

# INVESTOR UPDATE

by  **PRIMA BIOMED**

EDITION  
JULY 2014

12



CEO Marc Voigt

## Message from the CEO

Welcome to the second issue of the Prima BioMed Investor update for 2014. It gives me great pleasure to be addressing Prima BioMed shareholders for the first time as Chief Executive Officer.

First of all and before going into the operational details I would like to

thank all our Shareholders for their considerable loyalty and support and reassure you that the whole Prima team is fully committed to bringing CVac™ to market.

It is therefore most encouraging that the past three months have delivered a series of very positive announcements related to our clinical development program and regulatory milestones in the US for CVac. These achievements are the culmination of a lot of hard work by the Prima team. I would especially like to acknowledge the significant contribution of Matthew Lehman as CEO in building the Company to where it is today. Matt will continue to consult with the Prima team on the clinical development program.

I am grateful to the Board for putting their faith in me to lead Prima into the future. I am firmly committed to successfully executing Prima's clinical trial program for CVac, while also assessing other market opportunities that may arise.

### Strategic Update

Most recently we announced that the United States Patent and Trademark Office (USPTO) has granted Prima a patent for CVac, along with a patent term adjustment of almost four years. This takes patent expiry in the US out until August 2022, providing Prima with essential protection over its commercial development. This was the final patent in the Prima portfolio to be granted.

This news followed the United States Food and Drug Administration (FDA) grant of Fast Track status for CVac's clinical development program in May. There is a clear unmet medical need in ovarian cancer and the potential application of CVac as a maintenance therapy for this disease.

Fast Track status means we will have higher levels of engagement with the FDA through the clinical development program and faster review timelines, which could significantly shorten the approval time after completion of our clinical trials.

I would also like to take this opportunity to acknowledge and address shareholder concerns about a fall in the Company's

share price after a perceived clinical trial failure of CVac late last year. Our recent presentations of data at the American Society of Clinical Oncology (ASCO) conference in May revealed very promising CVac data which we explain in some detail in this newsletter. We are very excited about this data and hope that this will go some way towards helping our investors understand why, more than ever, we believe CVac is a very promising therapy.

Our focus remains on getting CVac through the clinical trial program successfully to meet the clear unmet medical need. To that end, our new CAN-004B clinical trial of second remission ovarian cancer patients will greatly assist in bringing CVac to market as quickly as possible. As outlined in more detail in Professor Frazer's Q&A section, we have decided to focus on second remission patients because this group demonstrated an earlier clinical benefit during the CAN-003 trial. As the disease progresses, the remission window shortens and we are able to achieve statistically meaningful data, more readily than with first remission patients.

In late April we announced that enrolment for the CAN-004B clinical trial for second remission patients had commenced. By way of a progress update, we have increased the number of clinical sites across Europe and these are in the process of being initiated to allow enrolment of patients into the trial. This is a rigorous and time consuming process which requires all clinicians to be properly vetted and trained.

The increasing political instability in the Ukraine has caused some disruption to Prima's clinical trial enrolment as we are no longer able to ship CVac to our site in Donetsk. Prima will continue to monitor the situation closely to assess whether withdrawals from its other Ukrainian clinical trial sites is necessary. We will provide a further update once the impact of any further site closures has been fully assessed.

### ASCO Presentation

As mentioned briefly earlier, the most important event that took place during the quarter was the presentation at ASCO by Dr. Heidi Gray, the Lead Investigator on Prima's CAN-003 clinical trial, at the end of May.

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## Message from the CEO

Dr. Gray presented extremely positive final progression free survival (PFS) data and a very strong indication in overall survival (OS) interim data for CVac treatment in second remission ovarian cancer patients.

This was most encouraging and fully supports the launch of Prima's new CAN-004B clinical trial, which has a very robust clinical trial design. Should the CAN-004B results demonstrate trends similar to CAN-003 in a larger population, it would be a major step towards securing approval for CVac in this target patient population.

Clearly, this process will still take some time given the nature of these trials, but the Directors of Prima, along with its clinical and scientific advisory board members, share my optimism that the Company has a clearly defined development plan for CVac supported by strong data and which has every chance of success. Along with the rest of the Prima team, my priority is to bring this treatment to market at the earliest opportunity for the benefit of advanced stage ovarian cancer patients around the world.

