ISSN 1443-850X

In this edition...
Sales of Relenza have zoomed ahead in the March quarter, and with it so have royalties that are to be received by Biota. We regard Biota as one of the most important Australian biotech stocks to watch, with revenues and profitability among the many reasons for investors considering this stock as an essential biotech portfolio holding.
Alchemia, another stock closely followed by Bioshares announced developments on several fronts this week, including the preliminary results of its Phase II trial of HyCAMP, a program that came to it through the acquisition of Meditech Research. The signing of a new marketing and manufacturing partner for Alchemia resolves a key question hanging over the future of its synthetic generic heparin product.
The editors
Companies covered:
ACL, BTA,BDM,CGS

	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)	14.6%
Cumulative Gain	**219%**
Average Annual Gain	**26.3%**

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).

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9671 3633
Email: info@bioshares.com.au
David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 213 (27 April 2007)
ISSN 1443-850X

Bioshares

27 April 2007
Edition 213

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

Relenza Royalty Stream Gains Traction For Biota

Sales of Relenza are starting to accelerate. Sold by **GlaxoSmithKline (GSK)**, Relenza delivers a 7% royalty stream to Biota Holdings (BTA: $1.72). GSK sold $220 million (US$183 million) worth of Relenza in the last three months, which put in perspective, is about same sold during all of 2006. Of that, Biota will receive $16 million, a 120% increase over the December quarter (note that 1% of the royalties Biota is commercially obliged to pass to other parties involved in the development of Relenza).

What is of interest is that GSK appears to ramping up its production capacity more quickly that previously anticipated. We estimate that its capacity has now exceeded 30 million courses a year. To date for this financial year, Biota should receive $28.7 (net $24.6 million) million for the first nine months alone. And there appears to be continued growth ahead. It's a surprising development as GSK's estimated capacity at the end of last year was only 15 million courses.

Roche sells that competing product, Tamiflu, which has secured about 90% of stockpiling orders. To date, Roche has received orders for 215 million treatment courses of Tamiflu. If we assume a sale price of US$20 per course, then the government stockpiling of Tamiflu is valued at US$4.3 billion.

With the expectation that this stockpile will need to be turned over every four to five years, then it represents an annual stockpile replenishing market of around US$1 billion. With the seasonal market approaching US$1 billion as well (although it can be assumed that some of the seasonal sales have gone towards individual stockpiling), then it represents an annual market size of up to US$2 billion a year.

Gilead Sciences, which receives royalties from Tamiflu sales from Roche, received royalties last year of US$364 million! Roche's capacity to manufacture Tamiflu has now exceeded demand, reaching 400 million treatments a year.

Since 2006 GSK has sold about US$360 million of Relenza, largely for government stockpiling, which is less that 10% of the government orders placed for Tamiflu. Whilst Roche may have satisfied government demand for its Tamiflu, we expect demand for Relenza will continue.

There are acknowledged concerns over the potential resistance of the flu virus to Tamiflu and resistance concerns are far lower for Relenza because of the nature of the bonding of the drug to the virus. Also health concerns emerging in Japan with Tamiflu which remain unexplained argue for a more representative stockpiling of the two neuraminidase inhibitor drugs. There are also some drug interaction restrictions with Tamiflu that do not exist with Relenza.

Cont'd over

Although Roche has been able to satisfy government demand for its drug now, we expect the proportion of Relenza stockpiling will increase, up to 30%, as GSK capacity increases and as governments turnover stockpiles and seek a more representative mix of drugs. Currently Ireland's proportion of Relenza stockpiling of neuraminidase inhibitors sits at 40%, France at 30% and the US at 20%.

Patents
The Gilead patent over Tamiflu expires in 2016. Biota's patents expire between 2011 - 2103, which gives Biota a royalty income stream from Relenza sales for the next four to six years.

Institutional investor interest
Excluding current royalties payable, Biota Holdings had $42 million in cash at the end of last year. The company is now capitalized at $310 million. With Biota now a profitable biotech company, institutional investors are taking stakes in this company, which has previously retained a primarily retail shareholder base. At the current level of Relenza sales, Biota will receive $55 million in net royalties annually, and this may continue to increase as GSK manufacturing capacity continues to increase.

Other assets and activities
It appears that almost no value is being attributed to the current litigation claim against GSK, which at this stage sits at over $400 million in claims. Biota also has three key development assets. Its next generation long acting neuraminidase inhibitor (LANI) program is being developed with **Daiichi-Sankyo** in Japan (which has annualized sales of $10 billion a year) and has recently completed Phase I trials. Its LANI lead has also shown in *in vitro* studies recently conducted to be effective against the avian flu strain (H5N1). Phase II trials are expected to begin in October this year. The company has partnered its preclinical programs for respiratory syncytial virus therapeutics with **MedImmune** (in December 2005) and its Hepatitis C program is partnered with Boehringer Ingelheim (in November last year). Biota's rhinovirus program, aimed at developing antiviral drug to treat the common cold, is currently unpartnered in Phase I clinical trials.

