

NASDAQ: PBMD, ASX: PRR

JANUARY 2017
CORPORATE PRESENTATION

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# **Company Overview**

- Biopharmaceutical company developing novel immunotherapeutic products for cancer and autoimmune diseases
- Deep expertise and understanding of the LAG-3 immune control mechanism:
  - Prof. Frédéric Triebel (Prima's CSO & CMO) discovered LAG-3 in 1990 and is a leading LAG-3 thought leader
  - LAG-3 plays a vital role in the regulation of T cell immune response and is one of the four primary checkpoint inhibitor targets
- Lead product candidate, IMP321 is in ongoing clinical development (Phase IIb + I studies)
  - IMP321 is an antigen presenting cell (APC) activator and fusion protein and is a soluble dimeric form of LAG-3
- Multiple industry partnerships including, GSK and Novartis
- Poised for meaningful news and data flow in 2017



## **Directors & Officers**



Lucy Turnbull, AO, Non-executive Chairman Businesswoman and philanthropist; previously on the boards of the Cancer Institute of NSW and Australian Technology Park





Marc Voigt, Executive Director & Chief Executive Officer 17+ years in leading positions in finance, venture capital and biotech industry



Prof. Frédéric Triebel, MD PhD, CSO & CMO/Immutep S.A.S.

Clinical haematologist, and PhD in immunology (Paris University) and successfully developed several research programs in immunogenetics and immunotherapy, leading to 144 publications and 16 patents



Pete A Meyers, Non-executive Director

CFO of Motif Bio; previous Co-Head of Global Health Care Investment Banking at Deutsche Bank



Russell J. Howard, PhD, Non-executive Director

Scientist entrepreneur; previously CEO of Maxygen & Oakbio, positions at NIH, DNAX, Affymax

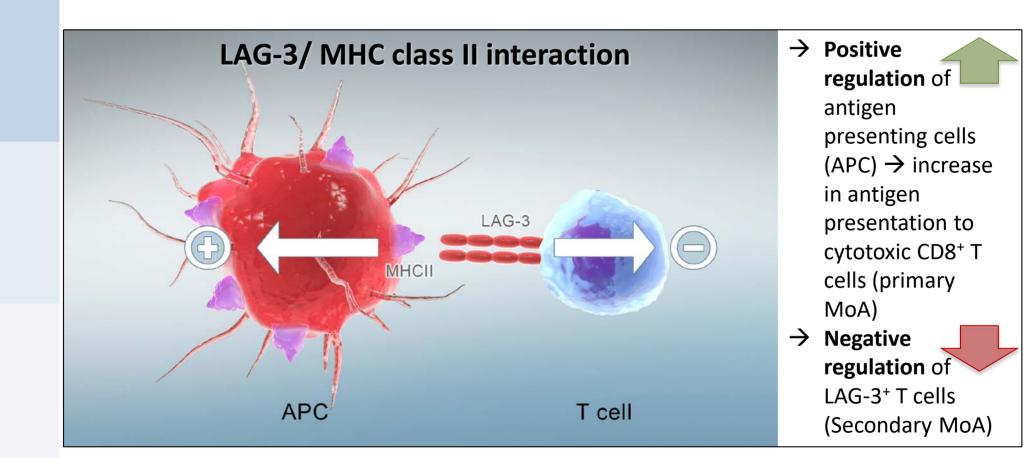


Deanne Miller, General Counsel, Company Secretary & COO

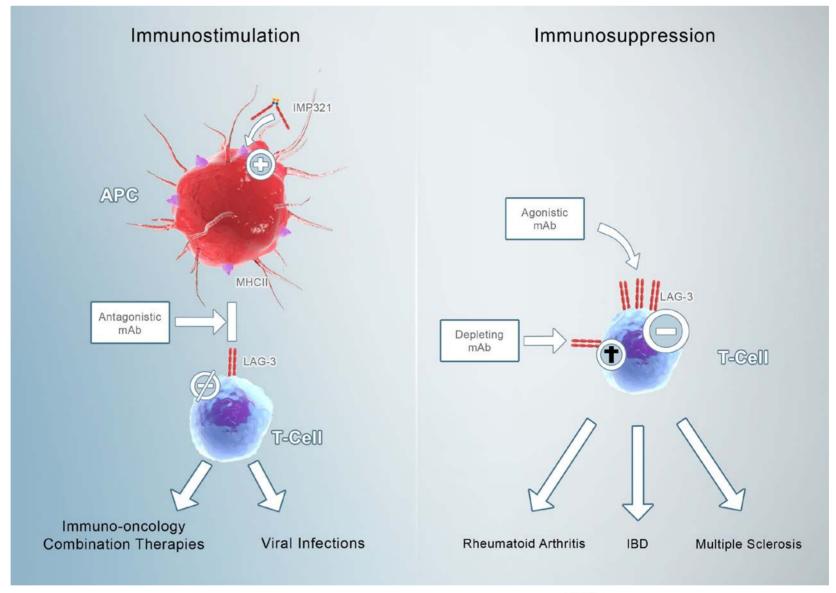
Lawyer; previous positions at RBC Investor Services, Westpac, Macquarie and ASIC

