



Lucy Turnbull, AO

## Message from the Chair

Dear Fellow Shareholders,

A lot has happened for Prima BioMed in the six months since our last newsletter. In December 2014 we completed the acquisition of Immutep, and since then our team has been hard at work getting ready for clinical studies with our new lead product, IMP321. In late February we an-

nounced that we are seeking a development partner for our CVac™ product. Finally, we announced in May a A\$15m capital raising with the US-based specialist healthcare investor, Ridgeback Capital Investments L.P. which will be put to shareholders at an Extraordinary General Meeting (EGM) to be held on 31 July 2015.

Ridgeback Capital Investments has built a reputation since its founding by Wayne Holman in 2006 as an astute investor in Life Science companies both in America and around the world. Ridgeback knows the immuno-oncology field very well, having invested in a number of other companies in our space. Having and maintaining Ridgeback as a strategic cornerstone investor for the full \$15 million significantly raises our profile among other sophisticated investors as well as industry participants, and we will benefit from their considerable knowledge base and commercial insights.

I want to take this opportunity to thank Wayne and his team for the investment into Prima and we look forward to working with Ridgeback to grow shareholder value in Prima.

The other gratifying aspect of the proposed capital raising is that our company would be funded through to late 2016, by which time we expect to have created considerable value with IMP321 and the other immuno-oncology products in the Immutep portfolio. Subject to the Ridgeback funding being approved, we expect clinical work by Prima on IMP321 to commence later this year. As recently announced, our development plan and the design of our AIPAC clinical registration trial has been endorsed by the European Medicines Agency (EMA).

In the meantime our licensee GlaxoSmithKline (GSK) recently initiated Phase I with their GSK2831781 product, which started life as Immutep's IMP731. Furthermore, we are hopeful that Novartis will soon commence clinical trials with their version of Immutep's IMP701. With these multiple compounds in clinical development we believe the Company's prospects have greatly

improved. Our expanded portfolio of therapies for oncology and autoimmune disease has potential to benefit the lives and wellbeing of our patients and their families, and also provide investment returns for our shareholders.

The market has responded well to the news that we are now funded for the next stage of our growth, subject to shareholder approval of Ridgeback's investment.

In parallel with the Ridgeback investment we are offering existing shareholders the opportunity to participate in a Share Purchase Plan (SPP), allowing shareholders to further benefit from future value growth as we develop our exciting LAG-3 programs that have attracted a growing level of investor and industry interest.

I would like to thank our CEO Marc Voigt who has put in an extraordinary effort across multiple time zones and many months to navigate the company through, firstly acquiring Immutep with its portfolio of very promising therapies, and secondly and just as importantly, in securing the investment by Ridgeback Capital. Marc has shown true leadership, vision and great negotiating skills.

I would also like to thank our General Counsel and Company Secretary, Deanne Miller, who has similarly worked around the clock for many months in advising and supporting Marc and assisting greatly in many negotiations.

As mentioned, the investment by Ridgeback will need to be approved at an EGM of shareholders to be held in Sydney on 31 July 2015. I encourage you to read the Notice of Meeting before casting your vote. If you are in Sydney at the time of the meeting, please consider attending. I very much look forward to seeing you there and presenting an update of what we are doing.

Yours sincerely,  
Lucy Turnbull

### >> In this Issue:

- **Message from the Chair**
- **Message from the CEO**
- **Q&A with Stuart Roberts**
- **A message from Professor Triebel**
- **Prima in the news**



*Marc Voigt, CEO*

## Message from the CEO

### Dear Fellow Shareholders,

As Lucy has noted, we have seen many changes in the last few months.

The acquisition of Immutep was finalised in December 2014 for a total

value of approximately US\$25 million. This was approximately \$3 million less than the originally announced consideration due to the subsequent reduction in the value of warrants based on the Black Scholes calculation, reflecting a good outcome for shareholders. I believe however, that the intrinsic value of the acquired assets is significantly higher and that the level of attention we have received since the acquisition foreshadows further potential upside.

As part of the consideration for the acquisition, in January 2015 a multi-million dollar milestone payment from GSK triggered a payment of approximately the same amount to the former owners of Immutep, so it was partly a “self-funding” transaction. All potential future GSK milestone payments, which are substantial, as well as all potential future royalties, will be retained by Prima.

