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In this edition...
Move! Move! Move! is a dictum for biotech companies, who should move as quickly as possible to commercialise their discoveries in as many ways as possible. Xceed Biotechnology's subsidiary Polynovo has done exactly that, by firing up a joint venture with an Adelaide burns surgeon to investigate wound healing applications of Polynovo's fascinating polymer technology.

We also describe the connection between Chemgenex's Ceflatonin and Novartis' Gleevec, whose market success may breed success in turn for Ceflatonin. And the cash registers have pinged at Cytopia and Genesis R&D, with both companies shoring up their cash positions.
The editors

Companies covered: CYT, CXS, GEN, XBL

	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)	-10.8%
Cumulative Gain	**148.0%**
Average Annual Gain	**22.1%**

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.

Strategies & Issues

Tax Loss Selling Contributes to Strong Price Falls in Biotechs

The last three weeks have seen some strong price corrections in biotech stocks. This in part may be attributed to the fall in the broader equity markets. Also a factor, particularly in thinly traded stocks, is tax loss selling of biotechs which has accentuated these falls.

When the true and consistent market-based valuing of emerging technology stocks is difficult to achieve, the result is an over-selling of these stocks, biotechs included, escpecially when sentiment turns negative or when broader market conditions become more turbulent. Conversely, when sentiment returns to these stocks and widespread interest is resurrected, emerging technology stocks will invariably become overbought, and an argument can be made for the continuing need to remember to take profits.

Few investors need to be reminded of the latter at the moment. Most biotech stocks have fallen over the last few weeks and a number of these appear to also have been victim to tax loss selling as well, a phenomenon that is becoming more of a regular event in this sector before June 30. The stocks that appear to have been sold down heavily for this reason include **Prima Biomed**, **Agenix**, **Biosignal**, **Clinical Cell Culture**, **Living Cell Technologies**, and **Ventracor**.

Although the sector is experiencing selling pressure across the board, *it should be noted that this is being driven largely by factors external to the biotech sector.* To the contrary, the sector has never before been in such a strong position with a growing number of companies (14 at last count) either conducting registration trials or due to begin Phase III studies in the next 12 – 18 months, with a further emphasis coming from several recent very positive licensing and collaboration deals. It's also worth being aware of the biotech investment cycle, which has followed a fairly consistent four year cycle over the last two decades. With the last global surge in biotech stocks occurring in 2003 (triggered by the Phase III Avastin result), we are poised for a strong year for biotech stocks in 2007. On the next page we have reprinted a chart showing the fluctuations in the US AMEX Biotech Index, which we first printed in Bioshares in September last year.

