

# INVESTOR UPDATE

by  PRIMA BIOMED

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# 18



Marc Voigt, CEO

## Message from the CEO

Dear Fellow Shareholders,

In our August operational update we outlined the trial designs and timelines for our two clinical programs, AIPAC and TACTI-mel, both of which are progressing on schedule. Data read out from the open-label, safety run-in cohorts of both trials is expected by the end of the current quarter.

We have recently filed a protocol amendment for the TACTI-mel trial to include patients that have brain metastases. We had previously excluded such patients, pending the generation of the initial safety data on the first six patients in the trial. We are pleased to be able to offer these patients a chance to be treated with IMP321 in conjunction with their KEYTRUDA® therapy.

The operational update also highlighted that the Company's cash reach has extended well into the fourth quarter of 2017 due to a rigorous focus on cost management.

In our recent Annual Report to shareholders we also provided a comprehensive review of key activities for the financial year ended 30 June 2016. In this investor update therefore, we have focused on what is transpiring in the broader biotech market with respect to immuno-oncology and the current trials targeting LAG-3.

In this investor update we feature the vital work our laboratory staff in Paris are undertaking to support our clinical studies, and introduce our Director of Clinical Development, Mr Christian Mueller.

Lastly, we provide an overview of an innovative investigator initiated study called INSIGHT on which we are collaborating with Professor Doctor Al-Batran, which will explore the potential for IMP321 as an activator of dendritic cells found within solid cancer tumours in new settings.

## Immuno-oncology Landscape

Immuno-oncology (I-O) remains one of the hottest areas in our industry, with recent market reports predicting peak global sales of \$34Bn by 2024<sup>1</sup>. Immunotherapy is a collective term given to treatments including vaccines and antibodies to treat cancers and infectious disease. I-O is the use of specific types of immune therapies to treat cancer by controlling a patient's immune responses. Recently, one of our partners, Novartis, announced its decision to intensify its focus on I-O and move away from cell and gene therapies. Novartis has announced multiple collaborations in various I-O combinations throughout this year.

The current market leader, however, is Bristol Myers Squibb which dominates the I-O market with an impressive 10 different products targeting different immune checkpoints. One of these checkpoints is LAG-3.

In 2015, the value of deals done in the I-O space exceeded US\$10.8Bn<sup>2</sup>. The growing level of industry interest in this space has continued in 2016 as illustrated by the table below of recent acquisitions in the past few months of I-O assets. There have also been numerous collaborations for combination approaches announced.

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LAG-3 clinical development is gaining momentum with some of the world's largest pharmaceutical companies conducting trials of their version of an antibody that removes the brakes from the immune system or that depletes the chronically LAG-3 activated T cells involved in auto-immunity (IMP731). Large pharma including Merck and Boehringer Ingelheim have recently

Parties	Value of deal
Novartis and Xencor: bispecific antibodies	\$150M upfront and \$2.4Bn milestones
BMS acquired Flexus Biosciences	\$1.25Bn
Advaxis and Amgen collaboration	\$40M upfront and \$25M investment plus \$475M in milestones
Pfizer acquiring Medivation oncology portfolio	\$14Bn cash
Astellas acquiring Ganymed	€422M upfront and €860M in milestones

announced they too are trialing their own versions of LAG-3 antibodies. Coupled with our own IMP321 programs and the INSIGHT trial (which we discuss in more detail in this newsletter), the table below reproduced from a recent research report by Van Leeuwenhoeck Research (US) Inc shows how Prima is either directly or indirectly involved in 5 of the 13 clinical trials currently targeting LAG-3.

