

INVESTOR UPDATE

by  PRIMA BIOMED

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16



Lucy Turnbull, AO

Message from the Chair

Dear Shareholders,

Welcome to our first newsletter for 2016 in what I envisage will be a year of continued success for our Company.

Over the past 12 months we and our partners have progressed from one LAG-3 product in clinical development to three products in four clinical trials: quite a remarkable achievement for a small biotech company. We have also received milestone payments from our partners GSK and Novartis as their products have entered Phase I trials.

In our last newsletter we profiled our recently launched AIPAC clinical trial in metastatic breast cancer. In this newsletter, we discuss our recently initiated TACTI-mel clinical trial, a Phase I trial in melanoma, in a bit more detail. The trial, to be conducted in multiple sites around Australia, will be the first human study combining IMP321 as an immune activator together with a PD-1 checkpoint inhibitor. This is another illustration of how Prima is leading the way in discovering new avenues for the treatment of cancer.

Our staff in the Paris laboratory have continued their research and development efforts and this has resulted in the filing of a number of new patents. In January, we were granted a patent in the US for our GSK licensed depleting antibody, the first ever patent to be granted for LAG-3 depleting antibodies anywhere in the world.

The excitement around immuno-oncology and immune checkpoints in particular has continued to grow in recent years. A market research report in 2013 by the Citi Equity Research Group valued the market potential for immunotherapies at \$35 billion per year over the next 10 years. Elsewhere in this newsletter we highlight some of the more recent market sentiment in immuno-oncology and for LAG-3 in particular.

Prima is well positioned to be a part of this immuno-oncology revolution and we look forward to announcing data from our clinical trials over the months and years ahead.

Yours sincerely,

Lucy Turnbull
Chairman Prima BioMed Ltd



Marc Voigt, CEO

Message from the CEO

Dear Shareholders,

2015 was indeed a transformational year for Prima. The receipt of regulatory approvals for our two new trials and the commencement of AIPAC are attracting interest from a variety of audiences and we look forward to conducting our new melanoma trial in Australia. Australia has a reputation for conducting excellent Phase I trials. Australia is also known as the sunburnt country and as a consequence, it suffers from a very high incidence of melanoma. It is therefore gratifying to be able to offer Australian melanoma sufferers the opportunity to participate. Details on this exciting new trial are featured later in this newsletter.

Our partners' clinical trials appear to be progressing well and it is exciting to think that GSK may begin their Phase II trial with GSK2831781 (derived from IMP731) in 2016. We are very pleased that GSK presented this first-in-class antibody in November 2015 at their R&D Investor Day in New York.

► <http://www.gsk.com/media/851136/r-and-d-event-full-presentation.pdf>

As previously mentioned, Novartis started a Phase I clinical trial in August 2015 with LAG525 (derived from IMP701) with 240 patients in several different indications in oncology. Our Japanese collaboration with Yamaguchi University and NEC Corporation is also progressing well. The signing of a material transfer agreement (MTA) was concluded at the end of 2015, under which we will provide clinical grade IMP321 to Yamaguchi University for a fee. They will test IMP321 as an antigen presenting cell activator in a cancer vaccine trial together with their proprietary cancer peptides in an investigator led clinical research study.

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As we outlined at our AGM in November, we have been in active discussions regarding CVac™; however, given their confidential nature, we are not in a position to comment further at this stage. We will make further announcements to the market as and when appropriate.

Financial Update

We finished 2015 in a solid position with approximately \$25.5m cash in the bank. During October we executed two smaller share placements to sophisticated investors raising approximately \$3.55m. Given the overall market conditions, especially in January, we believe that this was a wise decision. R&D expenditure has been increasing as we initiate our new IMP321 trials, and we expect this to continue in 2016. Taking this into account, Prima is funded till approximately mid calendar year 2017.

I have been very encouraged by the initiation of research coverage by three independent investment banks: HC Wainwright in October, followed by FBR Capital and Roth Capital in December. All reports (including historical reports) are available on the Prima website in the investor tab under news and reports > analyst reports.

