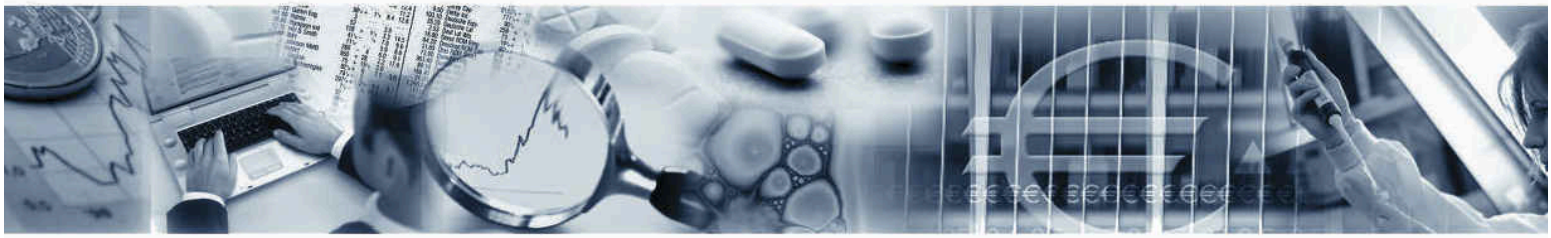

Research Note

Prima BioMed

Ongoing strong data support LAG-3 pipeline

PRIMA BIOMED

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Name:	**Prima BioMed**
Country:	**Australia**
Price:	**AUD 0.035**
ISIN Code:	**US74154B2034**
Reuters Code:	**PRR.AX, NASDAQ: PBMD**
Market Cap (AUD m):	**72.6**
EV (AUD m):	**51.7**
Cash & cash eq. (AUD m):	**20.9**
Shares outstanding (m):	**2,058**
Volume:	**1,258,985**
Free float:	**100%**
52-week Range:	**0.03-0.05**

	2014A	2015A	2016A
Total Revenues	3.1	2.1	2.0
Net (Loss)/Profit	(13.4)	(32.2)	(62.0)
Net loss per share (cents)	(0.93)	(2.02)	(2.77)
R&D costs	11.9	9.0	7.1
Cash increase/(decrease)	(8.6)	(8.5)	15.1
Cash and marketable sec.	14.2	6.8	20.9

Executive Summary

- Prima BioMed Ltd (ASX:PRR, NASDAQ: PBMD) is a leading biotech company in the development of product candidates in immune oncology and autoimmune diseases.. With the acquisition of French private biotech company Immutep late 2014, the company has evolved into a front runner in the so called LAG-3 technology. LAG-3 is a major factor involved in the regulation of T-cells in immune responses. With the out-licensing of its dendritic cell vaccine CVac (in development for ovarian and pancreatic cancer) to US biotech company Sydys Corporation, the company has a complete focus on its pipeline in LAG-3.

- Its lead product IMP321 is in Phase II development against metastatic breast cancer and also in Phase I development in melanoma in combination with pembrolizumab (Keytruda). It also has two partnered programs with Novartis and GSK. Novartis is running a Phase I/II in various cancers and recently increased its clinical program to 416 patients from 240 patients. Recently, first clinical data were announced for its trial in metastatic melanoma patients, which showed that IMP321 is safe and well tolerated. As a consequence, the company commenced recruitment for a second cohort of six patients with metastatic melanoma.

- With IMP321, Prima also announced interim data from its Phase IIb trail in metastatic breast cancer. Data from all 15 patients in the safety run-in phase demonstrated that IMP321 is safe and well tolerated at both the 6mg and 30mg dosage levels. The company will now commence the randomised phase of the trial in January 2017. IMP321 has been shown in an open-label Phase I study to be able to double the expected six month response rate in HER-2 negative metastatic breast cancer patients receiving standard-of care paclitaxel; from a 25% historic response rate, to 50% when combined with IMP321.

