



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

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

**Date & Time:** Thursday, 10 June 2021, at 7:00 am Australian Eastern Standard Time (AEST) / Wednesday, 9 June, at 5:00 p.m. U.S. Eastern Daylight Time

Register: Interested parties join the webcast by registering via  
<https://fnn.webex.com/fnn/onstage/g.php?MTID=ebcdb72840d84111e57730c2b6cccd2c1>

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

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

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# Overview

## Immute<sup>p</sup>

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



## Global leadership position

in LAG-3 with 4 product candidates in immuno-oncology and autoimmune disease



## Clinical Potential

Immute<sup>p</sup>'s product candidates have demonstrated clinical potential in a range of indications with high unmet need



## Collaboration deals

executed with industry leaders



Merck KGaA,  
Darmstadt, Germany



# LAG-3 Overview & Product Candidates

# LAG-3 Pioneer: French immunologist

Frédéric Triebel, PhD, MD

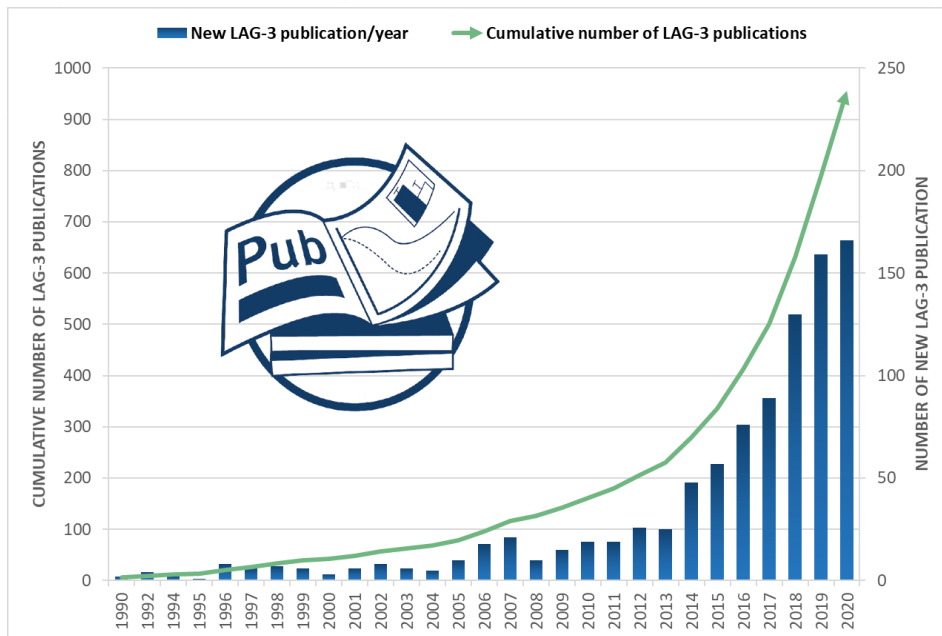
Immutep CMO & CSO



# Acceleration in the LAG-3 Space

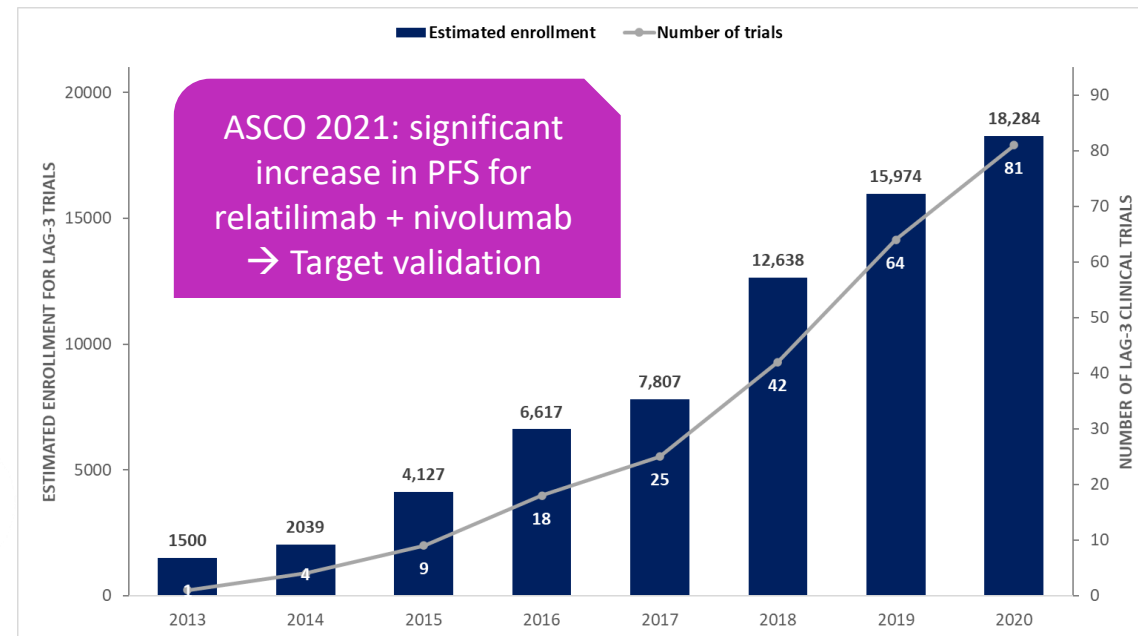
- Over 900 scientific publications dealing with LAG-3
- More than 80 clinical trials evaluating 19 LAG-3 product candidates
- Close to 20,000 patients estimated to be enrolled in clinical trials around the globe

## LAG-3 Scientific Publications



Source: PubMed


## LAG-3 Clinical Trials



Source: GlobalData, May 2021

**Immutep is the only company with four LAG-3 related compounds each with a different mechanism of action**

# LAG-3 Therapeutic Landscape Overview

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

Sources: GlobalData, Company websites, clinicaltrials.gov, and sec.gov, as of **June 2021**. The green bars above represent programs conducted by Immute<sup>p</sup> &/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.

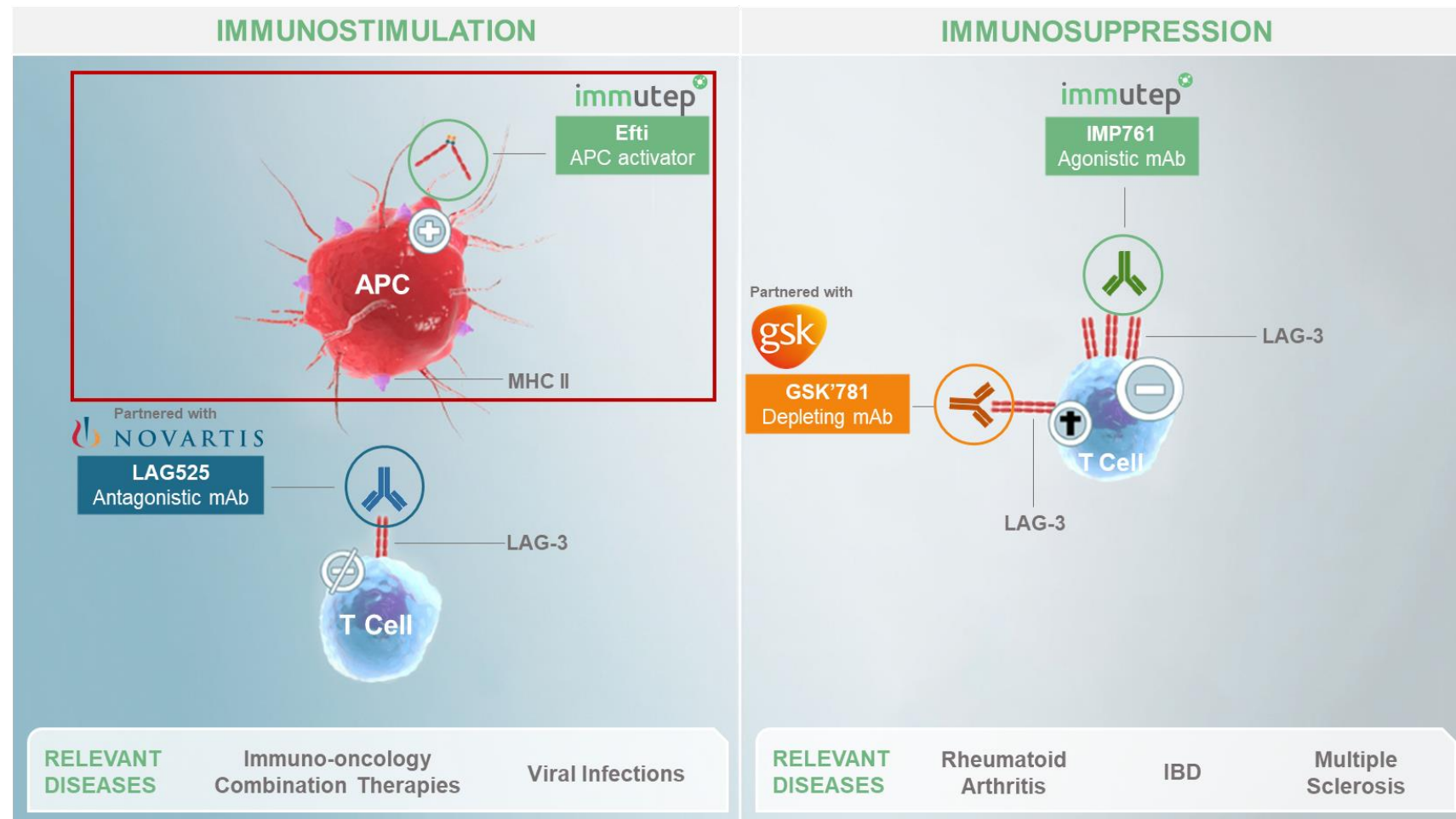
- As of January 7, 2019 Regeneron is in full control of program and continuing development ([https://www.sec.gov/Archives/edgar/data/872589/000110465919000977/a19-1325\\_18k.htm](https://www.sec.gov/Archives/edgar/data/872589/000110465919000977/a19-1325_18k.htm))
- On 3 Apr. 2020 Les Laboratoires Servier Acquires Symphogen
- 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/))