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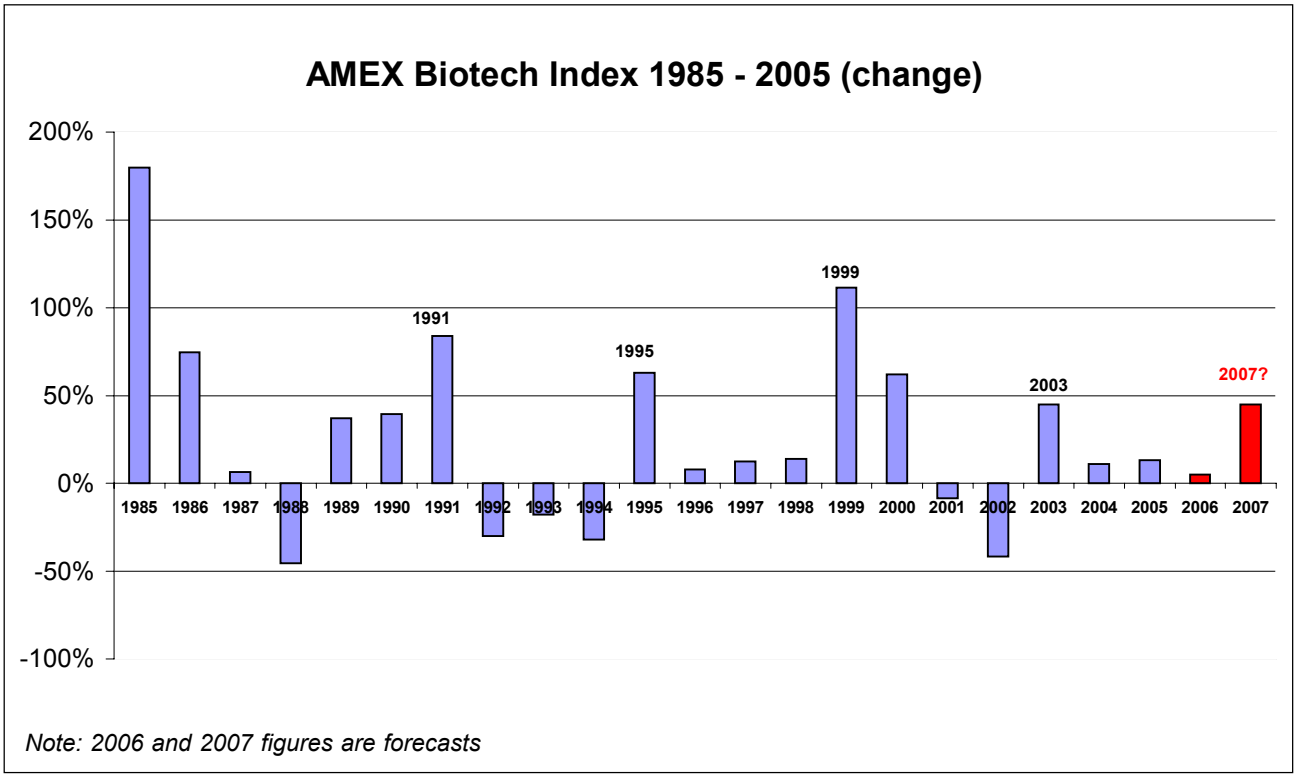

Xceed Biotechnology Expands Technology Application with Wound Healing JV

Xceed Biotechnology (XBL: 21 cents) is executing what most other platform technology companies are slow to deliver on – leveraging the core technology asset through multiple collaborative arrangements. This week Xceed's investee company, Polynovo, announced the formation of a joint venture – called **NovoSkin** – to apply its biodegradable polymer technology to the development of wound treatment products. Xceed has a 60% equity interest in Polynovo.

What makes the Polynovo technology useful is the design flexibility to modify the core polyurethane material that allows selection of mechanical and biological properties. By manipulating the active compounds, Polynovo has shown it can change the time its polymers take to biodegrade, and also can adjust the elasticity and mechanical strength of the material.

In January this year, Polynovo signed a collaborative deal with **Medtronic** to incorporate its polymers into coronary stent coatings that can release anticoagulant compounds, and is also working on a fully biodegradable stent product. Its second core application is in the area of orthopedics, for potential use in spine fusion and/or bone glue for treatment of complex fractures.

Polynovo has formed a joint venture with Adelaide plastic surgeon, Dr John Greenwood. Dr Greenwood is Director of the Burns Unit at the **Royal Adelaide Hospital.** Polynovo will retain an 80% interest in the JV. Both parties will contribute intellectual property to the JV, with Dr Greenwood's IP relating more to know-how in skin regeneration and burns treatment. Importantly, the link with Dr Greenwood will help facilitate pilot clinical studies of the technology through the **Adelaide Skin Engineering Laboratory** run by him.

There are two main products that will be developed under this program; one for treating superficial wounds to the top layer of the skin, the epidermis, and the second for the treatment of full thickness wounds.

