

In this edition...

At the end of the day, drug development is about treating diseases more safely to either eradicate them, or extend life or improve quality of life if the disease is chronic. Cancer therapy developer Prima Biomed faces a critical point this year when data from its Phase II trial becomes available and its potential as a new, safer way to treat cancer by harnessing the immune system is made clear. We re-visit the Prima proposition in a reader friendly Q&A format.

We also update readers on Evogenix's osteoporosis protein drug prospect, Cogstate's distribution deal in Japan and Sirtex's strong profit result.

The editors

Companies covered: **CGS, EGX, PRR, SRX**

	Bioshares Portfolio
Year 1	21.2%
Year 2	-9.4%
Year 3	70.0%
Year 4	-16.3%
Year 5 (to date)	67.6%
Cumulative Gain	162%
Average Annual Gain	26.6%

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

Extract from Bioshares 159

Prima Biomed's Cancer Immunotherapy Approaches Crucial Revaluation Point

Prima Biomed (PRR: 7.3 cents) is conducting a trial of a therapeutic technology that may contribute significantly to the way in which a number of cancers can be treated. The company has developed a therapeutic cancer vaccine, otherwise termed immunotherapy. The approach uses a particular cell from a patient's own immune system, called the dendritic cell. This dendritic cell is presented (*ex vivo*, or outside the body) with an antigen prolific on a number of cancer cell surfaces, in particular ovarian and renal cancers, called the MUC1 protein. This presentation effectively trains the immune system to recognise the MUC1 protein, so when re-introduced into the body it can induce a sequence of events that destroy or halt tumour growth.

The outcome from the company's Phase II trial in 20 patients in coming months is set to be a critical milestone for the company, investors and patients with a range of aggressive cancers. If successful, the technology could one day be used as a standard early cancer treatment.

We have set out below five questions, that presented in a Q&A format, will hopefully help investors grasp what the Prima Biomed investment proposition is about.

- What is Prima's business model?
- Why is Cell Therapies so important to Prima?
- What was revealed in the Phase I trial results?
- What will be a good result in the Phase II trial underway?
- Why is Dendreon a company to keep a close eye on?

I. What is Prima's business model?

Prima has developed a therapeutic cancer vaccine that uses a person's *own* dendritic cells to stimulate a patient's immune system. It involves harvesting those cells from the patient (apheresis), expanding those cells in culture, and fusing the cells with the MUC1 surface protein. The rights to use MUC1 have been in-licensed from a Canadian biotech, **Biomira**. The MUC1 protein is in high abundance on the surface of ovarian cancer cells and the logic is that if the immune system's T-cells can be trained to recognise cancer cells in the body through this protein, then the cancer cells could be selectively destroyed.

It's also believed that the MUC1 protein is also heavily expressed on pancreatic, kidney and breast cancer cells, and to a lesser extent on colon and lung cancer cells. In normal tissues, MUC1 is expressed to a lower level in ducts and glands in the body.

In the agreement with Biomira, Biomira has the option to commercialise Prima's vaccine technology throughout the world except for Australasia, where Prima retains

Cont'd over

commercial rights. Prima will receive a royalty from any Biomira sales of this product.

Prima is expecting interim results in April/May this year, with final data from the current Phase II study expected towards the end of this year. The interim results may or may not be released, depending on Biomira, although the final results will be released when available. It is expected that Biomira will exercise its option to develop the technology should the results be favourable.

If the final results are positive, Biomira may undertake a large Phase IIb/III study and Prima may decide to conduct its own 100+ patient trial in Australia, potentially in women with less advanced disease. Other options that may also be explored are for evaluating the vaccine in other cancers, such as renal or pancreatic cancer.

Prima may consider selling the treatment in Australia and New Zealand, and in other regions where Biomira may elect not to distribute the product. In Australia, it's likely the patient would be treated using the Cell Therapies contract processing facility which, in its currently size, would have a capacity of 1,000 patients a year. It's expected that an annual treatment course might cost in the order of \$25,000 a year, with cell harvesting and processing only required once over that period and surplus product frozen for later use.

