TACTI-mel, Two ACTive Immunotherapies in Melanoma: Combination of IMP321 (LAG-3Ig) with an Anti-PD-1 Antagonist in a Phase I Trial

Frédéric Triebel, CSO/CMO

24th International Molecular Medicine Tri-Conference - Cancer Immunotherapy
February 20, 2017
San Francisco, CA.

PRIMA BIOMED

ASX:PRR; NASDAQ:PBMD

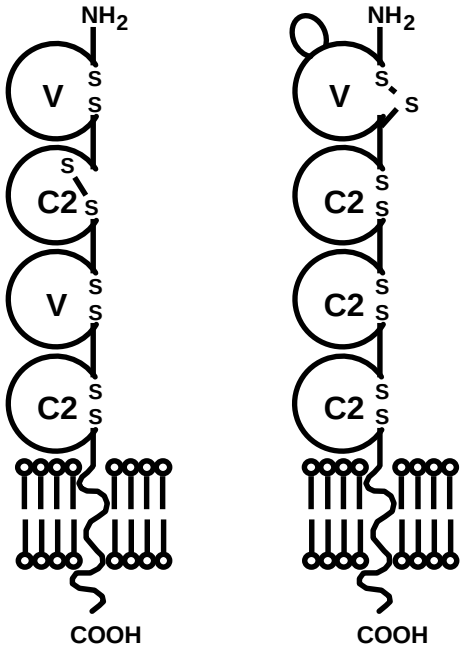
Notice: Forward Looking Statements

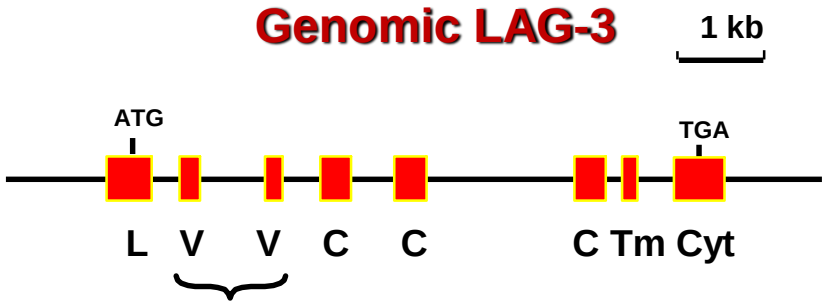
The purpose of the presentation is to provide an update of the business of Prima BioMed Ltd ACN 009 237 889 (ASX:PRR; NASDAQ:PBMD). These slides have been prepared as a presentation aid only and the information they contain may require further explanation and/or clarification. Accordingly, these slides and the information they contain should be read in conjunction with past and future announcements made by Prima BioMed and should not be relied upon as an independent source of information. Please refer to the Company's website and/or the Company's filings to the ASX and SEC for further information.

The views expressed in this presentation contain information derived from publicly available sources that have not been independently verified. No representation or warranty is made as to the accuracy, completeness or reliability of the information. Any forward looking statements in this presentation have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside Prima BioMed's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this presentation include known and unknown risks. Because actual results could differ materially to assumptions made and Prima BioMed's current intentions, plans, expectations and beliefs about the future, you are urged to view all forward looking statements contained in this presentation with caution. This presentation should not be relied on as a recommendation or forecast by Prima BioMed. Nothing in this presentation should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

PRIMA BIOMED

Lymphocyte Activation Gene-3 (LAG-3 or CD223)