### Financial Update

As reported in our Appendix 4C for the quarter and financial year ended 30 June 2014, Prima has \$23.20 million in cash and term deposits. Prima benefits from up to €7.9 million funding grant from the Saxony Development Bank in Germany to carry out its CVac program in Europe.

This is one of the fundamental reasons for the Company focusing its operations in Europe, where we are also able to achieve greater efficiencies both in our clinical trials and in the manufacturing of CVac. During the year we also benefited from a R&D tax refund from the Australian Federal Government of \$1.6 million.

Continued tight management of the company's cash outflows remains a high priority for Prima.

### Outlook

In addition to successfully delivering the development program for CVac, part of my role is to assess future growth opportunities for Prima. The licensing agreement we reached with the Neopharm Group earlier this year is a small example of the kind of commercial opportunities that are available to Prima and is symbolic of the kind of interest we receive from other industry players. As a Board and management team we will assess any opportunities that arise and only enter into agreements which we consider to be value accretive for shareholders.

Finally, an important part of my role will be to market the Company to a broad spectrum of industry participants as well as other key stakeholders including investors. This is an area to which I will be dedicating considerable time and effort and I look forward to updating Prima's many shareholders, both in Australia and internationally, on its future achievements.

Marc Voigt | Chief Executive Officer

## Understanding the CAN-003 data presented at ASCO

On 31 May 2014, Dr. Heidi Gray presented the final progression free survival (PFS) and interim overall survival (OS) results for the CAN-003 trial of patients in first and second remission ovarian cancer.

ASCO is one of the largest annual oncology conferences attended by industry professionals in the world. This year there were 34,750 registered attendees. Out of 5,530 abstracts submitted for ASCO this year from numerous applicants around the world, only 210 were selected for oral presentation at the ASCO Annual Conference. Hence, it was a real privilege to have the data from our CVac CAN-003 trial presented at this highly prestigious oncology industry event.

The purpose of this section of the newsletter is to assist our readers in understanding the significance of this data.

Dr. Gray's presentation showed that there were multiple accomplishments of the CAN-003 trial. One goal was to evaluate the ability to manufacture CVac

outside Australia. This was successfully completed with the transfer of manufacturing to the USA. The trial also confirmed that CVac is very safe and well tolerated with minimal side effects. The results showed that the drug appears to be working as expected: patients who received the CVac treatment were able to produce an immune response that was cellular (driven by T cells) and very targeted or specific to the cancer type (mucin 1).

Most importantly, Dr. Gray's presentation revealed that the CAN-003 data was generating a very positive PFS and OS signal in second remission patients.

**PFS** is a measure of the length of time during or after the treatment of a cancer, that patients continue to live without disease progression (i.e., are in remission). It is used to measure the efficacy of a new treatment compared with patients receiving standard of care or a placebo control. **OS** on the other hand, is a measure of the percentage of patients in a treatment group who are still alive for a certain period of

time after diagnosis or commencement of treatment. It is important to look at OS in a treatment arm relative to that of the standard of care.

When examining the clinical impact in the PFS period, while there was not a significant difference between the treated and standard of care patients in the first remission group, those patients in second remission showed a clinical benefit of greater than 8 months. Similarly, when looking at the patients' OS, although this is still an early analysis, the data shows a similar trend to that of PFS. Possible reasons for the differences observed between the first and second remission groups are discussed in the Q&A section with Professor Fazer but it is important to understand that it doesn't mean CVac will not benefit first remission patients.

One of the primary conclusions from CAN-003 was that a larger clinical trial focused on second remission patients was justified, leading to a trial redesign and enrolment into the enlarged CAN-004B clinical trial commencing in April 2014.