2. Why is Cell Therapies so important to Prima?

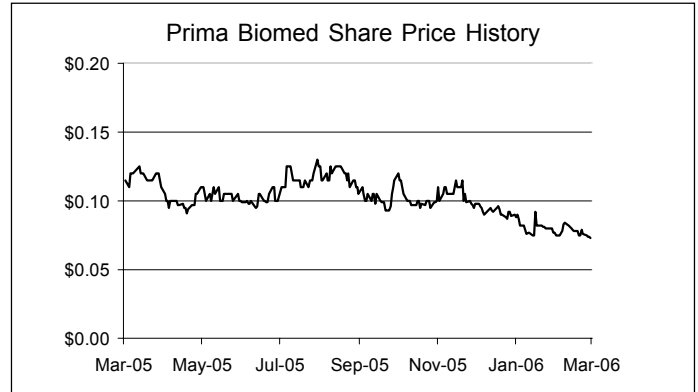
One of the reasons Prima has been able to progress its Phase II trial is because of the existence of **Cell Therapies Pty Ltd.** Based at, and 51% owned by, the **Peter MacCallum Cancer Centre** in Melbourne, Cell Therapies is producing cellular therapeutic products for a number of clients in Australia, including **Mesoblast** and **Cygenics**, and clients in the US and Europe.

The company received a TGA license in 2003 to manufacture therapeutic products. Cell Therapies can assist clients such as Prima across the entire process, including recruitment of patients (through the Peter Mac.), submitting data and regulatory packages to the TGA, cell harvesting and processing, and treatment of patients.

There are only four or five such facilities operating throughout the world and Cell Therapies is now expanding its own business model into the US in recent weeks. Called the **Cell Alliance**, it provides similar contract services for cellular therapeutics in conjunction with **Apptec** (which will conduct the cell processing) and **Lifeblood Biological Services** (which will harvest the cells from the patients). Cell Therapies will manage the projects.

3. What was revealed in the Phase I trial results?

Previous attempts by scientists who developed the Prima technology at the **Austin Research Institute** failed to achieve the requisite T-cell response, with only an antibody response recorded. However Prima's Phase trial in 10 patients with a range of advanced malignancies showed that adding an adjuvant to the vaccine allowed a cellular immune response to be recorded in all 10



patients and outstanding survival accounts in two of the patients in the trial.

The results were published in *Clinical Cancer Research* last month. One 64 year-old woman in the trial had been diagnosed with stage III ovarian cancer 26 months before enrolling in the study. She had undergone surgery and been through six cycles of chemotherapy treatment of carboplatin and paclitaxel. This woman may have been expected to live for another 18 months. However, after continuing with Prima's vaccine treatment well after completion of the trial, the woman was clinically stable for three and a half years. What was particularly impressive about this result was the direct effect on CA125 (a marker for ovarian cancer) levels following injection of the cancer vaccine, and it is this result that has been a major reason that ovarian cancer was selected as the target in the current Phase II trial.

The second patient was a 69 year-old man with renal cell carcinoma. The man had surgery 22 months before enrolling in the trial and there were signs of progressive disease in mediastinal nodes at the commencement of the Phase I trial. He was earlier classified as a patient with Stage IV disease. Over the three months of the vaccine trial, the disease remained stable and for eight months after completion of the trial. The patient then recommenced vaccine treatment at 14 months from the trial start date. Scans showed that earlier disease states were stable or had reduced in size. After three years of ongoing vaccine therapy, the disease remained stable in the patient.

4. What will be a good result in the Phase II trial underway?

Prima Biomed is currently conducting a Phase II trial of its therapeutic cancer vaccine in 29 women (20 evaluable patients) with Stage II and III ovarian cancer. As with the previous (Phase I) trial, the chief investigator is Dr Paul Mitchell. Mitchell is the Director of Cancer Services at Austin Health, which is currently engaged in 50 different cancer trials for various pharmaceutical products.

