ISSN 1443-850X

In this edition...
Sirtex Medical has only penetrated a small portion of the global liver cancer market. Will its Sir-Spheres treatment ever become a mainstay therapy for unresectable primary liver cancer and how is it positioned against drug therapies such as Sorafenib and TACE? We answer these questions in this edition, following a briefing from one of the leading global authorities in this space.

And with reporting season underway, we look at two Melbourne-based pharmaceutical businesses, Medical Developments Int. and Probiotec.

The Editors
Companies Covered:MVP, PBP, SRX

	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 - May'11)	45.4%
Year 11 now commenced	-27.3%
Cumulative Gain	**206%**
Av. annual gain (10 yrs)	**21.2%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.
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) 9329 3350
Email: info@bioshares.com.au

David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph:03 9348 9317
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$375 (Inc.GST)
Edition Number 444 (24 February 2012)
ISSN 1443-850X

Bioshares

24 February 2012
Edition 444

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

Sir-Spheres Consolidates its Position for Treating Primary and Secondary Liver Cancer

The global adoption of the Sirtex (SRX:$5.03) liver cancer therapy, Sir-Spheres, continues to progress. This week Professor Bruno Sangro, Professor of Hepatology in the Liver Unit of the Clinical University of Navarra, Pamplona, Spain, visited Australia to explain his findings on the use of the Sir-Spheres for the treatment of *primary* liver cancer.

Key Terms
Radioembolisation (RE) – This includes Sir-Spheres and TheraSpheres (a similar glass bead product from Nordion)

TACE – Trans-arterial chemo-embolisation

HCC – Primary liver cancer

ENRY – European Network on Radioembolisation with Yttrium-90 Resin Microspheres analysis

Sir-Spheres were approved initially for the treatment of *secondary* liver cancer that has spread from the colon. There is potentially a much larger market for those people who have primary liver cancer (called HCC for short), with around 750,000 cases diagnosed globally each year. The effectiveness and suitability therefore of Sir-Spheres for the treatment of HCC is a very important issue for the company in terms of increasing its adoption.

Professor Sangro was the chair of the ENRY analysis, a review that looked at 325 people with inoperable HCC who had previously been treated using Sir-Spheres. The results from that analysis were published in the journal *Hepatology* in September in 2011.

Professor Sangro presented a summary from not only the ENRY analysis, but data from other studies with radioembolisation (Sir-Spheres and the glass beads developed by Nordion whitrh also contain Yttium-90), and other therapies including TACE (trans-arterial chemo-embolisation) and the drug Sorafenib.

Outcomes

The outcome from this wider analysis suggests that radioembolisation (including Sir-Spheres) – RE for short – has a place in the treatment of HCC. The main competition is TACE and according to Professor Sangro, who would be considered a leading authority in this area, there is a place for both therapies.

There is no head-to-head comparison between TACE and RE and according to Professor Sangro, this is unlikely to occur as it would require over 1,000 patients to gain a clear result. Looking at historical data, a similar survival is achieved from both therapies however RE is better tolerated than TACE. The main side effects of pain, fever and nausea are transient for RE. Patients generally only require mild pain killers for a very short term. With TACE, the side effects are more prolonged.

Cont'd over

– from Page 1

The survival benefit of RE is comparable also to Sorafenib but is better tolerated than Sorafenib with 38% of patients discontinuing Sorafenib drug therapy. The major side effect with Sir-Spheres treatment is gastrointestinal ulceration, although rates are low at 3.7%, according to the ENRY analysis. The delivery of Sir-Spheres has improved significantly since the therapy first made it to market in 2002. Professor Sangro said the delivery, including the catheter used, is extremely important.

This is not to suggest that RE will replace existing therapies. Professor Sangro stressed that more, not less, treatments need to be made available for patients with HCC.

