

In this edition...

The testing of drugs and devices in humans, as opposed to mice, pigs and sheep, is where the cis-polyisoprene (rubber) hits the road for new products. It's a numbers game where recruiting patients on time means that you can also (probably) meet the budget for the job. That appears to be the case for Starpharma which has completed recruitment for two Phase III trials of Vivagel for the treatment of bacterial vaginosis. In stark contrast, cancer immunotherapy company Prima Biomed's enrollment for its Phase III trial of CVac has had a very slow start, and interim data from a Phase II trial is only providing weak evidence of benefit, if any. Interim data from Viralytics' CAVATAK Phase II trial is positive as are the results from Calzada's first two patients treated with its Novosorb BTM product.

Companies Covered: CZD, PRR, SPL, VLA

	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 (May '11 - May '12)	-18.0%
Year 12 (May '12 - current)	-12.5%
Cumulative Gain	202%
Av. annual gain (11 yrs)	17.8%

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Bioshares

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

Extract from *Bioshares* –

Calzada – First Human Implants Successful

Calzada (CZD: 5.1 cents) has successfully used its wound repair product in treating full thickness wounds in two patients requiring flap donor site treatment. The treatment, called the Novosorb Biodegradable Temporizing Matrix (BTM), is a biodegradable polyurethane polymer.

Early Clinical Results Positive

The results from the treatment of the first two patients in the Novosorb BTM trial are important because proof-of-concept in man has now been achieved. Animal studies have shown the implanted polymer wound dressing works well, but in-human studies have now confirmed its positive features. There was no discomfort from the polymer implant and the wounds have been effectively sealed with a final skin graft treatment.

A free flap application was used because it is a scheduled procedure. In such cases, the skin is taken from one part of the body and is used to replace skin or tissue structures in other areas of the body.

Advantage 1 – Avoids Immediate Skin Graft

The Novosorb BTM has a number of functions. Firstly it allows the wound to be sealed, reducing the chances of infection in a major burn wound. It also importantly stops water loss from the wound.

The alternative is to immediately give the patient a skin graft from another area of the body. However, in the case of major burns, patients first need to be stabilised, skin grafts then need to be taken once the patient is stabilised, and for large wounds there may be insufficient body areas to deliver a graft. Often there is an additional delay, of more than 10 days, to allow the donor site to regrow to allow a second and third graft to be taken. In the meantime the wound is open to infection and water loss occurs.

Novosorb BTM has been designed to offer immediate wound closure, and to be followed by a skin graft at a later stage, once the patient has been stabilised.

Advantage 2 – Less Skin Graft

The second advantage from having a polymer implant is that the thickness of the skin graft required is much lower, with the skin graft only the final layer placed on top of the Novosorb BTM implant

This reduces the demand on skin grafts from other areas of the body. In the two patients treated in this trial, the Novosorb BTM product was 5-6mm in depth.

Advantage 3 – Less Wound Contraction

The third advantage in using a polymer to immediately close the wound is that it results in less contraction in the wound and therefore less disfiguration of the skin. The body

Cont'd over

naturally tries to close a wound if it is not sealed, thereby contracting the skin.

Also if there is not sufficient skin depth in the skin graft, the treated wound is lower than the surrounding skin and this adds to the contraction in the skin. In the first two patients treated, the wounds were full thickness and the final treated wound area was level with the surrounding skin, achieving a visually appealing result (see announcement 15 October 2012 for images). Contraction of the skin can also restrict the mobility in the limbs.

Advantage 4 – Robust and Easy to Use

The fourth advantage with Novosorb BTM is that it is robust and easy to use, compared to the Integra product in the market which is more delicate. Calzada also believes its technology is more reliable than Integra, with reliability being a very important issue. Integra has several limitations, one of those being its very high cost.

The appeal of Novosorb BTM in a mass casualty situation (see BARDA Contract Submission) is that it is durable, easy to use, reliable, much less expensive to produce than Integra (Integra is made from bovine collagen and shark chondrocyte), and can be mass produced and stored.

Additional Patient Recruitment

Novoskin (the joint venture between John Greenwood and Calzada's subsidiary Polynovo) will continue to enrol more patients into this trial and on the back of the positive results to date, it may look to expand the trial into burn wounds, looking to recruit around a further 10 patients in the next 12 months.

Next Product – Composite Cultured Skin

A major advance in wound treatment is using the Novosorb technology to create a complete bilayer skin product that would potentially replace the need for a skin graft. The company has already developed proof-of-concept in an animal study that it can develop a bilayer skin product.

This involves producing two layers of skin, where the skin is grown up in a bioreactor from a small biopsy. The process takes 21 days. It forms a dermal structure from fibroblast cells and a second

BARDA Contract Submission

The technology from Calzada's subsidiary Polynovo is being championed by burn surgeon Dr John Greenwood in Adelaide. Dr Greenwood was the only non-US burn surgeon invited to advise the US government on its disaster planning response to a potential major catastrophe in the US.

This is an important point because Novoskin, which is 80% owned by Calzada and 20% by Dr Greenwood, was invited to submit a proposal for a US BARDA contract to develop a product for the treatment of mass burn casualties. Calzada expects a decision on its application for a \$16.9 million contract with BARDA to be decided in the next six months. The Novosorb BTM could potentially be stockpiled by BARDA for use in event of a major catastrophe. Novosorb BTM can be mass produced and can be readily stored for emergency use.

layer using epidermis cells. The cells are held in place using the Novosorb biodegradable polymer scaffold, allowing vascularisation to occur to provide nutrients to the cells.

In the two patients treated to date with the Novosorb BTM scaffold, tissue ingrowth into the scaffold and vascularisation was observed.

Summary

Calzada's wound therapy technology appeals on a number of levels. It has now achieved early proof-of-concept evidence in two patients showing that it works as designed, potentially offering a much needed wound healing therapy. And it has a burns surgeon to champion its use and coordinate clinical assessment.

Calzada is capitalised at \$18 million. It had \$4.8 million in cash at the end of June.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

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

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