

# INVESTOR UPDATE



EDITION **6**  
FEBRUARY 2012



## Message from the CEO

*Welcome to the first issue of the Prima BioMed Investor Update for 2012.*

*The New Year has begun in a very positive fashion for Prima BioMed and it shapes as a watershed year for the Company, as we commence our major late-stage trial for the CVac™ immunotherapy ovarian cancer vaccine.*

*Those of you who follow our public releases would be aware that we completed two major milestones in the early part of the year.*

*In February the Company commenced patient enrolment in to the CVac™ CANVAS (**C**ANcer **V**accine **S**tudy), with the first patient being enrolled in to the trial. We now expect patient enrollment to ramp-up throughout the balance of the year. Details of CANVAS are provided in this Investor Update.*

*It also gives me great pleasure to bring you the news that the Company has been cleared for its NASDAQ listing in the United States.*

*The listing has been a long time coming, but we are delighted to have filed a registration statement for the listing and now look forward to being admitted to the NASDAQ. I would like to thank all our shareholders for their patience and understanding throughout this process, and I would also like to thank all those involved for their tireless work to make the listing a success.*

*Also, in this issue of your Investor Update, we have a Q & A session with Dr Dominic Wall, Chief Scientific Officer for Cell Therapies Pty Ltd in Melbourne, on the importance of the CVac™ manufacturing process and potency assay, and there is also an update on the progress of the Company's other clinical programs.*

*Welcome to the New Year and I look forward to sharing the positive progress of your Company with you throughout the year.*

**Martin Rogers**  
Chief Executive Officer

## Prima BioMed cleared for NASDAQ listing

The Company is delighted to report that it has filed a registration statement with the US Securities and Exchange Commission to enable a listing on the NASDAQ Global Market (NASDAQ) of American Depositary Receipts (ADR).

Over the past two years, the Company has continued to attract an increasing level of support and interest from the US market. This had been generated, in part, by the success of NASDAQ-listed company Dendreon, which has successfully completed the commercialisation of its Provenge vaccine product, for the treatment of prostate cancer.

Prima BioMed uses similar technology in its CVac™ ovarian cancer vaccine, and this has contributed to the interest from US investors in Prima's plans.

Prima announced plans to list on the NASDAQ Global Market in September 2010. After what proved to be a drawn out lead time, it is delighted to have now filed a registration statement for its listing, and it looks forward to being admitted to trade on the NASDAQ, under the ticker **PBMD**.

Prima's listing on the NASDAQ will be a Level II ADR compliance listing, and as a result the Company will have dual listings of its securities on both the Australian Securities Exchange (ASX) and NASDAQ. There will be one NASDAQ share for every 30 Prima ASX-listed shares.

NASDAQ is the largest electronic screen-based equity securities trading market in the US, and the aim of the NASDAQ listing is to provide a structure that better meets the needs of both Prima's Australian and US investors, and to provide increased liquidity for Prima's shares.

The listing process is being managed by Bank of New York Mellon and US broking houses and US brokering houses Deutsche Bank AG, Noble Financial and Aegis.

The NASDAQ listing will come at a significant point in the Company's development timeline for Cvac™, and the timing should offer US investors an outstanding opportunity to share in this growth phase of the Company.

## In this Issue

- Company cleared for NASDAQ listing
- Patient enrolment for CANVAS commences
- Q&A on the importance of manufacturing and potency assay for CVac™
- Update on other clinical programs
- Staff profile – Matt Lehman, Chief Operations Officer ... and more

## Patient enrolment for CANVAS underway

The Company has been busy at work in its preparations for its major late-stage clinical trial for CVac™ for some time, and is excited to report the news that patient enrolment for the CANVAS (CANcer VAccine Study) trial has now commenced.

In February Prima advised that the first patient has been enrolled into the trial. The patient was recruited in the United States.

With the first patient now enrolled in to the trial, the Company expects to ramp-up enrolment through sites in Europe, Australasia and the US through 2012.

The commencement of patient enrolment for Prima's major CVac™ trial represents a significant milestone in its development timeline. The ability to embark on such a large scale study across multiple sites, in different continents, is a testament to the commitment and expertise of the Prima team, and also for the potential for CVac™ to provide a viable, commercially available treatment option for ovarian cancer patients globally.

### About CANVAS

CANVAS is a multinational, multi-centre, randomised, double-blinded, placebo-controlled trial of CVac™ as a maintenance treatment for epithelial ovarian, primary peritoneal, or fallopian tube cancer in complete remission.

