrux prepared fact sheets but also wrote an Information Memorandum, which was a 30-40 page document that was published immediately after the Phase III results were announced. This contained detailed information on the product, including development status, information about IP, the partnering process and the time table. The time table included the deadline for submission of offers, when finalised term sheets should be delivered, dates for due diligence and an expectation of the format of an offer.

Web-based communications were delivered using **Cisco**'s Webex and a data room was managed using software supplied by **Ansarada**. The data room gave Acrux the ability to control access to different levels, note when people had accessed documents and what documents they had accessed and for how long.

### Evaluating the Offers

A final challenge for Acrux was how to evaluate offers. Acrux developed three principles for evaluating offers. These were the maximising of value, maximising the certainty of receiving value and thirdly allowing for flexibility on the structure of the offer.

One of the most important assumptions in the offers was that of sales, with deal values proving very sensitive to sales assumptions. Acrux evaluated deal offerings by applying the same sales assumptions to each offering. This was followed by analysing sales using the assumptions supplied by each potential licensee. It was important to use both methods, said Pilcher.

The deals were also assessed according to execution risk, in other words taking into account the likelihood that a potential partner could achieve their sales forecasts.

### A Clear Purpose

Pilcher said that in 2007 when Acrux announced a change of strategy it did so with a very clear purpose: to complete the Phase III and then partner the product.

Management developed a detailed business plan that contained three main elements:

– Activities need to develop Axiron
– A costing of the process
– A timeline for the process

Acrux then went to shareholders with a very clear proposition. Pilcher said that Acrux was raising money for a specific proposal, and not for working capital and was able to say to shareholders 'We are raising this much money, this is why we need it, this is what we are going to do with it.'

Pilcher said that the company also decided to publicly commit to outcomes and timelines. " We were putting ourselves on the line." However, Pilcher believes this helped them raise capital for the project in less than 48 hours.

### The Challenge of 'Executing to Perfect'

Although the program was delivered on time and within sbudget, Pilcher said that the process was not without issues. "There were issues everywhere – issues in the trial, in manufacturing, and right in the middle we had the GFC. We raised capital at $1.60 and the price plummeted to 40 cents. There was nothing we could do about it. The exchange rate went from 90 cents to 60 cents and back to 90 again through the execution period. It was not plain sailing."

"But we developed a culture of dealing with problems immediately as they came up and put the collective brains of the company on to dealing with them. All of us were all over the detail of everything."

In summing up, Pilcher said that diligence was a key discipline for the Acrux team. "We paid attention to every minute detail". And Acrux constantly refined its assumptions as it progressed through the partnering process.

**Bioshares**

# *The Application of Starpharma's Dendrimer Platform to Drug Delivery*

Starpharma's CEO, Jackie Fairley, gave a very enlightening presentation on another aspect of the Starpharma portfolio. While much has been communicated about Starpharma's Vivagel product and its application as a microbicidal condom coating, the company was asked to present on the rapidly strengthening interest in the use of the company's dendrimers for the application of drug delivery. The presentation clearly showed just why there is so much interest in the Starpharma story.

Starpharma is using its dendrimers as a chemical scaffold that can be attached to existing pharmaceuticals to enhance their properties. Starpharma has drug delivery partnerships with **Eli Lilly** (for pharmaceuticals), with **Stiefel Laboratories** which is now part of **GlaxoSmithKline** (for dermal products), with **Elanco**, the animal health division of **Eli Lilly**, and some earlier stage deals including in agrochemicals.

The specific properties of drugs and agrochemicals that dendrimers can improve include: better efficacy of drugs through tissue targeting; drug half life extension; reduced toxicity; product life cycle management; and better drug solubility. It was perhaps the data from the preclinical studies that really confirms how much progress the company has made in drug delivery.

## Cancer Drugs

Paclitaxel (or Taxol) is normally almost completely insoluble in water (only 0.8 ug/ml). However when Starpharma covalently bonded that drug with its dendrimer, the solubility was increased by more than 9,000 times.