### The future of CVac

I would like to focus on our strategic decision regarding CVac, which might have caused some concerns for shareholders. This product, you recall, is a cancer vaccine in which we take a cancer antigen called MUC1 and conjugate it to a sugar called mannan. Our thesis with CVac was that this combination, when exposed outside the body to a patient’s dendritic cells – the “orchestrators” of the immune system - would generate a tumour-destroying immune response in ovarian cancer patients.

This is indeed what seems to have happened in ovarian cancer patients we treated, where those patients were in their second remission after chemotherapy. Specifically, in our CAN-003 study, where we had a total of 20 ovarian cancer patients in second remission, the median overall survival (OS) for the standard of care group was 25 months, consistent with other studies. For our treatment group – those that were treated with CVac – we still had not hit the median OS when we stopped measuring at 42 months. That means at least a 16 months survival advantage for CVac, and an encouraging trend ( $p=0.07$ ).

As mentioned at our AGM in November, we undertook a strategic review of the entire Prima portfolio. After careful

consideration, we made the decision to consolidate the clinical development of the CVac program. We believe it is a financially responsible decision given a number of factors.

The CVac program had undergone a number of significant changes over the past few years as we collected data from the CAN-003 trial. Our early data from this trial indicated that CVac had a much more positive result in second remission patients rather than with first remission ovarian cancer patients. This finding prompted a very significant refocusing and redesign of the trials but subsequently also experienced much greater complexity with recruitment and clinical approval than anticipated.

In addition, in December last year the manufacturing grants in Germany from the Saxony Development Bank ceased.

Our long term shareholders will remember that it took from 2010 to about mid-2015 to reach a final data point for CAN-003 with 63 patients. The same considerations would have applied to the CAN-004 clinical trial had it proceeded as planned – the time, complexity and cost constraints for a small company like Prima weighed heavily on us as we considered the best path forward for the Company and our shareholders

While the nature of the data generated so far warrants further investigations with this therapy, Prima’s strategic review led to the conclusion that a company with Prima’s limited resources, both financial and human, was not in a position to simultaneously run clinical trials for both the CVac and IMP321 therapies in a reasonable time frame. We believe that it is in the best interests of the Company and its shareholders to aim for a partnering transaction based on the final CAN-003 OS data.

### Developing IMP321

IMP321 reflects a unique biological mechanistic concept; it addresses large potential patient populations; it has so far demonstrated a very good safety and activity profile; is generating significant interest from many parties; and has comparably low production costs. For these multiple reasons we believe it is commercially responsible to concentrate on this clinical opportunity.

Our focus will now be on initiating two new clinical trials of IMP321. The first is a Phase IIb chemo-immunotherapy trial for metastatic breast cancer in conjunction with paclitaxel called

AIPAC (Active Immunotherapy PAClitaxel). After a smaller safety run-in phase that will extend into 2016 and will yield valuable safety, pharmacokinetic and pharmacodynamic data, AIPAC will proceed to recruit around 200 patients with HER-2 negative metastatic breast cancer, randomising them 1:1 with double-blinding (i.e. neither the patient nor the investigator knows about the nature of the injected product) to either standard-of-care paclitaxel plus placebo or paclitaxel plus IMP321. The second new clinical trial of IMP321 is a Phase I trial together with an immune checkpoint inhibitor.

These two clinical trials will underpin our position as a central player in the rapidly emerging field of immuno-oncology, where we believe the greatest commercial opportunity currently resides. In addition we have been able to generate new and exciting intellectual property in our research lab outside of Paris. The year ahead for Prima is undoubtedly going to be a busy one. The acquisition of Immutep has provided us with a strong pipeline of multiple products, an asset base that is essential for an emerging biotechnology company.

The planning for IMP321 clinical trials has begun in earnest, with manufacture of IMP321 already completed. The European Medicines Association (EMA), the agency responsible for evaluating medicines use in the European Union, has endorsed the development program of IMP321 in metastatic breast cancer. We expect to start the clinical development of IMP321 in the fourth quarter of this calendar year and are very excited about the potential of this interesting cancer immunotherapy program. In addition, Prima BioMed now has an active research and clinical discovery laboratory headed by our Chief Scientific Officer, Frédéric Triebel, that we believe will generate exciting new LAG-3 based products over the longer term.