Biota has also been awarded two NIH grants, valued at US$14.1 million to develop LANI and aerosol forms of LANI as part of preparation for a flu pandemic.

Summary
Biota is forming the complete biotech company which makes it an attractive asset to retail and institutional investors. We believe the stock is undervalued with significant growth opportunities ahead that are not acknowledged in the current market price.

Bioshares recommendation: **Buy**

AstraZeneca Buys MedImmune – What It Means for Biodiem

AstraZeneca this week launched a US$15.2 billion takeover bid for **MedImmune**. The primary interest for AstraZeneca was MedImmune's flagship product, Synagis, for the treatment of respiratory syncytial virus. Synagis is a monoclonal antibody that last year generated sales of just over US$1 billion. It extends on AstraZeneca's push to move into the monoclonal antibody space following its acquisition last year of **Cambridge Antibody Technology**, and it is line with the move by most major pharmaceutical companies to gain exposure to the biopharmaceutical industry over the last two years, including **CSL** which last year acquired **Zenyth Therapeutics** (Amrad).

However what was also relevant for AstraZeneca in bidding for MedImmune was that company's vaccine business, primarily the Flumist influenza vaccine. And this has relevance for Biodiem (BDM: 33 cents) (see last week's edition) which is developing the only other live attenuated influenza vaccine (LAIV).

The threat of an influenza pandemic and the expected success of CSL/Merck's Gardasil cervical cancer (HPV) vaccine has made the vaccine market attractive for the major players. When **Schering-Plough** bid for **Organon** recently, it also specified that the Organon acquisition would give that company entry into the vaccine business, and importantly for Biodiem once again, through its LAIV primarily, which has been licensed Biodiem to Organon's subsidiary **Nobilon**.

In AstraZeneca's press release announcing its bid for MedImmune, the company referred to the attractive marketed products of Synagis and Flumist and also two late stage assets, the next generation follow-on assets of Synagis, called Numax, and the refrigerated form of Flumist which will be released at the end of this year.

The Flumist asset was acquired from Aviron in 2002 for US$1.5 billion, largely for that product, however MedImmune has failed to commercialise that product successfully. In the hands of a more experienced group such as AstraZeneca, observers may see the inhaled flu vaccine product achieve much greater success, which should help recognise the potential of the Biodiem LAIV asset being developed by Nobilon. Biodiem is capitalised at $17 million with $4.2 million in cash assets.

Bioshares recommendation: **Speculative Buy Class A**

Correction
In last week's edition of *Bioshares*, we indicated that the LAIVs from Biodiem and from MedImmune are made from the same strain. In fact, Biodiem's LAIV is made from a less mutated strain and the company believes that this potentially gives its vaccine superior properties to MedImmune's LAIV.

Earnings Update – Cogstate

Cogstate (CGS: 20 cents) reported its sales revenue this week for the third quarter of this financial year. The company sells a cognitive testing software program and service – based on a proprietary playing card software program where response time and memory are measured and assessed against individual changes and benchmark levels – primarily for use in the clinical trial setting by pharmaceutical and biotech companies developing neurological drugs.

For the three months to March this year, the company generated sales of $782,000 which brings the total sales for the year to $1.97 million. Whilst this is a small company with a small market capitalisation ($9 million), the company is well run and is approaching profitability, with a largely consistent sales growth trend over the last eight quarters. In the quarter just passed, Cogstate generated a positive cashflow of $124,000 although this was due to receipt of some larger individual payments. The company needs to increase sales by approximately 25%, to around $1 million a quarter, to move to profitability.

Cogstate has increased its team in the US this year to six staff. It is nearing a position where its clinical trials product is established in the market place and profitable allowing the company to enter other product markets, such as testing alertness in the workplace (Alert 4 Work) and using the test to measure cognitive decline in the broader community (CogHealth).

Cognitive testing in the clinical trial setting is an established commercial area where competing companies have formed successful and profitable businesses. Cogstate's product and service is competitive with that offered by its competitors and is arguably better offering advantages. However it is less established in the market place and this is the main obstacle to growth, as with any new entrant to an existing sector.

Cogstate has shown solid corporate management over the last two years with sales displaying a consistent growth path. As the company extends its position into the market place, with the first goal to secure a second major pharmaceutical group (in addition to Pfizer) as a repeat customer, a continued strong sales growth from a higher base should be achievable. There is also untapped upside from expansion into other product areas that should occur as resources become available to company.