Fairley pointed to the very interesting case study of **Abraxis Biosciences**. Taxol is largely insoluble and its 'oily' formulation includes cremoforms that cannot be removed in manufacturing. These cremoforms cause hypersensitivity reactions with patients. This means the drug needs to be administered very slowly over many hours with patients resting in a hospital bed.

Abraxis improved the water solubility of taxol in a re-engineered product called Abraxane. A consequence is that Abraxane can be delivered quickly in an out-patient setting. Abraxane generates sales of around US$350 million and recently **Celgene** announced its acquisition of the company for US$2.9 billion.

## Patent Expiration Driver

One of the issues driving the strong interest in drug re-engineering according to Fairley is the number of patents expiring for existing drugs. It is a lower risk option to, in a creative way, modify an existing drug than to go right back to the beginning with a new chemical entity said Fairley. Starpharma is working with all categories of drugs, including small molecules, proteins, peptides and even antisense drugs.

## Increased Half Life Means Less Frequent Delivery

By changing the size of the dendrimer, Starpharma can increase the half-life of pharmaceuticals. For the drug methotrexate, the company has shown it can extend the half-life out from 24 minutes to over 50 hours. For cancer drug doxorubicin, the half-life can be extended from about 30 minutes to 34 hours. Fairley said doxorubicin is still the most widely used cancer drug in the world.

This increased half-life has also been achieved with protein drugs. Insulin is another product Starpharma is working on. Even though this is an on old off-patent drug, insulin generates sales of $16 billion a year and there is still interest in improving the delivery aspects of this drug. Starpharma has shown extended glucose suppression in a diabetes animal model by combining its dendrimer scaffold with insulin, thereby potentially offering less frequent injections for patients.

## Reduced Toxicity

For the area of cancer treatment, Starpharma has shown in a mouse model that a dendrimer-doxorubicin structure could maintain efficacy but deliver lower cardiac toxicity. According to Fairley, this is because the large construct is too big to get through tight capillary junctions into normal tissues such as the heart but the large molecules can seep through the leaky blood vessels that exist in a tumour. This becomes a passive targeting mechanism, said Fairley.

This reduced toxicity has shown to increase the maximum tolerated dose of the dendrimer-doxorubicin construct to twice that of the PEGylated liposomal doxorubicin in a mouse model. The implication is that a sustained and perhaps an improved treatment with cancer drugs such as doxorubicin can potentially be achieved with a dendrimer-doxorubicin construct. Fairley said this proof-of-concept data has been compelling when talking to partners.

## Advantages over Liposome Drug Carriers

An advantage over liposomal drug carriers is that liposomes tend to be less stable and break down and are not always reliable as drug carriers. Dendrimers can be more highly loaded with active drugs than liposomes. Liposomes can also be difficult to dissolve, unlike dendrimers, forming an oily viscous liquid. Dendrimers have at least twice as long a shelf life over liposomal drug carriers. And the manufacture of dendrimers is easier than liposomes, said Fairley.

## Targeted Delivery

Different sized dendrimers can target different tissues said Fairley. Also, Starpharma has been able to add monoclonal antibody fragments onto the dendrimer scaffold for targeted drug delivery. The larger compounds have also shown to achieve higher blood levels of drugs in the lymphatic system, giving a more concentrated drug dose in the lymph nodes where the cancer cells accumulate and spread.

## Attractive Business Model

Starpharma believes it has an attractive business model. The company produced proof-of-concept data to demonstrate the concept of using dendrimers to provide the drug delivery benefits (as previously mentioned). It was then able to sign collaboration deals such as the Eli Lilly deal, where that company provides the active drug, Starpharma conducts the chemistry work which is paid for by the partner, and then all the subsequent development work is completed by the partner.

