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In this edition...
It's a turbulent time for equity markets, and biotech stocks have not been immune to the current sell down. Company's such as Prima Biomed and Cytopia are making exceptional progress and this is not being reflected by the market. However, the sector has never been in such a fundamentally strong position, with at least 14 companies either in or approaching (next 12 months) pivotal trials. In this edition we profile two such companies with attractive investment features, Starpharma Holdings and Avexa.

We also introduce readers to Giaconda, which listed in September 2005.

The editors

Companies covered: AVX, GIA, 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)	-8.6%
Cumulative Gain	**155.0%**
Average Annual Gain	**22.5%**

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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Edition 171

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

Avexa Approaching Crucial Milestone

One of the quality stocks to keep a close watch on is Avexa (AVX: 24 cents). The company specialises in the development of antiviral medicines and its focus at the moment is on a Phase IIb trial of AVX754 for the treatment of HIV, which commenced in July last year. The 60 patient trial is expected to be fully enrolled by the end of this month and results are due in the third quarter of 2006.

The trial is measuring changes in viral load after 21 days of treatment in resistant forms of HIV, in particular, M184V mutations. M184V mutations are common in patients being treated with 3TC (lamivudine) and FTC (emtricitabine). Avexa's compound, AVX754 (now called apricitabine), was originally developed by **Biochem Pharma** in Canada which was subsequently bought by **Shire Pharmaceuticals** in the UK in 2001 and licensed to Avexa for development in January 2005.

Apricitabine is very chemically similar to 3TC. The design rationale broadly is that a small change in the compound which has produced apricitabine is sufficient to maintain efficacy against the wild type virus but also efficacy against resistant strains such as M184V (and TAMS (multiple thymidine analogue mutations)). Whilst the virus mutates to develop drug resistance, each mutation reduces the strength of the virus relative to the original wild-type virus. In a Phase IIa trial conducted by Shire on the wild-type virus, the compound produced a 25-fold decrease in viral load. The minimum level of efficacy for this Phase IIb trial is a four-fold reduction in viral load. Anything less and it's likely the program will be discontinued.

Preclinical programs

Avexa has three preclinical programs, of which two are being actively progressed. The company is developing another HIV drug, which is an HIV Integrase compound, and this program is on track to enter the clinic in the first quarter of next year. Avexa is also developing a novel antibiotic to treat drug resistant bacterial infections. Results from preclinical studies are expected in the third quarter of 2006.

Avexa has split marketing rights for apricitabine with Shire. Shire has marketing rights for the US and Avexa for the rest of the world, with each company to receive royalties from sales in regions outside of its own allocation.

Funding for an 800 patient Phase III trial will be a major decision for the company if data from the Phase IIb trial is positive. The company has the option of raising $30 million from equity markets, although the company's capitalisation would need to exceed $100 million for this to occur, or more likely, the company could partner with a major partner, one who specialises in HIV. There are some obvious choices here, including **Gilead Sciences**, which has built a major antiviral business specializing in HIV and has a market capitalisation of US$27 billion. Combination therapy is the standard in

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Thredbo Biotech Summit

July 21- 22, 2006

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Founder of Axon Instruments

Geoff Brooke
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Julian Chick
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For full details, visit the Bioshares website - http://www.bioshares.com.au/thredbo2006.htm

Program and speakers subject to change. Accommodation is filling quickly. There are few accommodation & registration packages remaining. Please email pachacz@bioshares.com.au for details

HIV care and collaborations between market players are common.

Summary
Avexa has a capitalisation of $48 million. It is holding an estimated $22 million in cash. If a technology value can be ascribed for the company's preclinical program of $10 million, the apricitabine program is currently being valued at $18 million, or 33% of the company. This represents the possible downside should the current Phase IIb trial fail. The data to date suggests there is a strong chance the results from current trial will be positive and allow the company to move into a Phase III clinical program. The company's goal is to have the product on the market in 2009. With a global US$6.6 billion market for HIV drugs, the average sales for a HIV drug is in the order of US$300 million a year.

Avexa News Flow
- Phase IIb trial results (3rd qtr 2006)
- Results from antibacterial preclinical program (3rd qtr 2006)
- Commencement of Phase III HIV trial, pending positive Phase IIb results (2006)
- Commencement of Phase I studies for HIV Integrase program (1st qtr 2007)

Bioshares Recommendation: **Speculative Buy Class A**

Starpharma's VivaGel Delivers Added Bonus

Commercialisation of Starpharma Holdings' (SPL: 42 cents) dendrimer technology is on track to move to a pivotal phase in the next 12 months as the company plans for two population-based efficacy studies in 2007. If the company is successful, it may be in a position to file two products for regulatory approval in 2008 that will mark the significant transformation of this biotechnology company.

