

# The global leader in developing LAG-3 therapeutics

Investor Presentation January 2019

(ASX: IMM, NASDAQ: IMMP)

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#### **Company Snapshot**



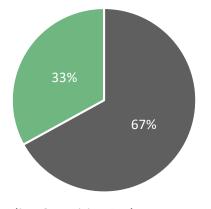
- Globally active biotechnology company with operations in Australia, Europe and U.S.
- Four LAG-3 related product candidates in development in immuno-oncology and autoimmune disease
- Committed partnerships with five of the world's largest pharmaceutical companies - Merck (MSD), Pfizer/ Merck KGaA,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

#### **Capital Structure**

Ticker symbols	IMM (Australian Securities Exchange) IMMP (NASDAQ)
Securities on issue <sup>(1)</sup> (as at 3 January 2019)	3.38 billion ordinary shares 11.2 million American Depository Shares (ADSs)
Cash & Term Deposits (as at 31 December 2018)	A\$26 million (~US\$18 million)
Market Cap (as at 3 January 2019)	A\$100.3 million (~US\$69.86 million)
Avg. Vol. (3 months) (as at 31 December 2018)	3.1 million ordinary shares on ASX 85 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

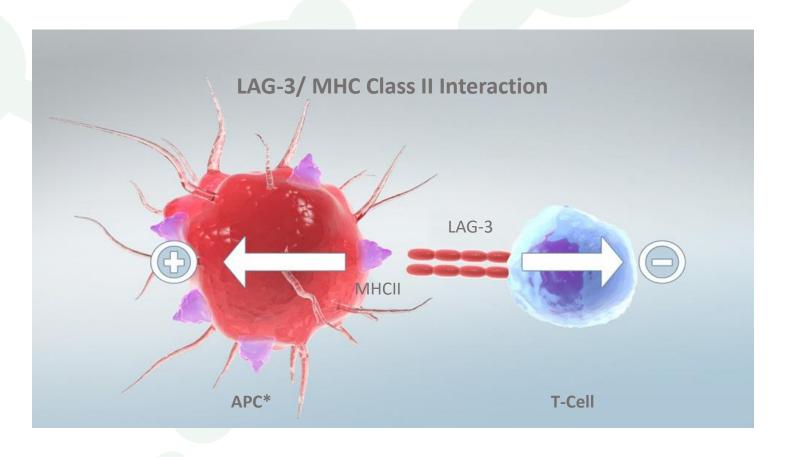


# LAG-3 Overview & Product Candidates

#### 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



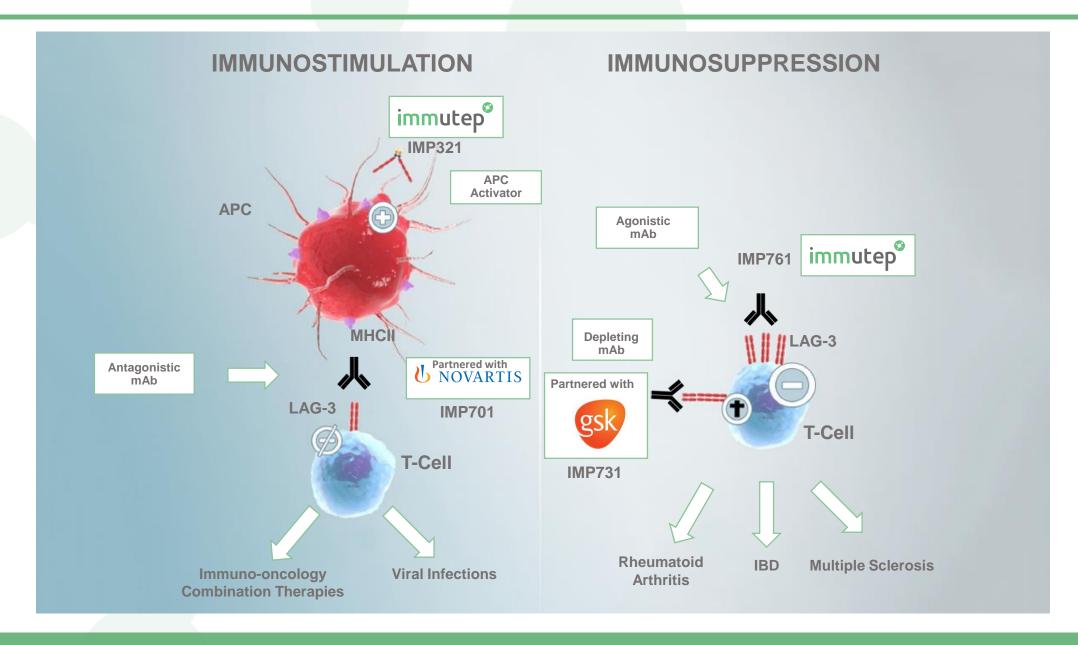
- → Positive regulation of antigen presenting cells (APC) → increase in antigen presentation to cytotoxic CD8+ T cells
- → Negative regulation of LAG-3+ T Cells

