

**immutep**  
LAG-3 IMMUNOTHERAPY



## Immutep TACTI-002 Clinical Results & Update Global Webcast Slides

Immutep will present these slides as part of its global webcast, as follows:

Date & Time: Wednesday, February 26, 2020, 8:00 am Australian Eastern Daylight Time /  
Tuesday, February 25, 2020, 4:00 pm US Eastern Standard Time

Register: Interested parties can join the webcast by registering via [FNN](#).

A replay of the webcast will also be available at [www.immutep.com](http://www.immutep.com) from the day after the event.

**(ASX: IMM, NASDAQ: IMMP)**

# Notice: Forward Looking Statements

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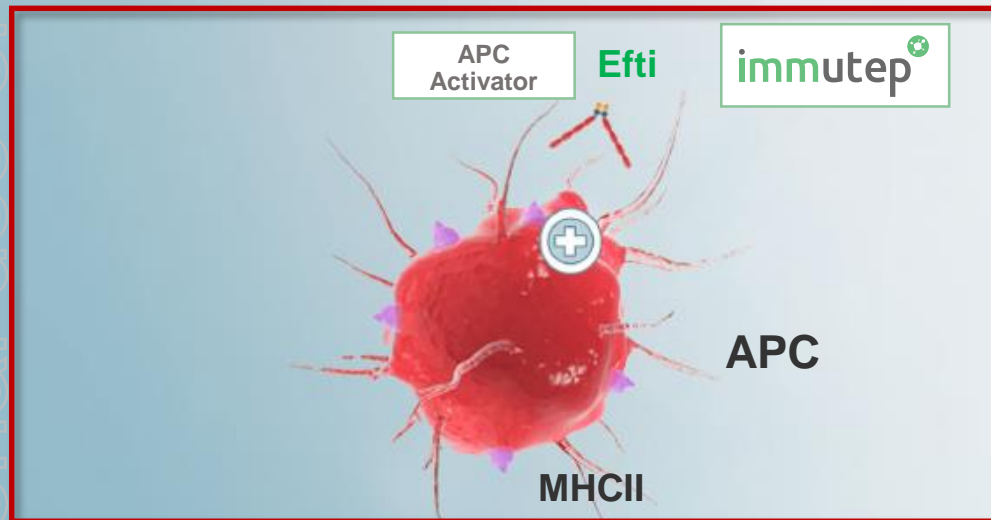
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# Eftilagimod Alpha (efti or IMP321)

# Targeting LAG-3 / MHC II may lead to multiple therapeutics in numerous indications

## IMMUNOSTIMULATION



Antagonistic mAb

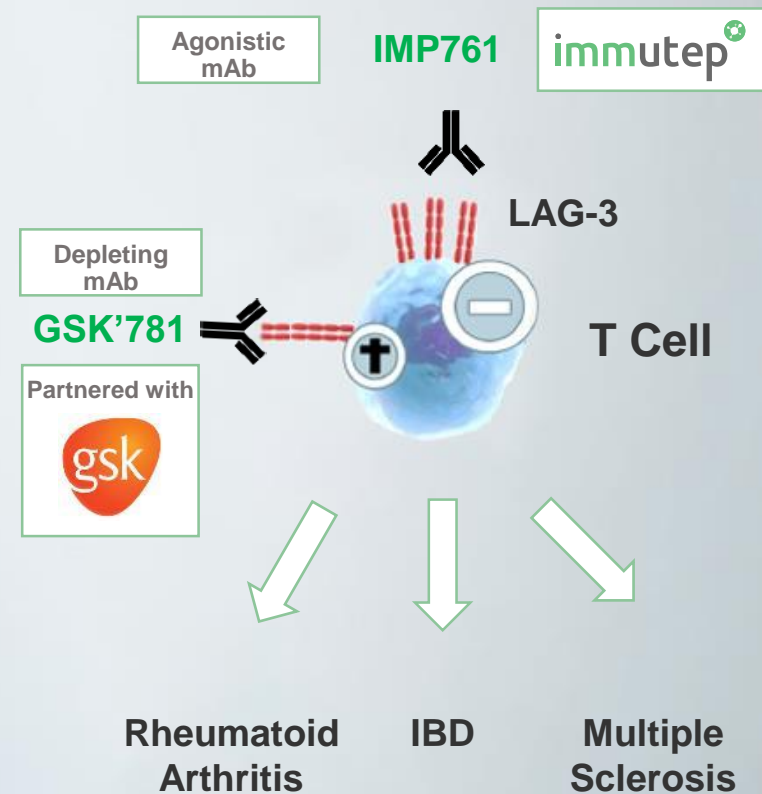
LAG525

Partnered with  
NOVARTIS

Immuno-oncology  
Combination Therapies






Viral Infections

## IMMUNOSUPPRESSION



# Immutep Controlled Immunotherapy Pipeline (Oncology)\*

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Program	Preclinical	Phase I	Phase II	Late Stage <sup>(4)</sup>	Commercial Rights
<b>Oncology</b>  <b>Eftilagimod Alpha (efti or IMP321)</b>  APC activating soluble LAG-3 protein	<b>Metastatic Breast Cancer (Chemo – IO)</b> <b>AIPAC</b>				Global Rights 
	<b>Non-Small-Cell Lung Carcinoma (IO – IO) <sup>(1)</sup></b> <b>TACTI-002</b>				
	<b>Head and Neck Squamous Cell Carcinoma (IO – IO) <sup>(1)</sup></b> <b>TACTI-002</b>				
	<b>Solid Tumors (IO – IO) <sup>(2), (3)</sup></b> <b>INSIGHT-004</b>		 Merck KGaA, Darmstadt, Germany		
	<b>Melanoma (IO – IO)</b> <b>TACTI-mel</b>				
	<b>Solid Tumors (In situ Immunization) <sup>(2)</sup></b> <b>INSIGHT</b>				
	<b>Metastatic Breast Cancer (Chemo – IO)</b>				Chinese Rights 