- In the beginning of this year, the company announced that it has developed a new candidate, IMP761. IMP761 is the first agonist antibody of LAG-3. So far, therapeutic antibodies with agonistic properties have not been described for any of the three major immune checkpoints, CTLA-4, PD-1 or LAG-3. IMP761 promises the first opportunity for fine tuning of the immune response to an immune checkpoint target, which could benefit sufferers of certain autoimmune diseases

- Major pharmaceutical companies like Merck, BMS, GSK and Novartis are taking an interest in LAG-3. Prima BioMed clearly is very well positioned with two own clinical programs and the two advanced partnerships with Novartis and GSK. We feel that each of these programs have blockbuster potential. Next to that, the increased interest from big pharma will make it more likely that the company will be able to make a substantial deal on IMP321 once it concludes the Phase II clinical trials in metastatic melanoma and breast cancer.

- Based on our adjusted NPV valuation, we believe **Prima BioMed** is substantially undervalued at the current share price of AUD 0.035. We have increased our valuation of the company to AUD 260 million or AUD 0.127 per share from AUD 0.11 per share. New programs like IMP761 offer additional upside potential

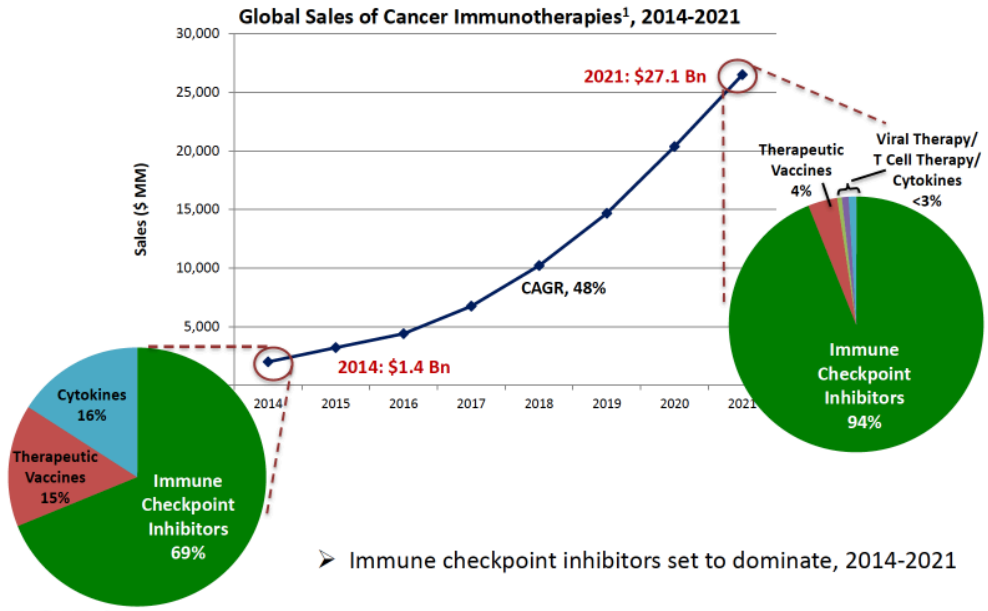
Immune Checkpoint Inhibitors New Holy Grail?

In the past few years, the rapidly advancing field of cancer immunology has produced several new methods of treating cancer, called immunotherapies, that increase the strength of immune responses against tumors. Immune Checkpoint Modulators blocks the ability of certain proteins, called immune checkpoint proteins, to limit the strength and duration of immune responses. These proteins normally keep immune responses in check by preventing overly intense responses that might damage normal cells as well as abnormal cells. But, researchers have learned that tumors can commandeer these proteins and use them to suppress immune responses. LAG-3 is an example of an Immune Checkpoint (others include CTLA-4, TIM3 and PD-1).

