

ASX/Media Release (Code: ASX: IMM; NASDAQ: IMMP)

Immutep Reports Positive Final Efficacy Data from TACTI-mel Trial in Melanoma

Key Trial Findings

- Favourable safety profile of efitlagimod alpha in combination with pembrolizumab
- Deep and durable responses have been observed with tumour shrinkage in 56% and 66% of patients in part A and B respectively
- Disease Control Rate of 66% of patients in each Part A and B (24 patients in total)

SYDNEY, AUSTRALIA – October 15, 2019 – [Immutep Limited](#) (ASX: IMM; NASDAQ: IMMP) (“Immutep” or “the Company”), a biotechnology company developing novel immunotherapy treatments for cancer and autoimmune diseases, today announces mature positive efficacy data from its TACTI-mel Phase I clinical study combining its lead product candidate, efitlagimod alpha (“efti” or “IMP321”) with KEYTRUDA® (pembrolizumab) in metastatic melanoma.

The data will be presented by Dr. Frédéric Triebel, Chief Scientific Officer and Chief Medical Officer of Immutep at the World Immunotherapy Congress as part of the Festival of Biologics 2019 being held in Basel, Switzerland on 15th October 2019.

Commenting on the positive results, Dr. Triebel said, “The combination therapy with efti shows very encouraging efficacy signals of synergy with KEYTRUDA along with a favourable safety profile so far in this high-risk patient population. Patients are responding well to the combination treatment, their tumours are shrinking and not growing back over a long follow up period. In addition, we have seen the complete disappearance of all target tumour lesions for six patients plus one patient with a metabolic complete response on the PET-scan. The efficacy data is now final with a long follow up, the safety assessment is ongoing.”

Overview of Trial

TACTI-mel evaluated the combination of efti with anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in 24 patients with unresectable or metastatic melanoma. Patients participating in the trial had a very late stage of disease: 75% classified as M1c (associated with lowest probability of survival), 67% had lung metastasis, 50% had liver metastasis, 50% had elevated LDH (poor prognosis marker) and many had either a suboptimal response or disease progression with pembrolizumab treatment as a monotherapy. All patients received subcutaneous injections of efti every two weeks, with a treatment duration of up to either six or 12 months.

TACTI-mel is a multi-centre, open label clinical trial involving four cohorts of six patients per cohort:

- **Part A** includes the first three cohorts testing different dosages of efti (1mg, 6mg and 30mg) in combination with pembrolizumab, with efti treatment given for six months only and commencing at cycle five of pembrolizumab treatment.

- **Part B** includes the remaining cohort testing a 30mg dosage of efti given for 12 months in combination with pembrolizumab, starting at cycle 1, day 1 of pembrolizumab treatment.

The primary endpoint of the trial is safety and tolerability, with the outcome to determine the recommended dose for a Phase II trial. The trial also evaluated efficacy through Overall Response Rate (ORR), tumour shrinkage and Disease Control Rate (DCR).

Key Findings

- Efti has a favourable safety profile in combination with pembrolizumab with no dose-limiting toxicities.
- The recommended dosage level for a Phase II trial is 30mg of efti, which is the dosage level currently used in the ongoing TACTI-002 Phase II trial.
- Deep (with 12 patients (50%) having a decrease of $\geq 75\%$ in the target lesions) and durable (9 patients (38%) being treated for ≥ 12 months with pembrolizumab \pm efti) responses have been observed.

The key efficacy findings from the trial are:

Measured according to irRC	Part A* N=18	Part B** N=6	Part A + B C1D1 analysis*** N=24
Overall Response Rate (ORR)	6 (33%)	3 (50%)	14 (58%)
Patients with tumour shrinkage	10 (56%)	4 (66%)	17 (71%)
Disease Control Rate (DCR)	12 (66%)	4 (66%)	Not reported
Progression free at 6 months	Not reported	4 (66%)	14 (58%)

* Part A: Combination treatment began at cycle 5 of pembrolizumab treatment with patients having suboptimal response to pembrolizumab monotherapy and included a dose escalation of efti.

**Part B: Combination treatment started from cycle 1 day 1 of pembrolizumab.

*** Part A+B C1D1 analysis: Performed exploratory analysis starting from cycle 1 day 1 of pembrolizumab, including the 4 cycles pembrolizumab monotherapy (“C1/D1 Analysis”) and includes patients from part B.

The full presentation is attached below to this announcement and will be available on the Company’s website at <http://www.immutep.com/investors-media/presentations.html>

About the TACTI-mel clinical trial

The TACTI-mel (Two ACTIVE Immunotherapies in melanoma) Phase I clinical trial is a multicentre, open-label study evaluating the combination of eftilagimod alpha (“efti”) with pembrolizumab, in unresectable or metastatic melanoma patients that have had either a suboptimal response or had disease progression with pembrolizumab monotherapy (clinicaltrials.gov identifier NCT 02676869).

About Immutep

Immutep is a globally active biotechnology company that is a leader in the development of immunotherapeutic products for the treatment of cancer and autoimmune disease. Immutep is dedicated to leveraging its technology and expertise to bring innovative treatment options to market for patients and to maximize value to shareholders. Immutep is listed on the Australian Securities Exchange (IMM), and on the NASDAQ (IMMP) in the United States.

