



Update Report

## Immutep

*Moving Ahead in LAG-3*



Chief Research Analyst

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<b>Name:</b>	<b>Immutep</b>
<b>Country:</b>	<b>Australia</b>
<b>Price:</b>	<b>AUD 0.023</b>
<b>ISIN Code:</b>	<b>US74154B2034</b>
<b>Reuters Code:</b>	<b>IMM.AX, NASDAQ: IMMP</b>
<b>Market Cap (AUD m):</b>	<b>69.6</b>
<b>EV (AUD m):</b>	<b>41.9</b>
<b>Cash &amp; cash eq. (AUD m):</b>	<b>27.7*</b>
<b>Shares outstanding (m):</b>	<b>3,026</b>
<b>Volume:</b>	<b>3,300,323</b>
<b>Free float:</b>	<b>100%</b>
<b>52-week Range:</b>	<b>0.02-0.04</b>

*\*) includes recent AUD 13.2m capital raise and AUD 0.7m R&D Tax rebate*

	2015/16A	2016/17A	2017/18E
<b>Total Revenues</b>	2.0	4.2	6.0
<b>Net (Loss)/Profit</b>	(61.7)	(9.6)	(8.0)
<b>Net loss per share (cents)</b>	(3.08)	(0.45)	(0.11)
<b>R&amp;D costs</b>	7.1	7.5	10.0
<b>Cash increase/(decrease)</b>	14.5	(8.5)	12.0
<b>Cash and marketable sec.</b>	20.9	12.2	24.2



## Executive Summary

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- Immutep (ASX:IMM, NASDAQ: IMMP), formerly known as Prima BioMed is a leading biotech company in the development of personalized immunocellular therapeutics for the treatment of cancer. Its pipeline is based on four products using a LAG-3 immune control system: IMP321 for cancer chemo-immunotherapy and two partnered products IMP731 (GSK) and IMP701 (Novartis). Its program IMP761 is currently in preclinical development for autoimmune diseases.
- Its lead product IMP321 (eftilagimod alpha or efti) is in Phase IIb development against metastatic breast cancer (MBC) in combination with chemotherapy and also in Phase I development in melanoma in combination with pembrolizumab (KEYTRUDA®). It also has two partnered programs with Novartis and GSK. Recently, updated clinical data were published for its Phase I trial in metastatic melanoma patients (TACTI-mel), which showed that IMP321 is safe and well tolerated. Full recruitment of the third cohort of patients was completed in December 2017. The data from all 3 cohorts are expected mid 2018. Besides, Immutep recently announced a clinical trial collaboration with Merck MSD to evaluate the combination of efti with Merck's KEYTRUDA® in patients with NSCLC, head&neck cancer or ovarian cancer in a Phase II trial.
- With efti, Immutep also announced interim data from its Phase IIb trial in metastatic breast cancer. The ongoing Phase IIb AIPAC clinical trial in metastatic breast cancer reported positive safety and efficacy data from its safety run-in phase in Europe in June 2017. The trial remains on track to be fully recruited by mid-(calendar) 2018Q3. Following a pre-IND meeting with the FDA, it intends to file an IND in 2018H1.



- Immutep is the leading company in LAG-3 with three programs in clinical development. Only Bristol Myers has more clinical trials running. The company is very well placed to take advantage of the growing importance of LAG-3 in immuno oncology or immunotherapy. Two of its programs are licensed to Novartis (IMP701 in various cancer types) and GSK (IMP731 or GSK2831781 in autoimmune disease). Novartis, which is developing IMP701 (or LAG525), an anti-LAG-3 antibody, is currently recruiting a total of 675 patients for its two ongoing clinical trials. GlaxoSmithKline is developing IMP731 for the treatment of autoimmune diseases and has now fully recruited 67 patients for its Phase I, first-in-human clinical trial which was completed in March. We feel that each of these programs have blockbuster potential.
- The interest in LAG-3 from major pharmaceutical companies like Merck, BMS, GSK and Novartis is clearly increasing. This makes it likely that Immutep will be able to make a substantial deal on IMP321 supported by potentially strong data from the clinical trials in metastatic breast cancer and melanoma. With three own clinical programs and two advanced partnerships (Novartis and GSK), Immutep clearly is very well positioned in this area.
- Recently, Immutep successfully raised AUD 13.2 million, AUD 6.85 via an institutional placement and AUD 6.3 million through a share purchase plan (SPP) with existing shareholders. The funds raised from the SPP and Placement will be used to support Immutep's ongoing and planned immuno-oncology clinical development programs, its pre-clinical program in autoimmune disease and for general working capital purposes. Total cash reach should be enough till end of 2019.
- Based on our adjusted NPV valuation, we believe Immutep is substantially undervalued at the current share price of AUD 0.023. Following the positive development of its programs in LAG-3 we have revised our valuation model upwards. We have calculated the present valuation of the company should be AUD 397 million or AUD 0.13 per share.



## Immune Checkpoint Inhibitors Moving to the Forefront

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Cancer survival rates are generally increasing in the United States and Europe. According to the National Cancer Institute, approximately 39% of all Americans will develop cancer at some point in their lifetime. However, the overall mortality rate of those diagnosed with cancer has declined, in part due to improvements in therapeutic approaches. The development of immunotherapies reflects a new approach to cancer treatment involving activation of the immune system against cancer. Immune checkpoint inhibitors, in particular, have demonstrated considerable promise in their recent approval for the treatment of melanoma, non-small cell lung cancer, and other cancers. 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).