Unlike other immunotherapies or cancer vaccines that work by strengthening the immune system or training it to attack tumor cells, checkpoint inhibitors work to defeat a cancer resistance mechanism that causes immune cells to see tumorcells as “self”. Once this veil or “brake” is lifted, the immune response may be enough to defeat the cancer cells on its own, but a wide ranging array of therapeutic combinations is being tested. Blocking the activity of immune checkpoint proteins releases the "brakes" on the immune system, increasing its ability to destroy cancer cells. Several immune checkpoint inhibitors have been approved by the Food and Drug Administration (FDA). Checkpoint inhibitor interest started with iplimumab (Yervoy), which is an antibody directed to the CTLA4 receptor, an important inhibitory regulator of T-cell activation. More recently, the drugs Nivolumab (Opdivo) and pembrolizumab (Keytruda) have received a lot of attention – they are checkpoint inhibitors that are mediated by Program Cell Death pathways. Keytruda received breakthrough therapy status by the FDA in 2014 for the treatment of NSCLC. CTLA4 acts as a "switch" to inactivate these T cells, thereby reducing the strength of immune responses; ipilimumab binds to CTLA4 and prevents it from sending its inhibitory signal. Opdivo and Keytruda, work in a similar way, but they target a different checkpoint protein on activated T cells known as

PD-1. Nivolumab is approved to treat some patients with advanced melanoma or advanced lung cancer, and pembrolizumab is approved to treat some patients with advanced melanoma. Researchers have also developed checkpoint inhibitors that disrupt the interaction of PD-1 and proteins on the surface of tumor cells known as PD-L1 and PD-L2.

Several researchers estimate that the market for immunotherapeutic approaches in cancer treatment is expected to exceed USD 30 billion by 2023, driven by novel agents, combination therapy, longer treatment times and the emergence of predictive Biomarkers. Within cancer immunotherapy, immune checkpoint inhibitors are taking the bulk of the market with and expected CAGR more than 50%.



Source: DR/Decision Resources LLC

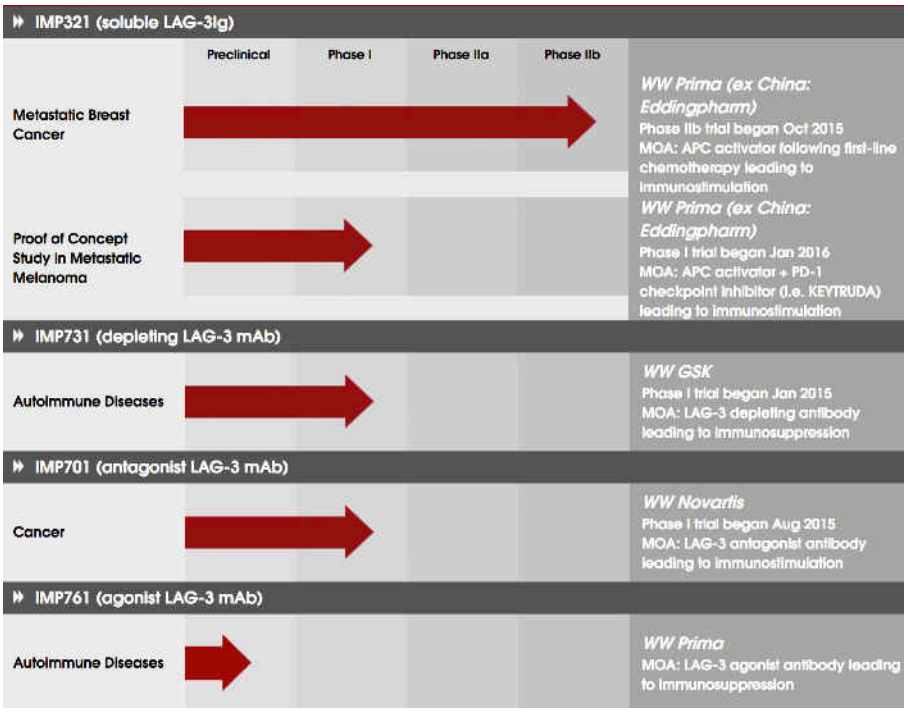
Clinical Overview LAG-3 Pipeline

With the acquisition of Immutep late 2014, Prima BioMed has focused its clinical portfolio to LAG-3, a very important Immune Checkpoint Modulator. The LAG-3 platform provides a good combination for a total approach in cancer immunotherapies. With the LAG-3 antibodies IMP731 and IMP701 the effect is to release the brakes on the immune system, whereas the LAG-3 activator IMP321 has the function to push the accelerator as a strong immune activator. It therefore makes perfect sense for each of the three products to be developed in parallel, as they are complimentary therapies with their use dependent on the condition of the individual patient.