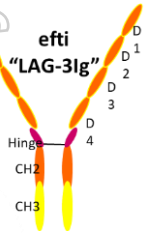
## Notes

\* Information in pipeline chart current as at 25 February 2020

- 5 (1) In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC")  
 (2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

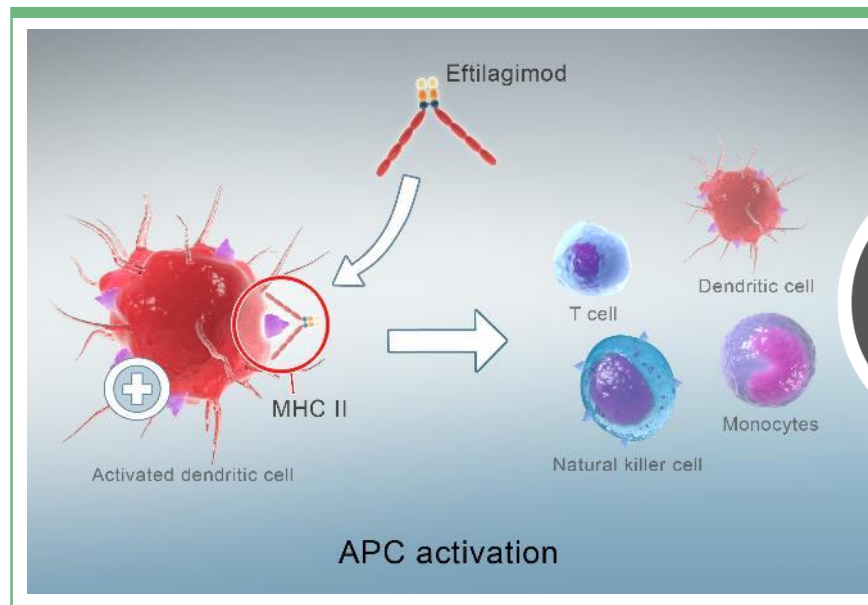
- (3) In combination with BAVENCIO® (avelumab)  
 (4) Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials

# 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. I-O agents or chemotherapies

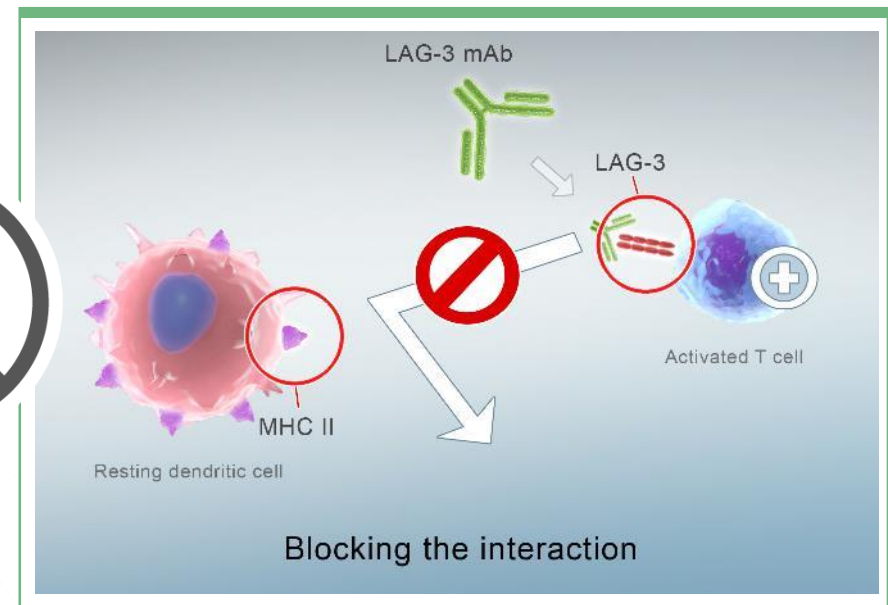
## “PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”



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”