- Includes two completed Phase I studies and one discontinued Phase 2 study
- Including IITs, two planned trials (MBC trial by EOC and HNSCC trial) and the EAT COVID trial
- 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-Opdovo-nivolumab-in-Patients-with-Previously-Untreated-Metastatic-or-Unresectable-Melanoma-Meets-Primary-Endpoint-of-Progression-Free-Survival/default.aspx>)



# Immutep Mission: Targeting LAG-3 / MHC II

Multiple product candidates in numerous diseases



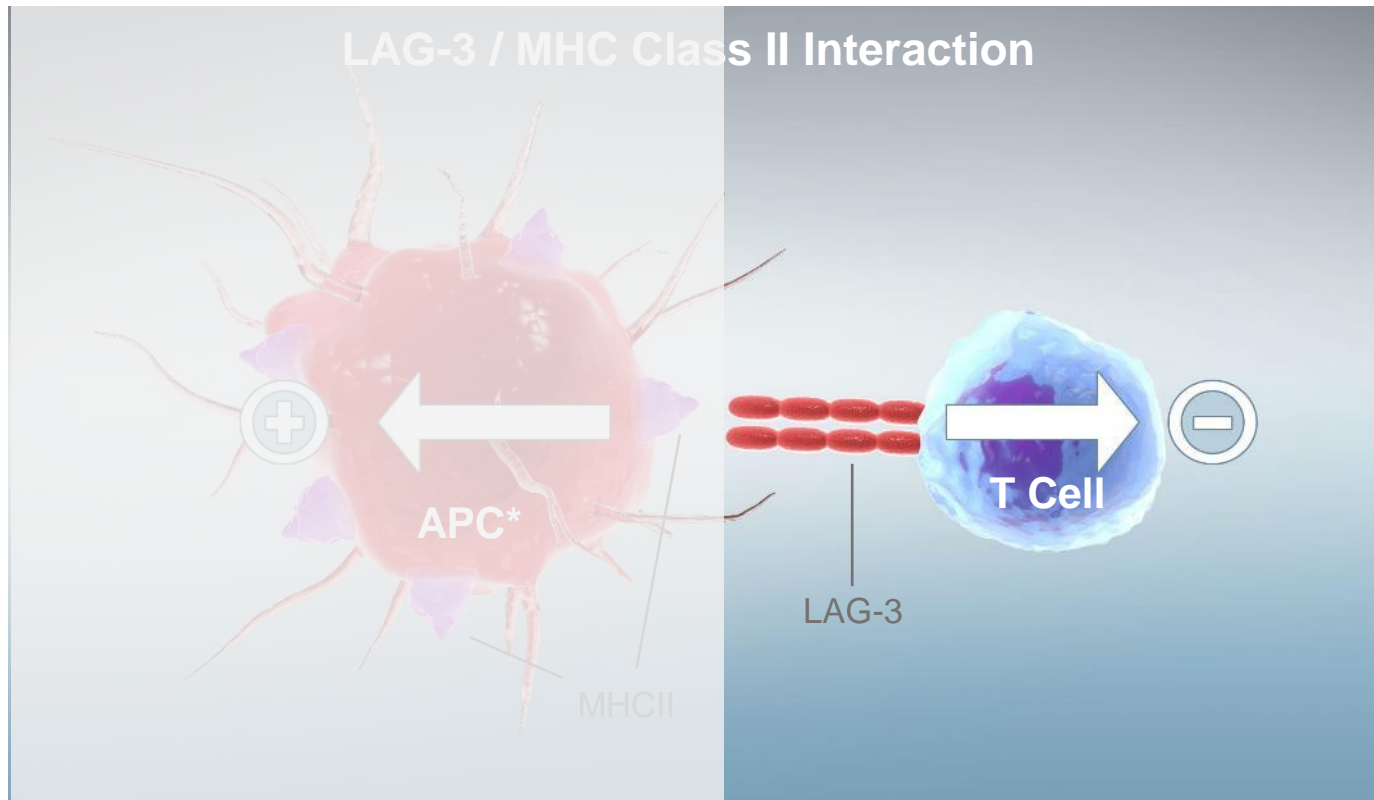
- ✓ Immutep is the only company with four LAG-3 related compounds, each with a different mechanism of action for treatment of numerous diseases
- ✓ Two major partnerships with pharma and two products under own development



# MHC II / LAG-3 Interaction 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 APCs

→ **Prime target for immune therapy**

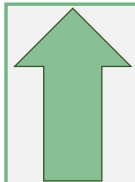


**Negative regulation of LAG-3<sup>+</sup> T Cells**

- Relatlimab + 15 more products in clinical development
- Clinical validation at ASCO 2021 (RELATIVITY-047 - relatlimab + nivolumab in melanoma)

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

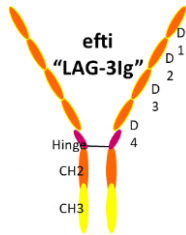
**This APC / T cell interaction is now a validated target since ASCO 2021 → 3<sup>rd</sup> validated checkpoint in immuno-oncology**



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

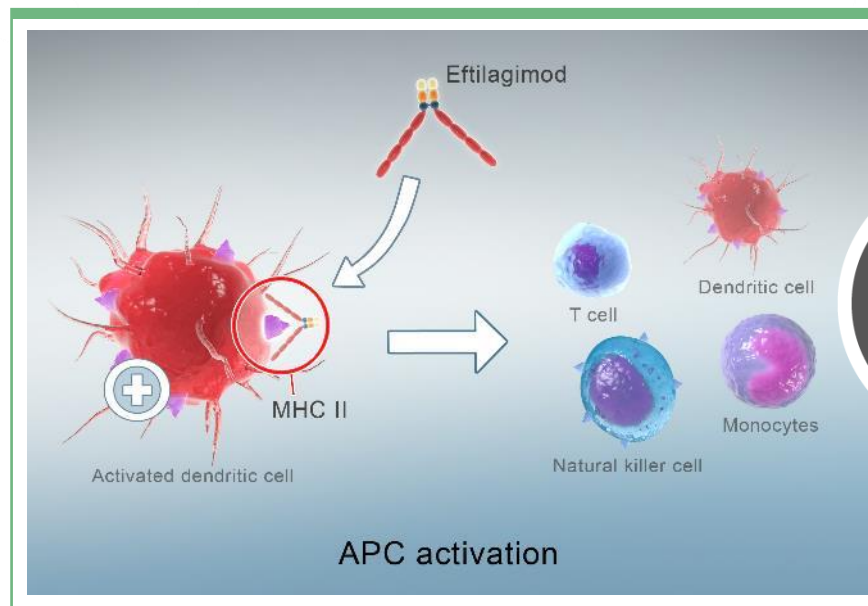
# Eftilagimod Alpha (efti or IMP321)

