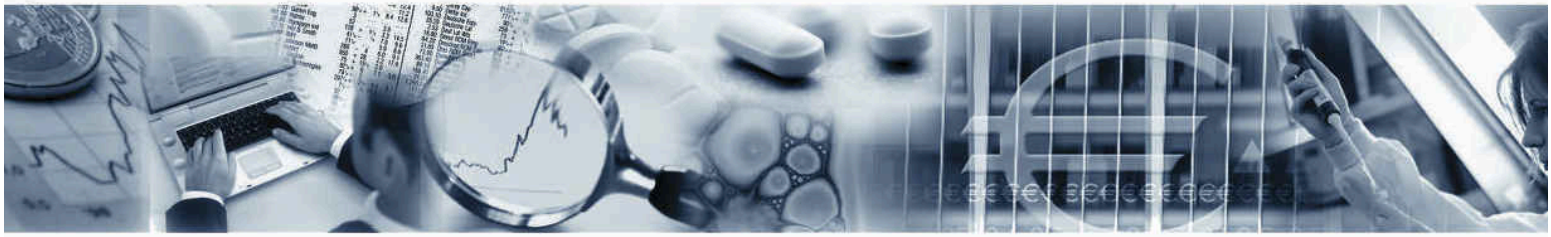

Update Report

# Prima BioMed

## At the forefront in LAG-3

PRIMA BIOMED


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Date: 1 September 2016

| | |
|---|---|
| **Name:** | **Prima BioMed** |
| **Country:** | **Australia** |
| **Price:** | **AUD 0.039** |
| **ISIN Code:** | **US74154B2034** |
| **Reuters Code:** | **PRR.AX, NASDAQ: PBMD** |
| **Market Cap (AUD m):** | **80.3** |
| **EV (AUD m):** | **60.2** |
| **Cash & cash eq. (AUD m):** | **20.1** |
| **Shares outstanding (m):** | **2,058** |
| **Volume:** | **1,478,626** |
| **Free float:** | **100%** |
| **52-week Range:** | **0.04-0.07** |

| AUD mln (ending June 30th) | 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) | 14.5 |
| **Cash and marketable sec.** | 14.2 | 6.8 | 20.1 |


# Contents


# Executive Summary

- Prima BioMed Ltd (ASX:PRR, NASDAQ: PBMD) is a leading biotech company in the development of personalized immunocellular therapeutics for the treatment of cancer. 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 late stage 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. GSK indicated that it intends to commence with Phase II in psoriasis before the end of this year.

- LAG-3 is a very important emerging target within the so called immune checkpoint inhibitor/modulator, which is currently the largest growth driver in oncology sales. Checkpoint inhibitors can be used to "release the brakes" on the immune system, allowing a stronger immune attack against cancer, whereas immune modulators are drugs that "step on the gas" of the immune response. Immune checkpoint inhibitors are the major growth area in immune oncology market with an expected CAGR of 48% to a market size USD 27.1 billion.

- 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.

- Based on our adjusted NPV valuation, we believe **Prima BioMed** is substantially undervalued at the current share price of AUD 0.039. We have increased our valuation of the company to AUD 260 million or AUD 0.127 per share from AUD 0.11 per share.


# Company Profile

Prima BioMed Ltd is a leading biotech company in the development of personalized immunocellular therapeutics for the treatment of cancer. Late 2014 the company acquired French private immunotherapy company Immutep for a sum of USD 20 million. Immutep's pipeline three products are based on pathways in the Lymphocyte Activation Gene 3 (LAG-3) immune control mechanism. With the acquisition Prima BioMed decided to focus on the development of its lead LAG-3 product IMP321, a first-in-class fusion protein over its previous sole product CVac (a dendritic cell therapy) and has recently out-licensed CVac to Sydys Corporation.

The Immutep acquisition brought sizable partnerships with China based Eddingpharm, and the large pharma companies GSK and Novartis. These partnerships will potentially bring in milestones of more than USD 100 million plus royalties. Immutep's founder, Professor Frédéric Triebel, who is a leading expert on LAG-3, joined Prima BioMed as CMO/CSO.

Prima BioMed is listed on the Australian stock exchange (ASX:PRR) and on the NASDAQ (PBMD) in the US.