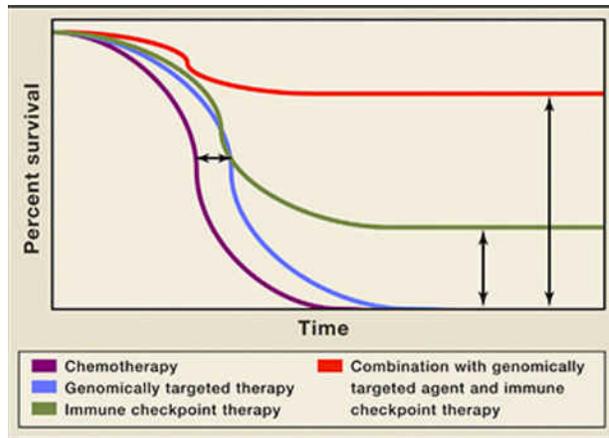
Unlike other immunotherapies or cancer vaccines that work by strengthening the immune system or training it to attack tumor cells, checkpoint inhibitors work to defeat a cancer resistance mechanism that causes immune cells to see tumor cells as “self”. Once this veil or “brake” is lifted, the immune 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 ipilimumab (Yervoy), which is an antibody directed to the CTLA4 receptor, an important inhibitory regulator of T-cell activation. The last few years, the drugs Nivolumab (Opdivo) and pembrolizumab (KEYTRUDA®) have received a lot of attention –



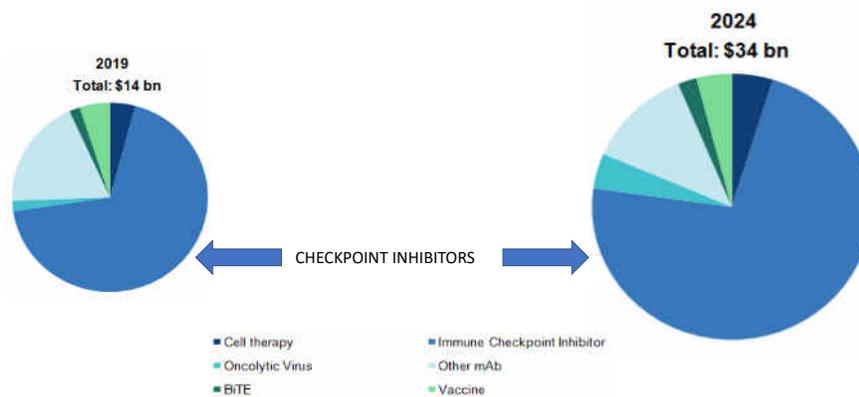
they are checkpoint inhibitors that are mediated by Program Cell Death pathways. KEYTRUDA® received breakthrough therapy status by the FDA in 2014 for the treatment of NSCLC. CTLA4 acts as a "switch" to inactivate these T cells, thereby reducing the strength of immune responses; ipilimumab binds to CTLA4 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 34 billion by 2024, 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 an expected CAGR more than 50%. The growth is driven by:

- High adoption rates in Western countries, given immunotherapies have a largely well tolerated adverse event profile compared with conventional chemotherapy;
- Immunotherapy treatment months/patient to likely materially expand due to improved progression free survival (PFS) associated with immunotherapy, multiple lines of therapy during a patient's disease and maintenance usage;
- Likely use of repeat immunotherapy based approach in patients who lose their partial response, given well tolerated adverse event profile and mechanistic rationale;
- Combination strategies with chemo/radio/MAb/cryotherapy or other checkpoint inhibitors (like IMP32 for melanoma as a combination therapy with KEYTRUDA® and for MBC in combination with paclitaxel) will likely expand the potential indications for checkpoint agents. These combination therapies also have considerably improved survival rates as the graph below shows.



Source: Cell, April 2015



Source: Global Data, Immuno-Oncology Strategic Insight: Multi-Indication and Market Size Analysis

As the table below shows, various large pharmaceutical companies are taking an interest in LAG-3

Immutep is very well positioned with three own clinical programs and two advanced partnerships with Novartis and GSK. IMP321 and IMP731 are unique in terms of mechanism of action and currently do not face a direct competition. LAG-3 as a target is clearly (given clinical development and data) moving to the forefront.



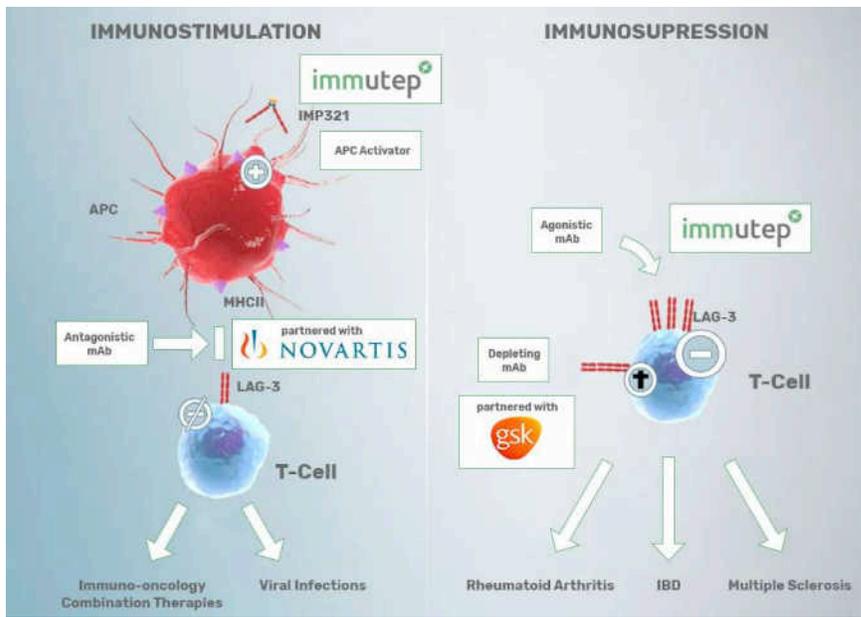
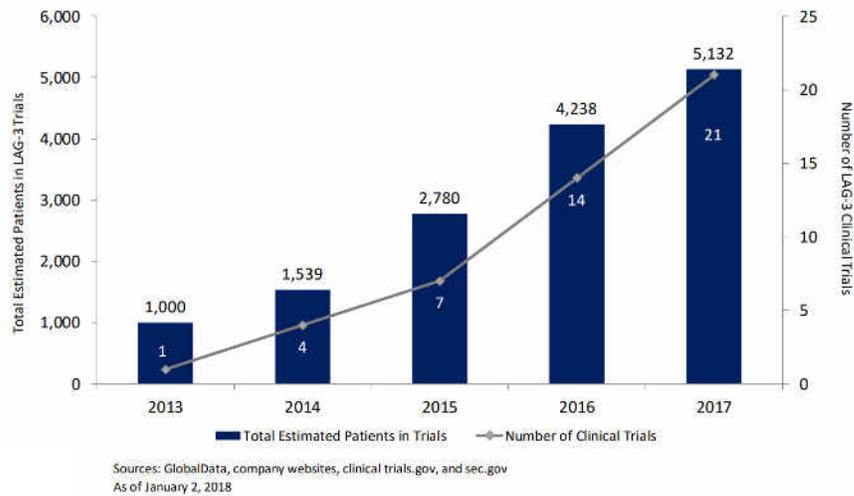
## Competitive Landscape LAG-3 with enrolment of more than 5,000 patients