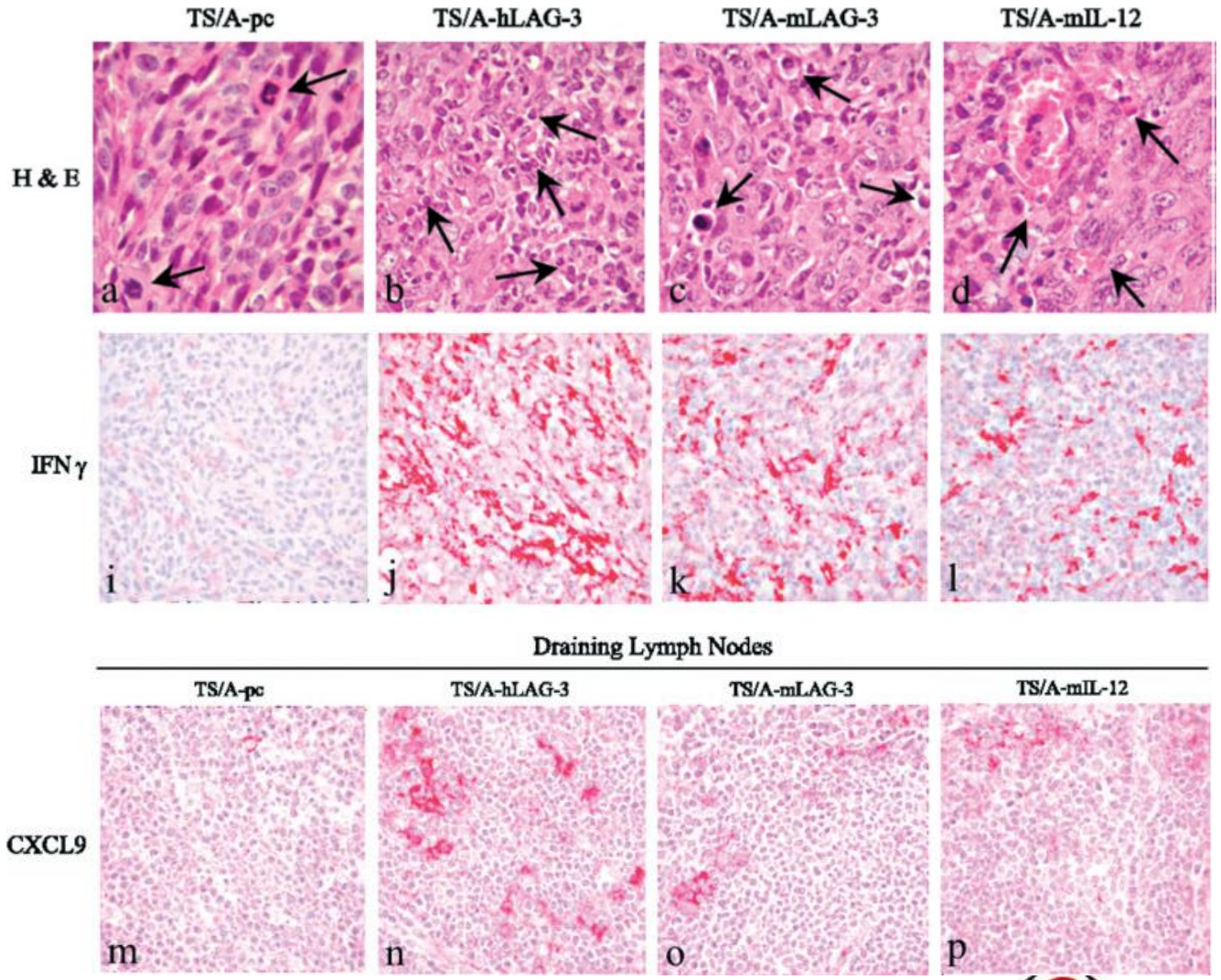




- 4-IgSF domain transmembrane proteins.
- Same genomic organization
  (intron in D1, duplication event D1D2 vs D3D4)
- Close proximity on 12p13.

PRIMA BIOMED

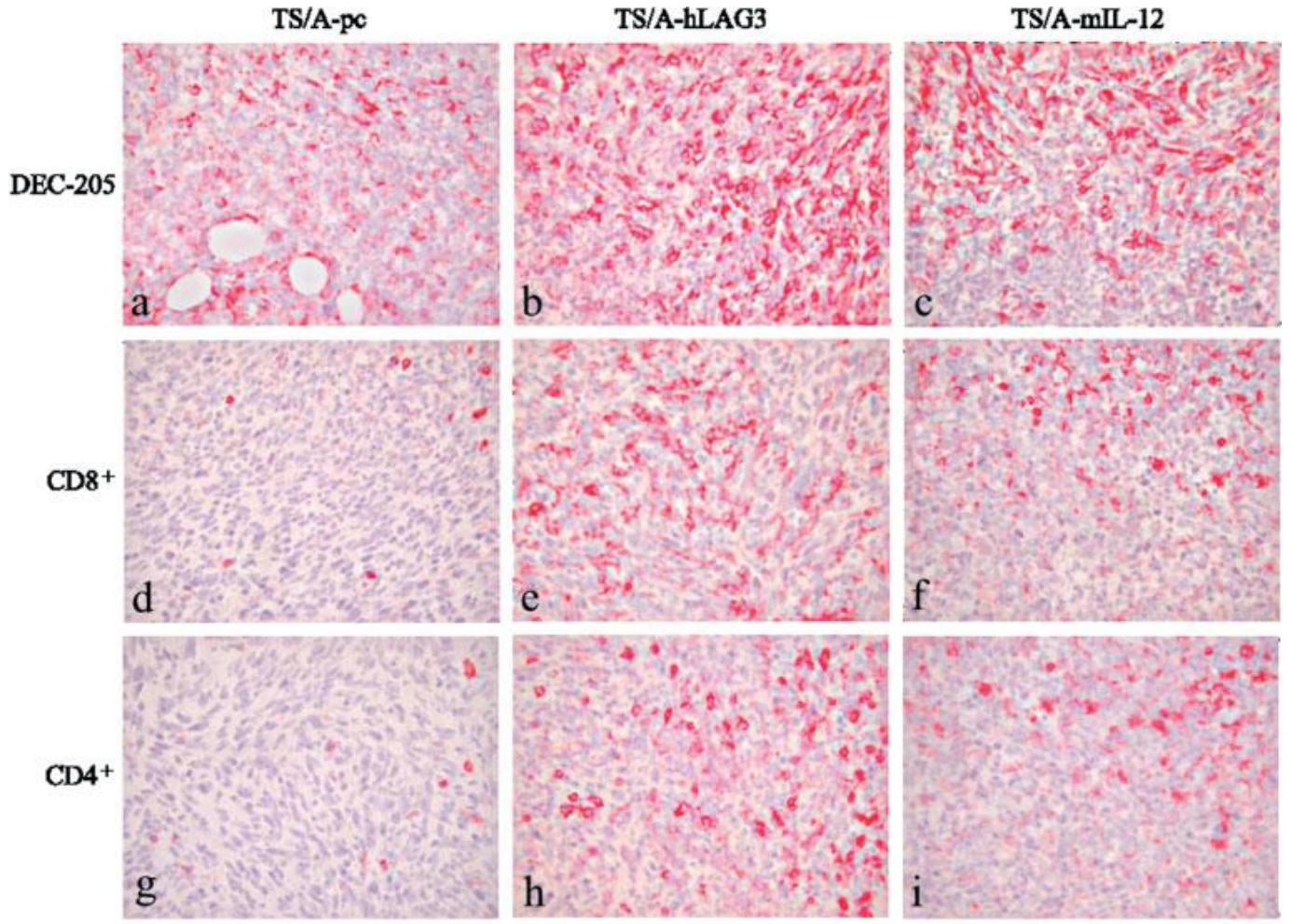
Immunological mechanisms elicited at the tumour site by LAG-3 versus IL-12: sharing a common Th1 anti-tumour immune pathway