Contraceptive effect
This week, the company had a surprising positive development to announce regarding its lead product, VivaGel, a vaginal microbicide being trialed for the prevention of sexually transmitted diseases. In an animal model, the product was shown to have contraceptive activity, reducing the conception rate by up to 95%.

Although this figure is not high enough for Vivagel to be marketed as a stand alone contraceptive, the additional potential marketing claim could be very valuable in improving usage rates of the microbicide either as a stand alone product or used as a condom coating.

In the second half of this year, Starpharma will begin expanded safety studies in healthy volunteers for its VivaGel product in Kenya, the US and Australia. It's anticipated these trials will be completed early next year. Initial Phase I safety studies in 36 volunteers were successfully completed at the end of 2004.

Major studies in 2007
Next year, the company is confident it will commence major efficacy studies with its single use VivaGel applicator product for the prevention of HIV and genital herpes (HSV-2). These studies will be conducted in Sub-Saharan Africa and also potentially in the US and Australia. The trials may involve in excess of 1,000 people who will likely trial VivaGel for 12 months. Starpharma has set itself aggressive timelines for completing these studies – by mid 2008 – with the products to be submitted for regulatory review by the end of 2008. To fund the completion of this pivotal efficacy study, the company may need to raise further funds or seek further collaborations or partnerships.

Using the same active component, Starpharma intends to develop three products. The first would be a single use applicator product for the prevention of HIV and HSV-2 in developing countries. The second product would be for the prevention of HSV-2 primarily in developed countries. And the third product would be for use as a condom coating. Development of this product would require an early collaboration with a major condom manufacturer, which the company is seeking.

Whether VivaGel is to be used as a prophylactic treatment for the prevention of HIV or HSV-2, the added potential claim for the product as having contraceptive properties would be an obvious additional feature that would improve usage rates.

Summary
Starpharma is evolving into a more commercially focused business as key clinical milestones approach for the company. In the past the company could be criticised for the delay in moving its preclinical programs forward and lacking in external commercial validation. Over the next 12 months the company will be judged on its ability to progress its critical program and over the next two years on its ability to form commercial partnerships to bring its products to market.

At current prices, Starpharma is a very attractive investment to consider. The company is capitalised at $62 million with $15.4 million in cash at the end of March this year. It also owns a 33% stake in Dendritic Nanotechnologies in the US and has been awarded two important grants from the NIH, one for US$20.3 million for its HIV prevention program. The other, awarded in April this year, was for an undisclosed amount and will fund a clinical trial for the prevention of HSV-2.

Bioshares recommendation: **Speculative Buy Class A**

Giaconda's Myoconda Planned for a 2008 Market Entry

Giaconda (GIA: 40 cents) was established in February, 2004, as a commercialisation vehicle for the Sydney based **Centre for Digestive Diseases Pty Ltd** (CDD). The CDD is a privately run clinic that performs upwards of 5,000 procedures (eg colonoscopies) per annum. Giaconda listed in September 2005, issuing 12 million shares at 50 cents to raise $6 million.

Giaconda is developing Myoconda to treat Crohn's disease as a rescue treatment, that is where the front line treatment Remicade has failed.

It is also developing Hepaconda to treat HCV infection, where interferon and ribavirin have failed, Heliconda for the treatment of resistant strains of *Helicobacter pylori* and Ibaconda for the treatment of constipation in patients with Irritable Bowel Syndrome.

These therapies comprise combinations of existing approved drugs. For example, the company's most advanced therapy Myoconda is a combination formulation of three antibiotics: rifabutin, clarithromycin and clofazimine. The scientific hypothesis underpinning the treatment of Crohn's disease with a suite of antibiotics is that this disease is caused by the bacterium *Mycobacterium avium paratuberculosis* (MAP).

The company has patents granted in the USA covering the use of the rifabutin, clarithromycin and clofazimine as a combination therapy for the treatment of Crohn's disease.

That gastro-intestinal cancer can be caused by pathogens was recognised by the awarding of the Nobel Prize for Medicine in 2005 to Robin Warren and Barry Marshall from the University of Western Australia. Marshall and Warren proved *H. pylori* infection caused gastric and duodenal ulcers, which in turn correlate highly with gastric cancers. Marshall established a company **Trimed** that develops and markets tests and therapeutics for *H. pylori* infection. Tri-med markets De-Nol, a bismuth based chemical that undergoes a reaction in ulcerated regions of the G-I tract and creates a protective lining for the diseased tissues. It also markets furazolidone, an antibiotic for the treatment of patients with metranidazole resistent *H. pylori* infection.