Company	Program	Indication	Phase	Pat.	Comments	Study Completion
Immutep	Eftilagimod Alpha	Metastatic Breast Cancer	IIb	241	Adenocarcinoma Breast Stage IV. 2arms: Paclitaxel + IMP321 at the RPTD and Active Comparator: Comparator: Paclitaxel + Placebo	2019
Immutep	Eftilagimod Alpha	Metastatic Melanoma	I	18	Multicentre, Open Label, Dose Escalation, Phase 1 Study in Patients With Unresectable or Metastatic Melanoma	2018
Novartis (partnership Immutep)	LAG525	Various Cancers	I/II	675	Open Label, Multicenter Study of the Safety and Efficacy of LAG525 Single Agent and in Combination With PDR001 Administered to Patients With Advanced Malignancies,	Apr 2019/ Feb 2021
Bristol Myers Squibb	Relatlimab	Melanoma	II/III	700	April 2018: A Randomized, Double-Blind Phase 2/3 Study of Relatlimab Combined With Nivolumab Versus Nivolumab in Participants With Previously Untreated Metastatic Melanoma	March 2022
Bristol Myers Squibb	Relatlimab	Solid Tumors	I/IIa	1,000	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	Oct 2019
Bristol Myers Squibb	Relatlimab	Solid Tumors	I/II	230	April 2018: Relatlimab (Anti-LAG-3 Monoclonal Antibody) Administered in Combination With Both Nivolumab (Anti-PD-1 Monoclonal Antibody) and BMS-986205 (IDO1 Inhibitor) or in Combination With Both Nivolumab and Ipilimumab (Anti-CTLA-4 Monoclonal Antibody) in Advanced Malignant Tumors	May 2022
Bristol Myers Squibb	Relatlimab	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 B-Cell Malignancies	May 2020
Bristol Myers Squibb	Relatlimab	Glioblastoma	I	68	Jan 2016: A Phase I Trial of Anti-LAG-3 or Anti-CD137 Alone and in Combination With Anti-PD-1 in Patients With Recurrent GBM	Dec 2019
Bristol Myers Squibb	Relatlimab	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)	April 2021
Bristol Myers Squibb	Relatlimab	Various Cancers	I/II	500	Combination therapy with Nivolumab/ipilumab/daratumumab. Recruitment since October 2015	Dec 2019
Bristol Myers Squibb	Relatlimab	Metastatic Colon Cancer	II	340	Combination therapy with Nivolumab/Ipilumab/Daratumumab/Cobi Recruitment since March 2014	Dec 2018
Bristol Myers Squibb	Relatlimab	Advanced Renal Cancer	II	200	Combination therapy with Nivolumab/Ipilumab Recruitment since January 2017	Jan 2022
Bristol Myers Squibb	Relatlimab	Advanced Gastric Cancer	II	300	Combination therapy with Nivolumab/Ipilumab Recruitment since November 2016	Nov 2021
Merck	MK4280	Solid Tumors	I	260	March 2022: Phase 1/2a Dose Escalation and Cohort Expansion Study of the Safety, Tolerability, and Efficacy of MK4280 (Anti-LAG-3 mAb) Administered Alone or in Combination With Pembrolizumab (Anti-PD-1 mAb) in Patients With Advanced Solid Tumors	Oct 2020
GSK (partnership Immutep)	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. Fully enrolled March 2018	Mar 2018
Boehringer Ingelheim	BI754111	Neoplasms	I	70	An Open Label, Phase I Dose-finding Study in Combination With BI 754091 in Patients With Advanced Solid Cancers and of BI 754111 Monotherapy With Subsequent Combination With BI 754091 in Patients With Follicular Lymphoma,	Nov 2019
Regeneron/ Sanofi	REGN3767	Advanced cancers	I	301	Open-Label, Dose-Escalation and Cohort Expansion First-in-Human Study of the Safety, Tolerability, Activity and Pharmacokinetics of REGN3767 (Anti-LAG-3 mAb) Administered Alone or in Combination With REGN2810 (Anti-PD-1 mAb) in Patients With Advanced Malignancies	Oct 2020

