

The global leader in developing LAG-3 therapeutics

Investor Presentation 2019

(ASX: IMM, NASDAQ: IMMP)

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Investment Highlights



Global Leader in Development of LAG-3 Therapeutics More clinical-stage LAG-3 programs than any other company

 Dr. Frédéric Triebel, MD Ph.D., Chief Scientific Officer and Chief Medical Officer, discovered the LAG-3 gene in 1990

Best-and-First-in-Class/
Potential Pipelines in
Product Candidates

LAG-3 fusion protein that is a MHCII agonist and APC activator for oncology

LAG-3 agonist mAb for autoimmune diseases

Near-Term Phase II Clinical Data Expected for Eftilagimod Alpha

- Data updates from Phase II clinical study in combination with Keytruda⁽¹⁾ expected in Q4 2019 and in 2020
- PFS data from Phase IIb double blind placebo-controlled study of 227 patients with HER2-negative / HR positive MBC expected in Q1 2020

Leading Industry
Partners

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

Company Snapshot



Globally active biotechnology company with operations in Australia, Europe and U.S.

Four LAG-3 related candidates in immuno-oncology

and autoimmune disease

- Two out-licensed: LAG525 (Novartis) & GSK'781 (GSK)
- Two controlled by Immutep: Eftilagimod Alpha (efti or IMP321)* & IMP761

Committed partnerships with five of the world's largest pharmaceutical companies - Merck (MSD), Pfizer / Merck KGaA, Novartis and GSK

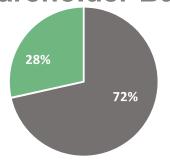
Financial Snapshot

Ticker symbols	IMM (Australian Securities Exchange) IMMP (NASDAQ)			
Securities on issue ⁽¹⁾ (as at 23 September 2019)	3.87 billion ordinary shares 10.9 million American Depository Shares (ADSs)			
Cash & Term Deposits ⁽²⁾ (as at 30 June 2019)	A\$16.6 million (US\$11.2 million)			
Market Cap ⁽³⁾ (as at 23 September 2019)	A\$97 million (US\$66 million)			

Notes:

- (1) Each ADS represents 100 ordinary shares
- (2) Balance as per latest Appendix 4C. Does not include net proceeds of A\$9.3M from capital raise completed in August 2019 and GSK milestone payment of A\$7.4M announced on 23 September 2019 which would increase total cash & term deposits to A\$33M (US\$22.32M)
- (3) Market capitalization based on ASX share price. For a detailed summary of all securities on issue refer to latest Appendix 3B released on ASX

Shareholder Base



*EOC, an affiliate of Eddingpharm holds the Chinese rights for efti via a licensing agreement that is revenue bearing to Immutep