## *Business Strategy*

Given the high costs, long development times and high attrition rates associated with drug development, many biotechnology companies seek the assistance of a pharmaceutical partner to advance their products through clinical trials. Earlier this year, Prima BioMed executed a spin out agreement with US based Sydys Corporation that will oversee the development of the CVac immuno oncology program. Prima BioMed received a 9.9% equity stake in Sydys for the assets being transferred. Should CVac be successfully commercialized, the company could receive over AUD 400 million in milestone payments as well as low single digit royalties on sales. to market

The various LAG-3 products have been commercially partnered with different companies:

- The Phase II program for metastatic Breast Cancer IMP321 is partnered with Eddingpharm and licensed in China and Taiwan; Eddingpharm is a fast growing specialty pharmaceutical company in the Chinese market, committed to actively introducing quality products into China's pharmaceutical market. Prima BioMed holds the Worldwide rights excluding China and Taiwan.
- The Phase I program IMP731 in autoimmune diseases (psoriasis) is partnered with GlaxoSmithKline. GSK has indicated that this program is expected to be progressed into Phase II this year with the potential to file after 2021.
- The Phase I program IMP701 (LAG525) in immune checkpoint blockade for cancer immunotherapy is partnered with Novartis. In June 2016 Novartis added a third treatment group to the trial and increased the size of the trial to 416 patients, a substantial increase from the original target of 240 patients The focus on this trail is Melanoma, Lung Cancer and Renal Cancer.


# Immune Checkpoint Inhibitors Fastest Grower in Immunotherapy

The immune system's natural capacity to detect and destroy abnormal cells may prevent the development of many cancers. However, cancer cells are sometimes able to avoid detection and destruction by the immune system. Cancer cells may:

- reduce the expression of tumor antigens on their surface, making it harder for the immune system to detect them
- express proteins on their surface that induce immune cell inactivation
- induce cells in the surrounding environment (microenvironment) to release substances that suppress immune responses and promote tumor cell proliferation and survival

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. Immunotherapies either stimulate the activities of specific components of the immune system or counteract signals produced by cancer cells that suppress immune responses. These advances in cancer immunotherapy are the result of long-term investments in basic research on the immune system—research that continues today.

There are several approaches to cancer immunotherapy, the most important are:

- Immune Cell Therapy
- Therapeutic Antibodies
- Cancer Vaccines
- Immune System Modulators
- Immune Checkpoint Modulator

### *Immune Checkpoint Modulators*

This approach 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). The first such drug to receive approval, ipilimumab (Yervoy®), for the treatment of advanced melanoma, blocks the activity of a checkpoint protein known as CTLA4, which is expressed on the surface of activated immune cells called cytotoxic T lymphocytes. 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.

Two other FDA-approved checkpoint inhibitors, nivolumab (Opdivo®) and pembrolizumab (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%. See also the graphs on the next page.

The growth is driven by:

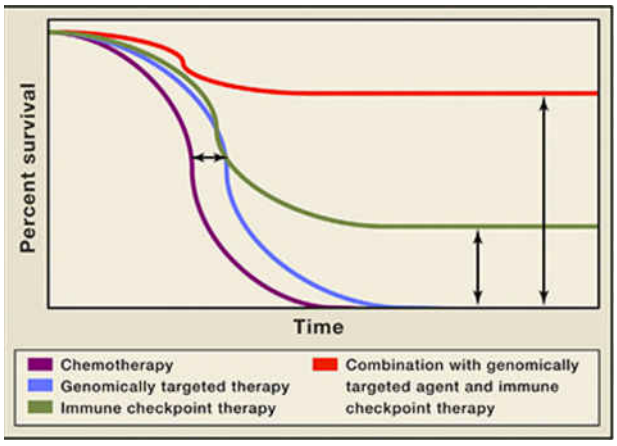
- High adoption rates in Western countries, given immunotherapies have a largely well-tolerated adverse event profile compared with conventional chemotherapy;

- 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;

