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In this edition...
Prima Biomed's prospects may well be about to change with the progress made by a US competitor, Dendreon, in getting the first therapeutic cancer vaccine on the market and a surging share price capitalising that company at over US$1 billion, a sign that investors may warn to cancer vaccines after all! Biota Holdings has filed an Amended Statement of Claim against GlaxoSmithKline, which makes for very interesting reading. Not only does it show how serious the company is with its litigation, but there are sure to be wider implications for the biotech and pharmaceutical sector if Biota is successful.
And on the other side, Evogenix has reported positive results from its collaboration with GSK and is the most significant validation to date of its technology platform.

The editors
Companies covered: BTA,EGX. PRR

	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)	17.1%
Cumulative Gain	**226%**
Average Annual Gain	**26.7%**

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.

Prima Biomed's Fortunes Change as Dendreon Soars to US$1 billion Market Cap

On Friday night in the US, cancer immunotherapy group **Dendreon** saw its share price soar 147% to US$1 billion after a positive decision from an FDA Advisory Committee that decided its therapeutic cancer vaccine for prostate cancer was shown to be both safe and effective. It's been a big week for cancer vaccines and this has major implications for **Prima Biomed** (PRR: 4.7 cents), who's fortunes may have been dramatically altered. These developments may be crucial to Prima Biomed, which is seeking to develop its own therapeutic cancer vaccine for the treatment of ovarian cancer.

In other key developments in this field during the week, **Oxford Biomedica** in the UK signed a US$690 million deal with **Sanofi-Aventis** to develop its cancer vaccine, TroVax, for a number of indications. On the same day, the **US Department of Agriculture** granted conditional approval to **Merial** for its canine melanoma vaccine, which makes it the first therapeutic cancer vaccine approved in the US for either animals or humans.

Dendreon leads the way for cancer vaccines
Dendreon is developing a therapeutic cancer vaccine (Provenge) which has commonalities with Prima Biomed's vaccine program (CVac). Both companies utilize the body's own dendritic cells to help stimulate the immune system to recognize existing cancer cells as foreign. Both companies use an autologous approach whereby the patient's dendritic cells are removed, treated *ex vivo* and then returned to the blood stream of the patient. Dendreon uses the PAP (prostatic acid phosphatase) antigen fused with GM-CSF to prime the immune system (PAP is found on the outside of prostate cancer cells). Prima Biomed uses the mucin-1 antigen found on the outside of ovarian cancer cells and is also over-expressed on a number of other tumour types.

The FDA Advisory Committee decision on Provenge
Dendreon completed a Phase II study with Provenge in 127 patients with prostate cancer. The primary endpoint was safety and a reduction in cancer progression. Whilst the vaccine was found to be largely safe, the primary efficacy endpoint was not met. The company then measured a survival difference between the two groups and found that Provenge-treated patients lived for 4.5 months longer than those on placebo. The Advisory Committee voted 17-0 in favour of Provenge that it was safe and 13-4 in favour of Provenge that it was effective.

Cont'd over

Easter Break
Please note there will be no Bioshares published next week due to the Easter break. The next edition of Bioshares will be out on 14 April.

The FDA is due to give a decision on or just before 15 May on the approval of Provenge. It's a major milestone for the cancer immunotherapy field and extremely significant for other players in this field. Dendreon is paving the way for this sector. If it can (a) get approval and (b) generate considerable sales and profit margins from this business, then investment interest in this space will continue to increase. It's a development of great relevance to Prima Biomed, which needs to raise funds soon to continue the development of its own cancer vaccine program, which recently generated positive data from its Phase IIa study.

As Dendreon moves through the regulatory approval process, the barriers to commercialising this technology will be removed. During the Advisory Panel meeting, members needed to be reminded that this was a first-in-class therapeutic candidate for this type of cell therapy and that the benchmarks used for chemotherapeutics could not be used in assessing this application. Provenge is slotted as a potential treatment option post hormone therapy in patients with prostate cancer but before chemotherapy.

More details emerge on the Provenge product

Provenge is delivered in a series of three injections, two weeks apart. The dendritic cells are removed (through apheresis) from the patient, separated out through density separation, primed with the PAP GM-CSF fusion protein for 36-44 hours at 37 degrees, and then harvested and delivered back to the patient. Dendreon uses fresh cells taken from the patient each time, whereas Prima takes one sample and then freezes those cells for a subsequent course of 7-10 cycles.

Price of the immunotherapeutics such as Provenge remains unknown, although some are suggesting that it will be similarly priced to other biologics such as antibodies, in excess of US$40,000 per treatment.

Risks

The risks with this therapy is to safeguard that the correct processed cells are returned to the patient. Other concerns in the Phase II trial completed by Provenge is the slight increaser in the incidence of stroke, 3.9% versus 2.6% in the placebo group.