# 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 or chemotherapies

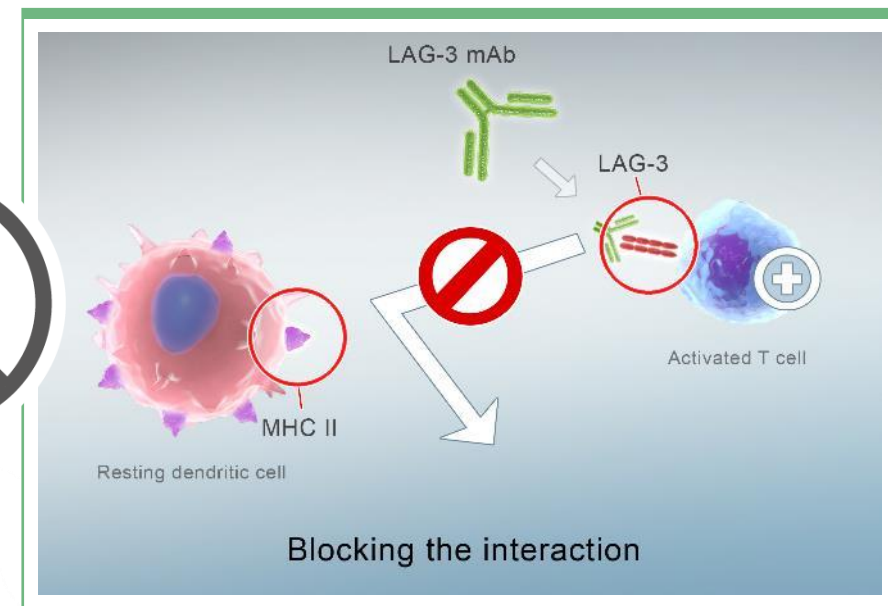
## “PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”



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”



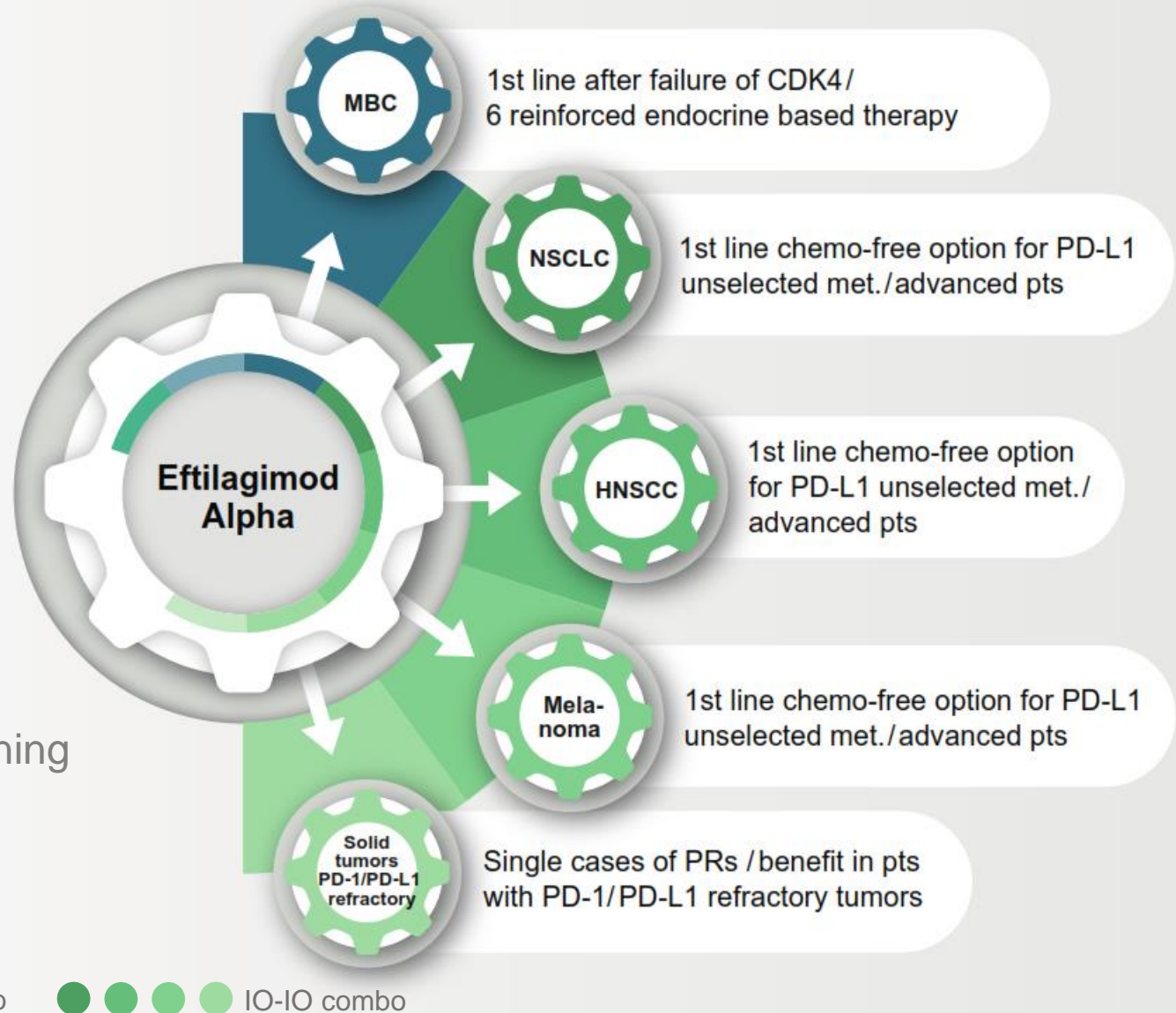
**LAG-3 antagonist**, or blocking, antibodies:  
**Immune checkpoint inhibitor**

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

# Efti: Potential Pipeline in a Product

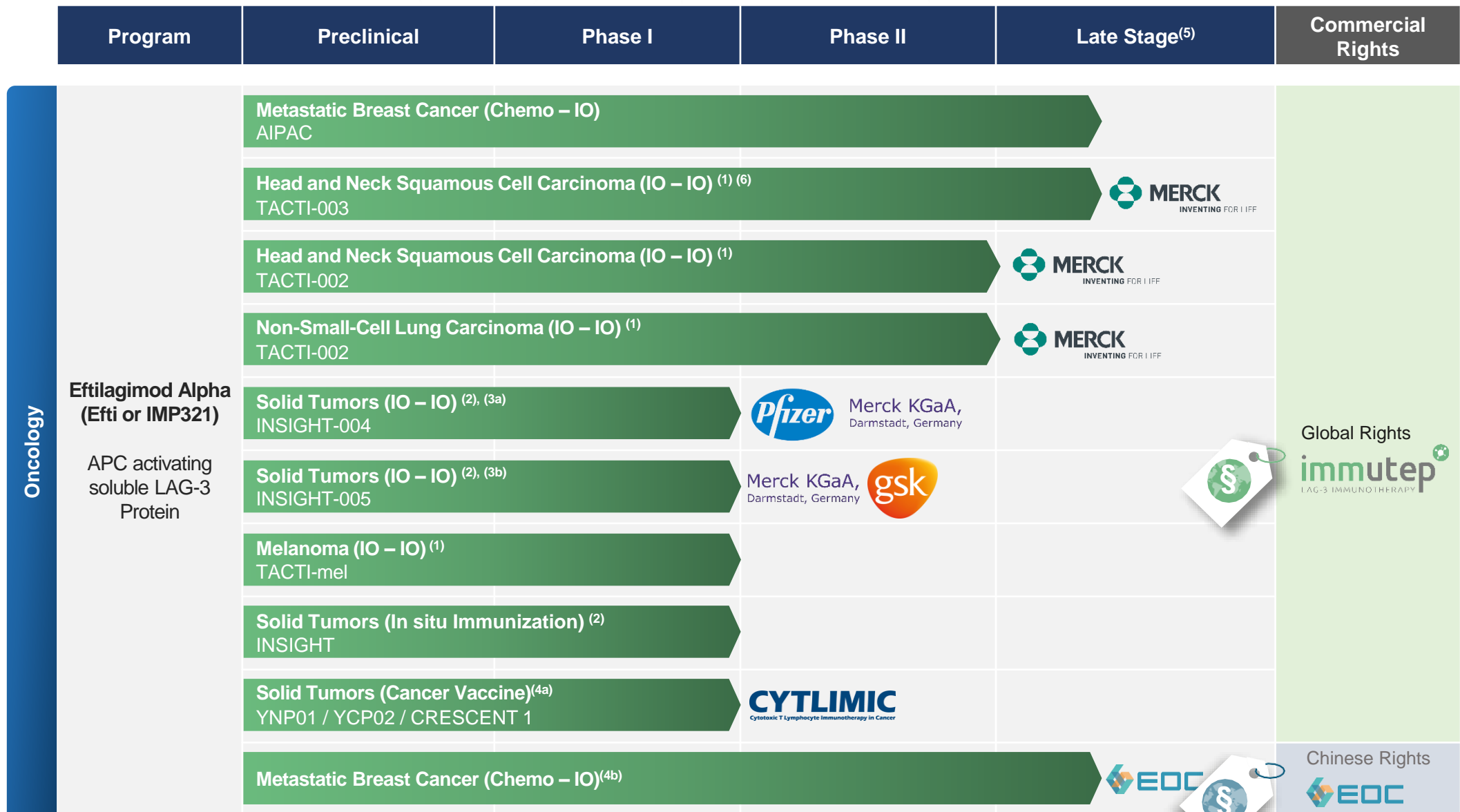
Potential for use in various combination settings

