ISSN 1443-850X

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%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

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Individual Subscriptions (48 issues/year)
$350 (Inc.GST)
Edition Number 369 (27 July 2010)
ISSN 1443-850X

Bioshares

27 July 2010
Edition 369

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

Extract from Bioshares –
The 6th Bioshares 2010 Thredbo Biotech Summit - Event Coverage

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.

– Cont'd over

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.

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

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

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