## LAG-3 As a Therapeutic Target

- LAG-3 is widely expressed on tumor infiltrating lymphocytes (TILs) and cytotoxic T cells
  - → Prime target for an immune checkpoint blocker (such as PD-1)
- Functionally similar to CTLA-4 (targeted by Yervoy®) and PD-1 (Keytruda®)



# Targeting LAG-3 May Lead to Multiple Therapeutics in Numerous Indications





# LAG-3 is an Important I-O Target

- In 1990 **Prof. Triebel discovered LAG-3** and subsequently also discovered the LAG-3 ligand MHC class II and its importance in the immune system
- LAG-3 is the subject of 363 PubMed publications:
  - 102 publications of LAG-3 in immune system
  - 141 publications of LAG-3 in context of I-O
  - 16 publications of promising pre-clinical data on LAG-3 and cancer immunotherapy<sup>1</sup>
- Multiple companies developing anti-LAG-3 mAb in pre-clinical and clinical studies (including Prima BioMed and partners)
- LAG-3's potential synergistic function with PD-1 and PD-L1 is very promising<sup>1</sup>: "Simultaneous blockade of LAG-3 and PD-1 synergistically enhance T-cell activity and antitumor immunity in mouse models"<sup>2</sup>

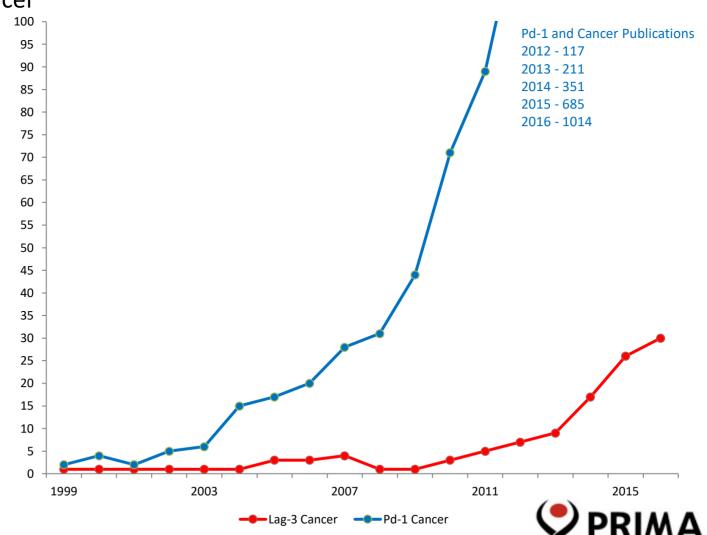


promote tumoral immune escape. Cancer Res. 2012

2 Woo et al. Immune inhibitory molecules LAG-3 and PD-1 synergistically regulate T-cell function to

# **Growing Interest in LAG-3**

- Overall understanding and appreciation of the importance of LAG-3's role in the immune system continues to grow
- Trajectory of the PubMed articles on LAG-3 cancer is similar to that of PD-1 cancer



