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# The global leader in developing LAG-3 therapeutics

*Corporate Presentation  
September 2021*

*(ASX: IMM, NASDAQ: IMMP)*

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*This presentation was authorised for release by the CEO, Marc Voigt.*

# Overview

## Immutep

is an innovative biotechnology company developing novel immunotherapies for cancer and autoimmune disease



## Globally active



## Leadership position in LAG-3

with 4 product candidates in immuno-oncology and autoimmune disease



## Clinical Potential

Immutep's product candidates have demonstrated clinical potential in a range of indications with high unmet need



## Collaborating with industry leaders



## LAG-3 Pioneer

French immunologist  
Prof. Frédéric Triebel, **Immutep**  
CMO & CSO







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# 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	
Oncology	Agonist		Eftilagimod Alpha <sup>(5)</sup>		10	4		14	967	
	Antagonist	BMS	Relatlimab		7	32	2		41	9,706
			Ieramilimab		1	4			5	960
		Merck & Co. Inc.	Favezelimab		1	5			6	1066
		Macrogenics	Tebotelimab		3	3			6	1422
		H-L Roche	RO7247669		1	2			3	538
		B.I.	BI754111		4	1			5	649
		Regeneron <sup>(1)</sup>	Fianlimab		1	1			2	836
		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
		Innovent	IBI110		1				1	268
Xencor	XmAb-22841		1				1	242		
Autoimmune	Agonist		IMP761					--	--	
	Depleting AB		GSK2831781 (IMP731)		2	1		3	207	

PDUFA meeting  
March 19, 2022

Sources: GlobalData, Company websites, clinicaltrials.gov, and sec.gov, as of **September 2021**. The green bars above represent programs conducted by Immuprep &/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

([https://www.sec.gov/Archives/edgar/data/872589/000110465919000977/a19-1325\\_18k.htm](https://www.sec.gov/Archives/edgar/data/872589/000110465919000977/a19-1325_18k.htm))

2) On 3 Apr. 2020 Les Laboratoires Servier acquired Symphogen

3) Tesaro was acquired by and is now part of GSK ([www.gsk.com/en-gb/media/press-releases/gsk-completes-acquisition-of-tesaro-an-oncology-focused-biopharmaceutical-company/](http://www.gsk.com/en-gb/media/press-releases/gsk-completes-acquisition-of-tesaro-an-oncology-focused-biopharmaceutical-company/))

4) Includes two completed Phase I studies and one discontinued Phase 2 study

5) Including IITs, two planned trials (MBC trial by EOC and HNSCC trial) and the EAT COVID trial

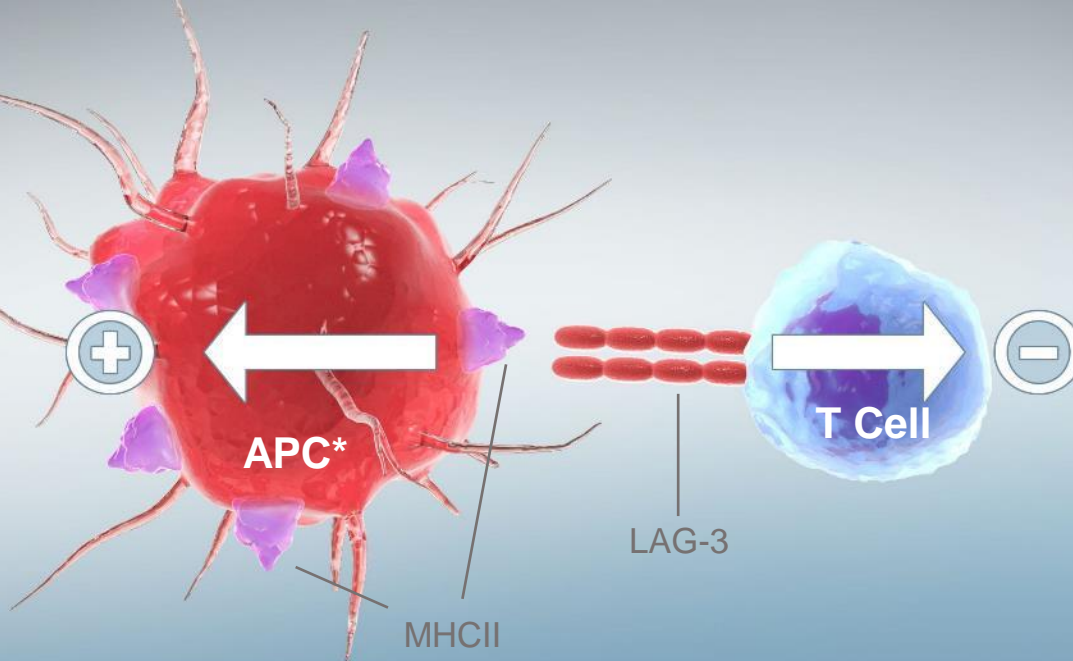
6) RELATIVITY-047 (<https://investors.bms.com/iframes/press-releases/press-release-details/2021/Bristol-Myers-Squibb-Announces-RELATIVITY-047-a-Trial-Evaluating-Anti-LAG-3-Antibody-Relatlimab-and-Opdivo-nivolumab-in-Patients-with-Previously-Untreated-Metastatic-or-Unresectable-Melanoma-Meets-Primary-Endpoint-of-Progression-Free-Survival/default.aspx>)

# MHC II / LAG-3 Interaction is Clinically Validated as a Therapeutic Target

LAG-3, an immune checkpoint, is widely expressed on tumor infiltrating lymphocytes (TILs) and cytotoxic T cells, and interacts with MHC class II molecules on antigen presenting cells (APCs)

→ Prime target for immune therapy

## LAG-3 / MHC Class II Interaction



**Positive regulation** of antigen presenting cells (APCs) via MHC II transferred activating signals → increase in antigen presentation to cytotoxic CD8<sup>+</sup> T cells

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

- Relatlimab + 15 more products in clinical development
- Clinical validation at ASCO/ESMO 2021 (RELATIVITY-047 - relatlimab + nivolumab in melanoma)
- PDUFA target action date is March 19, 2021\*

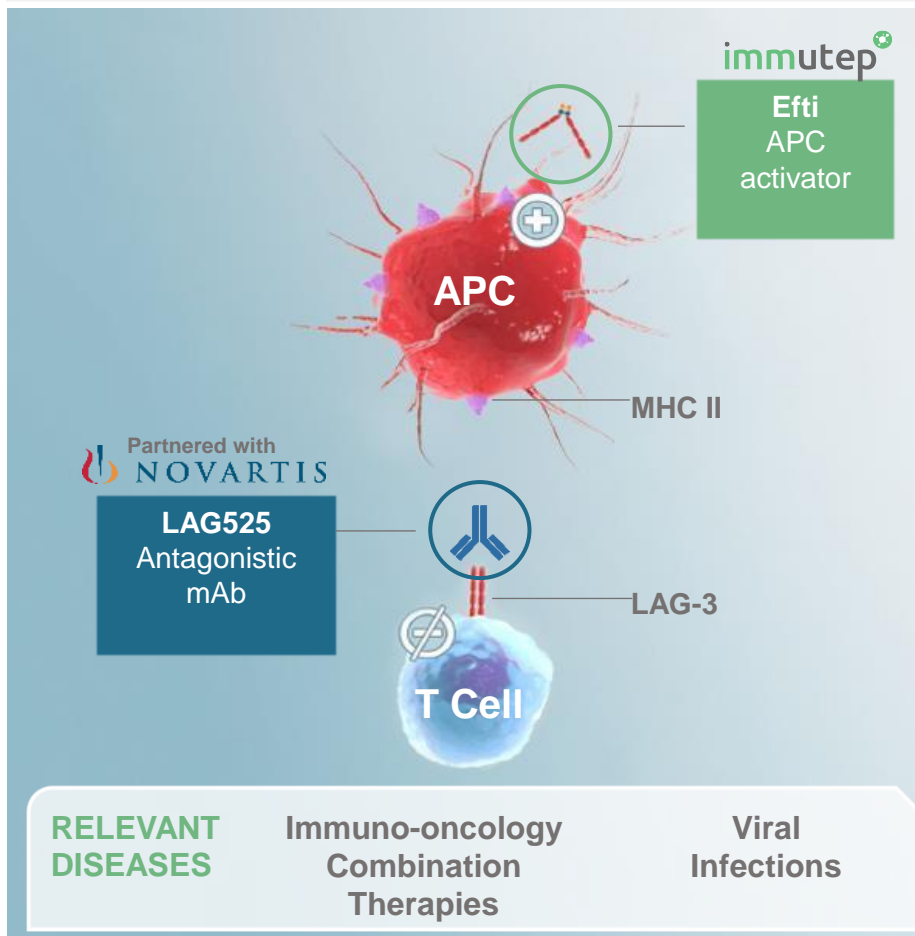
## MHC II (APC) / LAG-3 (T cell) interaction is important for tumor immunology

- This APC / T cell interaction is now a validated target since ASCO 2021 → 3<sup>rd</sup> validated checkpoint in immunology

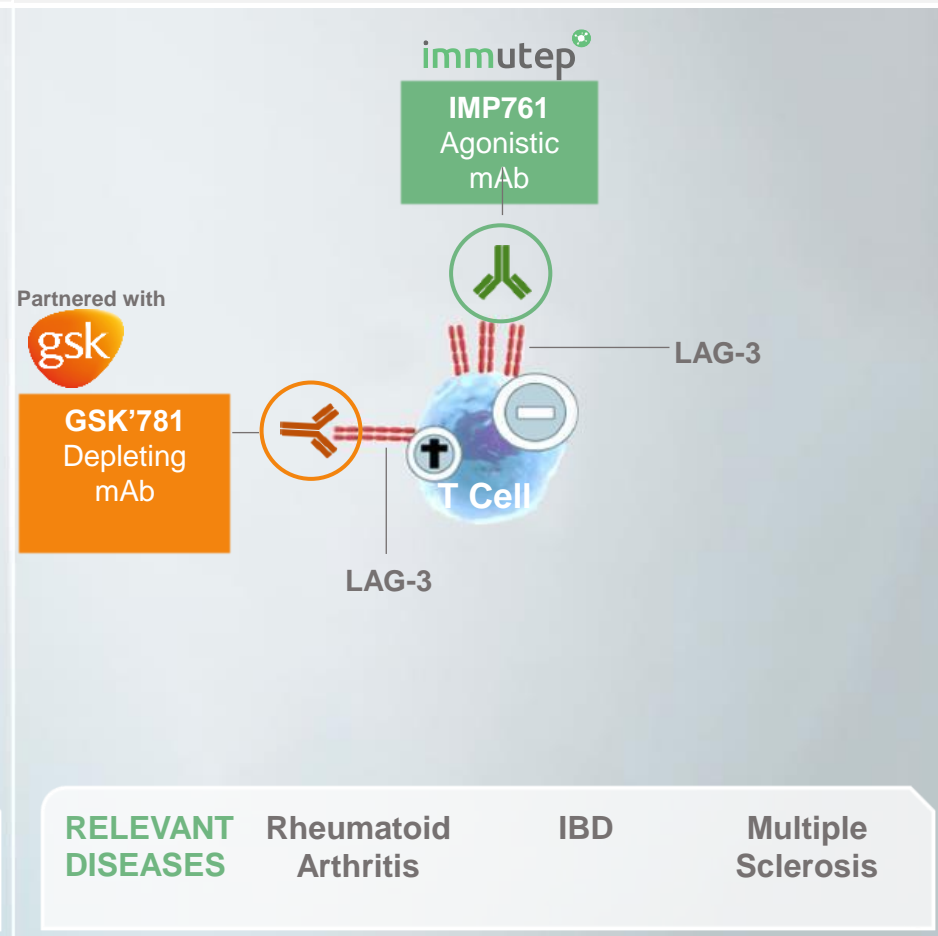
# Targeting LAG-3 / MHC II:

Immutep has multiple therapeutics in numerous diseases

## IMMUNOSTIMULATION



## IMMUNOSUPPRESSION



- ✓ Immutep is the only company with four LAG-3 related compounds, each with a different mechanism of action for treatment of numerous diseases
- ✓ Two major partnerships with pharma and two products under own development

# Immutep's LAG-3 Trial Pipeline\*

Program	Preclinical	Phase I	Phase II	Late Stage <sup>(5)</sup>	Commercial Rights	Market Size <sup>(6)</sup>	
<b>Eftilagimod Alpha</b> (efti or IMP321)  APC activating soluble LAG-3 protein	Metastatic Breast Cancer (Chemo – IO) AIPAC				Global Rights 	US\$29.9 billion	
	Head and Neck Squamous Cell Carcinoma (IO – IO) <sup>(1b)</sup> TACTI-003					US\$1.9 billion	
	Head and Neck Squamous Cell Carcinoma (IO – IO) <sup>(1)</sup> TACTI-002					US\$22.6 billion	
	Non-Small-Cell Lung Carcinoma (IO – IO) <sup>(1)</sup> TACTI-002						
	Solid Tumors (IO – IO) <sup>(2), (3a)</sup> INSIGHT-004			Merck KGaA, Darmstadt, Germany			
	Solid Tumors (IO – IO) <sup>(2), (3b)</sup> INSIGHT-005			Merck KGaA, Darmstadt, Germany		Chinese Rights 	US\$2.3 billion
	Solid Tumors (IO – IO – chemo) <sup>(2)</sup> INSIGHT-003						
	Solid Tumors (Cancer Vaccine) <sup>(4a)</sup> YNP01 / YCP02 / CRESCENT 1						
	Metastatic Breast Cancer (Chemo – IO) <sup>(4b)</sup>						
Inf. Dis.  Autoimm.	Efti	COVID-19 disease (Monotherapy) <sup>(7)</sup> EAT-COVID			Global Rights <sup>(8)</sup> 		
	IMP761 (Agonist AB)				Global Rights 	US\$149.4 billion (2025)	

Notes

- (1) Information in pipeline chart current as at September 2021
- (1) In combination with KEYTRUDA® (pembrolizumab) (1b) Planned new trial for 1<sup>st</sup> line HNSCC patients
- (2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial
- (3) a) In combination with BAVENCIO® (avelumab); b) in combination with Bintrafusp alfa
- (4) a) Conducted by CYTLIMIC in Japan; b) Conducted by EOC in China. Immutep has no control over either of these trials.
- (5) Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials
- (6) GlobalData Market Size forecast for US, JP, EU5, Urban China and Australia; [KBV Research: https://www.kbvresearch.com/autoimmune-disease-therapeutics-market/](https://www.kbvresearch.com/autoimmune-disease-therapeutics-market/)
- (7) IIT conducted by University Hospital Pilsen. Immutep has no control over this trial.
- (8) Ex China



# Immutep Out-Licensed Immunotherapy Pipeline\*

Program	Preclinical	Phase I	Phase II	Late Stage <sup>(1)</sup>	Commercial Rights/Partners	Updates
<b>Oncology</b> LAG525 (Antagonist AB)	Solid Tumors + Blood Cancer (IO-IO Combo)				Global Rights 	Novartis currently has five clinical trials ongoing for LAG525 in multiple cancer indications for approx. 1,000 patients <sup>(4)</sup>
	Triple Negative Breast Cancer (Chemo-IO Combo)					
	Melanoma (IO-IO-Small Molecule Combo)					
	Solid Tumors (IO-IO Combo)					
	Triple Negative Breast Cancer (Chemo-IO-Small Molecule Combo)					
<b>Autoimmune</b> GSK'781 (Depleting AB)	Ulcerative Colitis <sup>(6)</sup>				Global Rights 	Two successful Phase I studies. Phase II clinical study in up to 242 ulcerative colitis patients was discontinued.
	Healthy Japanese and Caucasian Subjects <sup>(2)</sup>					
	Psoriasis <sup>(3)</sup>					

Notes

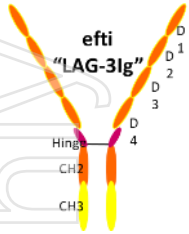
- (1) Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials
- (2) Reflects completed Phase I study in healthy volunteers
- (3) Reflects completed Phase I study in healthy volunteers and in patients with plaque psoriasis

- (4) <https://clinicaltrials.gov/ct2/results?cond=&term=LAG525&cntry=&state=&city=&dist=>
- (5) <https://clinicaltrials.gov/ct2/results?cond=&term=GSK2831781&cntry=&state=&city=&dist=> and <https://www.gsk.com/media/5957/q1-2020-results-slides.pdf>
- (6) Discontinued in Jan 2021

# Eftilagimod Alpha (efti or IMP321)

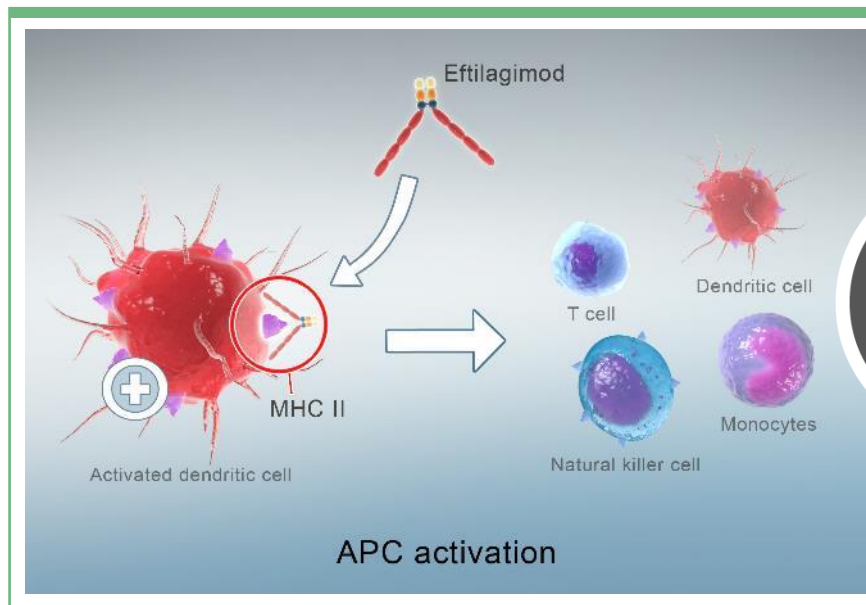
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# Efti: an Innovative LAG-3 I-O Product Candidate



- Efti is a soluble LAG-3 protein targeting a subset of MHC class II on APC
- Potentially synergistic with other therapeutic agents e.g. immuno-oncology (I-O) agents & chemotherapies

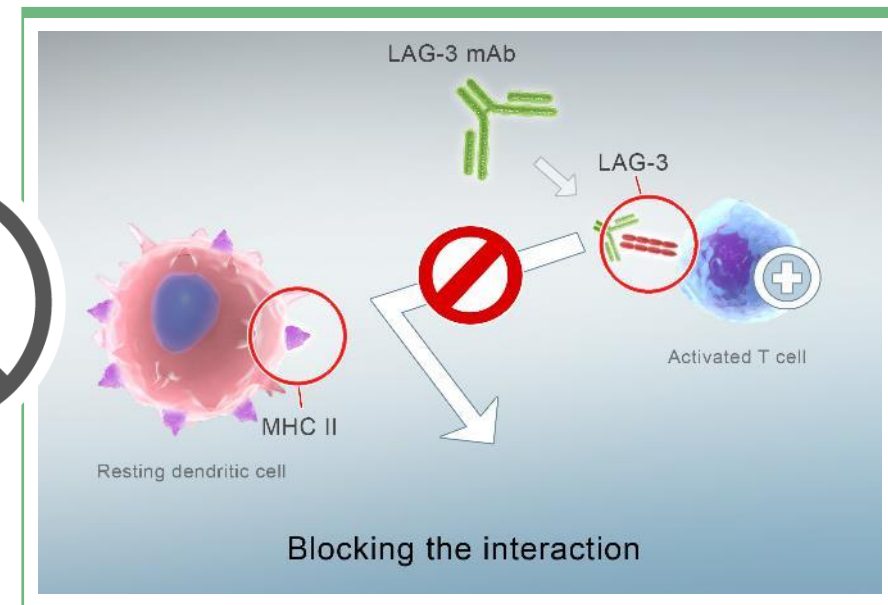
## “PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”



Efti is an **MHC II agonist:**  
**APC activator**

- boost and sustain the CD8<sup>+</sup> T cell responses
- activate multiple immune cell subsets