Source: Van Leeuwenhoek Research, Company Reports, clinicaltrials.gov



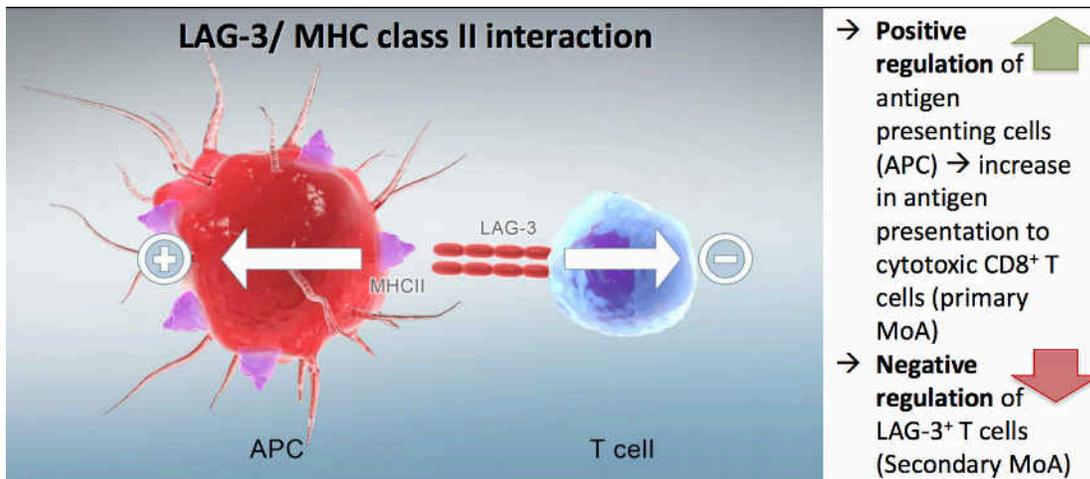
### Increasing Number of Trials Targeting LAG-3



Source: Immutep

## Clinical Overview LAG-3 Pipeline

The LAG-3 platform provides a good combination for a total approach in cancer immunotherapies. 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.



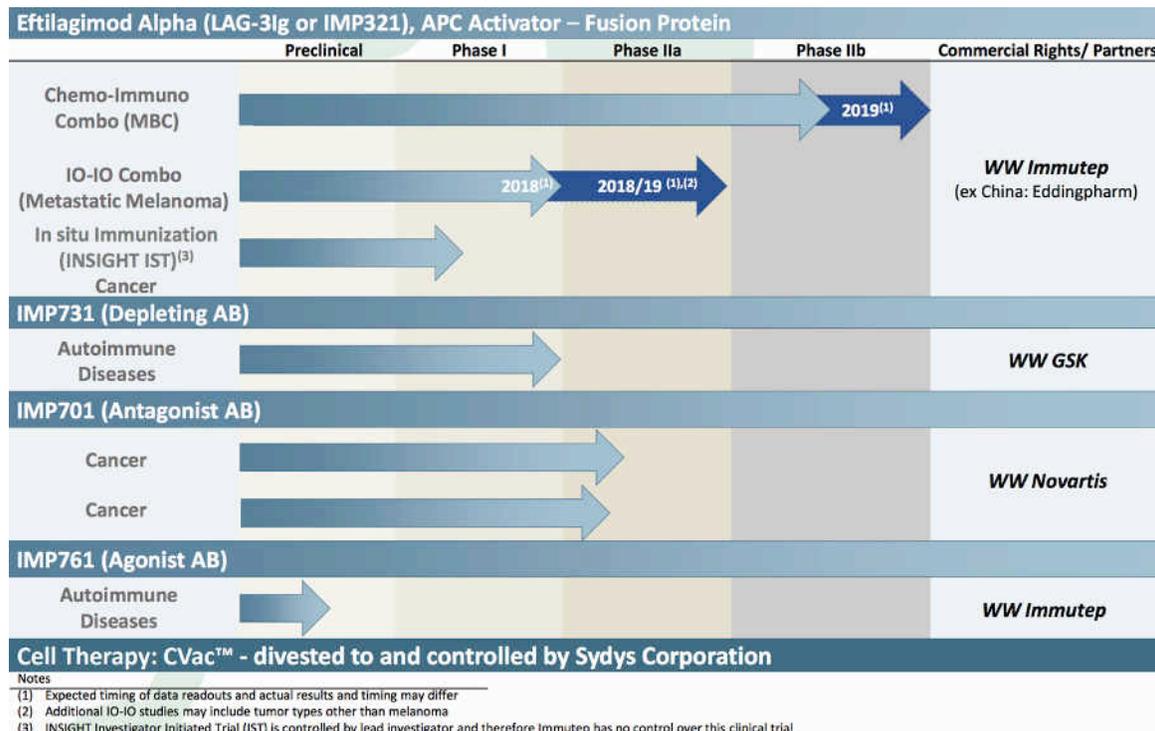
With the LAG-3 antibody IMP701 the effect is to release the brakes on the immune system, whereas the LAG-3 activator IMP321 has the function to push the accelerator as a strong immune activator. It therefore makes perfect sense for each of the products to be developed in



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.