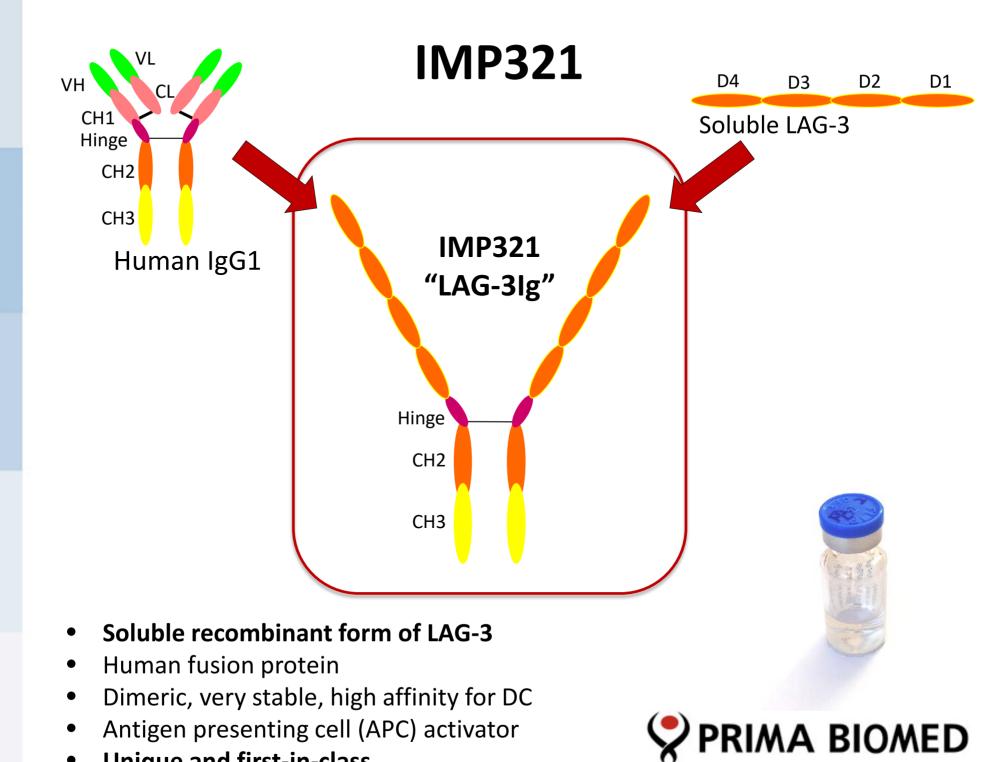
# **Pipeline**

#### LAG-3 Technologies **IMP321** Preclinical Phase I Phase IIa Phase IIb **WW Prima Metastatic Breast** (ex China: Eddingpharm) Phase IIb trial began Oct 2015 Cancer MOA: APC activator following first-line chemotherapy **WW Prima Proof of Concept** (ex China: Eddingpharm) Study in Metastatic Phase I trial began Jan 2016 Melanoma MOA: APC activator + PD-1 checkpoint inhibitor (i.e. KEYTRUDA) **IMP731** WW GSK **Autoimmune** Phase I trial began Jan 2015 **Diseases** MOA: LAG-3 depleting antibody **IMP701 WW Novartis** Cancer Phase I trial began Aug 2015 MOA: LAG-3 antagonist antibody **IMP761 Autoimmune WW Prima Diseases** MOA: LAG-3 agonist antibody **Autologous Dendritic Cell Therapy** CVac<sup>™</sup> **WW Sydys Corporation Ovarian Cancer** (ex Israel: Neopharm)

Phase IIb completed (CAN-003)

# **LEAD PRODUCT IMP321**

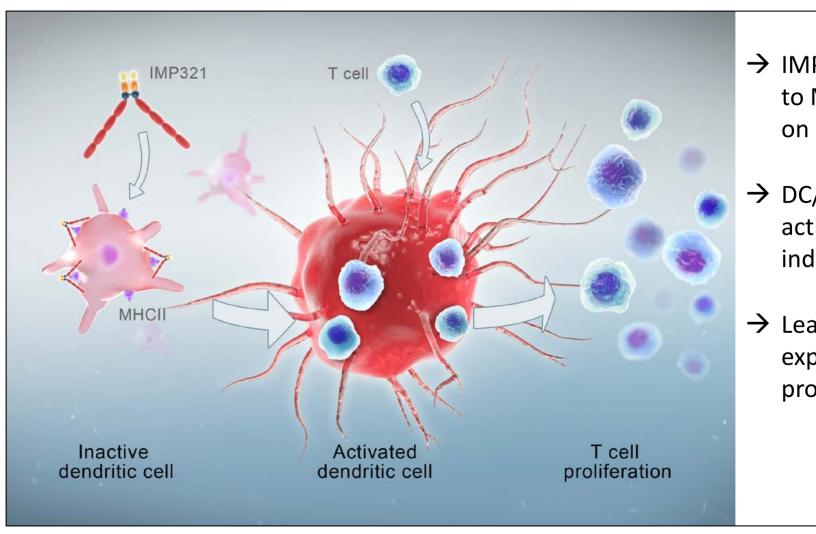




**Unique and first-in-class** 

## **IMP321**

### Soluble dimeric recombinant form of LAG-3lg (fusion protein)



- → IMP321 binds to MHC class II on monocytes
- → DC/ monocyte activation induced
- → Leads to T cell expansion and proliferation