## “RELEASING THE BRAKE ON THE T CELL”



**LAG-3 antagonist** (blocking) antibodies:  
**Immune checkpoint inhibitor**

- increase cytotoxicity of the pre-existing CD8 T cell response

# Efti: Potential Pipeline in a Product

Potential for use in various combination settings

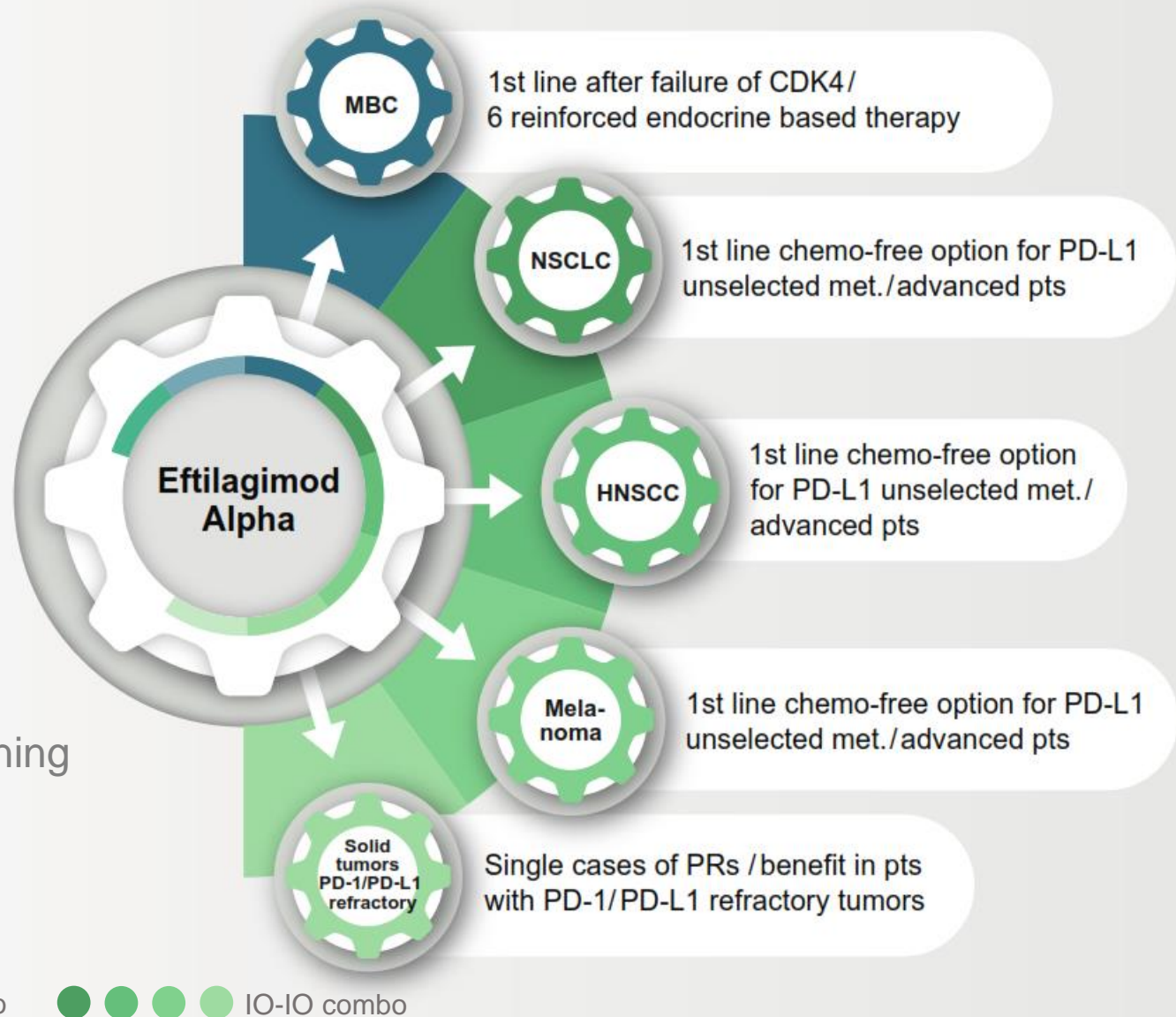
Unique MHC II agonist

Excellent safety profile

Encouraging efficacy data

Low cost of goods

Unique protective IP positioning  
(unlike ICI mAbs)



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# **Efti + anti-PD-1 Combination**

## **TACTI-002**

**Update from ASCO 2021**

# TACTI-002 (Phase II)

## Design & Status

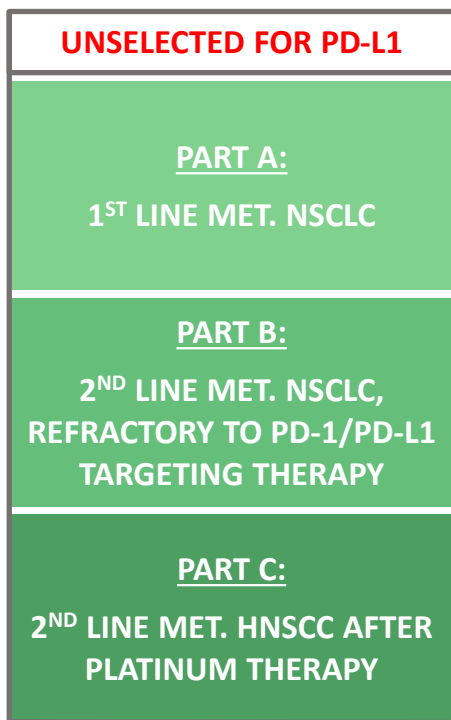
### TACTI-002: Two ACTIVE Immunotherapeutics in NSCLC and HNSCC

In collaboration with



ORR, PFS, OS, PK,  
biomarker, safety and  
tolerability

**COMBINED  
IMMUNOTHERAPY**  
PEMBROLIZUMAB + EFTI FOR 12  
MONTHS + 12 MONTHS  
PEMBROLIZUMAB MONO



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<b>Treatment</b>	30 mg efti (IMP321) s.c. 200 mg pembrolizumab (Keytruda <sup>®</sup> ) i.v.
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#### Recruitment Status Report

- ✓ Fully approved in all countries
- ✓ Up to 183 patients in three indications
  - Part A (N=36) completed; extension cohort (N=74 recruiting)
- ✓ Part C (N=39) completed
- ✓ Part B (N=36); completed

#### Sites in Europe / US / Australia



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# TACTI-002 Results<sup>(1)</sup>

## 1<sup>st</sup> line NSCLC (Part A)

- **PD-L1 distribution as expected (~70% with < 50% PD-L1 expression) → PD-L1 all comer trial**
- **Patients are typical NSCLC 1<sup>st</sup> line pts**

Baseline parameters	N (%)	Best overall response, iRECIST, N = 36	Local Read (investigator) N (%)	Blinded Read (BICR) N (%)
Age (years), median (range)	68.5 (53-84)	<b>Complete Response</b>	<b>2 (5.6)</b>	<b>2 (5.6)</b>
Female	11 (30.6)	Partial Response	11 (30.6)	13 (36.1)
Male	25 (69.4)	Stable Disease	11 (30.6)	10 (27.8)
ECOG 0	15 (41.7)	Progression	8 (22.2)	6 (16.7)
ECOG 1	21 (58.3)	Not Evaluable**	4 (11.1)	5 (13.9)
Current / Ex-smokers	34 (94.4)	Disease Control Rate	24 (66.7)	25 (69.4)
Non-smokers	2 (5.6)	<b>Overall Response Rate* [95% CI interval]</b>	<b>13 (36.1) [20.8-53.8]</b>	<b>15 (41.7) [25.5-59.2]</b>
Squamous pathology	15 (41.7)	<b>Overall Response Rate – Evaluable pts*** [95% CI interval]</b>	<b>13 (40.6) [23.7-59.4]</b>	<b>15 (48.4) [30.1-60.9]</b>
Non-squamous pathology	21 (58.3)			
Patients with liver metastasis	14 (38.9)			

\* - All patients stage 1 and 2 (N=36) with ≥ 1 treatment

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

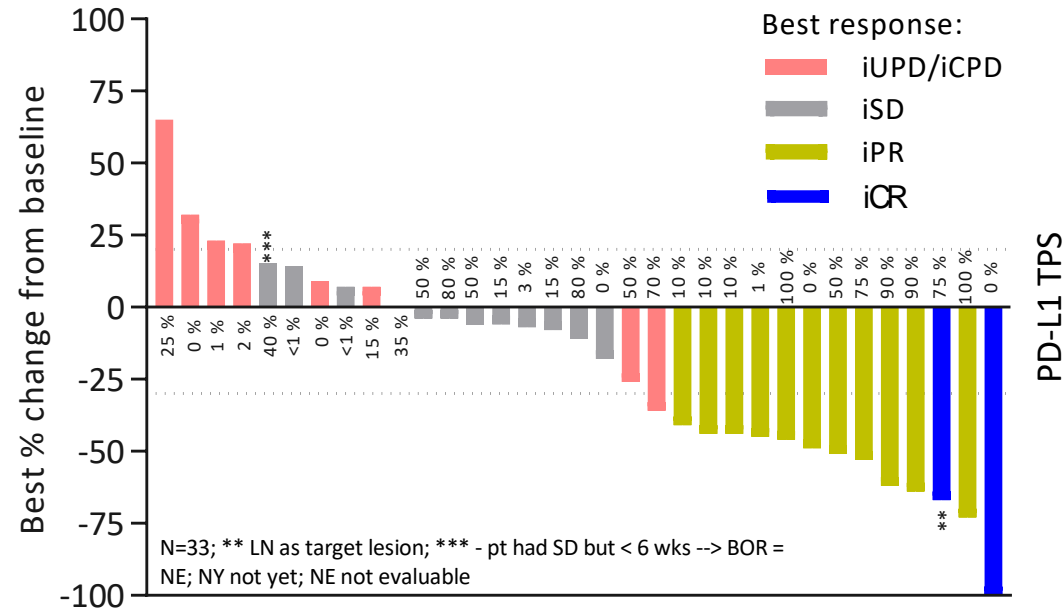
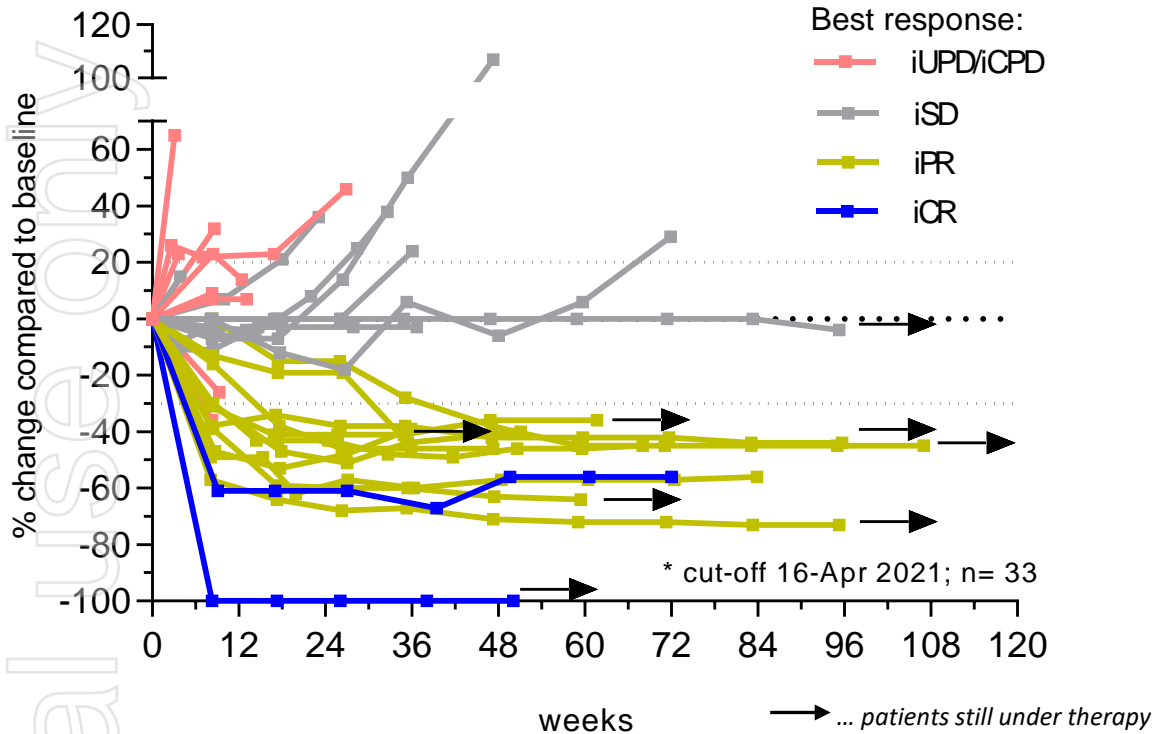
\*\*\* - Evaluable for efficacy meaning ≥ 1 treatment and ≥ 1 post baseline tumor staging