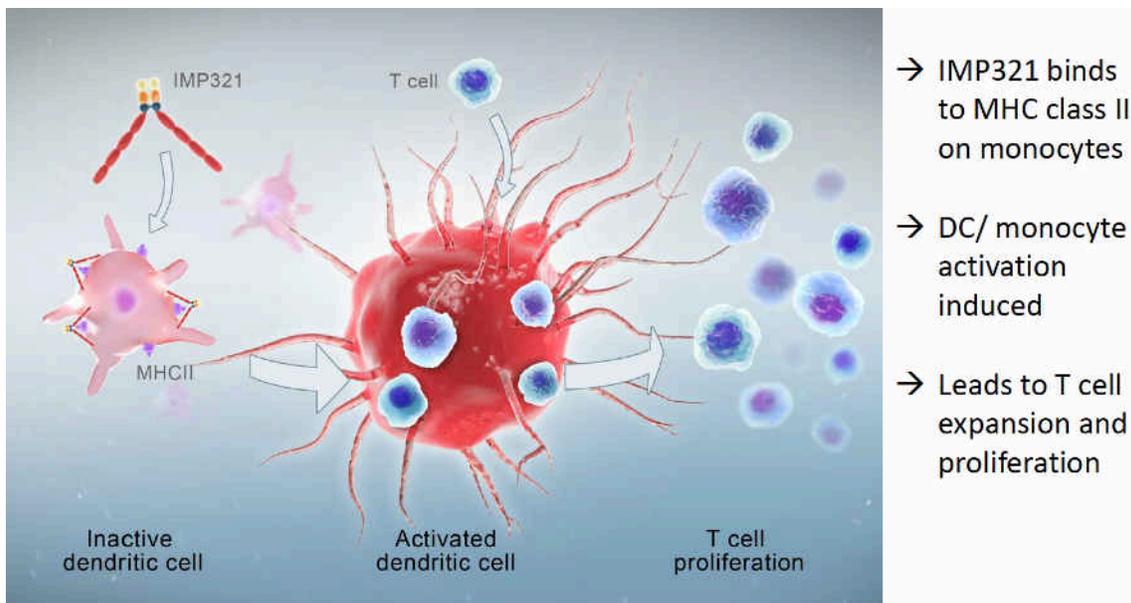
### Clinical Overview



Source: Immutep

*Eftilagimod Alpha (IMP321): Combination Therapy in Development for MBC and Melanoma*

Eftilagimod alpha (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).



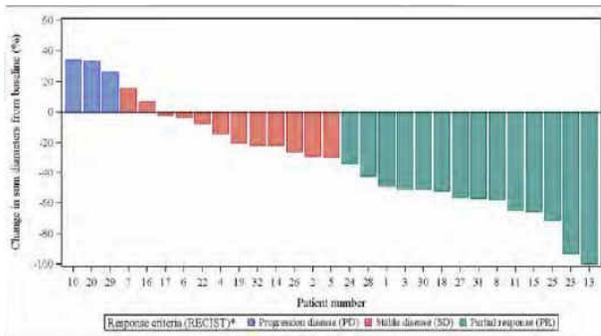
As announced earlier in June 2017, data from the open-label safety run-in cohort of 15 patients, who received 6mg and 30mg doses of eftilagimod alpha in combination with paclitaxel, were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL, USA. Final results received in December 2017 confirm the data presented at ASCO. These data showed very encouraging interim results from the safety run-in phase of its AIPAC Phase IIb clinical trial as a chemo-immunotherapy for metastatic breast cancer (MBC). AIPAC (Active Immunotherapy PAClitaxel) is Prima’s multicentre, Phase IIb, randomised, double-blind, placebo-controlled study in hormone receptor-positive MBC patients receiving IMP321 or placebo as adjunctive to first-line



weekly chemotherapy, paclitaxel.

The safety run-in phase trialed the safety, immune-monitoring and activity of 15 patients. At both the 6mg and 30mg dose levels, IMP321 was shown to be safe and well tolerated. The higher 30mg dose demonstrated a stronger immune response, and was determined to be the recommended phase II dose (RPTD) for the ongoing randomised phase of 226 patients. A total of 15 patients received between 1-18 IMP321 injections. The preliminary efficacy results showed that the ORR was 47% accompanied by a Disease Control Rate (DCR) of 87%. The ORR is consistent with the 50% response rate reported from the earlier Phase I trial that tested 6mg dose in combination with paclitaxel in 30 patients.

P005 – Phase I

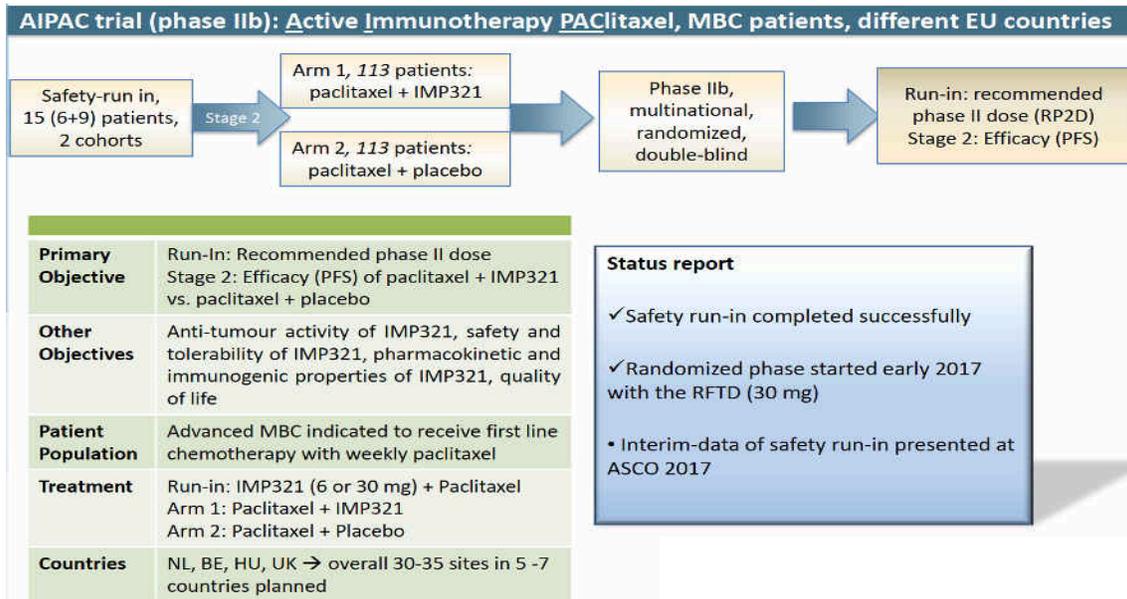


AIPAC (P011) – Phase I

Response parameter	Paclitaxel + IMP321 (n = 15)
Complete Response (CR)	0/15 (0%)
Partial Response (PR)	7/15 (47%)
Stable Disease (SD)	6/15 (40%)
Progressive Disease (PD)	2/15 (13%)
Overall Response Rate (ORR)	7/15 (47%)
Disease Control Rate (DCR)	13/15 (87%)

In total, the randomized double blind phase will enroll 226 patients with half receiving paclitaxel chemotherapy plus 30mg of IMP321 while the other half receives paclitaxel plus placebo.