- Unique MHC II agonist
- Excellent safety profile
- Encouraging efficacy data
- Low cost of goods
- Unique protective IP positioning (unlike ICI mAbs)



# Clinical Development

## Efti: Main Trials\*



Notes:

- \* Information in pipeline chart current as at June 2021
- (1) In combination with KEYTRUDA® (pembrolizumab)
- (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) Not yet recruiting

# Combining efti and anti-PD-1 pembrolizumab

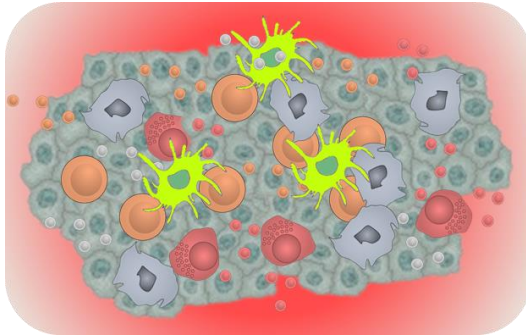
## TACTI-002



# APC activator – ICI combinations

## Three types of patient tumors

H  
O  
T



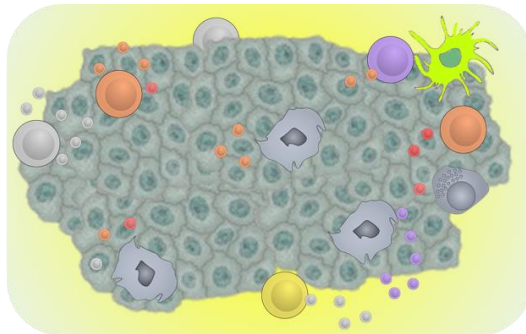
IFN $\gamma$

### Inflamed responder

- Considerable immune cell infiltration e.g.: CD8+ Tc; Macrophages
- **High** levels of IFN- $\gamma$  produced  $\rightarrow$  inducing high PD-L1 expression on tumor cells

Likely responds to Immune Checkpoint Inhibition  
e.g.: anti-PD-1

T  
E  
P  
I  
D

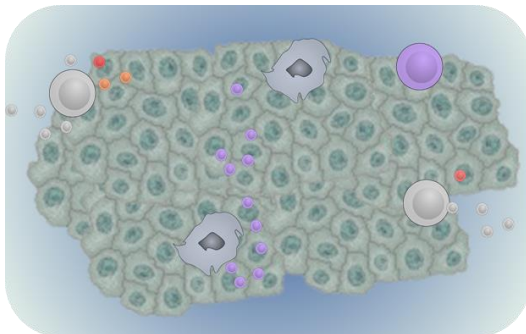


### Inflamed non-responder

- Some infiltrates in the tumor margins but no response.
- **Medium** levels of IFN- $\gamma$  produced  $\rightarrow$  inducing low PD-L1 expression on tumor cells

Due to low level of TH1 (IFN- $\gamma$ ) driven T-cell activation  $\rightarrow$  **unlikely to respond to ICI treatment**

C  
O  
L  
D



### Non-inflamed non-responder

- Minimal to no immune cell infiltration on the tumor margins.
- **Low** levels of IFN- $\gamma$  produced  $\rightarrow$  no induction of PD-L1 expression on tumor cells

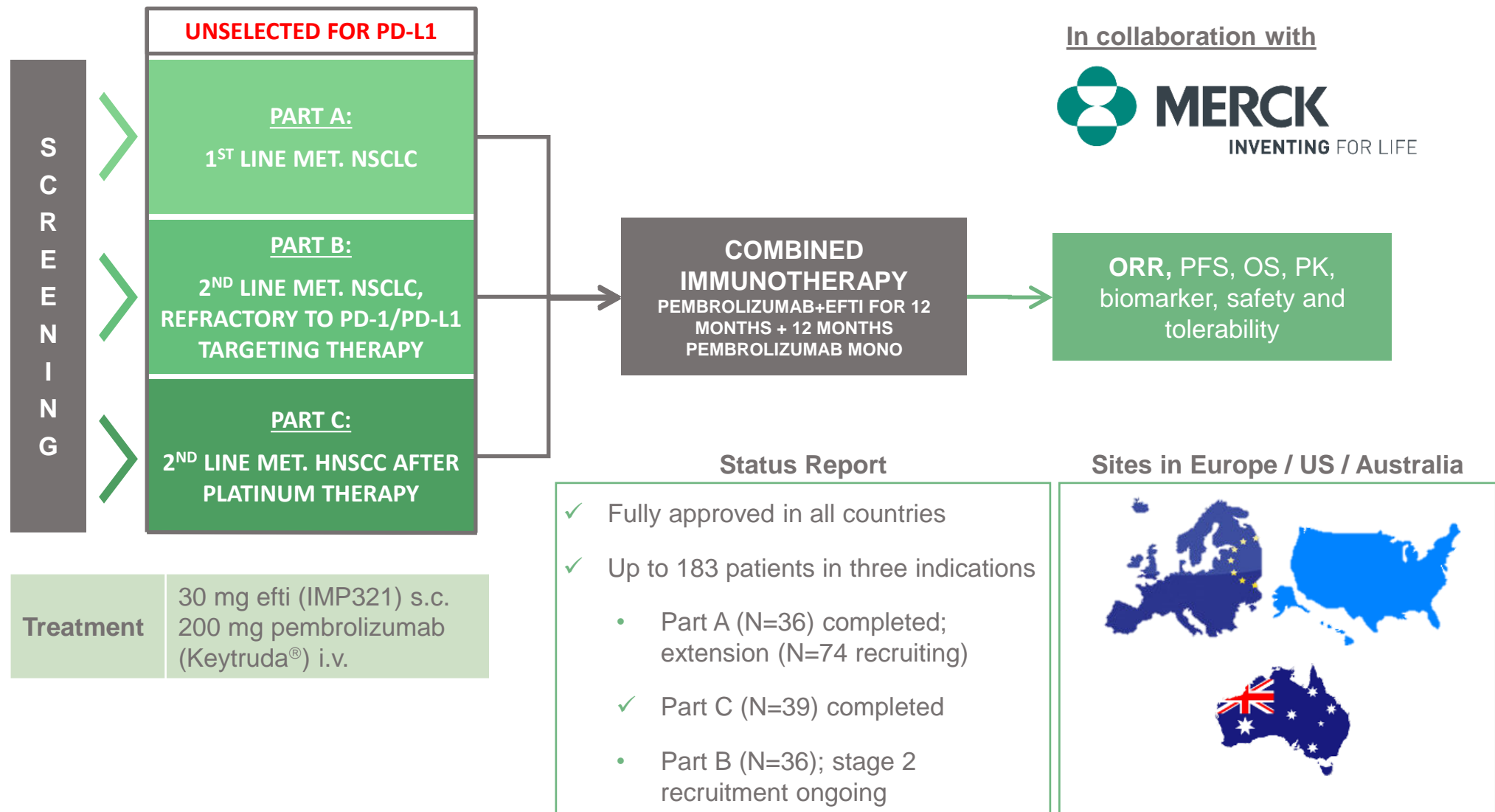
Due to low numbers of infiltrating T-cells  $\rightarrow$  **unlikely to respond to ICI treatment**



