ISSN 1443-850X

In this edition...
A surge in volume sales in the US for Sirtex Medical's liver cancer product Sir-Spheres may see the company deliver a record volume sales result for FY2012, despite weakness continuing in Europe. Sirtex is a standout stock and well suited to the patient long term investor.
Calzada, through its subsidiary company Polynovo's joint venture with an Adelaide burns surgeon, is finally entering the all important clinical proof of concept stage for its wound and burn treatment products. By the end of the year clinical data should be available to confirm the efficacy of the PolyNovo's polymer technology for treating burns and other wounds.
A clinical trial slowdown for its partnered product, Urocidin, has caused Bioniche to tighten its cash spend and obtain debt finance.

The Editors
Companies Covered: BNC, CZD, 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)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 now commenced	-20.0%
Cumulative Gain	**236%**
Av. annual gain (10 yrs)	**21.4%**

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

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Individual Subscriptions (48 issues/year)
$375 (Inc.GST)
Edition Number 450 (14 April 2012)

Bioshares

14 April 2012
Edition 450

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

Sirtex Sales Boom in the US

Shares in Sirtex Medical (SRX: $5.90) surged this week after it announced strong March quarter volume sales figures. Sirtex shares increased 13% from the last trading day before Easter.

Sirtex markets Sir-Spheres, a targeted radiation therapy product that is currently used to treat liver cancer that has spread from the colon, both for secondary and in some regions for primary cancers.

The company reported that March quarter sales grew 34% on a volume basis, from the previous corresponding quarter. We estimate unit sales for the quarter of 1,632 and 4,330 for the financial year to date. This is the highest ever quarterly figure for volume sales recorded by Sirtex covering 31 consecutive quarters of sales growth.

Sales were driven by a very strong performance in the US where volume sales increased 47% from the previous corresponding quarter, with the Asia Pacific region recording a growth rate of 46% pcp and Europe 8% on pcp.

Sir-Spheres is progressing from gaining initial market acceptance to now seeing growth from interventional radiologists and oncologists applying the treatment on the basis of familiarity with the approach. Sir-Spheres treatment in the US is reimbursed at US$15,800 per treatment.

The much larger but longer term opportunity that Sirtex is addressing through several clinical trials is for Sir-Spheres to be accepted as a treatment for primary liver cancer and to be used earlier in the treatment regimes for liver cancer, rather than as the third line salvage position it now occupies.

For the half-year ended December 31, 2012, Sirtex posted sales of $36.8 million and a net profit of $6.1 million. Sirtex is capitalised at $329 million.

Bioshares recommendation: **Buy**

Unit Sales - SirSpheres

	FY2006	FY2007	FY2008	2009	2010	2011	FY2012 H1	FY2012 YTD (estimate)
US	1,077	1,444	1,805	2,298	2,490	2,969	1,702	
% ch. pcp		*34%*	*25%*	*27%*	*8%*	*19%*	25%	
Europe	140	332	454	985	1,288	1,603	738	
% ch. pcp		*137%*	*37%*	*117%*	*31%*	*24%*	-3%	
Asia Pacific	182	332	332	375	393	405	258	
% ch. pcp		*82%*	*0%*	*13%*	*5%*	*3%*	28%	
Total	1,399	2,108	2,591	3,658	4,171	4,977	2,698	4,330
% ch. pcp		*51%*	*23%*	*41%*	*14%*	*19%*	16%	21%

Big Year for Calzada Ahead with Two Clinical Trials Underway

Calzada (CZD: 5.7 cents), through its subsidiary **Polynovo Biomaterials**, has commenced its second clinical trial this year with its biodegradable wound healing technology. It should be a significant year for the company with the company's products now being investigated in the clinical setting after many years of development. Results from the two trials are expected by year's end.

The Polynovo technology, called NovoSorb, uses a biodegradable form of polyurethane. It has many potential medical applications, including use as a bone void filer, fracture fixation and even as a drug delivery vehicle. The leading application is for use in the treatment of burns and other skin wounds.

The skin wound application is being commercialised through a joint venture with Adelaide-based burns and plastic surgeon, John Greenwood. Polynovo (Calzada) owns 80% of the joint venture, called **NovoSkin Pty Ltd**. Greenwood is particularly important to this program, providing the clinical guidance and expertise for commercialising these products.