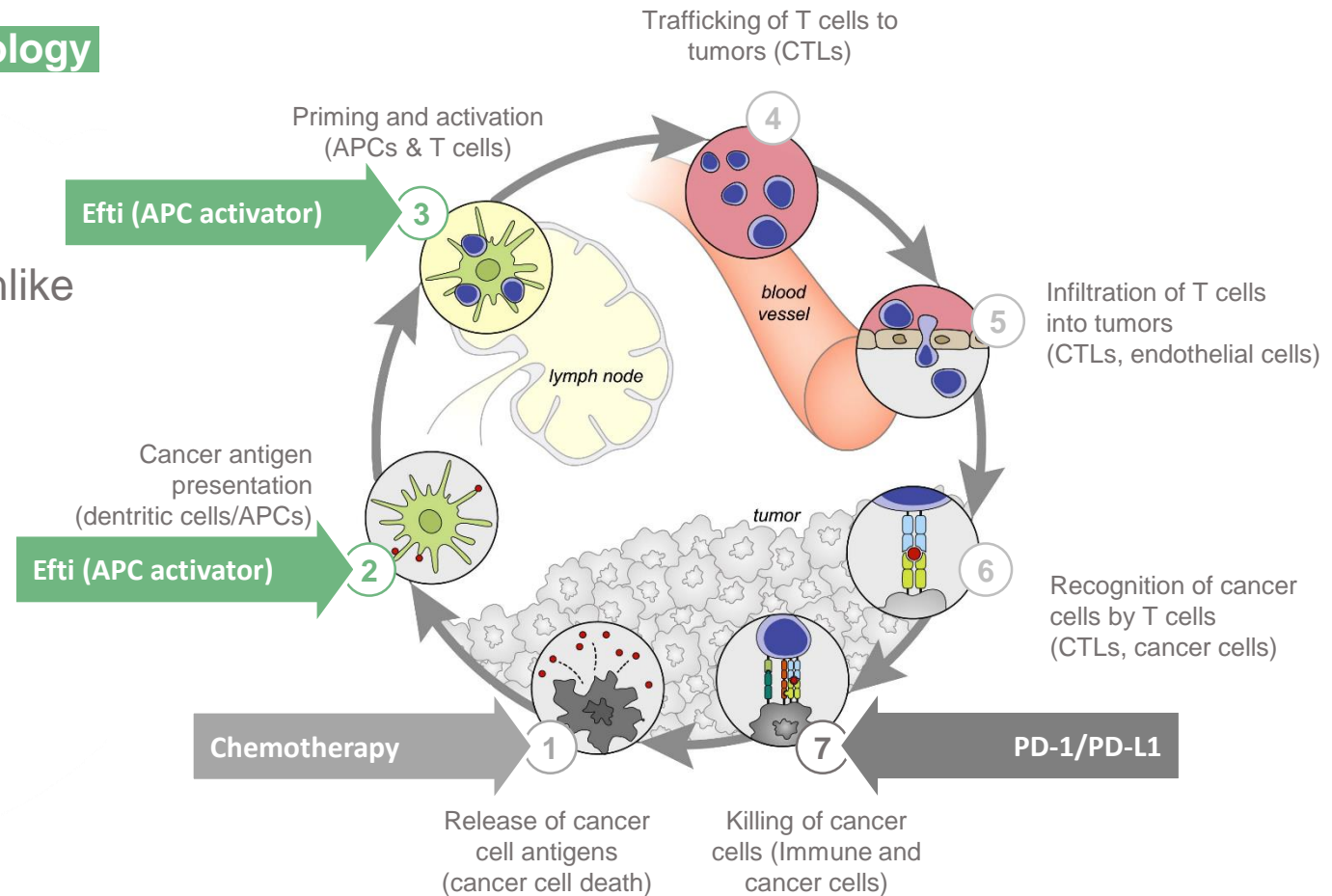
**LAG-3 antagonist**, or blocking, antibodies:  
**Immune checkpoint inhibitor**

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

# Efti: a pipeline in a product

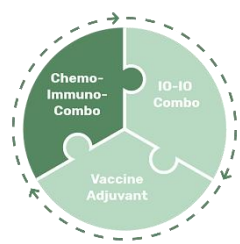
## Efti has disruptive potential for oncology

- ✓ **First-in-Class** MHCII agonist
- ✓ good safety profile
- ✓ unique protective IP positioning (unlike ICI mAbs)
- ✓ encouraging efficacy data
- ✓ low cost of goods
- ✓ potential for use in various combination settings →  
**efti is a “pipeline in a product”**



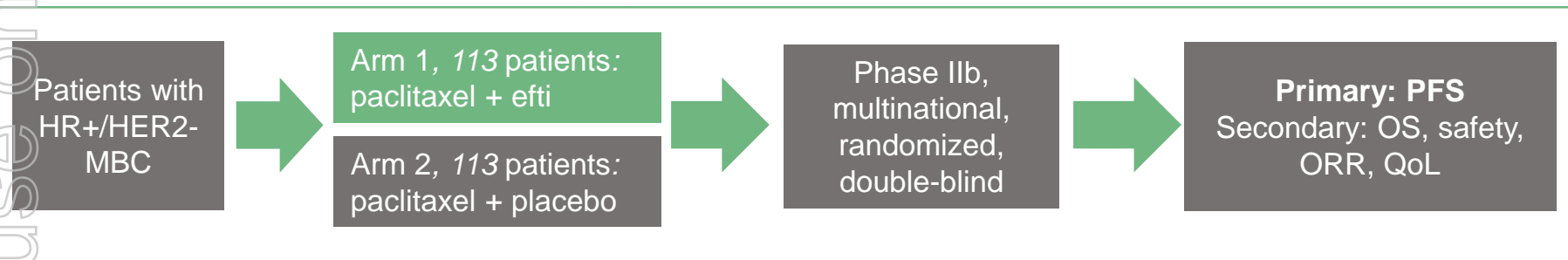
# AIPAC update





# Efti: Clinical Development AIPAC (Phase IIb)

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



Primary endpoint will include:

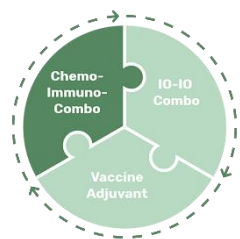
- median PFS including confidence intervals, and
- Hazard Ratio: relative risk of progression compared to placebo; e.g.  $HR = 0.75 \rightarrow$  risk of progression in a group is 25% lower compared to the other group

## Status Report

- ✓ Fully recruited in 7 EU countries (227 pts)
- PFS & ORR data expected by end of March 2020

## Key features:

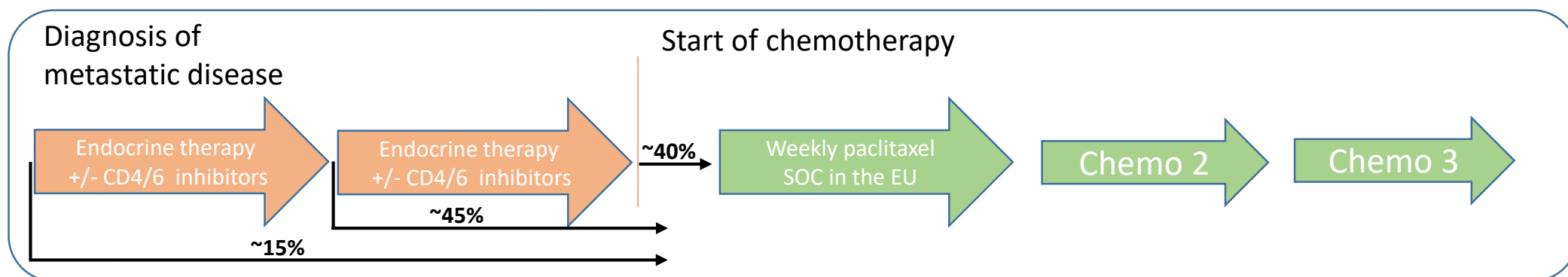
1. double blinded potentially pivotal trial in MBC patients  $\rightarrow$  conditional marketing authorization in the EU depending on data
2. broader perspective: validation of Antigen Presenting Cell activators  $\rightarrow$  a new class of active I-O products after the Immune Checkpoint Inhibitors



# Efti positioning in HR+/HER2- MBC

## Epidemiology:

- 812,500 HR+/ HER2- diagnoses per annum worldwide<sup>(1)</sup>
- approximately 250,000 develop metastatic disease and are eligible to receive chemotherapy



## Current Status:

- despite all changes for early treatment lines → no improvement for patients receiving first-line chemotherapy
- taxane monotherapy widely used in first line chemotherapy setting
- no active IO approved / or in late stage trials

## Typical Patient Population in MBC:

- number of pre-treatments have increased over recent years → patients receive chemo at a later stage → shortened expected benefit
- expected that most patients starting with chemotherapy have:
  - visceral disease
  - usually 1 or 2 previous anti-cancer therapies

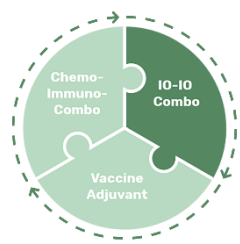
**Efti will be a differentiator for chemotherapies → combination will likely be used more than single-agent paclitaxel right now**

# Recent MBC approvals and late stage approaches: Selected PFS results and Hazard Ratios

Approval status	Drug	Indication	Trial	Results		
				PFS T+nP	PFS PI-nP	HR
APPROVED (2019)	Tecentriq (atezolizumab)	1 <sup>st</sup> line in combo with nab- paclitaxel for mTNBC	<b>Impassion130</b> : Tecentriq + nP vs. Placebo + nP	7.5	5.3	<b>0.63</b>
				PFS piqr.+fulv.	PFS PI+fulv.	HR
APPROVED (2019)	Piqray (alpelisib)	2 <sup>nd</sup> line in combination with fulvestrant for PIK3CA-mutated HR+ HER2- mBC	<b>SOLAR-1</b> : Piqray + fulvestrant vs. Placebo + fulvestrant	11.0	5.7	<b>0.65</b>
				PFS marg+chemo	PFS Tr+chemo	HR
BLA submitted (2019)	Margetuximab	2 <sup>nd</sup> line HER2+ mBC	<b>SOPHIA</b> : margetuximab + chemo vs. Trastuzumab + chemo	5.8	4.9	<b>0.76</b>