Phase III trial

Giaconda has conducted a Phase III trial of Myoconda, otherwise known as anti-MAP therapy. The trial, completed in September 2004, and partnered with **Pharmacia**, showed that at 16 weeks, 67% of patients achieved remission, a statistically significant result. The is result can be compared to a 39% remission rate achieved at 30 weeks with Remicade, the TNF-alpha targeted monoclonal antibody treatment marketed by **Centocor/Johnson & Johnson**. **Pfizer's** acquisition of Pharmacia stymied further development of Myoconda, with the license left to expire.

However, the Phase III trial also revealed that, after remission was achieved, the therapy did not achieve statistically significant outcomes at the 12, 24 or 36 month stages of the protocol. In other words, after remission was achieved, Myoconda was not found to be better than using conventional therapy in controlling relapses.

The company held a pre-IND meeting with the US FDA in December 2004 to discuss an IND filing in support of a Phase IIIb registration trial for the US market. Key issues discussed included dosing and patient stratification. Of interest to the FDA is work conducted by Saleh Nasser at the University of Central Florida towards the development of a real time PCR (RT-PCR) test for MAP. This test could be incorporated in the clinical study.

The company will employ a Canadian clinical trials company to manage a Phase III study that utilises US and Canadian sites. The trial is estimated to cost in the order $10 million. However, rebates from several Canadian governments may be obtained that would offset up to half this cost (where work is conducted in Canada), with the balance to be secured from a licencee partner.

The duration of the Phase III trial would possibly be for 26 weeks, with a follow up period. The company is hoping to achieve US market approval in 2008.

Giaconda intends to seek orphan drug status for Myoconda in the US and Europe, where the failure rate with conventional treament is estimated to create patient population that falls within the market parameters for orphan drugs. Certain exclusivity and market protection benefits accrue to drugs with orphan drug status.

Letter of intent

The company has signed a letter of intent with **Forrest Laboratories (UK)** for the licensing of Myconda for the territories of the UK and Ireland. The license would be executed prior to the start of the Phase IIIb trial. In Europe, the company is seeking license partners for Germany, Italy, Spain and France.

Key milestone

The next most important milestone for the company is the submission and acceptance of its IND with the FDA. This is may take place in the second half of 2006.

Issues and risks

There are two investment risks with Giaconda that stem from the substantial shareholding that the company founder, Professor Thomas Borody, has in the company. Brody accounts for 70% of issued stock. Together with several other investors, 77% of the issued stock will be held in escrow till September 28, 2007. A problem is that with 23% of stock available on market, certain types of investors may be reluctant to invest because of a low level of available stock, especially if clear and positive progress occurs in the company and value is represented in the share price.

A second problem is that one shareholder in particular has overwhelming control, and this can provide significant risk for other shareholders. This risk could transpire, for example, when that

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shareholder chooses to set and implement strategies that run counter to soundly based strategies devised by company management with credible product, industry and market experience. Another risk is that such shareholders often fail to recognise the important and generally necessary trade-off between dilution and funding, and hence can precipitate the destruction of much of the potential value in a company.

A solution for the company's problem of low available stock may be that it undertakes a placement to fund managers and professional investors in the not too distant future. A fund raising of this type would also improve the company's balance sheet. Giaconda had cash at hand of $4.8 million at the end of the March quarter. The company raised $6 million at its IPO, which after costs of $445,000, was specified as sufficient for two years of operations.

Although the company's strategy is to sign up partners for various territories, who would fund Phase III clinical trial and other costs, a risk exists that the company will not be able to finalise such licences. This would then see the company's funding requirements challenged. This is, therefore, a second reason for the company to consider a modest capital raising.

Summary

Giaconda's strengths stem from the clinical background and insights of its founder, Professor Borody. Like several other listed drug development companies, there is low 'molecule' risk with Giaconda. At the same time the composition of the company's share register poses some problems for potential investors. Acceptance of an IND by the USA will serve as a clear entry point for investors interested in this stock. Giaconda is capitalised at $29 million.

Bioshares recommendation: **Speculative Hold Class B**

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Bioshares Model Portfolio (16 June 2006)

Company	Price (current)	Price added to portfolio
Acrux	$0.75	$0.83
Agenix	$0.15	$0.22
Alchemia	$1.15	$0.67
Avexa	$0.24	$0.15
Biolayer	$0.20	$0.195
Bionomics	$0.17	$0.210
Biosignal	$0.16	$0.22
Cytopia	$0.95	$0.46
Evogenix	$0.56	$0.47
GroPep	$1.65	$1.43
Optiscan Imaging	$0.50	$0.35
Neuren Pharmaceuticals	$0.47	$0.70
Pharmaxis	$1.99	$1.90
Prima Biomed	$0.071	$0.09
Sirtex Medical	$2.25	$1.95

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

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