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In this edition...
This week Bioshares takes a look at two Melbourne biotechs that have undergone transformational change over the last 2 years.

Metabolic Pharmaceuticals is well on the way to finsishing the repeat of a Phase II trial of its obesity compound AOD9604. Starpharma's proposed acquisition of Dendritic Nanotechnologies looks to be a nice completion to a set of reforms and changes made to the company, starting from the day it decided give up its PDF investor status in March 2004.
The message from both of these companies is that, with time, effort and patience, difficult business challenges can be addressed.

The editors
Companies covered: MBP, 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 (from 5 May '06)	-9.8%
Cumulative Gain	**151%**
Average Annual Gain	**22.3%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd. The company also provides market and company analysis of the Australian pharmaceutical and biotech industries for local and international funds management institutions, venture capital funds and other related industry groups. For further details contact David Blake (see details below).

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Bioshares

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

Bioshares 20 Index Posts Strong Gains

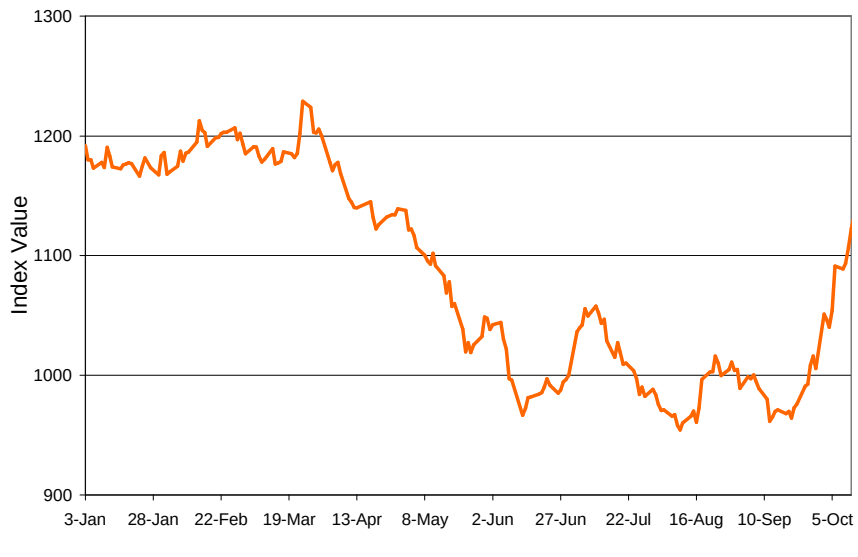
The Bioshares 20 Index has posted its strongest gains since June over the last two weeks. The index increased 3.8% from a week ago. This followed an 8.5% increase in the previous week. From June 30, the Bioshares 20 Index has increased 13.2%. Over the same period the Nasdaq Biotech Index has increased 6.9%.

The Bioshares 20 Index	
Change from June 30, 2006	**13.2%**
Change - week ago	**3.8%**
Nasdaq Biotech Index	
Change from June 30, 2006	**6.9%**
Change - week ago	**2.1%**

The increase observed in the Bioshares 20 Index has occured because of strong gains in the stock prices of **Metabolic Pharmaceuticals** (up 29.2%), **Pharmaxis** (+12.8%), **Mesoblast** (+10.2%) and **Cellestis** (+8.7%). Only four stocks recorded price falls, with **Life Therapuetics** registering the greatest fall of 3.3%.

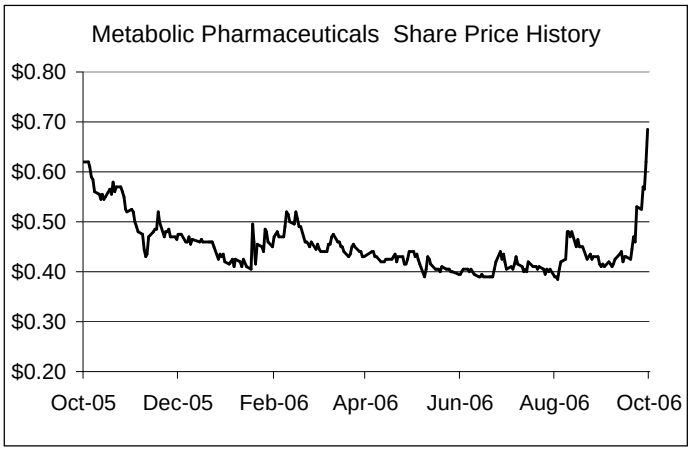
This recent recovery in the Bioshares 20 Index indicates that some interest has returned to the biotech sector and confirms the view posited in the last week's Bioshares (edition 187) that the sector had bottomed in the September quarter in terms of investor sentiment.