► www.primabiomed.com.au/investor

The stock markets became more difficult in the last weeks of 2015 and even more so at the beginning of 2016. The NASDAQ biotech index has seen 18 month lows. Not surprisingly our share price has been affected as well. However, I would like to emphasise that we do not see this as a Prima-specific issue or reflection of any disappointment regarding our development. Instead, I believe we are strategically and fundamentally better positioned than six months ago, for the following reasons:

- We have multiple ongoing clinical developments with several value inflection points during 2016;
- We have strong partners with continued development and progress in clinical phases; and
- We have a solid cash position with no need for any short term action.

I am proud of the efforts of our team over the past 12 months as we have repositioned ourselves in the immune checkpoint space and I look forward to a year of further data-driven progress.

Marc Voigt
CEO Prima BioMed Ltd

Clinical Update

It was an exciting year for both Prima and our partners in terms of the clinical development of our LAG-3 products in 2015 and this will continue into 2016. In January 2015 we announced receipt of a milestone payment from partner GSK after the dosing of their first patient with GSK2831781, a depleting antibody currently in development for the treatment of autoimmune disease. By all accounts this trial is progressing well. At a recent investor presentation GSK announced their intention to progress these trials into Phase II studies in 2016, an exciting validation of the promise of this treatment modality. In August 2015, we announced Novartis had treated their first patient with LAG-525, an antibody for the treatment of cancer. We hope this trial will also progress to Phase II trials.

We have previously outlined the success of IMP321, our first-in-class Antigen Presenting Cell Activator (“APC Activator”), in combination with chemotherapy in treating metastatic breast cancer (mBC) in a Phase I/IIa clinical trial in 30 patients. A larger 211 patient randomised, double-blind, placebo controlled Phase IIb trial has now commenced in Europe with Belgium and the Netherlands having been initiated. The AIPAC (Active Immunotherapy plus PAClitaxel) trial will take approximately three years to complete.

Our Phase I trial called TACTI-mel (Two ACTIVE Immunotherapies in melanoma) was initiated in January 2016. Australia has the highest incidence of melanoma in the world. This trial will combine IMP321 as an immune activator, together with a PD-1 checkpoint inhibitor (in this case KEYTRUDA®). Other combination trials currently in progress are predominantly focusing on the combination of two inhibitors. Prima is at the forefront of a potential new clinical frontier in combining checkpoint therapies. Accordingly, we filed a patent in 2015 to support combination therapy using IMP321. It is hoped that combining an activator (“pushing the gas”) and an inhibitor (“releasing the breaks”) will lead to synergistic treatment in a safe manner and especially improve the outcome for the subpopulation of patients who are otherwise suboptimal responders to a single immune checkpoint inhibitor treatment.

The trial has been designed as an open label study (patients and physicians will know they are receiving treatment) with the primary endpoint of measuring safety and tolerability of the two treatments together. Secondary endpoints will include efficacy measures such as progression free survival and objective response rates. The trial will be conducted in three patient cohorts (n=8) with escalating doses of IMP321 to measure pharmacokinetics of the combined treatment and to ensure safety. First interim results could be expected in the second half of calendar 2016.

We will continue to monitor the progress of all trials throughout the year and update our shareholders as news arises.

Increasing interest in LAG-3 from large pharma and institutional biotech investors

In recent newsletters we have explained a little about immune checkpoints and how they work, as well as about the role of LAG-3. Technologies aimed at controlling these checkpoints are a hot space in life sciences at the moment, underpinned by good data and product approvals. Prima feels confident that LAG-3 has already been scientifically validated as a target. Looking at the competitive landscape for LAG-3, there are a number of pharma companies working towards the clinical validation of LAG-3 for treatment of cancer.

Currently a blocking antibody to LAG-3 is being developed by Bristol Myers Squibb (BMS). The antibody is in a Phase I trial in conjunction with a PD-1 inhibitor. The basis of these trials is the removal of “2 brakes” on the activity of T cells to allow a patient’s immune system to respond to his cancer (in contrast to our TACTI-Mel study which tests an activator and inhibitor combination). BMS have recently increased the recruitment of patients in their trial from 160 to 540; however, no data has been published yet.