*– Cont'd on page 6*

# *Understanding Drivers of the Pain Market – Case Studies*

In developing pain therapeutics, **QRxPharma**'s Chief Operating Officer Phil Magistro said that market research is a key and important piece of the puzzle. Magistro spoke on drivers in the pain therapeutics market, having been intimately involved with the commercial success of several pain drugs.

Magistro said pain therapeutics constitute a very large market that is getting bigger, with over 150 million people in major pharmaceutical markets suffering from pain. The pain market is expected to increase from US$36 billion in 2010 to US$49 billion in 2020, partly due to the aging population.

For opioid drugs, the focus at the moment is on reducing abuse of these drugs, and also on providing drugs with fewer side effects. Magistro said that according to an article in the *British Journal of Pharmacology*, the search for the holy grail in opioid drugs over the last 75 years – finding an opioid-like drug the provided opioid-like analgesia without the side effects – has been a failure.

Magistro said the acute pain market in the US is dominated by generics, with 190 million annual prescriptions with an estimated value of US$3.3 billion in the US. The chronic pain market is more dominated by branded drugs. That market is generally more appealing with a larger market estimated at being worth US$4.9 billion in 2010.

## Case Study 1 – Neurontin

Magistro was involved in the pre- and post-market commercialisation of Neurontin at **Parke Davis**, having worked there for 15 years. The market for neuropathic pain in the US was worth only US$178 million in 1994, being a highly generic market. That market in 2001 jumped to US$1.3 billion with Gabapentin (brand name Neurontin) making up for most of that growth (sales of almost US$1 billion).

The anti-epileptic drug Neurontin was found to be as effective as the older antidepressants in treating neuropathic pain, which were effective in treating about 50% of patients. However the side effects were so severe said Magistro that many patients discontinued treatment. However the side effect profile of Neurontin was starkly different with largely benign side effects.

Sales of Neurontin were US$440 million in the US around 1997/98 said Magistro however in Europe sales were stagnant at US$50 million. Magistro and his team then did some market research and found that their affiliates in Europe simply required better education from some US key opinion leaders around the benefits of using Neurontin for the treatment of neuropathic pain. Over the subsequent three years, sales accelerated by US$300 million in Europe as a result.

## Case Study 2 - Kadian

After Parke Davis, Magistro worked on the Kadian product for the Australian company **F. H. Faulding**. Faulding developed Kadian, which was a delayed release version of morphine sulphate. It was initially licensed to **Astrazeneca** but was returned when it only generated sales of US$3 million in 1996. Faulding put on 24 sales people in North Carolina but sales remained stagnant at around US$5 million between 1997-2000.

### *A diamond in the rough*

When Magistro joined Faulding in 2000, he conducted market research on the Kadian product and found it was a 'diamond in the rough'. The problem was that it was being sold on the benefit of being a once a day treatment against other pain products taken three to four times a day that did not deliver consistent pain relief.

However Kadian once a day was not sufficiently effective. However, when it was taken twice a day it was very effective with very consistent serum levels achieved throughout the day, said Magistro.

Faulding conducted a large Phase IV trial in 1200 patients and the product was relaunched in 2001 being repositioned as a twice a day product. In the first year sales of US$35 million were achieved, US$80 million in the second year and eventually sales of US$275 million were achieved with the drug in the US.

Magistro said that if the drug had been launched correctly in the first place, it could have been a US$600 million drug.

## Case Study 3 – MoxDuo, A Work in Progress

Magistro's third case study is a work-in-progress. He says that by combining morphine with oxycodone (MoxDuo), QRxPharma is potentially addressing the holy grail in opioid therapy. Magistro said this combination of opioids is achieving a 50%-75% reduction in side effects while achieving equal analgesic effect against other opioids such as Percocet (oxycodone plus paracetamol). The most clinically significant adverse events according to Magistro of opioids are nausea, vomiting, dizziness, sedation and constipation. MoxDuo addresses both these acute and chronic use side effects.