Oxford Biomedica deal

Under the terms of this deal, Oxford Biomedica will receive US$39 million up front from Sanofi Aventis, future near term payments of US$25 million and total payments of US$690 million if all targets are met with royalties. The deal gives Sanofi-Aventis access to Oxford Biomedica's TroVax cancer vaccines. The company's lead program is a Phase III trial in 300 patients with renal cell carcinoma, which began in November last year.

The vaccine is delivered using a pox virus vector, a modified vaccinia virus Ankara and targets the 5T4 tumour antigen. Over 150 patients have been treated generating an anti-tumour immune response in over 95% of patients. The company has also generated positive Phase II results in colorectal cancer with a 3000 patient Phase III trial being planned and a 120 patient Phase II breast cancer trial also in the planning. Oxford Biomedica has a market capitalisation of US$447 million.

Summary

The development of monoclonal antibodies took several decades to translate into commercial success. Cancer immunotherapy is slowly moving through a gate towards commercial opportunity and validation. If one or two companies can successfully proceed in coming years, then investment support for this field should naturally increase to deliver on this much anticipated additional cancer treatment modality.

Prima Biomed may have been thrown a late lifeline as a result of these developments this week. The company is running very low on cash, which is a major risk, and has struggled to gain investment support for its own cancer vaccine program. That may change this week. The funding risk with Prima Biomed remains. However the company's ability to raise money now should have improved substantially. And with that funding, the company needs a new and more experienced management team, with its caretaker CEO, Eugene Kopp, expected to leave at the end of this year. The company is moving to a Phase IIb trial where efficacy of its vaccine and its mucin-1 antigen needs to be properly established following promising earlier studies. We have upgraded our recommendation to a Speculative Buy, although caution investors about the immediate funding risk that exists with this company. Prima is capitalised at $9 million.

Bioshares Recommendation: **Speculative Buy Class C**

Evogenix – More Validation of Platform

Evogenix (EGX: 87 cents) received arguably its clearest validation to date this week for its protein optimization platform. In October last year the company delivered to **GlaxoSmithKline** improved versions of a protein drug from GSK. The improved proteins were tested by GSK and found to have exceeded a 20-fold increase in binding affinity that had been targeted when the collaboration was formed.

There few remaining independent groups that provide outsourcing services of antibody humanization and optimisation. As of last week, there is now one less, with **Morphotek** being acquired by **Eisai Corporation** for US$325 million. Morphotek is a very useful comparator for Evogenix, with both companies having antibody humanisation and optimisation platforms.

Morphotek is a larger company in terms of employees, approximately double that of Evogenix. It is more advanced than Evogenix with two earlier stage, in-house clinical programs underway. Evogenix has collaborations with GSK, **CSL** and **Vegenics** and its in-house programs have yet to enter the clinic.

That CSL and GSK have both made acquisitions recently of biopharmaceutical groups (CSL acquired **Zenyth Therapeutics** and GSK has acquired **Domantis**), adds weight to the possibility of Evogenix being a target for acquisition. And that the Evogenix technology could potentially be applicable to single domain antibodies may increase the interest to GSK. Evogenix is currently capitalised at $121 million.

Bioshares recommendation: **Speculative Buy Class A**

Biota Files Amended Claim Against GlaxoSmithKline

Biota Holdings has filed an Amended Statement of Claim (ASOC) in the Supreme Court of Victoria in respect of its dispute with **GlaxoSmithKline** (GSK). Biota claims in summary that GSK did not use its it best efforts to promote and support the sale of Relenza (zanamivir), an antiviral drug.

According to Biota, the ASOC provides greater support of its claim that "GSK consistently mismanaged its legal obligation to develop and market the anti-viral drug Relenza". The legal obligation to which Biota refers has a number of elements including the obligation of GSK to use its best endeavours to "advertise and promote Products pursuant to the Licence on a proper commercial basis".

Biota is seeking loss and damages between $308 million and $430 million, for what it has suffered and will suffer. The ASOC exists as a result of Biota's lawyers examining 200,000 documents under the process of discovery.

Description

The ASOC is structured such that the performance of what is called 'The Main Agreement" is set out according to various phases (eg Research, Exploitation, Full Development), according to activities in various territories (eg Australia, USA, Japan) and according to various 'influenza seasons' in various territories (eg First Australian Season, First USA Season, Second Australian Season, Second Italian Season).

The claim details and alleges numerous acts and omissions by GSK that Biota believes breach the terms of the licence agreement. These include failures of trial design and execution, inappropriate inhaler device and selection, poor regulatory approval management, failures of global marketing and promotion, inventory and production (being) too limited to respond to demand, and failure to exploit existing and new markets.

Biota also claims that because of GSK's "consistent failures in marketing and promoting Relenza" that Relenza has been "denied its proper place as a major defence for global populations against the threat of influenza pandemic".