### Current Clinical Trials targeting LAG-3<sup>3</sup>

Company	Product	Indication	Phase	Patients	Remarks
Prima BioMed	IMP321	Metastatic Breast Cancer	IIb	211	Adenocarcinoma Breast Stage IV. 2arms: Paclitaxel + IMP321 at the RPTD and Active Comparator: Comparator: Paclitaxel + Placebo
Prima BioMed	IMP321	Metastatic Melanoma	I	24	Multicentre, Open Label, Dose Escalation, Phase 1 Study in Patients
Novartis (partnership Prima)	LAG525	Various Cancers	I/II	416	May 9, 2015: Safety and Efficacy of LAG525 Single Agent and in Combination With PDR001 in Patients With Advanced Malignancies
Bristol Myers Squibb	BMS986016	Solid Tumors	I/IIa	360	Sep 25 2013: Phase I/2a Dose Escalation and Cohort Expansion Study of the Safety, Tolerability, and Efficacy of Anti-LAG-3 Mab Alone and in Comb with Anti-PD-1 Nivolumab, in Solid Tumors
Bristol Myers Squibb	BMS986016	Hematologic Neoplasms	I/IIa	132	Feb 12, 2014: Phase 1/2a Dose Escalation and Cohort Expansion Study of the Safety, Tolerability, and Efficacy in Combination With Anti-PD-1 Nivolumab, in Relapsed or Refract BCell Malignancies
Bristol Myers Squibb	BMS986016	Glioblastoma	I	68	2016_01_19: A Phase I Trial of Anti-LAG-3 or Anti-CD137 Alone and in Combination With Anti-PD-1 in Patients With Recurrent GBM
Bristol Myers Squibb	BMS986016	NSCLC	II	504	April 21, 2016: A Phase 2, Fast Real Time Assessment of Combination Therapies in Immuno-Oncology Study in Subjects With Advanced NSCLC (FRACTION-Lung)
Merck	MK4280	Solid Tumors	I	70	March 22, 2016 : A Phase 1 Trial as Monotherapy and in Combination With Pembrolizumab in Subjects With Advanced Solid Tumors
GlaxoSmithKline (partnership Prima)	GSK2831781	Psoriasis	I	67	July 17, 2014: A Randomised, Double Blind Placebo-Controlled, Single Asc Dose Study of Safety, Tolerability, Pharmacokinetics of a IV Dose in Healthy Subjects and Patients With Psoriasis
Tesaro	TSR033	Various cancers	Preclinical		Antibodies to Human TIM3 and LAG3 Demonstrate Potent Activity in a Dendritic Cell / T Cell MLR and Have Increased Activity in Combination with Anti PD 1
Agenus/Incyte	-	Undisclosed	Preclinical		
Macrogenics	MGD013	Various cancers	Preclinical		At its 2015 R&D Day, pre-clinical data showing that the co-blockade of PD-1 and LAG-3 via a PD-1 x LAG-3 DART molecule significantly enhanced T-cell response
Sanofi/Regeneron		Cancer	Preclinical		

We still have a bit to learn about LAG-3, the role it plays and how we can target it to treat diseases like cancer. Even though Prima is still a small company, we occupy a prominent position in the LAG-3 field and we are very pleased by the increasing awareness of this promising immune checkpoint.

1 <http://finance.yahoo.com/news/global-immuno-oncology-strategic-insight-131800166.html>

2 <https://www.linkedin.com/pulse/immuno-oncology-deals-worth-over-1089-billion-2015-nicholas-longworth>.

3 Van Leeuwenhoeck Update Report: Prima BioMed at the Forefront of LAG-3. September 1, 2016:

<http://nebula.wsimg.com/9c18c5f45768f11347291024199b3730?AccessKeyId=F1B3D293B900048B2E3E&disposition=0&alloworigin=1>

## Insights into 'INSIGHT'

In July we announced to the market that we have entered into a collaborative study investigating the intra-tumoral injection of IMP321. This investigator sponsored study will be conducted by the Institute of Clinical Cancer Research (IKF), Krankenhaus Nordwest GmbH in Frankfurt Germany.

Unfortunately, many solid tumours have evasive mechanisms to prevent the active killing of their cells. The tumour microenvironment can often contain a complex cocktail of immune system inhibitors generated by the tumour to switch off our normal mechanisms of controlling cancer.

This new study will explore the potential for IMP321 as an activator of local dendritic cells found within solid cancer tumours, as opposed to AIPAC that is looking at boosting all antigen presenting cell (APC) responses to solid tumours post chemotherapy, or TACTI-mel where we aim to boost APC responses to help improve suboptimal responses to KEYTRUDA®. Both AIPAC and TACTI-mel are directed at improving the responses of circulating APC (dendritic cells and monocytes) while INSIGHT will look to activate those APC's that are already directly infiltrating a tumour.