■ Australian Securities Exchange ■ Nasdag

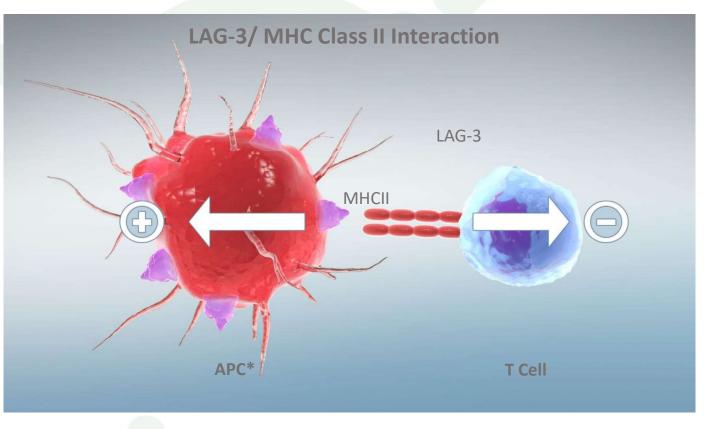
LAG-3 Overview & Product Candidates

LAG-3 as a Therapeutic Target



or personal use (

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

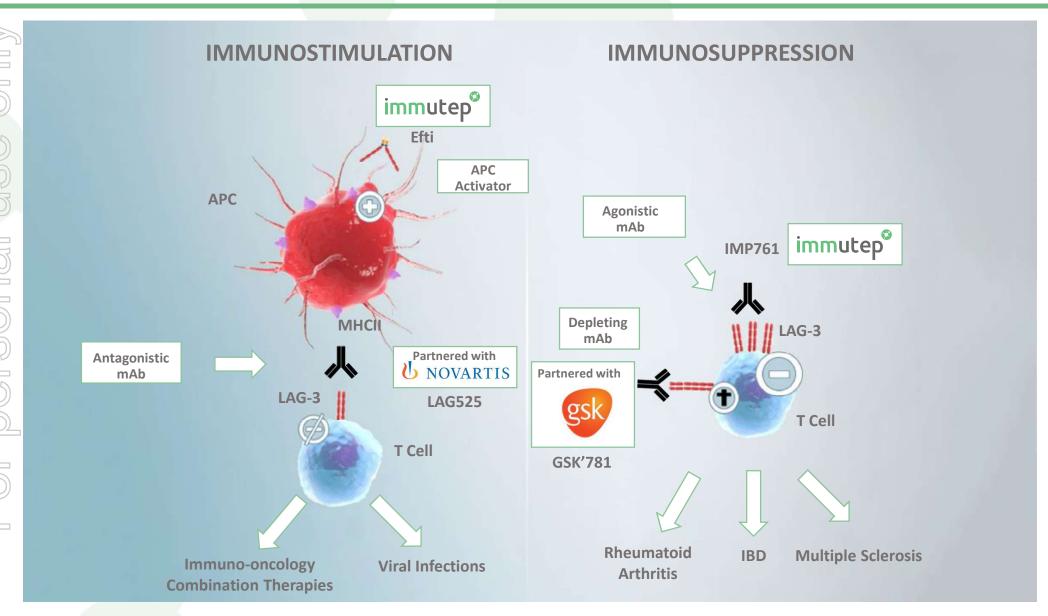


Notes

^{*} APC: antigen presenting cell

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





Immutep Controlled Immunotherapy Pipeline* immutep



	Program	Preclinical	Phase I	Phase II	Late Stage ⁽⁵⁾	Commercial Rights
		AIPAC (Chemo-IO Combo) Metastatic Brea	st Cancer			
		TACTI-002 ⁽¹⁾ (IO-IO Combo) NSCLC (1 st /2 nd L.) HI	NSCC (2 nd)		MERCK INVENTING FOR LIFE	
	Eftilagimod Alpha (LAG-3lg or IMP321),	INSIGHT-004 (2), (3) (IO-IO Combo) Solid Tumors		Merck KGaA, Darmstadt, Germany		Global Rights immutep®
\(\text{\text{\$\infty}} \)	APC activating Soluble LAG-3 Protein	TACTI-mel (IO-IO Combo) Melanoma				
		INSIGHT (2) (In Situ Immunization) Solid Tumors				
		EOC 202 ⁽⁴⁾ (Chemo-IO Combo) Metastatic Breas Cancer	st	♦ E0C		Chinese Rights
Autoimmune	IMP761 (Agonist AB)					Global Rights innute LAG-3 IMMUNOTHERAPY

- Information in pipeline chart current as at 1 August 2019
- - In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC") 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)
- EOC Pharma is the sponsor of the EOC 202 clinical trial which is being conducted in the People's Republic of China
- Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials

Out-Licensed Immunotherapy Pipeline*



	Program	Preclinical	Phase I	Phase II	Late Stage ⁽¹⁾	Commercial Rights/Partners
		IO-IO Combo: Solid Tumors	+ Blood Cancer			
		Chemo-IO Combo: Triple No	egative Breast Cancer			
Oncology	LAG525 (Antagonist AB)	IO-IO-Small Molecule Comb	o: Melanoma			Global Rights
		IO-IO Combo: Solid Tumors				
		Chemo-IO-Small Molecule C Triple Negative Breast Cand				
		Ulcerative Colitis			,	
Autoimmune	GSK'781 (Depleting AB)	Healthy Japanese and Cauc	asian Subjects			Global Rights
Ř		Psoriasis ⁽²⁾				