J Pathol 2005; 205: 82–91

PRIMA BIOMED

Immunological mechanisms elicited at the tumour site by LAG-3 versus IL-12: sharing a common Th1 anti-tumour immune pathway



J Pathol 2005; 205: 82–91

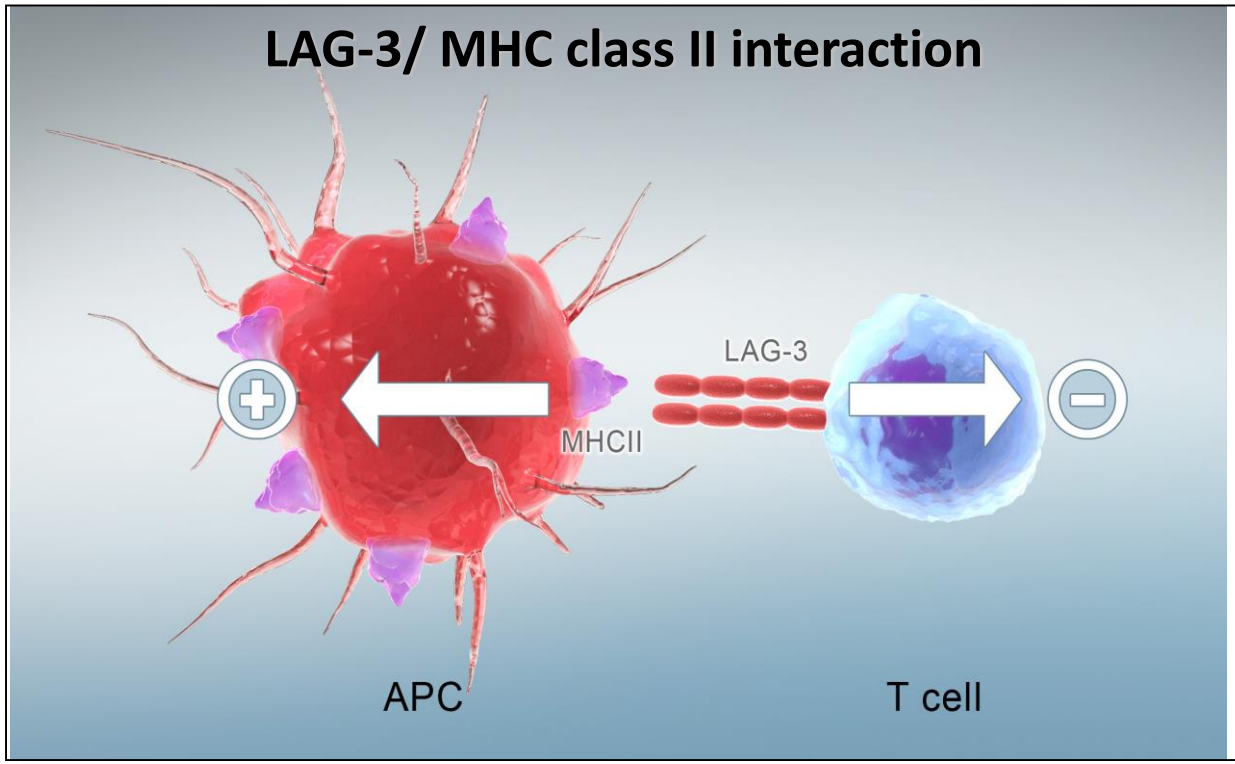
PRIMA BIOMED

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®)