Although each of the products are standalone products they can be potentially combined with other immuno-therapies, such as checkpoint inhibitors or chemotherapy, and these combination therapies are increasingly being recognised in the scientific and medical community as optimal approaches for fighting cancer.

LAG-3 stands for "Lymphocyte Activation Gene-3" and is involved in the regulation of T cells in immune responses. On activated T cells it is an inhibitory receptor that down-modulates their proliferation and activation. LAG-3 is one of the few key molecules that have been identified as being responsible for the regulation of T cells. LAG-3 is important as it plays a number of roles that can both activate or suppress immune responses, which makes it an attractive target for immunotherapy, both in cancer treatment and autoimmunity. Both fields are similar in essence as human tumors are frequently deeply infiltrated by active T cells, and the tumor could then be considered as an autoimmune site where the T cell response has just not been strong enough to eliminate these abnormal tissue cells. In immuno-oncology multiple tumor masses disappear in advanced metastasized cancer by just unleashing the power of this tumor infiltrating T cell.

Clinical Overview



Source: Prima BioMed

IMP 321

IMP321 is a recombinant protein consisting of a dimer of LAG-3 that has been engineered to be soluble rather than expressed on the surface of cells. It is a first-in-class antigen presenting cell (APC) activator, which has been proven to induce sustained immune responses in cancer patients when used at low dose as a cancer vaccine adjuvant or used at higher doses to get a systemic effect (i.e. general APC activation. IMP321 is currently in a Phase IIb clinical trial as a chemo-immunotherapy for metastatic breast cancer termed AIPAC and in a Phase I combination therapy trial in metastatic melanoma termed TACTI-mel. End of last year, the company announced interim data. The Database Safety Monitoring Board (DSMB) confirmed that IMP321 is safe and well tolerated at the first dose level when used in combination with a PD-1 blocking antibody and

dose escalation can continue as planned. Initial data show no safety concerns from the combination with IMP321 at 1 mg dosage. No drug related serious adverse events have been reported and the DSMB approved the continuance of the dose escalation as planned. The trial proceeded to the next dose level of 6 mg and the first patient has been dosed. This second cohort will recruit up to six patients with unresectable or metastatic melanoma that have had a suboptimal response to KEYTRUDA. Further data updates in terms of safety and activity could be expected throughout 2017.

AIPAC: Active Immune Therapy PAClitaxel

Active Immunotherapy PAClitaxel (AIPAC) is a Phase IIb trial in metastatic breast cancer (MBC). The multi-national, randomized, double-blind, placebo-controlled Phase IIb study of IMP321 is conducted in Europe in over 200 patients. IMP321 is tested in combination with a taxane based chemotherapy in hormone receptor positive metastatic breast cancer patients. 211 patients are planned to be enrolled with 15 patients in a safety run in phase and additional 196 patients thereafter. Patients will be administered with subcutaneous doses of IMP321 on days 2 and 16 of a weekly regimen of paclitaxel, the day after their paclitaxel infusion for six months. The primary endpoint from the randomized stage of the trial is improvement in progression-free survival (PFS), while overall survival (OS) is a secondary endpoint. The European regulator (EMA) has indicated that this trial could be sufficient to support a marketing authorization if it achieves certain (undisclosed) clinical endpoints.

