



# The global leader in developing LAG-3 therapeutics

Investor Presentation  
May 2019

*(ASX: IMM, NASDAQ: IMMP)*

# Notice: Forward Looking Statements

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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

## Capital Structure

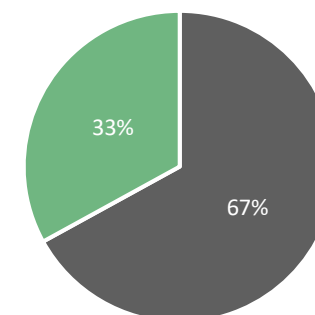
<b>Ticker symbols</b>	IMMP (NASDAQ) IMM (Australian Securities Exchange)
<b>Securities on issue<sup>(1)</sup></b> (as at 30 April 2019)	11.1 million American Depositary Shares (ADSs) 3.38 billion ordinary shares
<b>Cash &amp; Term Deposits</b> (as at 31 March 2019)	US\$15 million (A\$21 million)
<b>Market Cap<sup>(2)</sup></b> (as at 6 May 2019)	US\$67 million (A\$93 million)
<b>Avg. Vol. (3 months)</b> (as at 30 April 2019)	271 k ADSs <sup>(1)</sup> on NASDAQ 2.4 million ordinary shares on ASX

Notes:

(1) Each ADS represents 100 ordinary shares

(2) Market capitalization based on Nasdaq share price. For a detailed summary of all securities on issue refer to latest Appendix 3B released on ASX

## Shareholder Base



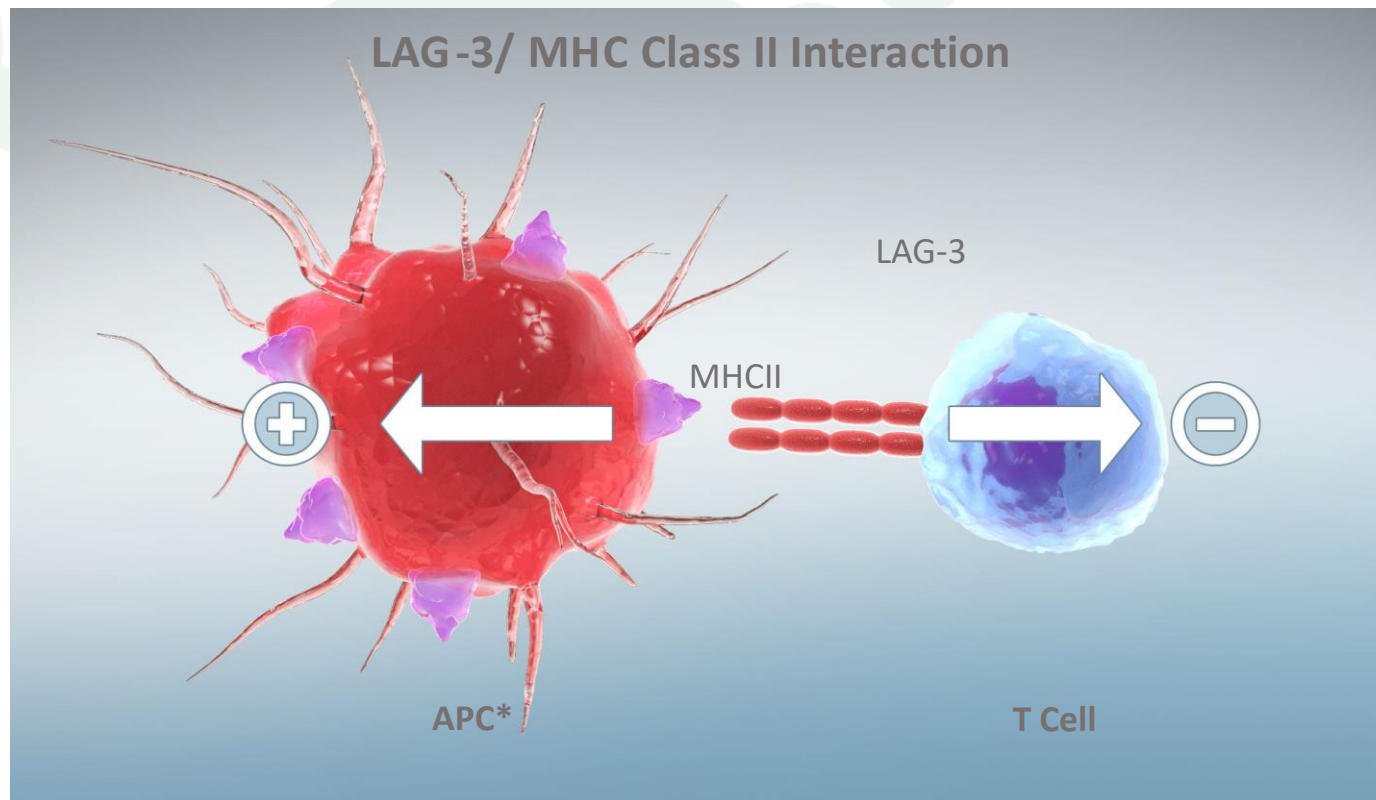
■ Australian Securities Exchange ■ Nasdaq



# 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**



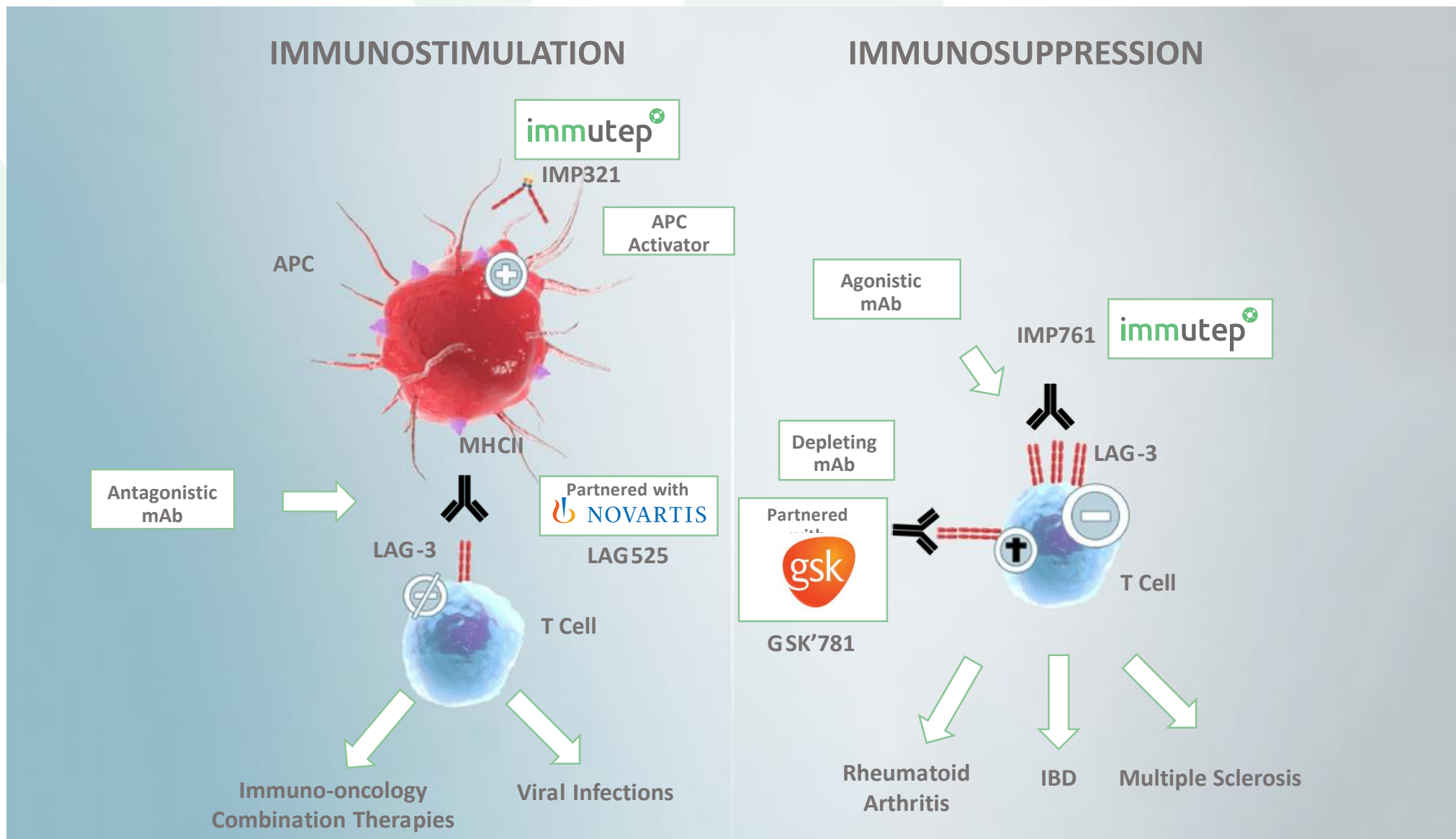
→ **Positive regulation** ↑  
of antigen  
presenting cells  
(APC) → increase  
in antigen  
presentation to  
cytotoxic CD8<sup>+</sup>  
T cells