Immutep's current lead product candidate is eftilagimod alpha ("efti" or "IMP321"), a soluble LAG-3Ig fusion protein based on the LAG-3 immune control mechanism, is a best-and-first-in-class MHC II agonist. This mechanism plays a vital role in the regulation of the T cell immune response. Efti is currently in a Phase IIb clinical trial as a chemoimmunotherapy for metastatic breast cancer termed AIPAC; a Phase II clinical trial being conducted in collaboration with Merck & Co., Inc., Kenilworth, NJ, USA (known as "MSD" outside the United States and Canada) referred to as TACTI-002 (Two ACTIVE Immunotherapies) to evaluate a combination of efti with KEYTRUDA® (or pembrolizumab, an anti-PD-1 therapy) in several different solid tumours (clinicaltrials.gov identifier NCT03625323); a Phase I clinical trial being conducted in collaboration with Merck KGaA, Darmstadt, Germany and Pfizer Inc. referred to as INSIGHT-004 to evaluate a combination of efti with avelumab (clinical trials.gov identifier NCT03252938); and a Phase I combination therapy trial in metastatic melanoma termed TACTI-mel (clinicaltrials.gov identifier NCT02676869). Immutep is also developing a LAG-3 agonist monoclonal antibody for autoimmune diseases (IMP761) that is currently in preclinical development.

Further information can be found on the Company's website www.immutep.com or by contacting:

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A soluble LAG-3 protein (eftilagimod alpha) with an anti-PD-1 antibody (pembrolizumab): a new combination in immuno-oncology.

Frédéric Triebel MD, PhD
World Immunotherapy Congress
Basel, October 15, 2019

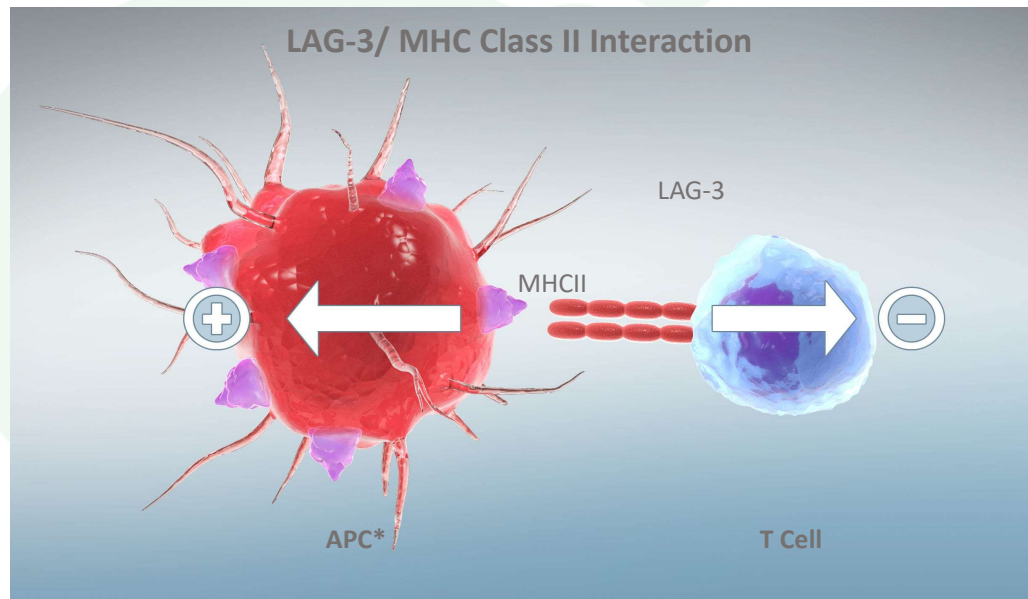
Notice: Forward Looking Statements

The purpose of the presentation is to provide an update of the business of Immunetep 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 Immunetep and should not be relied upon as an independent source of information. Please refer to the Company's website and/or the Company's filings to the ASX and SEC for further information.

The views expressed in this presentation contain information derived from publicly available sources that have not been independently verified. No representation or warranty is made as to the accuracy, completeness or reliability of the information. Any forward looking statements in this presentation have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside Immunetep's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this presentation include known and unknown risks. Because actual results could differ materially to assumptions made and Immunetep's current intentions, plans, expectations and beliefs about the future, you are urged to view all forward looking statements contained in this presentation with caution. Additionally, the INSIGHT investigator sponsored clinical trial described in this presentation is controlled by the lead investigator and therefore Immunetep has no control over this clinical trial. This presentation should not be relied on as a recommendation or forecast by Immunetep. 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.

