ISSN 1443-850X

In this edition...
The approach of discovering antibodies made by the human body to target cancer is being opened up with Patrys overcoming key manufacturing hurdles. Patrys has two planks to its value proposition, firstly from cancer antibody drug development, and secondly from a proprietary position covering a suite of novel targets.
Alchemia is edging closer to seeing its generic anticoagulant receive FDA approval. Its commercial prospects look solid and prospective revenues should set the company for a next phase of drug development.
Somnomed is now profitable and facing a promising future as sales of its dental splint for treating obstructive sleep apnea surge. Unit sales of the Somnodent product have grown at a compound rate of 56% since 2006.
The Editors
Companies Covered: ACL, PAB, SOM

	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 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - May '10)	49.2%
Year 10 (May '10 - Current)	12.2%
Cumulative Gain	**225%**
Av Annual Gain (9 yrs)	**18.5%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

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Individual Subscriptions (48 issues/year)
$350 (Inc.GST)
Edition Number 384 (5 November 2010)
ISSN 1443-850X

Bioshares

5 November 2010
Edition 384

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

Patrys Sets a New Pace for Natural Human Antibody Drug Development

Patrys (PAB: 12.5 cents) has been purposefully quiet in the last year. Patrys has maintained a low profile while it had been busy preparing for the launch of its clinical program. That effort and investment in that preparation can not be underestimated. The company is now well financed, well positioned and ready to progress its cancer antibody arsenal.

When developing antibody drugs, quite different to most small molecule drugs, getting the manufacturing process completed is a major effort and a very significant expense. Antibody drugs are manufactured via recombinant (biological fermentation) processes and those processes are difficult to get right. In Patrys' case, it had to work out how to manufacture human (not humanised) antibodies, and is the first company in the world that has shown it can manufacture these antibodies on a commercial scale. That has been a major achievement and in itself is a major portion of the company's intellectual property assets.

One point to remember about antibody drugs is that whilst they are much more difficult to get into the clinic because of the manufacturing issues, the chances of clinical success are historically much greater than for small molecule drugs. This is largely because of their greater selectivity for specific targets than small molecule drugs in general terms.

Having completed all of the relevant preclinical studies and manufacturing process, Patrys has now dosed its first antibody drug candidate in a Phase I study into two patients and so far so good. Patrys is aiming to treat cancer with a completely different approach to existing therapies. It has isolated cancer antibodies found in people that are naturally present to fight off aberrant cancer cells.

Current Phase I Melanoma Trial

A Phase I trial recently started by Patrys is in patients with melanoma trailing its PAT-SM6 drug candidate. Nine patients will be recruited (with maybe one or two extra) and recruitment is expected to be completed by mid 2011. The trial with look at three different doses in a single IV infusion. The first two patients have been dosed and the aim is to recruit one patient per month.

The trial is being conducted at Royal Adelaide Hospital. Once further product is manufactured in the first half of 2011, the company will seek to expand the Phase I trial to patients with other types of solid tumours, possibly even before the current trial is completed.

The patients being recruited into this melanoma treatment study will vary. Some of the patients may have had the disease for seven years and relapsed twice before. Some may progress very quickly. The melanomas are visible and biopsies will be taken before and after excision. The issue is that tumours are not obvious will continue to grow in patients.

– Cont'd over

The Patrys proprietary target for PAT-SM6 is GRP78, which was found to be present on over 98% of 200 different tumours screened. There is also a strong correlation between the expression of this target and the aggressiveness of melanoma diseases progression.

Patrys Hires Ideal CMO

In August this year Patrys appointed a Chief Medical Officer, Marie Roskrow. This is an outstanding appointment for Patrys. Roskrow was trained as an oncologist and haematologist and was previously University Professor/Research Group Leader in Translational Medicine at the Institute of Molecular Immunology in Munich. She then became a director of investment bank **Lazard** in San Francisco before moving to Australia, taking on a healthcare investment banking role with Lazard in Australia (formerly Carnegie Wylie). Roskrow brings invaluable investment banking and medical expertise (in oncology and immunology) to the company. Her interest in Patrys also helps confirm the potential in this company.

