



**The global leader in developing  
LAG-3 therapeutics**

**Investor Presentation  
November 2018**

***(ASX: IMM, NASDAQ: IMMP)***

# Notice: Forward Looking Statements

*The purpose of the presentation is to provide an update of the business of Immutep Limited ACN 009 237 889 (ASX:IMM; NASDAQ:IMMP). 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 Immutep 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.*

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*Additionally, the INSIGHT investigator sponsored clinical trial described in this presentation is controlled by the lead investigator and therefore Immutep has no control over this clinical trial. This presentation should not be relied on as a recommendation or forecast by Immutep. 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.*

# Company Snapshot

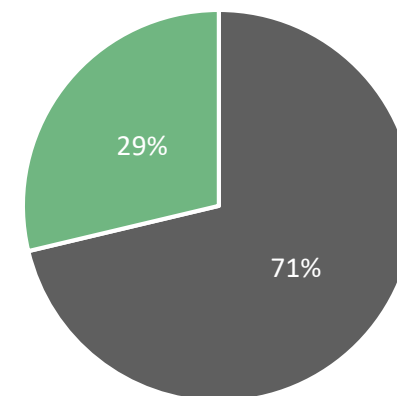
- Globally active biotechnology company with operations in Australia, Europe and U.S.
- Four LAG-3 related product candidates in development in immuno-oncology and autoimmune disease
- Committed partnerships with five of the world's largest pharmaceutical companies - Merck (MSD), Pfizer/ Merck KGaA, Novartis and GSK, along with Eddingpharm in China

## Capital Structure

<b>Ticker symbols</b>	IMM (Australian Securities Exchange) IMMP (NASDAQ)
<b>Securities on issue<sup>(1)</sup></b> (as at 6 November 2018)	3.08 billion ordinary shares 8.82 million American Depositary Shares (ADSs)
<b>Cash &amp; Term Deposits</b> (as at 30 September 2018)	A\$21.3 million (~US\$15.4 million)
<b>Market Cap</b> (as at 6 November 2018)	A\$138.6 million (~US\$100 million)
<b>Avg. Vol. (3 months)</b> (as at 6 November 2018)	6.0 million ordinary shares on ASX 180 k ADSs <sup>(1)</sup> on NASDAQ

<sup>(1)</sup> Market capitalisation based on ASX ordinary share price. For a detailed summary of all securities on issue refer to latest Appendix 3B released on ASX. Each ADS represents 100 ordinary shares.