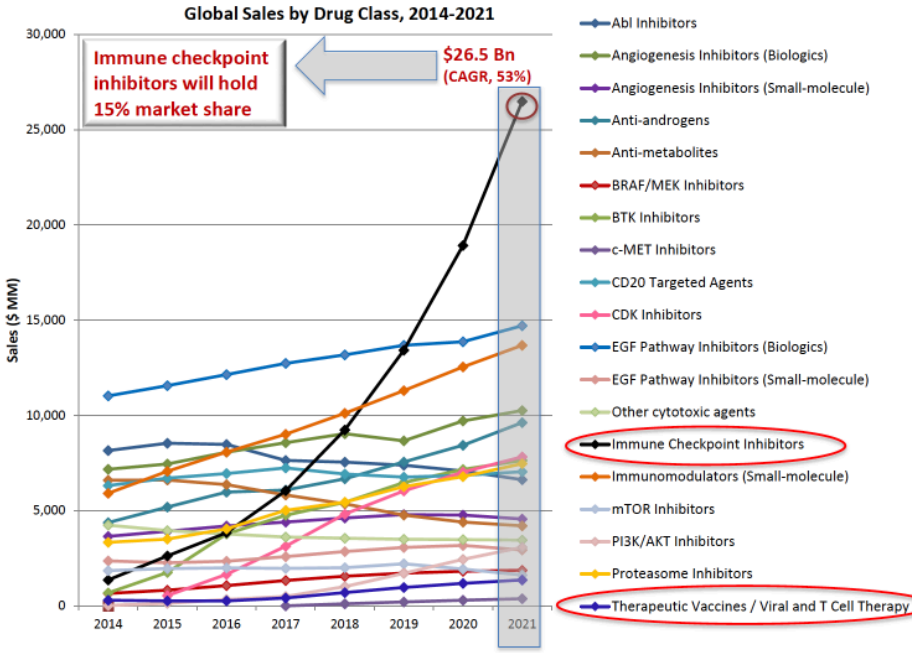
- Combination strategies with chemo/radio/MAb/cryotherapy or other checkpoint inhibitors (like the current Phase I of IMP32 for melanoma as a combination therapy with Keytruda) will likely expand the potential indications for checkpoint agents. These combination therapies also proof to improve survival rates considerably as the graph below shows.

*Improved Overall Survival as a Result of Combination Therapy.*

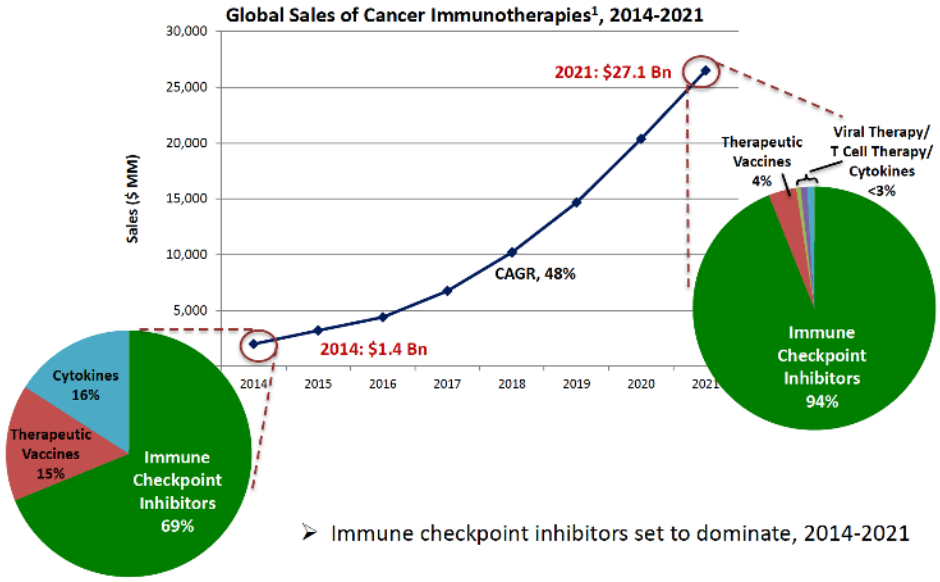



*Source: Cell, April 2015*

The graph shows depiction of Kaplan-Meier survival curve with genomically targeted agents (blue line) as compared to standard therapies (purple line), indicating an improvement in median overall survival but lack of durable responses. Improved median overall survival and durable responses in a fraction of patients treated with immune checkpoint therapy (green line); possibility for improved median overall survival with durable responses for the majority of patients in the setting of combination treatment with genomically targeted agents and immune checkpoint therapy (red line).




*Source: DR/Decision Resources LLC*




*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.