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

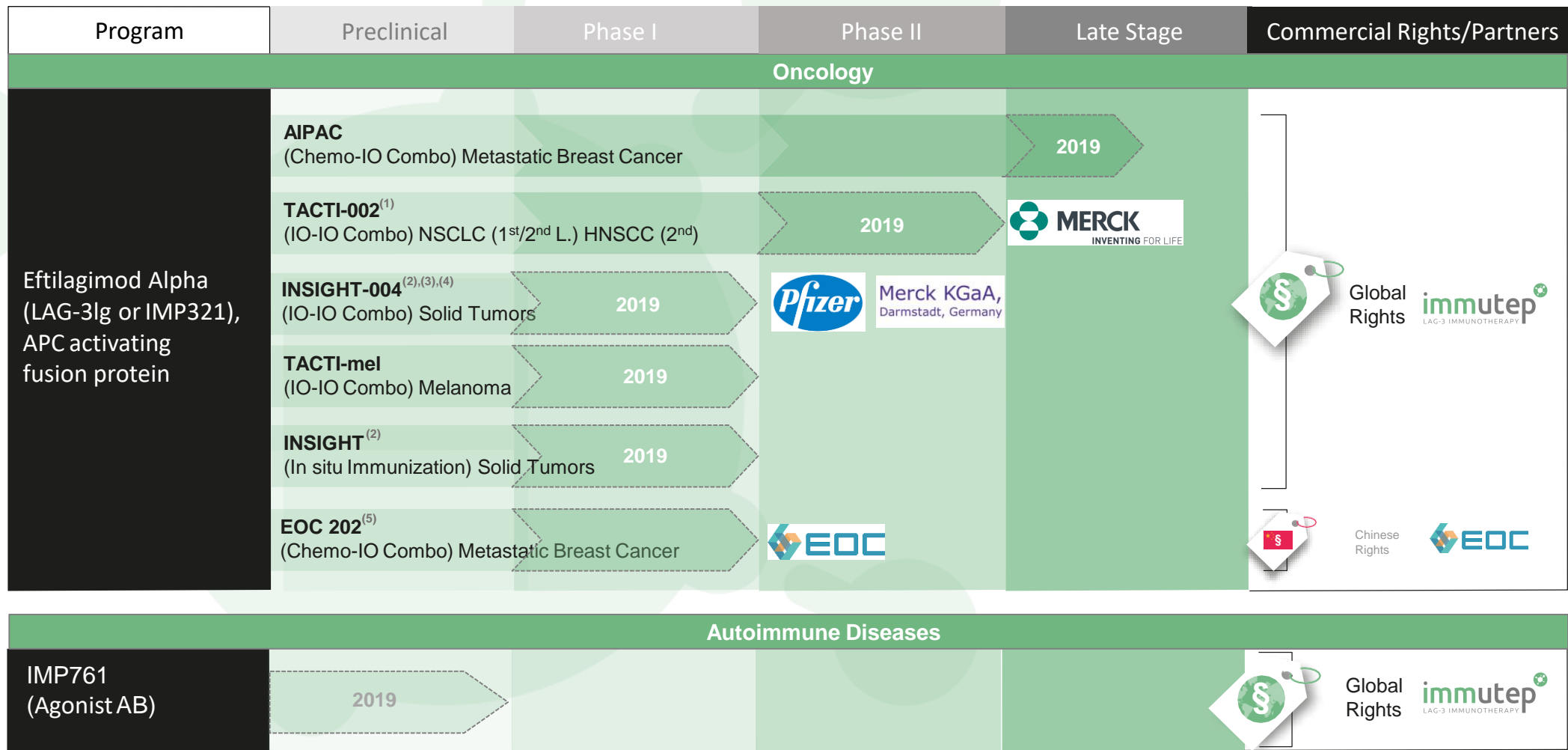
*Notes:*

\* APC: antigen presenting cell

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



# Immutep Controlled Immunotherapy Pipeline\*

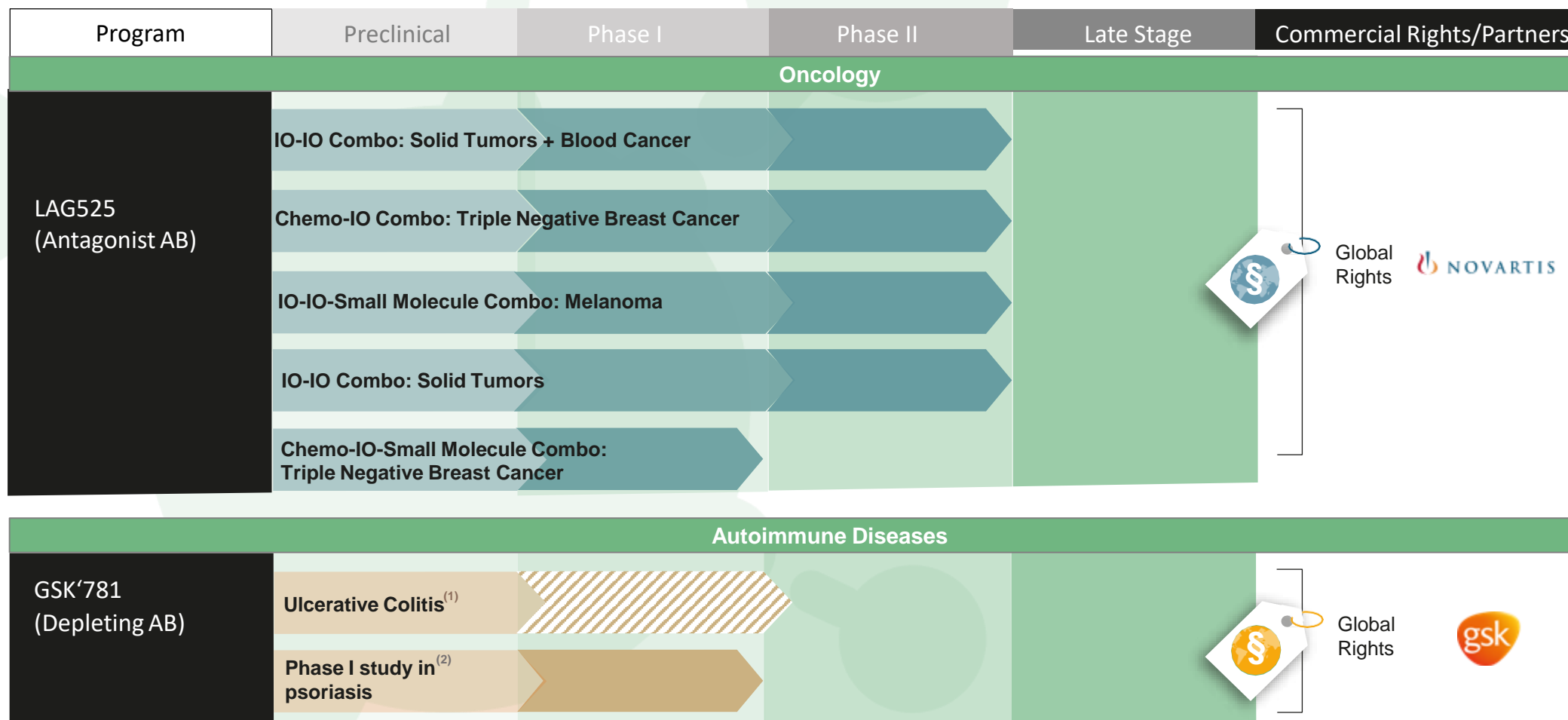


Notes

- \* Actual timing of data readouts may differ from expected timing shown above. Information in pipeline chart current as at 12 February 2019.
- (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 Immutep has no control over this clinical trial