Notes

<sup>\*</sup> APC: antigen presenting cell

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





#### **Oncology and Autoimmune Pipeline\***



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

- \* 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

INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

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



# Lead Program Eftilagimod Alpha (IMP321)

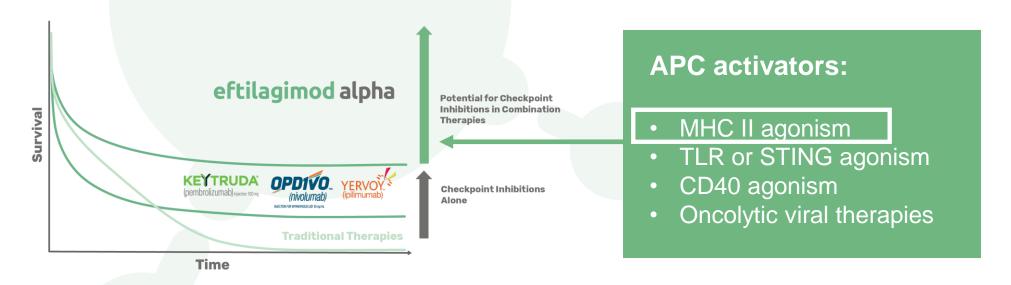
#### **IO Therapy Oncology Response Rates**



Approximately 70-80% of patients do no 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 <u>ideal combinatory therapeutic in the</u> <u>oncology treatment regiment</u> that could improve the prognosis for patients

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

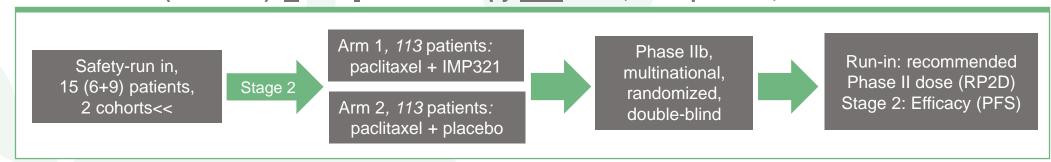
- First-in-class MHCII agonist
- Good safety profile and encouraging efficacy data thus far
- Potential for use in various combination settings (e.g. IO, chemo, vaccines or in situimmunization)
- Estimated favorable (low) cost of goods based on current flat dosing regimen and manufacturing process



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



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



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

#### **Status Report (November 2018)**

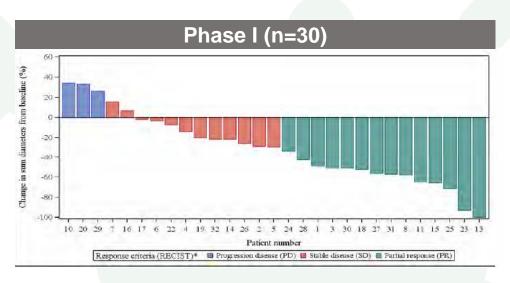
- √ Safety run-in completed successfully
- √ Randomized phase started early 2017 with the RP2D (30 mg)
- ✓ Interim-data of safety run-in presented at ASCO 2017
- √ To-date, efficacy and safety data in-line with historical control group/ prior clinical trials (Brignone et al Journal Translational Medicine 2010, 8:71)
- √ Regulatory approval to conduct trial in 7 EU countries
- ✓ Mid-point of patient enrolment reached (June 2018)
- √ >160 patients recruited in Stage 2
- Primary read out expected in H2/2019



### 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 Ru	ın 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)

<sup>\*</sup>Overall Response Rate \*\*Disease Control Rate Preliminary data, status Interim CSR April 2018, best response acc. To RECIST 1.1



#### 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



7 sites in Australia

- 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 and initial data presented in November 2018
- Pembrolizumab (Keytruda®) 2 mg/kg every
   3 weeks i.v. part A and B



## TACTI-mel Part A Summary Baseline Characteristics and Efficacy



Baseline Characteristics	N = 18 (%)		
Age (median)	67 yrs		
Sex (f/m)	1 (6%) / 17 (94 %)		
Elevated LDH	7 (39%)		
Metastasis stage M1c	14 (78%)		
Pre-treated with BRAF/MEK/ipilimumab	5 (28%)		
irPD/irSD to pembro after 3 cycles	11 (61%)		