The Bioshares 20 Index



Metabolic Pharmaceuticals Impressive Turnround

Metabolic Pharmaceuticals (MBP: $0.685) epitomises some of the features that attract biotech investors: drug candidates approaching major clinical milestones, potential new medicines that represent a very large market potential, but also high technical risk with the reciprocal high investment reward. Two years ago Metabolic Pharmaceuticals failed to achieve a major clinical milestone for its obesity treatment compound, AOD9604, in a Phase II trial. In December this year, a repeat of that study will be completed with results due for release in March next year. Between now and March 2007, there will be considerable anticipation and speculation about this trial result. Once again there are investment opportunities with this stock as the company seeks to make a definitive impact on the Australian biotechnology sector.



Two years later...

When Metabolic Pharmaceuticals released its Phase II results for AOD9604 in December 2004, the result was disappointing on two fronts. Firstly the trial did not represent statistical significance in its primary measure, that of overall weight loss. However the second failure was by the company in not recognising the shortfall in the result, with the trial result hailed as an overwhelming success.

In the last two years the company has successfully sought to correct both of these failures. A management change with the appointment of Roland Scollay as CEO has effected an improved dialogue with analysts, media commentators and investors with previous shortcomings recognised.

The company has also acknowledged the need to conduct an additional trial with larger patient numbers and different dosing points in an effort to deliver statistically significant results that were not achieved in the previous trial. The turnaround by the company over this time is impressive.

In March this year, the company completed a $13 million capital raising at 43 cents. In December 2004, Metabolic was effectively a binary play, with the focus overwhelmingly on AOD9604. The company now has two Phase II programs underway both with very large market potential, the second a neuropathic pain therapeutic that has moved in Phase II clinical trials.

The company is also expecting to have a third program in Phase II clinical testing next year, with the same AOD9604 but for the treatment of osteoporosis. AOD9604 is a growth hormone fragment and that it may have effect on promoting bone growth is not altogether surprising. The market for osteoporosis is also extremely large, in excess of US$7 billion last year.

Trial design

The current trial of AOD9604 involves 536 people. There are some positive aspects to this trial. Firstly, the trial numbers are higher than the previous obesity trial, which involved 300 subjects. Interest in this drug and the capability of the company in conducting the trial has been positively reflected in the early full recruitment of subjects in the trial, which was completed in May this year.

Each person is treated for 24 weeks and to date 100 subjects have completed the trial. In total, each person is enrolled for 32 weeks, which includes eight weeks of pre- and post-treatment observation.

The primary endpoints are weight loss over 12 weeks and also safety and tolerability. The secondary endpoints include weight loss over 24 weeks, waistline reduction, body fat reduction and improvements in risk factors such as glucose control and lipid levels.

The trial includes equal numbers of obese men and women. There will be four dosage groups, these being 0.25 mg, 0.5 mg and 1 mg of AOD9604 and a placebo group. Each person will also be placed on an exercise program and a diet.

Probability of success in current obesity trial

We expect there will be a variation in results in men and women and variation due to body weight and metabolism of the drug, which will complicate the trial. That the dose response curve is an inverted bell-shaped curve as revealed in the previous study, and is inverse to that previously expected, also makes selecting the correct dosage for each patient more difficult.