# TACTI-002 (Phase II)

## Design & Status

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



# TACTI-002 (Phase II)

## Safety

Efti + Pembro combination has a favourable safety profile

### Summary TACTI-002 (N=115 in total)

- No (0%) treatment-related death
- 4 (3.5%) subjects with treatment (efti and/or pembro) related adverse events leading to discontinuation
- 57 pts (49.6%) had  $\geq 1$  adverse events  $\geq$  grade 3
- No new safety signals of this combination identified until cut-off

### Selected safety aspects of other treatment regimens

Regimen <sup>(2)</sup>	Treatment related adverse events leading to discontinuation	Treatment related adverse events leading to death
Double Chemo	8-22%	1-6%
Ipi + Nivo	20%	< 2%
Chemo + Pembro	23-33%	3-8%
Pembro alone	10-15%	< 2%

✓ **Efti + pembrolizumab combination has a very good safety profile**

✓ **Favorable compared to any combination which included chemotherapy**

# Non-Small Cell Lung Cancer (NSCLC)

## Introduction

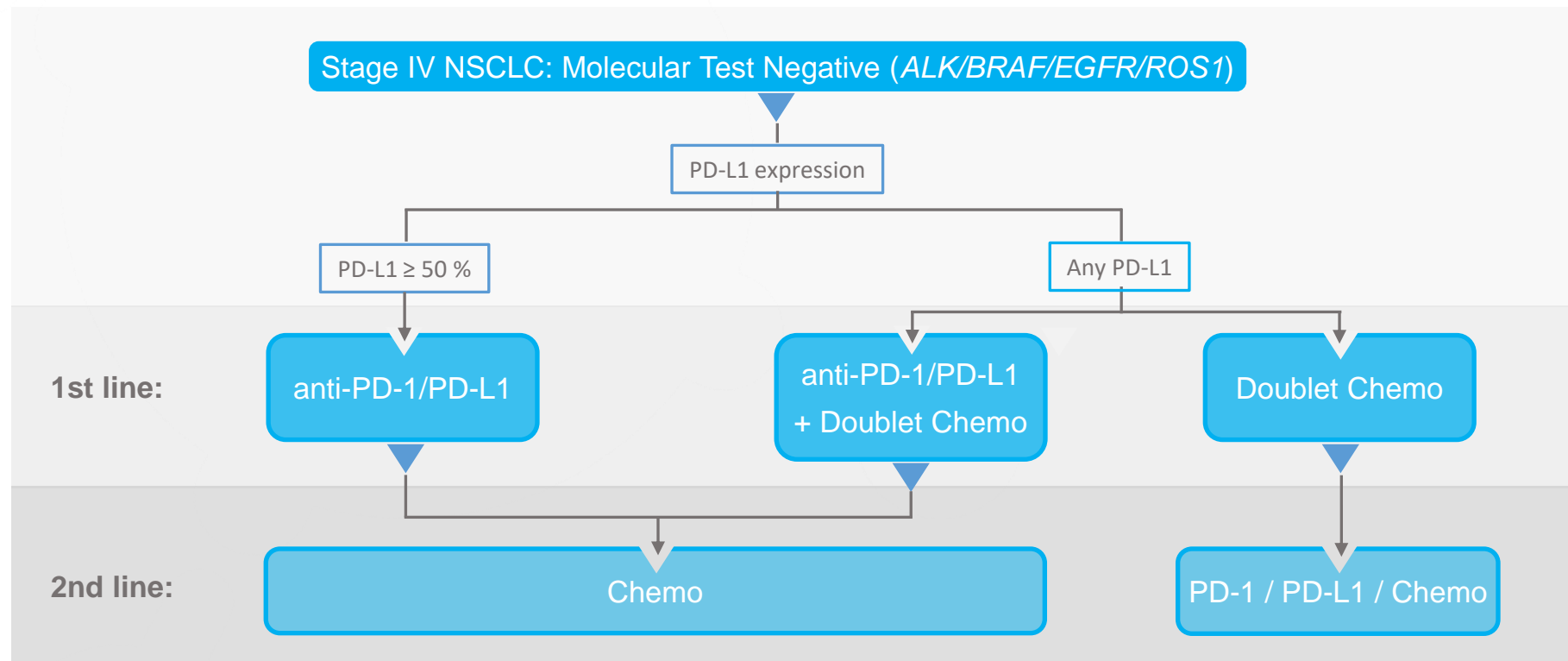
### High unmet medical need for well tolerated and efficacious treatment options

#### Epidemiology<sup>(1)</sup>:

- 1,850,000 NSCLC diagnoses per annum worldwide growing by 1.5% p.a.
- Approximately 1,300,000 develop metastatic disease and are eligible to receive anti-PD-1/PD-L1

#### Unmet need:

- Modest efficacy of anti-PD-1/PD-L1 for pts with < 50% PD-L1 (**~70% of total population**)
- Toxicity for patients / costs for health care systems of doublet chemo + PD-1/PD-L1 is relatively high



#### Notes:

- (1) Calculated from Global Cancer Observatory (WHO), 2018 data
- (2) Informa Pharma Intelligence Report 2018 for US, Japan and EU5
- (3) Based on ESMO Guidelines

# 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 (%)
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)
Current / Ex-smokers	34 (94.4)
Non-smokers	2 (5.6)
Squamous pathology	15 (41.7)
Non-squamous pathology	21 (58.3)
Patients with liver metastasis	14 (38.9)

Best overall response, iRECIST, N = 36	Local Read (investigator) N (%)	Blinded Read (BICR) N (%)
<b>Complete Response</b>	<b>2 (5.6)</b>	<b>2 (5.6)</b>
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)
<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>
<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>