Recent data from all 15 patients in the safety run-in phase demonstrated that IMP321 is safe and well tolerated at both the 6mg and 30mg dosage levels. Immune monitoring data has also confirmed that IMP321, as an Antigen Presenting Cell (APC) activator, is working to generate the desired immune responses. The data demonstrated activation and an increased level of blood monocytes, dendritic cells and CD8 T-cells. Subject to the confirmation of the dose escalation

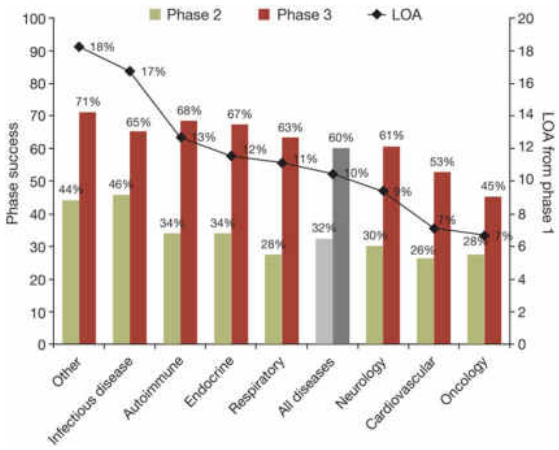
committee on December 30th 2017, the company will now commence the randomised phase of the trial in January 2017. Patients will receive paclitaxel treatment plus placebo or paclitaxel in conjunction with IMP321. The company expects the trial to take about three years to complete, so results should be available in early 2019. Positive results could potentially allow the company to file for approval in Europe in 2019, with approval possible in 2020. US approval could potentially be achieved in 2023 following a Phase III trial. Prima announced that the first patient has been dosed in January following the approval of the 30mg dosage level for IMP321 by the Dose Escalation Committee.

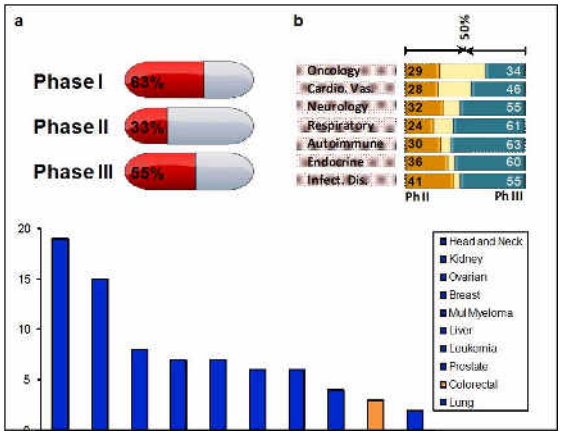
Improvements in the use of traditional breast cancer therapies have decreased the morbidity and mortality of breast cancer treatment, and improved the overall survival of women with early stage disease. The development of targeted drugs such as aromatase inhibitors (anastrozole (Arimidex), letrozole (Femara), and exemestane (Aromasin)), fulvestrant (Faslodex), and trastuzumab (Herceptin) has improved the quality of life for women with advanced disease. Current adjuvant trials are likely to demonstrate that these newer therapeutics will add an additional survival benefit for women with early breast cancer. Despite these remarkable advances, approximately 40% of women continue to fail current primary management strategies for early breast cancer, and ultimately succumb to their disease. Furthermore, although women with metastatic disease can enjoy a good quality of life on therapy, metastatic breast cancer remains incurable. The failure of current management approaches is generally attributed to the outgrowth of breast tumor cells that are inherently resistant to standard treatments. Together, these observations underscore the need for unique approaches that can either overcome or circumvent intrinsic mechanisms of resistance to standard therapies. Manipulating the immune system to recognize and eradicate breast tumor cells is a highly attractive alternative approach to disease management.

Valuation LAG-3 pipeline: Blockbuster potential

We value Prima BioMed at AUD 260 million or AUD 0.127 per share using a risk-adjusted NPV valuation. This is valuing the potential of the LAG-3 clinical programs IMP321, IMP731 and IMP701. At this moment we do not address value to the outlicensed CVac program. This is a potential upside for the company.

In estimating a value for each separate clinical program in Prima's pipeline and its partnerships, we made use of several studies that were done on the clinical development success rates for investigational drugs and specifically on immune therapy. No data were available specifically for Immune Checkpoint Inhibitors. Therefore, we used the data available for monoclonal antibodies as another example of immune therapy. These results were published in Nature Biotechnology[1] and Pharmaceutical Outsourcing[2].