PAT-SC1

In October last year Patrys was returned the rights to PAT-SC1 from **Debiopharm**. This compound had successfully completed a Phase II trial in treating patients with gastric cancer. In that trial in 35 patients with gastric cancer, when treated with PAT-SC1 prior to tumour removal, the patents showed around a 90% improvement in survival benefit compared to historical survival rates.

Patrys this week received orphan drug status for PAT-SC1 for the treatment of gastric cancer. The company is converting the manufacture of the drug to its own now proven process. Subject to financing – and this depends on the company's share price, interest in the company and its ability to raise more funds – Patrys may start a Phase II trial next year, potentially in South Korea. One Phase I/II trial would cost around $6 million, including manufacturing costs.

Roskrow said at a recent briefing that gastric cancer is treated differently around the world and so will dictate the way PAT-SC1 is commercialised. In the US, patients receive a gastrectomy, where part of their stomach is removed, followed by chemotherapy and radiation therapy. In Europe, gastrectomy is generally followed by radiation therapy, or chemotherapy, or nothing at all. In South Korea, patients undergo a gastrectomy and are then sent home. This represents a very good opportunity to trial PAT-SC1 according to Roskrow. One clinic in South Korea will see 1,000 patients each year with gastric cancer said Roskrow.

Difficult to Recruit in US for Clinical Trials

Patrys will seek to gain evidence of efficacy first in Australia. Recruitment into clinical studies has become very competitive in the US and this is one of the reasons Australia has been chosen for the first clinical study with PAT-SM6. Even Genentech is now conducting trials in China because of the difficulty recruiting in the US.

If the company had only one drug candidate it would take a more global approach from the start. However, the company also believes that showing early efficacy will help support the approach the company is taking with using naturally occurring human antibodies as a treatment for cancer.

Competitors

Patrys is not without competitors. At its recent briefing, the company listed five other competitors in the human antibody space. (This is always a good sign when biotech companies are prepared to list their competitors straight up.) Morphotek/Esai has a Phase I trial in a number of cancers, Chugai/Roche has a Phase I/IIa trial in melanoma, Nascent Biologics has a Phase II trial in brain cancer, Kenta Biotech has a Phase I/IIa trial in treating pneumonia, and Acorda has a preclinical program with a human antibody in treating CNS diseases.

The existence of competitors helps validate the approach Patrys is taking. Patrys believes it has a leading position in this field. One of its competitors, Patrys says, can't make its drug and can't find its target. Another company, Kenta Biotech, has a current production process that only delivers one-tenth the yield that the Patrys process currently achieves. Patrys CEO, Dan Devine, said that the company has been approached by some of its competitors to manufacture their drug candidates but has so far declined to assist.

Patrys' manufacturing yields have so far achieved 1g/L for three compounds, which is the yield that is targeted by other antibody companies. The current PAT-SM6 trial is supported by drug made in a 30-litre reactor. By April next year the company plans to have PAT-SM6 product manufactured in a 250 litre reactor (regulators allow only a 10-fold increase in manufacturing in each expansion) that will provide material for an expanded Phase I trial.

Patrys believes it has head start on its competitors and with such a good IP position, it is not concerned about its competitors. It is also the first company to complete large scale manufacturing of natural human antibodies.

CSL Collaboration

In January this year, Patrys started a collaboration with **CSL**. CSL has rights to two Patrys antibody drug candidates, which does not include any of the lead programs Patrys is working on, with an option to a further two antibodies. Devine said CSL is an ideal partner as it already sells natural antibody products in the form of IVIG (not in oncology).

The collaboration is progressing well said Devine, having just completed a quarterly review and already having received some payments under the collaboration. One of the distinct interests from CSL is in the novel targets that Patrys has discovered. Devine expects announcements from the collaboration in the next six months.