- (3) In combination with BAVENCIO® (avelumab)
- (4) Clinical trial is currently planned and not active
- (5) EOC Pharma is the sponsor of the EOC 202 clinical trial which is being conducted in the People's Republic of China

# Out-Licensed Immunotherapy Pipeline



## Notes

- (1) Clinical trials currently planned and not yet active (as depicted by diagonal striped lines). Proof of concept data in Ulcerative Colitis for GSK'781 expected in 2H 2020.
- (2) Reflects completed Phase I study in healthy volunteers and psoriasis.



The background of the slide is a solid green color. It is decorated with several semi-transparent, light green speech bubbles of various sizes. Some bubbles are simple circles, while others have a small tail pointing in different directions, giving the impression of a conversation or a network of ideas.

# Lead Program Eftilagimod Alpha (IMP321)

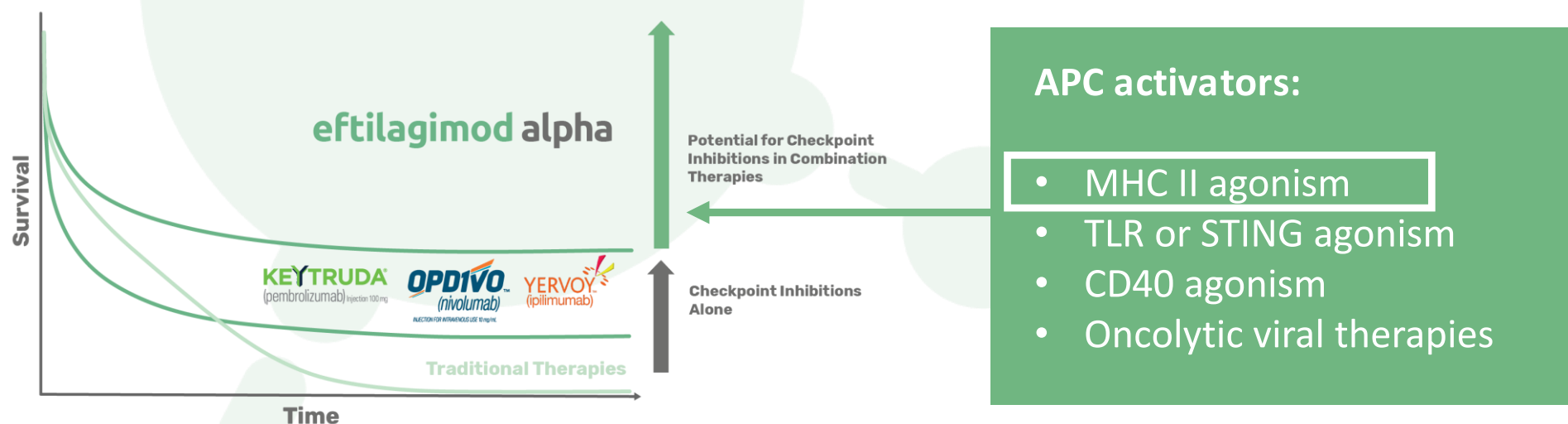
# IO Therapy Oncology Response Rates

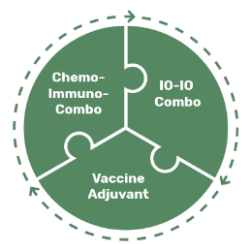
Approximately 70-80% of patients do not respond to anti-PD1 monotherapy

## 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

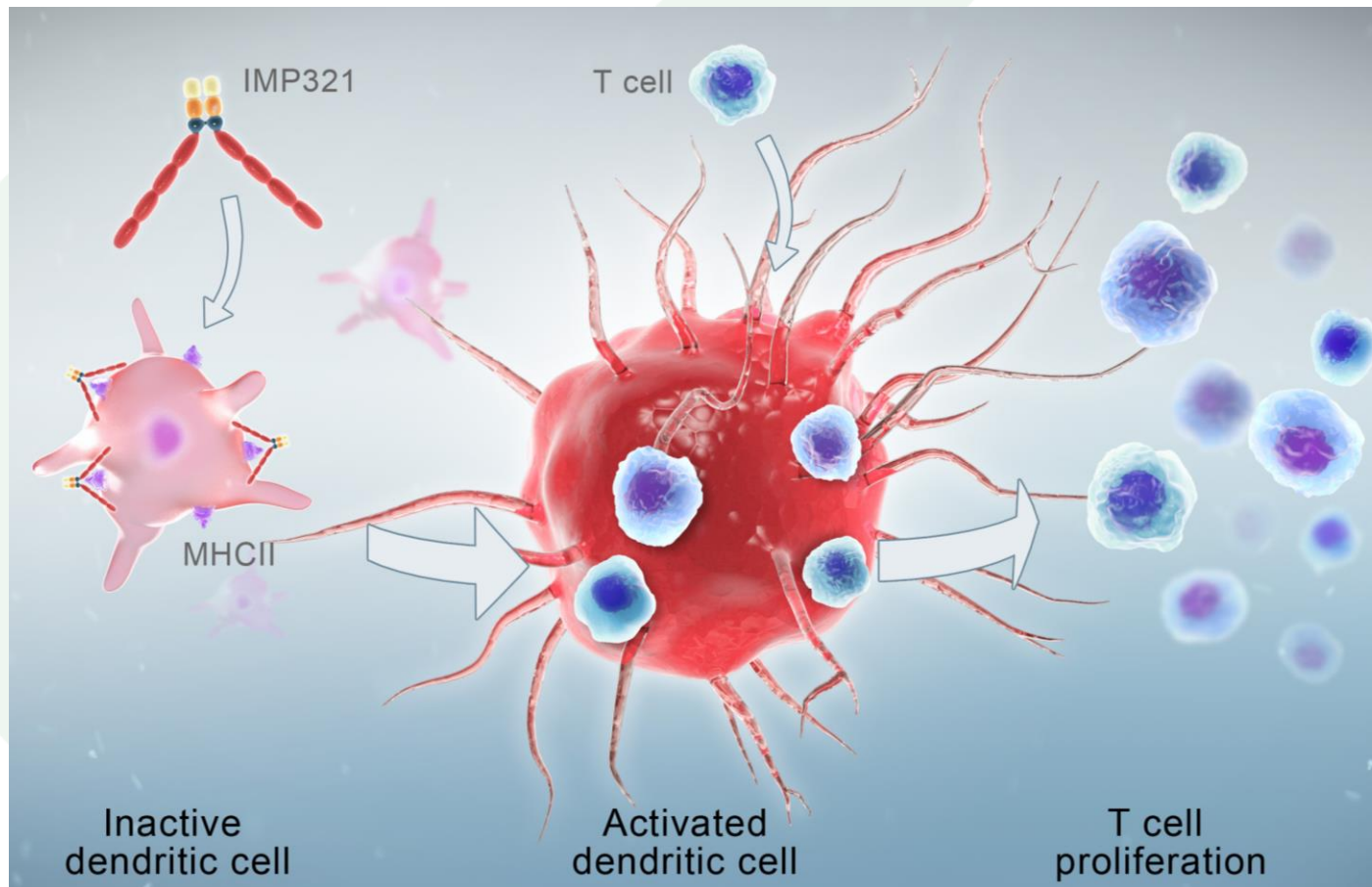
Eftilagimod has the potential to be an **ideal combinatory therapeutic in the oncology treatment regiment** that could improve the prognosis for patients