**A more detailed look at the CAN-003 data**

The final PFS and OS data from CAN-003 was presented at ASCO in the form of Kaplan-Meier curves. **A Kaplan Meier (KM) curve is a widely used graphical presentation that compares the proportion of patients that are either disease free (for PFS) or surviving (for OS) for each treatment arm.** For CAN-003, the treatment arms were either receiving CVac (blue line) or standard of care (in this case observation; yellow line). The steepness of the curves demonstrates the efficacy of the

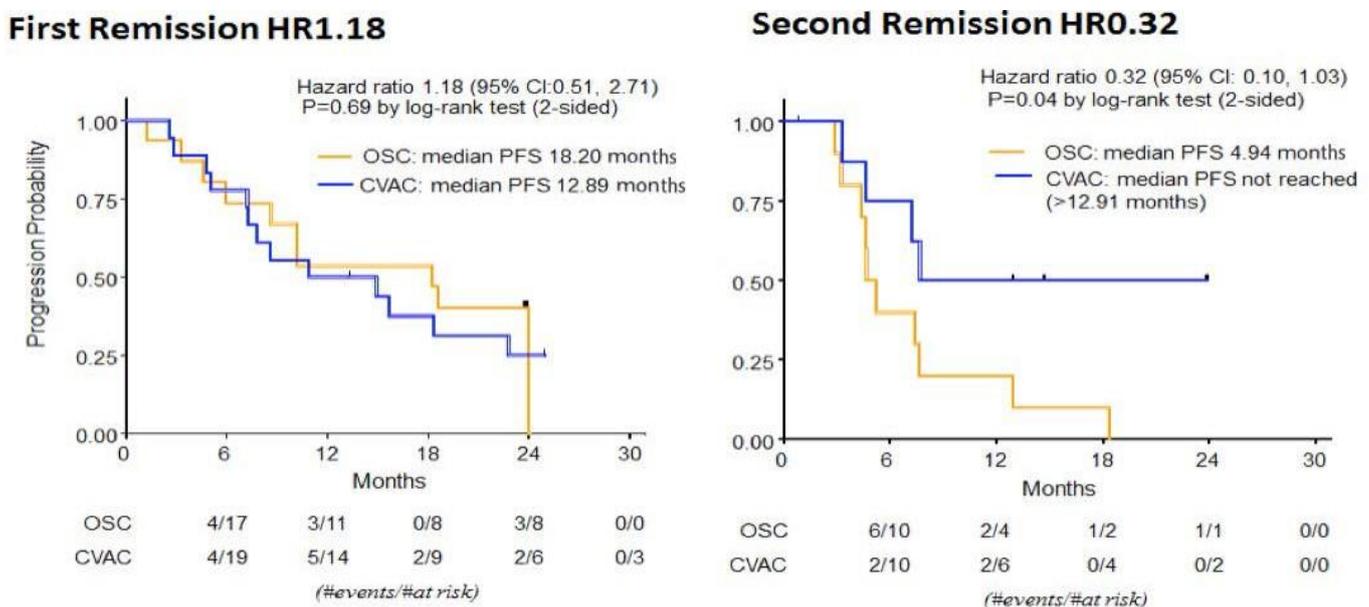
treatment being investigated. The shallower the survival curves, the more effective the treatment because patients either are in remission longer or surviving longer. If the KM curves have similar patterns, it suggests that there is only a small amount of difference between the arms of the study. No differences between the two different arms of the studies are measured if the curves meet.

Looking at PFS data in Figure 1, for patients in the first remission group, there is little difference in PFS seen between patients who received CVac versus observation (the blue and yellow curves are close together). Possible reasons for this are discussed in the Q&A section with Professor Ian Frazer. However, encouragingly in the second remission graph there is a separation of the blue and yellow curves, indicating a significant difference between the control and treatment groups.

Looking more closely at the second remission graph, patients in the CVac arm have a median PFS that has not yet been reached after more than 13 months (because the trial finished and no more data can be collected) while median PFS for the observation group is about 5 months. From the difference in PFS between the two arms it can be concluded that the CVac treatment resulted in at least 8 months of benefit for patients in the second remission group.

Statistical analysis of the data calculated a hazard ratio of 0.32 for the PFS of second remission patients. **A hazard ratio (HR) is a way of calculating the relative risk of experienc-**

**Figure 1 Final PFS analysis for first and second remission patients**



ing an event (e.g. disease progression or death) being measured in one trial arm when compared with the other arm, over the entire time period of the trial. A HR of 1 indicates there is no difference between the treatment and control group. A HR of less than 1 means that the treatment arm is at less risk of progression or death.