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



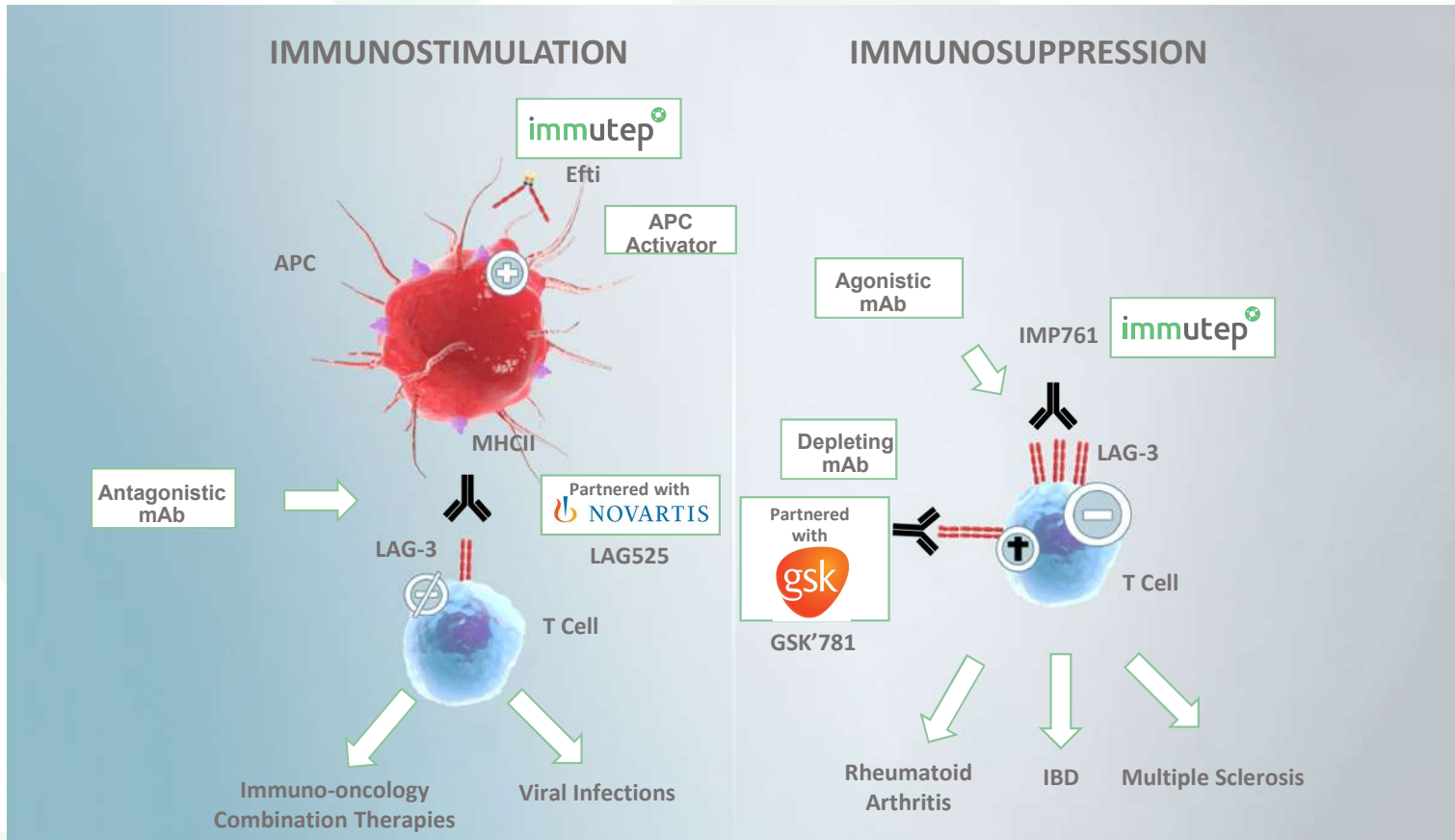
→ **Negative regulation**
of LAG-3⁺ T Cells



Notes:

* APC: antigen presenting cell

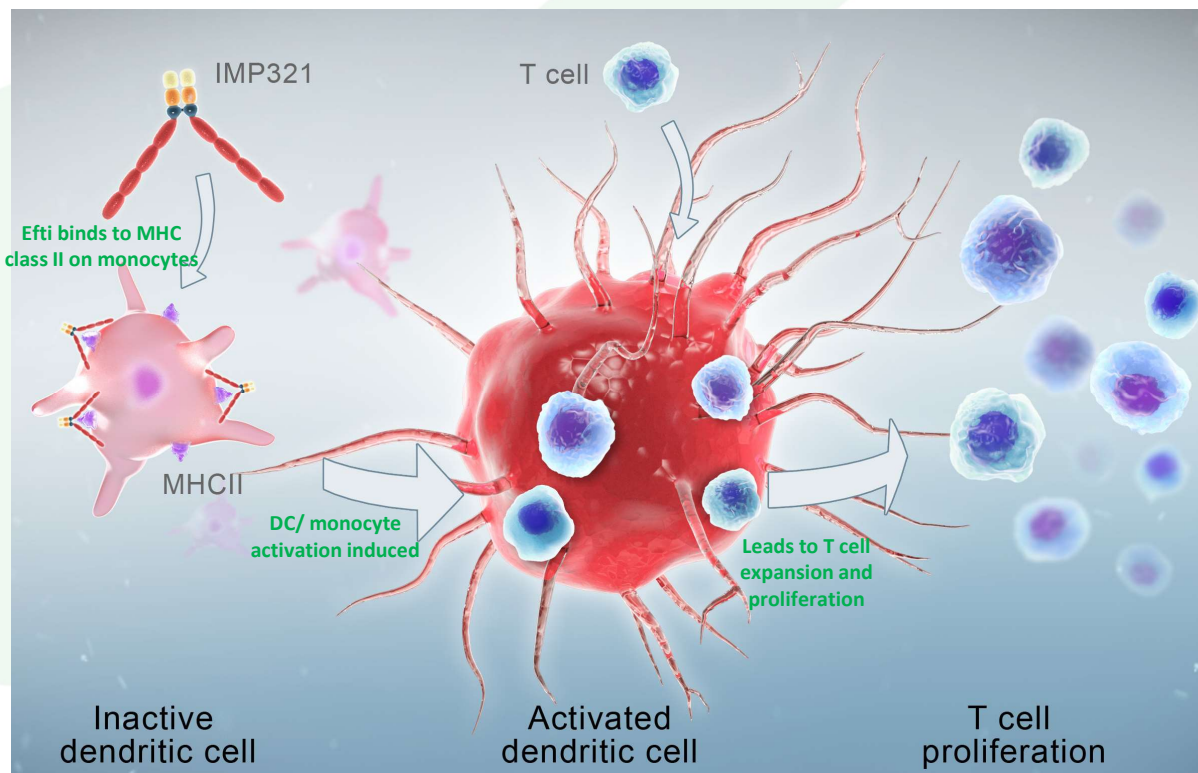
Targeting LAG-3/MHC II May Lead to Multiple Therapeutics in Numerous Indications