**Combining efti  
and anti-PD-1:**

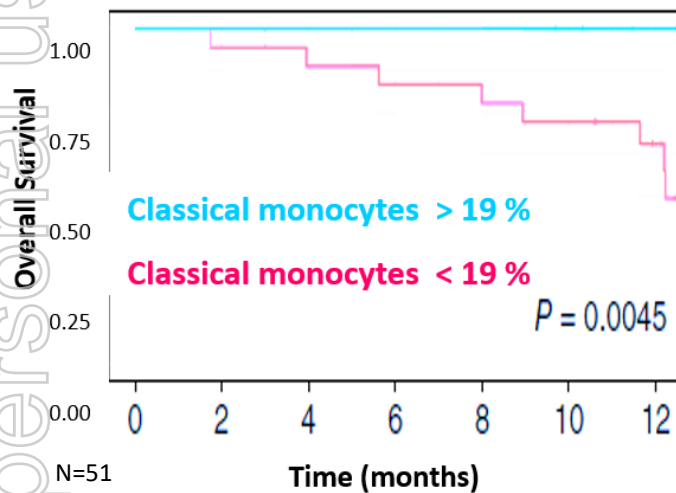
**TACTI-002**



# Rationale for combining efti with PD-1 antagonists

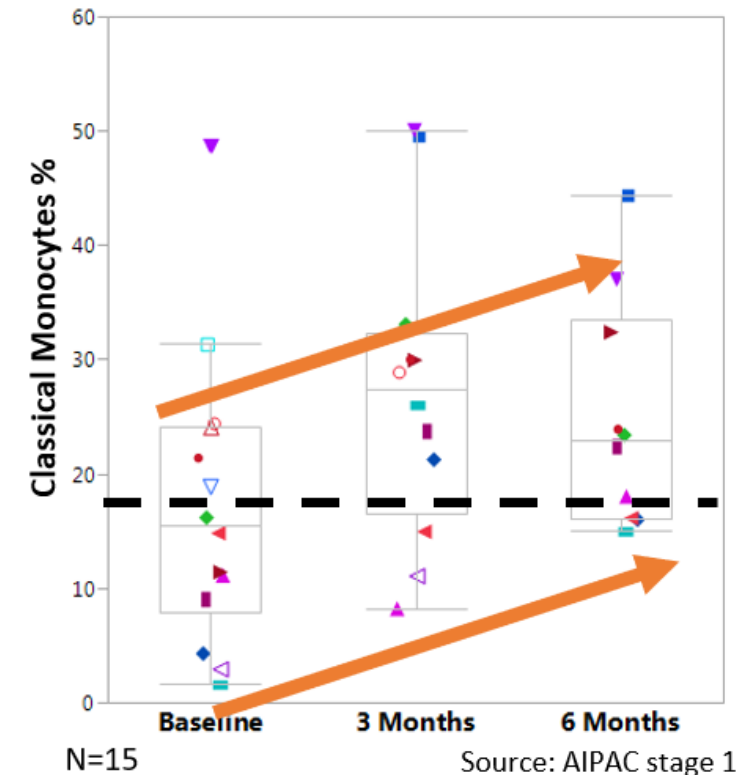
*Efti increases monocyte number in cancer patients*

## Melanoma

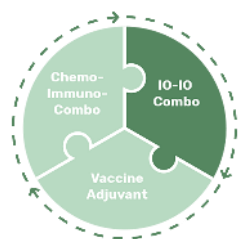


- baseline innate immunity status seems to be important for the response (OS) to pembrolizumab
- data suggests that low monocyte numbers at baseline are associated with poor efficacy of anti-PD-1 therapy in melanoma patients
- data shows that the APC activator, efti, boosts innate immunity

Source: Krieg et al., Nat. Med. 24, 2018.



Source: AIPAC stage 1



# Efti: Clinical Development TACTI-002 (Phase II)



## Trial Design + Introduction

- Phase II, multi-national, open label, Simon`s 2 stage design; PD-L1 all comer
- In collaboration with Merck Sharp & Dohme (MSD)

### Eligibility

- Available tumor tissue
- ECOG 0-1
- Adequate organ functions
- PD-L1 all comer

Part A:  
1<sup>st</sup> line met. NSCLC

Part B:  
2<sup>nd</sup> line met. NSCLC,  
refractory for PD-  
1/PD-L1

Part C:  
2<sup>nd</sup> line met. HNSCC  
after platinum

30 mg efti SC  
+  
200 mg pembrolizumab IV  
  
Up to 12 months then  
pembrolizumab alone for  
another 12 months

**Primary endpoint: iORR  
(iRECIST)**

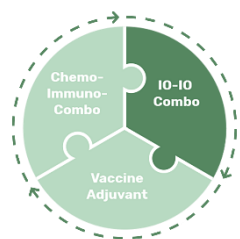
**Secondary endpoints: PFS,  
OS, PK, biomarker, PD, safety  
and tolerability**

Study – Part*	Stage 1 (N) Actual/target	Stage 2 (N) target
Part A	17/17	10/19
Part B	14/23	-/13
Part C	18/18	3/19

Notes:

NSCLC – non-small-cell lung cancer, HNSCC – head and neck squamous cell cancer, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK – pharmacokinetics, PD-X – any PD-1 or PD-L1 treatment

\*as of Feb 20th 2020



# Efti: Clinical Development TACTI-002 - Safety

## TACTI-002: Preliminary results – Safety, all parts

### Summary

- In total 48 pts were enrolled between Mar 2019 and Jan 2020<sup>(1)</sup>. Pts received median 7 (range 1-20) IMP321 injections and median of 5 (range 1-16) pembrolizumab (Keytruda®) infusions.
- No grade 4 or 5 for the TEAEs described above
- Injection site reactions (n=18 events in 10 subjects, all grade 1) were reported for efti