Professor Sangro has treated hundreds of patients with Sir-Spheres since 2003. He has been an early adopter. Over that time, he has seen over 50 patients who had survived for more than five years. Over that time he has not seen cirrhosis occur as a result of the treatment.

An interesting aspect to RE therapy said Professor Sangro is that it is very robust and consistent across patient groups. Three different study groups have shown very similar survival periods based on their disease progression prior to receiving RE therapy. Disease control is between 80%-90% and tumour response is between 40%-50%.

Selection of RE Therapy

There are a number of factors that oncologists need to consider when choosing between TACE or RE therapy. These include the size of the cancer nodules, the number of nodules, their location and the vascular invasion of the tumour. In some cases Professor Sangro has used TACE for one lobe of the liver where there are smaller tumour nodules and RE therapy on the other lobe where there are larger tumours.

He has successfully used RE for patients on a liver transplant list and some patients following RE therapy can have their tumour downsized making them suitable for transplant as their overall tumour load has decreased.

The use of RE with Sorafenib also needs to be explored said Professor Sangro.

Trials Underway

HCC trials

Trials looking at Sorafenib treatment with Sir-Spheres are currently underway. A 360 patient trial, titled SORAMIC and run by Bayer and Sirtex, is comparing Sorafenib and Sir-Spheres against Sorafenib alone. It had recruited only 3% of patients at June 30 last year. In a 28 patient study from Singapore, results released in June 2010 showed that Sorafenib with Sir-Spheres was effective (11.75 months median survival) but there was no control arm. Another trial, SIRveNIB, was started last year comparing Sir-Spheres directly against Sorafenib. This trial was 15% recruited at the end of June last year.

Secondary liver cancer trials

Two large trials are underway (SIRFLOX and FOXFIRE) looking at Sir-Spheres as a first line therapy for metastatic colorectal cancer that has spread to the liver. SIRFLOX was 56% recruited at the end of June last year and FOXFIRE was only 9% recruited at the same time.

Earlier this month Sirtex announced that it will initiate a 400 patient trial comparing Sir-Spheres directly against Sorafenib in treating HCC in France. The trial will be sponsored by the Paris public hospital system and will involve 20 specialist treatment centres in France. It is an interesting development. Data compiled by Professor Sangro indicates that historical survival rates in patients treated by Sorafenib or by Sir-Spheres are similar. But up to 80% of patients on Sorafenib therapy experience side effects and 38% discontinue treatment. This trial is looking at whether Sir-Spheres deliver a better outcome for patients than Sorafenib.

Increasing Acceptance

Bioshares attended another Sir-Spheres medical seminar in 2011. There appears to be an increasing acceptance/interest in the Sir-Spheres technology from oncologists in the last year. The data that is emerging, including the data presented by Professor Sangro, supports the wider role of Sir-Spheres therapy in the treatment of liver cancer.

Adoption of Sir-Spheres for HCC

In the US, Sir-Spheres are only approved for the treatment of secondary liver cancer. However, in about 20% of cases, it is used off-label for treatment of primary liver cancer as well.

According to Professor Sangro, in Germany, all of the big medical institutions are making Sir-Spheres treatment available. In Italy many centres are using the approach and in the UK and France application of the therapy for HCC treatment has just started.

Summary

There are very few effective treatment options available for people with liver cancer, whether they be primary or secondary cancers. The Sir-Spheres treatment looks like it is on its way to being widely accepted as a treatment option for this disease. As results emerge from major trials, the therapy may be used more frequently both as a first line treatment for secondary liver cancer, and also for the treatment of primary liver cancer, either with Sorafenib, or potentially in place of Sorafenib pending trial outcomes.

For investors in this stock, our view is the increasing adoption of Sir-Spheres for the treatment of primary liver cancer should underpin strong top line growth of over 20% per annum for at least the next five years for Sirtex.

Sirtex Medical is capitalised at $281 million.