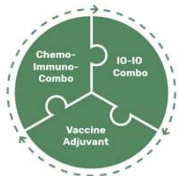


Lead Program Eftilagimod Alpha (IMP321)

Efti Mechanism of Action (MOA)

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



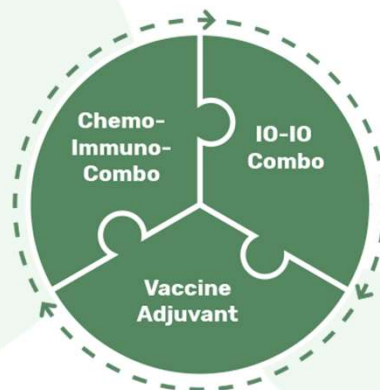


Opportunity for Eftilagimod Alpha

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 (Immute^{te}p)*

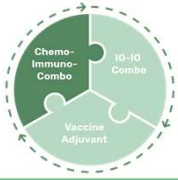


- *Phase I TACTI-mel (Immute^{te}p)*
- *Phase II TACTI-002 (Immute^{te}p⁽¹⁾)*
- *Phase I INSIGHT – Stratum D (Immute^{te}p⁽²⁾)*

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

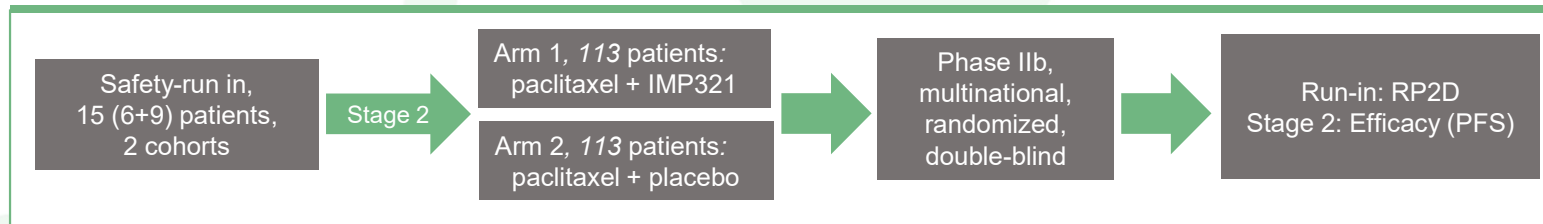
Notes

(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). This extension of INSIGHT is also referred to as INSIGHT-004
 (3) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immute^{te}p has no control over this clinical trial



Efti - Clinical Development AIPAC

AIPAC: Active Immunotherapy PAClitaxel in HER2-/ HR+ MBC

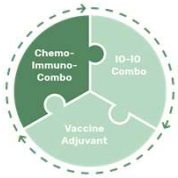


Other Objectives	Anti-tumor activity, safety and tolerability, PK, immunogenicity, quality of life
Patient Population	Advanced MBC indicated to receive 1 st line weekly paclitaxel
Treatment	Run-in: Paclitaxel + IMP321 (6 or 30 mg) Arm 1: Paclitaxel + IMP321 (30 mg) Arm 2: Paclitaxel + Placebo
Location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

Status Report (Sep 2019)