\* - 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

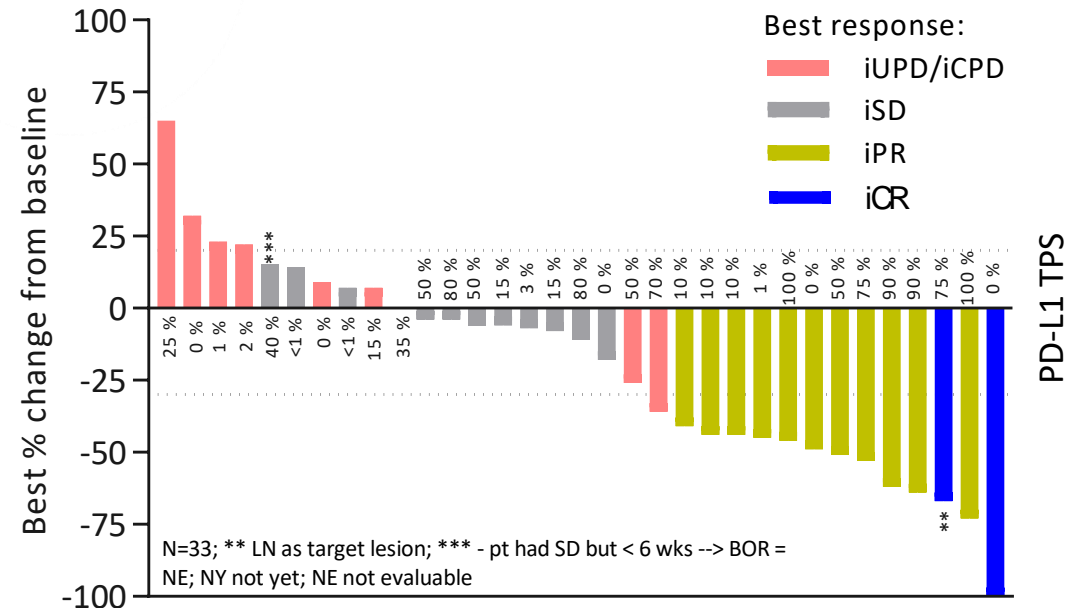
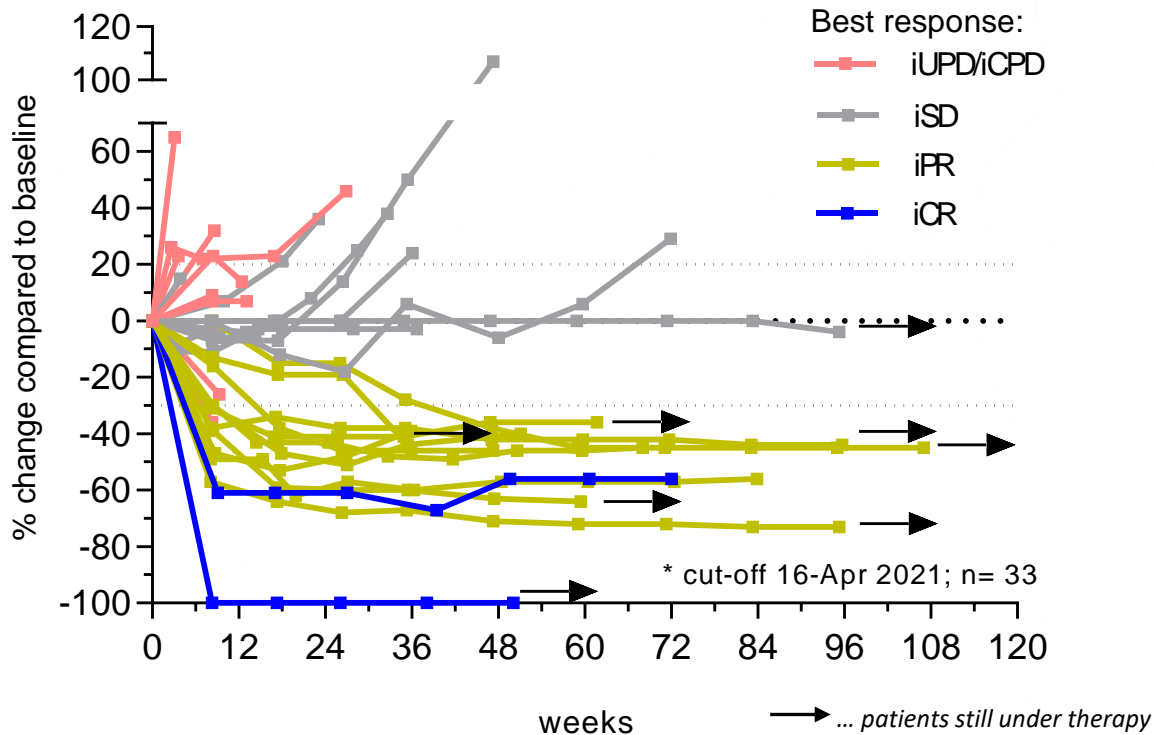
ECOG... Eastern Cooperative Oncology Group

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

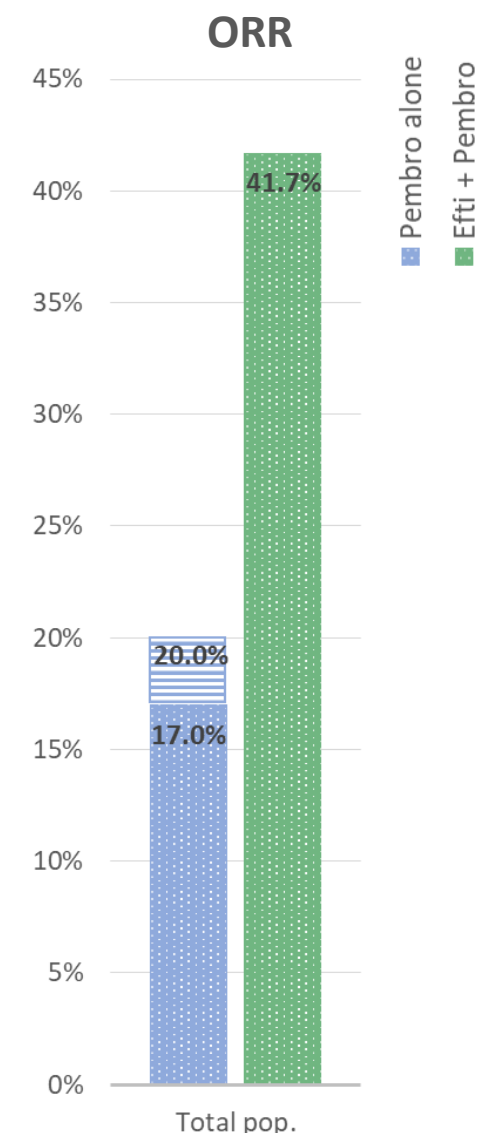
(1) Preliminary data, cut-off Apr 16, 2021

Graphs represent all patients with at least one post baseline assessment. One patient has no official RECIST assessment as this was done < 6 weeks and this does not qualify according to RECIST. Per local investigator assessment. iRECIST... Immune Response Evaluation Criteria In Solid Tumors

# 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)	Pembro + Chemo	
				NSQ	SQ
ORR (%)	≥ 50	39.5	53.8*	62.1	60.3
	≥ 1	27.3	44.0*	~ 55.8	~ 55.1
	< 50	--	31.6*	~ 40.7	~ 57.1
PFS (mths)	Overall pop.	--	8.2	9.0	6.4
	≥ 50	7.1	11.8	11.1	8.0
DoR (mths)	Overall pop.	20.2	NR (currently 13+)	12.4	7.7
Toxicity		Well tolerated	No significant add. toxicity	+ toxicity	
Co-med			No add. co-med required	+ cost of chemo co-med	



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

- Increased ORR & median PFS
- Responses in PD-L1 low expressors
- Comparable safety profile
- ORR & PFS comparable
- Improved DoR
- Less 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

(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 Gadgil 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)

# Head & Neck Squamous Cell Carcinoma (HNSCC)

## Introduction

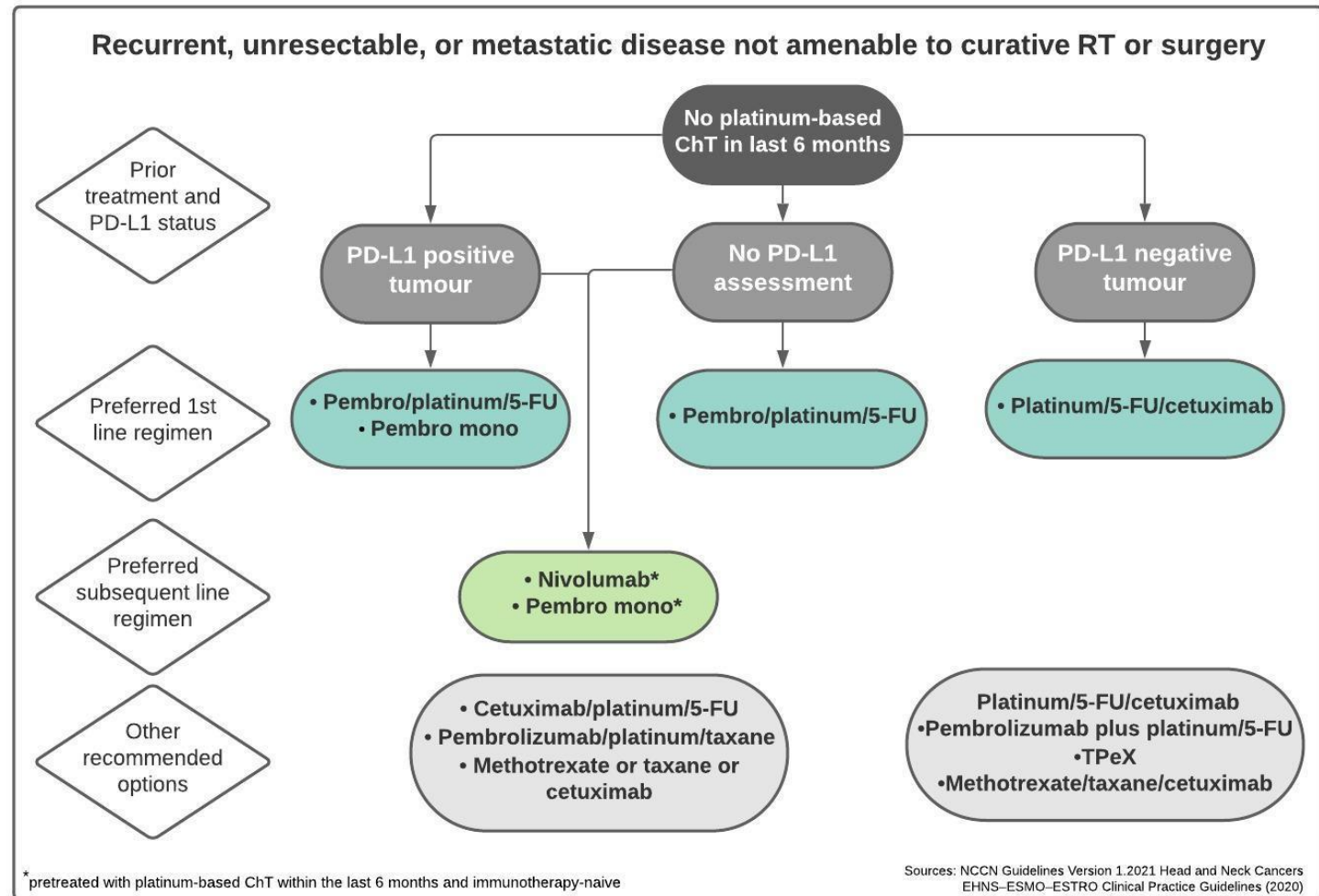
High unmet medical need for well tolerated and efficacious treatment options