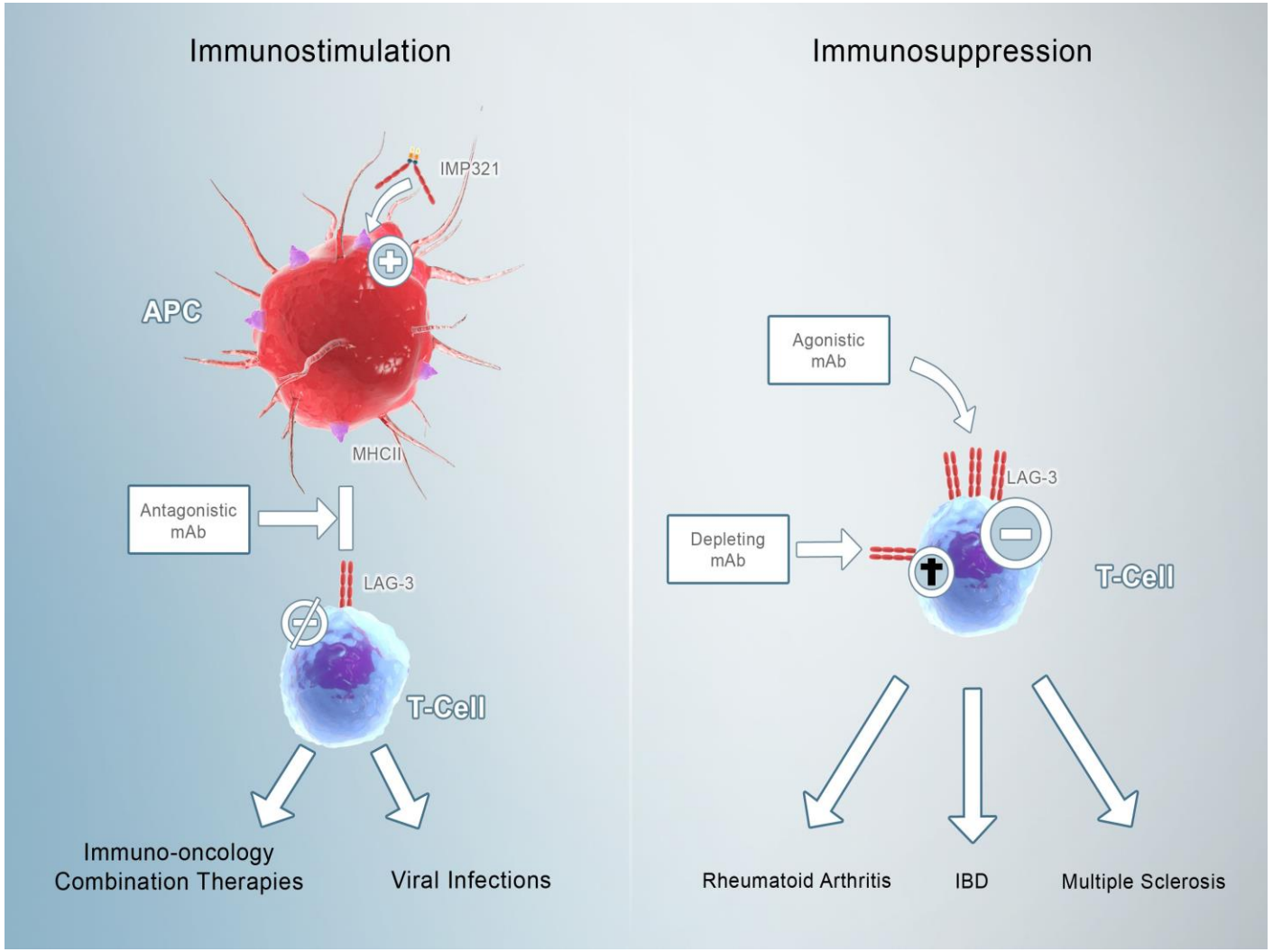


→ **Positive regulation** of antigen presenting cells (APC) → increase in antigen presentation to cytotoxic $CD8^+$ T cells