For both clinical trials underway, Greenwood is the principal investigator, although will not be the surgeon performing the treatments. Both trials are being conducted at the **Royal Adelaide Hospital**, where Greenwood is the Director of the Adult Burns unit.

There are two commercial phases of the wound application. The first is to deliver a better alternative to Integra (**Integra Life Sciences**), the current gold standard in treating full thickness wounds. This first stage of treatment involves sealing the exposed full thickness wound with a 'temporising' matrix. The aim is to immediately seal the wound and then to allow the split skin graft (taken from another part of the body) to be applied to complete treatment of the wound.

There are three reasons to properly seal the wound. The first is to prevent infection in the wound. The second is to prevent water evaporation from the site. And the third is to prevent contraction of the wound area. From an evolutionary perspective, the body naturally seeks to close the wound. If the wound is not sealed, the body contracts to achieve closure, which is the main visual distortion of the skin synonymous with burn wounds. This distortion is devastating on the face. From a functional perspective, rapid wound closure is particularly important around joints, where the body bends to achieve closure, thereby limiting joint movement when the wound has healed.

Preclinical Trial Result

A preclinical study was completed and published recently comparing Integra with Novosorb BTM. The study involved treatment of wounds in six pigs and was conducted by Greenwood and his team. Three of the key parameters that were measured were infection levels, the degree of contraction of the wound, and the level of scarring.

On all three measures, Novosorb BTM clearly outperformed Integra. With Novosorb BTM, there were no incidents of infection. With Integra, five of the six wounds became infected. A point to note was that a particular dressing was used on all wounds and this type of dressing is not generally used in the clinic with Integra. This could have contributed to the high infection rates with Integra.

The high infection rates with Integra may also have contributed to the increased contraction seen with Integra. With the sealed Novosorb BTM there was only a 23% contraction in the wound area, compared to a 55% contraction with Integra. The more contraction, the more cosmetic distortion of the skin.

With respect to scarring, with Novosorb BTM the scarring was very thin, between 0.16mm-1.0mm thick. Integra treated wounds left a thick scarring level, in some cases being up to 8.0mm.

On the downside with Novosorb BTM, in some of the wounds (in the tail), the wound sites had become disrupted, requiring repair and reattachment. There were also some issues with bonding the sealant to the BTM scaffold which the study report indicated the group was working on improving.

First Human Clinical Study – Vacuum Assisted Closure

The first clinical study with NovoSorb started in February this year. This trial will investigate the Novosorb polyurethane foam for use in a particular wound treatment, called vacuum assisted closure of pressure sores to deliver topical negative pressure.

This treatment method received FDA approval in 1995. It uses a vacuum pump over the pressure sore to remove wound fluid and waste material from the wound. The problem with this therapy is that in a small number of cases, the dressing material remains attached to the wound, causing bleeding or requiring surgery to remove the dressings. Between 2007 – 2011, the FDA received reports of 12 deaths and 174 injuries from the therapy and has issued a warning about the complications associated with this treatment.

Calzada believes its Novosorb material has better biocompatibility than current products on the market. Presumably, an advantage of the product should also be that if some of the polymer does remain in the wound, then it will eventually dissolve in the skin, within three to six months. The consumables market in this area is worth over US$400 million a year.

This trial will recruit 20 patients, 10 in the active arm using the Calzada product and 10 in the control using a commercially available product. The trial is designed to show that the Calzada product is not inferior to an existing product.

For Calzada, the trial will also provide early information on biocompatibility of its polymer. And commercially, it's a faster way to get its first product to market, potentially within the next two years. At the start of this month, four patients had been recruited into the trial.

Cont'd over

Second Trial – Free Flap Procedure

The second trial at the Royal Adelaide Hospital started this month. It will enrol 10 patients who are scheduled to undergo a 'free flap' procedure, where a full section of the tissue is removed, often from the forearm, to be used to rebuild another part of the body that has been removed due to injury or illness. Free flaps can be rolled up to make a section of the oesophagus or repair a section of the mouth. This controlled trial will be easier to coordinate than an emergency burns wound.

The NovoSorb biodegradable temporising matrix (BTM) that will be evaluated will include a sealing membrane on the top layer which will be removed just prior to a skin graft being placed as a final treatment of the wound.