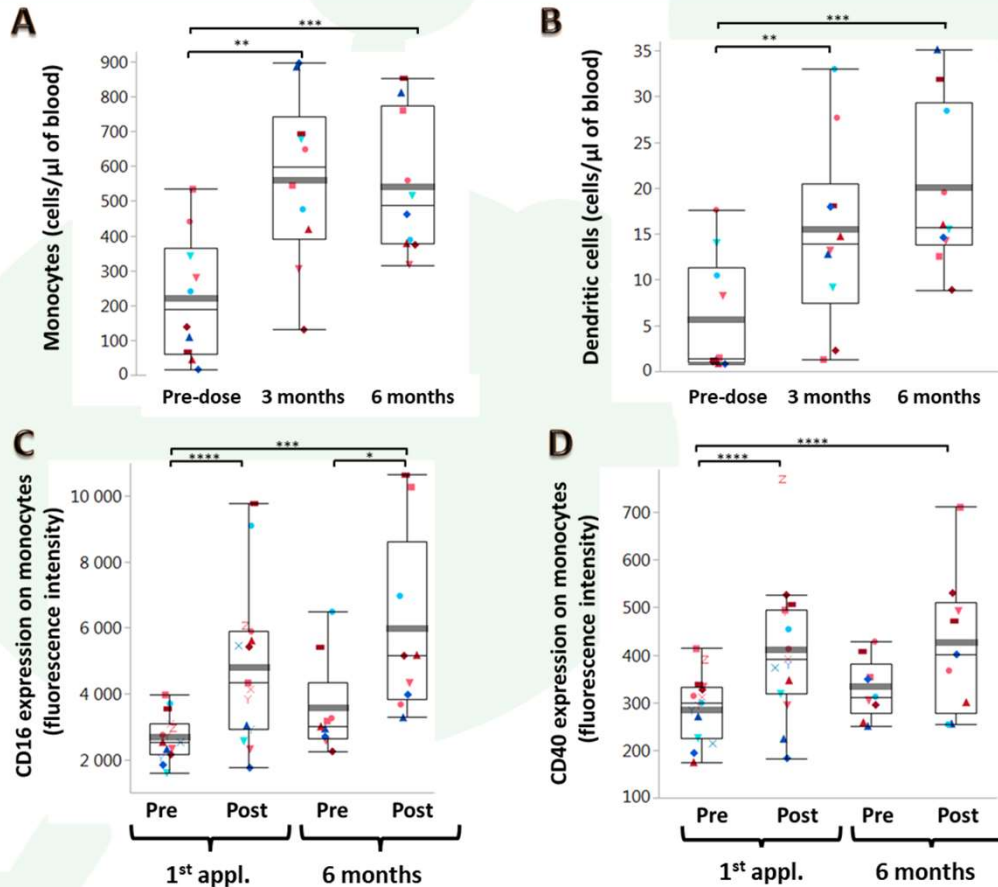
- ✓ To-date, efficacy and safety data (ASCO 2018) in-line with historical control group / prior clinical trials (Brignone et al J Trans Med 2010, 8:71)
- ✓ Regulatory approval in 7 EU countries
- ✓ 227 patients recruited in Stage 2 → LPI Jun 2019
- PFS data expected calendar Q1 2020

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

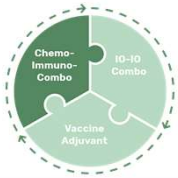


Efti Pharmacodynamic Effect

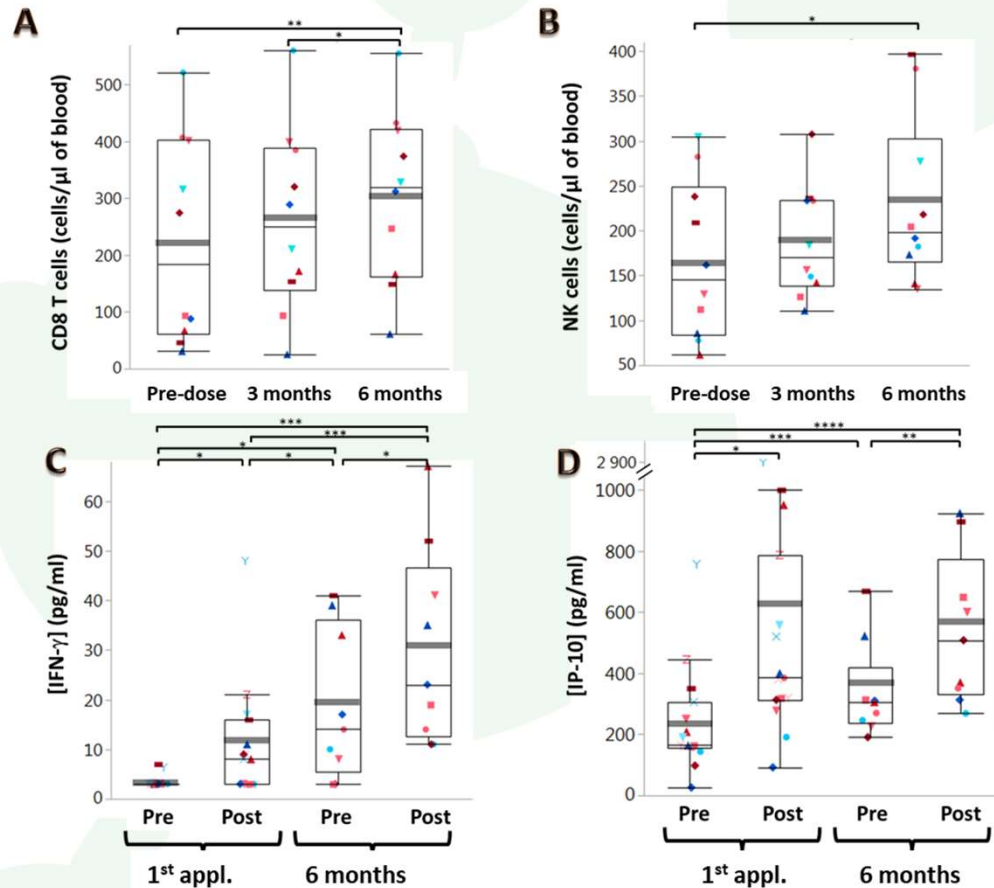
AIPAC Immunomonitoring: Primary Target Cells



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)).