Two applications for wound treatment

EASE

The first application, called EASE (easy application synthetic epidermis), would be a temporary bandage that is either sprayed on or pasted onto the wound. It would release pharmaceutical products, such as a local anesthetic and anti-bacterial agents, incorporated in the polymer compound. After being applied to the wound, the polymer dressing would be cured using a specific light source. The polymer bandage would be flexible and could be easily removed. Advantages over existing products are the ability to combine drug-eluting properties with the bandage. The bandage would also be solvent-free, reducing skin irritation, and when removed, any residual bandage material would biodegrade. This product could be in clinical testing in 18 months. One drawback for this technology is the requirement for light curing.

Biodegradable Temporising Matrix

The second product, which will take longer to develop, is a biodegradable bandage for full thickness wounds, called the biode-

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gradable temporizing matrix (BTM). Current treatment of such wounds involves cleaning the wound site, then placing a temporary nylon membrane to cover the wound whilst skin cells are grown in culture. Removing the bandage results in considerable bleeding, pain and an increased risk of infection. The Polynovo matrix could be applied immediately to the wound, and the skin graft or cultured cells would be placed on top of the matrix. The matrix will be designed to provide mechanical properties for six weeks and fully biodegrade after three months. It will include anti-bacterial compounds. The more defined matrix base may also give rise to more consistent skin cell distribution and reduce scarring.

Summary

Wound healing is not a core application for Polynovo although extends the use of this core asset and the joint venture helps identify and build upon the asset value. The Polynovo platform technology underpins an engine room of potential product development with many opportunities. Xceed Biotechnology is currently capitalised at $18 million. It had $5.8 million in cash (consolidated) at 31 March this year and also owns chemistry services company Boron Molecular, which it is seeking to divest.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares Model Portfolio (23 June 2006)

Company	Price (current)	Price added to portfolio
Acrux	$0.76	$0.83
Agenix	$0.17	$0.22
Alchemia	$1.15	$0.67
Avexa	$0.25	$0.15
Biolayer	$0.18	$0.195
Bionomics	$0.17	$0.210
Biosignal	$0.15	$0.22
Cytopia	$0.88	$0.46
Chemgenex Pharma.	$0.38	$0.38
Evogenix	$0.56	$0.47
GroPep	$1.55	$1.43
Optiscan Imaging	$0.47	$0.35
Neuren Pharmaceuticals	$0.42	$0.70
Pharmaxis	$1.90	$1.90
Prima Biomed	$0.067	$0.09
Sirtex Medical	$2.29	$1.95

Portfolio additions

Chemgenex Pharmaceuticals has been added to the portfolio at 38 cents.

Stock Briefs

Cytopia Shores up Cash Position

Cytopia (CYT:88 cents) firmed up its cash position this week by disposing of a major proportion of its shareholding in Alchemia. The company sold 11 million shares for a consideration of $11.6 million. The cost base of this component of its investment in Alchemia was approximately $5.1 million. Investors would do well to note that Cytopia would be subject to a concessional tax rate of 15% on the capital gain.

We estimate that with the net proceeds from this share sale, that Cytopia's cash position is $16 million.

Bioshares recommendation: **Speculative Buy Class A**

Genesis R&D Trades at 32% Discount

Genesis R&D (GEN: 88 cents) has finally received a settlement of US$5.7 million from its legal dispute with Arborgen, LLC. The company's cash reserves stand at a little under $10 million, or NZ$11.7 million. The company calculates these funds can support three years of operations.

The company is now led by the company's fomer CFO, Stephen Hall, who has applied a constructive and diligent approach to rebuilding the company's base following several clinical trial failures.

Genesis is currently trading at a 32% discount to its cash backing. The clearing of the litigation decks at Genesis is likely preface a return of investor interest in the stock.

Genesis is capitalised at $6.8 million.

Bioshares recommendation: **Speculative Buy Class C**

ChemGenex's Registration Trial of Ceflatonin to Commence in Q3, 2006

ChemGenex (CXS: 38 cents) is a biotech stock story with an unusual twist. The more **Novartis** expands and extends the market for one particular drug, Gleevec, which is a treatment for several different forms of leukemia (blood cancers), then the brighter the prospects are for ChemGenex's Ceflatonin.