This is a key trial for Calzada. What the company will be looking at is how easily the sealing membrane can be removed from the NovoSorb BTM, and how much the wound contracts.

From this trial, the company will be looking at the rate and quality of the integration of the product into the skin. A bad result from this trial would be significant contraction of the wound, or a negative reaction from the polymer material from patients.

Third Trial

The company is also looking to conduct a third trial, in 10-20 patients with burn wounds, towards the end of this year. This could also be followed with treatment of larger burn wounds.

Stages of Commercialisation

The first stage of the skin replacement product is to commercialise the Novosorb BTM product, which acts as a skin scaffold for full degree burns or wounds. A split skin graft would be used in the weeks following application of the Novosorb BTM.

A longer term project is the development of a composite skin product that could be used alone or with the Novosorb BTM skin scaffold. This would replace the use of skin grafting. It would taking a small sample of skin, culturing (growing) that skin sample and sealing it into the BTM polymer scaffold. This would thereby provide a dermis and epidermis for full thickness wounds.

At the earliest, the company could have two of its products on the market within two years.

Competition

The leading product on the market is called the Integra Dermal Regeneration Matrix, made by Integra Life Sciences Corporation. Estimated sales of the product are around $100 million a year. This product has its limitations. These include its high cost. It is a three dimensional wet sponge made from bovine collage fibres and shark cartilage. It also needs to be stored refrigerated.

By comparison, the NovoSorb BTM is produced as a foam and being a polymer, its cost of manufacture is substantially lower. This also makes the product lighter, with less material to be dissolved by the body. The product is not heat sensitive, so does not need refrigeration. This makes the product suitable for use by the military and also in second and third world countries.

The high cost of Integra limits its applications to more essential burns wounds. The incidence of infection with Integra is also an issue. The product is also very delicate, like a fibrous wet sponge and the product can be destroyed if the patient rolls over and lies on their wound.

Integra includes a dermal scaffold together with a silicon epidermis to seal the wound. Calzada's NovoSorb BTM is similar, including a dermal scaffold with a sealant layer. Other products on the market include Alloderm, which does not seal the wound, and Matriderm, which is a high cost product that also does not seal the wound.

With all of these products, a split skin graft is still required. However closing the wound whilst the patient is being stabilised and before the skin graft can be applied reduces the occurrence of infection. Both Integra and Novosorb BTM are absorbed by the body over time.

Commercialisation Model

The commercialisation plan for the NovoSorb products is based on Calzada partnering the products after completion of clinical studies, but retaining manufacturing.

AOD9604 Asset

Calzada also has the peptide AOD9604 which had previously been trialed as a treatment for obesity. It has licensed the application of its use to Phosphagenics as a cosmetic for the reduction of cellulite. It is continuing to investigate low cost options as to how any potential value could still be unlocked from this compound.

Summary

After 12 years of technology development, Calzada now has two products in clinical evaluation. Results from both of those studies are due by year's end, setting up some major milestones, with results from the second clinical trial to be more significant. With the clinical stewardship of burns and plastic surgeon, John Greenwood, commercialisation of the lead application of the technology is being well guided.

Through John Greenwood, Calzada can move products rapidly through the clinical proof of concept stage. The company can also move to clinical proof of concept at little cost. The first trial is expected to cost the company $150,000, and the second trial only $50,000.

Calzada is capitalised at $20 million. At the end of last year the company had cash (and short term investments) of $5.6 million. The company has a low spend rate of around $2.1 million a year.

Bioshares recommendation: **Speculative Buy Class B**

Bioniche Finalises Debt Financing and Focuses on Reducing Cash Burn

Bioniche (BNC: 56 cents) has finalised a debt financing arrangement in which **Capital Royalty LP** will loan Bioniche C$20 million, charging 15% interest per annum over a five year period. A portion of the loan will be capitalised for the first three years of the loan. Additionally, Bioniche must also pay Capital Royalty 2% of all sales revenues derived over the term of the loan

Following the completion of an interest-only period, the principal plus any 'paid in kind' principal will be repaid in eight equal instalments of C$2.5 million commencing June 30, 2015. For the first three years, the company will have repayments of around C$3 million a year, including the 2% of sales contribution. For the financier, it represents an internal rate of return of around 19% a year.

