



# The global leader in developing LAG-3 therapeutics

Jefferies Virtual Healthcare Conference
June 1 – June 4, 2021

(ASX: IMM, NASDAQ: IMMP)

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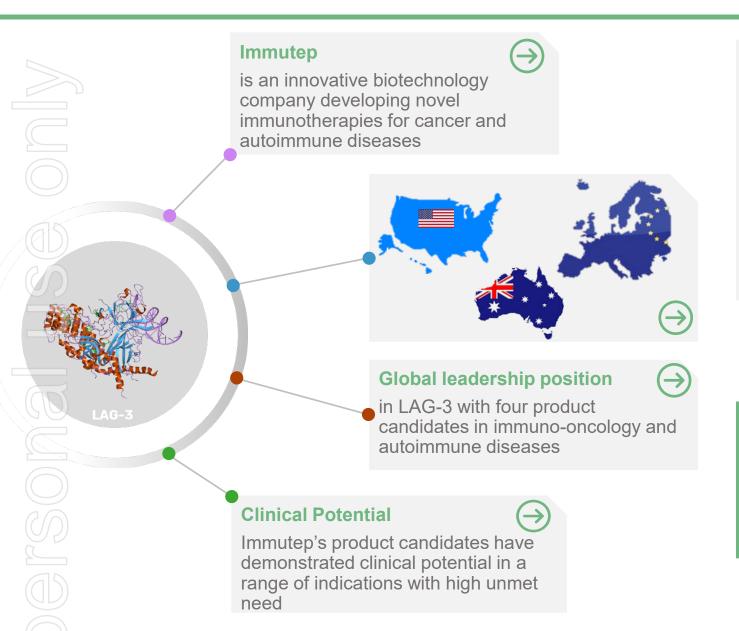
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# Overview





# **Collaboration deals** executed with industry leaders



















# **Corporate Strategy:**

To develop product candidates to sell, licence or partner with large pharmaceutical companies at key value inflection points





# LAG-3 Overview - The most promising immune checkpoint -

# **LAG-3 Therapeutic Landscape Overview**



		Company	Program	Preclinical	Phase I	Phase II	Phase III	Total Trials	Patients
	Agonist	LAG-3 IMMUNOTHERAPY	Eftilagimod Alpha <sup>(5)</sup>		10	4		14	940
		BMS	Relatlimab		7	32	2	41	9,509
		U NOVARTIS	leramilimab		1	4	Validation "demonstrate a benefit for	5	960
		Merck & Co. Inc.	Favezelimab		1	5	patients" <sup>(6)</sup>	6	1066
		Macrogenics	Tebotelimab		3	3		6	1514
λίξ		H-L Roche	RO7247669		1	2		3	538
Oncology	क्र	B.I.	BI754111		4	1		5	649
	Antagonist	Regeneron <sup>(1)</sup>	Fianlimab		1	1		2	836
	An	Tesaro <sup>(3)</sup>	TSR-033		1	1		2	139
		Incyte	INCAGN02385		1	1		2	74
		Symphogen <sup>(2)</sup>	SYM022		3			3	169
		F-star	FS-118		2			2	102
C		Innovent	IBI110		1			1	268
		Xencor	XmAb-22841		1			1	242
toimmune	Agonist	inmutep®	IMP761						
Autoim	Depleting AB	gsk (4)	GSK2831781 (IMP731)		2	1		3	164

Sources: GlobalData, Company websites, clinicaltrials.gov, and sec.gov, as of 1 June 2021. The green bars above represent programs conducted by Immutep &/or its partners. Total trials includes all active, completed &/or inactive trials. Patient totals are based on estimated total enrolled &/or to be enrolled. Not a complete list of currently existing LAG-3 products.

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

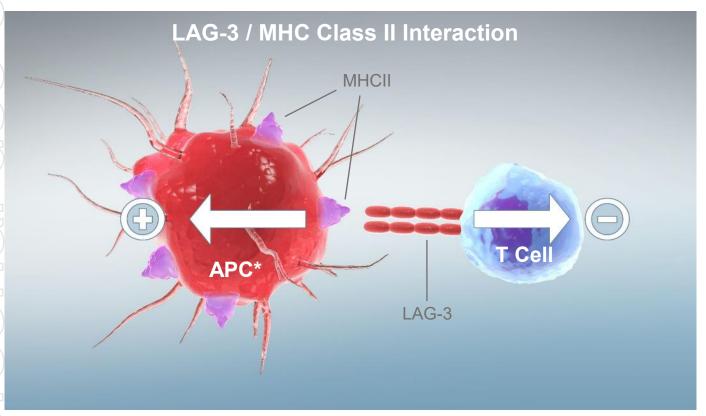
- 4) Includes two completed Phase I studies and one discontinued Phase 2 study (see slide 9)