Bioshares recommendation: **Speculative Buy Class B**

Correction - Benitec

We incorrectly listed Benitec's capitalisation in edition #211 of Bioshares. The correct capitalisation of Benitec at 31 March was $34 million, based on 233 million shares on issue.

The Bioshares 20 Index

Change from June 30, 2006	**77.4%**
Change from Dec 31, 2006	**40.5%**
Change - week ago	**0.9%**

Nasdaq Biotech Index

Change from June 30, 2006	**14.9%**
Change from Dec 31, 2006	**6.9%**
Change - week ago	**2.0%**

Bioshares Model Portfolio (27 April 2007)

Company	Price (current)	Price added to portfolio
Acrux	$1.30	$0.83
Alchemia	$1.20	$0.67
Biodiem	$0.33	$0.29
Biota Holdings	$1.72	$1.55
Cytopia	$0.73	$0.46
Chemgenex Pharma.	$0.81	$0.38
Optiscan Imaging	$0.44	$0.35
Neuren Pharmaceuticals	$0.43	$0.70
Peplin	$0.80	$0.83
Peptech	$1.83	$1.31
Phylogica	$0.34	$0.42
Probiotec	$0.95	$1.12
Sunshine Heart	$0.17	$0.19
Tissue Therapies	$0.49	$0.58

Alchemia Reports Positive Developments

HyCAMP Phase II results, New CEO, New Manufacturing and Marketing Partner

On Thursday, Alchemia (ACL: $1.20) announced the preliminary results of its Phase II trial of HyCAMP, in 80 patients with metastatic colorectal cancer who have failed treatment with 5-FU, a formulation of irinotecan and hyaluronic acid.

Irinotecan (Camptosar)

Irinotecan, also known by its trade name of Camptosar, is a topoisomerase inhibitor, currently marketed by **Pfizer**. The drug is approved for the first-line treatment for metastatic colorectal cancer in combination with leucovorin and 5-FU, and it is also indicated for the treatment of patients who have failed 5-FU therapy. Camptosar achieved world-wide sales of US$903 million in 2006, US$910 million in 2005, $US554 million in 2004 and $US299 million in 2003. The US patent for Camptosar expires in February, 2008. The drug was first approved by the FDA in 1996.

Treatment with irinotecan is known for a number of particularly unpalatable side effects, including diarrhea, neutropenia and vomiting.

Hyaluronic acid

Hyaluronic acid (HA) is a naturally occurring molecule found in joints and connective tissues that has been developed for use in a number of other medical applications by other companies, especially in the fields of opthamology and joint repair. HA has 'spongy' qualities and researchers at Alchemia and previously at Meditech Research have determined ways to incorporate active pharmaceutical ingredients and more recently monoclonal antibodies with HA. The technology has been termed HyACT. The specific incorporation of inrinotecan with HA is called HyCAMP

Potential of HA

The potential of HA, in which anti-cancer compounds are bound within, rests on the finding that the receptors that HA binds to (RHAMM and CD45) exist in relatively greater numbers on tumour cells. When HA, formulated with an active drug, binds to a CD45 receptor, a process takes place that imports the drug into the tumour cell. The drug then launches a cascade of events that destroys the tumour cell. The theory is that the direct targeting and specific import into a cancer cell using HA as a carrier means that much less active drug can be administered compared to the standard formulation and administration of an active drug.

A second but also important feature of the technology is based on the fact that tumours have leaky blood vessels. The theory is that HyACT compounds, encapsulating an anti-cancer compound, are injected and find their way to tumour sites, crossing the leaky blood vessel walls and end up becoming a drug depot within the tumour, thus prolonging the opportunity for the HyACT formulation to act on the tumour.

The theoretical potential of the HyACT technology is that existing anti-cancer drugs could be administered at lower doses to achieve an outcome equivalent to the same drug administered conventionally. Alternatively, increased doses could be administered using HyAct technology, but resulting in equivalent side effects occurring when same drug is administered at its conventional dose.

Preliminary Trial Results

The HyCAMP Phase II trial did not meet its primary of reducing the incidence of diarrhea in patients receiving HyCAMP after two cycles of treatment, in patients suffering metastatic colorectal cancer. The overall incidence of diarrhea was 14%, well under the expected rate of 30%. There was no difference in the rate of diarrhea reported in the HyCAMP arm or the control arm. The company suggested that improvements in disease management accounted for this low rate of diarrhea.

With HyCAMP, 93% of patients completed two cycles of therapy, versus 80% in the irinotecan control arm; 34% of patients completed eight cycles of HyCAMP therapy, versus 14% in the control arm. Neither of these endpoints achieved statistical significance.

The Median Progression-free Survival (PFS) was 5.2 months for patients receiving HyCAMP versus 2.4 months. This result was statistically significant.