 Very late stage of disease (M1c, elevated LDH) and majority not responding to pembrolizumab monotherapy

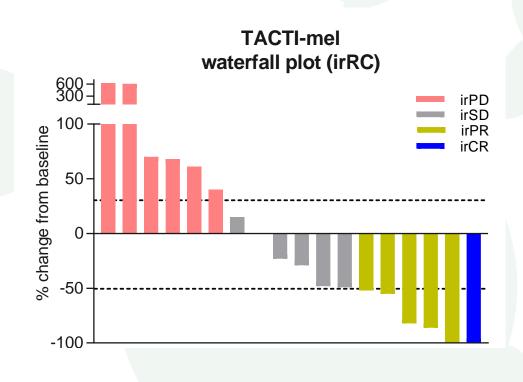
Best Overall Response acc. to irRC	N = 18 (%)
irCR	1 (6%)
irPR#	5 (28%)#
irSD	6 (33%)
irPD	6 (33%)
Best overall response rate (ORR)	6 (33 %)
Patients with tumor shrinkage	10 (56%)
Disease control rate	12 (66%)

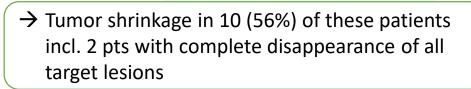
# - incl. 1 pt with complete disappearance of all target lesions

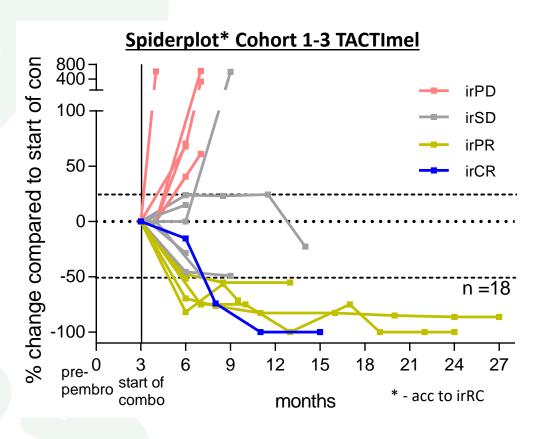
 If response is calculated from prepembro timepoint → ORR is 61% acc. to irRC











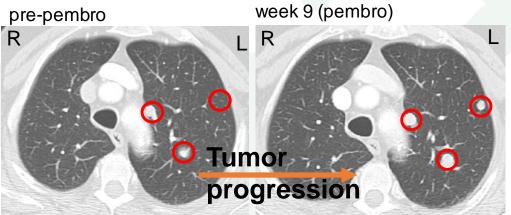
- → 1 pt with confirmed CR + 4 pts still on Tx after 12 months
- → 5 (28%) pts with long term (>12 mths) treatment/benefit

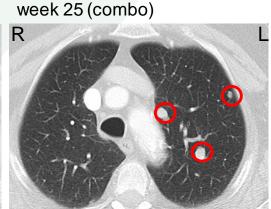


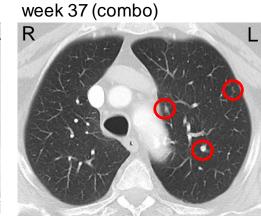
### Efti (IMP321) in Melanoma TACTI-mel (IO combination) – Single Case at 1 mg efti



#### **Efficacy: Metastatic Melanoma**







week 49 (Pembro mono)

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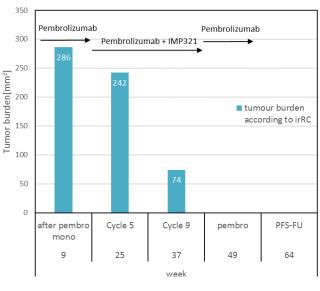
week 64 (PFS-FU)



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

Patient progressing on pembrolizumab monotherapy

Tumour burden (irRC)

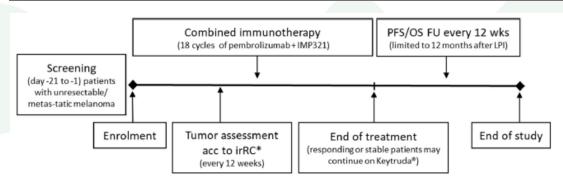




## Efti (IMP321) in Melanoma TACTI-mel Part B: Preliminary Results



#### **Study Scheme Part B:**



<sup>\*</sup>eligibility determined acc. to RECIST 1.1, but treatment decisions based on irRC