The study remains on track to be to be fully recruited with 226 patients in 2018Q3; Final data for the PFS primary endpoint are expected 2019Q3. The EMA already indicated that the trial would be sufficient to file for a marketing authorization if it received certain clinical endpoints.



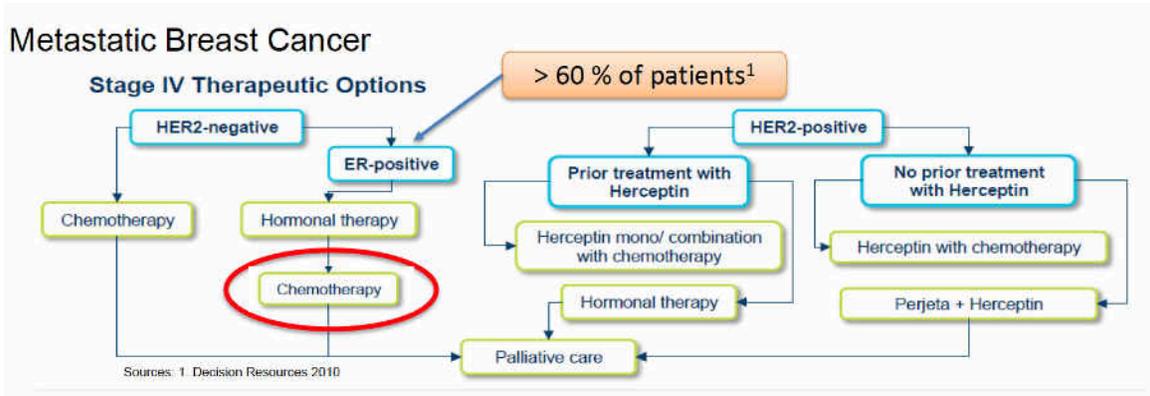
Source: Immutep

Six patients have now been recruited for the investigator-initiated Phase I clinical trial INSIGHT, which is being conducted in Frankfurt, Germany. These patients are receiving escalating doses of efti either via local (intratumoral) or loco-regional (intraperitoneal) injection. The objective of the study is to determine the recommended dose for each administration route for an intended Phase II clinical trial.

The primary target population for IMP321 are patients with HR+ and HER2neu MBC. Breast cancer that is ER+ or PR+ falls under the category of hormone receptor-positive (HR+) breast cancer. HER2+ cancer tends to be less responsive to hormonal treatment. This could be because HER2+ breast cancer tends to be more aggressive than other types of breast cancer. 30% of breast cancer patients are metastatic with 2 out of 3 HR+. After hormone therapy, patients receive taxane or



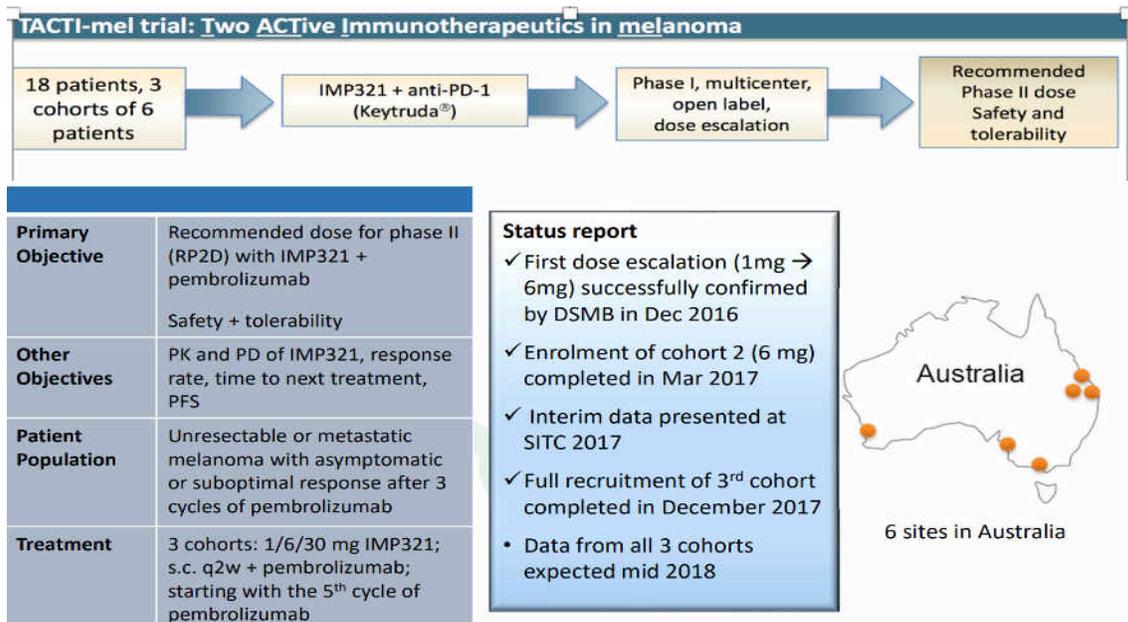
anthracycline based chemotherapy. The average PFS/OS is 5-9 months versus 24 months, so there is a high unmet medical need for which no major improvements were shown in the last few years.