In the past few months – which have been challenging for our shareholders - we have been working hard to create a new Prima BioMed with multiple product candidates, new research capabilities, new intellectual property, strong and significant pharma partners and very capable new colleagues like our CSO & CMO Prof. Dr Frédéric Triebel and Global Head of Investor Relations, Stuart Roberts. Enhancement of these attributes has led to increased interest from various third parties. I am very proud that Prima has been able to secure a funding agreement with Ridgeback Capital, one of the best fundamental biotech investors in the United States.

Significant investment interest is, in itself, a great achievement and means much more than just securing capital to fund our product development pipeline. I believe that this has increased our acceptance, especially in the United States - where we saw an all-time high in our share price and trading volumes since listing in the US in 2012. It also means our NASDAQ listing is of growing importance and we believe, is a positive sign of things to come.

In order to further concentrate volume and liquidity in the appropriate markets via the ASX and NASDAQ, we will delist from the Deutsche Börse.

Even though we have had our share of challenges, beyond those which are a normal part of being a small biotech company, I firmly believe that the future of Prima is very promising and I look forward to reporting on our further progress.

**Yours sincerely,  
Marc Voigt**



Stuart Roberts

## Q&A with Stuart Roberts

Stuart Roberts joined Prima in January as our Global Head of Investor Relations. He was formerly a well-respected and recognised analyst in the healthcare and biotechnology sectors at Baillieu Holst and Bell Potter Securities in

Sydney. Prior to that, in 2002, he established the market-leading Life Sciences equity research franchise at Southern Cross Equities. Stuart has a Master's Degree in Finance from Finsia.

**Question: You are an equities analyst by background. What got you interested in biotechnology?**

Answer: In 2002 I was asked by my firm to do some work on an ASX-listed antibody drug developer called Peptech. I took a lot of time with that report and came away impressed with three things: 1) That biotech had huge potential to benefit patients with new treatments; 2) that those treatments could make biotech companies a lot of money; and 3) that biotechnology was not well understood by the market. Hence one could acquire undervalued assets in the sector.

**Question: Has investors' understanding of biotech improved since 2002?**

Answer: Markedly. I think that as the population has aged their interest in healthcare has increased. There's nothing like being sick – or having a friend or family member who is sick – to teach you about the biology of illness and potential treatment solutions. Also, I've seen a lot of companies that have been good at teaching people about their technology, and the people who analyse the sector are getting better at explaining it.

**Question: What attracted you to come and work full-time for Prima?**

Answer: I had spent 12 years between 2002 and 2014 doing equities research focused on healthcare and biotech, so I felt I had a good eye for value. When Marc Voigt came to see me just after the Immutep acquisition I decided this was too good an opportunity to resist. Here was a company working successfully in one of the hottest areas of drug development today - cancer immunotherapy - where the stock was traded on NASDAQ (an important market for biotech globally) as well as ASX and where Prima's share price was still suffering from the legacy of our September 2013 PFS numbers in CAN-003. I felt a serious re-rating was in order.

**Question: Why is LAG-3 important to Prima?**

Answer: All through 2014 I kept on hearing about "checkpoint inhibitors" and how effective they were in cancer treatment by taking the brakes off an anti-cancer immune response. But when people were talking about checkpoints they generally meant PD-1, the target of Merck's very valuable Keytruda and BMS's Opdivo drugs. I felt that the search would quickly move to other checkpoints, and LAG-3 was well placed here because it is structurally and functionally similar. I believe LAG-3 has a lot of clinical and economic potential.

**Question: Why has Prima decided to delist from the Deutsche Börse?**

Answer: We were finding that most of the liquidity in our stock was coming from ASX and NASDAQ with relatively little from the Deutsche Börse. Our stock in Germany can continue to be traded via German OTC markets, at no cost to Prima.

**Question: What's important for Prima going forward, as far as the technology and clinical work is concerned?**

Answer: Definitely the upcoming Phase IIb with IMP321 in metastatic breast cancer. We showed in Phase IIa, which was an open label study that we could double the response rate (the percentage of patients whose tumours shrank by >30%) to the chemotherapy drug paclitaxel from 25% to 50% at the six month mark. With Phase IIb, which we expect will initiate in the second half of this calendar year in Europe, we'll be randomising patients to either paclitaxel or paclitaxel plus IMP321 and tracking for survival as well as responses. At the same time we want to see if our drug works synergistically with one of the newer immuno-oncology therapies, and before the year is out we'll start a Phase I proof of concept. This latter study is important because the ease with which drugs can be safely combined for greater effectiveness is important in oncology and particularly in immuno-oncology.