Comment

A rare insight

With the progression of Biota's statement of claim into an amended statement of claim and its resultant publication through the court process, investors now have a rare insight into the detail of a licensing agreement and the performance of the licensing agreement at least as is alleged by one party.

The ASOC is likely to be a document studied intensively not only by biotech investors around the globe, but by many other parties with an interest in this sector. This is because the modern therapeutic products industry is bound by the licensing of intellectual property to firms that either further develop or manufacture and market products.

The litigation between Biota and GSK, if followed through to full adjudication, looks set to become a test of the meaning and economic benefit of the licensing of intellectual property. If the Victorian Supreme Court finds there is no difference between licensing and whole ownership of a product, then a precedent may be set to cause other licencees to act in ways similar to the ways in which GSK is alleged to have acted.

A second area of analysis by biotech investors and owners of undeveloped intellectual property is likely to focus on the impact of large company mergers on small company licensors. The current dispute between Biota and GSK may cause the owners of undeveloped or partially commercialised intellectual property to revisit license agreements to ensure that agreements are effective in generating the performance anticipated under the license agreement, in the event of merger of the licensee with another firm.

Investment considerations

A consideration for investors is that the litigation costs for a small company such as Biota can mount up. There is the risk that the litigation could drag on and impose higher and ongoing burdens on Biota. Litigation also places a cost on management time. However, Biota is well managed and appears to have adjusted to the medium term imposition of a major litigation process. Furthermore, ironically, royalty income stemming from stockpiling orders of Relenza has improved Biota's cash position.

Bioshares recommendation: **Speculative Buy Class A**

Chronology of events

A chronology of events relating to the litigation and other aspects of the histories of Biota and GSK are set out below.

1985

Biota formed

1989

SmithKline Beckman and Beacham merge to form SmithKline Beecham

21 February 1990

Research and license agreement ("The Main Agreement") signed between Biota (and parties) and GSK (as it was then formed, as Glaxo Australia, the Australian arm of Glaxo Group plc, then later Glaxo Wellcome Australia).

26 May 1992

Research and license agreement amended

1993

Clinical trials of Relenza commence

1995

Glaxo and Burroughs Wellcome merge to form Glaxo Wellcome

30 March 1998
Second amended research and license agreement

March 1998
Glaxo filed application for marketing approval in Australia.

October 1998
Relenza was filed for approval with FDA.

March 1999
Relenza received approval from TGA in Australia

26 July 1999
The US FDA approves the use of Relenza to ***treat*** uncomplicated acute illness due to influenza virus infection in adults and adolescents 12 years or older

January 2000
Announcement of merger of Glaxo Wellcome with SmithKline Beecham to create GlaxoSmithKline

May 2000
Around this time, Biota alleges Glaxo decided to implement an "Exit Strategy" for Relenza

27 December 2000
Merger of GlaxoWellcome with SmithKline Beecham to create GlaxoSmithKline

28 November 2001
Consolidated research and license agreement

May 2002
Deed of agreement ("The Novation Agreement") entered into, in which GlaxoSmithKline Australia assumed the obligations and liabilities of Glaxo Welcome Australia under the Main Agreement. The research and licence agreement was also amended.

May 2004
Biota files its first Statement of Claim against GSK

July 2005
Biota files a document in the Supreme Court of Victoria estimating loss and damages at between $308 million and $430 million, for what it has suffered and will suffer

Nov 2005
Court ordered mediation between Biota and GSK takes place but no settlement is reached

29 Mar 2006
Relenza approved by US FDA for ***prevention*** in adults and children above five years of age

28 Mar 2007
Biota files Amended Statement of Claim

April 1, 2008 (Ann. 30/8/2006)
The trial is set down to commence in the Commercial and Equity Division of the Supreme Court of Victoria

Bioshares Model Portfolio (30 March 2007)

Company	Price (current)	Price added to portfolio
Acrux	$1.35	$0.83
Alchemia	$0.98	$0.67
Biodiem	$0.35	$0.29
Biota Holdings	$1.56	$1.55
Cytopia	$0.70	$0.46
Chemgenex Pharma.	$0.79	$0.38
Optiscan Imaging	$0.47	$0.35
Neuren Pharmaceuticals	$0.50	$0.70
Peplin	$0.78	$0.83
Peptech	$1.88	$1.31
Phylogica	$0.38	$0.42
Probiotec	$1.06	$1.12
Progen Pharmaceuticals	$7.34	$3.40
Sunshine Heart	$0.18	$0.19
Tissue Therapies	$0.55	$0.58

The Bioshares 20 Index

Change from June 30, 2006	**52.0%**
Change from Dec 31, 2006	**17.8%**
Change - week ago	**-2.1%**

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, Cytopia, Biodiem, Peptech, Starpharma Holdings, Cogstate, Xceed Biotechnology, Incitive, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Medical Therapies

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