In the CVac treatment arm for second remission patients, a HR for PFS of 0.32 indicates there is a 68% reduction in the risk of disease progressing or for the patient coming out of remission. This means that at any given point during the trial, 68% of the patients receiving CVac are doing better than the standard of care patients.

The other numbers in the graph include a P value and confidence intervals. These are also statistical measures for analysing the data. A **P value** is used to represent the strength of a conclusion drawn from clinical trial data. If the P value is small (less than 0.05), this means there is less than 5% probability that the outcome of the trial happened by chance and the result is statistically significant. The **confidence interval (CI)** is a measure of certainty or reliability around the outcome of a result. A 95% CI means there is 95% confidence that under the same study conditions the same outcome or result would fall within that range again. Collectively the statistical data support the conclusion that there is a PFS benefit seen in second remission patients

Looking at Figure 2, the interim OS data for CAN-003 is still early, but is very promising. In the first remission group, neither treatment arm has reached their median OS, but this is not

unexpected as much of the available literature suggests that OS for ovarian cancer patients is up to 5 years from diagnosis. There is a small separation of the curves, but the data is still early and hence inconclusive.

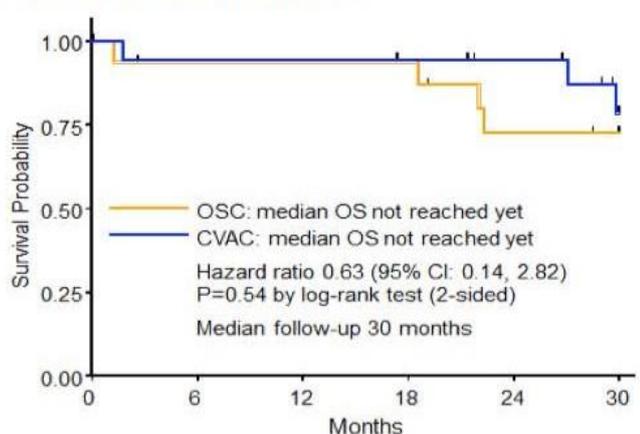
In contrast, in the second remission group, median OS for the standard of care observation arm (yellow line) has been reached at 26 months, whereas the OS for the CVac arm (blue line) has not been reached after more than 30 months from the treatment commencing. As you refer back to our previous explanation regarding of the HR, note the HR in the second remission group for OS is 0.17.

This HR indicates that at any point during the trial, this group of patients receiving CVac are doing 83% better than the observational group. This result is very encouraging. There is likely to be a significant benefit in the OS of second remission patients, greater than the 4 month OS benefit seen so far. Prima will provide an update on the status of OS of both patient groups in late 2014.

While the patient numbers in CAN-003 were small, our results are strongly indicative of CVac's utility as a maintenance therapy in a disease with a high unmet medical need. These results support our decision to modify the CAN-004 trial to focus on patients in second remission. The protocol has been amended, revised and approved by the Prima clinical advisory board and filed to those countries that are participating in enrolling CAN-004 second remission patients (CAN-004B). The protocol has been approved in many countries across Europe and patient enrolment has commenced.

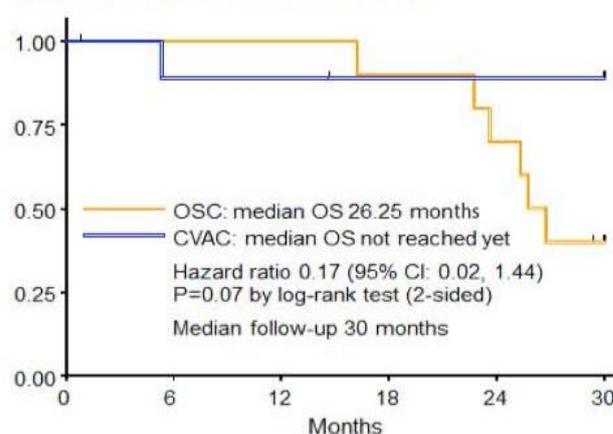
Figure 2 Interim OS analysis for first and second remission patients