All the patients in Phase II have progressive disease and the aim is to investigate if Prima's cancer vaccine can stabilize CA125 levels. As a secondary endpoint, the cellular immune response will also be measured. Recruitment of the trial was completed last month. Interim results will be recorded when all patients

Cont'd over

have finished 10 weeks of treatment which includes three vaccine injections (weeks two, six and 10). Patients will continue on the trial with injections every 10 weeks.

The first 10 patients had stage III disease and the remaining 20 patients were less advanced (Stage II), although all patients were relapsing, (meaning that their CA125 levels were increasing) when enrolled into the trial.

The trial data will be categorised in the following manner:

Major response:

more than a 50% decline in CA125 values over one month

Minor response:

more than a 25% decline in CA125 values over one month

Stable disease:

CA125 levels +/- 25% over three months

The aim of this trial is to stop the patient relapsing. A good result will be if four of the 20 evaluable patients have stable disease at 10 weeks. Two major responses alone might be enough for the company to launch a pivotal study based on this data in ovarian cancer and a second study in renal cancer.

5. Why is Dendreon a company to keep a close eye on?

To date, no therapeutic cancer vaccines have been approved by the FDA. However, all eyes in this field are on **Dendreon** in the US, which is developing an autologous therapeutic cancer vaccine, initially for the treatment of men with asymptomatic, metastatic, androgen-independent prostate cancer. In two Phase III studies in 225 men, the company's vaccine, called Provenge, was found to achieve a median 23.2 month survival, compared to 18.9 month median survival in the placebo group.

The company is conducting a third Phase III study in prostate cancer in 170 men and enrolment has now been completed. The company expects to file its BLA (Biologics License Application) with the FDA in the second half of 2006 and has been granted Fast Track status from the FDA.

The chances that Provenge will be approved are high, given the product's good safety profile, as there appears to be no rate limiting toxicity with the product. The company expects to have its 150,000 square foot processing facility completed by mid year and the product may be on the market in the next 12 months. If it's successful, it will be a significantly positive event for Prima Biomed, validating its own business model. Dendreon is currently capitalised at US\$268 million.

Risks

The risks with Prima are twofold. Firstly, there is a technology risk, that the company's therapeutic cancer vaccine will not be sufficiently efficacious to gain regulatory approval. The second is the risk of the company's business model of selling an autologous cancer therapeutic product that can generate a strong profit margin and revenues. The existence of, and access to the commercial cell processing facility, Cell Therapies, substantially lowers the manufacturing risk for the company. In earlier days, the

absence of certified manufacturing infrastructure would have been a reason for investors to disregard the stock.

Summary

Prima Biomed is approaching a crucial re-valuation point this year with the results from its current Phase II trial in 29 women with advanced ovarian cancer due to be released. There is a clear biomarker (CA125) with which to accurately judge the immunotherapy's efficacy in halting progression of ovarian cancer. Each year in Australia alone approximately 1500 women are diagnosed with ovarian cancer and the aim no doubt would be to make this therapeutic vaccine available to women immediately after diagnosis as a standard treatment. A glimpse of efficacy first needs to be established in patients with more advanced malignancies before the product can be used in earlier up the line treatments, where extension of life should be more pronounced. There is also further blue sky that the product use could be extended to other cancers. Investors should also keep in mind, that it is potentially a very safe therapy, in contrast to many highly toxic, non-specific chemotherapies that in many cases damage healthy tissues and weaken the immune system, thus exposing patients to infection from pathogens.

The field of autologous therapeutic cancer vaccines has yet to be proven as a viable commercial model and Dendreon is a company that should be watched closely. Prima's Phase I trial with its cancer vaccine produced some very positive results in two patients and it's a project that certainly contains merit and may offer many in the future another important modality for treating a number of cancers.

Prima is capitalised at \$13 million and had \$5.1 million in cash at the end of last year.

Bioshares recommendation: **Speculative Buy Class A**

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.

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, Psivida, Cytopia, Biodiem, Peptech, Starpharma Holdings, Cogstate, Xceed Biotechnology

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