## Shareholders

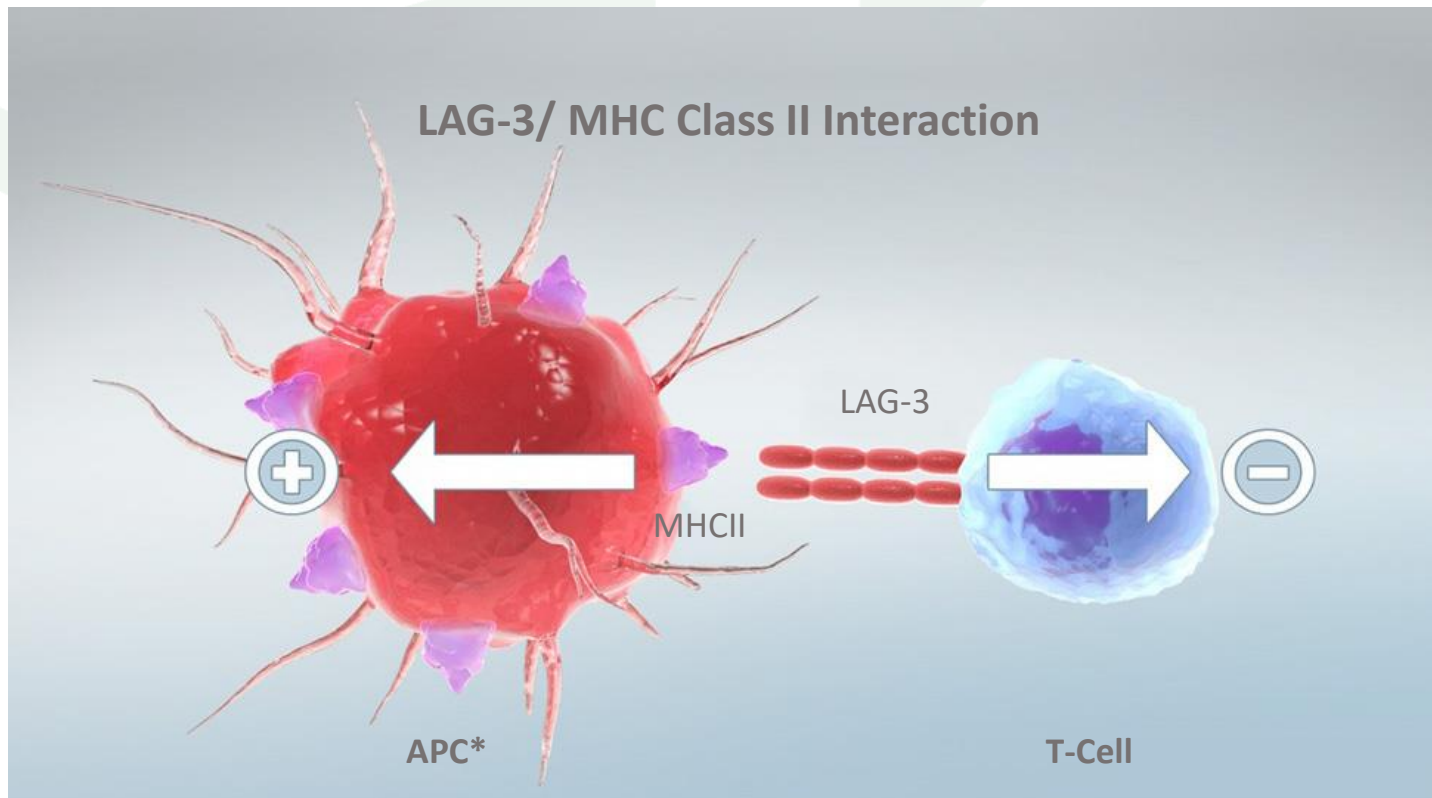


■ Australian Securities Exchange ■ Nasdaq

# LAG-3 Overview & Product Candidates

# 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**



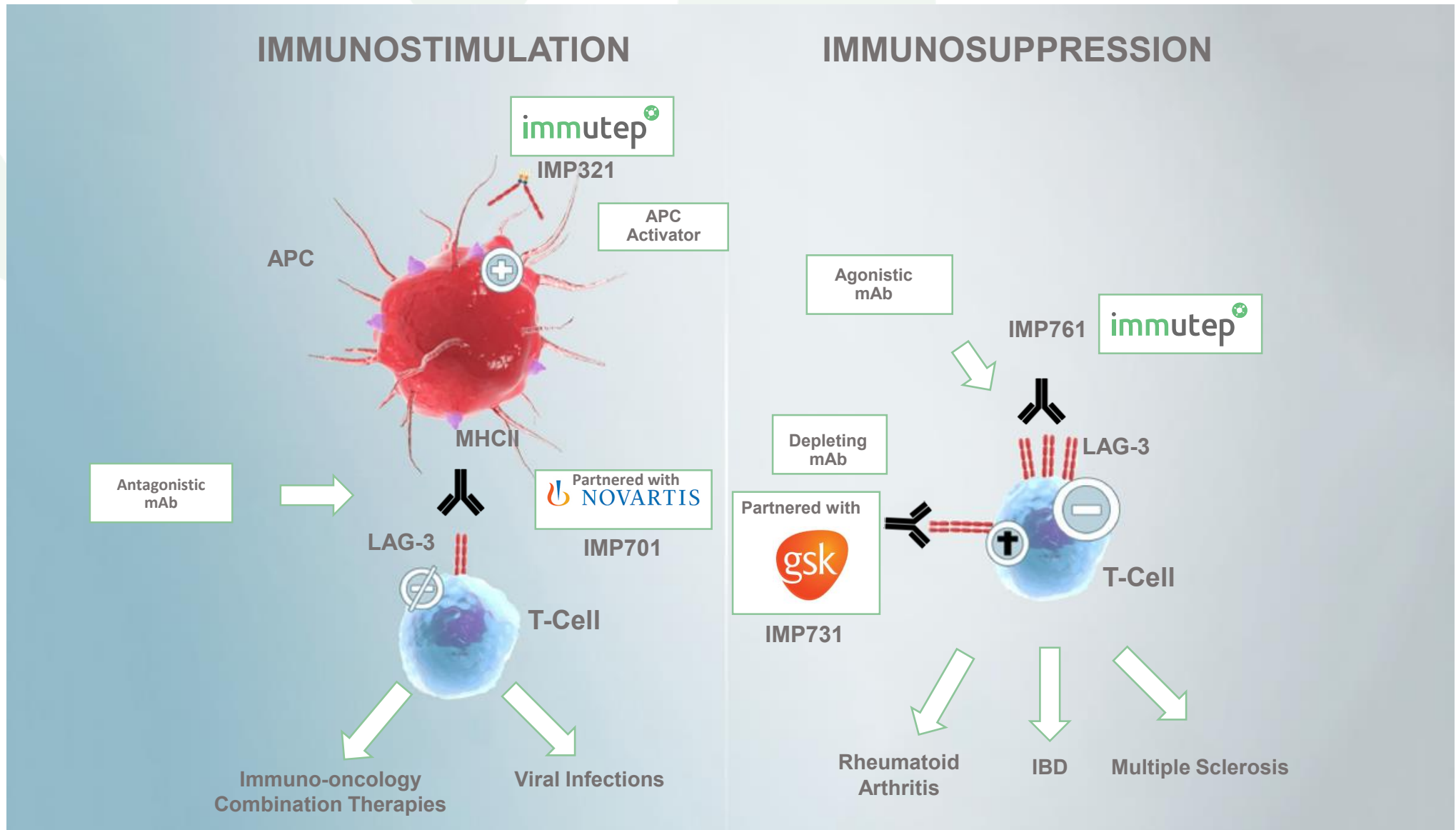
→ **Positive regulation** ↑  
of antigen presenting cells (APC) →  
increase in antigen presentation to  
cytotoxic CD8<sup>+</sup> T cells

→ **Negative regulation** ↓  
of LAG-3<sup>+</sup> T Cells













*Notes:*

\* APC: antigen presenting cell

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



# Oncology and Autoimmune Pipeline\*

Program	Preclinical	Phase I	Phase II	Late Stage	Commercial Rights/Partners
Eftilagimod Alpha (LAG-3Ig or IMP321), APC activating fusion protein	<b>AIPAC</b> (Chemo-IO Combo)			2019	 Global Rights   Chinese Rights 
	<b>TACTI-002</b> <sup>(1)</sup> (IO-IO Combo)		2019/2020		
	<b>INSIGHT-004</b> <sup>(2),(3),(5)</sup> (IO-IO Combo)	2019/2020	 Merck KGaA, Darmstadt, Germany		
	<b>TACTI-mel</b> (IO-IO Combo)	2018/2019			
	<b>INSIGHT</b> <sup>(2)</sup> (In situ Immunization)	2018/2019			
IMP731 (DepletingAB)	<b>Autoimmune Diseases</b> <sup>(4)</sup>				 Global Rights 
IMP701 (AntagonistAB)	IO-IO Combo: solid tumors IO-IO Combo: solid tumors + blood cancer Chemo-IO combo: metastatic breast cancer IO-IO Combo: melanoma <sup>(5)</sup>				 Global Rights 
IMP761 (AgonistAB)	<b>Autoimmune Diseases</b>				 Global Rights 

## Notes

- \* Actual timing of data readouts may differ from expected timing shown above.
- (1) In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC"); clinical trial is currently planned and not active.
- (2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immunetep has no control over this clinical trial.

- (3) In combination with BAVENCIO® (avelumab).
- (4) Reflects completed Phase I study in psoriasis and anticipated Phase II trial in ulcerative colitis.
- (5) Clinical trial is currently planned and not active.