Notes:

(1) Preliminary data, cut-off Apr 16, 2021  
 ECOG... Eastern Cooperative Oncology Group  
 iRECIST... Immune Response Evaluation Criteria In Solid Tumors  
 BICR... Blinded Independent Central Review

# TACTI-002 Results<sup>(1)</sup>

## 1<sup>st</sup> line NSCLC (Part A)



### Duration of response (DoR)

- 92% responses confirmed
- 58% confirmed responses ongoing with 6+ months
- 42% of confirmed responses progressed after 6.5-13.8 months
- Median DoR estimated 13+ months

- Responses at all PD-L1 levels including 1 Complete Response with TPS of 0%
- At data cut-off, 7 pts still under therapy and 1 patient completed the 2 years of therapy

(1) Preliminary data, cut-off Apr 16, 2021



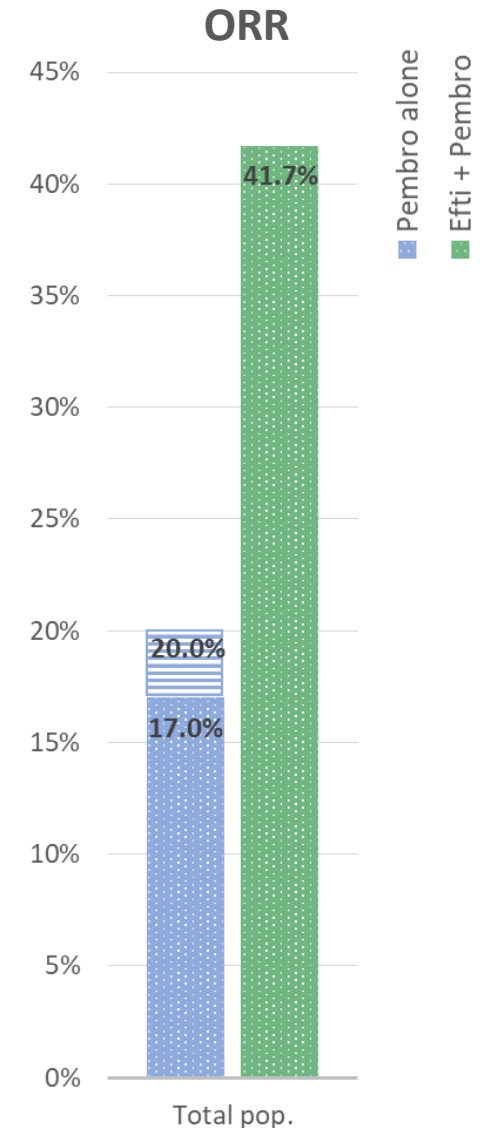
# TACTI-002 Results<sup>(1)</sup>

## 1<sup>st</sup> line NSCLC (Part A) - Benchmarking

	PD-L1 (TPS)	Pembro alone** (NSQ+SQ)	Pembro + Efti*** (NSQ+SQ)
ORR (%)	≥ 50	39.5	53.8*
	≥ 1	27.3	44.0*
	< 50	--	31.6*
PFS (mths)	Overall pop.	--	8.2
	≥ 50	7.1	11.8
DoR (mths)	Overall pop.	20.2	NR (currently 13+)
Toxicity		Well tolerated	No significant add. toxicity

\* Pts with PD-L1 results available and ≥ 1 post baseline RECIST assessments (32/36); \*\* Data for pembro derived from KN042, KN189, KN-407<sup>(2)(3)(4)</sup>; \*\*\* According to investigator read

- Increased ORR & median PFS
- Responses in PD-L1 low expressors
- Comparable safety profile



Data for pembro derived from KN042 and KN001<sup>(2)(5)</sup>

(1) Preliminary data, cut-off 16 Apr 2021 for TACTI-002  
 (2) KEYNOTE-042: TSK Mok et al, The Lancet 2019, [http://dx.doi.org/10.1016/S0140-6736\(18\)32409-7](http://dx.doi.org/10.1016/S0140-6736(18)32409-7)  
 (3) KEYNOTE-189: S Gadgeel et al, J Clin Oncol 2020, <https://doi.org/10.1200/JCO.19.03136>

(4) KEYNOTE-407: L Paz-Ares et al, N Engl J Med 2018;379:2040-51. DOI: 10.1056/NEJMoa1810865  
 (5) KEYNOTE-001: NB Leigh et al, The Lancet 2019, [http://dx.doi.org/10.1016/S2213-2600\(18\)30500-9](http://dx.doi.org/10.1016/S2213-2600(18)30500-9)

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# TACTI-002 Results<sup>(1)</sup>

## 2<sup>nd</sup> line HNSCC (Part C)

- 2<sup>nd</sup> line treatment for patients after platinum therapy. PD-L1 all comer population

• Doubling the ORR compared to historical pembro mono results with **13.5% Complete Responses**

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 / Ex-smokers	33 (84.6)
Non-smokers	6 (15.4)
Previous chemotherapy	39 (100)
Previous cetuximab	16 (41.0)
Lung lesions	19 (48.7)
Liver lesions	6 (17.6)

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

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

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

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

\*\*\* - evaluable patients (N=31): ≥ 1 treatment and ≥ 1 post baseline tumor staging

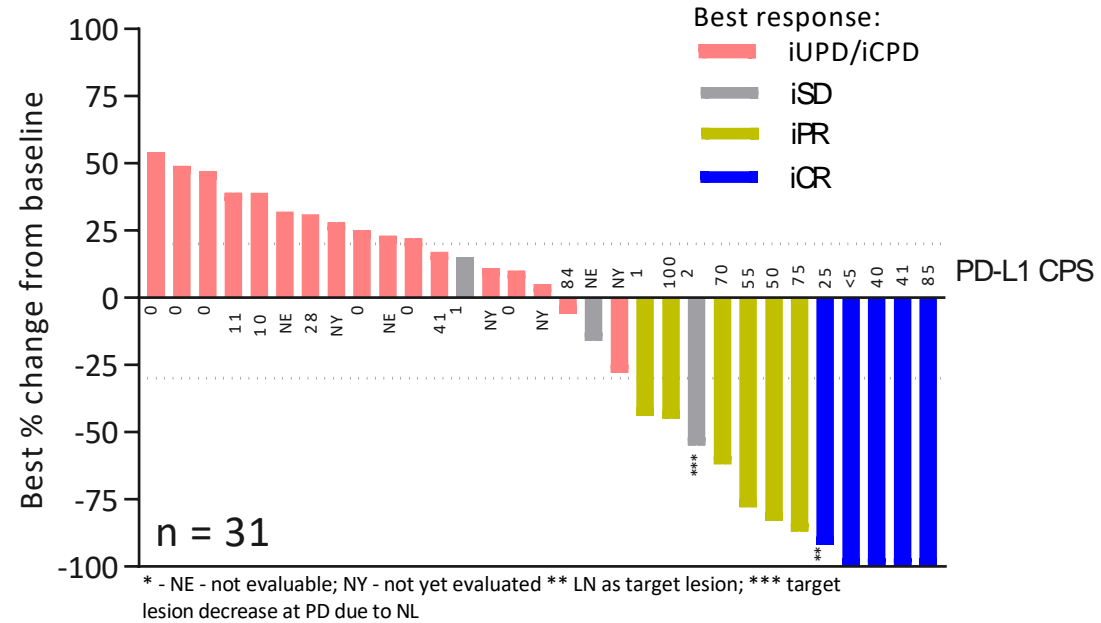
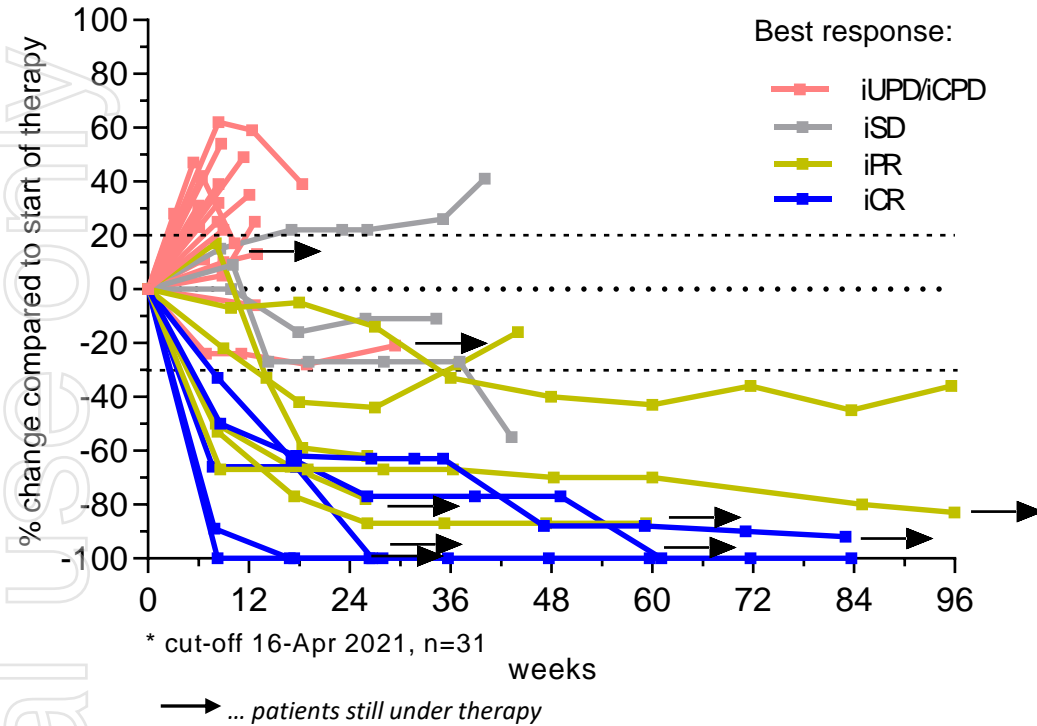
**All four pathologies enrolled**

Note:

(1) Preliminary data, cut-off 16 Apr 2021

# TACTI-002 Results<sup>(1)</sup>

## 2<sup>nd</sup> line HNSCC (Part C)

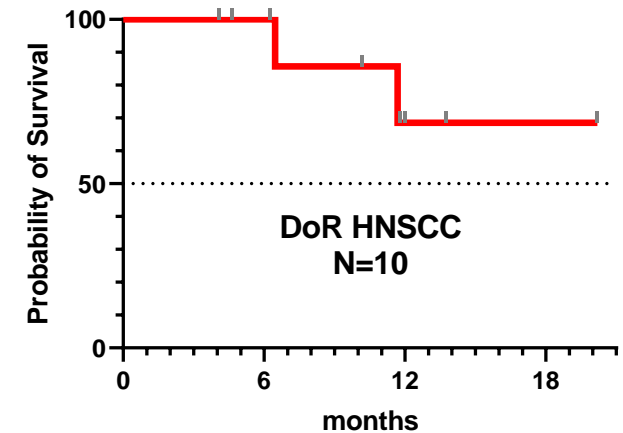


### Deep responses with 5 Complete Responses

#### Duration of response (DoR)

- 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

Figure 3: Duration of response (DOR) for confirmed responders



Note:

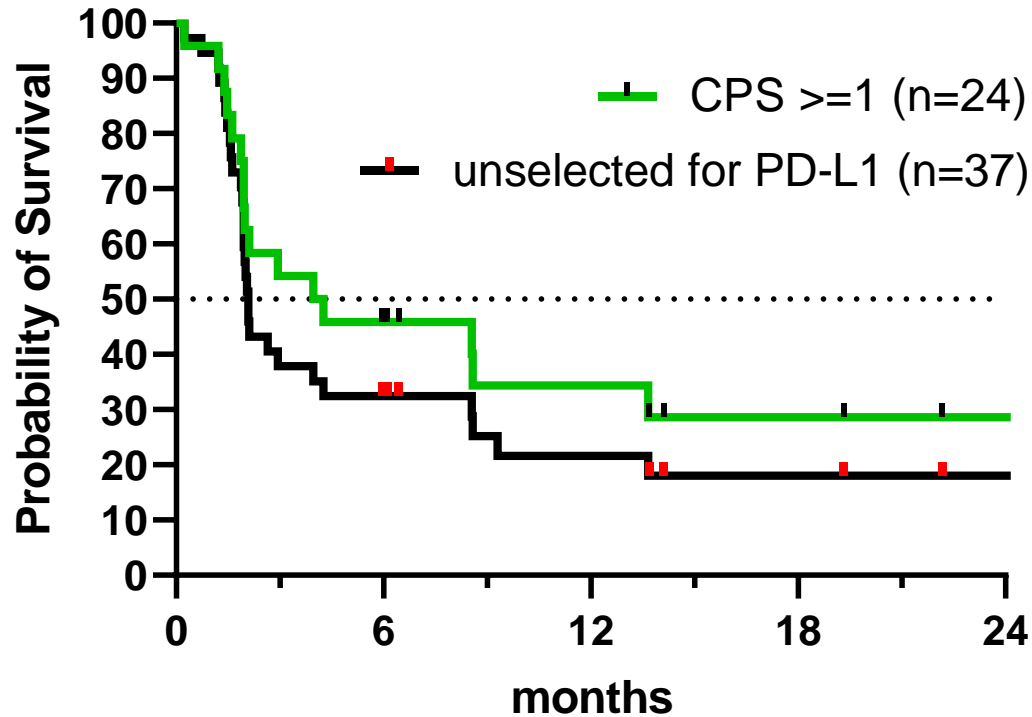
(1) Preliminary data, cut-off 16 Apr 2021

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

# TACTI-002 Results<sup>(1)</sup>

## 2<sup>nd</sup> line HNSCC (Part C)

Kaplan-Meier Plot PFS\*



### Overall population (unselected for PD-L1)

- Median PFS 2.1 mths
- 30+% progression free at 6 mths

### Selected for PD-L1 expression, CPS ≥ 1\*

Median OS (58% events)

12.6 mths

Median PFS (71% events)

4.1 mths (45% prog. free at 6 mths)

ORR iRECIST (95% CI)

45.8% (25.6-67.2)

Note:

(1) Preliminary data, cut-off 16 Apr 2021

(2) \* ≥ 1 treatment and no death due to COVID-19 prior to first post-baseline staging (N=37)

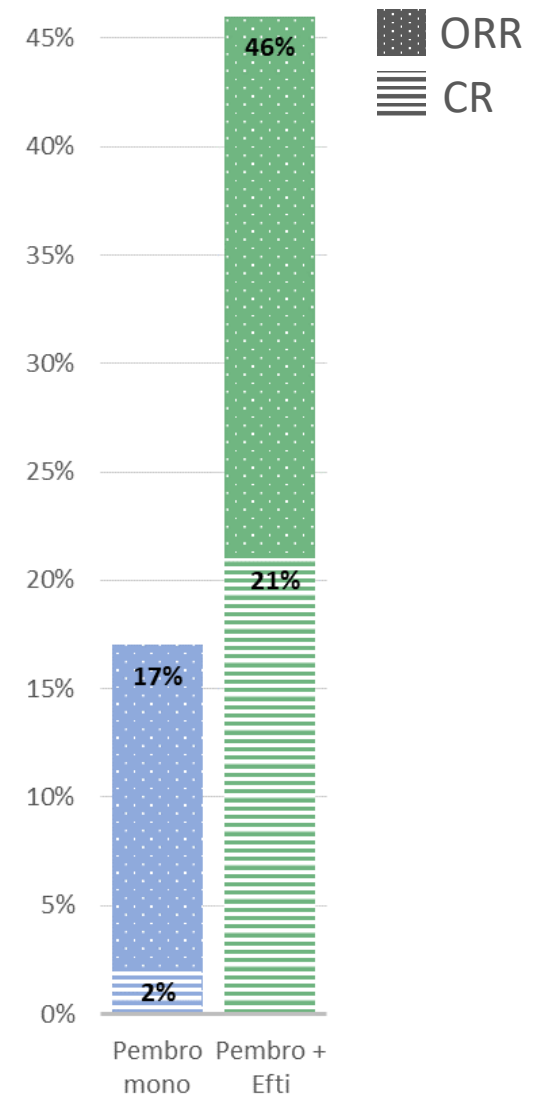
# TACTI-002 Results<sup>(1)</sup>

## 2<sup>nd</sup> line HNSCC (Part C) – Benchmarking

	PD-L1 (CPS)	Pembro alone**	TACTI-002
ORR (%)	≥ 1	17.3 (2% CR)	45.8* (20.8% CR*)
	Overall pop.	14.6	35.5 <sup>#</sup>
mPFS (mths)	≥ 1	2.2 28.7% PFS rate at 6 mths	4.1* 45% PFS rate at 6 mths
	Overall pop.	2.1 25.6% PFS rate at 6 mths	2.1 <sup>§</sup> 30+% PFS rate at 6 mths
mOS (mths)	≥ 1	8.7 40% alive at 12 mths	12.6* 54% alive at 12 mths
	Overall pop.	8.4 37% alive at 12 mths	12.6 <sup>§</sup> 50+% alive at 12 mths

\* - only patients evaluated where PD-L1 results available (N=24); <sup>#</sup> - only evaluable patients (N=31);  
<sup>§</sup> - total pop. (N=37) ; \*\* Data for pembro derived from KN040<sup>(2)</sup>

- ORR of pembro mono generally low → increase to 22% (≥ 20 CPS) and 28% (≥ 50 CPS)<sup>(3)</sup>
- Duration of response drops dramatically if you add chemo<sup>(4)</sup> – not the case with efti
- ORR is clearly higher with high rates of CRs; duration of response very promising (only 1 pt. with PR discontinued in TACTI-002 so far)



TACTI-002 Part C - Historical comparison of ORRs and CRs in metastatic HNSCC for patients who has a PD-L1 CPS of ≥1. ORR for Pembrolizumab monotherapy was taken from KEYNOTE-040.

Notes:

- (1) Preliminary data, cut-off 16 Apr 2021
- (2) Keynote-040 results: EEW Cohen et al., *The Lancet* 2018; [http://dx.doi.org/10.1016/S0140-6736\(18\)31999-8](http://dx.doi.org/10.1016/S0140-6736(18)31999-8)
- (3) E Cohen et al; *Annals of Oncology* 2019; Volume 30 | Supplement 5 | September 2019
- (4) KN-048; *The Lancet*. 2019; [https://doi.org/10.1016/S0140-6736\(19\)32591-7](https://doi.org/10.1016/S0140-6736(19)32591-7)

# **Efti + anti-PD-L1 Combination**

## **INSIGHT-004**

**Update from ASCO 2021**

# INSIGHT Platform Trial in Solid Tumours

## INSIGHT-004: Efti + Avelumab Combination

INSIGHT-004 is a dose escalation study evaluating efti in combination with Bavencio® (avelumab).  
Conducted as the 4<sup>th</sup> arm i.e. **Stratum D** of the INSIGHT trial.

In collaboration with  **Merck KGaA**,  
Darmstadt, Germany  Institut für Klinisch-Onkologische Forschung  
 **KRANKENHAUS  
NORDWEST**



### Phase I

Open label trial



12

Patients: 2 cohorts of  
6 patients each



### 6 months

Combination treatment,  
then 6 months avelumab  
monotherapy



### One site

Germany

### Inclusion

#### Solid tumors

- histologically confirmed locally advanced or metastatic
- received  $\leq 3$  prior lines of therapy
- no selection for immunogenic markers (e.g. PD-L1 expression levels, msi high or tmb)

### Treatment

- 1) **Avelumab + Efti (6 mg - 30 mg) s.c.**  
qw 2 for a maximum of 6 months
- 2) **Avelumab monotherapy (maintenance)**  
qw 2 for a maximum of further 6 months

### Results

RP2D, Safety,  
ORR, PFS, PK, PD

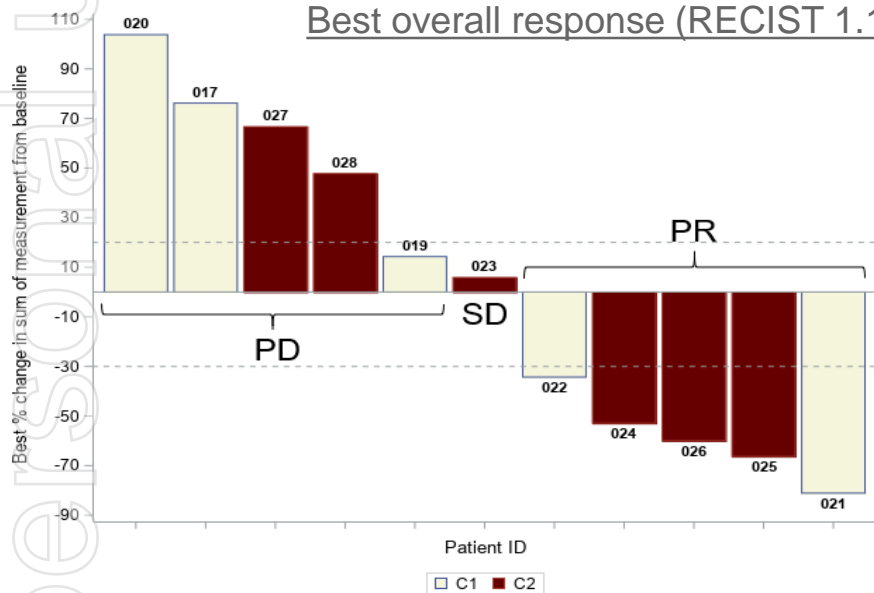
# INSIGHT-004 (Stratum-D)