The Gleevec Story

Since Gleevec first hit the market in 2002, it has earned a cumulative US$6.5 billion in sales. It posted sales of US$2.17 billion in 2005, an increase of 33% from the previous year. In the first quarter of 2006, Gleevec registered US$560 million in sales.

Global Sales of Novartis' Gleevec

	Bill. (USD)	Change - PCP
2001	$0.33	
2002	$0.61	84%
2003	$1.13	84%
2004	$1.63	45%
2005	$2.17	33%
2006 Q1	$0.56	13%

Gleevec has been an outstandingly successful drug that has commanded a very high price (USD$4,400 per 30 400mg doses, or US$52,500 per 12 months treatment) because of a very high success rate in treating patients suffering from a number of different forms of leukemia.

Results from a Phase III study (the IRIS study) of Gleevec administered to Chronic Phase Chronic Myeloid Leukemia patients show that the complete hematological response (CHR) rate at 38 months was 96% of patients. This meant that for 96% patients, leukemic blood cells were reduced to normal or low levels (eg the number white blood cells $<10x10^9/L$). The measure of complete cytogenetic response was 81%. A cytogenetic analysis investigates the presence of leukemic cells bearing the unique genetic features that give rise to the disease. (Unlike cancers characterised by solid tumours, the impact of drugs on blood-based cancers can be measured effectively by counting blood cell types.)

Response rates of this magnitude are almost unheard of in oncology. The CHR rate in the other arm (interferon-alpha plus cytarabine) of the Phase III (IRIS) trial was 16% at 30 months, compared to 84% for Gleevec. The table on page 6 records response rates for a number of recently approved cancer drugs, with best being 38% for Velcade, which interestingly is approved to treat a blood-based cancer. This data indicate that just how diffcult cancer drug development is, and what an achievement the development of Gleevec has been.

Bio-marker data from earlier stages of advanced clinical trials of Gleevec has been sufficiently convincing for the FDA to grant the compound accelerated review for six out of seven approvals granted to date. The accelerated review is a process that can allows the use of surrogate endpoints (such as a biomarker) that is not a "direct measurement of how a patient feels, functions, or survives, but is still considered likely to predict therapeutic benefit fo the patient". When permitted, accelerated review can offer substantial advantages to a drug developer.

The Downside for Gleevec

However, there is a downside to Gleevec treatment. Over time mutations occur in a particular protein in the stem cells that give rise to the leukemic cells. This protein also exists in the adult cell, where Gleevec is targted. To date, 13 mutations have been determined, and one of the most frequently occurring mutations is termed the T315i mutation. These mutations then limit the ability of Gleevec to control the leukemic cells.

ChemGenex's Ceflatonin attacks both the adult and precursor leukemia cells, found in bone marrow, which is an advantage over Gleevec.

Ceflatonin has been administered to more than 450 patients to date. It has achieved response rates ranging from 67%-92% in a smaller number of patients, which places it in a position comparable to Gleevec. More significantly, its potential is as a prospective therapy where resistance to Gleevec is emerging.

The Upside for Ceflatonin

The upside for Ceflatonin is that as Gleevec increases the survival of CML patients then the numbers, or pool, of Gleevec resistant patients will be expected to increase significantly. There are approximately 40,000 current cases of CML in the US, with new cases per year in the order of 4,600. Gleevec treatment could increase the pool to 55,000 in four years, based on a 90% response rate. The increase in the pool of Gleevec treated patients will increase the demand for a drug that deals with resistance. There is very similar to what has happened in HIV drug development as each wave of HIV drug class and therapy regimes has extended patient life, but also created demand for newer drugs that manage drug resistance.

Two Phase II studies of Ceflatonin have shown that in nine Gleevec-resistant patients, 80% reverted to the chronic stage of the disease, and that in another ten Gleevec-resistant patients, a 70% reduction in expression from the underlying gene defect that causes the disease was generated.