In the previous trial, the dosage levels selected were 0 mg, 1 mg, 5 mg, 10 mg, 20 mg and 30 mg. The best result in weight loss over 12 weeks was an average 2.8kg at the 1 mg dose, compared to a 0.8kg loss in patients on a placebo. However there were insufficient patient numbers at that efficacy level to achieve the statistically significant level (the probability value was 0.1, which equates to a 10% chance that result was not reproducible).

To counter this unknown, Metabolic has increased the enrolment numbers from 300 to 536 fully recruited (with a target of 480 patients to complete the trial). The number of treatment groups have decreased from six to four, which all equates to 2.4 times the number of people in each treatment group compared to the

Cont'd over

previous Phase II trial. The company has indicated that the trial has been structured such that it will have an 80% chance of achieving statistical significance ($p<0.05$) in the 1 mg treatment group if similar results from the previous trial are obtained.

We believe the trial will viewed as very successful if there are no common adverse side effects and if the average weight loss over 12 weeks can exceed 2kg taking into account the placebo effect. The reason for this is that a competing product on the market, Xenical, achieves an average weight loss of 1.8 kg over three months.

Perhaps more important will be whether this weight loss can be sustained over the six month period, which was not measured in the previous trial that lasted only three months. Also of great relevance will be the effect on lipid levels and glucose control, which should not be underestimated. If this drug can be shown to help manage and control Type 2 diabetes, it could significantly expand the market for this drug.

Steady IGF-1 levels will also be a vital parameter to check. Escalating IGF-1 levels could potentially lead to unwanted self proliferation of cells resulting in a cancer-promoting risk. Previous trial results showed steady IGF-1 levels.

Our estimate at this stage is that the company has a 30% chance of returning a very good result from this trial, and a 60% chance of achieving reasonable result with some key questions still unanswered. The logic behind the mechanism of action of this compound is highly suggestive that the compound will promote weight loss. However, the variable response curve of this growth hormone fragment significantly increases the complexity in bringing this drug to market.

Competition

There are a number of drugs on the market with the leading drug being Xenical. At present, Xenical sales are approaching US$1 billion a year after the drug was approved by the FDA for sale without prescription in January this year. (The drug is also being advertised for sale on local television in Australia). The drug was first approved in the US in 1999. Unpleasant aspects of this drug are the side effects of oily spotting and oily stools.

Other Projects

1. Therapeutic pain

Lat month, Metabolic commenced a trial with its second drug, ACV1, for the treatment of neuropathic pain. This compound was in-licensed from the **University of Melbourne** in 2003 and the company has made rapid progress to move it into Phase II clinical studies.

The drug, a peptide, was derived from venom found in an Australian marine cone snail. This compound has powerful analgesic properties. The current trial, which will involve 40 patients, will assess ACV1 delivered by subcutaneous injection. This proof-of-concept study is expected to be followed by trials with an oral version of the drug. The company has experience in the modification of peptide drugs into oral form with the development of AOD9604 (this drug was originally trialed as an injectable). Metabolic announced that it has invented an oral version of this drug and clinical studies are expected to begin once the current Phase IIa trial has been completed.

A major milestone for this company is evidence that it has developed an effective oral version of the drug, with the market for injectable pain drugs significantly lower than that for orally available pain drugs.

2. Osteoporosis

Metabolic is investigating the lead drug, AOD9604, for properties in the treatment of osteoporosis. In January this year the company announced it had produced positive preclinical data with the drug. Of interest also is that this study, conducted by scientists in Canada, also showed that a side effect in the animal model for osteoporosis was weight loss. The clinical use of growth hormone in the treatment of osteoporosis has been documented. With safety studies already completed with this drug, the company is expecting to be in a position to move into Phase II clinical studies for osteoporosis next year.

Valuation

When Metabolic shares hit their peak of $2.20 in December 2004, just prior to the release of the last Phase II results (and just after), the company was valued at $508 million. With the existing shares on offer, this capitalisation equates to a share price today of $1.78.

However, Metabolic is substantially better placed in the lead up to the release of results from the current trial compared to December 2004. Metabolic is no longer a one product biotech company, with two other Phase II trials expected to be underway next year.

The company will have gained considerable information from the previous obesity trial and this current trial should be better structured and is better powered for a statistical result.