# LAG-3 as a Therapeutic Target



LAG-3, an immune checkpoint, is widely expressed on tumor infiltrating lymphocytes (TILs)

and cytotoxic T cells → LAG-3 / MHC II interaction is a validated target for IO



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



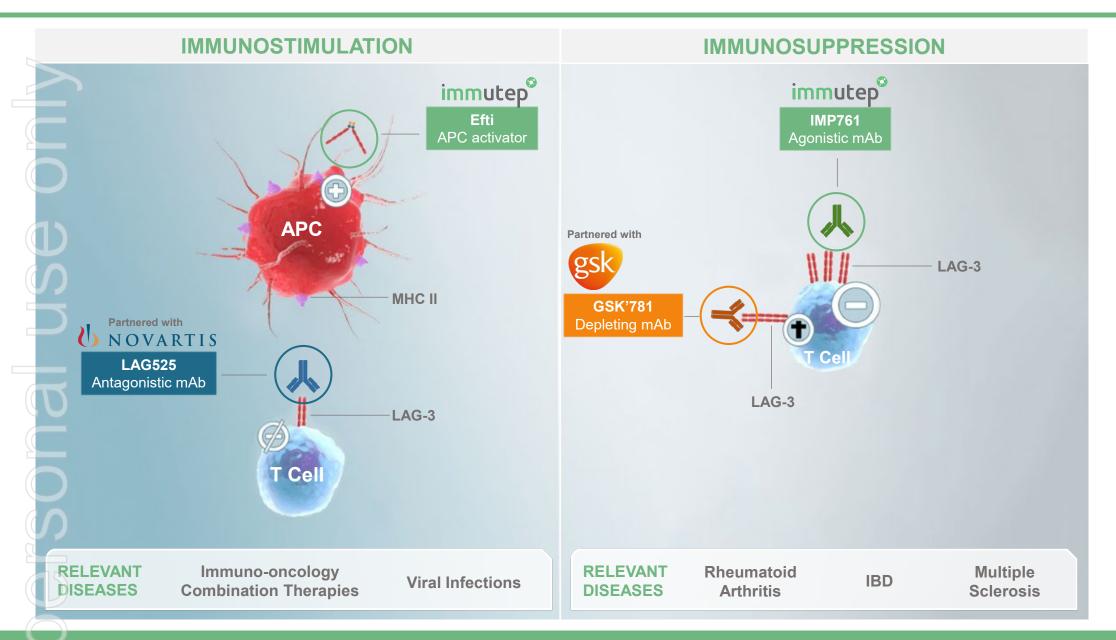
→ Negative regulation of LAG-3<sup>+</sup> T Cells



# Targeting LAG-3 / MHC II:

# Multiple Therapeutics in Numerous Diseases





# **Immunotherapy Pipeline\***



_		tiliciapy i					
	Program	Preclinical	Phase I	Phase II	Late Stage <sup>(5)</sup>	Commercial Rights	Market Size <sup>(6)</sup>
>		Metastatic Breast Cancer (C	Chemo – IO)				US\$29.9 billion
=		Non-Small-Cell Lung Carcii TACTI-002	noma (IO – IO) <sup>(1)</sup>		MSD INVENTING FOR LIFE		US\$22.6 billion
		Head and Neck Squamous TACTI-002	Cell Carcinoma (IO – IO) <sup>(1)</sup>		MSD INVENTING FOR LIFE		US\$1.9 billion
J	Eftilagimod	Head and Neck Squamous TACTI-003	Cell Carcinoma (IO – IO) <sup>(1b)</sup>		MSD INVENTING FOR LIFE		Hollild E.1 &CO
(Rollowin)	Alpha (efti or IMP321)	Solid Tumors (IO – IO) (2), (3) INSIGHT-004	a)	Merck KGaA, Darmstadt, Germany		Global Rights	
	APC activating soluble LAG-3	Solid Tumors (IO – IO) (2), (3) INSIGHT-005	b)	Merck KGaA, QSK Darmstadt, Germany	S	immutep <sup>©</sup>	
5	protein	Melanoma (IO – IO) <sup>(1)</sup> TACTI-mel					US\$4.5 billion
		Solid Tumors (In situ Immo	unization) <sup>(2)</sup>				
<b>5</b>		Solid Tumors (Cancer Vacc YNP01 / YCP02 / CRESCEN		CYTLIMIC Cytotoalc T Lymphocyte Immunotherapy in Cancer			
_		Metastatic Breast Cancer (C	Chemo – IO) <sup>(4b)</sup>	•	PEOL	Chinese Rights	US\$2.3 billion
Dis.	Efti	COVID-19 disease (Monoth	erapy) <sup>(7)</sup>		§	Global Rights <sup>(8)</sup>	
	IMP761	LATIOUVID			S	Global Rights	US\$149.4 billion
	(Agonist AB)				§	immutep"	(2025)
s		surrent as at June 2021					

- (2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this (6) GlobalData Market Size forecast for US, JP, EU5, Urban China and Australia; KBV Research:

- https://www.kbvresearch.com/autoimmune-disease-therapeutics-market/)
  (7) IIT conducted by University Hospital Pilsen. Immutep has no control over this trial.