Lead Investigator of this pilot trial is Prof. Doctor Salah-Eddin Al-Batran, the Director of Oncology at the IKF. Prof. Doctor Al Batran is also featured in the Q&A section of this investor update. Prima will provide the IMP321 clinical supply for the trial but there will be no material funding required from us. The commencement of the study is subject to all necessary regulatory and ethical allowances.

We believe this is an ideal opportunity to investigate further clinical applications for IMP321. Direct injection into tumours, if shown to be successful, could much more rapidly activate a patients' immune system to respond to their disease.

### INSIGHT SYNOPSIS

<b>Title of Study</b>	<b>INSIGHT:</b> An explorative, single center, open-labeled, phase I study to evaluate the feasibility and safety of intra-tumoural, intra-peritoneal, and subcutaneous injections with IMP321 (LAG-3lg fusion protein) for advanced stage solid tumor entities
<b>Objectives</b>	<ul style="list-style-type: none"><li>• Feasibility, safety and toxicity</li><li>• Immune response in whole blood and tumour tissue</li><li>• Identification of biomarkers that correlate with clinical response / clinical outcome</li></ul>
<b>BMS acquired Flexus Biosciences</b>	Monocenter, open-labeled, phase I study
<b>Planned Sample size</b>	Up to 40 patients
<b>Clinical trial identifier:</b>	To be determined

## Do we have your correct email address?

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.

## Immune Monitoring in Paris Laboratory

In addition to some research and development activities regarding LAG-3, staff at our laboratory in Châtenay-Malabry, south of Paris, are kept busy conducting immune monitoring for both our AIPAC and TACTI-mel clinical trials.

Patients in each of these trials are intensively monitored for their responses to treatment with IMP321, including their immune response. Blood samples are collected at pre-specified intervals and shipped to Paris from different centers in Europe. The staff in the lab are experts in conducting specially designed assays that are capable of analysing subtle changes in the immune status of patients. A separate vendor in Paris measures inflammatory cytokine levels and activation markers on blood samples. This is an essential activity to ensure the health and safety of our patients but also for measuring and analysing the magnitude of responses to treatment with IMP321.

In parallel, for our TACTI-mel clinical trial in melanoma being conducted in Australia, blood samples are collected and assessed at a local vendor in Melbourne by flow cytometry. These assays are evaluating the number of activated T cells and number of antigen presenting cells over the course of the treatment.

We then collectively analyse all of the data generated, together with the investigators at each of our clinical sites in order to have a more complete picture of our patient responses.

## Q&A with Professor Doctor Salah-Eddin Al-Batran MD

### Q. What is an investigator sponsored study?

An investigator sponsored study is typically an academic study planned and conducted by an investigator with expertise in his or her field to investigate a new therapeutic strategy or a new drug application, for example in a new indication. This can be prior to, or after market authorisation. Companies producing the drug may provide material or support for the trial, but unlike clinical trials sponsored by biotech or pharmaceutical companies, they do not manage the trial or the data.

Investigator sponsored studies represent an important component of clinical research and drug development. They facilitate the exploration of innovative drugs in other indications or within alternative combinations. They also help to cross-link high-end academic research with clinical drug development.

### Q. Can you tell us a little about yourself?

I am Director of the Institute of Clinical Cancer Research and Director of GI Oncology at the Krankenhaus Nord-west-University Cancer Center, Frankfurt. I am a qualified haematologist and oncologist and my main fields of interest are upper GI malignancies, specifically esophageal and stomach cancer. Approximately 10 years ago, I founded the FLOT Gastric Cancer Network, which comprises more than 180 medical centers.

### Q. What are you hoping to achieve with the INSIGHT study?

As its title suggests, we are seeking new insights into the immunological and anti-tumoral effects of IMP321 when administered using alternative methods like direct intratumoral injection or intraperitoneal application. We aim to gain a better understanding of the mechanism of action of this very interesting and highly innovative drug following promising results from previous studies and the favourable safety profile of IMP321. We will also explore the potential to extend the positive results obtained by subcutaneous injections of IMP321 in metastatic renal cell and breast carcinomas to further solid tumour entities.