Another Core Asset

Another of the core assets for Patrys are the novel targets it has found, which can be very valuable in their own right. Once a novel human antibody is isolated, Patrys' research team of 12 scientists in Germany works out what target that antibody is binding with. That target, in many cases, is completely novel and patented. Outside of the CSL collaboration, Patrys has nine antibody drug candidates which all hit novel targets that have been patented by Patrys.

– Cont'd over

Risks

One of the key risks is that the use of human antibodies as a cancer therapy remains an unproven approach. Patrys is one of the leaders in this field and the increasing presence of competitors helps validate the approach. In 99.8% of the population, cancer cells are successfully held at bay due the body's immune response, including from antibodies, so this is a logical approach.

Summary

Patrys has had its delays. Clinical trials were originally expected to begin in 2009. The shut down of a third party manufacturing facility contributed to the delays. Successful drug development requires multiple products in the pipeline. Patrys has over 200 human antibodies in its library. As the lead antibodies selected move through the development process and are partnered out, the aim is to refill pipeline will new drug candidates from its library.

The Patrys approach applies antibodies that are extremely specific to aberrant cancer cells, which trigger a cell-mediated immune response.

Patrys has a lead position in this field and also has a very secure IP position that covers the manufacturing process, the targets and also the antibodies.

Patrys is capitalised at $24 million. At the end of September, Patrys had $5.5 million of cash in the bank. It also has access to a $15 million convertible note facility, of which $500,000 had been drawn at 16 October.

Bioshares recommendation: **Speculative BuyClass A**

Bioshares

Alchemia – Almost There!

After almost seven years as a listed company, Alchemia's (ACL: 55 cents) first product should only be weeks away from reaching the market. The generic version of Arixtra, fondaparinux or Fonda for short, is edging closer to approval by the US FDA. This week the CEO of Alchemia's partner, **Dr Reddy's**, indicated that he expected Fonda to be approved a week after the inspection of a third party filling facility in India, the latter being expected to occur in November.

Arixtra sales by **GlaxoSmithKline** (GSK) in the US are holding up at around $270 million a year. Alchemia/Dr Reddy's are aiming to get at least 40% of that market, which should translate into a profit share for Alchemia of around $36 million.

Of interest in the US heparin market is that the sales of Arixtra have remain largely unchanged in the last quarter ($67 million versus $69 million in previous quarter). This is in contrast to the dramatic fall in Lovenox sales, which globally fell by 26% and with the introduction of a generic competitor.

This has a number of implications for the fondaparinux market. Firstly it confirms that generic drugs in the heparin space can indeed make very quick inroads into this market once approved. The generic competition to Lovenox (from **Sandoz**/**Momenta**) was launched only at the end of July 2010 in the US. This caused sales to plummet 47% in the US due to presumably a price fall and also significant market share erosion in only two months!

Lovenox (enoxaparin) held a massive global market position, selling $4.57 billion in 2009. That stronghold has now been broken in the US market, immediately with the introduction of a generic competitor. The second implication for Alchemia investors is that the destablisation of the Lovenox market has so far left the Arixtra market unchanged.

The question going forward is whether the fondaparinux market will hold steady, continue to grow or decline with the Lovenox market in total dollar value. With the fondaparinux generic coming to market in coming weeks, it is likely GSK will significantly reduce its marketing of Arixtra, thereby limiting sales growth in the US. Our expectation is that the Arixtra/Fonda market should hold steady and serve up a solid revenue stream for many years to come.

That revenue stream will be put to productive use almost immediately, funding a Phase III HA-irinotecan study for Alchemia. That study will cost Alchemia $20 million to conduct. Alchemia has been granted two concessions from the FDA, those being that it only needs to conduct one Phase III study and Progression Free Survival will be an acceptable endpoint. It should be an appealing product from the FDA's standpoint, delivering a chemotherapy with far fewer side effects if the Phase II study results can be confirmed in a Phase III setting.