Note

Information in pipeline chart current as at 1 August 2019

⁽¹⁾ Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials

²⁾ Reflects completed Phase I study in healthy volunteers and psoriasis

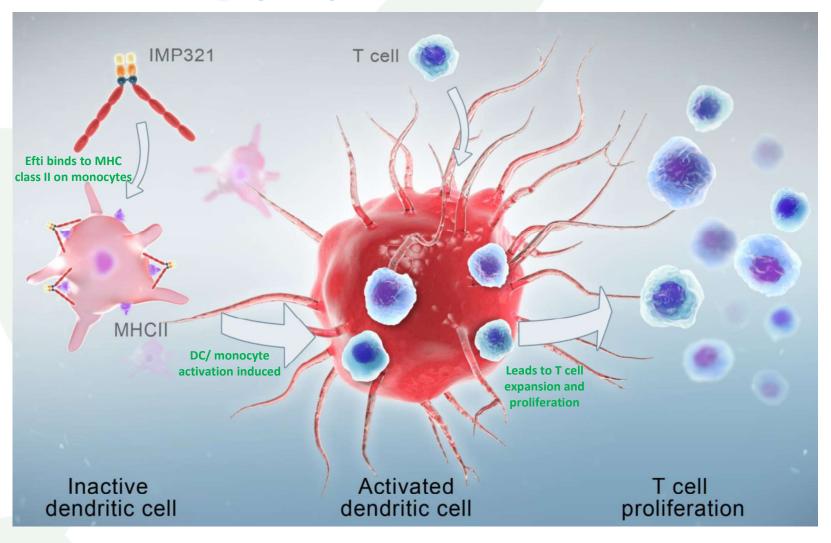
Lead Program Eftilagimod Alpha (IMP321)

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Efti Mechanism of Action (MOA)



Efti's unique agonistic MOA leads to T cell expansion and proliferation => pushing the gas on the immune response





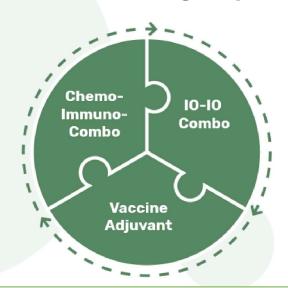
Opportunity for Eftilagimod Alpha



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

- Best-and-First-In-Class MHCII agonist
- Good safety profile and encouraging efficacy data thus far
- Estimated favorable (low) cost of goods, current flat dosing and manufacturing process
- Potential for use in various combination settings potential pipeline in a product

 Late Stage European Phase IIb AIPAC (Immutep)



- Phase I TACTI-mel (Immutep)
- Phase II TACTI-002 (Immutep⁽¹⁾)
- Phase I INSIGHT Stratum D (Immutep⁽²⁾)

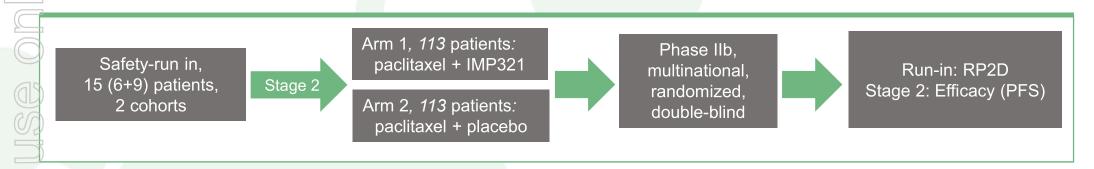
- Phase I Solid Tumors (Cytlimic)
- Phase I INSIGHT Stratum A+B (IKF(3))



Efti - Clinical Development AIPAC



AIPAC: Active Immunotherapy PAC litaxel in HER2-/ HR+ MBC



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

Status Report (Sep 2019)

- √ To-date, efficacy and safety data (ASCO 2018) inline with historical control group / prior clinical trials (Brignone et al J Trans Med 2010, 8:71)
- ✓ Regulatory approval in 7 EU countries
- \checkmark 227 patients recruited in Stage 2 \rightarrow LPI Jun 2019
- PFS data expected calendar Q1 2020

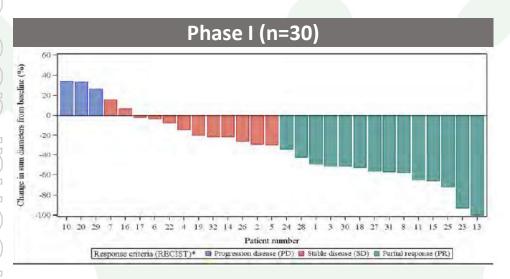
Key features: double blinded, potentially pivotal trial in metastatic breast cancer patients



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%)				