### Q. What interests you about immuno-oncology or more specifically about IMP321?

Immunotherapy is the future of cancer therapy. In 20 years, immunotherapy will be the mainstay of every cancer treatment. IMP321 belongs to a new class of immuno-oncology drugs that will help more effectively control cancer than with classic PD-1/PD-L1 inhibitors. It is the way the industry is heading and Prima is right at the forefront of this movement with its portfolio of LAG-3 product candidates.

### Q. What is the expected timeframe for receiving the required approvals and for the trial itself?

We expect to have all the necessary approvals in place within the next two months and to be ready to commence the trial within the next three months.

## Prima Conference and Abstract Presentations

### Christian Mueller at ESMO

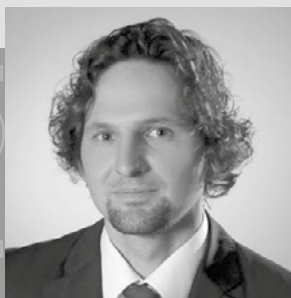
Prima's Director of Clinical Development, Christian Mueller (separately profiled), presented two Poster Presentations during the ESMO Symposium on Immunology - Advances in cancer immunotherapy; From vaccines to antibodies and cell therapies from 4-6 November 2016 in Lausanne, Switzerland. The first abstract is titled "TACTI-mel (Two ACTIVE Immunotherapeutics in melanoma): A Phase 1 trial in patients with unresectable or metastatic melanoma receiving IMP321 (LAG-3Ig fusion protein) as an adjunctive therapy to anti-PD-1 therapy with pembrolizumab." The second abstract is titled "AIPAC (Active Immunotherapy PACli-taxel): A Phase IIb trial in hormone receptor-positive metastatic breast carcinoma patients receiving IMP321 (LAG-3Ig fusion protein) or placebo as adjunctive to a standard chemotherapy regimen of paclitaxel."

### Professor Triebel at SITC

Prof. Triebel was selected to be a guest speaker for a rapid fire presentation in the New Cancer Immunotherapy section at the Society for the Immunotherapy of Cancer (SITC) conference in November. The meeting is being held in National Harbor (MD) in the USA (Nov 9-13 2016). Prof. Triebel spoke at the conference about the combination of IMP321 with a PD-1 checkpoint inhibitor.

His presentation slides are available at the following link: <http://primabiomed.com.au/investor/TriebelSITC2016.pdf>

Prof. Triebel was also interviewed on LAG-3 treatments including IMP321 ahead of the SITC conference. For further details on this interview and the other companies presenting at SITC please refer to the following link: <http://bit.ly/2fegmo2>



*Christian Mueller*

## Meet our Clinical Director Christian Mueller

Our German office welcomed our new clinical director Mr Christian Mueller in June. Christian has more than 10 years experience in the field of oncology drug development. Christian's previous roles include the assembly of a clinical team responsible for the development of the lead product at Medical Enzymes AG. More recently Christian oversaw the clinical development of the lead immuno-oncology antibody at Ganymed Pharmaceuticals AG where he successfully ran an approved regulatory Phase II, 200+ patient clinical trial. Based on this clinical data the company was successfully sold to Astella.

## Coming up for Prima in Calendar Year 2016 & 2017

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

## Company Calendar

<b>November 25, 2016</b>	Annual General Meeting, Sydney, Australia
<b>January 09-13, 2017</b>	J.P. Morgan 35th Annual Healthcare Conference, San Francisco, California

## 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.

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

- TACTI-mel trial is NCT02676869
- AIPAC is NCT02614833

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## Prima BioMed – Fast Facts

### Listings

Australian Securities Exchange (ASX), NASDAQ

### Stock Codes

ASX: PRR, NASDAQ: PBMD

### Issued Capital – Ordinary shares

2.07B (approximate as at 8th November, 2016)

### Issued ADR's

21.3M (approximate as of 8th November, 2016)

### Market Capitalisation

72.5M (approximated as of 8th November, 2016)

## 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>	Executive Director and Chief Executive Officer
<b>Dr Russell J Howard</b>	Non-executive Director
<b>Mr Pete A Meyers</b>	Non-executive Director

## Senior Management

<b>Tom Bloomfield</b>	Company Secretary
<b>Prof Dr Frédéric Triebel</b>	Chief Medical Officer and Chief Scientific Officer
<b>Deanne Miller</b>	General Counsel and Company Secretary

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