The Study will enroll 800 women to assess those who are in complete remission after completing first-line treatment (surgery and chemotherapy) for ovarian cancer.

#### The goals of CANVAS are to;

- definitively establish that CVac™ is able to extend the time in remission after surgery and chemotherapy
- extend overall life expectancy
- improve quality of life for patients
- assess pharmacoeconomic parameters

Based on expected recruitment rates, full patient enrolment should be complete by around Q3-Q4 2013. CANVAS is an event driven study and actual study timelines will be dependent on patient outcomes in the trial (i.e. how long patients stay in remission and stay alive). As such, any timelines provided are indicative only and are provided only as a guideline.

**Contact details for interested parties and updated details of trial centres for all countries, as they open, will be available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov)**

## CVac™ - A 'Focused Cancer Killer'

In this issue of your Investor Update we have again included the double-page centre-piece, which provides an excellent graphical representation of how the CVac™ ovarian cancer vaccine actually works.

It is titled 'Focused Cancer Killer'. It shows a roadmap of the vaccine in action;

- from the body's own key cells being engaged,
- to the cells being selectively harvested from the patient's blood to make the vaccine, and finally
- to the vaccine being administered to the patient and the activated cells targeting the tumour cells

It also provides answers to a number of frequently asked questions on CVac™, and provides some key statistics on ovarian cancer, which help highlight the need for new, alternative treatment options.



*Dr Dominic Wall  
PhD FFSc*

## Q&A with Dr Dominic Wall on the importance of the manufacturing process and Potency Assay

*Dr Dominic Wall PhD FFSc (RCPA) is the Chief Scientific Officer for Cell Therapies Pty Ltd in Melbourne. They are a contract manufacturer of cell and tissue therapies, and are engaged by Prima BioMed to provide technical and production support to the Company in its development of CVac™ ovarian cancer vaccine.*

*As an important player in Australian medical innovation here he provides an insight into the importance of manufacturing and potency assay in Prima's development of CVac™.*

### Can you give some background on the manufacturing process and potency assay for CVac™?

There are two key aspects in a marketing approval for a new drug candidate; success in the clinical trials process, and a successful manufacturing process. As part of the manufacturing process, you need to be able to determine that the cell therapy treatment, in Prima's case CVac™, delivers the desired effect to the patient. This is referred to as a potency assay.

### What is the objective of a potency assay?

A potency assay needs to be developed, tested and validated. When that process has been successfully completed, the aim is to have a potency candidate that works to ensure that doses of a drug given to patients are immunologically potent – that is, that it has the desired effect.

### How important is a potency assay in the overall approvals process?

It is a critical component. A company won't get a marketing approval for a new drug with the FDA (Food and Drug Administration), EMA (European Medicines Agency) or TGA (Therapeutic Goods Administration) without a potency assay that has been developed, tested and validated.

### Is it difficult to achieve a successful potency assay?

The potency assay is the toughest challenge for a new drug candidate. It is different from safety and purity requirements, which are easier to satisfy. When you are dealing with cell and tissue therapies, as you are with CVac™, as distinct from a conventional drug product it is even more challenging. You are dealing with the area of immunology, with millions of proteins and the variability in cells, where as with a standard drug product you are dealing with a single molecule, so it is easier to find a method to determine if the drug has the desired effect.

### What are the main challenges in developing a potency assay?

The main challenge is that it needs to be robust to deal with patient variations, which are many and varied, and also be suitable for use in different manufacturing centres across the globe. It needs to be validated and controlled to fit in with the different set-ups of commercial manufacturers. Also, because you are dealing with cells and tissues each potency assay will be different. They are not off-the-shelf products.

### How far progressed is Prima with its potency assay for CVac™?

Prima is well advanced in its potency assay process. It has a potency assay project underway based on a complex immunological assay and an approved product development pathway. It is in clinical work to develop its potency assay which will be assessed as part of its late-stage clinical trials. Prima is confident it will have an approved potency method that will underpin its future marketing authorisations for CVac™.

## STATISTICS

Ovarian cancer represents the **6<sup>th</sup>** most commonly diagnosed cancer among women worldwide.