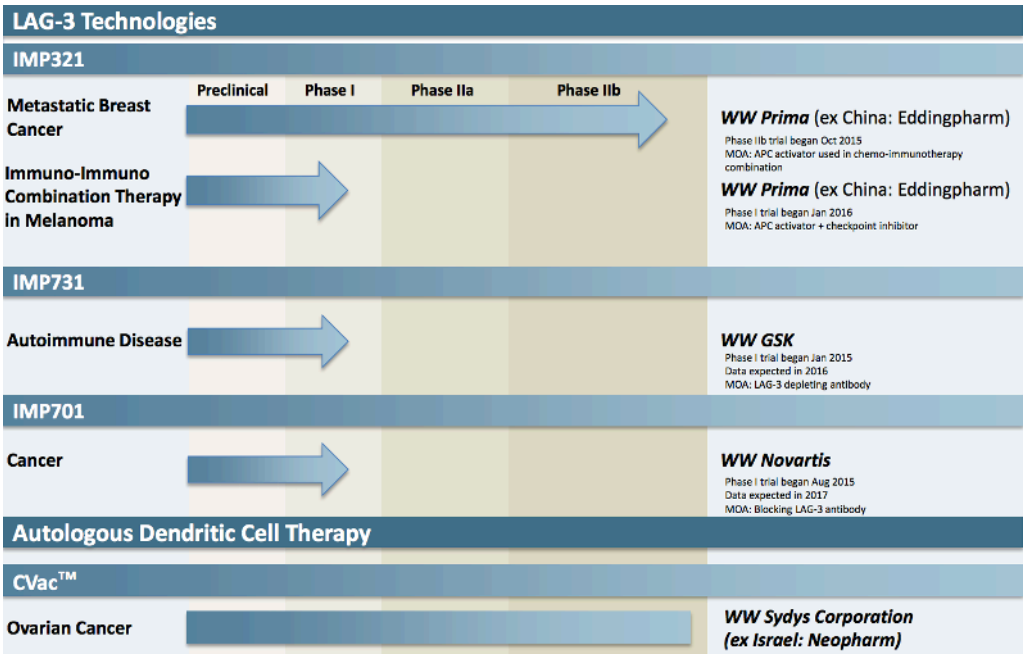
LAG-3 stands for "Lymphocyte Activation Gene-3" and is involved in the regulation of T cells in immune responses. On activated T cells it is an inhibitory receptor that down-modulates their proliferation and activation. LAG-3 is one of the few key molecules that have been identified as being responsible 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.


*Overview LAG-3 Clinical Development*

| 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 With Unresectable or Metastatic Melanoma** |
| **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 B-Cell 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 | | |

As the table above shows, various large pharmaceutical companies are taking an interest in LAG-3. Prima BioMed clearly is very well positioned with two own clinical programs and two advanced partnerships with Novartis and GSK. Novartis has actually increased the number of patients in the enrollment of the Phase I/II trial in various cancers (Melanoma, Lung Cancer and Renal Cancer) from 240 to 416 by adding a third treatment arm that involves treating Japanese patients.

## *Clinical Overview*




*Source: Prima BioMed*

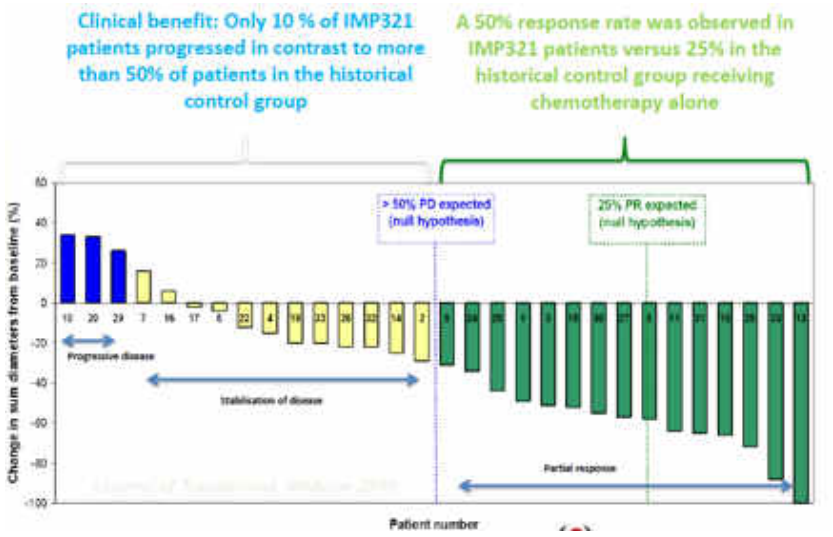
### *IMP 321*

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). In addition it has been shown to be safe and well tolerated.