- Highly efficacious in multiple animal models of cancer and infectious disease
- Shown to be safe, non-immunogenic and efficacious in humans

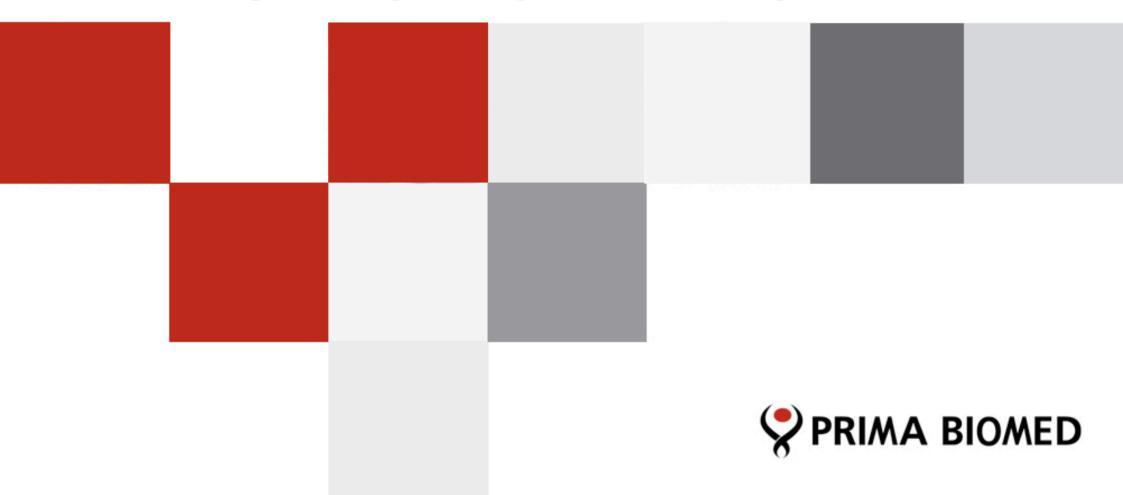
# **IMP321 – Potential Applications**

#### Potential combination therapy strategies:

- Chemo-immunotherapy in various cancer indications
  - Combination therapy with active agents such as Taxanes (e.g. Paclitaxel), anthracyclines, alkylating agents, anti-metabolites, vincas...
- I-O combination in various cancer indications
  - ➤ With PD-1, PDL-1 or CTLA-4 antagonists...
- Cancer vaccine
  - > To locally stimulate the immune system



## **IMP321 - CLINICAL DEVELOPMENT**



# **IMP321 – Clinical Development**

#### 1. Chemo-immunotherapy:

 IMP321 in combination with paclitaxel (immunogenic chemotherapy) in metastatic breast cancer → potentially pivotal trial in Europe ongoing (AIPAC)

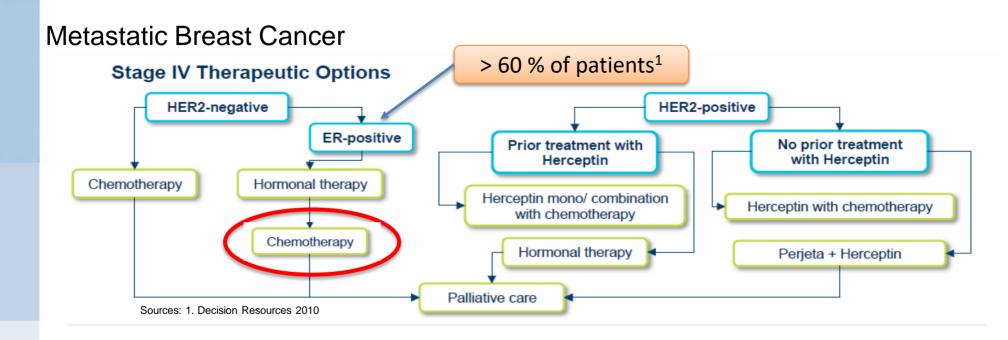
#### 2. I-O Combination:

• IMP321 in combination with pembrolizumab as a treatment for melanoma → phase I dose escalation trial ongoing (**TACTI-mel**)



# **IMP321** in Metastatic Breast Cancer (MBC)

**Potential Approval Pathway** 



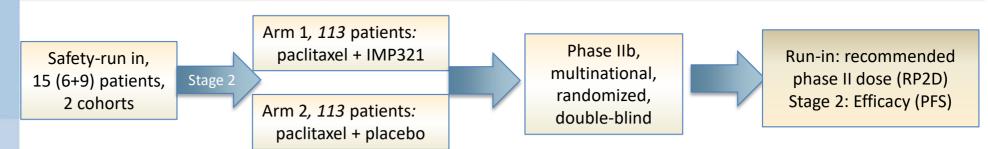
#### → Primary target population for IMP321 is HR+/HER2neu<sup>-</sup> MBC