Next to the AIPAC breast cancer trial, Prima has a Phase I combination therapy trial in metastatic melanoma termed TACTI-mel (Two ACTIVE Immunotherapeutics in melanoma) in development. TACTI-mel is using IMP321 to increase the efficacy in melanoma patients who have had a suboptimal initial response to KEYTRUDA®. Interim data results from the first patient cohort released in December 2016 indicate IMP321 at the 1mg dose level is safe and well tolerated. Out of the six patients in the first cohort (all with suboptimal response to KEYTRUDA® monotherapy) two patients had a partial or complete radiological tumour response according to immune related response criteria (irRC). The positive safety profile was also confirmed in the second cohort dosed with 6 mg of IMP321. None of the 6 patients treated with KEYTRUDA® plus IMP321 at this higher dose level experienced any serious adverse reaction nor dose limiting toxicity. As a result, the independent Drug Safety Monitoring Board (DSMB) has granted approval for the third cohort, at the 30mg dose level, to commence with the first patient to be dosed. The first two out of six patients of the additional cohort of the Company's TACTI-mel Phase I clinical trial in Australia have commenced their treatment. This follows the recruitment of all 18 patients in the initial three cohorts of TACTI-mel and the subsequent expansion of the trial to include an additional cohort of



six patients in February 2018. The TACTI-mel trial evaluates the combination of efti and anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in unresectable or metastatic melanoma patients, with the additional cohort receiving 30mg of efti in combination with pembrolizumab starting at cycle one of pembrolizumab. Last month, Dr Triebel, Immutep’s CSO, provided updated data from the first two cohorts of the study (since the previous data presented in November 2017 at the Society for Immunotherapy of Cancer (“SITC”). Data showed responses for TACTi-mel were sustained, in fact even slightly improved with one patient making Disease Control Rate (DCR) higher at 66%, previously 58%. The Company plans to present full data from the TACTI-mel trial in the middle of 2018.



TACTI-mel (Two ACTIVE Immunotherapeutics in melanoma) is a multicentre, open label, Phase I study in which patients with unresectable or metastatic melanoma will be dosed with IMP321 in combination with the PD-1 checkpoint inhibitor pembrolizumab (KEYTRUDA®). The study will evaluate safety as the primary endpoint and anti-tumour activity and the immune response to the combination as secondary endpoints.



In March, Immutep announced its clinical trial collaboration and supply agreement with Merck (known as MSD outside the United States and Canada), through a subsidiary, to evaluate the combination of Immutep's lead immunotherapy product candidate, efti with MSD's anti-PD-1 therapy KEYTRUDA® (pembrolizumab), Immutep is preparing to start its new clinical trial program TACTI-002 (Two ACTIVE Immunotherapies) in 2018H2. This new trial will evaluate the combination of efti with KEYTRUDA® in patients with advanced nonsmall cell lung cancer, head and neck cancer, or ovarian cancer. The TACTI-002 clinical trial will be a Phase II, Simon two-stage, non-comparative, open-label, single-arm, multicentre clinical study. Up to 120 patients across the three indications are planned to be treated in medical centres in Europe and the United States. The Company plans to file the respective Investigational New Drug application (IND) with the FDA in 2018H1 with the trial to commence in 2018H2.

The relevance of this collaboration is quite significant in the light of the recent news that the combination of Incyte's IDO-1 (epacadostat) and KEYTRUDA in melanoma did not meet its endpoint. IDO is a competitor of LAG-3. The data of the so-called ECHO-301 trial in first-line melanoma suggest that IDO-1 provided no additional benefit above KEYTRUDA alone. The ECHO program includes clinical trials designed to compare epacadostat with an IO inhibitor (KEYTRUDA or BMS' Opdivo) versus KEYTRUDA or Opdivo alone in five different tumors including melanoma, NSCLC, bladder cancer, renal cell cancer and H&N cancer.

### *Pharma Partners also Show Important Progress*

Both the programs partnered with Novartis (LAG525) and GSK (IMP731) recently reported important progress. Novartis, which is developing IMP701 (or LAG525), an anti-LAG-3 antibody, is currently recruiting a total of 675 patients for its two ongoing clinical trials. GlaxoSmithKline is developing IMP731, a novel LAG-3 depleting antibody, for the treatment of autoimmune diseases and has now fully recruited 67 patients for its Phase I, first-in-human clinical trial which is expected



to complete this month. Both Novartis and GlaxoSmithKline are responsible for all development costs with Immutep entitled to receive royalty and milestone payments. Eddingpharm owns the exclusive rights to develop and market efti in mainland China, Hong Kong, Macau, and Taiwan. Also setting Immutep apart from many other biotech companies, are that their partnerships are already generating revenue. Last year Novartis paid Immutep a milestone payment, its second payment in relation to the development of IMP701. The Company also recently received a milestone payment of USD 1 million from EOC Pharma, an affiliate of Eddingpharm, in relation to the development of efti in China. EOC Pharma applied in 2017Q1 for an Investigational New Drug (IND) in China, in preparation before starting clinical trials. Recent positive changes in the Chinese regulatory environment are likely to speed up development of efitagimod alpha in China.



## Financials

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For 2017/18H1 (ended 31 December 2017), Immutep reported total revenues of AUD 5.6 million. AUD 2.6 million was derived from licenses, whereas AUD 1.3 million was received from grants. Net loss amounted to AUD 3.8 million compared to AUD 4.6 in 2016/17H1. Expenses for the period totaled to AUD 10 million (2016: AUD 6.3 million). Research and development costs for the half year ended December 31, 2017 were AUD 4.6 million, compared to AUD 2.7 million last year.

Immutep's financial position was strengthened with the recent capital raise of approximately AUD 6.85 million via an institutional placement million and AUD 6.3 million through a share purchase plan (SPP) with existing shareholders. The funds raised from the SPP and Placement will be used to support Immutep's ongoing and planned immuno-oncology clinical development programs, its pre-clinical program in autoimmune disease and for general working capital purposes. Since July, a second milestone payment of USD 1 million was received from partner Novartis relating to Immutep's IMP701 LAG-3 antibody, also referred to as LAG525. Immutep is eligible to receive further potential development-based milestone payments and royalties as the program progresses. Immutep received its first milestone payment of USD 1 million from EOC Pharma on 31 January 2018. In February, Immutep received a AUD 686,704 cash rebate from the Australian Federal government's R&D tax incentive program. The cash rebate provided in respect of expenditure incurred on eligible R&D activities conducted in the 2017 fiscal year, mainly related to the Company's TACTI-mel trial, a Phase I clinical study in melanoma using its lead compound eftilagimod alpha ("IMP321"), conducted in Australia

At 31 December 2017, the consolidated entity had total funds of AUD 13.7 million comprising cash in hand at bank of AUD 8.3 million and short term deposits of AUD 5.4 million. Based on our current projections, total cash reach should be enough till end of 2019.