In July 2006 Immutep started a Phase I/IIa trial where IMP321 was given (0.25, 1.25 and 6.25 mg s.c. 12x q14, 30 patients) the day after paclitaxel (80 mg/m2) for 6 months, as a first line therapy for metastatic breast cancer. In this study Immutep used the weekly, 3 weeks out of 4, paclitaxel regimen which was introduced to reduce cumulative neurotoxicity observed with weekly paclitaxel administration. The repeated single doses of IMP321 were administered on day 2 and day 16 of the 28-day paclitaxel cycle. Thus, the injections of IMP321 were separated by 13-day intervals. This repeated dose injection protocol had previously been shown to be safe and well tolerated for doses up to 30 mg in advanced renal cell carcinoma patients. No clinically significant adverse event related to IMP321 was reported.

Fifteen tumor regressions out of 30 patients were observed at 6 months which is twice the response rate expected in this setting (i.e. a ~25 % response rate to first-line chemotherapy). There were also 12 stable disease and only three progressors (10%) giving a 90% clinical benefit. Both compared favorably with the historical control group as shown below:



*Clinical Overview IMP321 done by Immutep SA*

| Phase | Protocol | Population | Patients | Status | Remarks |
|---|---|---|---|---|---|
| I | P001 | Healthy volunteers with influenza antigen | 60 | Completed | . |
| I | P002 | Healthy volunteers with hepatitis antigen | 48 | Completed | |
| I | P003 | Stage IV renal cell cancer | 21 | Completed | Dose escalation study showing significant increases in activated CD8 and effector-memory CD8 T-cells in highest and repeated dosing |
| I | P005 | Metastatic breast cancer | 30 | Completed | 50% CR/PR rate. Median tumor regresssion of 40% during first 3-months, followed by added 29% reduction in subsequent 3-months |
| I/II | P006 | Disease free melanoma | 28 | Completed | randomized study with patients challenged with tumor peptides. Peptide alone arm all relapsed within one year. Other three arms saw median DFS of 33 months |
| I | P007 | Metastatic melanoma | 12 | Completed | adoptive T-cell transfer study showing no confirmed responses, but significant increases in MART-1 specific CD8 cells |
| I/II | P008 | Advanced pancreatic cancer | 18 | Completed | combinatin study with gemcitabine. No significant differences observed in pre- and post-dosing of monocytes, dendritic cells and T-cells. Company believes may have been due to suboptimal dosing. |
| I/II | P009 | Metastatic melanoma | 27 | Completed | |
| II | P010 | Prostate cancer | 20 | Completed | Study assessing combination of survivin peptides with |

*Source: Prima BioMed*

Immutep conducted and completed ten clinical trials with IMP321. The corresponding protocols are termed **P001** to **P010**. The first trial of IMP321 tested alone (monotherapy) has shown that 6 mg is the effective dose to increase over time the number of long-lived effector-memory CD8 T cells (i.e. immune cells responsible for tumour regression) in all patients. It also significantly

increases the percentage of progression-free survival patients at the post-study visit. The chemo-immunotherapy trials are to provide therapeutic efficacy proof-of-concept in man in indications with very large potential markets.

Overall, more than 600 s.c. injections of IMP321 have been administered since 2005 and the product has a good local and systemic tolerability profile. The product is also non-immunogenic (i.e. anti-IMP321 antibodies were not detected). 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.

### *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 will be conducted in Europe in over 200 patients. IMP321 will be 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.

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 Prima 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.