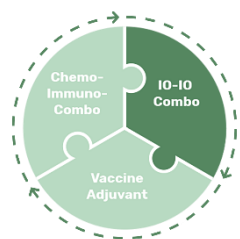
***Efti has a favorable safety profile in combination with pembrolizumab - no new safety signals observed***

### TEAEs\* occurred in > 10% of pts (N=48 in total)

Adverse event (PT)	Any Grade N (%)	Grade 3 N (%)	Grade 4/5 N (%)
Cough	15 (31.3)	5 (10.4)	-
Asthenia	11 (22.9)	4 (8.3)	-
Decreased appetite	9 (18.8)	5 (10.4)	-
Fatigue	9 (18.8)	2 (4.2)	1 (2.1)
Dyspnoea	8 (16.7)	2 (4.2)	3 (6.3)
Diarrhoea	7 (14.6)	2 (4.2)	1 (2.1)
Constipation	6 (12.5)	1 (2.1)	1 (2.1)

- 2 fatal TEAE\* (hemoptysis; respiratory failure) unrelated to therapy
- 2 TEAEs leading to permanent discontinuation:
  - Hepatitis grade 4 – both study drugs discontinued
  - Diarrhoea grade 3 – pembro discontinued

\*Treatment Emergent Adverse Event



# Efti: Clinical Development TACTI-002 - 1<sup>st</sup> line NSCLC (Part A)

## TACTI-002: Preliminary<sup>1</sup> results 1<sup>st</sup> line NSCLC – part A, stage 1

→ *PD-L1 distribution as expected → PD-L1 all come trial*

→ *Patients are typical NSCLC 1<sup>st</sup> line pts*

Baseline Parameters (n=17)	N (%)
Median age, yrs (range)	65 (53 – 76)
Sex	
Female	6 (35.3)
Male	11 (64.7)
ECOG	
0	12 (70.6)
1	5 (29.4)
Smoking status	
Never	1 (5.9)
Current / former	16 (94.1)
Histology	
Squamous	10 (58.8)
Non-squamous	7 (41.2)
Location of disease at study entry	
Lung	8 (47.1)
Bone	5 (29.4)

Central assessment of tumor cell PD-L1 expression done post enrollment		
PD-L1 (n=13) <sup>2</sup>	N (%)	Historical <sup>3</sup> Distribution
< 1%	3 (23%)	35%
1-49%	6 (46%)	35%
≥ 50%	4 (31%)	30%

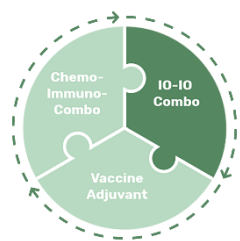
### Notes:

(1) Preliminary data, cut-off January 31 2020

(2) % in reference to evaluable samples; 4 specimens not evaluable by central lab using standard IHC kit

(3) Garon et al N Engl J Med 2015;372:2018-28





# Efti: Clinical Development TACTI-002 - 1<sup>st</sup> line NSCLC (Part A, Stage 1) - Results<sup>1</sup>

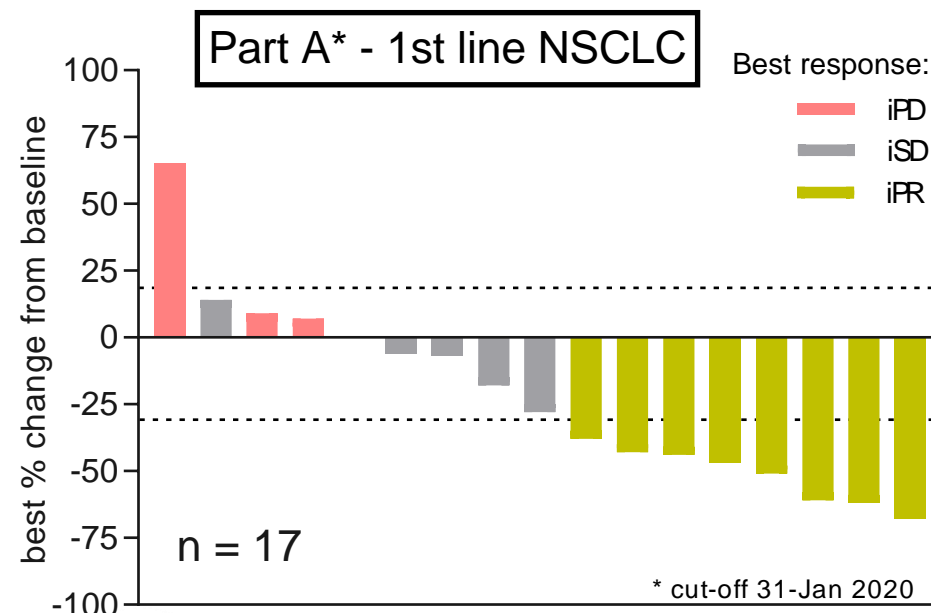
## Responses and Waterfall plot

→ 47.1% iORR acc. to iRECIST in this PD-L1 all comer trial

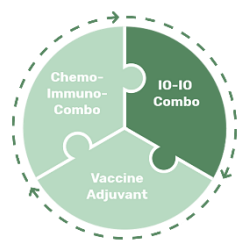
→ Responses in all PD-L1 subgroups

Tumor response - iBOR as per iRECIST	N (%) Total (N=17)
Complete Response (iCR)	0 (0.0)
Partial Response (iPR)	8 (47.1)
Stable Disease (iSD)	6 (35.3)
Progressive Disease (iPD)	3 (17.7)
<b>Objective Response Rate (iORR)</b>	<b>8 (47.1)</b>
<b>Disease Control Rate (iDCR)</b>	<b>14 (82.4)</b>