# Lead Program Eftilagimod Alpha (IMP321)

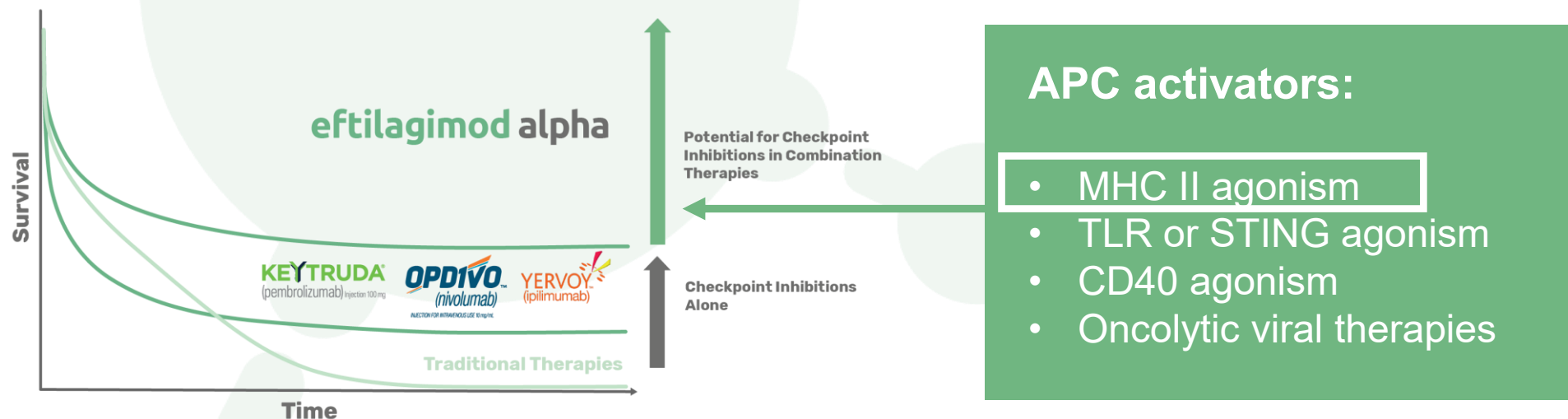
# IO Therapy Oncology Response Rates

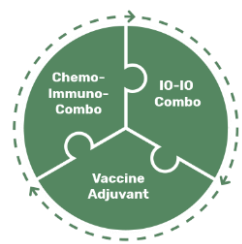
Approximately 70-80% of patients do not respond to anti-PD1 monotherapy

**How can we enable more efficacious T-cell responses?**

- Immunogenic cell death to liberate/uncover tumor antigens
- Cross-presentation of those antigens
- Recruitment of T cells into the tumor microenvironment
- Reversing the pathways driving a repressive tumor environment

**This could be achieved through the right APC activation**



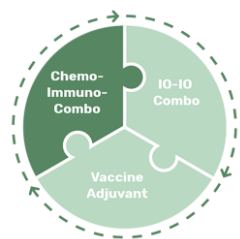


# Opportunity for Eftilagimod Alpha

**Eftilagimod has the potential to be an ideal combination candidate in oncology therapy that could improve the prognosis for patients**

## **Eftilagimod Key Characteristics (based on current data):**

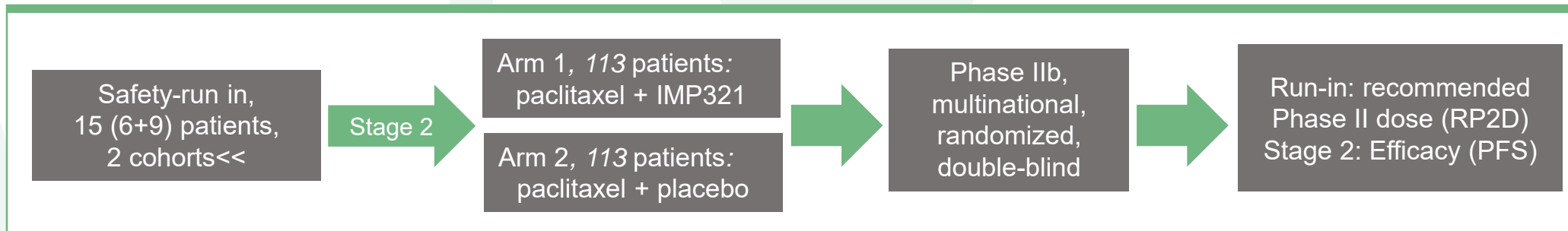
- First in class MHCII agonist
- Excellent safety profile and encouraging efficacy data thus far
- Potential for use in various combination settings (e.g. IO, chemo, vaccines or in situ immunization)
- Estimated favorable (low) cost of goods based on current flat dosing regimen and manufacturing process



# Eftilagimod Alpha in MBC (AIPAC) (chemo-immunotherapy)



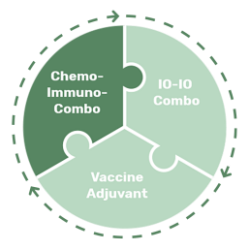
**AIPAC trial (Phase IIb): Active Immunotherapy PAClitaxel, MBC patients, different EU countries**



<b>Primary Objective</b>	Run-In: Recommended Phase II dose (RP2D) Stage 2: Efficacy (PFS) of paclitaxel + IMP321 vs. paclitaxel + placebo
<b>Other Objectives</b>	Anti-tumor activity, safety and tolerability, pharmacokinetic and immunogenic properties, quality of life of IMP321 plus paclitaxel compared to placebo
<b>Patient Population</b>	Advanced MBC indicated to receive 1 <sup>st</sup> line weekly paclitaxel
<b>Treatment</b>	Run-in: Paclitaxel + IMP321 (6 or 30 mg) Arm 1: Paclitaxel + IMP321 (30 mg) Arm 2: Paclitaxel + Placebo
<b>Countries</b>	NL, BE, PL, DE, HU, UK, FR → overall 30+ sites