It causes **more deaths** per year than any other cancer of the female reproductive system

It is the **5<sup>th</sup>** leading cause of cancer death among women globally

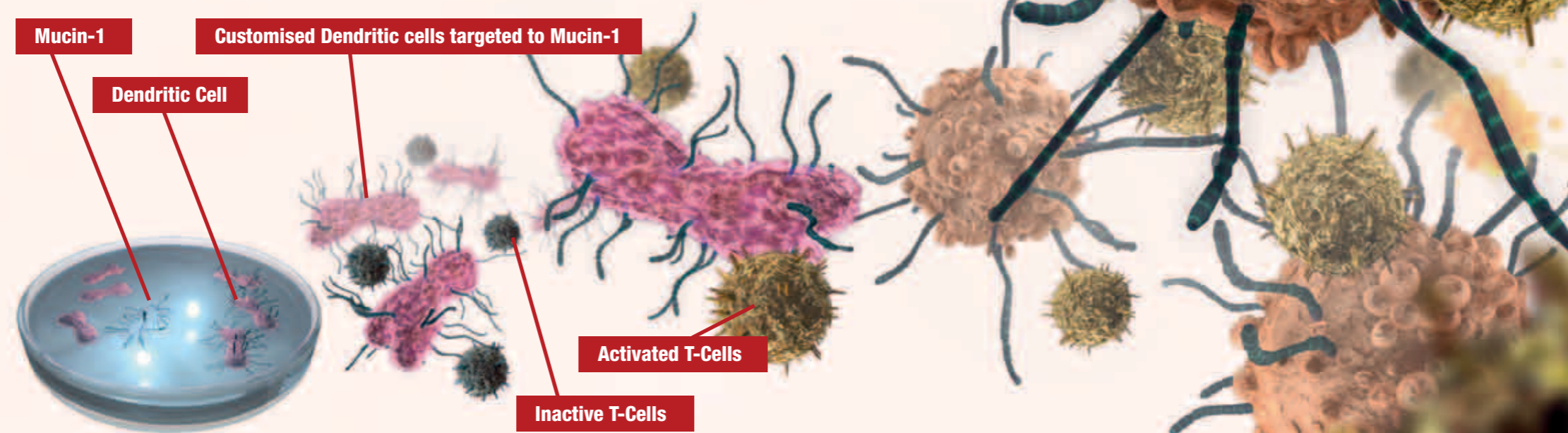
Only **3** out of **10** women with ovarian cancer live more than five years

# FOCUSED CANCER KILLER

Ever since the days of William Coley in New York, who pioneered in the year 1893 the use bacterial injections in an attempt to stimulate the immune system to fight cancer, physicians have attempted to harness the awesome power of the human immune system to fight tumours. Dr. Coley's patient lived for an additional twenty six years, and his tumour vanished. Such a success should have led to more and more sophisticated cancer immune therapies, but physicians chose the route of toxic chemotherapy, and harmful radiation to destroy rampaging tumours. Killing fast dividing cells by damaging their DNA seemed swifter than waiting for the body to mount a massive immune system attack

on the tumour. In April of 2010, Dendreon Corporation became the first company in history to get Food and Drug Administration approval in the United States for Provenge, a product consisting of patients own cells, primed to target PAP a protein found in high quantities in prostate tumour cells. Giving patients their own cells to boost the immune system proved an effective therapy, and patients lived on average 4.1 months longer than those given a sham treatment. Many new therapies are in development to target tumours, and an Australian company Prima Biomed Ltd is in the lead to develop a therapy for ovarian cancer that uses the patient's own cells to tackle their tumours.

## Fighting Cancer with a Vaccine Illustration by brandlovers.de



### THE KEY CELLS

The immune system is primed to find "foreign" proteins and to send killer cells to destroy them. The cells that find the foreign protein are antigen presenting cells, and dendritic cells are a key antigen presenting cell. The antigen presenting cell then picks up some of the bad protein, and shows it to T cells. The T cells then know what protein to find, and they kill any cell carrying that protein.

### VACCINE THERAPY

Therapy involves selectively harvesting cells from the patient's blood that can be matured into dendritic cells. These dendritic cells are then customised to the foreign protein or cancer antigen called mucin-1. The mucin-1 targeted dendritic cells are the treatment or in the case of PrimaBioMed, CVac™.

### TARGETING THE TUMOUR

When the cells are injected back into the patient's skin, they find T cells and show them the antigen. Activated T cells then hunt down tumour cells displaying Mucin-1 and destroy them.

## FREQUENTLY ASKED QUESTIONS

### HOW IS CVAC™ DIFFERENT FROM OTHER IMMUNE THERAPIES FOR CANCER?

In the case of Provenge®, the vaccine targets prostate cancer only. The cells are injected into a vein, whereas CVac™ is injected under the skin where it finds T cells in large numbers. Other immune therapies may take a sample of the patient's tumour, killing it and returning it to the patient in the hopes that the body will start treating the tumour as an invader, and attack it. Yet other therapies simply boost the whole immune system, running the risk that other tissues will be damaged by attack by T cells.