→ **Negative regulation** of $LAG\text{-}3^+$ T cells

PRIMA BIOMED

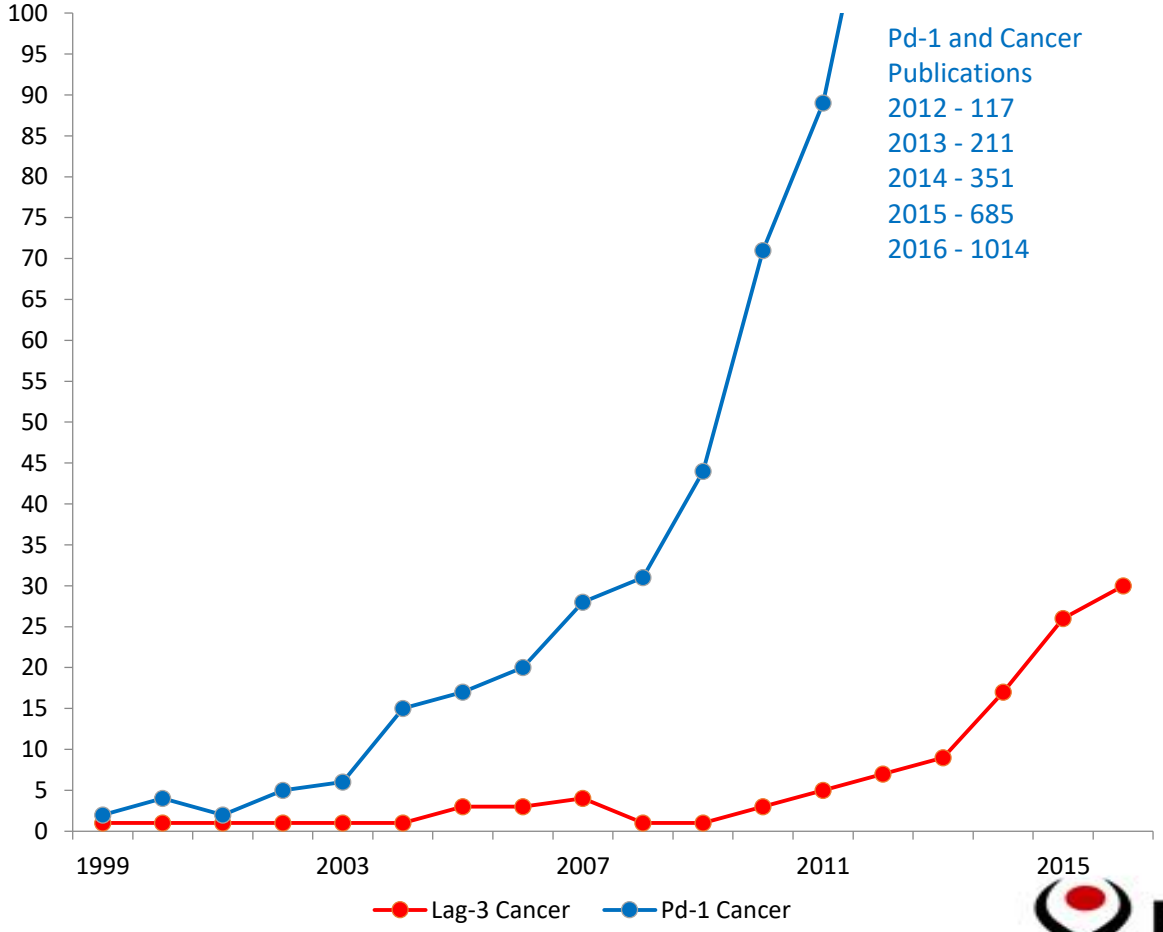
Targeting LAG-3 May Lead to Multiple Therapeutics in Numerous Indications



PRIMA BIOMED

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“



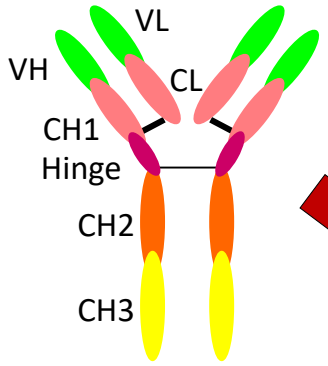
PubMed searches of “Lag-3 Cancer“ and “Pd-1 Cancer“ from January 1, 1999 – December 6, 2016