## Prima in the news

With our capital raising now announced, Prima will be working hard to market the story to investors and raising awareness of its position in the industry. A montage of some of the more recent media coverage is included here. This is in

addition to the extensive efforts of CEO, Marc Voigt and the team in marketing the business directly to potential investors and industry partners.



## Prima awarded Health Care Deal of the Year (Europe) 2014

Finance magazine Acquisition International's M&A Awards has awarded Prima the "Deal of the Year (Europe)" for the recent acquisition of Immutep. The magazine recognises excellence in all areas of M&A.

An article outlining the award was published in the January 2015 edition of the magazine, which is read by venture capitalists, financiers and investors.

The article can be viewed at [http://issuu.com/aiglobalmedia/docs/ai\\_january\\_2015\\_\\_issuu\\_/30?e=15629828/11549630](http://issuu.com/aiglobalmedia/docs/ai_january_2015__issuu_/30?e=15629828/11549630)



Frédéric Triebel, PhD

## A message from Professor Triebel

### Bonjour from Paris,

I have now been with Prima BioMed full-time for five months and it has been a privilege to work with Marc Voigt and his capable team of professionals as far afield Australia, the US and Germany. It gives me a lot of pleasure to see our LAG-3 science now positioned to move forward

quickly under the aegis of Prima, having been involved with this important checkpoint since its discovery in 1990, and watched it emerge into the limelight as the Immuno-Oncology Revolution got started around 2010.

Over the course of my scientific career I have collaborated with a number of biotech companies, and I firmly believe that LAG-3 will prove a 'company maker' in terms of our science for Prima. We have our core collaborations with GlaxoSmithKline and Novartis that should continue to generate revenues for Prima. We also have other collaborations that could potentially take on a life of their own. Consider for example that IMP321 is partnered with Eddingpharm in China and Taiwan. Prima and Eddingpharm have joined forces to have several clinical-grade IMP321 batches be manufactured by WuXi Apptech in Shanghai according to EU, US and Chinese pharmacopeias, which is now complete.

Eddingpharm will be armed to start clinical studies in China as local regulations require innovative products to be tested on Chinese patients in order to be manufactured in China. Considering the present size of the health care sector in China and its annual growth rate close to 15%, as well as China-specific regulations favouring local companies, it was important to secure such a deal early on to secure access to this market, which means for the time being milestone payments to Prima as well as substantial future royalties. Also, Prima is now working with a major Japanese company. Specifically, we announced on 11 May our collaboration with NEC Corporation and Yamaguchi University on a combination of IMP321 with a peptide vaccine. The work is being done at Yamaguchi University, in southern Japan, and NEC is funding it. The Yamaguchi team are looking to see whether our product will adjuvant (that is, 'boost') their vaccine in hepatocellular cancer, which is the primary liver cancer so common in Asia. We have generated data in the past showing that our product is a potentially powerful vaccine adjuvant, and for us the Yamaguchi collaboration suggests the potential to broaden the application of IMP321. I believe there will be many more such collaborations going forward.

### Understanding LAG-3

I want to focus now on what LAG-3 and IMP31 actually are, to help you understand why Prima paid approx. US\$25m to acquire Immutep, the company I co-founded in 2001.

LAG-3 is one of a growing number of molecules referred to as an "immune checkpoint" that are gaining popularity in the immuno-oncology field. To explain how they work, I often use the analogy of an intersection with traffic lights that control whether the body's natural immune response can proceed or not. The cells of a person's immune system need to proceed through a series of intersections to arrive at the location of the cancer cells they are targeting. If the immune cells are faced with a red light at any intersection, the immune system receives an inhibitory signal that stops it from proceeding. If the immune system receives a green light, the immune cells are allowed to proceed.

Tumour cells and viruses have evolved ways to control these signals and override the normal function of the immune system. In some cases, such as with autoimmune disease, we are born with defects that mean our signals don't work properly.

While we have learned a great deal over the last two decades, I think it is fair to say that scientists like myself and colleagues are just beginning to understand these new molecules and the way they interact with one another. The ability to influence the control of these signals will be a very powerful way of fighting cancer and autoimmune disease. It's a new field of science and LAG-3 is gaining a reputation as being a key player in future therapies.