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

- First-in-class MHCII agonist
- Good 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

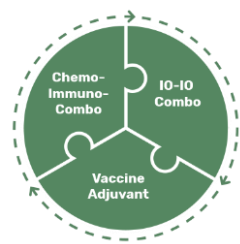
# Efti Mechanism of Action

*Efti's agonistic mechanism of action leads to T cell expansion and proliferation  
=> pushing the gas on the immune response*



- Efti 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



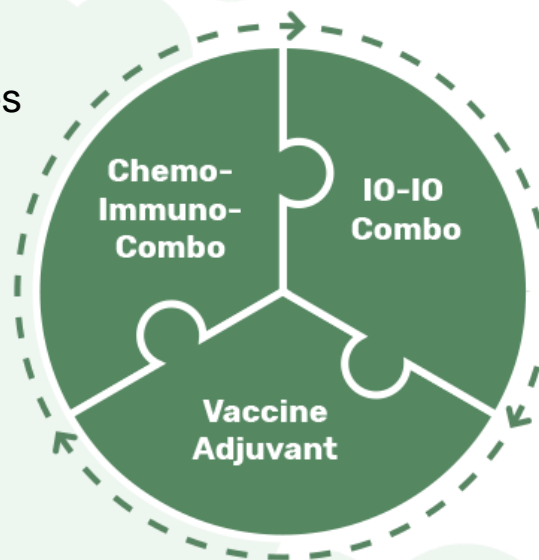
# Efti - Areas of Development Multiple Strategies

*Efti has multiple shots on goal in different indications and in different combinations*

## Chemo-immunotherapy

- Exploit the antigen debris from chemotherapy with an APC activator → combination with agents such as taxanes (e.g. paclitaxel)

- *European Phase IIb AIPAC (Immutep)*
- *Chinese Phase I Chemo Combo in MBC pts (EOC)*



## IO-IO combination

- Increase response rates and durability, overcoming resistance in combination with IO agents with complementary mechanisms (e.g. pembrolizumab, avelumab)

- *Phase I TACTI-mel (Immutep)*
- *Phase II TACTI-002 (Immutep<sup>1</sup>)*
- *Phase I INSIGHT – Stratum D (Immutep<sup>2</sup>)*

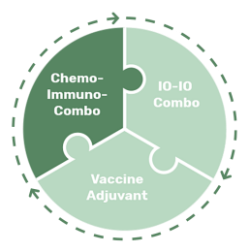
## Cancer vaccine or in situ vaccination

- Stimulate the immune system locally → intratumoral or in vaccination studies

- *Phase I Solid Tumors (Cytlimic)*
- *Phase I INSIGHT - Stratum A+B (IKF<sup>3</sup>)*

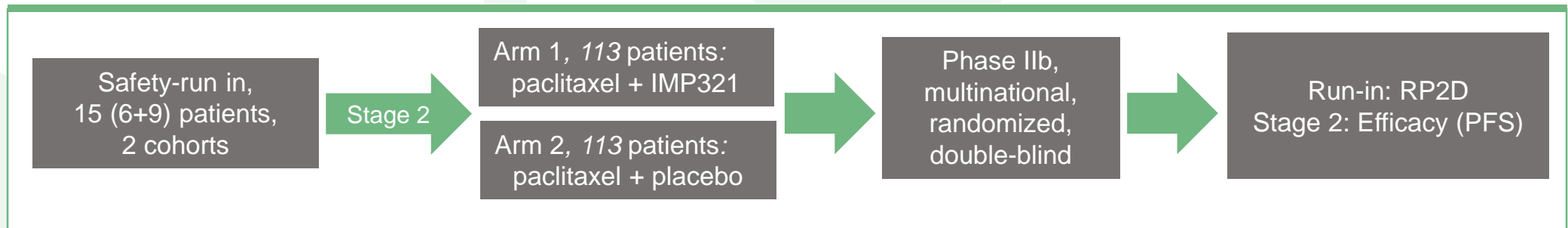
### Notes

- (1) In collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the United States and Canada) and in combination with KEYTRUDA® (pembrolizumab)
- (2) In collaboration with Merck KGaA, Darmstadt, Germany and Pfizer Inc. and in combination with BAVENCIO® (avelumab)
- (3) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial



# Efti - Clinical Development AIPAC

## AIPAC: Active Immunotherapy PAClitaxel in MBC

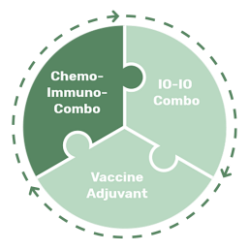


<b>Other Objectives</b>	Anti-tumor activity, safety and tolerability, PK, immunogenicity, quality of life
<b>Patient Population</b>	Advanced MBC indicated to receive 1 <sup>st</sup> line weekly paclitaxel
<b>Treatment</b>	Run-in: Paclitaxel + IMP321 (6 or 30 mg) Arm 1: Paclitaxel + IMP321 (30 mg) Arm 2: Paclitaxel + Placebo
<b>Location</b>	>30 sites in 7 (GB, DE, PL, HU, FR, BE, NL) EU countries

### Status Report (Apr 2019)

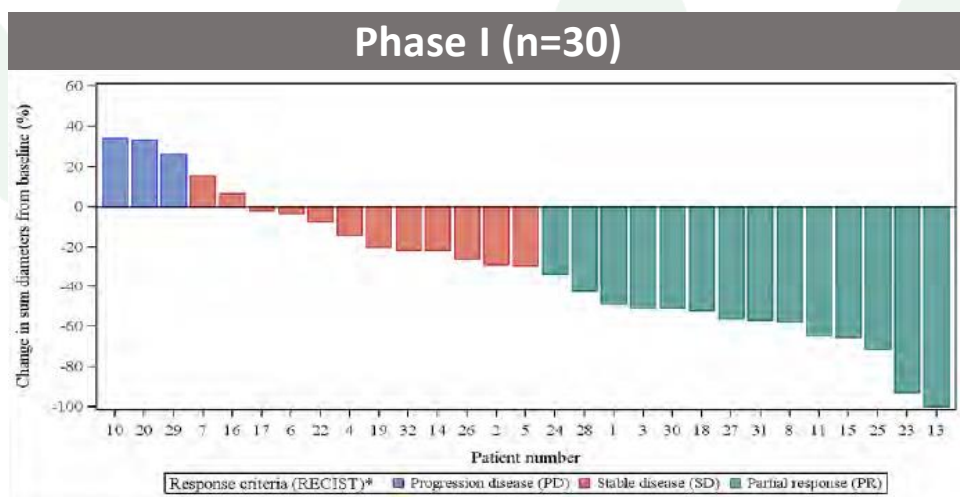
- ✓ To-date, efficacy and safety data (ASCO 2018) in-line with historical control group / prior clinical trials (Brignone et al J Trans Med 2010, 8:71)
- ✓ Regulatory approval in 7 EU countries
- ✓ >200 patients recruited in Stage 2 → LPI expected May/Jun 2019
- Primary read out expected within 12 months dependent on the number of events, but not before Q.4 2019

**Key features: double blinded, potentially pivotal trial in metastatic breast cancer patients**



# Eftilagimod Alpha Preliminary 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

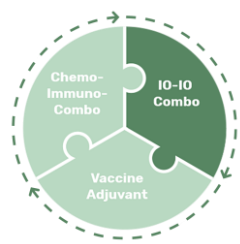
AIPAC – Safety Run Phase (n=15)	
Response Parameter	Paclitaxel + IMP321 (n = 15)
Complete Response (CR)	0/15 (0%)
Partial Response (PR)	7/15 (47%)
Stable Disease (SD)	6/15 (40%)
Progressive Disease (PD)	2/15 (13%)
Overall Response Rate (ORR)	7/15 (47%)
Disease Control Rate (DCR)	13/15 (87%)