### First Remission HR0.63



OSC	1/17	0/14	0/14	3/14	0/10
CVAC	1/19	0/17	0/17	0/16	2/14
	(#events/#at risk)				

### Second Remission HR0.17



OSC	0/10	0/10	1/10	2/9	3/7
CVAC	1/10	0/8	0/8	0/7	0/7
	(#events/#at risk)				



*Professor Ian Frazer, AC, is Chair of Prima BioMed's Scientific Advisory Board.*

## Q&A with Professor Ian Frazer

Professor Frazer is internationally renowned for the co-creation of the technology for the cervical cancer, HPV vaccines. He was awarded the 2005 CSIRO Eureka Prize for Leadership in Science and was selected as Queenslander of the Year, and Australian of the Year in 2006. He was also awarded the 2008 Prime Minister's Prize for Science, the 2008 Balzan Prize for Preventive Medicine, the 2009 Honda Prize, and, in 2011, was elected as a Fellow of the esteemed Royal Society of London. In 2012, Professor Frazer was appointed a Companion of the Order of Australia (AC) in the 2012 Queen's Birthday Honours. He is Chief

Executive Officer and Director of Research at the Translational Research Institute (TRI) Pty Ltd in Brisbane, Australia. In this role, he heads an expert cohort of over 650 researchers from four leading medical research institutes. He was appointed Chair of the Australian Cancer Research Foundation's prestigious Medical Research Advisory Committee in 2009.

**Q. CVac has been referred to as a "vaccine" by some but as a "maintenance therapy" by Prima. Can you please clarify how it is different to what most people would consider to be a traditional vaccine and how Prima defines CVac?**

Most people consider a vaccine to be of the traditional prophylactic or preventative type, like those you receive in childhood to prevent you from contracting a disease. People are less familiar with the concept of therapeutic vaccines or immunotherapies that help slow the progression of a disease once you have developed it. This is the category in which CVac belongs. To avoid any misunderstanding caused by the nuances between these two meanings of vaccine, Prima felt it would be better to start using the terminology of **maintenance therapy**. In oncology, this commonly used terminology refers to a treatment that is used to help maintain patients in a state of remission and to slow down the progression of their disease.

**Q. Would you consider CVac to be a stand-alone maintenance therapy or could it be used in conjunction with other therapies?**

At the moment, there is considerable excitement in the scientific and clinical community for the use of what is being termed "**combination therapy**", adopting more than one therapy to try and maximise the chances of eradicating cancers before they can implement their evasion mechanism. Approaches include the use of checkpoint inhibitors to help interfere with signalling mechanisms in cancer cells, the use of co-stimulatory molecules to help activate or boost immune responses and the use of various forms of cell therapies to actually kill or eradicate the cancer cells. Other approaches such as anti-angiogenesis inhibitors also aim to cut off the nutrition and blood supply to a cancer.

At the moment CVac is being trialled as a stand-alone therapy to obtain proof of concept however it is entirely feasible that it

could be combined with any of these other approaches in the future. CVac has the advantage of a good safety profile and minimal side effects. Some of these other forms of therapy have quite severe side effects limiting their use to specific cases or limiting the ability to combine them with certain other therapies.

**Q. In the CAN-003 results recently presented at ASCO, the first remission patients did not seem to respond as well as the second remission patients to CVac. Can you please explain why this might be the case and does it mean CVac won't work in patients in first remission?**

The data generated from the CAN-003 trial was from a small patient number of 63. The trial was designed to test the feasibility of using CVac to treat ovarian cancer but was not large enough to generate statistically significant results. The results are exciting and would suggest that the patients in second remission experience both an increase in progression free survival (PFS) and overall survival (OS). However the **results from the first remission patients are inconclusive** and a median for OS in this patient population has not yet been reached. This does not however mean that CVac has not worked for these patients.

Prima believes that in first remission patients the data may not have shown any conclusive effects because this group of patients is very heterogeneous in their response profiles. First remission patients have typically undergone their initial surgery to remove their tumour and then undergone their first round of chemotherapy with a platinum based therapy. They then commence CVac therapy within a month of completing their chemotherapy.