- After hormone therapy → taxane/anthracycline based chemotherapy
- Median PFS/OS at the start of chemotherapy is between 5-9 months/~24 months
- → Unmet medical need with no major improvements in recent years

PRIMA BIOMED

## AIPAC (chemo-immunotherapy)

#### AIPAC trial (phase IIb): Active Immunotherapy PAClitaxel, MBC patients, different EU countries



Primary Objective	Run-In: Recommended phase II dose Stage 2: Efficacy (PFS) of paclitaxel + IMP321 vs. paclitaxel + placebo
Other Objectives	Anti-tumour activity of IMP321, safety and tolerability of IMP321, pharmacokinetic and immunogenic properties of IMP321, quality of life
Patient Population	Advanced MBC indicated to receive first line chemotherapy with weekly paclitaxel
Treatment	Run-in: IMP321 (6 or 30 mg) + Paclitaxel Arm 1: Paclitaxel + IMP321 Arm 2: Paclitaxel + Placebo
Countries	NL, BE, HU, UK → overall 30-35 sites in 5 -7 countries planned

#### **Status report**

- ✓ Safety run-in completed successfully
- ✓ Both dose levels (6 + 30 mg) of IMP321 confirmed to be safe w/o DLTs by DEC at 30<sup>th</sup> Dec 2016
- Randomized phase to start early 2017
- Interim-data of safety run-in expected mid of 2017



## **AIPAC - Initial Data**

#### Safety as of Dec 2016:

#### •6 mg IMP321 + Paclitaxel (n=6):

➤ No DLTs, well tolerated and safe; increase of CD8 T-cell and monocyte count after treatment with IMP321

#### •30 mg IMP321 + Paclitaxel (n=9)

➤ No DLTs, well tolerated and safe; increase of CD8 T-cell and monocyte count after treatment with IMP321

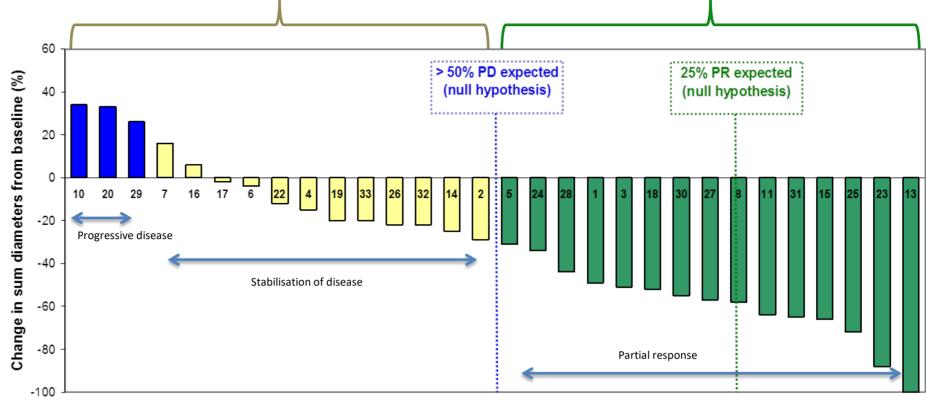


### **Completed Studies - Efficacy**

Efficacy results of a phase I trial of IMP321 + paclitaxel in MBC compared to historical paclitaxel monotherapy\*

Clinical benefit: Only 10 % of IMP321 patients progressed in contrast to more than 50% of patients in the historical control group

A 50% response rate was observed in IMP321 patients versus 25% in the historical control group receiving chemotherapy alone

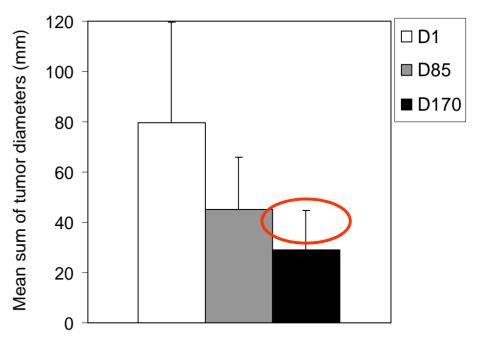


<sup>\* 254</sup> patients with measurable disease at baseline on weekly, 3 weeks out of 4, paclitaxel (ECOG 2100 study); J Clin Oncol. 2009 Oct 20;27(30):4966-72.