- Responses in all PD-L1 subgroups
- 6/8 iPR confirmed already → 7/8 pts with iPR still under therapy (none discontinued due to PD)
- 12/17 (71%) patients with target lesion decrease



Patients by PD-L1 category	No. of Responses	iORR
Low (< 1%)	1	33%
Medium (1-49%)	3	50%
High (≥ 50%)	3	75%
Not evaluable	1	25%
<b>Overall</b>	<b>8</b>	<b>47%</b>



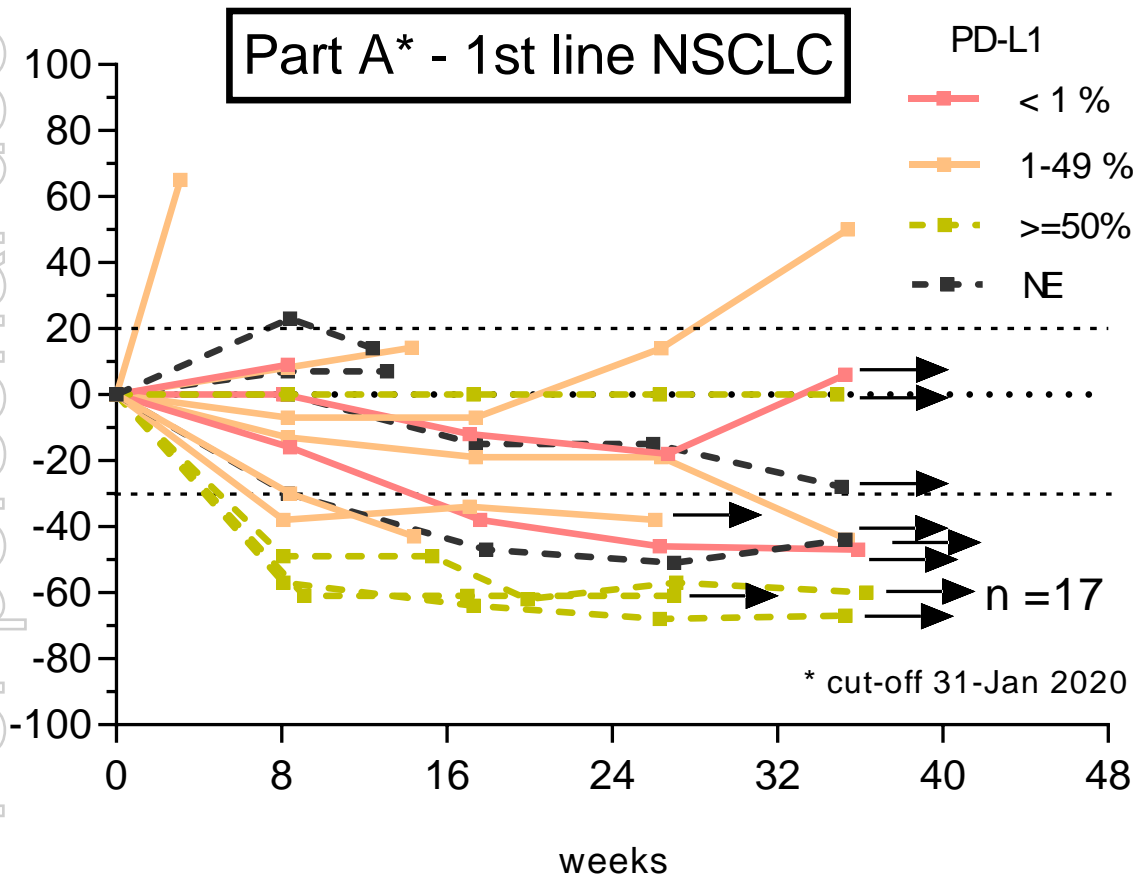
# Efti: Clinical Development

## TACTI-002 - 1<sup>st</sup> line NSCLC (Part A, Stage 1) - Results<sup>1</sup>

### Spiderplot

→ At data cut-off 10 pts (59%) still under treatment at 7+ months → median PFS not yet reached

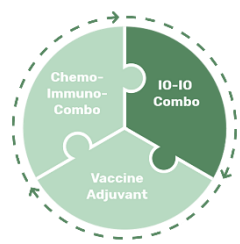
For release only



→ Patients continuing treatment

#### Main reason for discontinuation

- Progressive disease (n=4)
- Clinical deterioration (n=1)
- Adverse events (n=2):
  - G4 hepatitis (treatment related)
  - G5 hemoptysis (disease related)