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

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

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





# Efti in Melanoma

## TACTI-mel – 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

Other  
objectives

PK and PD of efti, response rate,  
PFS

Patient  
Population

Metastatic melanoma

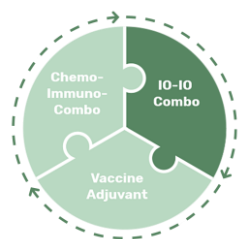


Australia

7 sites in Australia

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





# Efti in Melanoma TACTI-mel – Results Part A

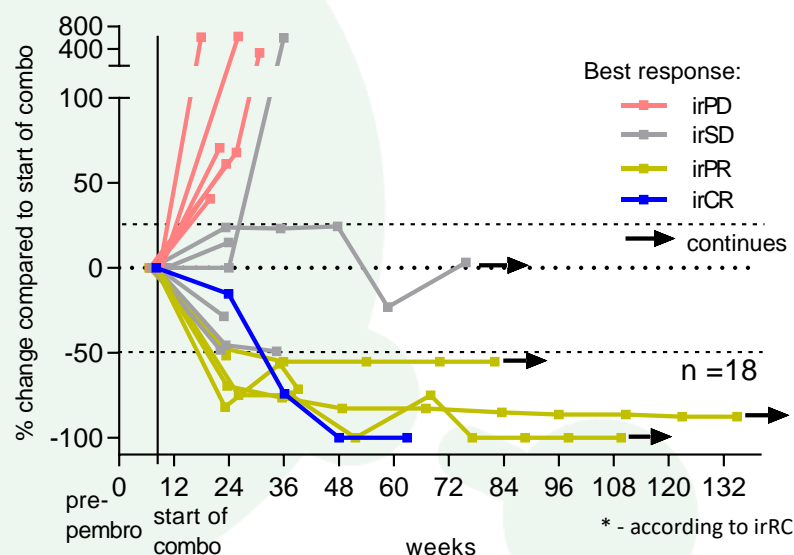
*Majority not responding to pembrolizumab monotherapy  
→ Tumor shrinkage in 56 % incl. 2 pts with disappearance of all target lesions*

Best Overall Response acc. to irRC	N = 18 (%)
irCR	1 (6 %)
irPR#	5 (28 %) #
irSD	6 (33 %)
irPD	6 (33 %)
<b>Best overall response rate (ORR)</b>	<b>6 (33 %)</b>
<b>Patients with tumor shrinkage</b>	<b>10 (56 %)</b>
<b>Disease control rate</b>	<b>12 (66 %)</b>

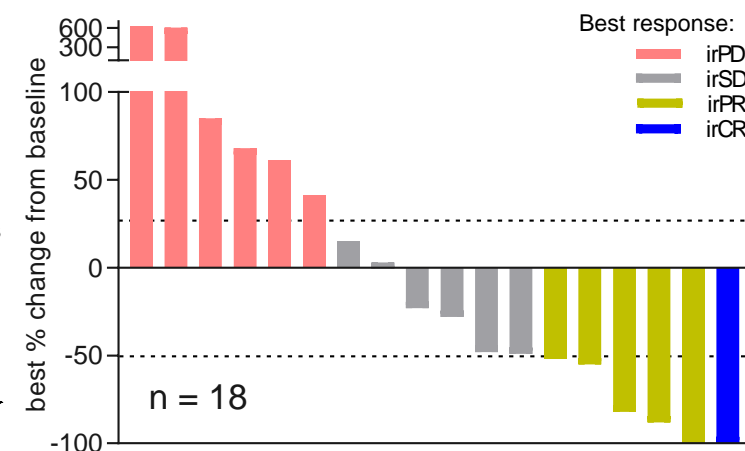
# - incl. 1 pt with complete disappearance of all target lesions; CR acc. to RECIST 1.1

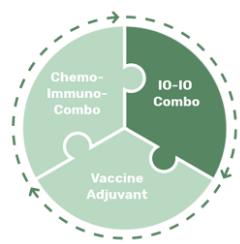
Exploratory analysis  
(C1D1 pembrolizumab):  
**ORR of 61 %**

**Spider plot\* (part A)**  
(starting with cycle 5 of pembrolizumab)



**Waterfall plot\* (part A)**  
(starting with cycle 5 of pembrolizumab)

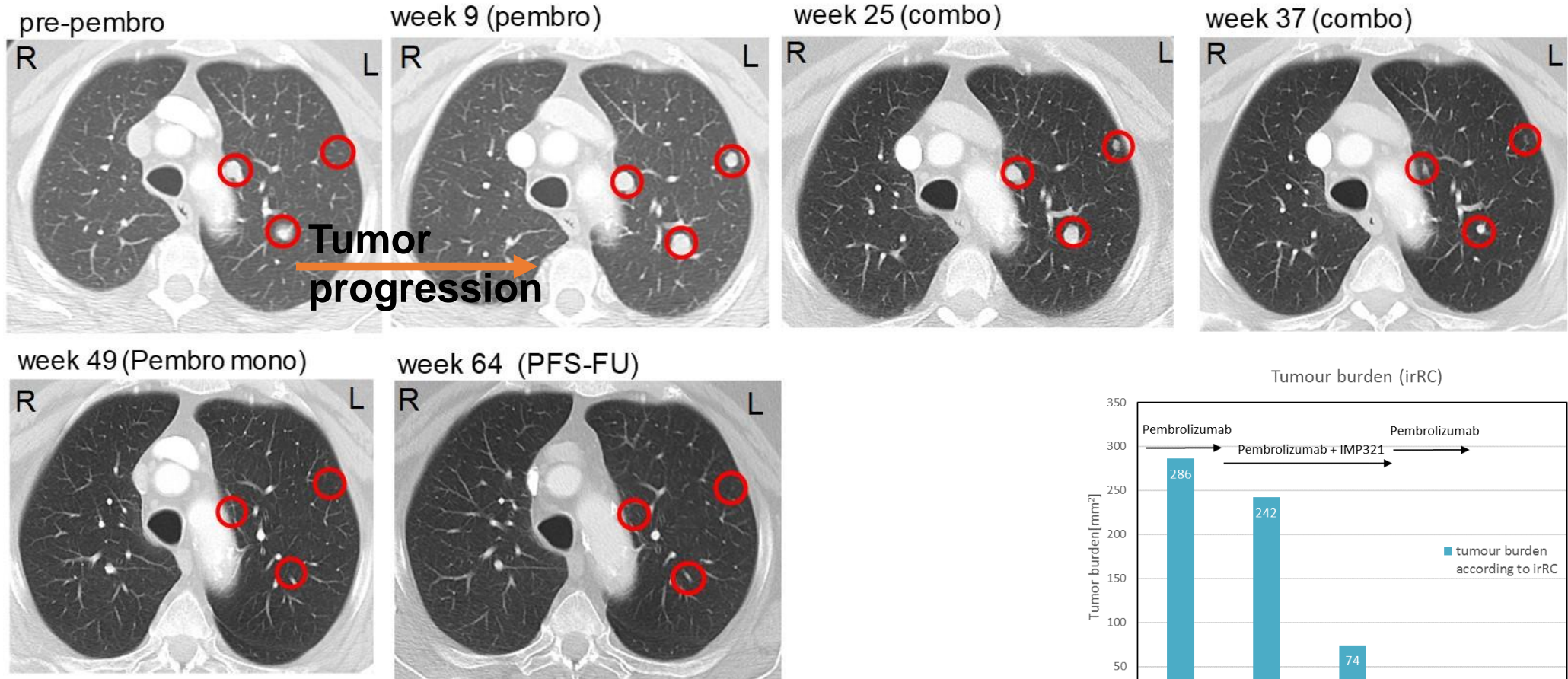




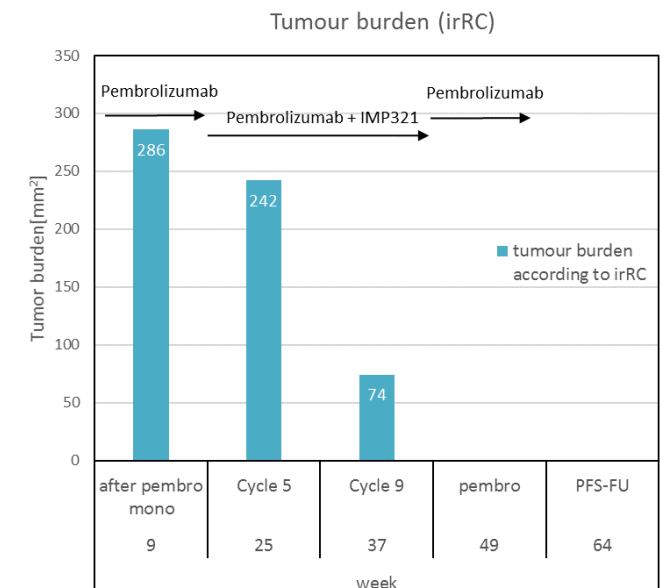
# Efti in Melanoma

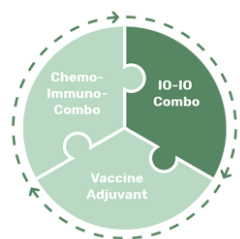
## TACTI-mel – Results Part A – Single Case