## Status Report (August 2018)

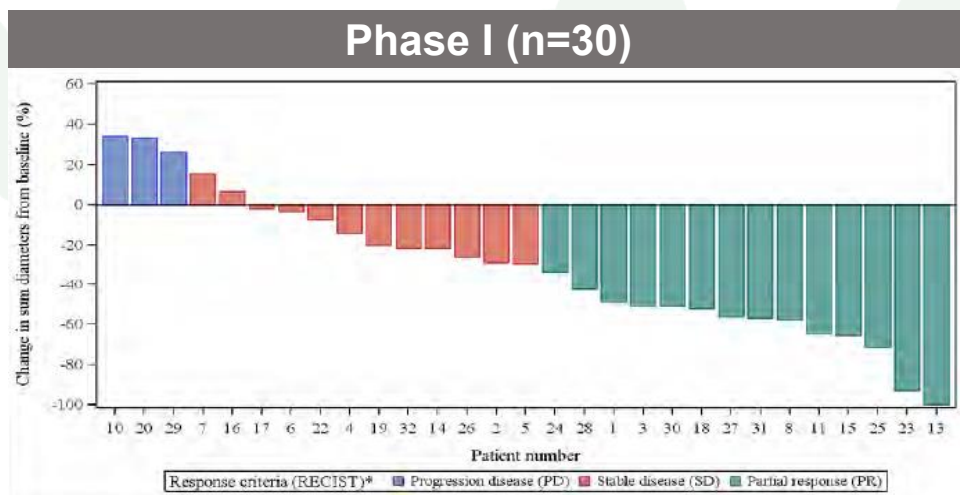
- ✓ Safety run-in completed successfully
- ✓ Randomized phase started early 2017 with the RP2D (30 mg)
- ✓ Interim-data of safety run-in presented at ASCO 2017
- ✓ To-date, efficacy and safety data in-line with historical control group/ prior clinical trials (Brignone et al Journal Translational Medicine 2010, 8:71)
- ✓ Regulatory approval to conduct trial in 7 EU countries
- ✓ Over 30 sites actively recruiting patients
- ✓ Mid-point of patient enrolment reached (June 2018)
  - Primary read out expected in 2019



# Eftilagimod Alpha Prelim. Efficacy Metastatic Breast Cancer



Observed response rates are substantially better than the 22-33% response rates seen in historical control groups with paclitaxel monotherapy



- **ORR\* of 47% and DCR\*\* of 83%**
- Responders had further tumor shrinkage between months 3 and 6

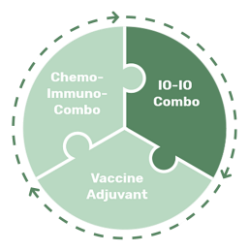
\*Overall Response Rate \*\*Disease Control Rate

Preliminary data, status Interim CSR April 2018, best response acc. To RECIST 1.1

## AIPAC – Safety Run Phase (n=15)

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%)

- **ORR of 47% and DCR of 87%**
- Two of the responses occurred relatively late (after ~6 months)



# Efti (IMP321) in Melanoma

## TACTI-mel (IO combination) – Trial Design

TACTI-mel = Two Active Immunotherapeutics in melanoma

24 patients,  
4 cohorts of 6 patients



Efti (IMP321) +  
anti-PD-1 (Keytruda®)



Phase I, multicenter,  
open label,  
dose escalation



Recommended  
Phase II dose,  
safety and  
tolerability

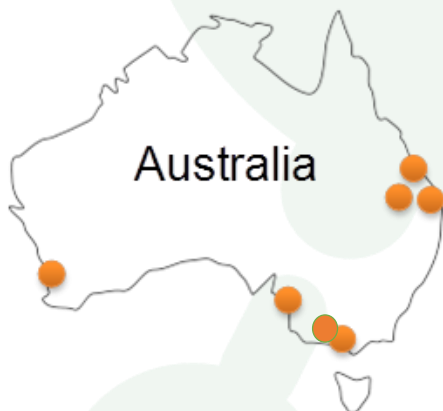
### Primary Objective

Recommended dose for Phase II with  
efti (IMP321) + pembrolizumab  
  
Safety + tolerability

### Other Objectives

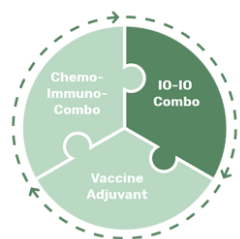
PK and PD of IMP321, response rate,  
time to next treatment, PFS

- Part A: efti (IMP321) at 1, 6 and 30 mg s.c. every 2 weeks starting with cycle 5 of pembrolizumab  
→ Status: recruitment completed; interim results on next slides
- Part B: efti (IMP321) at 30 mg s.c. every 2 weeks starting with cycle 1 of pembrolizumab  
→ Status: recruitment completed; data expected Q4
- Pembrolizumab (Keytruda®) 2 mg/kg every 3 weeks i.v. part A and B