Alchemia had $15.1 million in cash at September 30 and is capitalized at $105 million.

Bioshares recommendation: **Speculative Buy Class A**. *Investors with short term investment horizons may seek to take profits above 75 cents a share if 'Fonda' is approved by the FDA*

Bioshares

Somnomed – Breaking into Profitability

Somnomed (SOM: $1.07) develops and markets a range of dental products for the treatment of mild-to-moderate obstructive sleep apnea, bruxism (grinding of teeth while sleeping) and snoring.

The Somnomed dental splint (the SomnoDent) treats obstructive sleep apnea by preventing upper airway collapse by repositioning the lower jaw during sleep.

The devices offer an alternative approach to treating obstructive sleep apnea, such as through the use of CPAP, APAP and VPAP machines marketed, for example, by **Resmed**, **Respironics** and **Fisher & Paykel**. The key point of difference is that dental splint style products are not attached to machines and it can be argued offer advantages of comfort and convenience for patients who do not wish to wear a mask that is needed with CPAP machines.

Interestingly, in October 2009, Resmed acquired a French dental company, Laboratoires Narval, a manufacturer of the Narval MAS (a mandibular advancement splint), for EUR 8 million. This suggests that the CPAP companies recognise a role for mandibular advancement splint products in treating obstructive sleep apnea.

Somnomed was founded to commercialise the research and product development work of Richard Palmisano. Somnomed listed in 2004. To date, the company has raised $19 million through the issues of equity.

Somnomed employs 80 people, and this week it announced the appointment of two sales and marketing Vice-Presidents in North America, Anthony White (ex-Genetic technologies and Xtralis) and Jack Guthrie (ex- Novalar Pharmaceuticals).

Soft Lining – SMH B Flex

A key feature of the Somnomed device is the use of a special polycarbonate, the SMH B Flex, that lines the bite zone and ensures the device stays in position. This polycarbonate does not take on unpleasant odours over time and does not react to bacteria.

The SMH B Flex is used in 70% of devices sold in Australia, 90% sold in Europe, 100% in Japan and 50% in the US.

The company acquired 50% of **SMH Biomaterial** in August 2007. SHM Biomaterial holds the IP covering the SMH B Flex, and Somnomed has exclusive rights to the material. The material received FDA approval in January 2008.

Financials for FY2010

Somnomed has delivered impressive sales growth since FY2006, with sales growth at a compound annual growth rate of 56%. Gross margins have improved form 44% in FY2007 to 57% in FY2010.

Share Consolidation
Note that Somnomed undertook a 20:1 share consolidation on 26 November 2009.

Somnomed - Financial Summary

	FY2007	FY2008	FY2009	FY2010		Q3 2010*
Sales $(M)	$2.3	$3.7	$7.7	$10.7		$2.8
change		*61%*	*112%*	*38%*	*pcp*	*36%*
Units Sold	3503	7033	12544	19543		5160
change		*101%*	*78%*	*56%*	*pcp*	*29%*
Gross Margin	$1.00	$1.96	$4.06	$6.08		$1.68
GM as % Sales	*44%*	*53%*	*52%*	*57%*		*60%*
Pre-tax P/L	-$3.27	-$2.33	-$1.80	$0.11		
Profit/Loss	-$3.27	-$2.33	-$1.82	$0.79		$0.72
Cash ($M)	$3.2	$5.4	$4.0	$4.3		$3.6
Ave Unit Rev.	$1,541	$1,923	$1,621	$1,824		$1,843
Shares (M)				40		
CMP				$1.07		
Capitalisation				$43.1		
PE				54.9		

**unaudited*

The company posted its first full year profit of $0.79 million, although its pre-tax profit of $0.11 million is more representative of its performance.