### Efficacy: Metastatic Melanoma



- Patient progressing on pembrolizumab monotherapy
- At 1 yr all lesions disappeared → CR (confirmed)
- Patient without treatment and disease free → now lost to FU





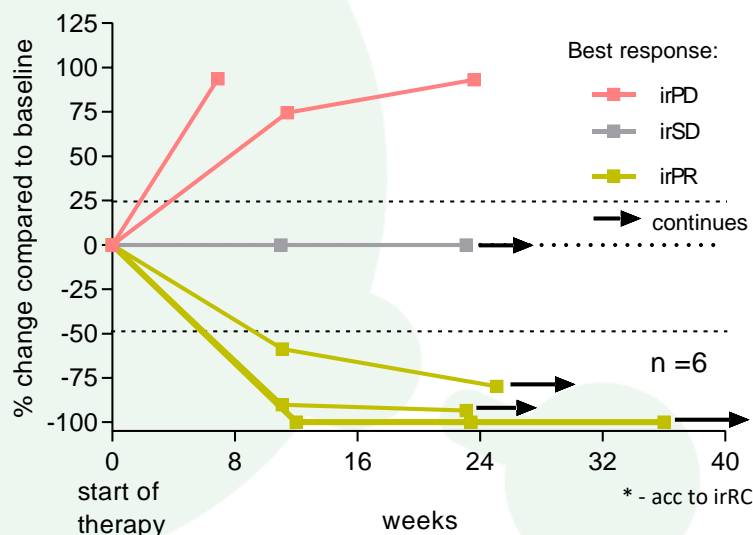
# Efti in Melanoma TACTI-mel – Results Part B

*Confirmed deep partial responses in 3 (50%) of the pts  
Treatment of 4 pts ongoing, all over 6 months*

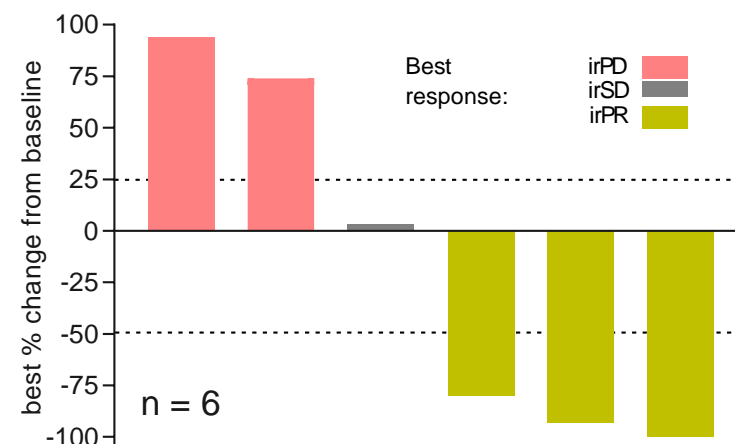
Best Overall Response acc. to irRC	N = 6 (%)
irCR	0 (0 %)
irPR#	3 (50 %)#
irSD	1 (13 %)
irPD	2 (25 %)
<b>Best overall response rate (ORR)</b>	<b>3 (50 %)</b>
<b>Patients with tumor shrinkage</b>	<b>3 (50 %)</b>
<b>Disease control rate</b>	<b>4 (66 %)</b>

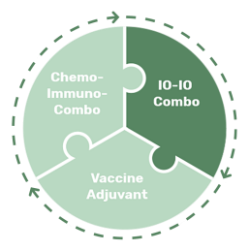
# - incl. 1 pt with complete disappearance of all target lesions

**Spider plot\* (part B)**



**Waterfall plot\* (part B)**





# Efti - Clinical Development TACTI-002 (Phase II)

## TACTI-002: Two Active Immunotherapeutics in different indications

Simon's 2 stage  
design; 3 indications;  
109 pts

Efti (IMP321) + Pembrolizumab  
(Keytruda®) for 12 months + 12  
months pembrolizumab mono

Phase II, multi-  
national (EU + US  
+ AU), open label

**ORR, PFS, OS, PK,  
Biomarker; Safety and  
tolerability**

### Patient Population

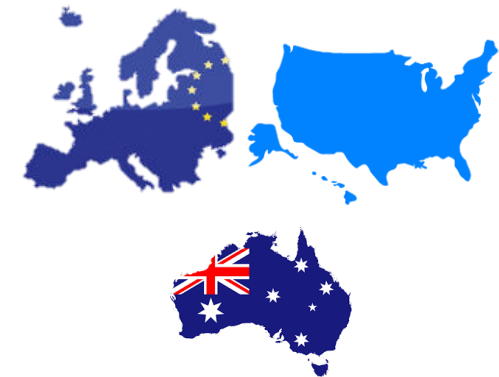
A: 1<sup>st</sup> line NSCLC PD-X naïve  
B: 2<sup>nd</sup> line NSCLC, PD-X refractory  
C: 2<sup>nd</sup> line HNSCC, PD-X naïve

### Treatment

30 mg Efti (IMP321) s.c.  
200 mg Pembrolizumab i.v.

### Status Report (Apr 2019)

- ✓ Fully approved in all countries  
(ES, GB, US, AU)
- ✓ >10 patients enrolled
- First data expected mid 2019

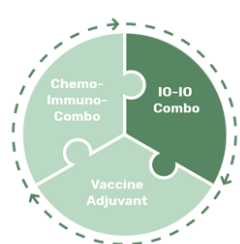


13 sites in Europe / US /  
Australia

### In collaboration with



**Key features: PD-X refractory patients (part B), chemo-free option for NSCLC, first FDA IND**



# Efti - Clinical Development INSIGHT-004 (Phase I)

## INSIGHT-004 – Dose escalation of efti in combination with avelumab

Dose escalation,  
solid tumors, 2  
cohorts of 6 pts each



Efti (IMP321) + Avelumab  
(Bavenico<sup>®</sup>) for 6 months + 6  
months avelumab monotherapy



Phase I,  
monocenter DE,  
open label, IIT



**RP2D, Safety, ORR,  
PFS, PK, PD**

### Patient Population

Solid tumors after failure of  
standard therapy

### Treatment

6/30 mg Efti (IMP321) s.c.  
800 mg avelumab i.v.;  
Both every 2 weeks

### Status Report (Apr 2019)

- ✓ 1 site in Germany
- ✓ Protocol approved by  
CA/ ED
- First patient expected in Q2 2019

### In collaboration with



**Merck KGaA,** I.K.F.  
Darmstadt, Germany

**Key features: safety with a PD-L1 antagonist avelumab**

# 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 ongoing

- 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; Clinical Trial Collaboration
- 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

The background features a solid green lower half and a white upper half, separated by a horizontal line. Several semi-transparent circles of varying sizes are scattered across the green area, some overlapping the white area. The text is centered in the green section.