### WHAT OTHER TUMOURS ARE BEING TARGETED BY VACCINE THERAPY?

There are many immune therapies in development for cancers, and many have shown promise during early development. Another company, Merck KgA, is developing a vaccine against Mucin-1, but in their case, they target lung and breast cancer. The vaccine is called Stimuvax™ and in early studies, patients lived 17 months longer on average than patients receiving a placebo.

### WHY DOES THE BODY NOT RECOGNIZE TUMOUR CELLS AS ABNORMAL BEFORE IT GETS THE VACCINE?

Tumour cells have escaped the normal patrolling T cells and hide in the background. It is only when the vaccine is given, and many new T cells are recruited to hunt down the tumour, then it can no longer remain undetected with such a focused attack.

### DO VACCINES WORK TO PREVENT CANCER?

They may do in the future. However, each vaccine tends to be targeted at one tumour type, and we would all have to receive thousands of vaccines to try to prevent any type of tumour from developing.

## Update on other clinical programs

In addition to its core focus on the CVac™ ovarian cancer vaccine, Prima has continued to make progress with its other clinical programs, which are in line with the Company's goal to develop commercial cancer treatment technologies and programs for global markets. Below is an overview on recent developments in the following programs;

### Research Program on Oral Delivery System for cervical cancer vaccines

In November 2009, the Company reported that it had engaged University of New South Wales (UNSW) and University of Queensland (UQ) to undertake a research program to develop an oral delivery system for vaccines for cervical cancer.

This research program has now progressed to the stage of testing various formulations of a nanoparticle oral vaccine delivery system in an animal (mouse) model. The work carried out to date has shown that a coated nanoparticle protein delivery system is feasible and can be administered safely in the mouse model.

In 2012, the UNSW and UQ laboratory teams will work to determine which oral formulation best delivers an immunogenic dose of protein to the lower gastrointestinal tract.

Also, Prima is pleased to report that this collaborative work will be supported, in part, by a competitive Australian Research Council (ARC) grant. The grant was determined on the merit of the research. The ARC grants are highly sought after and are highly regarded by the academic community.

The development of an oral delivery system for cervical cancer vaccines is potentially a major breakthrough in drug delivery for cervical cancer treatment as it would provide a suitable large scale alternative method of drug delivery to injection, which is currently the prime method of delivery.

### Cripto-1 immunotherapy cancer treatment program

Prima has also made progress on its pre-clinical testwork program on the Cripto-1 cancer monoclonal antibody (mAB) cancer treatment.

The Company entered into a licensing agreement for the development of a Cripto-1 mAB with leading Dutch antibody development company Bioceros in August 2010.

The development program for a Cripto-1 mAB has progressed well. Several hybrid mAB's have been synthesized from hybridoma cell lines. The lead mAB's that have been synthesized bind to Cripto-1 positive MCF-7 breast cancer cell lines.

In 2012 the focus of work by Bioceros will be the continued search for the most active humanized IgM or IgG mAB against the target.

Cripto-1 is a protein found in high levels on the surface of a number of different types of malignant tumor cells. It facilitates growth of the tumor cells, and contributes to their spreading throughout the body. The antibody works by binding to the Cripto-1 molecule interfering with local development of the tumor, and preventing distant seeding of tumor cells. The antibody may be administered in combination with cytotoxic drugs (chemotherapy drugs) to create an even more lethal potent additive effect on tumor cell destruction.

There is a large global market for mAB treatments. According to leading pharmaceutical industry research group, GBI Pharmaceutical Research, the global mAB market was worth US\$46.8 billion in sales, in 2010.

## Prima at the 2012 American Society of Clinical Oncology conference



Dr Jonathan Berek

Prima BioMed will again be well represented at the American Society of Clinical Oncology conference in Chicago, in June. The conference is a major annual event for those in the oncology field of medicine, and is attended by some of the world's leading oncologists.

At this year's conference, Dr Jonathan Berek from the Stanford Cancer Institute, Stanford University School of Medicine in California, will present a CANVAS study design, protocol and update on global recruitment, and Dr Jeffrey Goh from the Royal Brisbane Womens Hospital in Queensland, Australia, will make a presentation on the interim safety data from the CVac™ Phase IIb study.

Prima's Chief Medical Officer, Dr Neil Frazer, will again attend the conference. Dr Frazer made a presentation at last year's event on the progress of the clinical trials process for CVac™.