## Completed studies - Efficacy

Efficacy results of a phase I trial of IMP321 + paclitaxel in MBC "Late response effect"

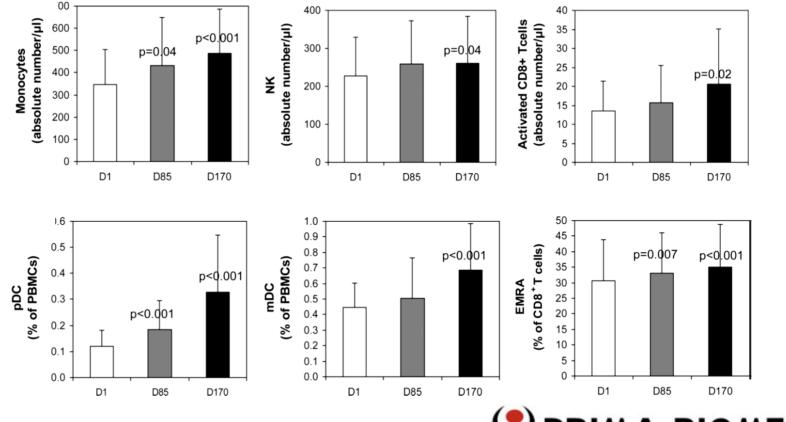
- → Clear evidence of immune involvement
- Further tumor regression between day 85 and day 170 <u>which is not seen</u> <u>with chemo alone</u>
- Such late responses are <u>characteristic</u> <u>of immunotherapy</u>

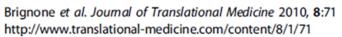




## Completed studies - "Proof of principle"

- Increased primary (monocytes and dendritic cells (DC)) and secondary target (Natural killer (NK) cells and activated CD8 and memory CD8 T cells) cell counts
- Sustained for ≥ 6 months (analyzed 13 days after the last injection and before the next IMP321 injection)







## **IMP321 MBC Market Opportunity**

- **30%** of breast cancer patients are metastatic (at diagnosis or more frequently through recurrence)<sup>1</sup> and 2 out of 3 are HR positive<sup>2</sup>
- Metastatic breast cancer (MBC) patients have a **median survival** of **2-4 years**<sup>3</sup>
- 5-year relative survival rate is only approximately 22%<sup>4,5</sup>
- MBC currently remains almost incurable<sup>6</sup>

• In the U.S., annual indirect cost to society attributable to MBC for women under 65 was

estimated to be **over US\$ 572 million** including<sup>7</sup>:

US\$ 270 million Premature deaths

US\$ 253 million Lost productivity

US\$ 50 million Caregiving

The global breast cancer treatment market will reach US\$17.2 billion by 2021.8

• HER2-HR+ patient group is our primary target: currently only hormone therapy followed by chemotherapy is applied with limited outcome improvement9

HER2+, HR~10%

HER2+, HR+
~15%

Primary target patients

ER/PR
ER/PR+

Other fields will follow → label extension



<sup>1.</sup> O'Shaughnessy I. Extending survival with chemotherapy in metastatic breast cancer. The Oncologist, 2005

<sup>2.</sup> American Cancer Society. (2014). Hormone therapy for breast cancer. Breast Cancer. Accessed on September 30, 2014 from http://www.cancer.org/cancer/breastcancer/detailedguide/breast cancer-treating-hormone-therapy.

<sup>3.</sup> Mosher, C. E., Johnson, C., Dickler, M., Norton, L., Massie, M. J., DuHamel, K. (2013). Living with metastatic breast cancer: A qualitative analysis of physical, psychological, and social sequelae.

<sup>4.</sup> http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-survival-by-stage

<sup>5.</sup> Madell. B. Metastatic breast cancer: Life expectancy and prognosis. Healthline. 2014 at http://www.healthline.com/health/breast-cancer/metastatic-prognosisF# Overview 1

 $<sup>6.\</sup> American\ Cancer\ Society.\ (2013).\ Detailed\ Guide:\ Breast\ cancer.\ American\ Cancer\ Society.\ Accessed\ on\ September\ 6,\ 2014\ at$ 

<sup>7.</sup> Sorensen, S. V. et al. (2012). Incidence-Based Cost-Of-Illness model for metastatic breast cancer in the United States. International Journal of Technology Assessment in Health Care, 28 1.http://dx.doi.org.proxy1.athensams.net/10.1017/S026646231100064X.