### Epidemiology:

- More than 585,000 HNSCC diagnoses per annum worldwide<sup>(1)</sup>
- Approximately 350,000 develop metastatic disease & are eligible to receive anti-PD-1 monotherapy or in combination with chemotherapy

### High unmet need:

- OS in 1<sup>st</sup> line barely exceeds 12 months
- ORR of 10-18% in 2<sup>nd</sup> line regardless of therapy



### Notes:

(1) F Bray et al.: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA CANCER J CLIN 2018;68:394–424

(2) Athanassios Argiris et al.: Evidence-Based Treatment Options in Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck. Front. Oncol., 09 May 2017 | <https://doi.org/10.3389/fonc.2017.00072>

(3) FDA and EMA approval differences. Pembrolizumab approval by the European Medicines Agency is for patients whose tumours express PD-L1 with a  $\geq 50\%$  TPS, which differs from FDA approval.



# 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

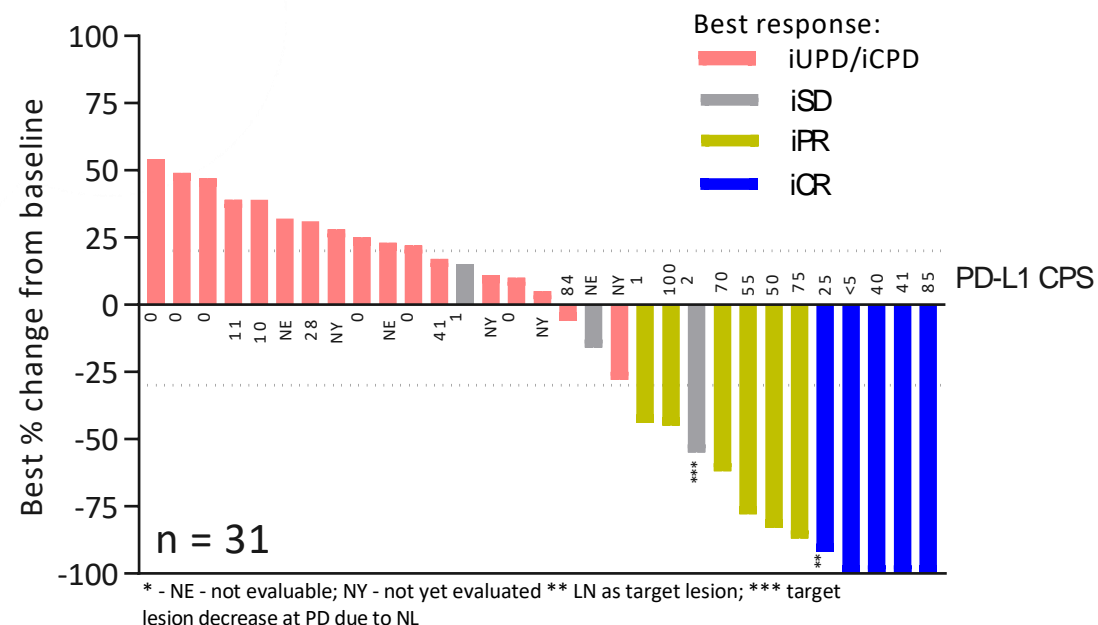
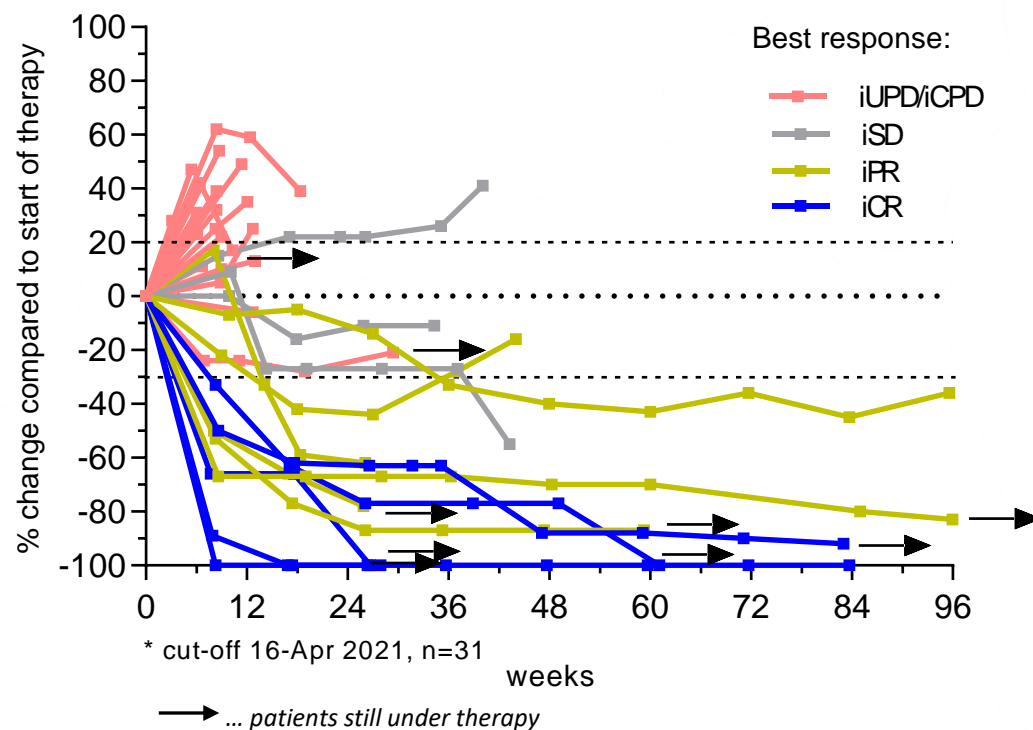
\*\* - dropped off prior to first staging or were not evaluable post-baseline for any reason