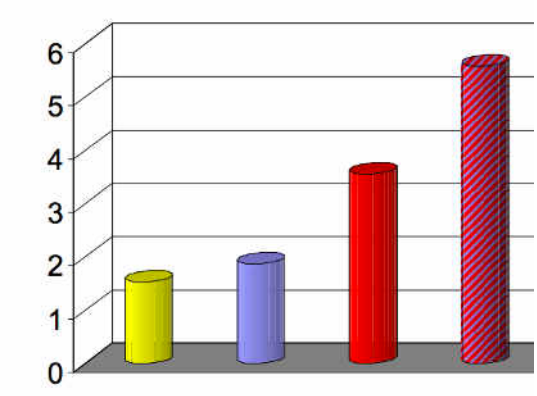
Improvements in the use of traditional breast cancer therapies have decreased the morbidity and mortality of breast cancer treatment, and improved the overall survival of women with early stage disease. The development of targeted drugs such as aromatase inhibitors (anastrozole (Arimidex), letrozole (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.

### *TACTI-mel: Two ACTive Immunotherapeutics in melanoma*

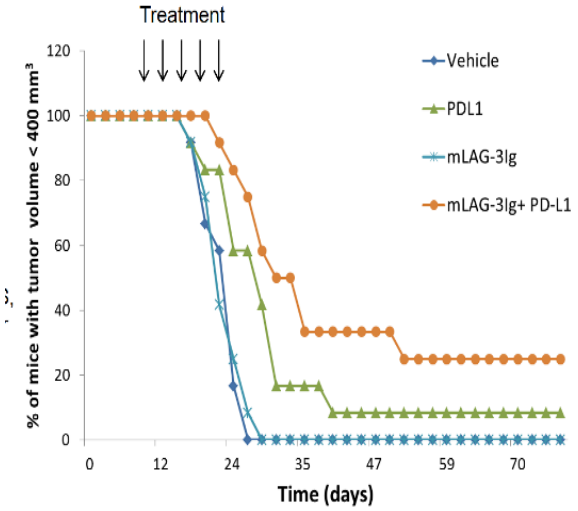
Two ACTive Immunotherapeutics in melanoma will be a safety and dose finding IMP321 study.. The clinical Phase I study is a combinatorial setting with a PD-1 checkpoint inhibitor (Keytruda). TACTI-mel will enroll up to 24 patients with Stage III/IV metastatic melanoma with ascending subcutaneous doses of IMP321 up to 30 mg per injection fortnightly for 13 injections. Safety, pharmacokinetics, pharmacodynamics and anti-tumor activity of IMP321 at the various doses as well as the nature of the immune response in the combination will be evaluated. The primary endpoint will be safety. The trial started in January 2016. This study is important because it combines the APC activation properties of IMP321, which helps to initiate an immune response, with an immune checkpoint inhibitor which 'releases the brakes' on the immune effector cells, enabling a stronger immune response. Prima has shown in preclinical studies that combining

IMP321 with immune checkpoint inhibitors increased the strength of an anti-cancer immune response and the speed and level of tumor regression.

The graphs below show that a combination of IMP321 with a PD-1 blocking antibody increases the activation of cytotoxic T-cells when white blood cells (peripheral blood mononuclear cells) were stimulated with a peptide antigen in vitro. In comparison with a mouse model of colon cancer, combination therapy with the mouse analogue of IMP321 (mLAG-3Ig) plus a PD-L1 blocking antibody inhibited tumor growth to a greater degree than either treatment on its own (see graph on the right side).




Yellow: Control
Blue: anti PD1 Mab
Red: IMP321
Purple: IMP321 + anti PD1 Mab




Combining two immunotherapy treatments with different mechanisms of action has already been proven to be an effective strategy. The FDA approved the combination of the ICIs Yervoy (ipilimumab) and Opdivo (nivolumab) in patients with advanced melanoma. Patients treated with the combination experienced a 60% overall response rate compared to 11% in those treated with Yervoy alone.

### *LAG525 (IMP701): Partnered with Novartis*

In 2012, Immutep licensed IMP701 (anti-LAG-3 antibody) to CoStim Pharmaceutical, a private biotech company CoStim, that was acquired by Novartis in the same year. Although terms were undisclosed, we expected a low single digit royalty on sales (3-5%) and an undisclosed amount in milestones.