A broad review of literature suggests this group has a wide variation of remission period from 12-28 months. Those relapsing in less than 6 months are called platinum resistant and then subsequently undergo different types of chemotherapy. In the CAN-003 trial, Prima had no way of predicting how first remission patients would respond to their chemotherapy and with a small patient number (n=36 of which 19 received CVac), cannot generate sufficient data to determine if by chance all those treated were at the lower end of the remission window or were perhaps platinum resistant. In contrast, the second remission patients are confirmed to be platinum sensitive and have less variation (12-13 months) in their remission windows.

Further investigations and larger patient numbers are required to determine if CVac will benefit first remission patients. There are 76 first remission patients that have been recruited to the Company's current CAN-004A trial which is ongoing.

**Q Trials of CVac are expected to commence soon in resectable pancreatic cancer. Is it possible that other cancers might also be treated by CVac?**

The CVac technology is based on stimulating a patient's T cells to recognise and kill cancer cells that are expressing a particular mutant form of the mucin 1 antigen. Mucin 1 is typically over expressed by epithelial derived cancers including breast, ovarian, pancreatic, prostate, colon and lung. It is therefore possible that the CVac technology could be used in the future to target other cancers.

## The addressable market for CVac

When considering the potential size of the market for CVac, it is important to distinguish between its **addressable patient numbers** and its **targeted patient numbers**.

**Addressable patient numbers** include all possible patients that can potentially be treated. CVac is currently in trials for ovarian cancer with trials in resectable pancreatic cancer expected to commence shortly. CVac is, however, capable of treating a number of cancer indications as discussed by Professor Ian Frazer. Patients with these types of cancer therefore represent the total addressable market for CVac.

**Targeted patient numbers** include the current population of patients being treated in a given clinical trial based on specific inclusion/exclusion criteria. When conducting clinical trials, it is normal to define more narrow populations of patients in which to test a drug or therapy. There are specific inclusion and exclusion criteria applied to target patient populations so that clinical trials can be designed to be successful and to provide statistically meaningful results more quickly. Longer term, multiple clinical trials may be conducted on a single drug to capture a wider target patient population.

When Prima commenced its CAN-003 trial the target patient population was patients in both first and second remission ovarian cancer. This trial was designed to test the feasibility of treating both of these groups.

Survival rates for these groups vary with the severity or stage of disease. CVac is targeting patients with stage 3 or 4 disease. Of all patients diagnosed with stage 3 or 4 disease, around 80% will achieve their first remission and of these patients, approximately 80% will experience a relapse and require subsequent treatment.

The results from the CAN-003 trial have not necessarily changed the addressable market for CVac because as mentioned in the Q&A with Professor Ian Frazer, it is simply too early to tell if CVac will benefit first remission patients. What has changed for the moment is that Prima now has a **more clearly defined target patient population** of patients in second remission that are likely to respond to treatment by CVac. So the initial target population that Prima will seek market authorisation for CVac with has become more defined based on specific inclusion and exclusion criteria. However, the long term addressable market for CVac in first remission ovarian patients and indeed in other indications remains to be further analysed.

### **Potential market opportunity**

Ovarian cancer is the seventh most common cancer in women worldwide in terms of new cases diagnosed (238,719 in 2012) and the sixth most common worldwide when including previously diagnosed patients based on 5 year prevalence data (586,624 in 2012) (GLOBOCAN 2012 database [http://globocan.iarc.fr/Pages/fact\\_sheets\\_population.aspx](http://globocan.iarc.fr/Pages/fact_sheets_population.aspx)).

The global market size for ovarian cancer therapy was estimated to be US\$460m in 2011 with an expectation that it will triple to US\$1.4 billion by 2021<sup>1</sup>. When considering the addressable market for CVac, the global cancer vaccines market was worth US \$1.6 billion in 2010 after increasing at a compound annual growth rate (CAGR) of 62.7% from 2006-2010. It is expected to record a CAGR of 20.0%, to reach \$ 7.08bn by 2018<sup>2</sup>.