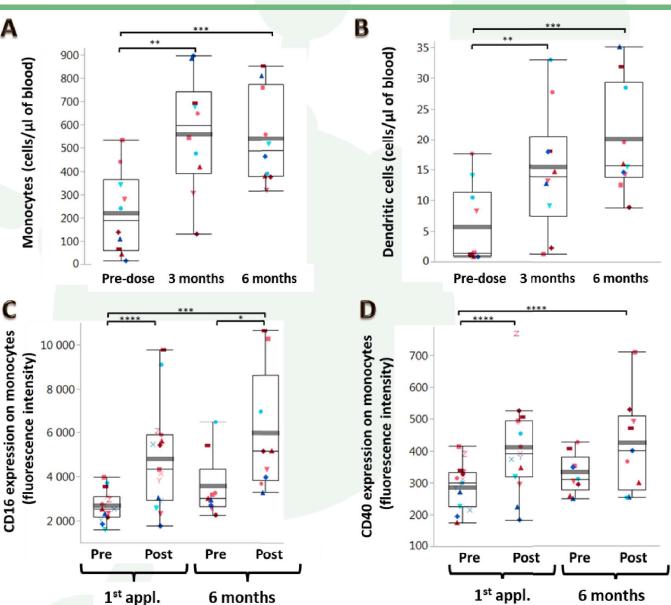
- ORR of 47% and DCR of 87%
- Two of the responses occurred relatively late (after ~6 months)

^{*}Overall Response Rate **Disease Control Rate
Preliminary data, status Interim CSR April 2018, best response acc. To RECIST 1.1



Efti Pharmacodynamic Effect AIPAC Immunomonitoring: Primary Target Cells





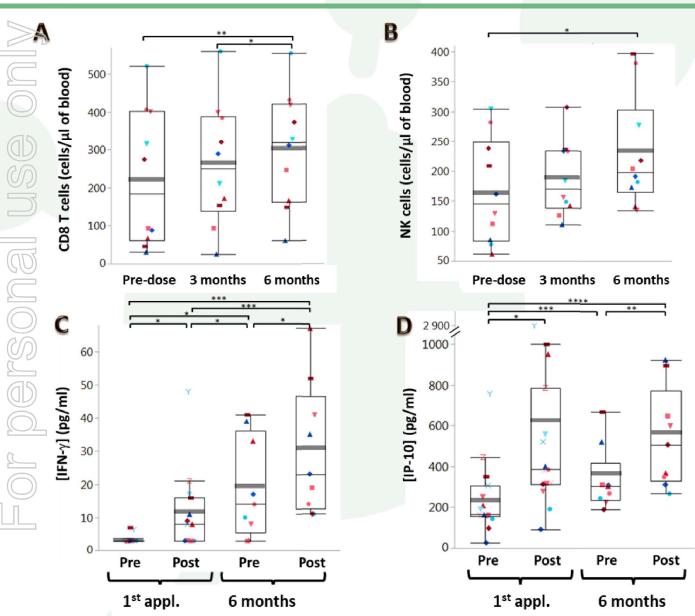
Primary target cells: Sustained increase of circulating Antigen-Presenting Cells (APCs) like monocytes (A) and dendritic cells (B). Rapid activation of monocytes (CD16 (C) and CD40 (D)).

or personal use



Efti Pharmacodynamic Effect AIPAC Immunomonitoring: Secondary Target Cells





Secondary target cells: Sustainable increase in absolute numbers of effector cells like i.e. CD8 T cells (A) and Natural Killer cells (B). IMP321 induces early and sustainable increase of Th1 biomarkers like IFN-γ (C) and IP-10 (CXCL10, D).





TACTI-mel: <u>Two ACT</u>ive <u>Immunotherapeutics in <u>Mel</u>anoma</u>

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	PK and PD of efti, response rate,
objectives	PFS

Patient Population Metastatic melanoma



7 sites in Australia

Status Report (Sep 2019)

- 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 + treatment completed; interim results on following slides
- Pembrolizumab (Keytruda®) 2 mg/kg every 3 weeks i.v. part A and B
- Final data expected in Q4 2019



Efti in Melanoma TACTI-mel – Results Part A



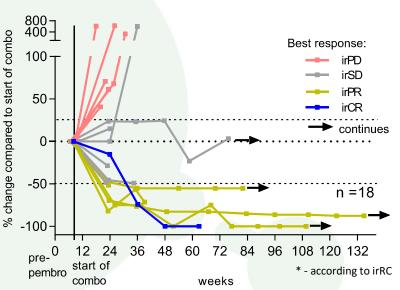
Majority not responding to pembrolizumab monotherapy → Tumor shrinkage in 56 % incl. 2 pts with disappearance of all target lesions

GIS.	
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 %)

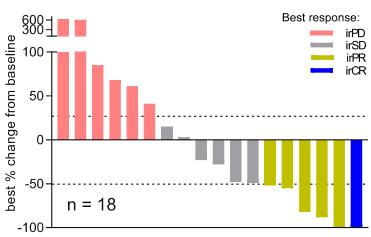
#- incl. 1 pt with complete disappearance of all target lesions; CR acc. to RECIST 1.1