Initially, Novartis started running a 240 patient, open label, Phase I/II study to test the safety and efficacy of LAG525 monotherapy for the Phase I portion and in combination with Novartis's PDR001 (anti-PD-1) for the Phase II portion. The Phase I primary endpoint is to identify the incidence of dose limiting toxicities (DLTs) and the primary endpoint of the Phase II portion is definition of overall response rate (ORR). An update from this study is expected by the end of 2016 or early 2017. However, earlier this year, Novartis increased the number of patients in the enrollment of the Phase I/II trial in various cancers (Melanoma, Lung Cancer and Renal Cancer) from 240 to 416 by adding a third treatment arm that involves treating Japanese patients. The trial is expected to be completed in 2018H2. In our view, Novartis clearly sees the importance of this trial with the expansion into more patients. Also combining IMP701 in the trial with its PD1 immune checkpoint inhibitor indicates that Novartis is focusing more on immune checkpoint inhibitors like LAG-3.

### *IMP731 in Autoimmune Diseases: Partnered with GlaxoSmithKline (GSK)*

IMP731 an autoimmune disease cytotoxic monoclonal antibody (mAb) that will kill the few LAG-3+ activated T cells that infiltrate autoimmune disease sites. It belongs to the next wave of innovative products that target the underlying cause of autoimmune diseases, that is the few auto-reactive T cells that accumulate at one organ site and destroy it.

At the present time, drugs such as corticoids or anti-TNF antibodies don't treat the underlying cause of the disease; they just control inflammation and therefore have to be given on a chronic basis. In contrast, it is expected that killing the few self-reactive T cells will have an enduring effect with long-term remissions induced by a single injection.

In December 2010, Immutep licensed the rights to IMP731 to GSK with total deal value of USD 100 million While the royalty has not been disclosed, we expect a low single digit royalty on sales as is the case with the Novartis partnership. GSK has developed a humanized form of the IMP731 mAb, which it has termed GSK2831781. GSK dosed the first patient in a Phase I study of GSK2831781 in January 2015 in patients with plaque psoriasis. GSK2831781 aims to kill the few activated LAG-3 positive T-cells that are autoreactive in autoimmune disease. At its R&D day in November 2015 GSK indicated that it expects to progress its anti-LAG-3 program into Phase II trials in immuno-inflammatory disease in 2016, with the potential for a regulatory filing in a 2021-25 time frame. The Phase II trial does not appear to have commenced yet.

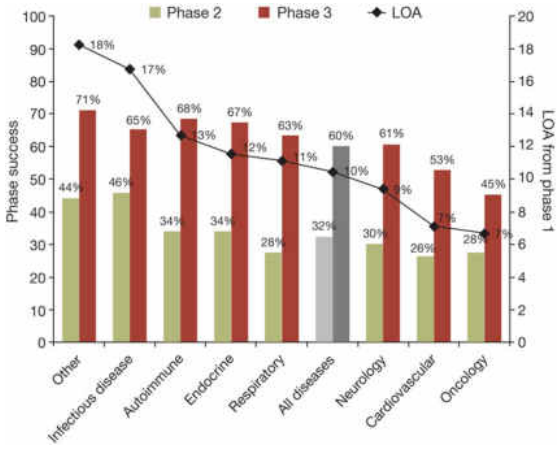

# SWOT

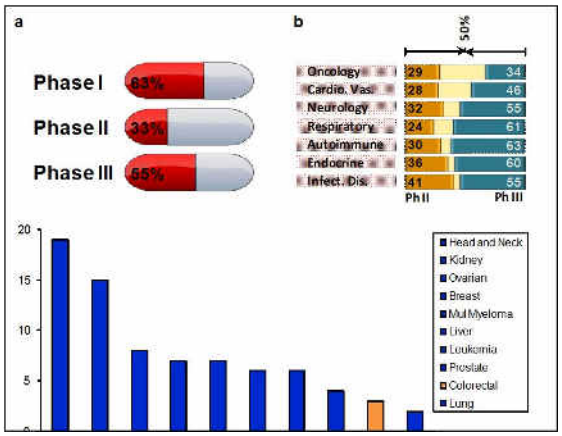
| Strengths | Weaknesses |
|---|---|
| Strong management with extensive relevant technical, scientific and financial expertise | Operating losses accumulating year-on-year |
| Vast expertise in fast growing area of immuno oncology | Dependency on LAG-3 technology |
| Sufficient cash position to finance its pipeline in the next few years | Potential delay in pipeline development |
| Partnerships with large pharma companies validate technology | |
| **Opportunities** | **Threats** |
| Profitable partnerhsips and license agreements | Uncertainty about the outcome of clinical trials |
| Front runner in LAG-3, thereby profiting from high expected growth in immune checkpoint stimulators and immune therapy | Higher level of expenditure than budgeted |