PRIMA BIOMED

LEAD PRODUCT IMP321

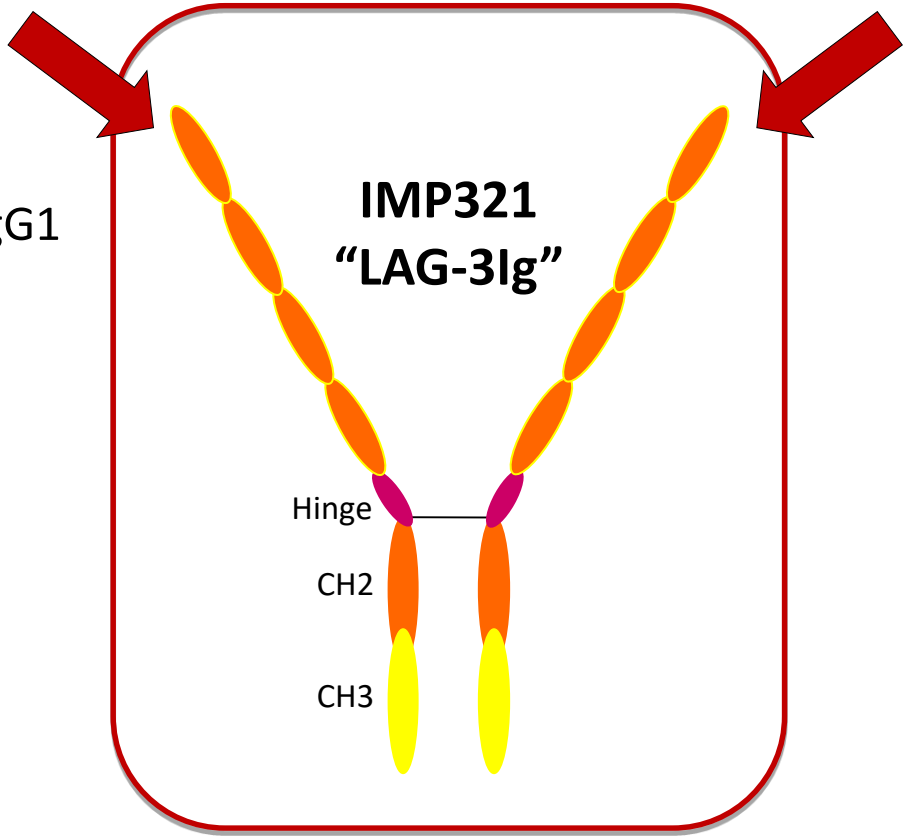
PRIMA BIOMED

IMP321



Human IgG1

Soluble LAG-3

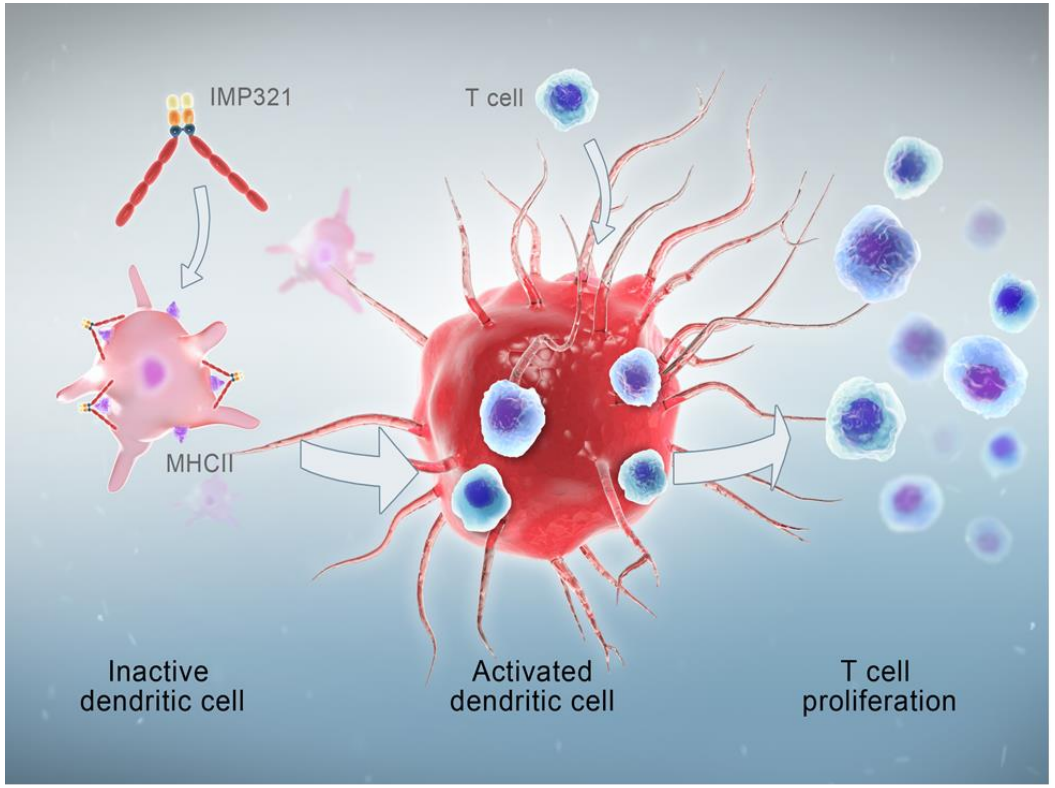


- **Soluble recombinant form of LAG-3**
- Human fusion protein
- Dimeric, very stable, high affinity for DC
- Antigen presenting cell (APC) activator
- **Unique and first-in-class**

PRIMA BIOMED

IMP321

Soluble dimeric recombinant form of LAG-3Ig (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

PRIMA BIOMED

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

PRIMA BIOMED

Three groups of patients responding to anti-PD-1 (IFN-γ signature)