## Results<sup>(1)</sup>

### Activity

- 5/12 (42%) with partial responses in different indications:
  - 1st line MSI high colorectal cancer; 1st line pleural mesothelioma; after radiochemo in squamous anal cell; pre-treated squamous cervical cancer (PD-L1 TPS < 1%) carcinoma; 3<sup>rd</sup> line gastroesophageal junction
- 75% (n=9) are still alive → 66.7% (n=4) of cohort 1 and 83.3% (n=5) of cohort 2

Best overall response (RECIST 1.1)

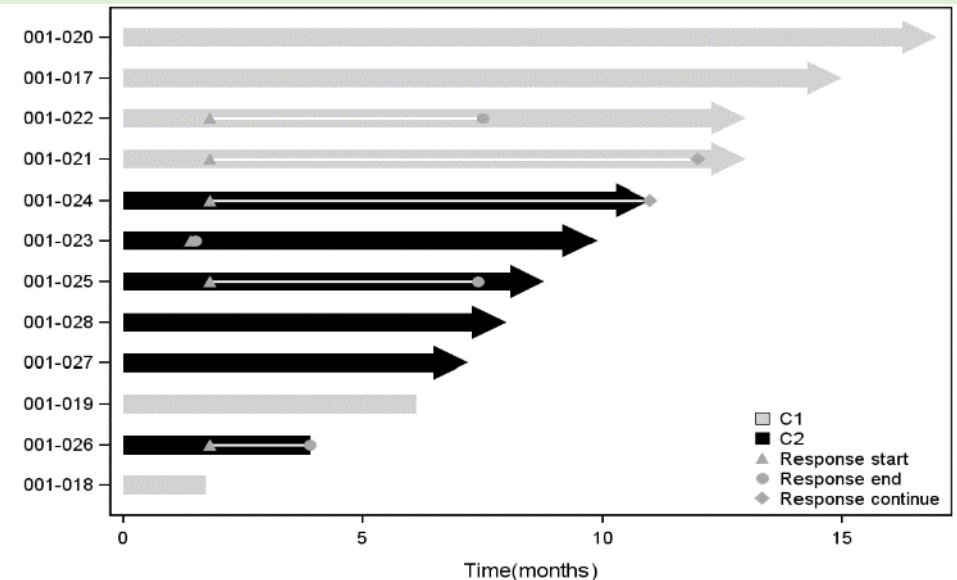


### Safety

- Combo of avelumab 800 mg + ehti 6 mg or 30 mg ehti s.c. is feasible and safe
- No unexpected AEs

### Conclusion

- Treatment with ehti + avelumab safe, with promising signals of efficacy
- Ehti + avelumab seems to be a potent combination for enhancing PD-L1 directed therapy and needs further evaluation in new trials



Triangles at the end of the chart represents the survival status



# Efti + Chemo Combination AIPAC

Exciting interim OS results presented at SABCS in December 2020

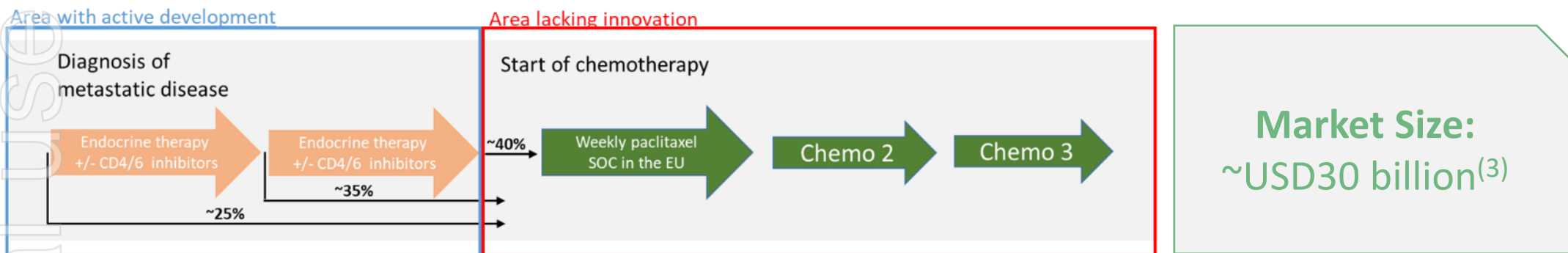
Final OS results to be presented at SITC, 10-14 November 2021

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# Goal: Improving OS while maintaining QoL in HR+/HER2- MBC patients

## Epidemiology:

- More than 2 million breast cancer (~70% HR+/HER2-) diagnoses per annum worldwide. 1.5 million of which are under the age of 65<sup>(1)</sup>
- Highest incidence rate among cancers: ~25% of all new cancer diagnoses among women and ~12% in the total population, including men.<sup>(1)</sup>
- Up to **350,000 patients younger than 65 develop metastatic disease** and are eligible to receive chemotherapy<sup>(1) (2)</sup>



High Unmet Medical Need



*efti addresses high unmet medical need with a good safety profile*

Paclitaxel



*Weekly paclitaxel well established SOC*

Lack of Innovation



*No innovation in decades & no significant innovations in the pipeline for pts receiving chemo*

### Notes

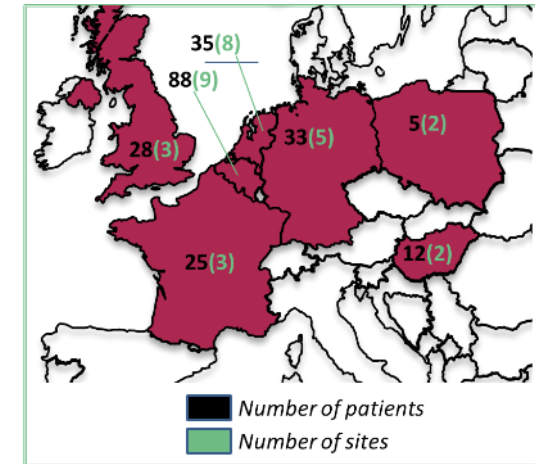
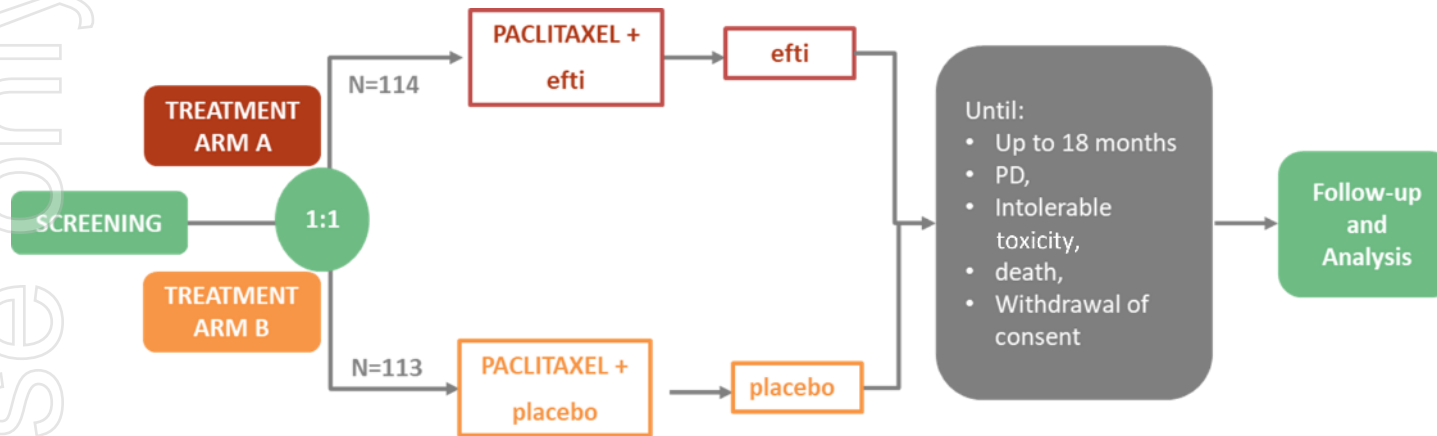
(1) Source: WHO Global Cancer Observatory 2020 and Informa Intelligence October 2020

(2) Wang et al. BMC Cancer (2019) 19:1091

(3) GlobalData Market Size forecast for US, JP, EU5, Urban China and Australia

# Efti: AIPAC (Phase IIb) design

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



### Primary endpoint<sup>(\*)</sup> (presented Mar. 2020) included:

- Assessment of Progression-Free Survival (PFS)

### Secondary endpoints<sup>(\*)</sup> (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 at SITC 2021

Notes:

\* No hypothesis testing

ORR – overall response rate, DCR – disease control rate, PFS – progression free survival, OS – overall survival, QoL – Quality of life

# AIPAC Phase IIb Clinical Interim OS Results\*

Subgroups: low monocytes and < 65 years – PFS / OS / ORR

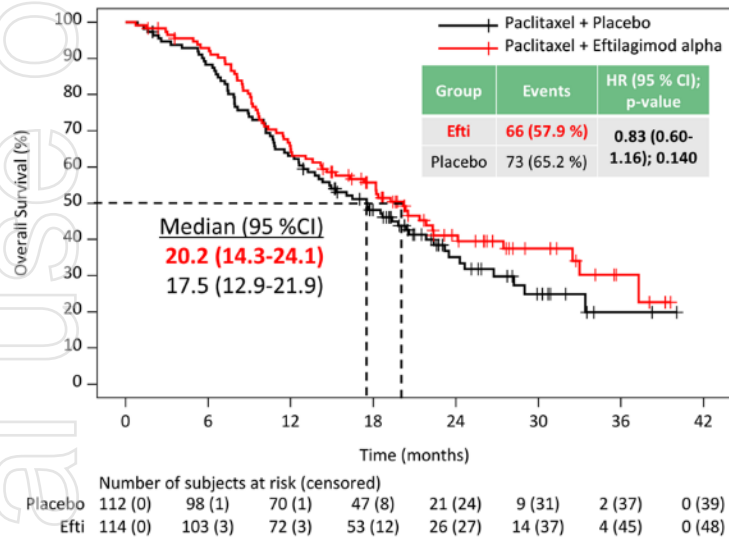


For predefined sub-groups:

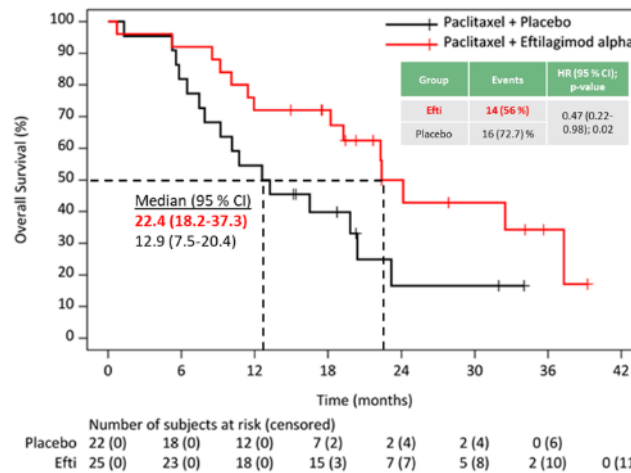
Clinically meaningful absolute and relative improvement for efficacy parameters, significance for OS

ESMO scale of magnitude\*\* = level 4 (makes reimbursement very likely)

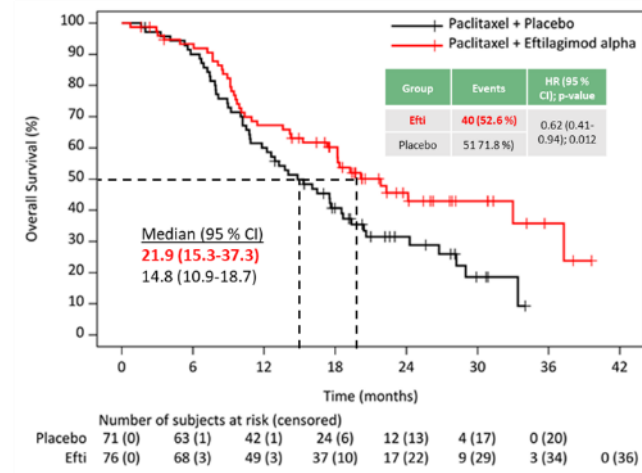
Overall Survival (Follow-up†) – Total Population



Patients with low monocytes - OS -



Patients with age < 65 yrs. - OS -



+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 **not** 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 **not** 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

Notes:

\* These results were presented at SABCS 2020. Data cut-off for interim overall survival results was 24 September 2020.

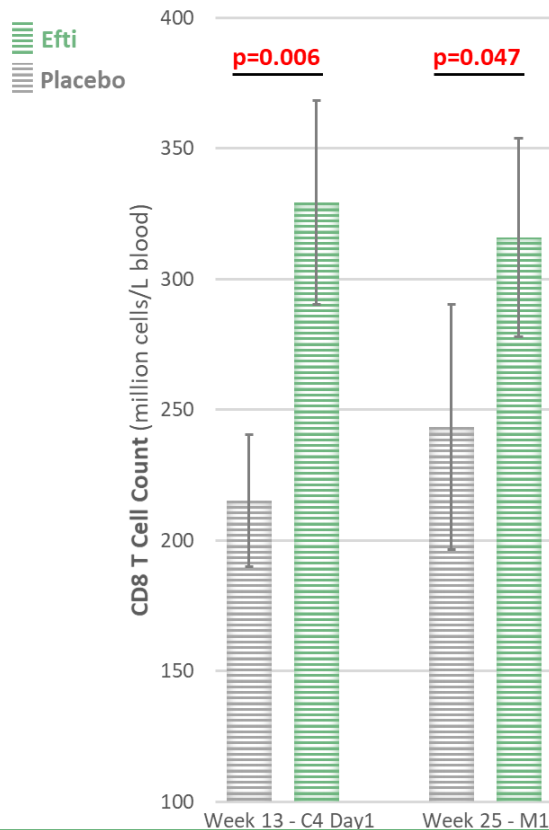
\*\* used for reimbursement in Europe: <https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1>

# AIPAC Phase IIb Clinical Results

Immune Monitoring on Fresh Blood (up to 70 patients)

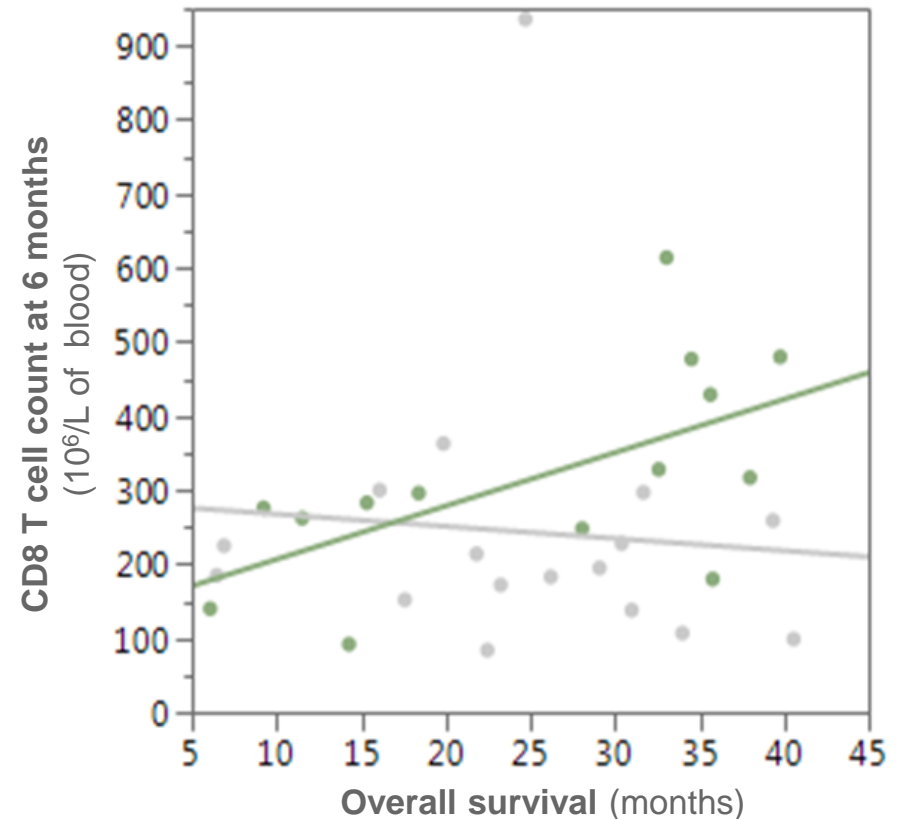
## Cytotoxic CD8<sup>+</sup> T Cell count over time

(Mean  $\pm$  SEM million cells/L of blood;  
p-value Wilcoxon)



Number of T cells increased in efti group, especially cytotoxic CD8<sup>+</sup> → Proof of Principle.

Stat. significant (**p=0.020**)  
Correlation: OS and cytotoxic CD8<sup>+</sup> T cell count



Increased number of cytotoxic CD8<sup>+</sup> T Cells correlated with improved OS in the efti arm → Proof of Concept.

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# AIPAC Phase IIb 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*

# Other Efti Partnerships



- EOC, an Eddingpharm spin-off holding the Chinese rights for efti, Phase I study in MBC completed with a Phase II trial in preparation
- Milestone and royalty bearing partnership



- Spin off from NEC, Japan: aims to develop cancer drugs discovered by artificial intelligence → mainly cancer vaccines
- Clinical Trial Collaboration (up to US\$5 million for ImmuteP); Phase I completed



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



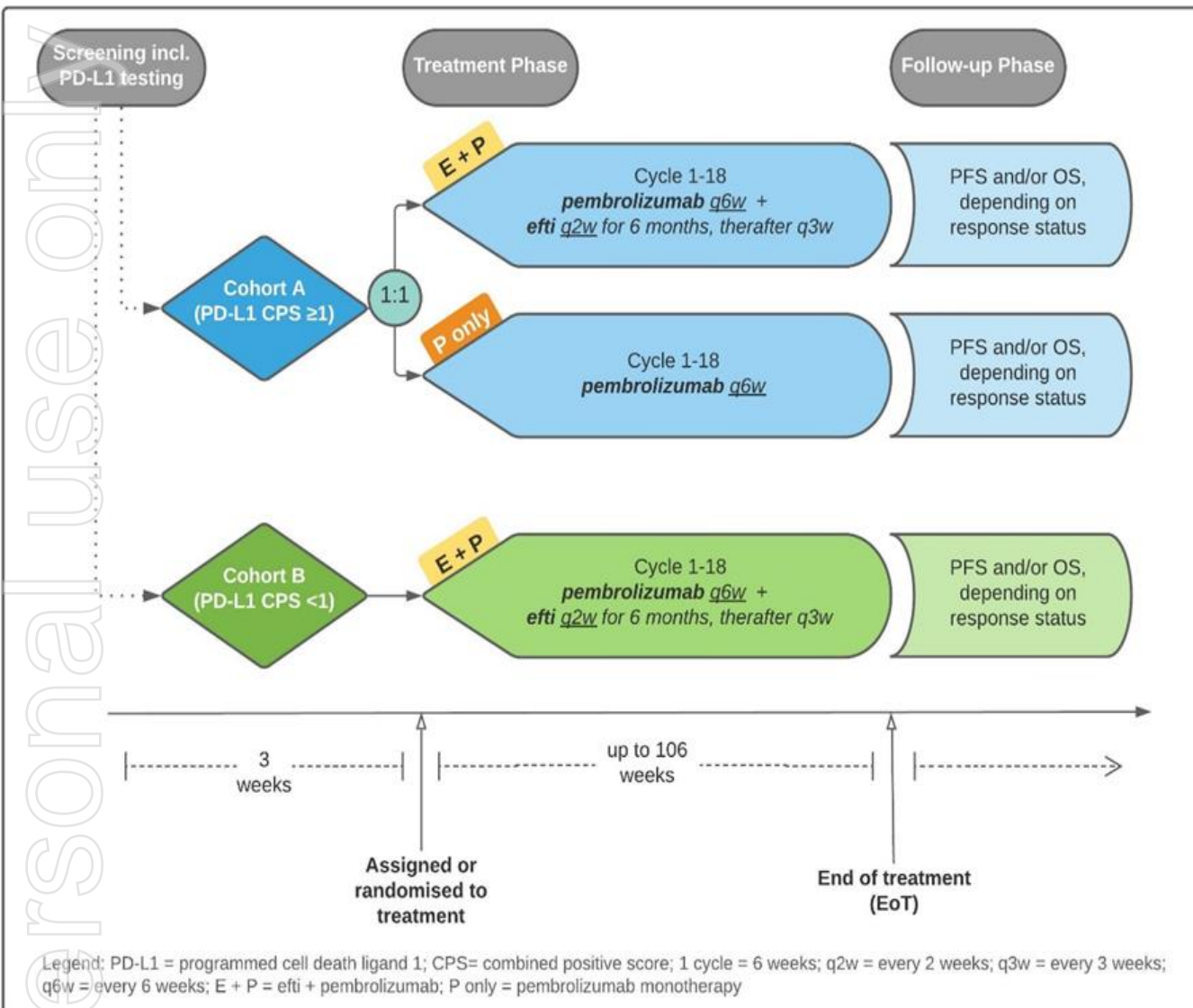
# New Trials

**TACTI-003, INSIGHT-003 and INSIGHT-005**



# TACTI-003 Trial in 1<sup>st</sup> line HNSCC

## Design + Status



In collaboration with



### Design:

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

### Status:

- First patient expected in 2H 2021
- **Fast Track designation granted by FDA in April 2021**

# INSIGHT Platform Trial in Solid Tumours

## Stratum-003: Efti + anti-PD-1 + chemo

To evaluate the feasibility and safety of **triple combination therapy** consisting of **efti** in conjunction with an existing approved **standard of care combination of chemotherapy and anti-PD-1** therapy.