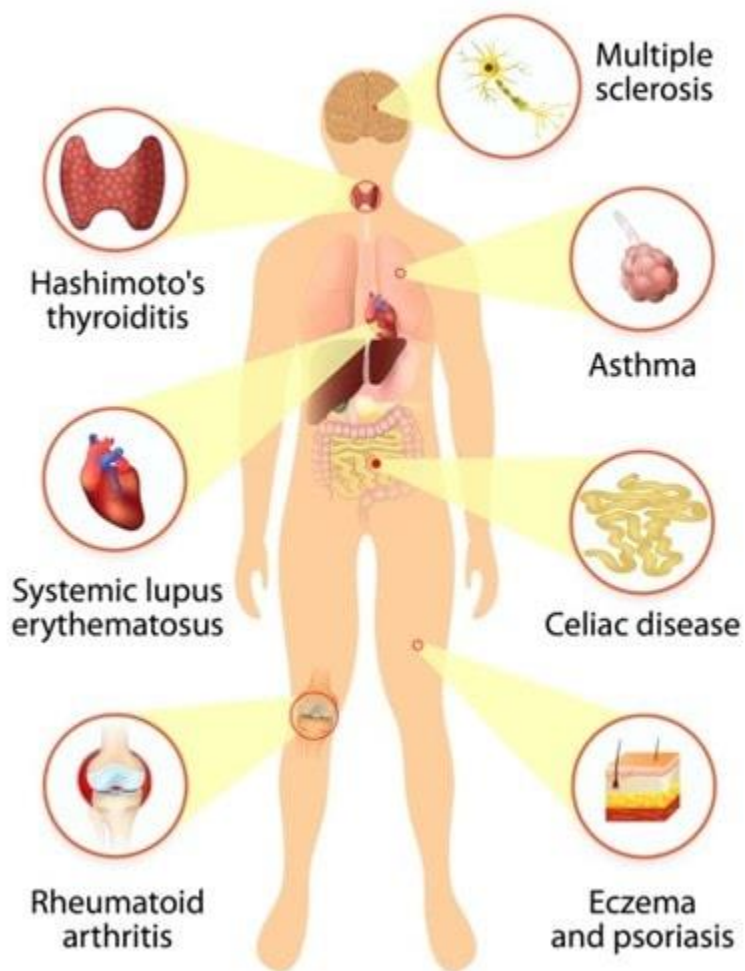
# IMP761

## (Autoimmune Diseases)



# Broad Potential in Targeting Auto-reactive Memory T cells with IMP761

## AUTOIMMUNE DISEASES



## THE PRESENT: FIGHTING SYMPTOMS

**Treating general inflammation:**  
corticoids, methotrexate,  
anti-TNF- $\alpha$ , -IL-6, -IL-17, -IL-23 mAbs

## THE FUTURE: FIGHTING THE CAUSE OF AID

**Treating the disease process:**  
silencing the few autoimmune memory T cells  
accumulating at the disease site with IMP761



# IMP761 – Agonist mAb

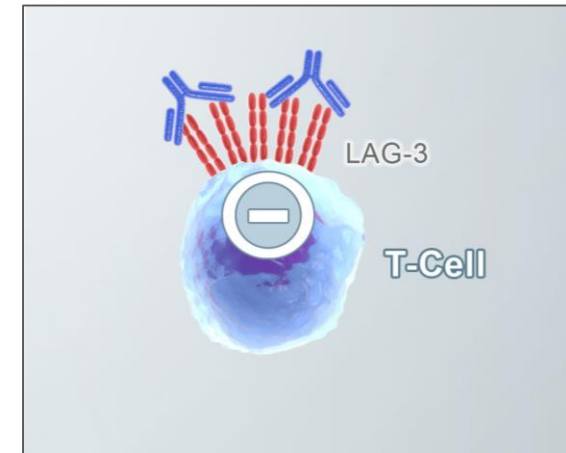
## Key Characteristics

- 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



The background features a solid green horizontal band across the middle. Above and below this band are several semi-transparent circles of varying sizes in shades of green and white, some with small stems, creating a bubble-like or molecular effect.

# Partnered Programs

# 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 (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 (now increased to 515 pts)
- 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 mid 2018 in TNBC (126 pts) and metastatic mel. (160 pts)
- Nov 2018: one new Phase Ib made public TNBC (220 pts)



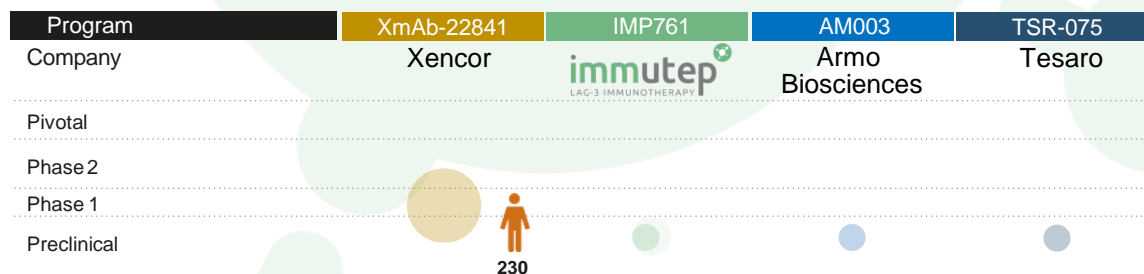
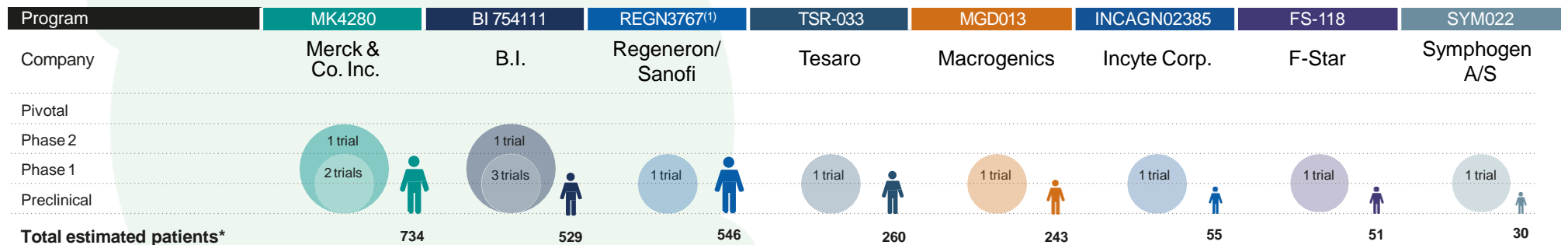
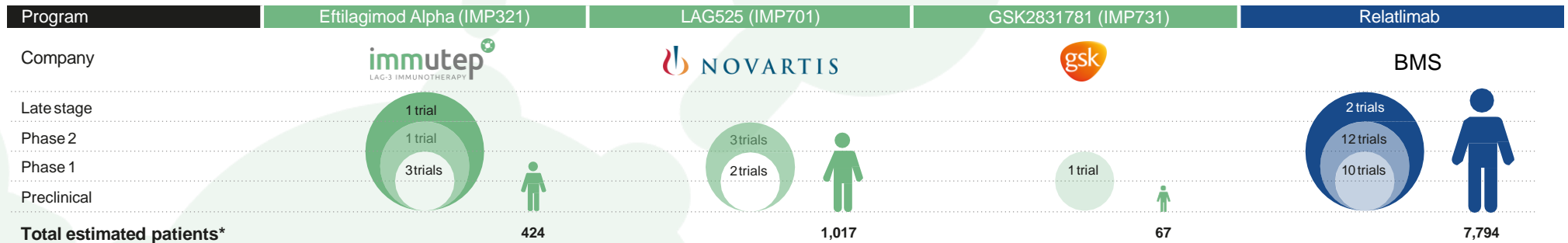
- **IMP701 is an anti-LAG -3 mAb that blocks LAG -3-mediated immune down-regulation**
- **LAG -3 is a prime target for immune checkpoint blockade as it is readily expressed at a high level in many human tumors**

The background features a solid green horizontal band across the middle. Above and below this band are several semi-transparent circles of varying sizes in shades of green and white. Some circles have small stems or tails, resembling bubbles or stylized figures. The text 'LAG-3 Landscape' is centered in the green band in a white, bold, sans-serif font.