Bioshares recommendation: **Buy**

Bioshares

Medical Developments' Profitable First Half; Holds $4 Million in Cash

Medical Developments International (MDI) (MVP: $0.62) has posted an impressive half year profit result, with a 43.8% lift in net profit. The company booked a net profit for the half year of $1.2 million, compared to $0.8 million for the previous corresponding period. Sales for the half year were $5.3 million, compared to $5.1 million for the same period a year ago, an increase of 3%.

Gross margins increased from 63% to 71%, and EBIT margins increased from 22.5% to 32%. Cash at the end of the period was $4 million, up from $3 million a year ago. However, MDI intends to pay a fully franked 3 cents dividend, a total sum of $1.54 million (and which is not reflected in the company's cash balance for December 31, 2012).

The company has a dividend reinvestment plan in place, which for its previous dividend saw 1.9 million shares issued, permitting the company to retain $0.9 million in cash, but paying out $0.6 million in cash dividends.

MDI's principal product is the Penthrox inhaler, which is used across Australian and New Zealand by ambulance paramedics to provide instant pain relief to trauma patients. Sales of Penthrox (and Anafane) for the half year rose 8%, whereas sales of asthma, spacers and oxygen products decreased by 3% from the previous corresponding period. Penthrox and Anafane sales accounted for 63% of total sales.

MDI is developing an improved, single-step version of Penthrox which does not require the separate step of opening a vial of methoyxflurane and dispensing it into the inhalation device. Such an improvement would make the device potentially more attractive to military users.

UK Clinical Trial

The company has been conducting a study of Penthrox in the accident and emergency departments of five UK hospitals in order to complete a submission that will meet the requirements of the European medical registration authority, the EMA.

We previously expected the trial to be completed in the earlier part of 2012. However, MDI now anticipates the trial will be completed by the third quarter of 2012. The study will enrol approximately 300 patients, with half enrolled to date.

The trial is a blinded, randomised, placebo controlled study. A Data Safety Monitoring Review Board examined safety data for the first 50 patients and supported the continuation of the trial.

Summary

Since we last discussed MDI in *Bioshares* 427, the stock has appreciated 37%. The stock is trading on a annualised price/earnings ratio of 14 and is capitalised at $33 million. A significant expansion to its revenue base from sales into European territories is not likely to begin until late 2014 at the earliest in our estimation (assuming a successful completion of its UK trial this year as well as registration). At this stage sales are mostly confined to existing market segments where growth prospects are more limited due to market saturation. However, MDI still has the capacity to generate improvements to profitability as it continues to apply strong management to its operations, including manufacturing and marketing, across its three main business segments.

Bioshares recommendation: **Hold**

Bioshares

Medical Dev. Int.	MVP			CMP	$0.62	PE	14
				Cap'n ($M)	$33		
	FY2007	FY2008	FY2009	FY2010	FY2011	FY2011 H1	FY2012 H1
Sales ($M)	$7.4	$9.2	$8.7	$8.3	$10.2	$5.1	$5.3
Change	13%	25%	-5%	-5%	23%		3%
EBIT ($M)	$1.66	$1.27	$1.19	$1.27	$2.50	$1.15	$1.69
Change	28%	-24%	-6%	7%	96%		47%
Net Profit ($M)	$1.21	$0.89	$0.81	$0.88	$1.74	$0.80	$1.16
Change	51%	-26%	-9%	9%	98%		44%
EBIT Margin	22.5%	13.7%	13.6%	15.4%	24.4%	22.5%	32.0%

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.70	$1.66	October 2011
Mayne Pharma Group	$0.300	$0.435	September 2011
Acrux	$3.64	$3.37	June 2011
Bioniche	$0.50	$1.35	March 2011
Somnomed	$0.91	$0.94	January 2011
Phylogica	$0.034	$0.053	September 2010
Biota Holdings	$0.76	$1.09	May 2010
Tissue Therapies	$0.36	$0.21	January 2010
Atcor Medical	$0.08	$0.10	October 2008
Impedimed	$0.50	$0.70	August 2008
Bionomics	$0.46	$0.42	December 2007
Cogstate	$0.27	$0.13	November 2007
Sirtex Medical	$5.03	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.82	$6.60	September 2007
Pharmaxis	$0.95	$3.15	August 2007
Universal Biosensors	$0.73	$1.23	June 2007
Alchemia	$0.415	$0.67	May 2004