# 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].




*Source: Nature Biotechnology, 2014*

[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 (AUD) |
|---|---|---|---|---|---|---|---|
| **IMP321 MBC** | 2020 EU | 20% | 5% | 700 | 15% | 32.0 | 0.016 |
| | 2023 US | | | 1,300 | 15% | 44.0 | 0.021 |
| **IMP321 Melanoma** | 2024 | 14% | 5% | 500 (EU) | 15% | 11.0 | 0.005 |
| | | | | 1,500 (US) | 15% | 34.3 | 0.017 |
| **IMP731 Psoriasis** | 400,000 | 14% | 5% | 1,200 (EU) | 5% | 40.5 | 0.020 |
| | | | | 1,450 (US) | 5% | 48.6 | 0.024 |
| **IMP701 Cancer** | 333,000 | 14% | 5% | 2,000 | 3% | 50.0 | 0.024 |
| **Total** | | | | | | **260.4** | **0.127** |

# Financials

For the financial year ended June 30th 2016, Prima BioMed ended the year with AUD 20.9 million in cash, which management believes is sufficient to fun operations to end-2017. That is actually longer than previously anticipated. Since May 2015, the company was successful to raise more than AUD 26 million. Net operating cash outflow for 2016FY amounted to AUD 11.3 million compared to AUD 7.8 million in 2015FY. Net loss amounted to AUD 62.0 million (2015: AUD 32.2 million).

In July and August 2015, the company completed a successful capital raising which was essential for initiating its two clinical trials for IMP321. The Share Purchase Plan ("SPP"), which was heavily oversubscribed, was increased from AUD 5 million to AUD 10 million. The decision to terminate the USD 37.4 million investment facility with Bergen Global Opportunity Fund, by mutual consent, was followed by two smaller placements with institutional investors. The aggregate amount of these two placements in October and November 2015 was AUD 3.55 million.

Shareholders ratified the issue of further securities to Ridgeback Capital Investments L.P. at the Extraordinary General Meeting held on 31 July 2015. In accordance with the approval by shareholders, the Company issued ordinary shares, a convertible note and warrants. Assuming that Ridgeback Capital Investments L.P. exercises all warrants and convertible notes, an additional 1,067,462,626 ordinary shares may be issued in future reporting periods. The total proceeds from the issuance of the above securities amounted to AUD 13,960,794.

In addition to the above cash financing from Ridgeback, it was disclosed at the Extraordinary General Meeting explanatory memorandum that Ridgeback also provides the company with additional benefits, including:

- Introductions to other well respected investment institutions which will help in future financing
- The ability to attract other top level executives and researchers to the company and the board
- Potential introductions for additional in-licensing opportunities; and
- Increased visibility to other biotechnology and pharmaceutical companies and potential partners and collaborators on Prima's internal assets


## *Profit & Loss Statement (USD mln)*

| For twelve months ended | June 30th 2016A | June 30th 2015A |
|---|---|---|
| **Revenues** | 2.029 | 2.093 |
| **R&D Costs** | (7.060) | (8.952) |
| **General & administrative expenses** | (6.983) | (5.723) |
| **Finance costs (income)** | (0.008) | (18.365) |
| **Share Bassed Payment to Strategic Investor** | (47.468) | - |
| **Depreciation and amortisation** | (1.993) | (1.341) |
| **Other** | (1.150) | - |
| **Loss (income) before income taxes** | (63.196) | (32.294) |
| ***Income tax benefit*** | 1.181 | 0.142 |
| ***Net Income (Loss)*** | *(62.015)* | *(32.151)* |

## *Consolidated statement of cash flows*

| For twelve months ended | June 30th 2016A | June 30th 2015A |
|---|---|---|
| Cash flow from operating activities | (11.310) | (7.787) |
| Cash flow from investing activities | 0.103 | (11.961) |
| Cash flow from financing activities | 25.720 | 11.268 |
| Cash and cash equivalents at beginning of the period | 6.760 | 14.200 |
| Net change in cash and cash equivalents | 14.513 | (8.480) |
| Cash and cash equivalents at the end of the period | 20.880 | 6.760 |


*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.*