Australia

7 sites in Australia



# Efti (IMP321) in Melanoma

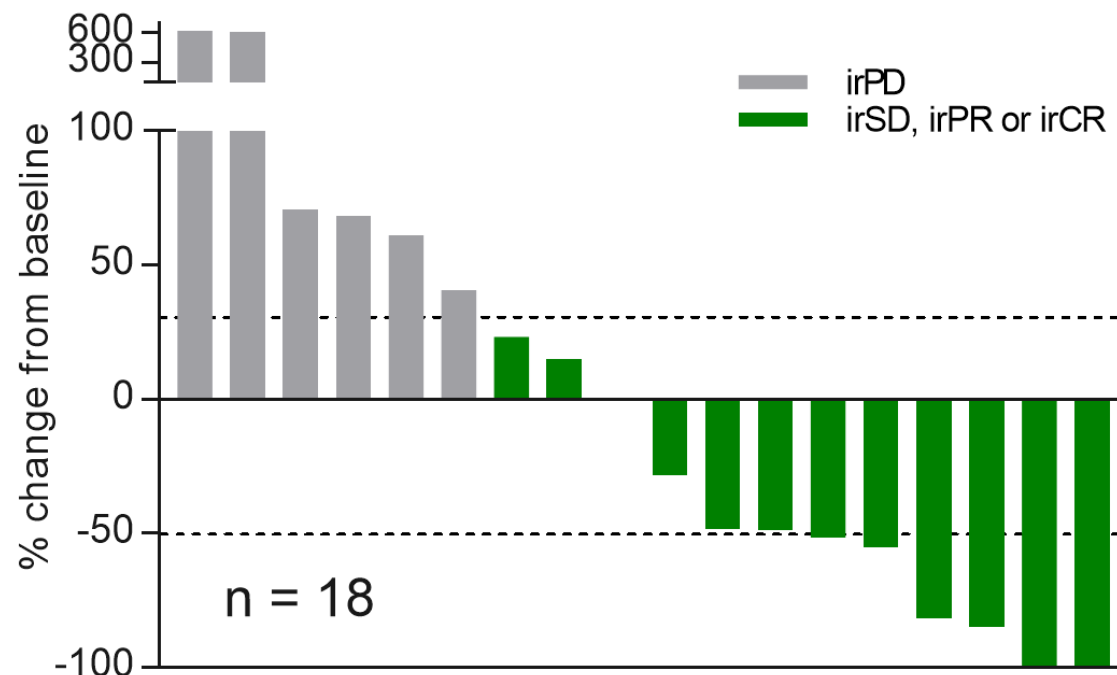
TACTI-mel (IO combination) – Results after Start of Combo (1)



Baseline Characteristics	N = 18 (%)
Elevated LDH	7 (39%)
Metastasis stage M1c	15 (83 %)
irPD/irSD to pembro after 3 cycles	12 (67 %)

Best Overall Response acc. to irRC	N = 18 (%)
Best overall response rate (ORR)	6 (33 %)
Patients with tumor shrinkage	9 (50 %)
Disease control rate	12 (66 %)

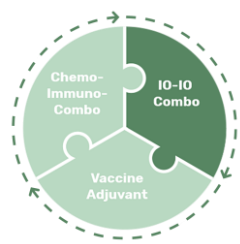
## Waterfall Plot\* (starting after 4 cycles of pembrolizumab)



\* - acc to irRC

- Patients very late stage of disease (M1c, elevated LDH)
- Majority not responding to pembrolizumab