# LAG-3 Landscape

# LAG-3 Therapeutic Landscape Overview

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



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

Indicates No. of patients on trials

Notes:

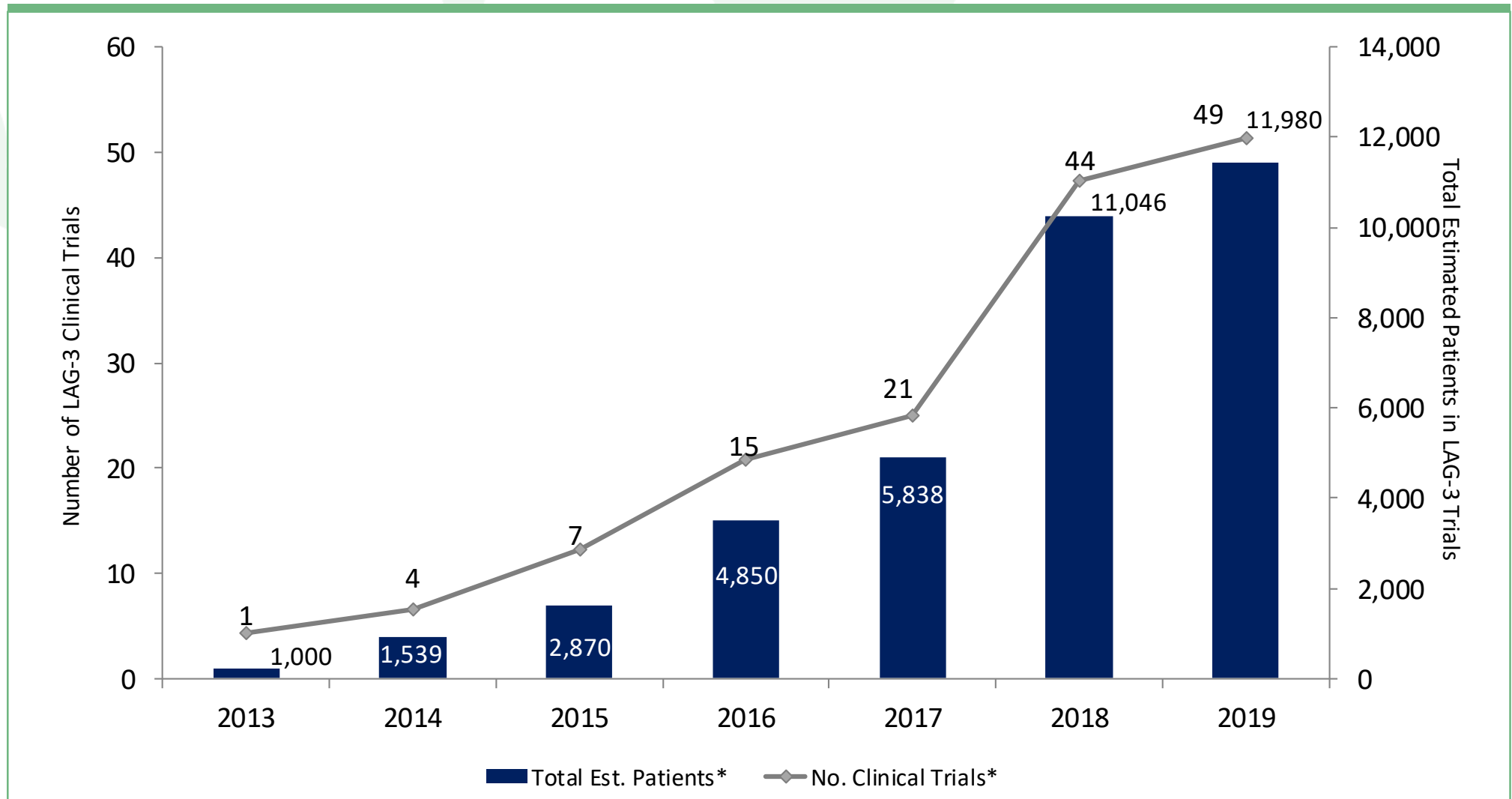
Sources: GlobalData, company websites, clinical trials.gov, and sec.gov

Information as of March 1, 2019, includes planned and completed trials, includes trials where the company may not be the sponsor

(1) As per Sanofi 6-K filing (February 2, 2019) development of REGN3767 has stopped

# 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 March 1, 2019

\*2019 includes planned and completed trials, includes trials where the company may not be the sponsor

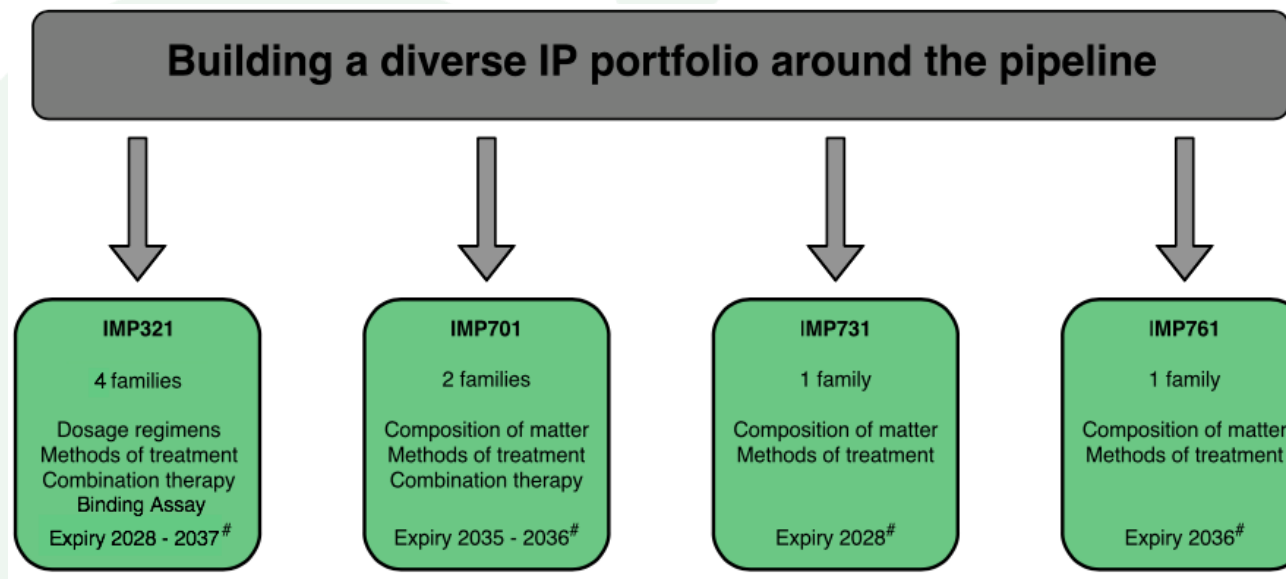
The background features a solid green horizontal band across the middle. Above and below this band are several semi-transparent circles of varying sizes in shades of green and white, some with small stems, creating a bubble-like or molecular aesthetic.

# IP & Outlook



# Intellectual Property

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.

# 2019 Clinical Guidance and Outlook

- ✓ TACTI-002 to commence, Phase II trial in collaboration with MSD: H1 2019
- ✓ TACTI-mel data from fourth patient cohort (30 mg dose at cycle 1) in 2019
- ✓ IMP761 program update: 2019
- INSIGHT-004 to commence, IIT Phase I trial in collaboration with Pfizer and Merck KGaA: Q2 2019
- TACTI-002 first data in mid-2019
- INSIGHT program updates: 2019
- TACTI-mel final assessment
- AIPAC fully recruited: Q2 2019
- AIPAC first progression free survival data (metastatic breast cancer trial): next four quarters, but not before Q4 2019

# Investment Highlights

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

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

Broad portfolio of LAG-3 product candidates developed by Company

Relationships with multiple industry leaders, including Merck (MSD), Pfizer/ Merck KGaA, GSK and Novartis

Clinical data readouts expected throughout 2019