[1] Michael Hay et al: Clinical development success rates for investigational drugs, Nature Biotechnology 32, 40-51 (2014)

[2] Laslo Otvos: Relative Success Rates by Drug Class, Pharmaceutical Outsourcing August 2014

We feel that each of the programs in clinical development has block buster potential, catering to large markets that are addressed with immune checkpoint inhibitors. Examples like Keytruda (sales 2015: USD 605 million), and Opdivo (sales 2015: USD 475 million) show that the uptake of such immune checkpoint inhibitors is very rapid with revenues in the first years growing quickly to more than USD 1 billion each. Analysts project sales of these therapies to be USD 5 billion and USD 8 billion respectively by 2020.

Phase Progression	Therapeutic Category	Molecule Classification	Probable Success Rate
Phase I – II	Oncology	Small Molecule NME	66%
		Peptides/Proteins	48%
		Monoclonal Antibodies	68%
	Non-Oncology	Small Molecule NME	65%
		Peptides/Proteins	65%
		Monoclonal Antibodies	72%
Phase II – III	Oncology	Small Molecule NME	29%
		Peptides/Proteins	31%
		Monoclonal Antibodies	29%
	Non-Oncology	Small Molecule NME	29%
		Peptides/Proteins	42%
		Monoclonal Antibodies	47%

Source: Pharmaceutical Outsourcing 2014

Input risk adjusted NPV

Cancer type	Prevalence (5yr) EUR	Prevalence (5yr) US	Prevalence (5yr) ROW	Pricing (monthly)	Market share
Secondary Breast	180,000	300,000	100,000	12,500	5%
Lung	440,000	410,000	700,000	12,500	5%
Melanoma	400,000	1,000,000	150,000	12,500	5%
Renal	333,000	400,000	235,000	12,500	5%

Source: Van Leeuwenhoeck Inc, National Cancer Institute, EUCAN, Remedica Journals, Metastatic Breast Cancer Network

We calculated specific risk factor per clinical phase: 68% success rate for concluding Phase I, 33% success rate for concluding Phase II and a success rate of 60% for concluding Phase III. This leads to a LOA (Likelihood of Approval) of 20% for IMP321 in Metastatic Breast cancer and 14% for IMP321 in Melanoma.

Valuation IMP321

In estimating a value for IMP321 in Metastatic Breast Cancer, we made use of a potential market of 50% from a total number of patients of 300,000 in the US, 180,000 in Europe and 100,000 in ROW, with a market launch in Europe in 2020 and 2023 in the US. For IMP321 in Melanoma we estimate launch is possible in 2022 in Europe and 2024 in the US. We calculate a Risk adjusted Discount Rate of 15%. Pricing per month treatment is set at USD 12,500 (USD 150,000 per year) which is comparable with pricing of Keytruda and Optivo. We estimate that Prima BioMed will partner IMP321 in Phase III for an estimated royalty of 15%. We estimate that a peak market share of 5% is possible. This leads to a total valuation of AUD 121 million or AUD 0.059 per share.

Valuation IMP731

In estimating a value of IMP731 in Autoimmune Disease, we apply the LOA of 14% to the potential milestones from GSK totaling USD 100 million. That would value IMP731 solely based on milestones at USD 14 million or AUD 18.5 million. Additionally, we take into account a royalty of 3-5% on sales. We estimate that market launch would be possible in 2022 with a peak market share of 5% in the market for moderate to severe psoriasis. Discounted at 15%, the total current value of expected royalties is AUD 54 million. Added the value for milestone leads to a total value of AUD 68 million or AUD 0.033.

Break down total valuation Prima BioMed

Program	Market	LOA	Market share	Peak Sales (US Million)	Royalty	Risk Adj. NPV (AUD m)	Per share
IMP321 MBC	2020 EU	20%	5%	700	15%	32.0	0.016
IMP321 Melanoma	2024	14%	5%	500 (EU)	15%	11.0	0.005
IMP731 Psoriasis	400,000	14%	5%	1,200 (EU)	5%	40.5	0.020
IMP701 Cancer	333,000	14%	5%	2,000	3%	50.0	0.024
Total						**260.4**	**0.127**

Analyst: Marcel Wijma MSc

Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.