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)

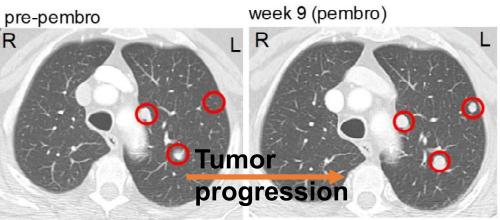


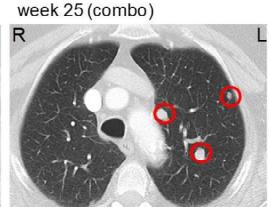


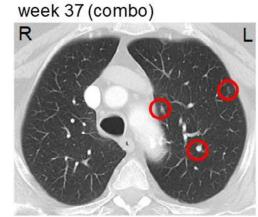
Efti in Melanoma TACTI-mel – Results Part A – Single Case



Efficacy: Metastatic Melanoma







week 49 (Pembro mono)



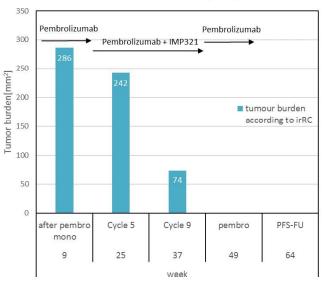
week 64 (PFS-FU)



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

Patient progressing on pembrolizumab monotherapy

Tumour burden (irRC)



or personal use



Efti in Melanoma TACTI-mel – Results Part B



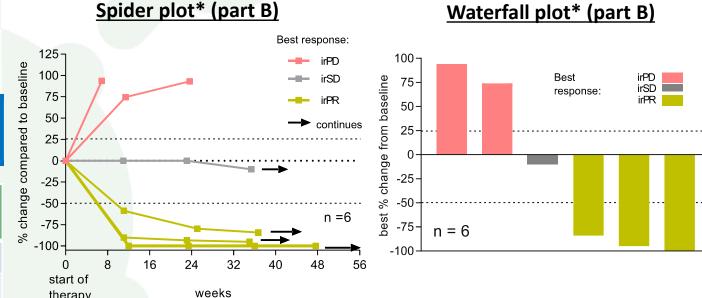
Confirmed deep partial responses in 3 (50%) of the pts Treatment of 4 pts ongoing, all over 9 months

therapy

Baseline Characteristics	N = 6 (%)
ECOG (0/1)	3 (50 %) / 3 (50 %)
Sex (f/m)	1 (13 %) / 5 (83 %)
Elevated LDH	5 (83%)
Metastasis stage M1c	6 (100 %)

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

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



- All patients with very late stage of disease (M1c, elevated LDH)
- No DLTs or new safety signals

* - acc to irRC

- → Confirmed deep partial responses in 3 (50%) of the pts
- → Treatment of 4 pts ongoing (currently 9+ months all)



Efti - Clinical Development TACTI-002 (Phase II)



TAGTI-002: <u>Two ACTive Immunotherapeutics in different indications</u>

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



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



Phase II, multinational (EU + US + AU), open label



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

Patient **Population** A: 1st line NSCLC PD-X naive

B: 2nd line NSCLC, PD-X refractory

C: 2nd line HNSCC, PD-X naïve

Treatment

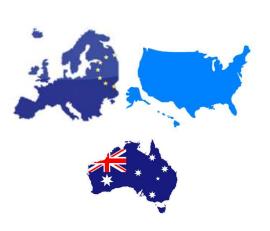
30 mg Efti (IMP321) s.c. 200 mg Pembrolizumab i.v.

In collaboration with



Status Report (Sep 2019)

- ✓ Fully approved in all countries (ES, GB, US, AU)
- ✓ Part A (PD-L1 all comers, 1st line NSCLC): 41 % ORR in stage 1 → 2nd cohort opened (Oct 19)
- 32 pts recruited in total



13 sites in Europe / US / Australia

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®) for 6 months + 6 months avelumab monotherapy



Phase I, monocenter DE, open label, IIT



RP2D, Safety, ORR, PFS, PK, PD

Patient	Sol
Population	sta
Treatment	6/3

Solid tumors after failure of standard therapy

ent 6/30 mg Efti (IMP321) s.c. 800 mg avelumab i.v.;

Both every 2 weeks

Both every 2 weeks

In collaboration with



Merck KGaA, Darmstadt, Germany

Status Report (Sep 2019)