Bioniche has been compelled to replenish its cash reserves which had fallen to C$6.8 million by December 31, 2011, compared to C$15.4 million at June 301, 2011 and compared to C$24 million as of December 31, 2010.

Cont'd over

Bioniche - Segment Results

	Human Health				Animal Health				Food Safety			
	2010	2011	H1 2011	H1 2012 (IFRS)	2010	2011	H1 2011	H1 2012 (IFRS)	2010	2011	H1 2011	H1 2012 (IFRS)
Sales					$27.0	$27.4	$12.8	$13.5				
% Change PCP						*1%*		*5%*				
Other	$18.0	$8.7	$5.7	$1.5	$0.9							
Total	$18.0	$8.7	$5.7	$1.5	$27.9	$27.4	$12.8	$13.5	$0.0	$0.0	$0.0	$0.0
Expenses					-$19.3	-$19.9	-$9.6	-$10.0	-$1.5	-$1.8	-$1.2	-$1.2
EBITA pre R&D	$18.0	$8.7	$5.7	$1.5	$8.6	$7.4	$3.2	$3.5	-$1.5	-$1.8	-$1.2	-$1.2
EBITA pre R&D/Sales					*32%*	*27%*	*25%*	*26%*				
Net R&D Expense	-$14.3	-$11.5	-$5.7	-$5.0	-$3.1	-$3.8	-$2.1	-$2.5	-$1.6	-$2.5	-$0.8	-$1.6
Segment Result before Tax	$2.7	-$3.7	-$0.4	-$3.6	$4.9	$2.9	$1.0	$0.9	-$3.2	-$4.4	-$2.2	-$2.9
Segment Assets	$11.3	$10.7		$8.9	$17.1	$19.6		$26.5	$10.8	$20.3		$28.4
Segment Liabilities				-$12.5				-$3.3				-$21.1

	Corporate				Total			
	2010	2011	H1 2011	H1 2012 (IFRS)	2010	2011	H1 2011	H1 2012 (IFRS)
Sales					$27.0	$27.4	$12.8	$13.5
% Change PCP								
Other					$18.9	$8.7	$5.7	$1.5
Total	$0.0	$0.0	$0.0	$0.0	$45.9	$36.0	$18.5	$14.9
Expenses	-$4.7	-$8.4	-$4.6	-$3.7	-$25.5	-$30.2	-$15.4	-$14.9
EBITA pre R&D	-$4.7	-$8.4	-$4.6	-$3.7	$20.4	$5.8	$3.0	$0.1
EBITA pre R&D/Sales								
Net R&D Expense					-$19.0	-$17.8	-$8.6	-$9.1
Segment Result before Tax	-$6.1	-$10.2	-$3.2	-$3.2	-$1.7	-$15.5	-$4.7	-$8.7
Segment Assets	$12.9	$19.0		$7.2	$52.1	$69.6		$71.0
Segment Liabilities				-$4.4				-$41.3

– Bioniche cont'd from page 4

Bioniche listed on the ASX in January 2011 after raising $12.5 million. At about the same time Bioniche also raised C$17.5 million in Canada where it is listed on the Toronto Stock Exchange.

Bioniche's high cash burn stems from its commitment to manufacture Urocidin, a potential treatment for non-muscle invasive bladder cancer, for its partner **Endo Pharmaceuticals**. Endo is currently conducting a second Phase III trial in 450 patients, which is possibly running a year behind schedule (Bioniche has not been updated on recruitment progress by Endo). Only 72 of the planned 120 sites for the trial are currently active. The trial was originally expected to be completed at the end of 2011.

The Urocidin manufacturing facility costs approximately C$7 million to operate at a minimum, and at the moment annual costs, including clinical trial support, is between C$10-$11. The more delays there are to the clinical and regulatory development of Urocidin, then the greater the financial burden is born by Bioniche. According to a filing with Clinicaltrials.gov, Endo expects recruitment to be completed by December 2013.

Why Has Bioniche Pursued Debt Financing?

One reason that Bioniche has pursued debt financing is that, according to Bioniche CEO Graeme McCrae, major shareholders did not want to be diluted as might be expected to occur with convertible note financing or with equity placements. McCrae said the company was under huge pressure from shareholders not to do an equity finance, which would have represented 25% of the company.