# **Immutep Out-Licensed Immunotherapy Pipeline\***





- (3) Reflects completed Phase I study in healthy volunteers and in patients with plague psor

- https://clinicaltrials.gov/ct2/results?cond=&term=GSK2831781&cntry=&state=&city=&dist= and

Discontinued in Jan 2021

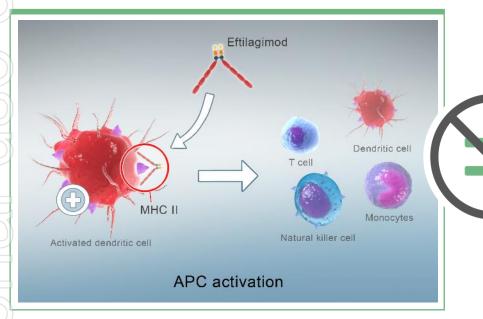


# Eftilagimod Alpha (efti or IMP321)

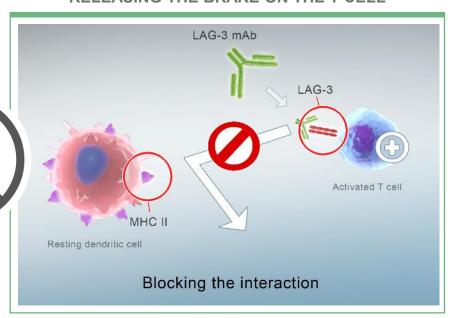
# Efti: an Innovative LAG-3 IO Product Candidate



- the only MHC II agonist (APC activator) product candidate currently in clinical development synergistic with other therapeutic agents and modalities e.g. IO agents or chemotherapy
- "PUSHING THE ACCELERATOR ON IMMUNE RESPONSES"



"RELEASING THE BRAKE ON THE T CELL"



Efti is an MHC II agonist

### **APC** activator

- boosts and sustains cytotoxic T cell responses
- activates multiple immune cell subsets

LAG-3 antagonist (or LAG-3 blocking) antibodies

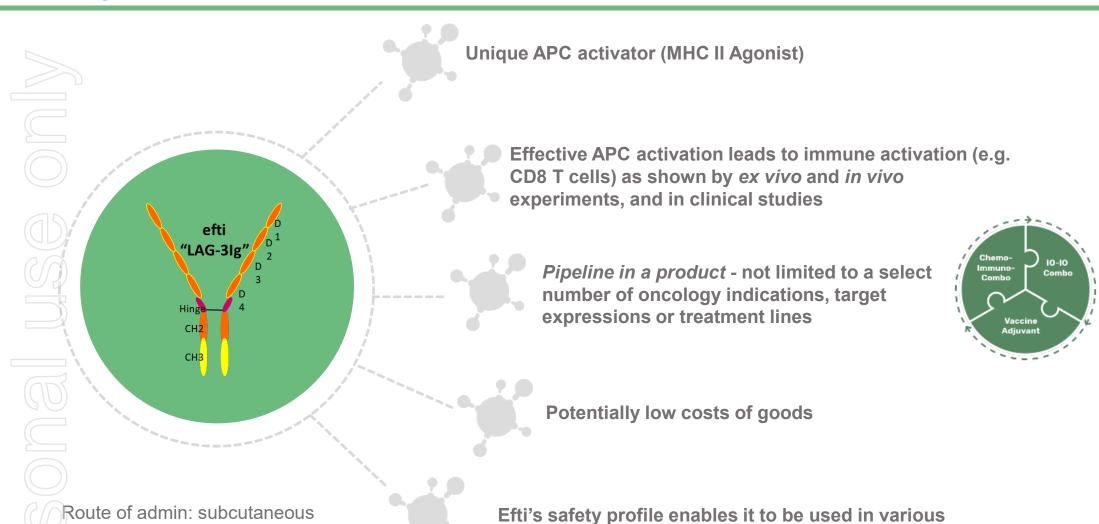
# Immune checkpoint inhibitor

 increases cytotoxicity of pre-existing CD8 T cell response

# **Efti: Potential Pipeline in a Product**

# High intrinsic value





combination settings

\* - can be extended to every 3 weeks after 6 months

Dose: 30 mg every 2 weeks\*



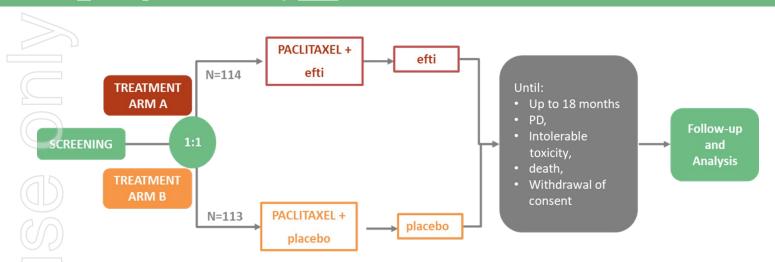
# Efti + Chemo Combination:

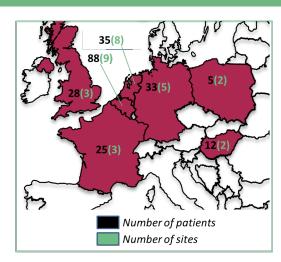
Exciting interim OS results
Presented at SABCS in December 2020

# Efti: AIPAC (Phase IIb) design



# AIPAC: Active Immunotherapy PAClitaxel in HER2-/ HR+ metastatic breast cancer (MBC)





# Primary endpoint(\*) (presented Mar. 2020) included:

Assessment of Progression-Free Survival (PFS)

# Secondary endpoints(\*) (presented Dec. 2020) included:

Overall Survival (OS)

Safety and tolerability

Overall Response Rate (ORR) and other efficacy parameters

Biomarker and Immune Monitoring

## **Fact sheet**

- √ Conducted in 7 EU countries
- √ Local and blinded independent central read
- √ Last Patient In enrolled Jun. 2019
- ✓ Primary analysis PFS (immature OS) Mar. 2020
- √ Follow-up 1 analysis OS Sep. 2020 (SABCS Dec. 2020) ~60% OS events
- ❖ 2<sup>nd</sup> OS follow-up analysis planned H2 2021

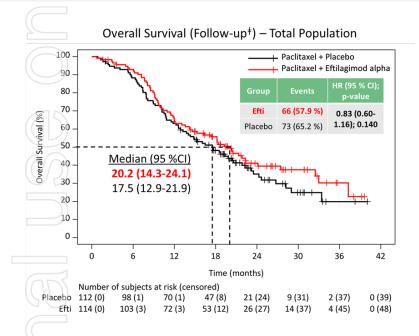
# **AIPAC Phase IIb Clinical Results**

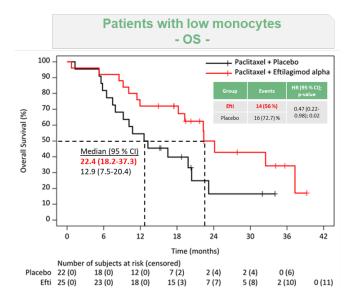


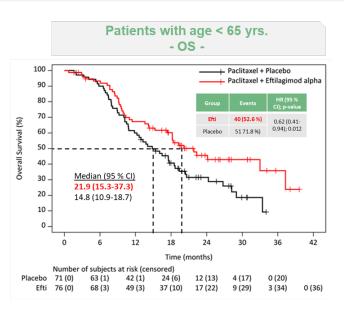


# For predefined sub-groups:

Clinically meaningful absolute and relative improvement for efficacy parameters, significance for OS ESMO scale of magnitude\* = level 4 (makes reimbursement very likely)







+9.1 months median OS

+7.1 months median OS

Quality of Life (QLQ-C30)

Significant deterioration of overall QoL in the placebo group at week 25, which was <u>not</u> observed in the efti group Very important for reimbursement → favorably for efti

Prior CDK 4/6

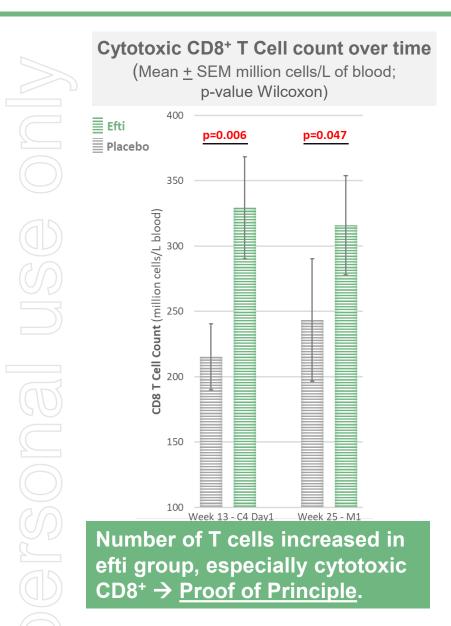
have negative impact on OS in placebo group (median reduced from 20.0 to 14.9 months), but <u>not</u> in the efti group (median OS 20.9 vs. 20.4 months)