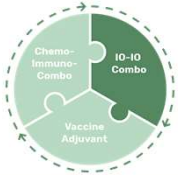
Efti Pharmacodynamic Effect AIPAC Immunomonitoring: Secondary Target Cells



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 trials: Two ACTIVE Immunotherapies

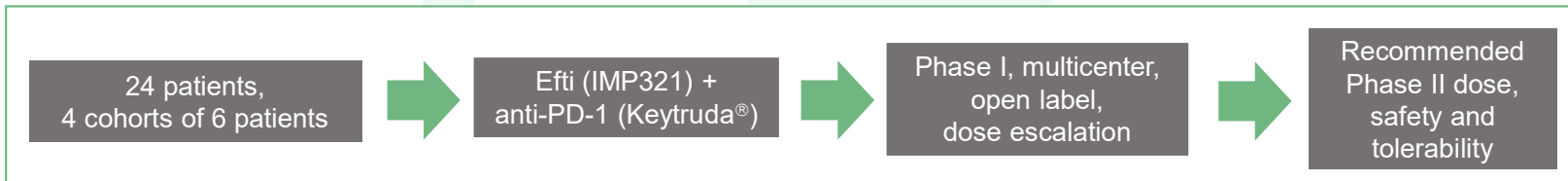
“Pushing the gas on the APC
while releasing the brake on the T cell”



Efti in Melanoma TACTI-mel – Trial Design



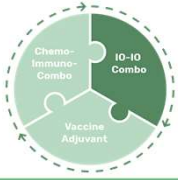
TACTI-mel: Two ACTive Immunotherapeutics in Melanoma



Other objectives	PK and PD of efti, response rate, PFS
Patient Population	Metastatic melanoma



- 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 – Safety Part A + B



*Efti has a favorable safety profile in combination with pembrolizumab -
No DLTs or MTDs and no new safety signals observed*

Frequent TEAE (selected if ≥ 15 % of pts)

Adverse Event*	Any grade N (%)	≥ Grade 3 N (%)
Abdominal pain (various terms)	5 (21)	-
Arthralgia	5 (21)	1 (4)
Cough	4 (17)	-
Diarrhea / Colitis	6 (25)	1 (4)
Fatigue	12 (50)	-
Headache	4 (17)	-
Injection site reaction	6 (25)	-
Nausea	7 (29)	-
Rash##	12 (50)	1 (4)

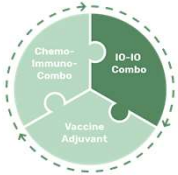
* - Adverse events occurred in > 15 % of pts
- any kind of rash

- 10 SAEs in 9 pts; one related to pembrolizumab, none to efti
- 6 pts (25 %) with ≥ 1 AE ≥ grade 3 (no grade 5)

Grade 3 / 4 TEAEs and rel. to study treatment

Reported term	Grade 3 N (%)	Grade 4 N (%)	Rel to efti / pembro
Maculo-papular rash	1 (4 %)	-	No / Yes
Decreased renal function	1 (4 %)	-	Yes / No
Colitis	1 (4 %)	-	No / Yes
Altered liver functions	1 (4 %)	-	No / Yes
Arthralgia	1 (4%)	-	No / Yes

- 2 pts died due to AE (grade 4 intracranial hemorrhage, not related to treatment; grade 4 Sepsis, not related to treatment)
- 1 pt disc. due to an AE (anaemia; not related to treatment)
- 6 pts experienced treatment delays due to AEs

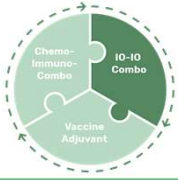


Efti in Melanoma TACTI-mel – Baseline Characteristics



Patients in very late stage of disease (M1c, elevated LDH, liver metastasis)

Baseline Characteristics	Part A N = 18 (%)	Part B N = 6 (%)	Overall N =24 (%)
Median Age	67 yrs	61 yrs	62 yrs
Sex (f/m)	6 % / 94 %	17 % / 83 %	8 % / 92 %
ECOG 1 / 0	22 % / 78 %	50 % / 50 %	29 % / 71 %
Pre-treated with BRAF/MEK/ipilimumab	5 (28 %)	0 (0 %)	5 (21 %)
Poor prognostic marker at study entry			
Elevated LDH (>ULN)	7 (39%)	5 (83%)	12 (50 %)
Liver metastasis	10 (56 %)	2 (33 %)	12 (50 %)
Lung metastasis	11 (61 %)	5 (83 %)	16 (67 %)
Metastatic, stage M1c	14 (78 %)	4 (66 %)	18 (75%)