# Efti: Clinical Development

## TACTI-002 - 2<sup>nd</sup> line HNSCC (Part C, Stage 1) - Results<sup>1</sup>

### Responses and Waterfall plot

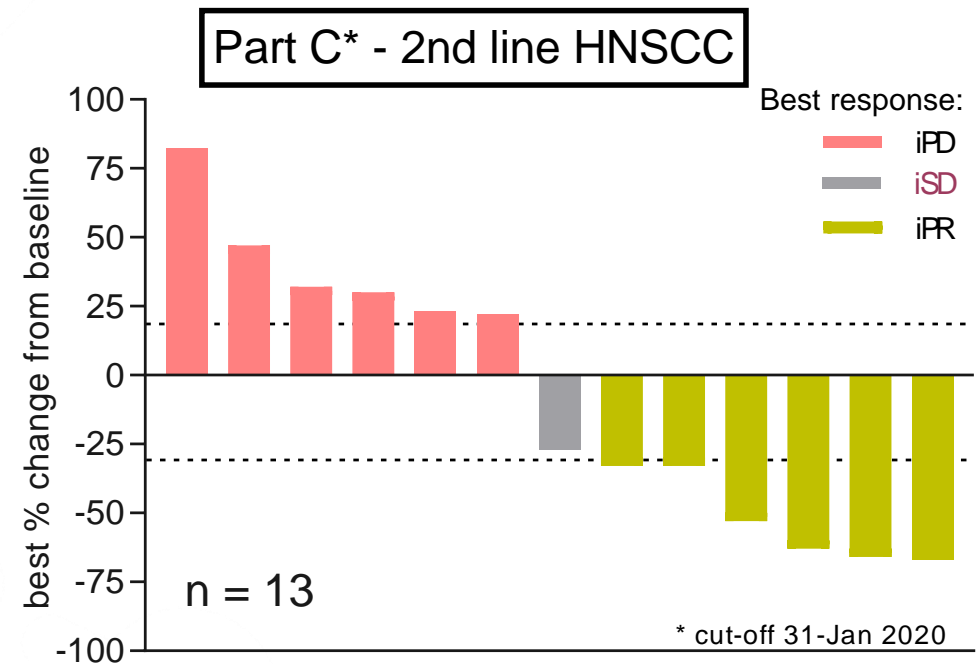
→ Initial iORR of 33.3% in this PD-L1 all comer HNSCC 2<sup>nd</sup> line patient

- Median Age of 66, mostly male (94%)
- ECOG 1 in 47%
- Different subtypes

Tumor response - iBOR as per iRECIST	N (%) Total (N=18)
Complete Response (iCR)	0 (0.0)
Partial Response (iPR)	6 (33.3)
Stable Disease (iSD)	1 (5.6)
Progressive Disease (iPD)	6 (33.3)
Not evaluable*	2 (11.1)
Not yet evaluated**	3 (16.7)
<b>Objective Response Rate (iORR)</b>	<b>6 (33.3)</b>
<b>Disease Control Rate (iDCR)</b>	<b>7 (38.9)</b>

\* - dropped out prior to first restaging

\*\* - not yet staged (on therapy < 9 weeks)

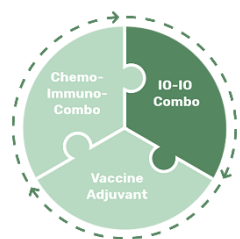


- LPI - Dec 2019 → 3 pts with outstanding imaging
- 7 pts (39%) had a decrease in target lesions
- All pts with iSD or iPR are still under treatment (median 6.4 months)

Note:

(1) Preliminary data, cut-off 31 Jan 2020

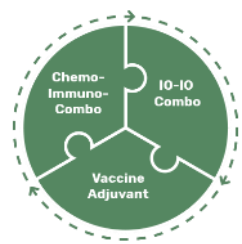
# Comparables and Outlook



# Efti: Clinical Development TACTI-002 (Phase II)

## TACTI-002: Trial design/status details

	Part A 1st line NSCLC	Part B 2nd line NSCLC	Part C 2nd line HNSCC
Details Indication	PD-L1 all comer; PD-X naive; SQ+NSQ	PD-L1 all comer; PD-X refractory	PD-L1 all comer; PD-X naive
Status	Stage 2 opened Nov 2019	Stage 1 opened	Stage 2 opened Jan 2020
Number of pts Stage 1 (actual / planned)	17/17	14/23	18/18
Number of pts Stage 2 (actual / planned)	10/19	NA/13 - Not yet opened	3/19
Preliminary results ORR etc	47% ORR (DKK 2020) 59% pts under therapy at 7+ months (DKK 2020) → median not yet reached	Not yet	33% ORR (6/18 patients with 3 patients not yet staged)
Expectation pembrolizumab alone	~20% ORR, ~5-6 months median PFS in ≥ 1% PD-L1 (label for pembro ≥50% PD-L1 e.g. in the EU)	./.	15-18% ORR in PD-L1 all comer



# Efti: a pipeline in a product

Efti is the ideal candidate to combine with  
✓ chemo and ✓ PD-1/PD-L1 antagonists

Chemotherapy

Eftilagimod  
Alpha

PD-1 / PD-L1

Taxanes

Huge  
Potential

Pembrolizumab

Nivolumab

Other Chemo

Avelumab

...

TACTI-002 NSCLC (1st line) & HNSCC (2nd line) results are very encouraging and - if further confirmed - support further clinical development.

If AIPAC is positive:  
validation of Antigen Presenting Cell (APC) activators and birth of a new class of active I-O products after the Immune Checkpoint Inhibitors!

Metastatic breast cancer would be the first entry point of possibly many other indications and combinations to come.

**Thank you!**