Since only preliminary findings were discussed, the secondary endpoints of median overall survival, 50% or greater decline in CEA levels (a biomarker of cancer activity) and time to treatment failure were not reported. Also, the preliminary results did not report response rates (ie Complete Response or Partial Response or Stable Disease) which are standard measures used in the clinical evaluation of cancer drugs.

Analysis of the Trial Results

The preliminary data for this Phase II trial of HyCAMP is interesting for several reasons, in spite of the fact that the primary endpoint was not met. In hindsight, it seems reasonable that patient management practice has improved since the trial began, with a positive impact on patients suffering the side-effect of diarrhea and that this part of the trial became obsolete in that regard.

However, some of the secondary endpoint data is encouraging, including the statistically significant difference in Median Progression free Survival where the PFS for the treatment arm was approximately twice that in the control arm.

The trial result of more patients completing a high number of treatment cycles than the control arm is also encouraging (a median of 6 cycles versus 2). The data suggests that patients in the HyCAMP arm were able to tolerate more doses of irinotecan, courtesy of the HyACT technology. However, this is a matter to be confirmed and better understood through further investiga-

Cont'd over

Alchemia - from previous page

tion. A key point to be investigated is not necessarily whether more doses can be tolerated, but whether an increase in the number of treatment cycles of HyCAMP can lead to increases in response rates, progression free survival (as seen in this trial) and median survival, compared to irinotecan treatment alone.

Next Steps

The presentation of the full results of the Phase II trial will be important for Alchemia, as these results will enable the company to decide what the next steps with development of HyCAMP might be. These next steps may include a Phase III trial HyCAMP in a larger number of patients, which in all likelihood would be done in partnership with another company. The results may give the company enough confidence to commence human studies of a number of other molecules, including the monoclonal antibodies bevacizumab (Avastin) and cetuximab (Erbitux) used to treat colorectal and other cancers. The company has completed a number of very promising pre-clinical studies of hyaluronic acid combined with bevacizumab (HyBEV) and hyaluronic acid combined with cetuximab (HyERB). The commercial argument for progressing studies with proprietary compounds such as these is that HyACT may enable even stronger performance from two drugs that are setting new benchmarks in cancer treatment and also dampen some of the side effects associated with these monoclonal antibody treatments. If superior outcomes are obtained, then the company may have several very attractive cross-licensing opportunities to play with.

Manufacturing and partnership change

A second announcement made by the company this week was the appointment of a new manufacturing and marketing partner for its synthetic heparin product, generic fondaparinux. The company has selected **Dr Reddy's Laboratories**, an Indian generics company listed on the New York Stock Exchange. Dr Reddy's posted global revenues of US$408 million for the nine months ending December 31, 2006. While this is a positive event for Alchemia, our concern is that Alchemia's target of launching generic fondaparinux in the US in 2008 may be delayed and this introduces a new risk for the company.

CEO Transition

Alchemia announced that its CEO Dr Tracie Ramsdale was stepping down to make way for the appointment of the very capable Dr Peter Smith as CEO, who came in as Director of Commercialisation in May 2006.

Cash Position

At the close of the March quarter Alchemia retained cash assets of $13.6 million. The company's net operational cash burn as annualised from its last cash flow report for the March quarter is $14 million per year. On this basis the company has less then a year's cash at hand. A capital raising can be expected shortly. Alchemia has raised $48 million since listing in December 2003.

Summary

Alchemia is now set to commence a new phase of growth and development under the leadership of a new CEO. The company has resolved an outstanding issue of finding a new manufacturing and marketing partner and this is a major development. The release of preliminary data from the Phase II trial of HyCAMP has provided some interesting data and the full results will be keenly waited on. Alchemia is capitalised $170 million.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Bioshares

Thredbo Biotech Summit

The Essential Biotech Investment Event

July 20-21, 2007 · Thredbo Alpine Hotel · Thredbo Village, NSW

Thredbo Biotech Summit 2007

The third annual Thredbo Biotech Summit is being held on Friday 20 and Saturday 21 July, 2007. Once again, the conference aims to provide the ideal turf-neutral venue for investment and commercial biotech participants to meet and discuss key issues affecting the Australian biotech sector.

Registration is now open, with the first early bird discount ending on Monday. Full conference details are available on our website http://www.bioshares.com.au/thredbo2007.htm

Building on the success of previous years, the aim is to provide a high quality networking opportunity with a challenging and relevant program geared to encourage lively discussion, all within the picturesque location of the Thredbo Alpine Village. If you only attend one biotech conference this year, make it the Thredbo Biotech Summit, the essential biotech investment event in Australia! And make sure you book your accommodation early.

*******Please note that the first early bird offer closes Monday April 30*******

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

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$320**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$520	2-3 email addresses
	$620	4-5 email addresses
	$750	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: 61 3 9671 3633

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____