# - incl. 1 pt with complete disappearance of all target lesions;  
CR acc. to RECIST 1.1

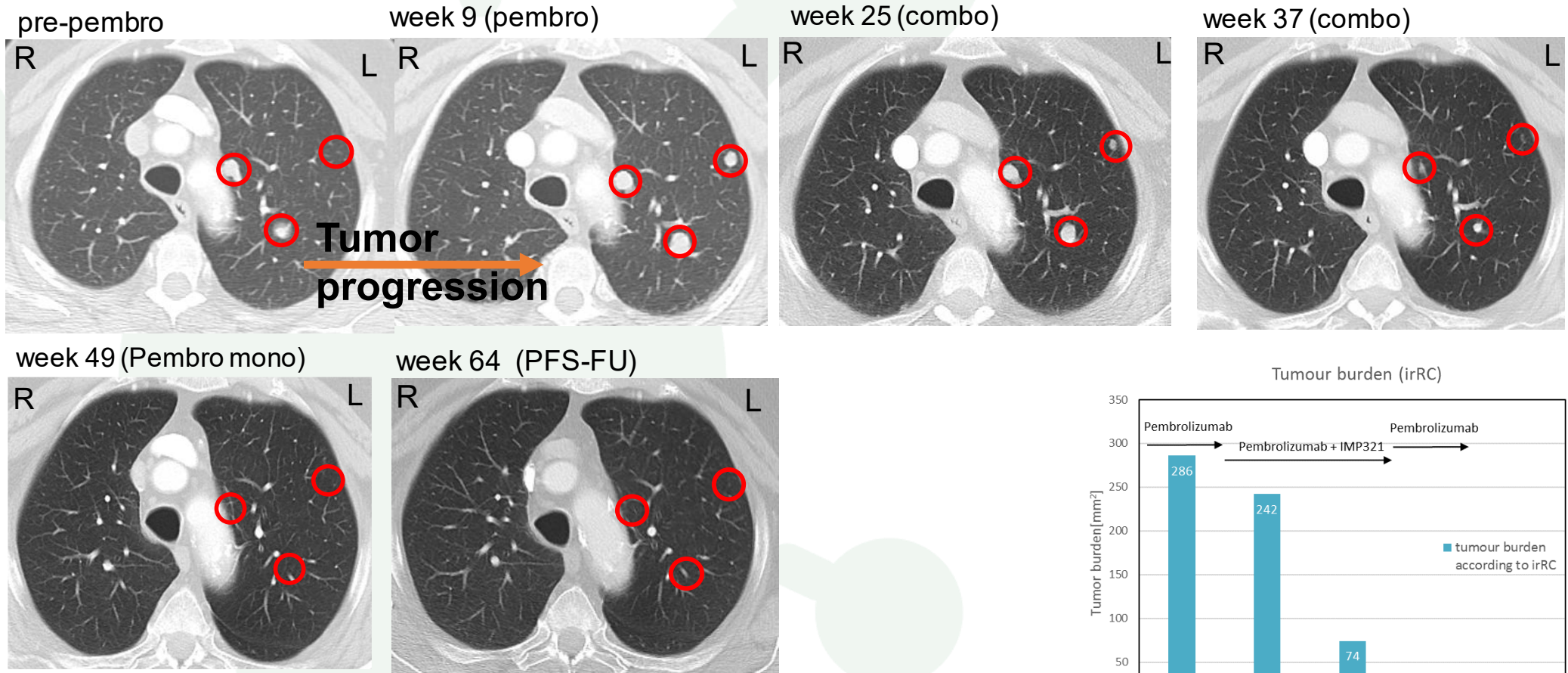


# Efti (IMP321) in Melanoma

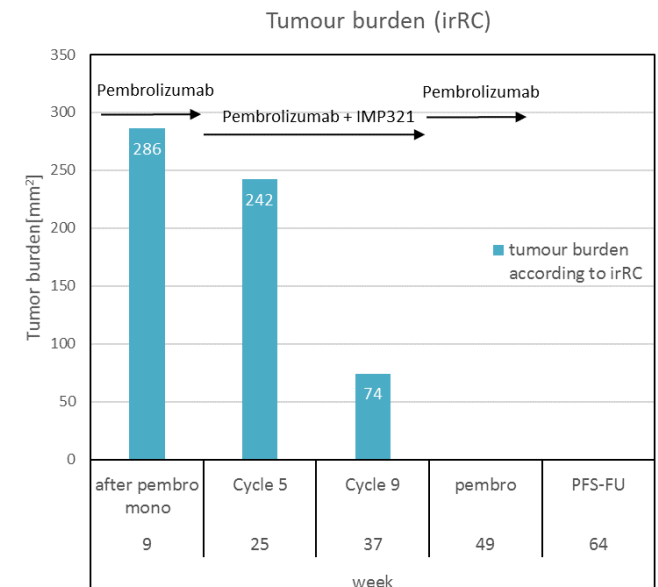
## TACTI-mel (IO combination) – Single Case at 1 mg efti



### Efficacy: Metastatic Melanoma



**All lesions disappeared → CR (confirmed)  
patient without treatment and disease free**



- In March 2018 ImmuteP entered into clinical trial collaboration and supply agreement with Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the United States and Canada) to evaluate the combination of eftilagimod alpha with MSD's anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in a new Phase II clinical trial
- The planned Phase II combinatory clinical trial, referred to as TACTI-002, will evaluate the safety and efficacy of this novel immunotherapy combination in patients in different cancer indications such as head and neck small cell carcinoma (“HNSCC”) or two different lines of non small cell lung cancer (“NSCLC”)
- The TACTI-002 clinical trial will be a Phase II, Simon two-stage, non-comparative, open-label, single-arm, multicentre clinical study
- Up to 110 patients across the three indications are planned to be treated in medical centres in Europe and the United States with the trial expected to commence in the second half of 2018

- In August 2018 ImmuteP entered into clinical trial collaboration and supply agreement with Merck KGaA, Darmstadt, Germany and Pfizer Inc., to evaluate the combination of ImmuteP's lead immunotherapy product candidate eftilagimod alpha ("efti" or "IMP321") with avelumab\*, a human anti-PD-L1 IgG1 monoclonal antibody, in patients with advanced solid malignancies
- The planned clinical evaluation will be an amendment to the existing INSIGHT Phase I clinical trial and will evaluate the safety, tolerability and recommended Phase II dose of efti when combined with avelumab in patients with advanced solid malignancies
- The Institute of Clinical Cancer Research, Krankenhaus Nordwest GmbH in Frankfurt, Germany ("IKF") will be the sponsor of the clinical trial and it will be conducted under the existing protocol of the ongoing INSIGHT clinical study. Prof. Dr. Salah-Eddin Al-Batran, the lead investigator of INSIGHT and member of ImmuteP's clinical advisory board, will continue to be the lead investigator of the trial

# Eftilagimod Alpha Partnerships



- Eddingpharm holds Chinese rights
- Chinese IND for IMP321 granted in Dec 2017 -> USD1m milestone paid to Immunetep
- EOC, an Eddingpharm spin-off holding the Chinese rights for IMP321, Phase I study in MBC expected to start Sep 2018
- Milestone and royalty bearing partnership for Immunetep



- Spin off from NEC, Japan. Est. Dec 2016; aims to develop cancer drugs discovered by artificial intelligence
- Multiple Material Transfer Agreements
- Preclinical and clinical research ongoing



- Strategic supply partnership for the manufacturing of eftilagimod alpha
- Through WuXi, Immunetep was first company ever to import and use a Chinese manufactured biologic in a European clinical trial

# IMP761 (Autoimmune Diseases)

# IMP761 – Agonist mAb

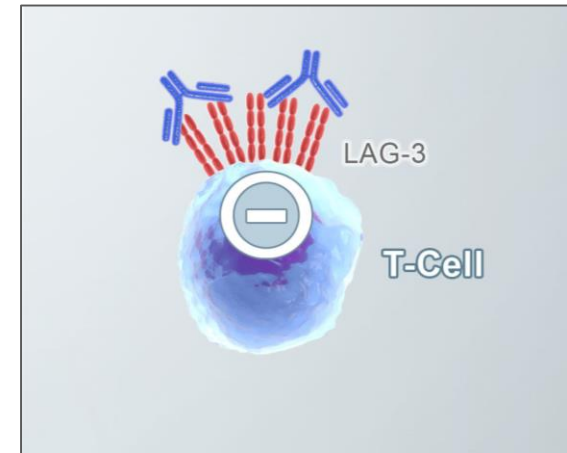
## Key Characteristics

- Humanized IgG4 monoclonal antibody
- First and best in class LAG-3 agonist mAb
- Mechanism of action: temporarily switches off LAG-3 positive chronically activated T-Cells

## Development Activities

- ✓ *In vitro/ in vivo studies* completed (cynomolgus monkey)
- ✓ Cross-reactivity studies completed
- ✓ CHO cell line development for GMP production started in Q3 2018

## IMP761



# IMP731 (Autoimmune Diseases)

# IMP731 (GSK'781) for Autoimmune Diseases



- GSK holds exclusive WW rights
- Jan 2015: ImmuteP received a single-digit million US\$ milestone payment
- Up to £64m in total upfront payments and milestones, plus royalties
- GSK2831781 in Phase I trials with potential regulatory filing expected within 2021-2025 timeframe<sup>1</sup>
- Portfolio review at GSK in 2017 -> IMP731 continued despite cancellation of 13 clinical and 20 preclinical programs
- Study completion date: March 2018 with 67 patients  
(see <http://www.gsk-clinicalstudyregister.com/study/200630#ps>)