Novartis is developing a similar approach in a 240 patient Phase I study with their Immutep licensed LAG-3 antibody coupled with their own PD-1 inhibitor. The Phase I trials of this antibody commenced in August this year and we are hopeful that the data will be promising.

In addition to “big pharma” there are a number of other early stage antibody products in development.

However, Prima BioMed is the worldwide leading company regarding LAG-3 with three assets in clinical development, ongoing research and the leading expert in the field.

Prima BioMed’s LAG-3 intellectual property portfolio is protected by 14 patent families. The majority of these are exclusively owned or licensed by Immutep. Information relating to 11 of these patent families is publically available in patent databases; others are yet to be published. Families are referred to by numbers 1-14 with 1-5 having been licensed from Merck Serono and providing important background coverage of the LAG-3 technologies which support various sub-licences to partners. Family 6 has been exclusively licensed from the Institut Gustave Roussy and the University of Paris South. Two further families are jointly owned with partners and relate to our sub-licences. The remaining six families are wholly owned by Immutep. Collectively these patents provide Prima and its licencees with the ability to manufacture and administer their various LAG-3 products.

While LAG-3 will hopefully be further clinically validated in the coming years, institutional awareness and understanding is also growing. JP Morgan (JPM) is the world’s largest healthcare conference for the year, attracting large and small pharmaceutical companies and investors to meet and update one another on their progress. The meeting is held in January each year at the Westin St Francis in Union Square San Francisco (pictured). The tone of the meetings can often set the landscape for institutional investment in the sector for the coming year.

This year’s meeting was once again full of buzz about immuno-oncology. Several staff members from Prima attended meetings with pharmaceutical companies and large institutional investors. While these meetings are conducted confidentially, we were pleased about the overall increase in the number of meetings we had this year compared with previous years – around 50% more. This signifies to us that the market is becoming more aware of the Prima story and that LAG-3 is a molecule of interest to many.



Westin St Francis



Union Square

US Patent 9,244,059 Granted

In January 2016, a US patent for our GSK licensed depleting antibody was granted. This was exciting for both parties as it was the first patent to be granted for these depleting antibodies. To our knowledge, there are no other companies that have yet generated an antibody capable of killing off LAG-3 expressing activated T cells.

In autoimmune disease, our own immune system is unfortunately chronically stimulated to attack our own tissues. LAG-3 is one of the checkpoints that, in normal healthy people, will generate negative signals that turn T cells off. In the inflamed tissues of autoimmune diseased organs, the T cells that have accumulated over time will over express LAG-3 in an attempt to switch themselves off. The LAG-3 protein on these auto-reactive T cells therefore makes a good target for therapeutic intervention with a depleting antibody, which will selectively remove only the T cells causing damage and stop any further tissue destruction. This new approach aims at treating the cause of the disease by eliminating these few nasty auto-reactive T cells rather than treating the symptoms of the disease (e.g. inflammation). It may therefore be considered a potential game changer in the field of auto-immune diseases.

The patent is entitled "Cytotoxic anti-LAG-3 monoclonal antibody and its use in the treatment or prevention of organ transplant rejection and autoimmune disease". In

the case of organ transplantation, activated T cells are responsible for recognising foreign grafts and killing or rejecting an organ that is not our own. An inflammatory reaction similar to autoimmune disease develops. The antibody being developed to deplete activated T cells expressing LAG-3 may therefore also have potential in helping to prevent transplant rejection. Currently GSK is developing the antibody for the treatment of plaque psoriasis but other indications in auto-immune diseases may follow with additional clinical development.

The claims that have been specifically granted for this US patent will provide protection to the sequences of these antibodies and their use in autoimmune disease. This would prevent someone from producing the exact same antibodies without a licence from us. Other applications have also been filed to seek broader protection to LAG-3 depleting antibodies and for other therapeutic uses. We will continue to provide updates on our patent portfolio in future newsletters.

Do we have your correct email address?

We recently checked the email addresses registered against shareholders at our share registry, Boardroom Ltd, and found that over 8% of them were no longer valid. If Boardroom has a valid email address for you then you can receive all communication from Prima, including investor newsletters like this one, electronically. To add an email address to your account, or change the email registered there, please call Boardroom Ltd on **1300 737 760** within Australia or **+61 2 9260 9600** outside Australia.