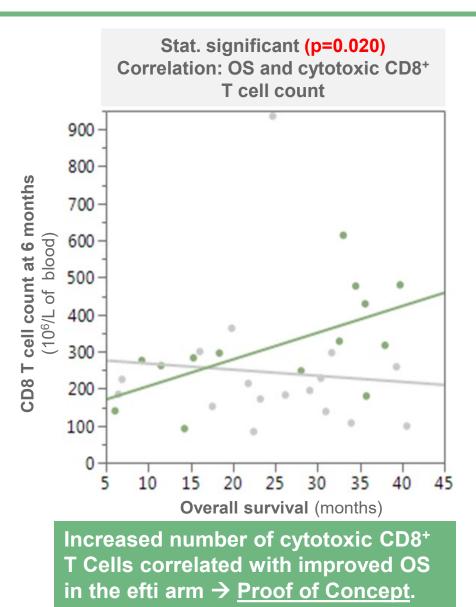
CDK4/6 are now standard, and most patients will have received it in future studies / real world → favorably for efti

# **AIPAC Phase IIb Clinical Results**









# **AIPAC Phase Ilb Clinical Results**

# **Summary and Conclusions**



# First time

an APC activator has shown meaningful increase in Overall Survival (OS) in a randomised setting

# **Proof of Principle**

Significant increase in cytotoxic T cell numbers compared to placebo

# **Proof of Concept**

Prolonged OS in the overall population and clearly linked to pharmacodynamic effect (increase in CD8 T cells)

# **Path Forward**

Regulatory (FDA and EMA) discussions are prioritised now



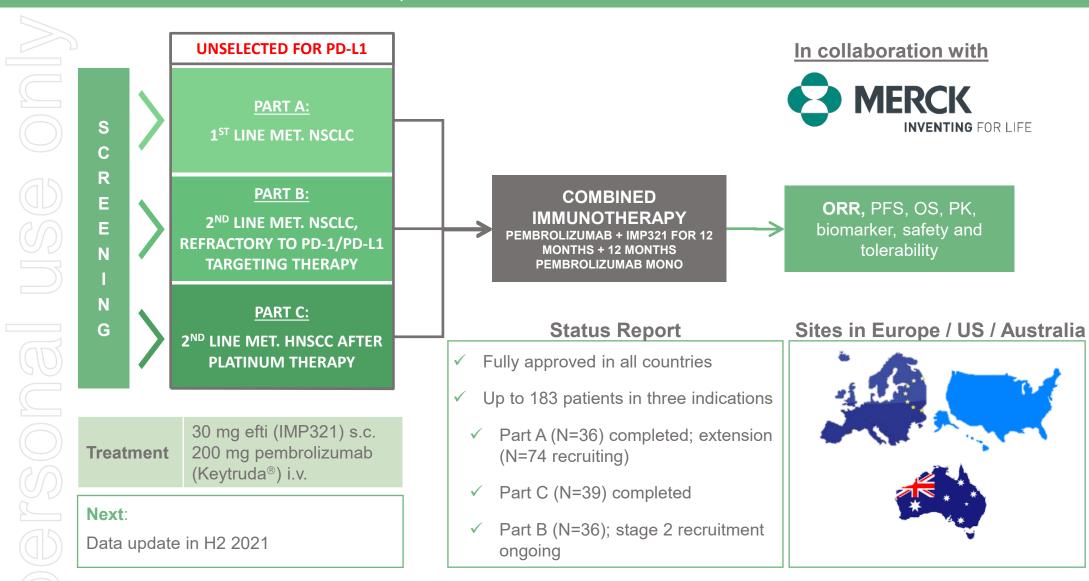
# Efti + anti-PD-1 Combinations Update from ASCO 2021

# **Key Clinical Trials**

TACTI-002 (Phase II) design & status



# TACTI-002: Two ACTive Immunotherapeutics in NSCLC and HNSCC



# TACTI-002: Phase II of efti and pembro in 1st line met NSCLC (Part A) BASELINE CHARACTERISTICS & EFFICACY\*



# Baseline Disease Characteristics\*

Baseline parameters	N (%)
Age (years), median (range)	68.5 (53-84)
Female	11 (30.6)
Male	25 (69.4)
ECOG 0	15 (41.7)
ECOG 1	21 (58.3)
Non smokers	2 (5.6)
Current / Ex-smokers	34 (94.4)
Squamous pathology	15 (41.7)
Non-squamous pathology	21 (58.3)
Patients with liver metastasis	14 (38.9)

# <u>Tumor Response\*</u>

Best overall response, iRECIST	Local Read (investigator) N (%)	Blinded Read (BICR) N (%)
Complete Response	2 (5.6)	2 (5.6)
Partial Response	11 (30.6)	13 (36.1)
Stable Disease	11 (30.6)	10 (27.8)
Progression	8 (22.2)	6 (16.7)
Not Evaluable**	4 (11.1)	5 (13.9)
Disease Control Rate	24 (66.7)	25 (69.4)
Overall Response Rate* [95% CI interval]	13 (36.1) [20.8-53.8]	15 (41.7) [25.5-59.2]
Overall Response Rate – Evaluable pts*** [95% CI interval]	13 (40.6) [23.7-59.4]	15 (48.4) [30.1-60.9]