Efti in Melanoma TACTI-mel – Results Part A

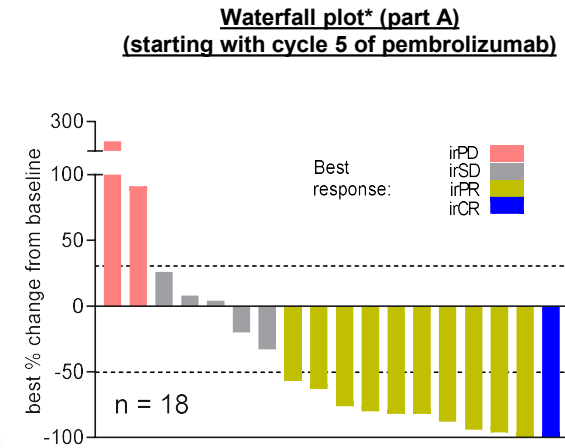
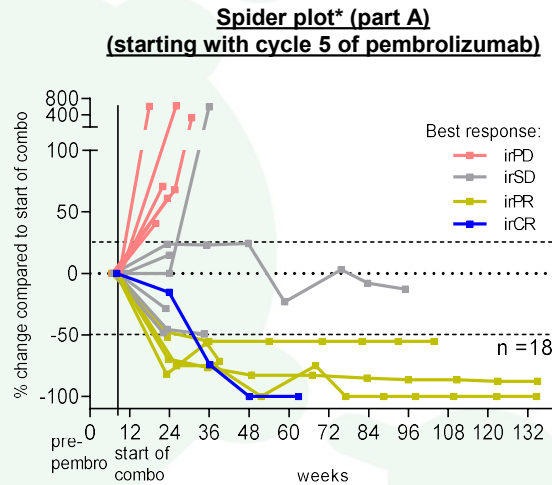


Majority not responding to pembrolizumab monotherapy
→ Tumor shrinkage in 56 % incl. 2 pts with disappearance of all baseline index lesions

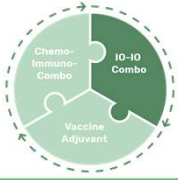
Best Overall Response acc. to irRC	N = 18 (%)
irCR	1 (6 %)
irPR#	5 (28 %) #
irSD	6 (33 %)
irPD	6 (33 %)
Best overall response rate (ORR)	6 (33 %)
Patients with tumor shrinkage	10 (56 %)
Disease control rate	12 (66 %)

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

Exploratory analysis
 (C1D1 pembrolizumab):
ORR of 61 %



* - according to irRC



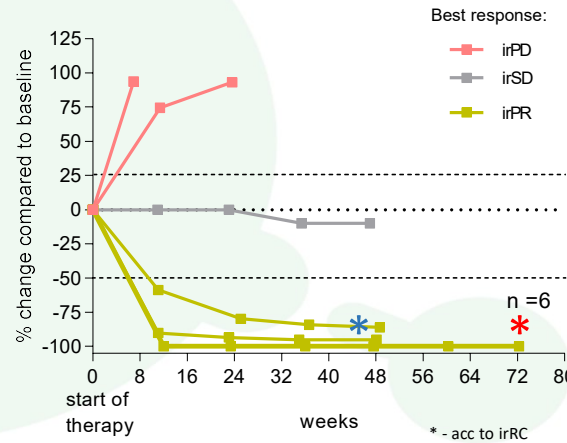
Efti in Melanoma TACTI-mel – Results Part B

Confirmed deep partial responses in 3 (50%) of the pts

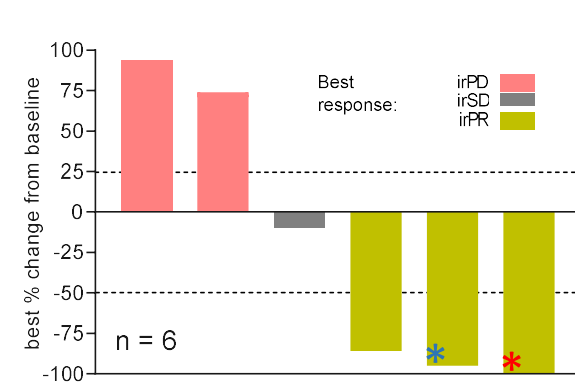
Best Overall Response acc. to irRC	N = 6 (%)
irCR	0 (0%)
irPR#	3 (50%)#
irSD	1 (17%)
irPD	2 (33%)
Best overall response rate (ORR)	3 (50%)
Patients with tumor shrinkage	4 (66%)
Disease control rate	4 (66%)

- incl. 1 pt with complete disappearance of all target lesions (red asterix, case 1) and incl 1 add. pt with no metabolic active disease as per PET-CT (blue asterix, case 2)

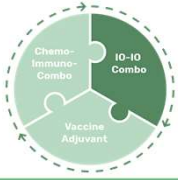
Spider plot* (part B)



Waterfall plot* (part B)

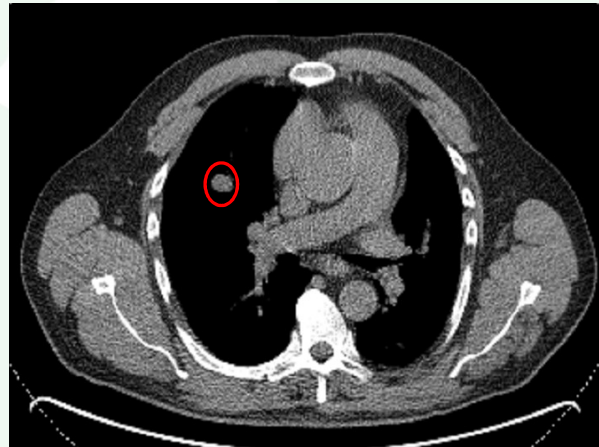


- 4 patients (all non-PD) continue on pembrolizumab monotherapy after completion of the trial