### *Profit & Loss Statement*

AUD mln	2016/17H1A	2017/2018H1A
Revenues	1.653	5.645
R&D Costs	(2.709)	(4.648)
G&A costs	(3.558)	(5.323)
Operating result	(4.615)	(4.325)
Finance expenses	0.552	(0.000)
Other	(0.491)	0.507
Net Result	(4.555)	(3.818)

### *Consolidated statement of cash flows*

AUD mln	2016/17H1A	2017/18H1A
Cash flow from operating activities	(4,118)	(4.452)
Cash flow from investing activities	(1.228)	(5.430)
Cash flow from financing activities	(0.006)	5.880
Cash and cash equivalents at start of the period	20.880	12.237
Net change in cash and cash equivalents	(4.125)	1.423
Cash and cash equivalents at end of the period	16.570	13.702

### *Balance Sheet*

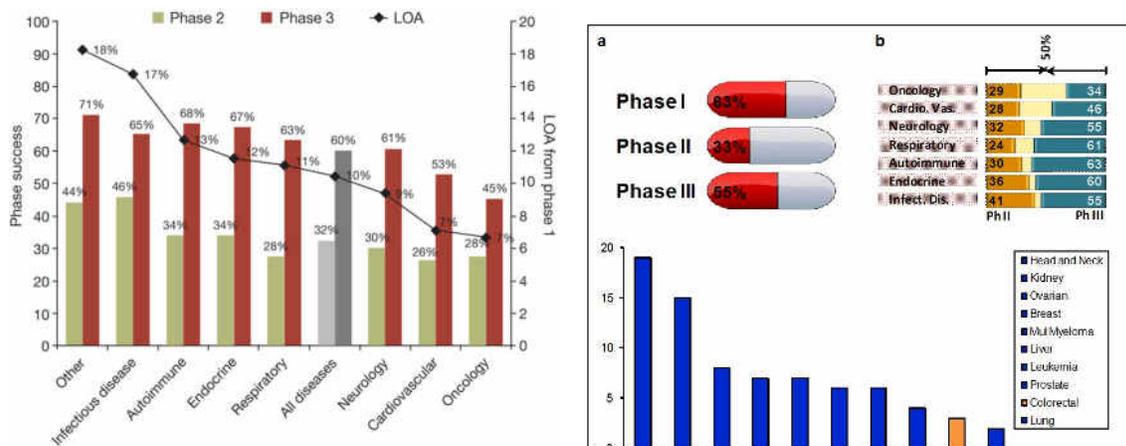
AUD mln	2016/17A (Dec 31)	2016/17A (June 30)
Current Assets	18.324	15.919
Cash and Cash Equivalents	13.701	12.237
Total Assets	37.046	34.964
Equity	27.127	26.532
Current Liabilities	2.255	2.632
Total liabilities	9.920	8.431



## Valuation LAG-3 pipeline: Blockbuster potential

We value Immutep at AUD 397 million or AUD 0.13 per share using a risk-adjusted NPV valuation. This is valuing the potential of the LAG-3 clinical programs IMP321, IMP731 and IMP701.

In estimating a value for each separate clinical program in Immutep'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<sup>1</sup> and Pharmaceutical Outsourcing<sup>2</sup>.



Source: Nature Biotechnology, 2014

<sup>1</sup>Michael Hay et al: Clinical development success rates for investigational drugs, Nature Biotechnology 32, 40-51 (2014)

<sup>2</sup>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 2017: USD 3.8 billion, +171% yoy), and Opdivo (sales 2017: USD 4.9 billion, +29% yoy) 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 6 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 2015



*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	10%
Lung	440,000	410,000	700,000	12,500	10%
Melanoma	400,000	1,000,000	150,000	12,500	10%
Renal	333,000	400,000	235,000	12,500	10%

Source: Van Leeuwenhoek 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. For MBC we have increased the LOA to 25% and for Melanoma to 18% respectively as a result of the positive interim results

*Valuation IMP321*

In estimating a value for IMP321 in MBC, 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 12%. 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 Immuteq will partner IMP321 in Phase III for an estimated high double digit royalty of 15-20%. We estimate that a peak market share of 10% is possible. This leads to a total valuation of AUD 200-225 million or AUD 0.07-0.08 per share.

*Valuation IMP731*



In estimating a value of IMP731 in Autoimmune Disease, we apply the LOA of 25% to the potential milestones from GSK totaling USD100 million. That would value IMP731 solely based on milestones at USD 25 million or AUD 32 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 8% in the market for moderate to severe psoriasis. Discounted at 12%, the total current value of expected royalties is AUD 60 million. Added the value for milestones leads to a total value of AUD 92 million or AUD 0.034.

*Break down total valuation Immutep*

Program	Market	LOA	Market share	Peak Sales (US Million)	Royalty	Risk Adj. NPV (AUD m)	Per share
IMP321 MBC	2021 EU	25%	10%	750	15%	200.0	0.066
IMP321 Melanoma	2024	18%	10%	400 (EU)	15%	25.0	0.01
IMP731 Psoriasis	400,000	18%	8%	800 (EU)	5%	92.0	0.030
IMP701 Cancer	333,000	18%	8%	1,500	3%	80.0	0.025
<b>Total</b>						<b>397.0</b>	<b>0.13</b>



*Analyst: Marcel Wijma MSc*

*Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoek 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.*

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