Status of Ceflatonin

ChemGenex will soon commence an open label Phase II trial (CGX-635-CML-202) of Ceflatonin in three classes of CML patients that are positive for the T315i mutation. The trial will enrol between 81 and 100 patients.

Ceflatonin will be administered subcutaneously, twice a day for 14 days every 28 days, for up to six cycles. Interim data is ex-

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pected to be available for review in the fourth quarter, 2006. The trial is expected to be completed in the second quarter of 2007, with an FDA submission a possibility for the second half of 2007. The end points will be the level of complete haematological response and the duration of response.

The company is confident that together with the data already collected for Ceflatonin, and following the forthcoming T315i trial, that it will be in a position to seek registration. Although the company has neither sought nor gained accelerated approval status from the FDA, we expect that it will seek such status after interim data is obtained at the end of this year. This will be a crucial development for the company and represents both a key milestone and risk going forward. However, we think there is a very strong liklihood that Ceflatonin could be granted accelerated review status

Four more Phase II trials for Ceflatonin underway or planned.

Funding position

ChemGenex recently completed a $15 million capital raising that now allows the company to fund the registration trial of Ceflatonin and support the company through to the end of 2007. The completion of this funding round removes a major short-to-medium term investment risk for ChemGenex.

Summary

Ceflatonin is one the most attractive cancer drugs in development by an Australian listed biotech company. It may even be the most attractive on a risk-reward basis, given the drug's established safety profile, the small number of T315i competitor compounds in development, which also lag Ceflatonin by a number of years, and the potentially very significant market that is emerging from Gleevec resistance.

The company has been supported by a bevy of highly regarded cancer physician opinion leaders, who lend credibility to the Ceflatonin program.

ChemGenex is capitalised at $58 million. With an estimated $16 million cash, ChemGenex has an implied technology valuation of $42 million, which is extremely attractive considering the low risk and rapid time to registration submission plan for Ceflatonin.

Bioshares recommendation: **Speculative Buy Class A**

Response Rates - Selected US FDA Cancer Drug Approvals, 2005-2006**

Drug	Indication	Company	Approval date	Study	No. Patients	Response Rate*
Nexavar (sorafenib)	**Advanced renal cell carcinoma**	Bayer	20/12/2005	Study 1	384	**2%**
Tarceva (erlotinib)	In combination with gemcitabine for the first-line treatment of patients with locally advanced, unresectable or **metastatic pancreatic cancer**	OSI	2/11/2005	Mono. Therapy	488	**9%**
Velcade (bortezomib)	Multiple myeloma patients who have received as least one prior therapy	Millenium	25/32005	Phase III	333	**38%**
Dacogen (decitabine)	**myelodysplastic syndromes** (MDS)	MGI Pharma	5/05/2006	Phase III	89	**17%**
				Phase II	66	**26%**
				Phase II	98	**24%**
Erbitux (cetuximab)	With radiation for locally or regionally **advanced squamous cell carcinoma of the head and neck** (SCCHN); or as a single agent for the treatment of patients with recurrent or metastatic SCCHN for whom prior platinum-based therapy has failed.	Imclone	1/03/2006	Mono.	103	**13%**
				Combination	218	**23%**

Accelerated Approval (clinical benefit ie survival, not established)

Arranon (nelarabine)	T-cell **acute lymphoblastic leukemia** and T-cell lymphoblastic lymphoma whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens	GlaxoSmithKline	28/10/2005	Pediatric Study	39	**23%**
				Adult Study	28	**28%**
Sutent (sunitinib maleate)	**Advanced renal cell carcinoma**	Pfizer	26/01/2006	Study 1	106	**26%**
				Study 2	63	**37%**

* Where a complete response rate was not published, the partial response rate was selected

** To June

Source: FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/) respective drug labels

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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