Portfolio Changes – 24 February 2011

IN:
No changes

OUT:
No changes

Probiotec Struggles to Perform

Altona-based Probiotec (PBP: $0.34) suffered a weak first half for FY2012, seeing sales from continuing operations decrease 3% from the previous corresponding period, although its headline net profit result of $2.6 million increased by 162.4%. Sales for the half year ending December 31, 2011 were $34.1 million, compared to $35.1 million a year ago.

Probiotec manufactures, markets and distributes prescription and OTC products and also provides contract manufacturing services.

Probiotec sold its Milton brand during the half year for $6 million, which resulted in EBITDA from continuing operation declining 15% from $5 million to $4.3 million. NPAT from continuing operation fell 48% from $2.2 million to $1.2 million.

Debt Burden

The company continues to carry a substantial debt burden, including $23 million in short term borrowings (PCP: $27 million). The company's net debt/equity ratio stands at 38%. However, financing costs on a cash flow basis increased to $1.2 million for the half year from $1.1 million for the previous corresponding period.

Analysis

The prospects for Probiotec have not yet improved and may not do so for some time. The company's forecasts a year ago of a strong profit performance for FY2011 did not materialise and were significantly off the mark. Its guidance of sales for FY2011 was $83.8 million compared to an actual result of $71.8 million. Profit guidance was for NPAT of $5.2 million compared to a loss of -$10.34 million.

In the second half of 2011, the performance of Probiotec's pharmaceuticals and consumer health business was dragged down by its underperforming meal replacement business. However, its contract manufacturing operations saw sales grow by 36.3% for the half year period ($8 million).

Probiotec's strategy of being a manufacturer of weakly differentiated (i.e. only weakly relying on evidence-based performance, novel technology or patents) pharmaceutical products is likely to be a matter of concern going forward. The company has a low spend on R&D (4.8% of sales for FY2011; by comparison, CSL's ratio is 8.2%) despite stating that it had (as of its 2011 AGM) 16 products under development and/or (in) registration.

Unlike Medical Developments which eventually saw the logic of investing in clinical trials (spending $1.5 million over the last 18 months) so that it could potentially gain market access for Penthrox in new territories, Probiotec will always face high levels of competition while it operates as a contract manufacturer and marketer of weakly differentiated pharmaceutical products.

Bioshares recommendation: **Sell**

Probiotec	PBP			CMP	$0.34	PE*	7.8
				Cap'n ($M)	$18		
	FY2007	FY2008	FY2009	FY2010	FY2011	FY2011 H1	FY2012 H1
Sales ($M)	$54.0	$65.8	$87.1	$74.8	$71.8	$35.1	$34.1
Change	30%	22%	32%	-14%	-4%		-3%
EBIT ($M)	$7.66	$10.41	$14.07	$11.84	$0.43	$3.34	$4.65
Change	85%	36%	35%	-16%	-96%		39%
Net Profit ($M)	$4.98	$6.31	$8.90	$9.43	-$10.34	$1.02	$2.67
Net Profit ($M) (Cont. Ops)							$1.14
Change	176%	27%	41%	6%	-210%		162%
EBIT Margin	14.2%	15.8%	16.1%	15.8%	0.6%	9.5%	13.6%

* from Cont. Operations

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

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Circadian Technologies, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Atcor Medical, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Genetic Technologies

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$375**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$590	2-3 email addresses
	$800	4-5 email addresses
	$1020	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

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 _____

_____

_____