<sup>\* -</sup> All patients stage 1 and 2 (N=36) with  $\geq$  1 treatment



<sup>\*\* -</sup> dropped off prior to first staging or were not evaluable post-baseline for any reason

<sup>\*\*\* -</sup> Evaluable for efficacy meaning  $\geq 1$  treatment and  $\geq 1$  post baseline tumor staging

# TACTI-002: Phase II of efti and pembro in 1st line met NSCLC (Part A) EFFICACY



# ORR by PD-L1 subgroup\*

PD-L1	ORR iRECIST* (%)
≥ 50% TPS	53.8
< 50% TPS	31.6
≥ 1% TPS	44.0

<sup>\*</sup> according to investigator read, evaluable pts only

N=33; \*\* LN as target lesion; \*\*\* - pt had SD but < 6 wks --> BOR =

NE: NY not vet: NE not evaluable

Best response:

iSD

iPR

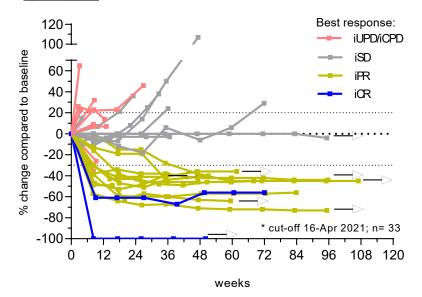
iUPD/iCPD

### Overall PFS estimates by PD-L1 subgroup\*\*

PD-L1	Median PFS iRECIST* (months)
Unselected	8.2
≥ 50% TPS	11.8
< 1% TPS	4.1

<sup>\*\*</sup> according to investigator read, minimum follow-up of 8.3 months, all patients stage 1 and 2 with  $\geq$  1 treatment

### Spider plot



# Duration of Response (DOR)

- 92% responses confirmed
- 58% confirmed responses ongoing with 6+ months
- Median DOR estimated 13+ months

 At data cut-off, 7 pts still under therapy and 1 pt completed the 2 yrs of therapy



Waterfall plot

100

75

50

-25

-50

-75

Best % change from baseline

# TACTI-002: Phase II of efti and pembro in 2<sup>nd</sup> line HNSCC (Part C) BASELINE CHARACTERISTICS & EFFICACY\*



# Baseline disease characteristics

Baseline parameters (N=39)	N (%)	
Age, median (years)	62 (37-84)	
Female	4 (10.3)	
Male	35 (89.7)	
ECOG 0	13 (33.3)	
ECOG 1	26 (66.7)	
Current smokers	6 (15.4)	
Ex- or non-smokers	33 (84.6)	
Previous chemotherapy	39 (100)	
Previous cetuximab	16 (41.0)	
Lung lesions	19 (48.7)	
Liver lesions	6 (17.6)	

## Primary tumor location

Primary tumour location (N=39)	N (%)	
Oral cavity	12 (30.8)	
Oropharynx	14 (35.9)	
Hypopharynx	7 (17.9)	
Larynx	6 (15.4)	

### Tumor response\*

Best overall response*, iRECIST	Investigator assessment N (%)	
Complete Response	5 (13.5)	
Partial Response	6 (16.2)	
Stable Disease	3 (8.1)	
Progression	17 (45.9)	
Not Evaluable**	6 (16.2)	
Disease Control Rate	14 (37.8)	
Overall Response Rate [95% CI interval]	11 (29.7) [15.9 – 47.0]	
Overall Response Rate - Evaluable pts*** [95% CI interval]	11 (35.5) [19.2 – 54.6]	

<sup>\* -</sup> All patients (N=37) with  $\geq$  1 treatment and no death due to COVID-19 prior to first post-baseline staging

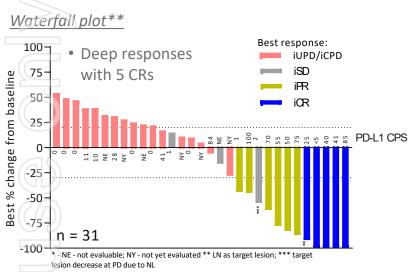
<sup>\*\*\* -</sup> evaluable patients (N=31):  $\geq$  1 treatment and  $\geq$  1 post baseline tumor staging



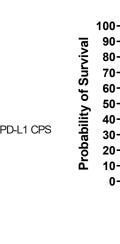
<sup>\*\* -</sup> dropped off prior to first staging or were not evaluable post-baseline for any reason