#### **Details:**

- 6 pts enrolled
- Patients received:
  - o 2 mg/kg pembrolizumab i.v. every 3 weeks
  - o 30 mg efti s.c. every 2 weeks for up to 12 months
- Imaging was done every 12 weeks

#### **Study Status & Results Part B:**

- Recruitment and safety observation period completed
- 5 pts had at least 1 post baseline CT

Baseline Characteristics	N = 6
Age (median)	65 yrs
Sex (f/m)	1 (13%) / 5 (83%)
ECOG (0/1)	3 (50%) / 3 (50%)
Elevated LDH	5 (83%)
Stage M1c	6 (100%)

- No DLTs or new safety signals detected
- 3/5 evaluable pts (60%) had irPR at 3 months
- Current disease control rate for this group is 66% (4/6)
- 4 pts still under treatment (1 pt died due to PD < 3 months, 1 pt left with confirmed irPD)

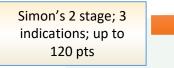
<sup>\* -</sup> tumor assessments done acc. to irRC irRC...Immune-Related Response Criteria, PFS- progression free survival, FU – follow-up



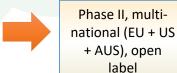
#### Efti (IMP321) in Melanoma **TACTI-002 Trial Design**



#### An umbrella trial: Two ACTive Immunotherapeutics in different indications

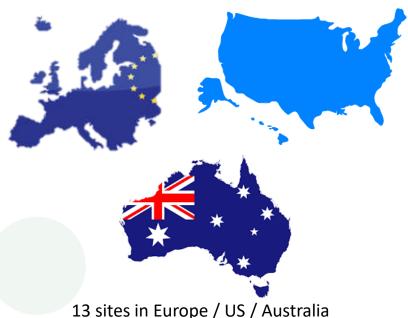


Efti (IMP321) + Pembrolizumab (Keytruda®) for 12 months + max. of 12 months pembrolizumab monotherapy





Primary Objective	Response rate (iRECIST)
Other Objectives	Safety, PFS+OS, PK, exploratory biomarker analysis
Patient Population	Part A: 1 <sup>st</sup> line NSCLC PD-X naive Part B: 2 <sup>nd</sup> line NSCLC, PD-X refractory Part C: 2 <sup>nd</sup> line HNSCC, PD-X naive
Treatment	30 mg Efti (IMP321) s.c. 200 mg Pembrolizumab i.v.





### Collaboration and Supply Agreement immul



- 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's 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



#### **Collaboration and Supply Agreement**



- 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 Immutep



- EOC, an Eddingpharm spin-off holding the Chinese rights for IMP321, Phase I study in MBC starting
- Milestone and royalty bearing partnership for Immutep



- 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, Immutep was first company ever to import and use a Chinese manufactured biologic in a European clinical trial



# IMP761 (Autoimmune Diseases)

#### IMP761 – Agonist mAb



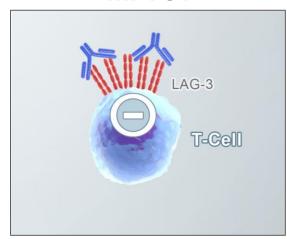
#### **Key Characteristics**

- 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 <a href="http://www.gsk-clinicalstudyregister.com/study/200630#ps">http://www.gsk-clinicalstudyregister.com/study/200630#ps</a>)

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>&</sup>lt;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 (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

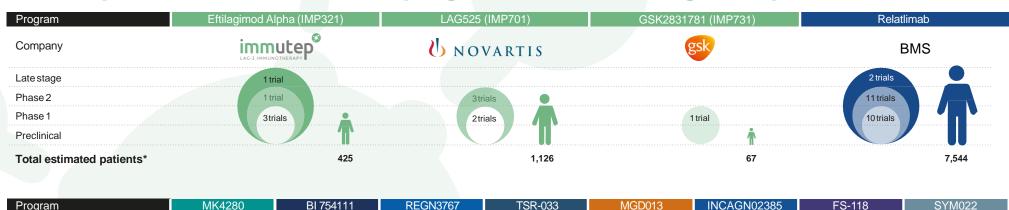


## LAG-3 Landscape

#### **LAG-3 Therapeutic Landscape Overview**

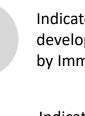


#### Immutep is the leader in developing LAG-3 modulating therapeutics



Program	MK4280	BI 754111	REGN3767	TSR-033	MGD013	INCAGN02385	FS-118	SYM022
Company	Merck & Co. Inc.	B.I.	Regeneron/ Sanofi	Tesaro	Macrogenics	Incyte Corp.	F-Star	Symphogen A/S
Pivotal								
Phase 2	1 trial	1 trial						
Phase 1	2 trials	3 trials	1 trial	1 trial	1 trial	1 trial	1 trial	1 trial
Preclinical				T		İ	İ	À
Total estimated patients*	734	529	546	260	131	55	51	30