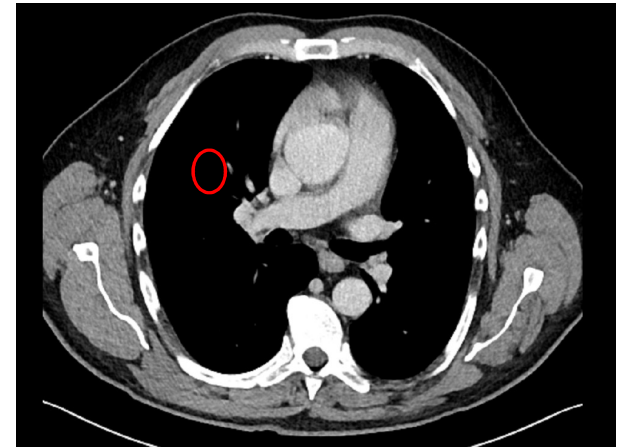


Efti in Melanoma TACTI-mel – Results Part B Single Case study (1)

- 61-year old male patient
- TxNxM1b at study entry in March 2018
- irPR reached by week 12 and maintained until end of study (week 72)

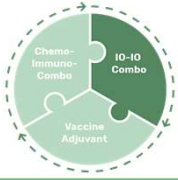


Baseline; lesion 17 mm



Week 72; lesion 0 mm

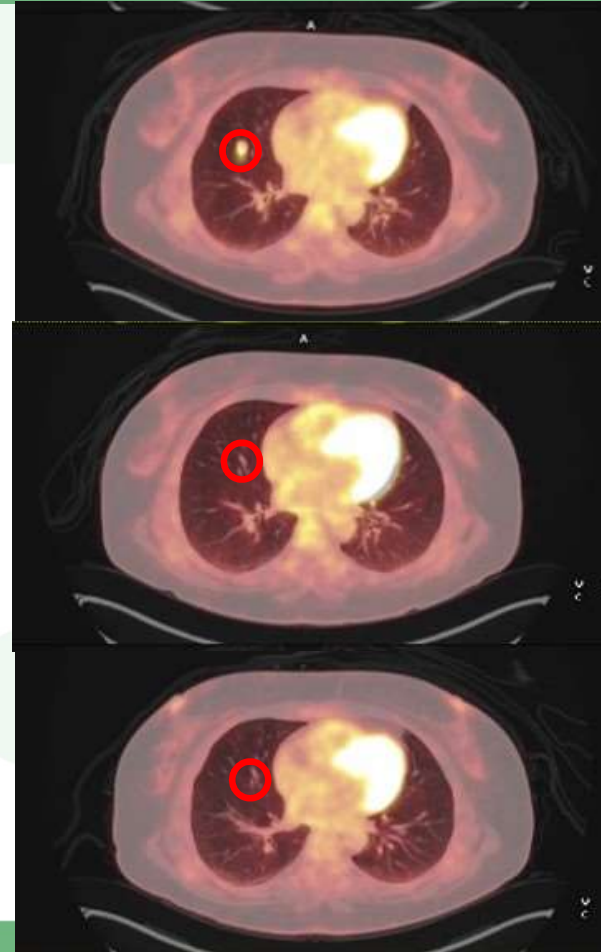
Single index (or target) lesion completely disappeared by week 12
Non-index lesions remained present



Efti in Melanoma TACTI-mel – Results Part B Single Case study (2)

- 46-year old female patient
- TxNxM1c at study entry in August 2018
- irPR reached by week 12 and maintained until end of study
- PET-scans negative on two occasions – at the time of end of treatment and after end of study

Deep irPR, residual tumor mass not metabolically active
(complete metabolic response, CMR)

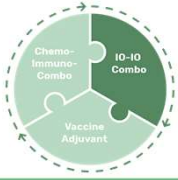


PET-scans

June 2018

May 2019

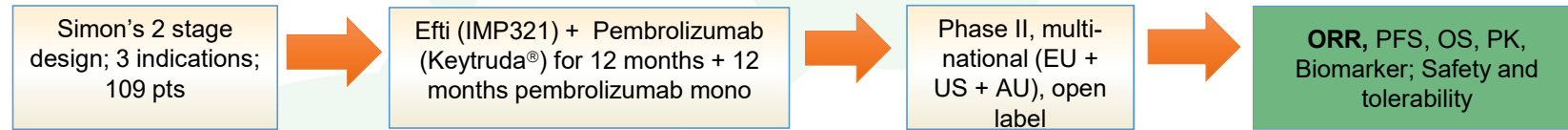
August 2019



Efti - Clinical Development TACTI-002 (Phase II)



TACTI-002: Two ACTive Immunotherapeutics in different indications



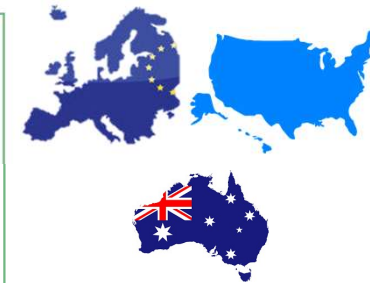
Patient Population	A: 1 st line NSCLC PD-X naïve B: 2 nd line NSCLC, PD-X refractory C: 2 nd line HNSCC, PD-X naïve
Treatment	30 mg Efti (IMP321) s.c. 200 mg Pembrolizumab i.v.

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 will be opened Q4 2019
- ✓ 32 pts recruited in total



13 sites in Europe / US / Australia

Updated results will be presented at SITC (under embargo until Nov. 9th, 2019)

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

Thank you

Frédéric Triebel MD, PhD
World Immunotherapy Congress
Basel, October 15, 2019