Summary

Metabolic Pharmaceuticals is a transformed company from two years ago. A new CEO, another shot at goal with its obesity treatment compound in what should be a far more illuminating trial, and a more advanced, diverse portfolio of projects makes this stock a worthy investment consideration. The company now has three shots at goal, each with large market potential, which should appeal to many investors, both retail and institutional, as the company progresses its pipeline. There should also be significantly increased interest in this stock in the lead up to the release of the results from the current Phase IIb trial. Investors should expect high volatility in this share over the next five months. While the stock has the potential to deliver strong gains, it will have a high risk profile while it approaches a major milestone event (in March 2007). The company is capitalised at $191 million with $23 million in cash at the end of June this year.

Bioshares recommendation: **Speculative Buy Class A**

The Rationale Behind Starpharma's Acquisition of DNT

In last week's edition we commented briefly on Starpharma's decision to buy out the other shareholders of **Dendritic Nanotechnologies (DNT)**, a company in which it has held a 33% stake. This week we examine the proposed transaction in some more detail.

Starpharma
Starpharma (SPL: $0.53) is a Melbourne-based developer of pharmaceutical applications of a large molecule chemistry scaffold technology known as dendrimers. Dendrimers are branched structures that are constructed around a core unit. Once one layer of chemical units that are the basic building block are laid down, then successive layers, or 'generations' can be added as desired. This concept allows for very precise structures to be made to order.

Starpharma was founded as a spin-out of the **Biomolecular Research Institute** (BRI) in 1996 and listed on the ASX in 2000. Starpharma has developed the first pharmaceutical application of dendrimers, Vivagel, which is a 'four-generations' polylysine dendrimer. Vivagel is being developed as topical application for the prevention of HIV and genital herpes (HSV2). The Vivagel program is the recipient of US$26 million in funding from the US **National Institutes of Health** (NIH).

Attached on the surface of the Vivagel dendrimers are 32 units of another chemical (napthalene disulfonate) that bind to a protein (gp120) on the HIV virus, thus inhibiting the virus from binding and infiltrating certain key immune system cells.

Dendritic Nanotechnologies
Dendritic Nanotechnologies is a privately owned US based dendrimer technologies company that was founded by Starpharma and Dr Donald Tomalia in August 2001. DNT was first established principally as a commercial supplier of dendrimers for research and development purposes and to generate income from the licensing of proprietary dendrimer architectures.

Deal value
The deal values DNT at approximately $14 million. The number of Starpharma shares on issue will increase from around 147.7 million to 168.7 million.

What is the rationale for this acquisition?
One of the problems of being a minority shareholder is the lack of control over a company's management and direction. By bringing Starpharma and DNT under the one management structure, the companies' combined resources can be more efficiently managed. A second rationale is that a number of investment attributes that were embedded separately in each company, yet linked through partnership arrangements, can be more clearly identified and evaluated in a combined entity.

These investment attributes include a company with revenue emanating from the sale of research chemicals and royalty income, which is currently in the order of $1.25 million per annum, two pharmaceutical and diagnostic products in development and a comprehensive intellectual property estate.

The consolidation of the IP assets may well be the most important aspect of the transaction because it may enable certain North American investors to approach the stock with a greater degree of interest, comfort and certainty.

In January 2005, **The Dow Chemical Company,** assigned all its dendrimer IP to DNT, including 41 patent families, in exchange for an equity holding. [Dow's holding at the time of the acquisition was 30%.]

Together with the 41 patent families contributed from Dow, 19 patent families are contributed by Starpharma and at least two by DNT to the combined entity. Although there are a reasonable number of dendrimer application patents granted to other parties, the newly formed Starpharma patent estate represents the largest with the most potential for blocking the activities of other parties wishing to practise other uses.

Another benefit for Starpharma includes control over a subsidiary based in the USA. US investors have built a 19% stake in Starpharma, including an 8.6% stake held by The Dow Chemical Company. The Dow stake may well prove beneficial to Starpharma as it seeks to increase the proportion of the firm held by investors outside Australia.