Program	IMP761	AM003	TSR-075	XmAb-22841	
Company	immutep <sup>©</sup>	Armo Biosciences	Tesaro	Xencor	
Pivotal					
Phase 2					
Phase 1					
Preclinical					



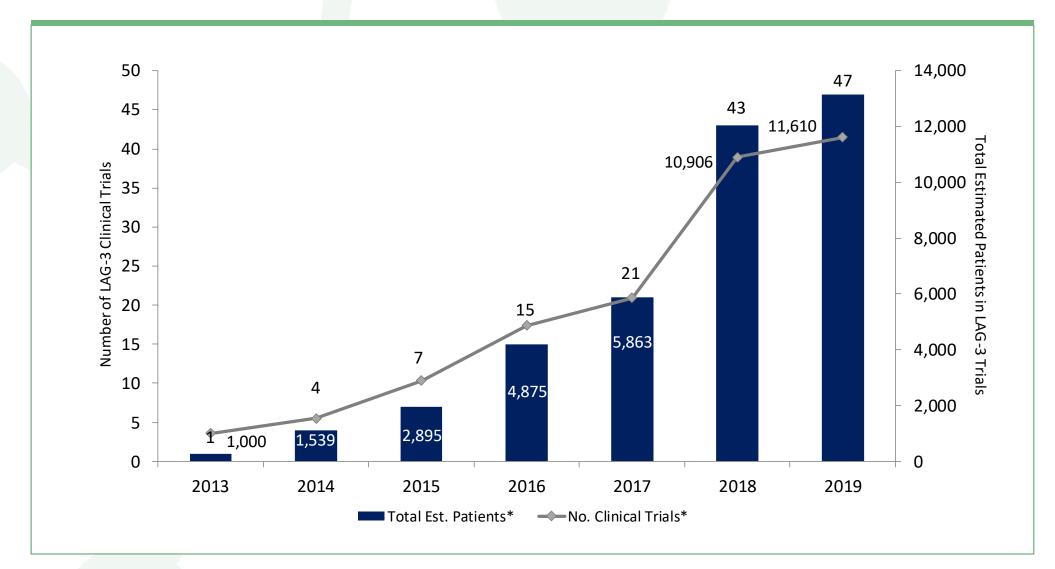
Indicates one product; size indicates stage of development, green = product either developed by Immutep or under license from Immutep

Indicates No. of patients on trials

#### **Increasing Clinical Trials Targeting LAG-3**



#### Industry increasingly deploying resources to development of LAG-3 therapeutics



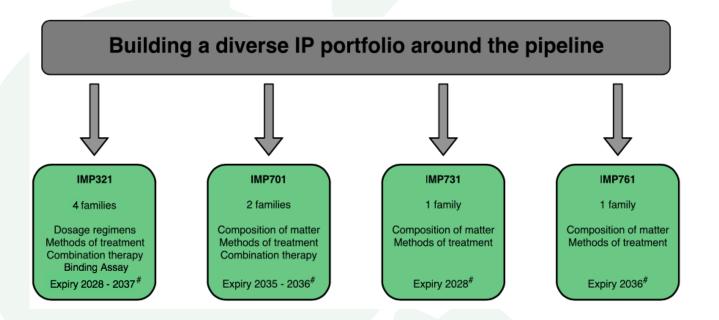


## IP & Outlook

#### **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.

#### **Outlook**



#### **Potential News Flow and Milestones**

R&D	TACTI-mel data from fourth patient cohort (30 mg dose at cycle 1) in 2019					
NGD	TACTI-002 to commence, Phase II trial in collaboration with MSD: H1 2019					
	TACTI-002 first data in 2019					
	INSIGHT-004 to commence, IIT Phase I trial in collaboration with Pfizer and Merck KGaA: H1 2019					
	IMP761 program updates: 2019					
	INSIGHT program updates: 2019					
	AIPAC first progression free survival data (metastatic breast cancer trial): H2 2019					
	Data presentations and posters at conferences					
Other	Potential milestone payments from clinical partners as trials progress					
	Participation at investor and investment bank healthcare investor conferences					
	Continued expansion of patent portfolio					
	Continued regulatory interaction					

#### **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 2019



## Thank you!