Website updates

Our website has been updated to reflect the changes since our Immuteq acquisition. Please take a look at www.primabiomed.com.au

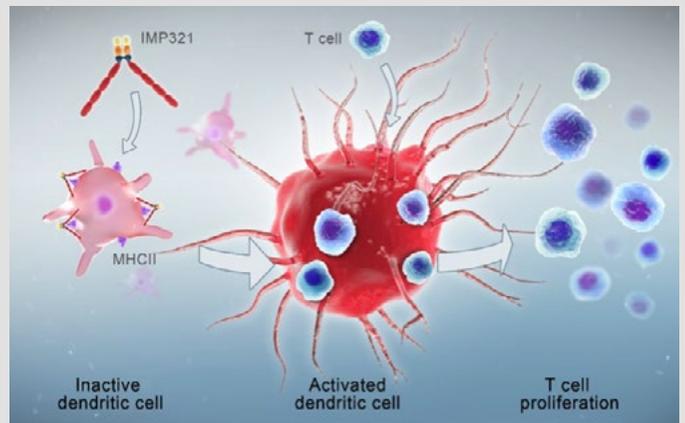
We have been developing some new images regarding our technology and we look forward to bringing you our new video soon. This figure has been created to help explain how IMP321 works to activate the immune system.

In the top left corner you can see IMP321 which has been conceptually injected into a patient. On the left hand side we see an inactive dendritic cell that would be present in the patients' skin at the site of injection. Dendritic cells are a form of antigen presenting cell (APC). APCs have some molecules on their surface called MHC class II. When IMP321 binds to MHC class II, the dendritic cell becomes activated and grows larger in size and grows long projections or arms. It is ready to start seeking foreign antigens in the body which might be bacteria, virus or cancer cell debris.

Once the APC has swallowed these antigens, it migrates to our lymph nodes where it will show or present these foreign antigens to the soldiers of our immune system, the T cells. The T cells will then proliferate/multiply and go out to find any other cells that have this antigen on their surface.

IMP321 therefore works to "push the gas" by causing the APCs to become activated and to have them switch on T cell responses.

In our AIPAC trial, the IMP321 is administered just after chemotherapy to prompt the APCs to pick up cancer antigens and present them to T cells. In our TACTI-mel trial the IMP321 is being used to activate the APCs while the PD-1 inhibitor is being used to remove the brake that has been put on the immune system. It's a two pronged approach that we expect to benefit those patients where removing the brake alone is not enough.



Did you catch our CEO Marc Voigt's interview on Sky Business while he was in Australia? If you missed it, you can still catch it [here](https://www.youtube.com/embed/MR44iP8DRdl).

► www.youtube.com/embed/MR44iP8DRdl

Coming up for Prima in Calendar Year 2016

- Ongoing Phase IIb trial with IMP321 (AIPAC)/Interim results
- Ongoing Phase I trial with IMP321 (TACTI-mel)/Interim results
- Ongoing Phase I trial for IMP701
- Start of Phase II trial for IMP731
- Continued expansion of intellectual property R&D for new products
- Ongoing: Business development

Company Calendar

March 13-16, 2016	28th Annual Roth Conference, Orange County, California
March 15-16, 2016	9th Annual European Life Science CEO Forum & Exhibition, Zurich, Switzerland
April 26-27, 2016	German Biotechnology Days, Leipzig, Germany
June 03-07, 2016	ASCO 2016, Chicago, Illinois

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**

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**

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.

Our ClinicalTrials.gov ID for our trials are as follows:

- TACTI-mel trial is NCT02676869
- AIPAC is NCT02614833

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► **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

2.06B (approximate as at 1st Feb 2016)

Issued ADR's

22M (approximate as of 1st Feb 2016)

Market Capitalization

91M (approximated as of 5th Feb 2016)

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

Ms Deanne Miller	General Counsel and Company Secretary
Prof Dr Frédéric Triebel	Chief Medical Officer and Chief Scientific Officer

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