Average unit revenue was $1,824 in FY2010, compared to $1,541 in FY2007. The US accounted for 68% of sales, with Australia and Europe each contributing 16% to total sales.

Latest September Quarter Figures

For the September quarter, the company recorded sales of $2.8 million, an increase of 36% from the previous corresponding year. Somnomed recorded a quarterly profit of $0.72 million (unaudited).

Somnomed sold more than 2,000 units in the month of September alone. The company improved its gross margin to 60% in the September quarter.

Patents

Patents covering Somnomed's Rapid Maxillary Expansion invention (apparatus and method for treating snoring) expire in April 2016 and Mandibular Advancement Split (the Somnodent product) expire in July 2019. The US patent for the Mandibular Advancement Splint has been granted.

However, the company filed further patents for Mandibular Advancement Split devices in 2002 and 2005, and another patent covering an 'oral appliance' in 2010.

Manufacturing

Somnomed operates twelve manufacturing sites world-wide, with nine managed under license and three are managed directly.

The Somnomed device is approved by the FDA as a medical tool device. Each device is hand-made by a technician, taking $1^{1/2}$ days to manufacture. Each device has a shelf life of between 3-5 years.

– Cont'd over

Bioshares Model Portfolio (5 Nov 2010)

Company	Price (current)	Price added to portfolio	Date added
Phylogica	$0.053	$0.053	September 2010
Sunshine Heart	$0.030	$0.036	June 2010
Biota Holdings	$0.96	$1.09	May 2010
Tissue Therapies	$0.47	$0.21	January 2010
QRxPharma	$0.93	$0.25	December 2008
Hexima	$0.40	$0.60	October 2008
Atcor Medical	$0.11	$0.10	October 2008
Impedimed	$0.79	$0.70	August 2008
Mesoblast	$2.75	$1.25	August 2008
Circadian Technologies	$0.59	$1.03	February 2008
Patrys	$0.13	$0.50	December 2007
Bionomics	$0.28	$0.42	December 2007
Cogstate	$0.27	$0.13	November 2007
Sirtex Medical	$5.90	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.18	$0.66	September 2007
Starpharma Holdings	$0.69	$0.37	August 2007
Pharmaxis	$2.83	$3.15	August 2007
Universal Biosensors	$1.52	$1.23	June 2007
Acrux	$3.06	$0.83	November 2004
Alchemia	$0.55	$0.67	May 2004

Portfolio Changes – 5 November 2010

IN:
No changes.

OUT:
No changes.

Summary

Somnomed has been on turn-around trajectory since the appointment of CEO Ralf Barschow in July 2007. Barschow has brought with him extensive experience in the dental and orthodontics areas gained at **Siemens AG**, **Align Technologies** and **Invoclar Vivadent**.

The company has set expectations for FY2011of achieving unit sales of greater than 28,000 for its sleep apnea product and unit sales of greater than 2,000 for its bruxism product, indicating a growth of close to 55% on a full year basis.

The company estimates that it can achieve sales of 36,000 units in FY2012.

The company also expects to increase staff numbers to around 100 during FY2011 and introduce two next generation products.

That the company could grow unit sales at >50% is a reasonable proposition. However, what the company may need to consider if it wants to accelerate growth is to add additional manufacturing capacity, but such expansion would require funding sourced through either debt or equity measures.

Somnomed is capitalised at $43 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Correction/Clarification – Pharmaxis, Bioshares 383
In last week's edition (383), we said that
"At 26 weeks, the CF302 trial reported a 106.5 ml improvement in FEV1 from baseline for patients that received Bronchitol. However this was not statistically significant (p=0.059)."

To be more precise, the improvement at 26 weeks and for week 6 – 26 weeks versus baseline was clinically significant (106.5ml; p<0.001). However, it was change in FEV1 between Bronchitol and control which was not significant (p=0.059).

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. For both groups, the rating "**Take Profits**" means that investors may re-weight their holding by selling between 25%-75% of a stock.

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

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