# TACTI-002: Phase II of efti and pembro in **2**<sup>nd</sup> line **HNSCC** (Part C) **EFFICACY\***





ORR, PFS, DoR, OS for pts with CPS ≥ 1 (N=24)\*



**ORR IRECIST** 

(95% CI)

45.8%

(25.6-67.2)

80-

70-

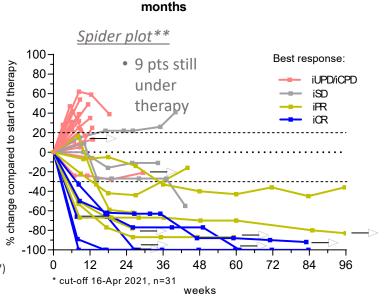
60

50

40

30-20-

10-



Kaplan-Meier Plot PFS\*

12

→ CPS >=1 (n=24)

Overall:

• 30+ %

Median PFS

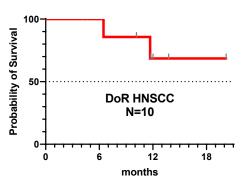
progression

free at 6 mts

2.1 mts

unselected for PD-L1 (n=37)

# Duration of response (DOR) for confirmed responders



## **Duration of response**

- 91% confirmed responses
  - 80% confirmed responses ongoing (censoring at 4-20 months)
  - No progression prior to 6 months DOR
- Median duration of response cannot be estimated yet

\*≥1 treatment and no death due to COVID-19 prior to first post-baseline staging (N=37)

**Median PFS** 

(71% events)

4.1 mts

45% PFS free at 6 mts

\*\* >= 1 post baseline tumor staging (N=31)

**Median OS** 

(58% events)

12.6 mts

54% alive at 12 mts



# INSIGHT-004\*: Phase I of efti and avelumab



- INSIGHT-004 is a dose escalation study evaluating efti in combination with Bavenico (avelumab). Conducted as the 4th arm of the INSIGHT platform trial.
- 12 pts (cohort 1: gastric, gallbladder, colon cancer, pleural mesothelioma; cohort 2: gastric, gastroesophageal, anal, rectum, cervix uteri)

### **Key findings**

- No DLTs and no new safety signals with standard dose of avelumab
- 5/12 (42%) patients with partial responses in:
  - o 1st line MSI high colorectal cancer
  - 1st line pleural mesothelioma
  - o after radiochemo in squamous anal cell
  - pre-treated squamous cervical cancer (PD-L1 TPS < 1%) carcinoma</li>
  - o 3rd line gastroesophageal junction
- Efti plus avelumab is safe and well tolerable
- Encouraging single cases in non ICI sensitive cancers

### In collaboration with



Merck KGaA, Darmstadt, Germany

Institut für Klinisch-Onkologische Forschung
KRANKENHAUS





Patients: 2 cohorts of 6 patients each



6 months

Combination treatment, then 6 months avelumab monotherapy





# INSIGHT-005: Phase I for efti and bintrafusp alfa



To evaluate the feasibility and safety of combined treatment with bintrafusp alfa (M7824) and eftilagimod alpha. Conducted as the 5<sup>th</sup> arm of the INSIGHT trial\*.

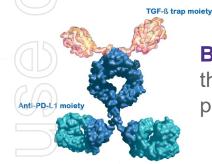
In collaboration with

Merck KGaA, Darmstadt, Germany

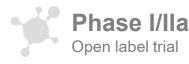


Institut für Klinisch-Onkologische Forschung





**Bintrafusp alfa:** bifunctional fusion protein that aims to block two immunosuppressive pathways, TGF-β and PD-L1.







**Efti:** LAG-3 fusion protein that activates antigen presenting cells (APCs), via the LAG-3 – MHC II pathway





### **Solid tumors**

- Histologically confirmed locally advanced or metastatic
- received ≤4 prior lines of therapy

### Q2W for maximum of 12 months

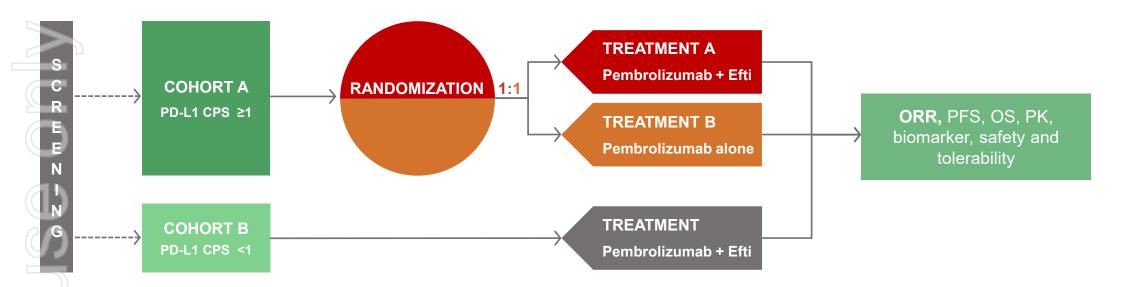
- bintrafusp alfa 1.200mg i.v.
- eftilagimod alpha 30mg s.c.