Imagine you are trying to navigate a series of intersections to get to your final destination; you might receive a red light at one intersection so you are diverted to take another route to try and get to your destination. Many intersections must be navigated and there are lots of immune checkpoints that can be involved in how easily you can get there. Some checkpoints may be a complete dead-end while others may send you along the wrong route. Getting the right checkpoints along the way will allow you to get to your destination and overcome any negative signals from the cancer cell or silence the wrong signals that happen in autoimmunity.

IMP321 is what we call an immune activator. It gives the immune system the green light to proceed with its beneficial activity to present cancer antigens to T cells so that they can start killing any cancer cells that have that antigen. Prima intends to use IMP321 as an "adjuvant to chemotherapy".

This means when used in addition to chemotherapy, the response generated to the cancer is greater than it would have been if chemotherapy was given on its own – it's a turbo boost.

When a patient is treated with chemotherapy first, there are lots of dying cancer cells that are being processed by our immune system. If we treat these patients with IMP321 the day after chemotherapy, the antigens from these dying cells can be better recognised and the turbo boost provided to the T cells allows them to proceed with their job of killing the cancer cells. Results to date in metastatic breast cancer have shown that IMP321 was able to increase the response rate at six months in these patients from the 25% expected of paclitaxel to 50% for IMP321 plus paclitaxel.

Prima will commence further trials using IMP321 with other immune checkpoint molecules in combination therapy in an attempt to fine tune more of the signals required to treat cancer. "Combo treatment" as this is now called, combining two immunotherapies with complementary mechanisms of action on immune cells, especially when these are synergistic, is now a key term in the immuno-oncology field. The goal is to raise the bar from 30% (i.e. the result obtained in metastatic melanoma or lung cancer patients treated with anti-PD-1 antibodies) to 50% and more in long-term remissions for the majority of advanced cancer patients (i.e. the ones with incurable disease).

Other LAG-3 products are being developed by our partners GSK and Novartis. The role these products play in generating red or green signals at their respective intersections are different to each other and different to IMP321.

The concept behind IMP731 (GSK) is that it depletes (that is, 'kills') the very few T cells that are attacking normal tissues and are involved in autoimmunity. This is potentially a game changer in the field as current treatments are addressing the symptoms (e.g. inflammation) and not the cause of the disease. Indeed, a single injection of a depleting LAG-3 antibody was shown to induce a long term remission in a monkey model of psoriasis. In autoimmunity, the cells of the immune system are essentially stuck at an intersection because they are waiting for a green light signal that will allow them to proceed through the intersection; that signal never comes because of a defect, so the 'stuck' cells then begin to attack their environment. The antibody that Immutep created cannot change the signals, but it can kill the cells that are stuck at the intersection so that they stop causing damage. GSK licensed the rights to that antibody in

2010 and over these last 5 years have improved it to work more effectively in patients.

IMP701, which is partnered with Novartis, is a blocking antibody that works to stop the immune system from receiving a negative signal at an intersection. By blocking that negative (red light) signal, the T cells are allowed to do their job and go forwards in their journey to start attacking the cancer cells.

The immune checkpoint system is complex and we are learning more all the time. Immutep has a laboratory in Paris South University and my staff there are working to both understand how the pathway works and to identify other ways of controlling the signals given at these intersections/ checkpoints so that we can attempt to more manually control immune responses.

**Yours sincerely,  
Frédéric Triebel**



## Coming up for Prima in Calendar Year 2015

- Start of Phase IIb with IMP321 (AIPAC)
- Start of immuno-combination study with IMP321
- Start of Phase I for IMP701
- Continued expansion of intellectual property
- R&D for new products
- Ongoing: Business development

## 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

### Stock Codes

ASX: PRR, NASDAQ: PBMD

### Issued Capital – Ordinary shares

1.75B (approximate as of 30 June 2015)

### Issued ADR's

17.71M (approximate as of 30 June 2015)

### Market Capitalization

A\$112.1M (approximate as of 3 July 2015)

## Board of Directors

**Ms Lucy Turnbull, AO** Non-executive Chairman

**Mr Albert Wong** Non-executive Deputy Chairman

**Mr Marc Voigt** Executive Director and Chief Executive Officer

**Dr Russell J Howard** Non-executive Director

**Mr Pete A Meyers** Non-executive Director

## Senior Management

**Dr Sharron Gargosky** Chief Technical Officer

**Ms Deanne Miller** General Counsel and Company Secretary

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