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

<sup>1</sup> see slide 108 of GSK investor presentation of 11/03/15

# IMP701 (Cancer)

# IMP701 (LAG525) for Cancer

- Novartis holds exclusive WW rights
- August 2015: Start of Phase I study of IMP701 in combination with PDR001 (anti-PD-1 mAb) in 13 different cancer indications in 240 patients
- 1st and 2nd Milestone payments received in Aug 2015 and August 2017, respectively
- Estimated study completion date is April 2019
- December 2017: new Phase II study of IMP701 in combination with PDR001 in advanced solid and hematologic malignancies in 160 patients made public
- April 2018: two new Phase II combination studies made public that planned to begin in June/ July 2018 in triple-negative breast cancer (126 patients) and metastatic melanoma (160 patients)

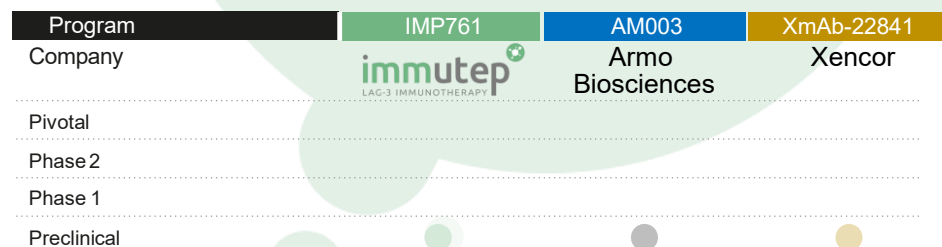
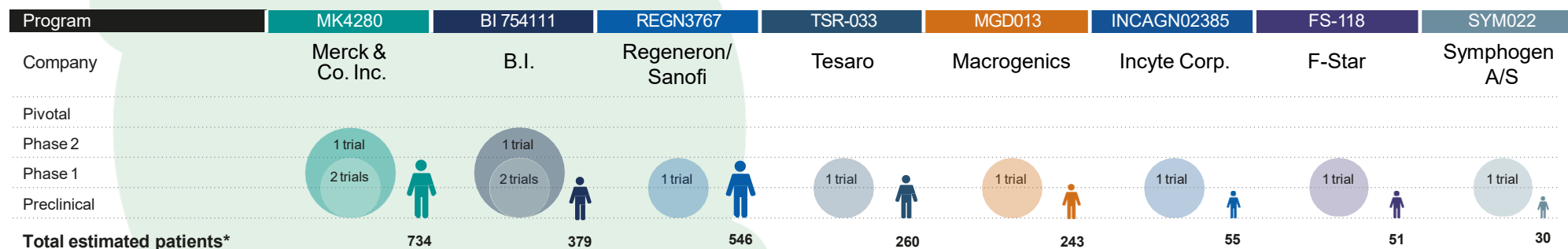
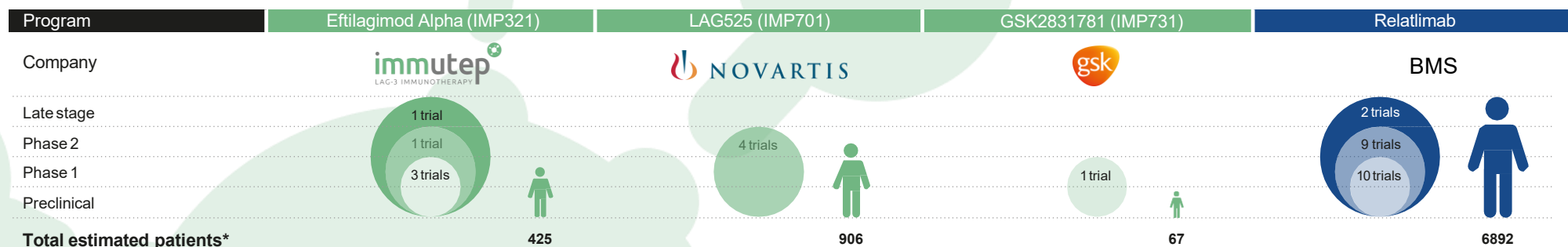


- **IMP701 is an anti-LAG-3 mAb that blocks LAG-3-mediated immune down-regulation**
- **LAG-3 is a prime target for immune checkpoint blockade as it is readily expressed at a high level in many human tumors**