RP2D, Safety, ORR, PFS, PK, PD

# TACTI-003 Trial in 1st line HNSCC

# Current Design + Status





# Design:

- Randomised study with ORR as primary endpoint
- Sites worldwide (AU, US, Europe)
- Approx. 154 pts: either to be randomized to have sufficient pts. in each group or in an experimental arm

## Status:

- Advanced planning & study start up expected in mid 2021
- Fast Track designation granted by FDA in April 2021

# In collaboration with



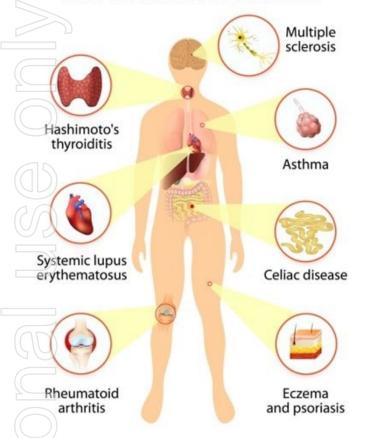


# **IMP761** - Autoimmune Diseases -

# Broad potential in targeting auto-reactive memory T cells with IMP761





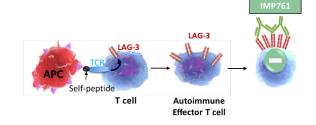


# THE PRESENT: FIGHTING THE SYMPTOMS Treating general inflammation:

corticoids, methotrexate, anti-TNF-α, -IL-6, -IL-17, -IL-23 mAbs

# THE FUTURE: FIGHTING THE CAUSE Treating the disease process:

silencing the few autoimmune memory T cells accumulating at the disease site with IMP761



POTENTIAL GAME CHANGER IN AUTOIMMUNE DISEASES (\$149.4 billion market size by 2025)<sup>1</sup>



# Corporate Snapshot & Outlook

# **Corporate Snapshot**



Ticker symbols	IMM (ASX) IMMP (NASDAQ)
Securities on issue <sup>(1)</sup> (as at 1 June 2021)	696.1 million ordinary shares
Cash & Cash equivalents (as at 31 March 2021)	~A\$51.7 million (US\$39.3 million)
Market Cap <sup>(2)</sup> (as at 1 June 2021)	A\$487.3 million (US\$377.3 million)

### Notes:

<sup>(1)</sup> As at 18 May 2021~38.46% of the ordinary shares are represented by ADSs listed on NASDAQ where 1 ADS represents 10 ordinary shares. For a detailed summary of securities on issue refer to latest Appendix 2A released on ASX.

<sup>(2)</sup> Market capitalization based on ASX share price and basic ordinary shares outstanding.

NB: US equivalent of amounts above are based on foreign exchange rate for AUD/USD of 0.7744 for market capitalization, and the US cash & cash equivalents amount was calculated using FX rate of 0.7602 as at 31 March 2021.

# 2020 & 2021 News Flow\*



# 2021 Final data from AIPAC: 2<sup>nd</sup> OS follow up

- ✓ AIPAC PFS, ORR and OS delivered
- ✓ US **IND** for MBC
  - **TACTI-002** recruitment & data delivered e.g. at ASCO, EMSO & SITC for
    - ✓ 1st line NSCLC
    - ✓ 2<sup>nd</sup> line NSCLC
    - ✓ 2<sup>nd</sup> line HNSCC
- ✓ Support of global **COVID** efforts (Phase II)
- ✓ New partnerships: LabCorp
- ✓ Progress from IMP761
- ✓ Expansion of IP portfolio
  - Strong financial position

- ✓ Data from **TACTI-002** & final data from **INSIGHT-004** at ASCO
- Recruitment & first data from TACTI-002 Part A extension
- Start & ongoing recruitment of **new trial in 1st** line **HNSCC** (TACTI-003)
- Ongoing regulatory engagement
- Updates from IMP761
- Updates from partnered programs (e.g. GSK, Novartis, EAT COVID, CYTLIMIC and EOC Pharma)
- Potential new partnerships and expansion of existing programs
- √ Validation of LAG-3/MHC-II interaction through readout of BMS's Phase III data for relatlimab + nivo combination

# Summary





Global leadership position in LAG-3 with four LAG-3 related product candidates in immuno-oncology and autoimmune disease

Multiple active clinical trials (including partnered candidates), with further significant data read-outs in 2021

Compelling clinical data from efti & strong rationale to combine with multiple FDA approved treatments

Established collaborations with e.g. Merck (MSD), Pfizer / Merck KGaA, Darmstadt; Novartis and GSK



Thank You