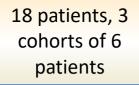
<sup>8.</sup> http://www.researchandmarkets.com/research/mg3gms/breast\_cancer

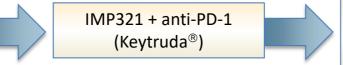
http://www.researchandi
 Decision Resources 2010

## **IMP321** in Melanoma

TACTI-mel (I-O combination)

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





Phase I, multicenter, open label, dose escalation Recommended phase II dose Safety and tolerability

Primary Objective	Recommended dose for phase II (RP2D) with IMP321 + pembrolizumab Safety + tolerability
Other Objectives	PK and PD of IMP321, response rate, time to next treatment, PFS
Patient Population	Unresectable or metastatic melanoma with asymptomatic or suboptimal response after 3 cycles of pembrolizumab
Treatment	3 cohorts: 1/6/30 mg IMP321; s.c. q2w + pembrolizumab; starting with the 5 <sup>th</sup> cycle of pembrolizumab

#### **Status report**

- ✓ First dose escalation (1  $\rightarrow$  6 mg) successfully confirmed by DSMB in Dec 2016
- Start of cohort 2 (6 mg) in Jan 2017
- Enrolment completion expected in 2017





# IMP321: COMPETITIVE LANDSCAPE



# **Competitive Landscape: APC Activators**

 Agonist anti-CD40 mAb: in development with anti-PDL-1 antibody by F. Hoffmann-La Roche Ltd

Phase Ib, 135 patients with locally advanced and/or metastatic solid tumors, estimated completion in Dec. 2017

- Toll-Like Receptors
  - Dynavax (DVAX) TLR9 agonist SD101 (in trials with Keytruda)
  - Immune Design (IMDZ) TLR4 agonist
  - Celgene (CELG) partnered with VentiRx (private) for TLR8 agonist



# LAG-3 Competitive Landscape (Blocking mAbs)

<b>Clinical Progra</b>	ms						Es	stimated
<b>Product Candi</b>	Company	Condition	Combination	Phase	Status	Start Date	Enrollment	Study Completion
BMS 986016	BMS	Glioblastoma; Gliosarcoma; Recurrent Brain	Nivolumab	1	Recruiting	August 2016	68	December 2019
BMS 986016	BMS	Neoplasms by Site	Nivolumab	1	Recruiting	October 2013	360	October 2019
BMS 986016	BMS	Hematologic Neoplasms	Nivolumab	1/2a	Recruiting	February 2014	132	January 2020
BMS 986016	BMS	Advanced Gastric Cancer	Nivo/ Ipi	2	Recruiting	November 2016	910	November 2021
BMS 986016	BMS	Advanced Cancer	Nivo/ Ipi/ Dasatinib	2	Recruiting	May 2016	504	April 2021
BMS 986016	BMS/Ono	Cancer	Nivolumab	1	Recruiting	November 2016	27	July 2020
BMS 986016	BMS	Advanced Renal Cell Carcinoma	Nivo/ Ipi	2	Not Open	January 2017	650	January 2022
MK4280	Merck & Co. Inc.	Advanced Cancer	Pembrolizumab	1	Recruiting	May 2016	70	August 2020
REGN3767	Regeneron/Sanofi	Malignancies	REGN2810	1	Recruiting	November 2016	283	July 2020
GSK2831781	GSK*/ Parexel	Psoriasis		1	Recruiting	July 2014	67	July 2018
LAG525	Novartis*	Advanced Solid Tumors	PDR001	1/2	Recruiting	June 2015	416	October 2016

Preclinical Programs		
Company (program)	Program	Condition
Agenus/ Incyte		Cancer
Boehringer Ingelheim/ Sarah Cannon Research	754091(anti- PD-1) and	Cancer
Institute	BI 754111 (anti-LAG 3)	
Macrogenics	(MGD013)	Cancer
Peregrine Pharmaceuticals		Cancer
RXi Pharmaceuticals/ Mirlmmune		Cancer
Tesaro	(TSR-033)	Cancer

<sup>\*</sup> Prima partner

Sources: company websites, clinical trials.gov, Biomedtracker, Medtrack, Datamonitor, and sec.gov As of January 3, 2017



# **PARTNERED PROGRAMS**



# **IMP731** for Autoimmune Diseases

GSK's investigational product, GSK2831781, which is derived from IMP731 antibody, aims to kill the few activated LAG-3+ T cells that are auto-reactive in autoimmune disease leading to long term disease control without generalized immune suppression

- GlaxoSmithKline holds exclusive WW rights to IMP731
- Jan 2015: Prima announced a single-digit million US\$ milestone
- Up to £64m in total upfront and potential milestones + royalties
- Study completion date: April 2018 with 63 pts. (see http://www.gsk-clinicalstudyregister.com/study/200630#ps)
- GSK2831781 in Phase I trials with potential regulatory filing expected within 2021-2025 timeframe (See from slide 108 of GSK investor presentation, 11/03/15)
- European Patent grants with patent number 142210 in August 2016



# **NOVARTIS** IMP701: Antagonist mAb for cancer

IMP701 is an anti-LAG-3 mAb that blocks LAG-3-mediated immune down-regulation

LAG-3 is a prime target for immune checkpoint blockade as it is readily expressed at a high level in many human tumors.