The debt financing addresses Bioniche's working capital requirements including (a) some as yet unspecified activity (b) the refurbishment of its MCC (Urocidin) plant in Montreal and (c) for business development in the animal health business. It does place conditions on the business. For example, if a change of control takes place the loan will have to be repaid in full if there is more than 50% of the loan outstanding.

Unlike many biotech companies with no steady income from product sales, one of the reasons Bioniche has been able to secure debt financing is because it operates a well established animal health business that generates revenues in the order of $27 million per annum, commanding gross margins of ~52% (C$14 million a year) and EBITDA margins (pre R&D) of ~25% (C$6.7 million a year).

Bioniche Focusing on Slowing Cash Burn

The timeline of the Phase III Urocidin trials having been extended significantly. With that there is extended cash burn associated with maintaining the facility and a delay in any milestone payments from the program and product sales. We would expect the next milestone payment to come with filing Urocidin for approval and a major milestone from Urocidin FDA approval. To date Bioniche has received $38 million from its licensing deal with Endo Pharmaceuticals.

Bioniche believes it is capable of reducing its cash burn going forward, having reduced its monthly cash burn to C$1 million per month in the 2011 Q4 from C$1.3 million per month in the 2011 Q3. Some R&D activities have been deferred and some costs with Urocidin commercialisation have been reduced.

Bioniche is seeking to generate stronger sales growth from its animal health business and is introducing several new products to this end. This includes a treatment for cancer in dogs, Immunocidin, using the same active product in Urocidin. This could generate sales of $5 million a year. Some positive results in treating cancer in dogs have already been achieved. It is also seeking to commercialise a new equine vaccine

The company's animal vaccine facility at its headquarters in Ontario is expected to be ready for commercial operation in mid 2012. The first product to be made at this facility will be an *E.coli* vaccine for cattle, called Econiche. The company will look to also conduct contract manufacturing at this new facility. The product is approved in Canada but is still awaiting approval in the USA. Bioniche is also working approval in Australia. Success with this product relies on either government mandating use of the vaccine, or demand from end users who are prepared to pay a higher price for a safer beef products.

Summary

Bioniche has a solid core business in the animal health field which generates sales of $27 million a year. However, the company has become financially exposed in its human development program. Sale of manufacturing assets is now a more difficult option with the current debt facility in place.

Bioniche's Econiche vaccine has yet to achieve a US regulatory clearance (expected on a conditional basis in 2011) in addition to commercial validation from sales to Canadian beef producers. The Canadian government has invested $25 million, for which $21 million sits as loans to be repaid by Bioniche.

Over the next 12 months there are a number of key events that need to occur for the business to improve. These include:

- Improvement in recruitment rates for the Phase III Urocidin trial being conducted by Endo Pharmaceuticals;
- Sales of Econiche vaccine;
- Initiation of contract manufacturing at animal vaccine facility;
- Increase in sales from the animal products business, including launch of new products; and
- Continued decrease in cash burn from current C$1 million per month.

With few drivers for this stock apparent in the short term, investors would be better placed to reconsider the stock in 12 months time.

Bioniche is capitalised at $58 million.

Bioshares recommendation: **Sell**

Bioshares

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.79	$1.66	October 2011
Mayne Pharma Group	$0.290	$0.435	September 2011
Acrux	$3.92	$3.37	June 2011
Somnomed	$0.85	$0.94	January 2011
Phylogica	$0.049	$0.053	September 2010
Biota Holdings	$0.96	$1.09	May 2010
Tissue Therapies	$0.44	$0.21	January 2010
Atcor Medical	$0.08	$0.10	October 2008
Bionomics	$0.46	$0.42	December 2007
Cogstate	$0.26	$0.13	November 2007
Sirtex Medical	$5.90	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.75	$6.60	September 2007
Pharmaxis	$1.31	$3.15	August 2007
Universal Biosensors	$0.65	$1.23	June 2007
Alchemia	$0.520	$0.67	May 2004

Portfolio Changes – 14 April 2012

IN:

Osprey Medical is due to list in the next two weeks. We have added Osprey to the model portfolio at its issue price of 40 cents a share.

OUT:

Bioniche has been removed from the portfolio. See analysis on page 4.

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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