# LAG-3 Landscape

# LAG-3 Therapeutic Landscape Overview

*Immute<sup>p</sup> is the leader in developing LAG-3 modulating therapeutics*

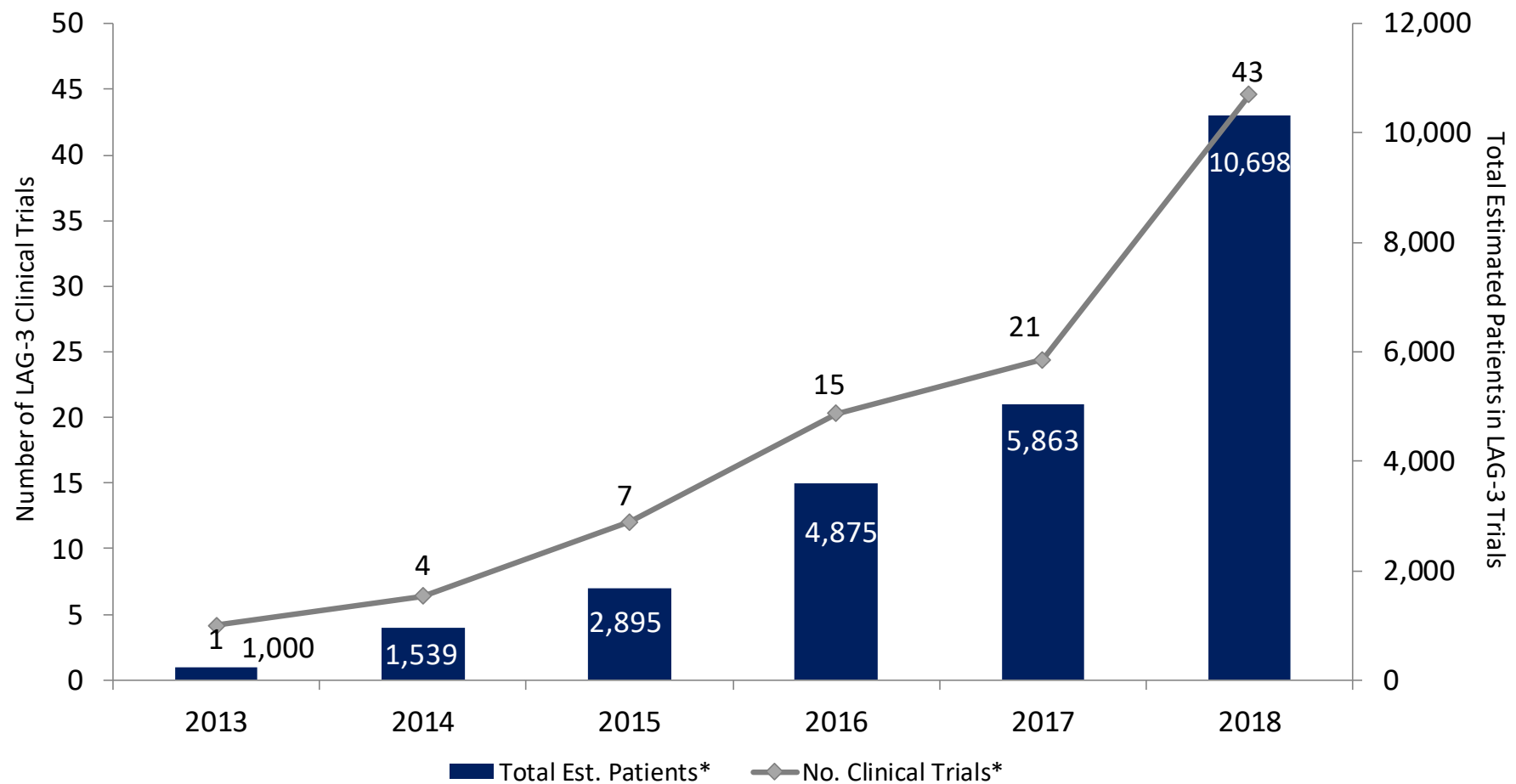


Indicates one product; size indicates stage of development, green = product either developed by Immute<sup>p</sup> or under license from Immute<sup>p</sup>

Indicates No. of patients on trials

# Increasing Clinical Trials Targeting LAG-3

Industry increasingly deploying resources to development of LAG-3 therapeutics



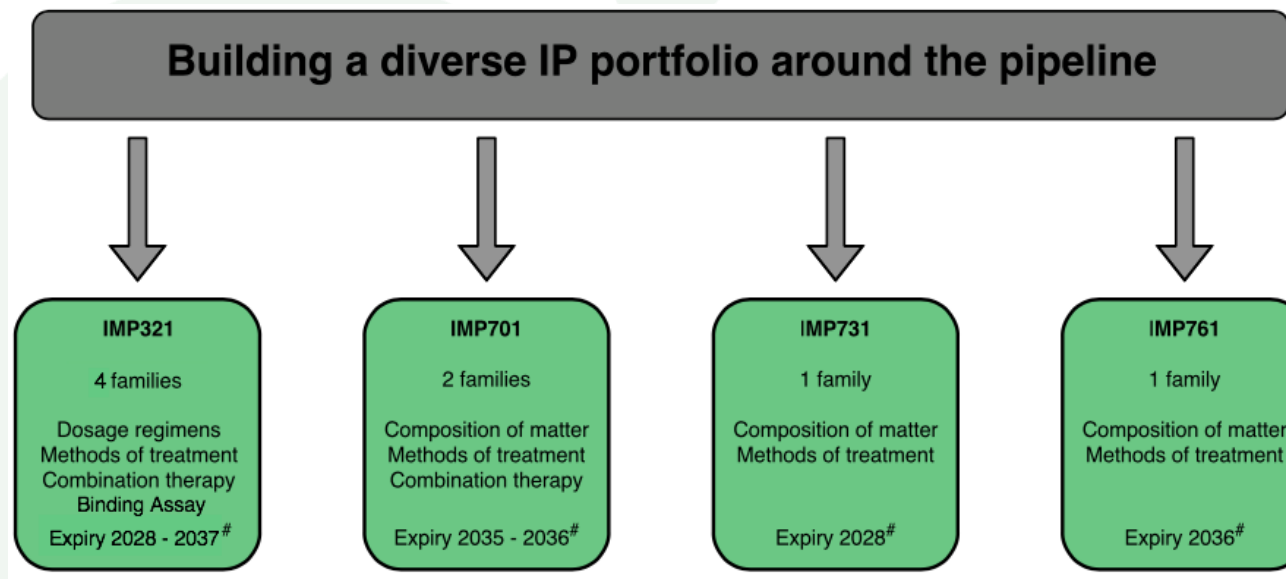
Sources: GlobalData, company websites, clinical trials.gov, and sec.gov

Information as of November 5, 2018

\*2018 includes planned and completed trials, includes trials where the company may not be the sponsor

# IP & Outlook

Immutep has a strong and continually expanding patent portfolio across major geographic markets and unrivalled expertise and understanding of the LAG-3 immune control mechanism



<sup>#</sup>Plus up to a 5 year extension of term available in some circumstances to compensate for delay associated with obtaining regulatory approval.

## Potential News Flow and Milestones

### Clinical

TACTI-mel data from fourth patient cohort (30 mg dose at cycle 1): H2 2018

TACTI-002 to commence, Phase II trial in collaboration with MSD: H2 2018

TACTI-002 first data in 2019

IMP761 preclinical data: 2018/ 2019

INSIGHT single cases from study: throughout 2019

AIPAC first progression free survival data (metastatic breast cancer trial): 2019

### Other

Potential milestone payments from clinical partners as trials progress

Continued expansion of patent portfolio

Continued regulatory interaction

Ongoing business development activities

# Investment Highlights

The global leader in developing LAG-3 therapeutics for immuno-oncology and autoimmune diseases

Deep expertise and IP in the LAG-3 immune control mechanism

Broadest LAG-3 portfolio with four product candidates, three of which are in nine ongoing or planned clinical trials

Multiple industry partnerships including Merck (MSD), GSK and Novartis

Expecting clinical results, regulatory updates, and business development news flow in 2018-2019

# Thank you!