- Novartis holds exclusive WW rights
- Aug 2015: Start of Phase I study by Novartis
- 13 different indications
- Estimated study completion date is October 2018
- Enlarged enrollment from 240 up to 416 pts.
- LAG-525 is used in combination with PD-1 in solid tumors



# **IMP761**

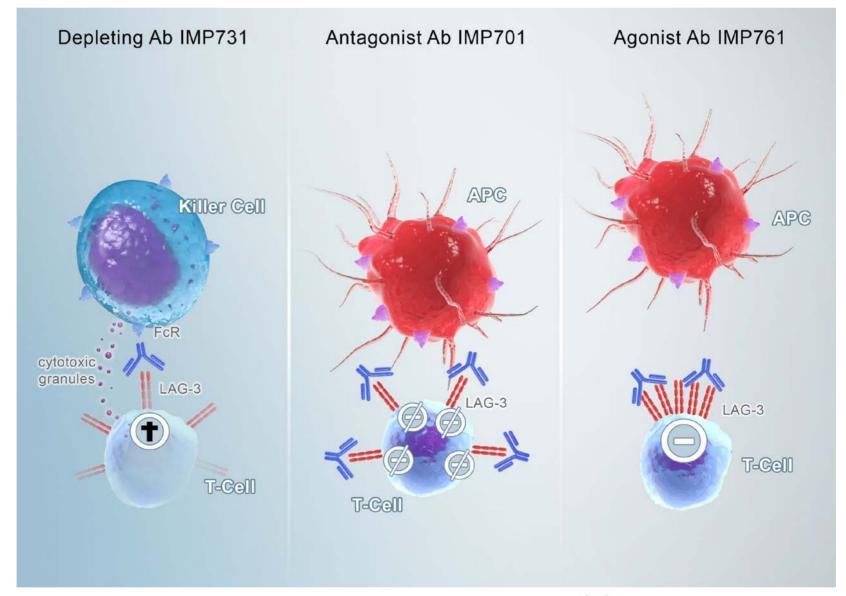


# **IMP761: Key Properties**

- IMP761: humanized IgG4 monoclonal antibody
- First ever agonist of LAG-3
- Pre clinical stage:
  - In vitro:  $\sqrt{\phantom{a}}$
  - In vivo: during 2017
- Supposed MoA: temporarily switching off activated LAG-3+ T cells



# **IMP761:** a different MoA





# POTENTIAL MILESTONES



# Expected LAG-3 data (2017)

- IMP321
  - AIPAC: immune monitoring and activity data (safety run-in phase), mid 2017
  - TACTI-mel: further dose escalation, safety and activity data throughout 2017
- IMP761: preclinical data
- IMP701: program updates
- IMP731: program updates



# **Corporate Snapshot**

Ticker symbol	PBMD (NASDAQ - ADRs) PRR (Australian Securities Exchange)
Securities on issue*	<ul><li>2.07 billion ordinary shares</li><li>77.38 million listed options @ A\$0.20</li><li>6.3 million issued ADRs***</li></ul>
Cash & Term Deposits**	~A\$16.57 million
Market Cap*	A\$74.63 million (US\$54 million)
Avg. Vol. (3 m)*	1,122,580 ordinary shares on ASX 156,890 ADRs on NASDAQ
Grant Support:	Australian tax credit (43.5% of eligible R&D spent) French tax credit (30% of eligible R&D spent)

<sup>\*</sup>Market references as of 2nd Jan 2017 summarizing listed securities on issue. For a detailed summary of all securities on issue refer to latest Appendix 3B released on ASX.

<sup>\*\*\*</sup> As of 28<sup>th</sup> December 2016 (i.e. the effective date of the announced ADR ratio change) each ADR represents 100 ordinary shares. Previously 1 ADR represented 30 ordinary shares.



<sup>\*\*</sup> As of 31st of Dec 2016



Thank you!