In collaboration with Institut für Klinisch-Onkologische Forschung  
 KRANKENHAUS  
NORDWEST



### Phase I

Open label trial



20

Patients with various solid tumours



### First patient

Enrolled and safely dosed  
August 2021



6 months

Combination treatment, then maintenance monotherapy or combination



Two sites

Germany

### Inclusion

#### Solid tumors

- histologically confirmed locally advanced or metastatic
- received no or max. 1 prior lines of therapy
- no selection for immunogenic markers (e.g. PD-L1 expression levels, msi high or tmb)

### Treatment

- 1) SoC (Chemo + a-PD-1 therapy) + Efti  
30 mg s.c., qw 2 for a maximum of 6 mts
- 2) Maintenance therapy  
Dependent on SoC maintenance schedule

### Results

RP2D, Safety,  
ORR, PFS, PK, PD

# INSIGHT Platform Trial in Solid Tumours

## Stratum-005: Efti + Bintrafusp Alfa Combination

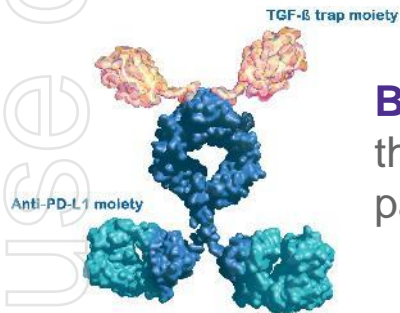
To evaluate the feasibility and safety of combined treatment with bintrafusp alfa (M7824) and eftilagimod alfa. Conducted as the 5<sup>th</sup> arm of the INSIGHT trial.

In collaboration with

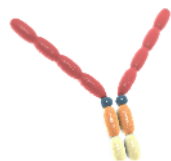
**Merck KGaA,**  
Darmstadt, Germany



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



**Phase I/IIa**  
Open label trial



**12**  
Patients in 3 cohorts



**12 months**  
Combination treatment



**Two sites**  
Germany

### Inclusion

#### Solid tumors

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

### Treatment

#### Q2W for maximum of 12 months

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

### Results

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

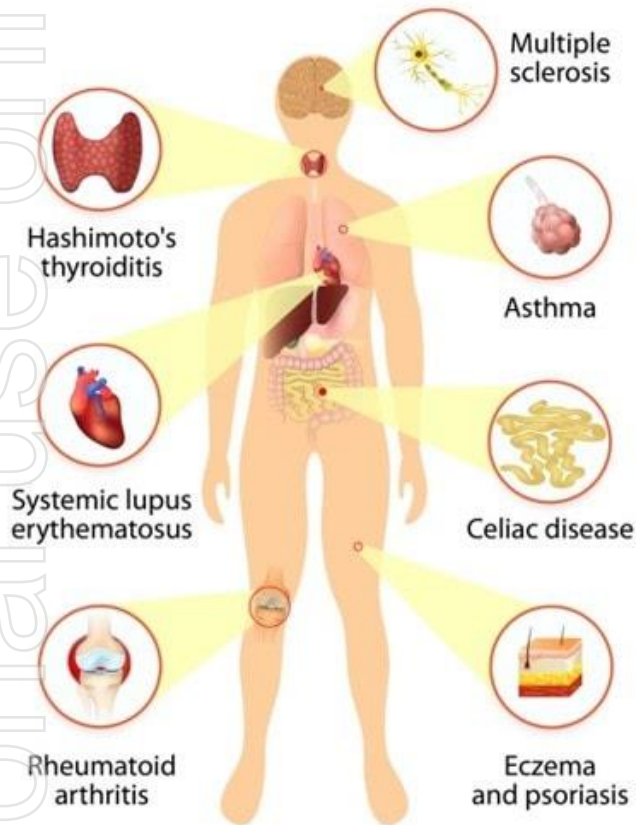
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**IMP761**

**- Autoimmune Diseases -**

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

## AUTOIMMUNE DISEASES

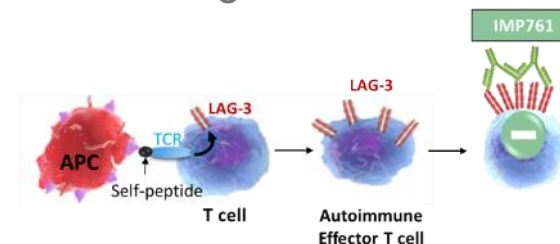


## THE PRESENT: FIGHTING THE SYMPTOMS

Treating general inflammation:  
corticoids, methotrexate,  
anti-TNF- $\alpha$ , -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 (US \$153.32 billion by 2025)<sup>1</sup>

**Out-Licensed  
Immunotherapy Pipeline  
&  
Other Collaborations**

# Ieramilimab (LAG525) for Cancer

- Novartis holds an exclusive WW licence to develop and commercialise Ieramilimab (which is derived from Immunetep's antagonist antibody known as IMP701)
- 1st and 2nd milestone payments received by Immunetep in August 2015 (undisclosed) and August 2017 (US\$1 million)
- In 2018 Novartis cancelled 90 other R&D programs but continued to invest heavily in progressing the development of LAG525<sup>(1)</sup>
- Novartis currently has five clinical trials for Ieramilimab in multiple cancer indications for over 1,000 patients<sup>(2)</sup>



- **Ieramilimab 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**

## Notes

(1) <https://www.fiercebiotech.com/biotech/novartis-dumps-20-programs-following-pipeline-review>

(2) For details on all trials of LAG525 conducted by Novartis see:

<https://www.clinicaltrials.gov/ct2/results?cond=&term=novartis+lag525&cntry=&state=&city=&dist=>

# GSK'781 (IMP731) for Autoimmune Diseases

- Exclusive WW licence continues with GSK to develop and commercialise GSK'781 (which is derived from Immunetep's depleting antibody known as IMP731)
- Up to £64 million in upfront payments and milestones, plus royalties
- GSK portfolio review in 2017 -> GSK'781 continued despite cancellation of 13 clinical and 20 preclinical programs<sup>(1)</sup>
- March 2018: Phase I trial in psoriasis completed in 67 subjects/patients<sup>(2)</sup>
- September 2019: 1<sup>st</sup> patient dosed in Phase II trial in ulcerative colitis in 242 patients triggered a £4 million (~US\$5.0 million) milestone payment to Immunetep<sup>(2)</sup>
- Phase I clinical study completed, evaluating GSK'781 in 36 healthy Japanese and Caucasian subjects, PK/PD study<sup>(2)</sup>
- Phase II in Ulcerative Colitis discontinued in January 2021

**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**





# Collaboration with LabCorp



- Licence and Collaboration Agreement for immuno-oncology products or services (entered in Oct 2020)
- Development of lab tests that may help oncologists select the right therapeutic options for their patients
- Upfront and potential commercial milestone and service-related payments to Immunetep
- Immunetep selected for its LAG-3 expertise

*Laboratory Corporation of America Holdings (LabCorp) is a leading global life sciences company focused on guiding patient care that provides diagnostic, drug development and technology-enabled solutions for more than 160 million patient encounters per year.*

**Enables Immunetep to enter the immuno-oncology diagnostics market through its technology and LAG-3 expertise**

# Outlook

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# 2021/2022 News Flow\*

H1 2021

- ✓ **Fast Track designation** granted for efti in 1<sup>st</sup> line HNSCC from US FDA
- ✓ Data from **TACTI-002** & final data from **INSIGHT-004** at ASCO
- ✓ Expansion of existing programs, adding:
  - ✓ Second collaboration with MSD for TACTI-003
  - ✓ First triple combination therapy with efti in INSIGHT-003
  - ✓ New collaboration with Merck KGaA for INSIGHT-005
- ✓ Patent protection strengthened
- ✓ Financial position significantly strengthened

- ✓ Validation of LAG-3/MHC-II interaction through BMS's Phase III results in melanoma

H2 2021

2022

- ❑ Final data from **AIPAC**: 2<sup>nd</sup> OS follow up at SITC
- ❑ Start & ongoing recruitment of **new randomised trial in 1st line HNSCC** (TACTI-003) in Q3 2021
- ✓ Part B of TACTI-002 fully recruited
- ❑ Recruitment into Part A extension & further data from **TACTI-002** in 2021 or early 2022
- ✓ **INSIGHT-003** first patient enrolled in Q3 2021 and first interim results in 2022
- ❑ Manufacturing scale up to 2,000 L
- ❑ Ongoing **regulatory** engagement
- ❑ Updates from **IMP761**
- ❑ Further updates from partnered programs (e.g. GSK, Novartis, EAT COVID, CYTLIMIC and EOC Pharma)

Notes:

\*The actual timing of future data readouts may differ from expected timing shown above. These dates are provided on a calendar year basis. A tick symbol indicates a completed item.

# Corporate Snapshot

<b>Ticker symbols</b>	IMM (ASX) IMMP (NASDAQ)
<b>Securities on issue<sup>(1)</sup></b>	~ 850.92 million ordinary shares
<b>Proforma cash balance<sup>(2)</sup></b>	~ A\$114 million (US\$85.7 million)
<b>Market Cap<sup>(3)</sup></b>	~ A\$459.50 million (US\$335.30 million)

Notes:

(1) Currently 32.82% of the ordinary shares are represented by ADSs listed on NASDAQ where 1 ADS represents 10 ordinary shares.

(2) Pro forma cash balance based on Immunetep's cash balance on 30 June 2021 plus the gross proceeds from the SPP and Tranche 2 share issuance as announced to the ASX on 30 July 2021.

(3) Market capitalization based on ASX share price of A\$0.54 on 24 September 2021 and basic ordinary shares outstanding.

US equivalent of amounts above are based on foreign exchange rate for AUD/USD of 0.7297 for market capitalization, and the US cash & cash equivalents amount was calculated using FX rate of 0.7518.

# Summary

Global leadership position in LAG-3 with 4 LAG-3 related product candidates in immuno-oncology and autoimmune disease

Multiple active clinical trials (including partnered candidates), with further significant data read-outs expected in 2021 and into 2022

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

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

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**immutep**<sup>®</sup>  
LAG-3 IMMUNOTHERAPY



**Thank You**