- √ 1 site in Germany
- ✓ Protocol approved by CA/ ED
- ✓ Five patients dosed thus far
- First data expected in 2019

Key features: safety with a PD-L1 antagonist avelumab

Eftilagimod Alpha Partnerships









- EOC, an Eddingpharm spin-off holding the Chinese rights for efti, Phase I study in MBC ongoing
- Milestone and royalty bearing partnership for Immutep where EOC bears all the costs of funding the trials -> Immutep received US\$1M milestone payment when Chinese IND was granted for efti in Dec 2017



- Spin off from NEC, Japan. Est. Dec 2016; aims to develop cancer drugs discovered by artificial intelligence
- Multiple Material Transfer Agreements; Clinical Trial Collaboration (up to USD 5M)
- Preclinical and clinical research ongoing
- Milestone bearing partnership for Immutep where CYTLIMIC bears all the costs of funding the trials -> USD 0.5M upfront payment paid to Immutep



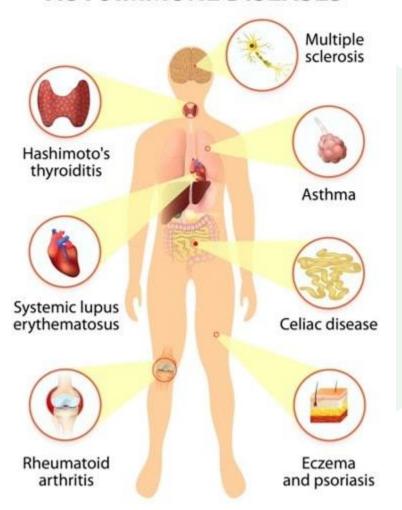
- Strategic supply partnership for the manufacture of efti
- Through WuXi, Immutep was first company ever to import and use a Chinese manufactured biologic in a European clinical trial

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-α, -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







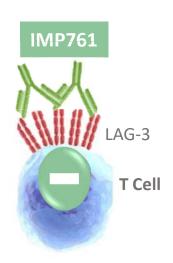


Key Characteristics

- Humanized IgG4 monoclonal antibody
- 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

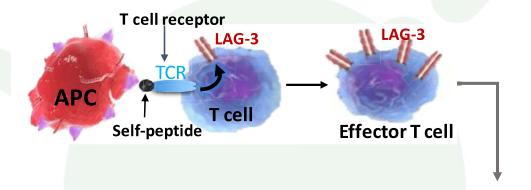


IMP761 Intervenes Upstream from Current Therapeutics





Auto-immune memory T cells are chronically stimulated by the same self-peptide, acquiring an 'exhausted' phenotype and expressing LAG-3 which down-modulates specifically TCR signaling. IMP761 increases this physiological down-regulation.



IMP761: blocking the activation of self-reactive memory T cells



Epigenetic reprogramming

(DNA methylation, histone modifications, miRNAs)



Th1 (e.g. RA, T1D)



Th2 (e.g. allergic asthma)



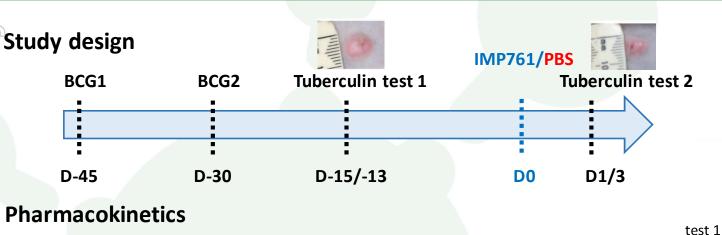
Th17 (e.g. IBD)



IL-23 (e.g. psoriasis)

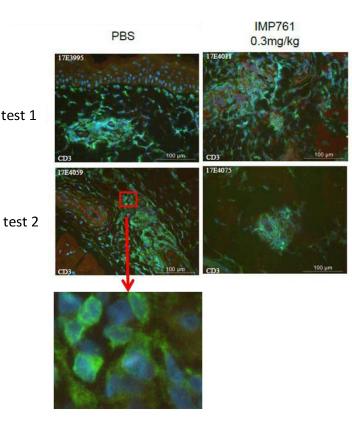
Delayed-Type Hypersensitivity Model in **Cynomolgus Monkey**