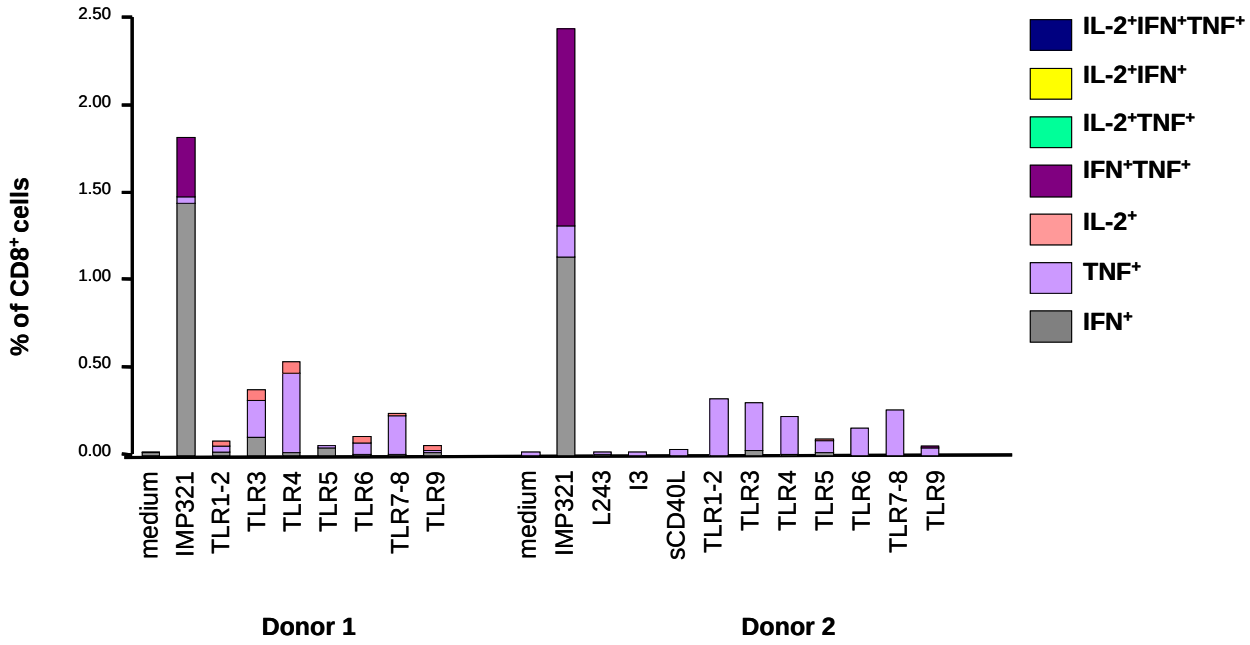
- A- Inflamed responders – respond to anti-PD-1
- B- Inflamed non-responders (some infiltrates in the tumor margins but no response)
- C- Non inflamed. “Cold tumor” with no response

- Optimal checkpoint combos will target groups B and C and help them:
  - Promote cross presentation of tumor antigens
  - Induce T cell recruitment into tumor microenvironment

PRIMA BIOMED

IMP321 induces a better Tc1 differentiation than sCD40L or TLR agonists

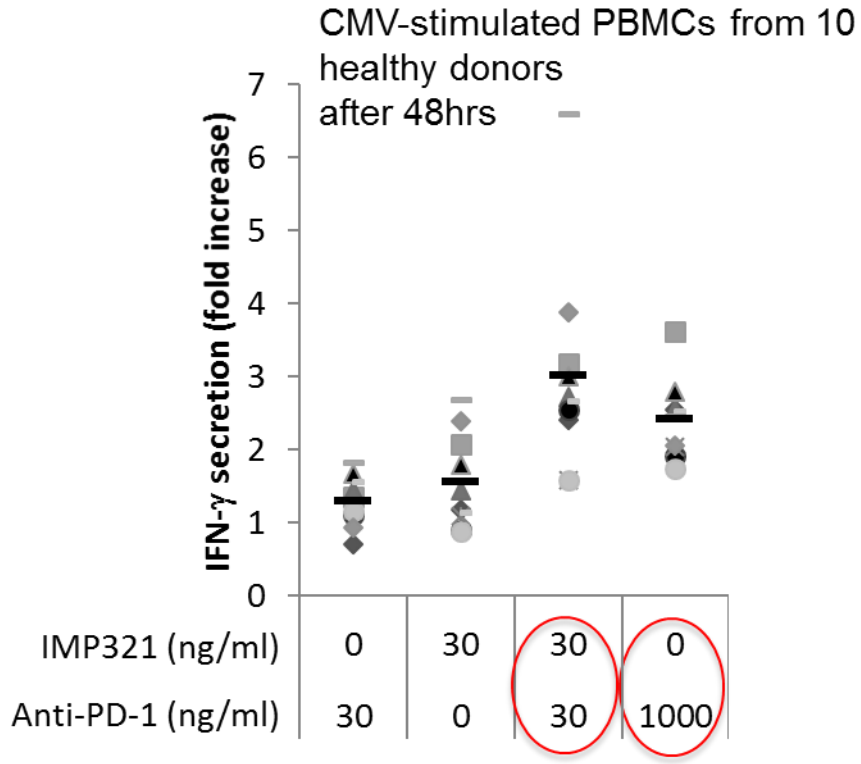
- **Human blood lymphocytes are analyzed in a 16 hr *ex vivo* assay**
- **Intracellular staining of CD8 T cells**
  - **Only IMP321 induces IFN$^+$ CD8 T cell responses**
  - **TLR agonists but not IMP321 induce IL-10 production which suppresses Tc1 differentiation**