Magistro believes QRxPharma will need to show the value proposition to payors. Time to discharge is a huge issue for managed care providers. If they can discharge a patient that day rather than having them on the books the next day then you have a clear winner said Magistro. If you can save them time, then they will be after your drug, where the health management cost savings completely outweigh the costs of the drug. (Presumably the better side effect profile will allow patients to be discharged earlier.)

Magistro believes MoxDuoIR is a market game changer, even though it is going into a generic market space, which can expand the immediate release (IR) opioid dollar market by commanding a premium pricing in the market.

## Implication

The implication from Magistro's talk is that highly successful commercial products can be achieved in the pain therapeutic space, even from small improvements in drug products and if the correct market research is conducted. However, MoxDuo potentially offers much more than just incremental benefits to existing pain treatment regiments.

**Bioshares**

**Bioshares Model Portfolio (26 July 2010)**

| Company | Price (current) | Price added to portfolio | Date added |
|---|---|---|---|
| Sunshine Heart | $0.033 | $0.036 | June 2010 |
| Biota Holdings | $0.97 | $1.09 | May 2010 |
| Tissue Therapies | $0.18 | $0.21 | January 2010 |
| QRxPharma | $1.00 | $0.25 | December 2008 |
| Hexima | $0.28 | $0.60 | October 2008 |
| Atcor Medical | $0.15 | $0.10 | October 2008 |
| CathRx | $0.20 | $0.70 | October 2008 |
| Impedimed | $0.67 | $0.70 | August 2008 |
| Mesoblast | $1.83 | $1.25 | August 2008 |
| Circadian Technologies | $0.59 | $1.03 | February 2008 |
| Patrys | $0.10 | $0.50 | December 2007 |
| Bionomics | $0.31 | $0.42 | December 2007 |
| Cogstate | $0.25 | $0.13 | November 2007 |
| Sirtex Medical | $5.14 | $3.90 | October 2007 |
| Clinuvel Pharmaceuticals | $0.25 | $0.66 | September 2007 |
| Starpharma Holdings | $0.54 | $0.37 | August 2007 |
| Pharmaxis | $2.16 | $3.15 | August 2007 |
| Universal Biosensors | $1.48 | $1.23 | June 2007 |
| Probiotec | $1.30 | $1.12 | February 2007 |
| Acrux | $1.86 | $0.83 | November 2004 |
| Alchemia | $0.43 | $0.67 | May 2004 |

### *Portfolio Changes – 26 July 2010*

**IN:**
No changes.

**OUT:**
No changes.

*– Starpharma...from page 4*

Under such arrangements, Starpharma is able to have many parallel programs underway, where in some cases the future upside for Starpharma could be a single digit royalty from billion dollar products. Fairley said the company has been careful not to contaminate or overlap the program areas, being careful not to license product applications for whole disease areas but for more specific drugs. Fairley believes this is a much lower risk strategy at the same time as maintaining upside across the programs.

### Agrochemicals Application

Starpharma has signed its first deal in the agrochemicals space and is hopeful it will sign several more. Some of the same properties of the dendrimers as with drug delivery can be very useful in agrochemicals, including higher solubility (therefore lower shipment volumes), patent extension and product differentiation. The multiple attachment sites of the dendrimers also make them quite sticky commented Fairley. This has the potential benefit that agrochemicals will not be washed off as easily in the rain and also provide protection against UV degradation.

The agrochemicals application has the same commercial structure, where the research is funded by partners and Starpharma maintains any future upside.

**Bioshares**

*Next week in Bioshares we will continue with coverage of the Thredbo Biotech Summit, covering the finance and investment themes discussed at the event.*

***Correction***

In *Bioshares* 368 we stated that Phosphagenics' alpha-tocopherol is a form of Vitamin A. This is incorrect, with alpha-tocopherol being a form of Vitamin E.

## 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.

### 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, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical, CathRx, BioMD, Tissue Therapies, Viralytics