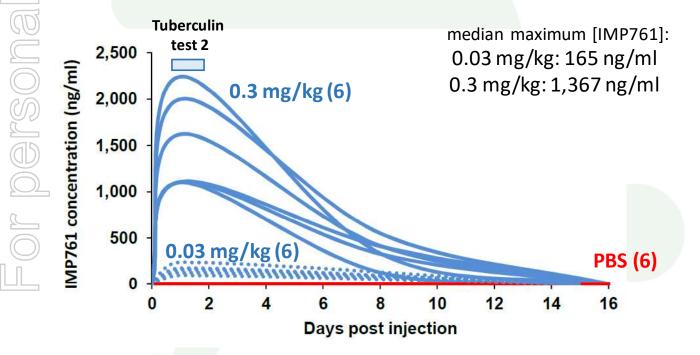




Immunofluorescence staining:

inflammatory T cell infiltration at tuberculin test site before and after IMP761/PBS injection

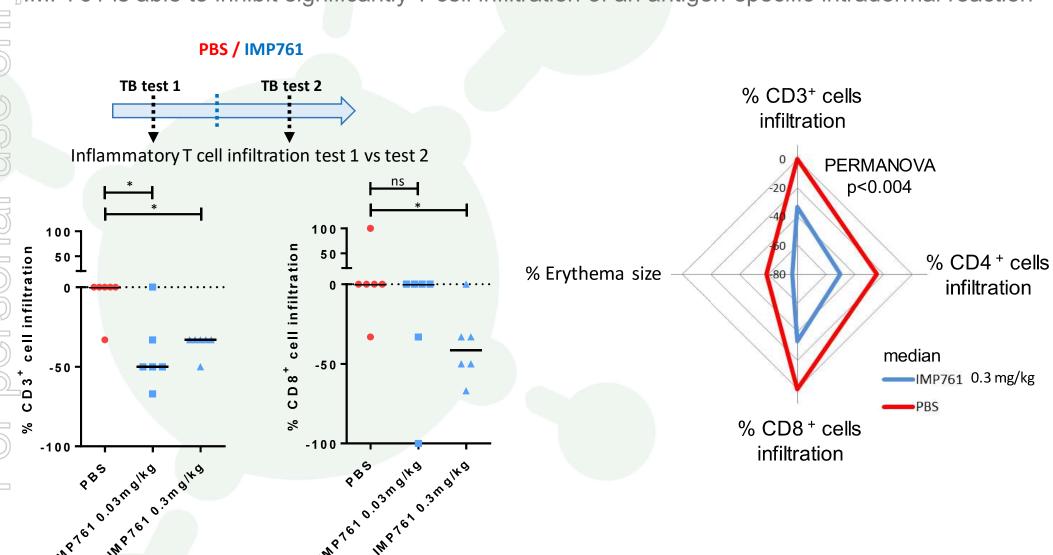




IMP761 Inhibits Inflammatory T Cell Infiltration in vivo



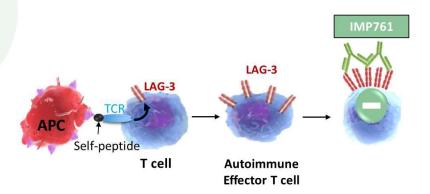
IMP761 is able to inhibit significantly T cell infiltration of an antigen-specific intradermal reaction



Conclusion



- The Concept: treating the cause of autoimmune diseases, not just the symptoms
 - The Target: the self-peptide specific memory T cells harboring LAG-3



- **The Tool**: an agonistic LAG-3-specific mAb down-modulating self-peptide-induced TCR signaling
- **The Evidence** (1): *in vitro* down-modulation of peptide-induced human T cell proliferation and activation
- The Evidence (2): in vivo down-modulation of peptide-induced T cell infiltration/inflammation at the tissue site in a NHP model
- Intellectual Property: 1 family composition of matter methods of treatment, expiry 2036
- The Status: cell line development ongoing and GMP manufacturing preparations underway in order to progress to clinical development

Partnered Programs

GSK'781 (IMP731) for Autoimmune Diseases Immute



- GSK holds exclusive WW rights
- Up to £64m in total upfront payments and milestones, plus royalties
- Sept 2019: 1st patient dosed in phase 2 trial triggered a £4m (~A\$7.4 million or ~US\$ 5.0 million) milestone payment to Immutep
- Portfolio review at GSK in 2017 -> GSK'781 continued despite cancellation of 13 clinical and 20 preclinical programs
- Study completion date of Phase 1 trial in psoriasis: March 2018 with 67 patients⁽¹⁾
- Phase II clinical study evaluating GSK'781 in ulcerative colitis in 280 patients initiated in May 2019 with estimated study completion date of August 2022⁽²⁾
- Phase I clinical study evaluating GSK'781 in 36 healthy Japanese and Caucasian subjects, PK/PD study