The US presence has a practical benefit, as DNT employs several business development personnel. Without adding much in the way of overheads, Starpharma can modestly increase its US-based business development activities, but significantly expand its capacity to address business development requirements for the combined entities' pharmaceutical operations.

Another benefit of the deal is that Starpharma has now built considerable expertise as a pioneer of the pharmaceutical applications of dendrimers, and has established infrastructure, such as analytical chemistry services to support this. DNT's diagnostic

Cont'd over

– Starpharma cont'd

dendrimer product could in theory benefit from the expertise developed in Starpharma's development work.

Assessment

The Starpharma/DNT transaction follows on from several restructuring activities undertaken by Starpharma since the company decided to rescind its Pooled Development Fund status in March 2004. Although this meant the company and its shareholders would forgo certain tax concessions, the decision signified its intention to move from being a manager of earlier stage projects to mature into a more focused developer of pharmaceuticals.

Since that date the company has transitioned its management with Dr Jackie Fairley taking over the CEO role from Dr John Raff in July 2006, although Dr Fairley had been appointed as Starpharma's Chief Operating Officer in March 2005.

In October 2005, Starpharma gained full ownership of key IP from the BRI, including three patent families. The BRI exchanged its 25% entitlement to the gross income that Starpharma might receive from any commercially successful products for 7 million shares in Starpharma.

It is not unusual for biotech companies to adapt or change their business more than once in a life spanning a decade or more, and Starpharma is no exception. What makes Starpharma unusual is that is has stuck with its original technology, achieving a measure of success with very substantial funding for Vivagel clinical studies from the NIH. Perhaps the main criticism that can be levelled at Starpharma is that its platform technology has not yielded more products suitable for clinical development. For example, no cancer therapeutics have been brought forward from the discovery stage.

In hindsight, a number of pharmaceutical products may not have been developed for reasons relating to cost of manufacture and DNT's next generation Priostar dendrimers that offer a much lower cost and ease of manufacture were only released in May 2005. However, the more basic reason for not developing a more comprehensive advanced portfolio is because of limited financial resources, with Starpharma's managers choosing one product (Vivagel) over others as being a more likely prospect for clinical and commercial success.

Summary

Assuming the DNT acquisition is completed, Starpharma looks set to begin a new and very positive phase as a biotech company. One key feature worth emphasising is that with the company now holding a comprehensive IP estate, its attractiveness as an acquisition target to pharmaceutical companies will have increased markedly. This is because large pharmaceutical companies place great value on being able to acquire assets that demonstrate clear freedom to operate, barriers to entry and no ongoing royalty obligations to other parties.

Starpharma is capitalised at $89 million, based on shares issued in consideration for the acquisition of DNT. As of June 30, Starpharma held $14.3 million in cash

Bioshares recommendation: **Speculative Buy Class A**

Bioshares Model Portfolio (13 October 2006)

Company	Price (current)	Price added to portfolio
Acrux	$0.81	$0.83
Alchemia	$0.69	$0.67
Avexa	$0.215	$0.15
Bionomics	$0.17	$0.210
Biosignal	$0.19	$0.22
Cogstate	$0.21	$0.20
Cytopia	$0.720	$0.46
Chemgenex Pharma.	$0.50	$0.38
Evogenix	$0.450	$0.47
Optiscan Imaging	$0.490	$0.35
Mesoblast	$1.370	$1.27
Metabolic Pharmaceuticals	$0.680	$0.53
Neuren Pharmaceuticals	$0.40	$0.70
Peptech	$1.35	$1.31
Pharmaxis	$2.73	$1.90
Prima Biomed	$0.064	$0.09
Sirtex Medical	$2.55	$1.95
Sunshine Heart	$0.15	$0.19

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: Phylogica, Neuren Pharmaceuticals, Pharmaxis, NeuroDiscovery, Prima Biomed, Biotech Capital, Cygenics, Psivida, Cytopia, Biodiem, Peptech, Starpharma Holdings, Cogstate, Xceed Biotechnology, Healthlinx, Incitive, Optiscan Imaging, Bionomics

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