PRIMA BIOMED

In vitro preclinical data supporting the combination

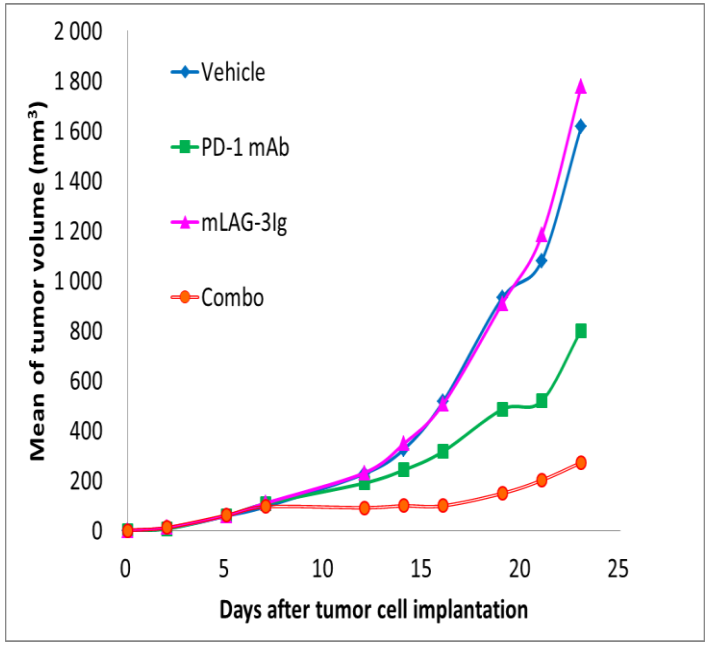
- **Synergistic effect for the combination at low dose: 30 ng/ml IMP321 + 30 ng/ml anti-PD1 mAb**
- **A better IFN-γ inducing effect than the blocking anti-PD-1 mAb concentration (1,000 ng/ml)**
  - **« Pushing the gas » (IMP321) and « releasing the brake » on CD8 T cell responses: a synergistic combination**



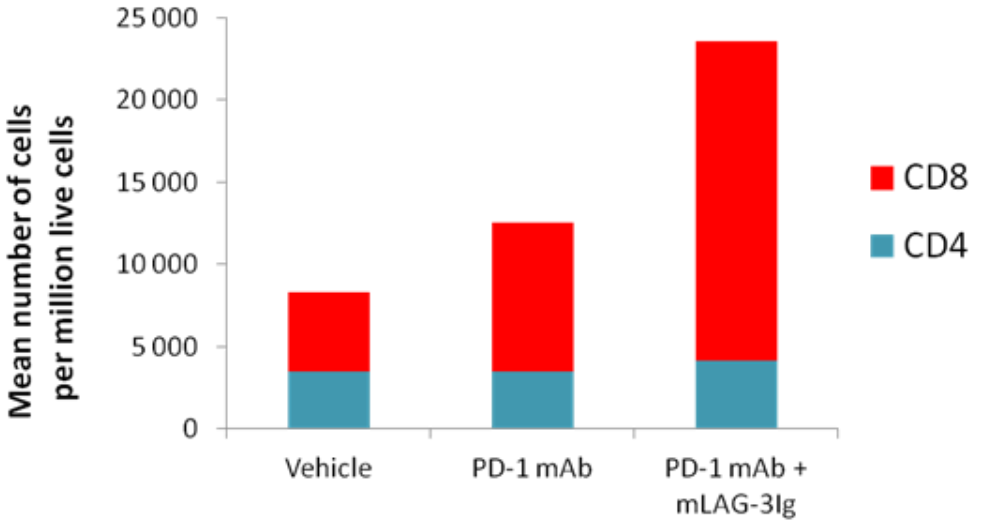
PRIMA BIOMED

In vivo preclinical data supporting the combination

Anti-PD-1 (10 mg/kg) + mLAG-3Ig (1 mg/kg)
in a subcutaneous CT26wt colon cancer model



Increase in the number of TILs at day 10
in a subcutaneous CT26wt colon cancer model



PRIMA BIOMED

IMP321 in Melanoma

TACTI-mel (I-O combination)

TACTI-mel trial: Two ACTive Immunotherapeutics in melanoma

18 patients, 3 cohorts of 6 patients → IMP321 + anti-PD-1 (Keytruda®) → 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 5th cycle of pembrolizumab

Status report

- Start of cohort 2 (6 mg) in Jan 2017
- Enrolment completion expected in Q3 2017

6 sites in Australia

PRIMA BIOMED

Thank you

Frédéric Triebel, CSO/CMO
24th International Molecular Medicine Tri-Conference - Cancer Immunotherapy
February 20, 2017
San Francisco, CA.

PRIMA BIOMED
ASX:PRR; NASDAQ:PBMD