## Japanese patent awarded for Cripto-1 antibody

The Company also recently reported some further positive news on its Cripto-1 cancer antibody, with the granting of a Japanese patent for Cripto-1.

The details of the patent are as follows:  
*The grant of patent was provided by the Japanese Patent Office. The patent number is 4854912 and it is titled, Antibodies against Cancer. It expires in March 2022. The patent has also been granted in Australia, New Zealand, China, South Korea and the USA.*

The granted patent claims protect the use of an antibody directed to the cancer antigen, Cripto-1.

## Meet the Prima team – Matthew Lehman, Chief Operating Officer



Matthew Lehman

In this issue of your Investor Update we are pleased to present the first in a series of profiles of members of the Prima team. We start with Matt Lehman, the Company's Chief Operating Officer.

Matt joined Prima in the role of COO, in January 2010, and has proved himself to be an invaluable member of the Company's management team. He plays a key role in leading the Company's global research and development plans and clinical trials for CVac™ from his European base.

His role with Prima sees him based in Berlin, Germany where he moved to work for Prima with his wife, two sons and a daughter.

Matt has extensive experience in the areas of clinical research, development programs and obtaining drug approval, and has specific expertise in clinical development strategies, operations and in-outsourcing.

Prior to joining Prima he was chief operating officer for SPRI Clinical Trials in Europe. In this position, he managed an operations team of 110 staff and consultants in all areas of clinical operations. Over the past decade Matt has been involved in approximately 150 clinical programs in a variety of roles.

Matt has a Master of Science from Columbia University in New York, and a Bachelor of Arts, Political Science and History from the University of Louisville, Kentucky, USA. He is also a member of the European Business Association and Association for Clinical Research Professionals.

## Links to additional information on Prima and CVac™

The Prima BioMed company website is set up with a range of different information on the CVac™ ovarian cancer therapy vaccine. Below are links to two different items that may be of interest for anyone wanting to know more about how CVac™ works and the demand for ovarian cancer treatment options.

Webcast of a recent Experts Conference Call;  
<http://www.investorcalendar.com/IC/CEPage.asp?ID=163542>

A short video which provides an overview of how the CVac™ vaccine works in practice;  
[www.primabiomed.com.au/movies/movie\\_3.php](http://www.primabiomed.com.au/movies/movie_3.php)





## OVARIAN CANCER AWARENESS MONTH

**February is Ovarian Cancer Australia's  
Ovarian Cancer Awareness Month**

Prima BioMed is a proud supporter of Ovarian Cancer Australia and their work in the area of ovarian cancer awareness, support and research.



OvarianCancerAustralia



**For further information please contact:**

**Mr Martin Rogers**  
Chief Executive Officer  
Prima BioMed

**Ph:** +61 (0) 2 9276 1242  
**E:** martin.rogers@primabiomed.com.au  
**W:** www.primabiomed.com.au

## Forward looking statement

Any forward looking statements in this newsletter have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside Prima BioMed Ltd's control. Important factors that could cause actual results to differ materially from any assumptions or expectations expressed or implied in this newsletter include known and unknown risks. As actual results may differ materially to any assumptions made in this newsletter, you are urged to view any forward looking statements contained in this newsletter with caution. This newsletter should not be relied on as a recommendation or forecast by Prima BioMed Limited, and should not be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

## Prima BioMed – Fast Facts

### Listings

Australian Securities Exchange (ASX), NASDAQ

### Stock Codes

ASX: PRR, NASDAQ: PBMD

### Issued Capital - Ordinary shares

1.064B

### Market Capitalisation

A\$191.6M (@ 15/02/12)

### Cash Position

A\$47.47M (@ 31/12/12)

## Board

<b>Ms Lucy Turnbull</b>	Non-executive Chairman
<b>Mr Albert Wong</b>	Non-executive Deputy Chairman
<b>Mr Martin Rogers</b>	Managing Director and Chief Executive Officer
<b>Dr Neil Frazer</b>	Executive Director and Chief Medical Officer
<b>Dr Richard Hammel</b>	Non-executive Director

## Senior Management

<b>Ian Bangs</b>	Chief Financial Officer
<b>Matthew Lehman</b>	Chief Operating Officer
<b>Dr Sharron Gargosky</b>	Senior Vice President, CVac™ Program
<b>Marc Voigt</b>	Senior Vice President, Business Development
<b>Marta Schilling</b>	Head of CMC
<b>Vanessa Waddell</b>	Business Development and Intellectual Property Manager
<b>Larisa Chisholm</b>	Intellectual Property Manager
<b>Dr Hind Al Saadi</b>	General Manager, Middle East