<sup>1</sup> Decision Resources market data retrieved 20 March 2014

<sup>2</sup> 2014 Cancer Vaccines - Pipeline Assessment and Market Forecast to 2018, Global Data, Jan 2012



## A patient's journey with CVac

### Sarah's story

This is the third and final instalment in our case study of a patient's journey with CVac. We continue with "Sarah", a patient who enrolled into the CANVAS clinical trial. We have learned about her experiences through the diagnosis of ovarian cancer, her decision to be part of the study and the collection process for mononuclear cell (MNC) blood collection.



“ Today after what seems interminable waiting, I am told by the study coordinator Karen that I have my product ready. It is an interesting part of this trial to not know if I am getting placebo or if I will take CVac, - the “real” thing, but I have a 50% chance of getting the actual product.

After all the work to get here and start the trial, the long consenting process, the testing to make sure I was the right type of patient, the MNC collection, to now be in remission and disease free is a fabulous feeling, and the trial needs were so simple.

I come for my regular appointments and have my weight checked, blood tested, and the usual assessments done. The unique part is the actual injection of CVac. The container it's shipped in reminds me of a small “dialek” with the domes plastic shell. Karen says we are aging ourselves! But this incredible container ships the product at extremely

low temperatures, -196 °C the monitor says on the device. Karen wears thick gloves to remove the tiny container of product. It's so small, I am shocked. The study staff check and double check I have the product that is mine by many numbers on the vial, then it's quickly thawed and injected into my upper arms and thighs. Done!

I will have 6 doses in total so Karen and I review my schedule for the next treatments and make sure the dates will work or I can work around them. I complete some questionnaires while we make sure I have no reaction and then I am let go.

It's a journey and who knows of our success but we have to try.

Signing off for now.  
Sarah

”

## Company calendar, social network contacts, fast facts; to be updated

**AUGUST 2014**

*Annual Report for FY14*

**NOVEMBER 2014**

*Annual General Meeting*

## Follow Prima's progress

Prima BioMed is dedicated to maintaining consistent and clear communications with our investors. In addition to our quarterly newsletter, we encourage our shareholders to continue following Prima's progress in a number of ways:

► **[www.primabiomed.com.au](http://www.primabiomed.com.au)**

The company website is a treasure trove for those in search of details about our company, our management team, and archived information. We encourage everyone to check it out regularly.

► **[www.clinicaltrials.gov](http://www.clinicaltrials.gov)**

Prima registers all of our clinical trials, and the details of enrolling doctors, on the ClinicalTrials.gov website, a service of the United States National Institutes of Health. This register is the largest such repository of clinical trial information around the world.

► **Twitter**

[twitter.com/PrimaBioMed](https://twitter.com/PrimaBioMed)

► **Facebook**

[www.facebook.com/PrimaBioMed](https://www.facebook.com/PrimaBioMed)

► **LinkedIn**

<http://us.linkedin.com/company/prima-biomed-ltd>

## Prima BioMed – Fast Facts

### Listings

Australian Securities Exchange (ASX), NASDAQ, Deutsche Börse

### Stock Codes

ASX: PRR, NASDAQ: PBMD,  
Deutsche Börse: ISIN: US74154B2304

### Issued Capital – Ordinary shares

1.23B (approximate as of 23 July 2014)

### Issued ADR's

3.05M (approximate as of 30 June 2014)

### Market Capitalization

A\$50.38M (approximate as of 23 July 2014)

### Cash Position

A\$23.20M (approximate as of 30 June 2014)

## Board of Directors

<b>Ms Lucy Turnbull, AO</b>	Non-executive Chairman
<b>Mr Albert Wong</b>	Non-executive Deputy Chairman
<b>Mr Marc Voigt</b>	Chief Executive Officer and Executive Director
<b>Dr Russell J Howard</b>	Non-executive Director
<b>Mr Pete A Meyers</b>	Non-executive Director

## Senior Management

<b>Dr Sharron Gargosky</b>	Chief Technical Officer
<b>Ms Deanne Miller</b>	General Counsel and Company Secretary

**[www.primabiomed.com.au](http://www.primabiomed.com.au)**