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

LAG525 (IMP701) for Cancer⁽¹⁾



- Novartis holds exclusive WW rights
- In 2015: Started Phase I study of LAG525 (derived from IMP701) in combination with PDR001 (anti-PD-1 mAb) in different cancer indications in 490 patients
- 1st and 2nd Milestone payments received in Aug 2015 (undisclosed) and August 2017 (of USD1M), respectively
- In 2018: started new Phase II study of LAG525 in combination with PDR001 in advanced solid and hematologic malignancies in 76 patients
- In 2018: started new Phase II combination studies in metastatic melanoma (230 pts) & new Phase II combination studies in Triple-negative Breast Cancer (96 pts)
- In 2019: started Phase Ib in Triple-negative Breast Cancer (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



9								
	Company	Program	Preclinical	Phase I	Phase II	Phase III	Total Trials	Patients on Trials
Agonist	immutep [©]	Eftilagimod Alpha		2	2		4	424
	BMS	Relatlimab		6	19	2	27	9,422
	U NOVARTIS	LAG525 (IMP701)		1	4		5	1,100
	B.I.	BI754111		4	1		5	849
	Merck & Co. Inc.	MK4280		2	1		3	910
***	Macrogenics	MGD013		1	1		2	1,105
Antagonist	Tesaro ⁽²⁾	TSR-033		1			1	260
Ant	Regeneron ⁽¹⁾	REGN3767		1			1	589
-	Xencor	XmAb-22841		1			1	242
	Symphogen A/S	SYM022		2			2	132
	Incyte	INCAGN02385		1			1	40
	F-Star	FS-118		1			1	51
Agonist	immutep®	IMP761					-	
Depleting AB	gsk (3)	GSK2831781 (IMP731)		2	1		3	383

Notes:

Sources: Company websites, clinical trials.gov, and sec.gov, as of September 27, 2019

B) Includes the Phase I study in psoriasis (completed March 2018)

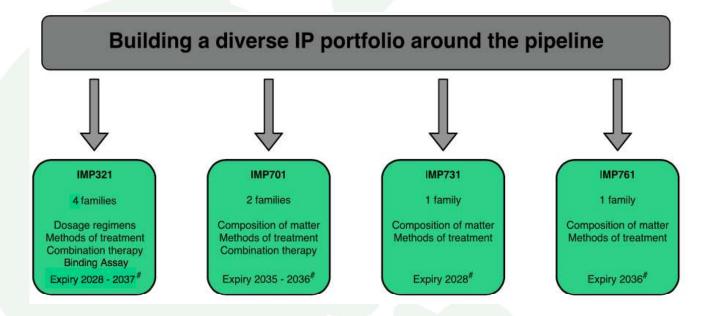
⁽¹⁾ As of January 7, 2019 Regeneron is in full control of program and continuing development (Sanofi discontinued)

⁽²⁾ Tesaro was acquired by and is now part of GSK

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



*Plus up to a 5 year extension of term available in some circumstances to compensate for delay associated with obtaining regulatory approval.

or personal use

2019/ 2020 Clinical Guidance*



- ✓ 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
- ✓ AIPAC fully recruited: Q2 2019
- ✓ TACTI-002 first data in September 2019
- o TACTI-002 data update: Q4 2019
- o INSIGHT-004 update: Q4 2019
- o TACTI-mel final assessment: Q4 2019
- o AIPAC PFS data (metastatic breast cancer trial): Q1 2020
- o TACTI-002 data update: H1 2020
- o INSIGHT-004 data update: H1 2020

^{*}The actual timing of future data readouts may differ from expected timing shown above. These dates are provided on a calendar year basis.

Investment Highlights



Global Leader in Development of LAG-3 Therapeutics • More clinical-stage LAG-3 programs than any other company

 Dr. Frédéric Triebel, MD Ph.D., Chief Scientific Officer and Chief Medical Officer, discovered the LAG-3 gene in 1990

Best-and-First-in-Class/
Potential Pipelines in
Product Candidates

- LAG-3 fusion protein that is a MHCII agonist and APC activator for oncology
- LAG-3 agonist mAb for autoimmune diseases

Near-Term Phase II Clinical Data Expected for Eftilagimod Alpha

- Data updates from Phase II clinical study in combination with Keytruda⁽¹⁾ expected in Q4 2019 and in 2020
- PFS data from Phase IIb double blind placebo-controlled study of 227 patients with HER2-negative / HR positive MBC expected in Q1 2020

Leading Industry

Partners

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