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

**All four pathologies enrolled**

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

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

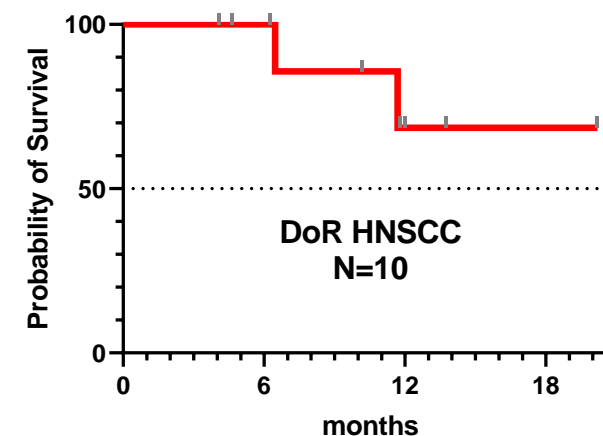


### Deep responses with 5 Complete Responses

#### 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:

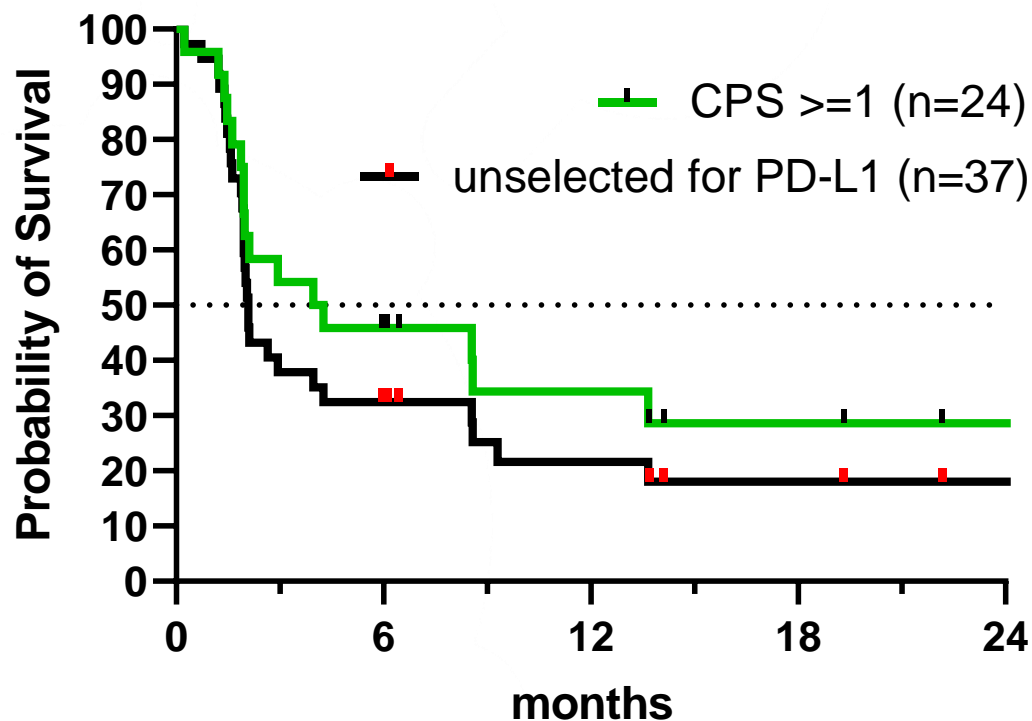
(1) Preliminary data, cut-off 16 Apr 2021

\*\* >= 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 $\geq 1$ \*

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

(3) \*\*  $\geq 1$  post baseline tumor staging (N=31)

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

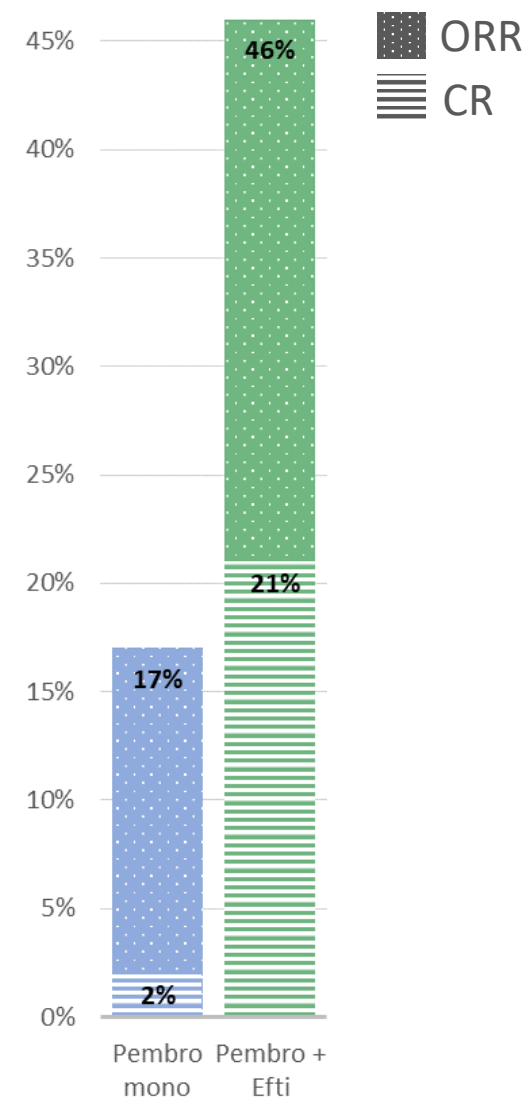
## 2<sup>nd</sup> line HNSCC (Part C) – Benchmarking

	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); # - only evaluable patients (N=31);

§ - 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>(4)</sup>
- Duration of response drops dramatically if you add chemo<sup>(5)</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 April 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) RL Ferris et al.: Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. *N Engl J Med* 2016;375:1856-67.

- (4) E Cohen et al; *Annals of Oncology* 2019; doi:10.1093/annonc/mdz252  
 (5) 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)

# Combining efti and anti-PD-L1 avelumab

## INSIGHT-004

# 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

 **Pfizer**

**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 ≤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

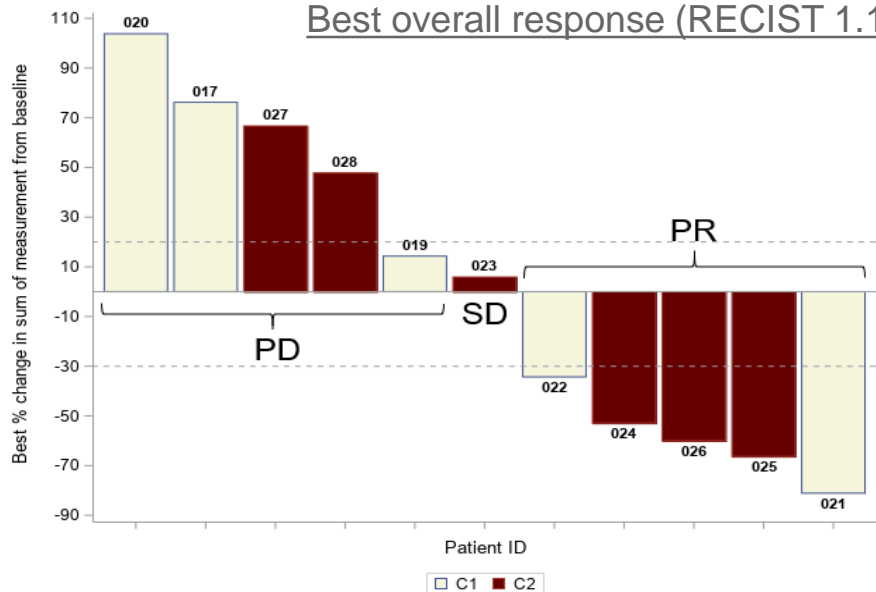
RP2D, Safety,  
ORR, PFS, PK, PD

# INSIGHT-004 (Stratum-D) Results<sup>(1)</sup>

## Efficacy

- 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)

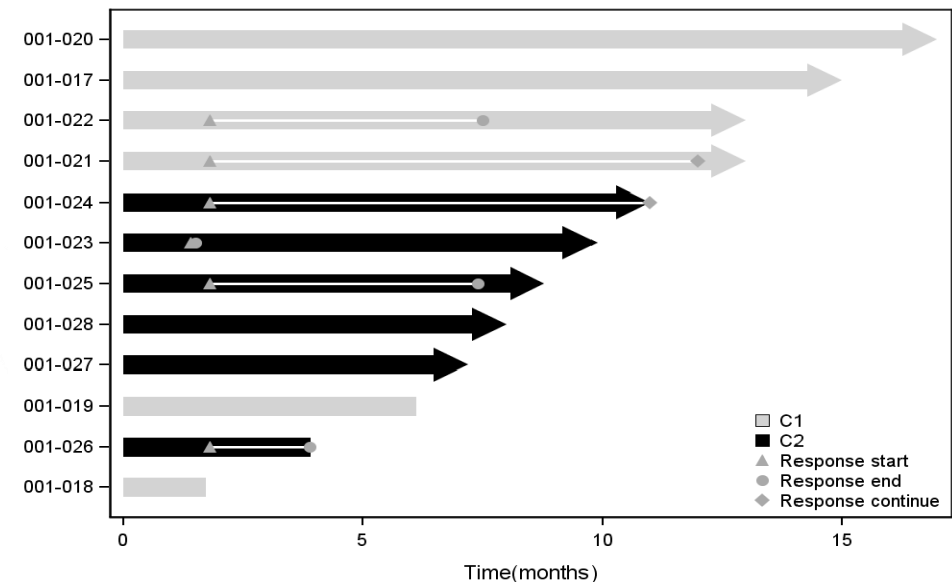


## Safety

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

## Conclusion

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



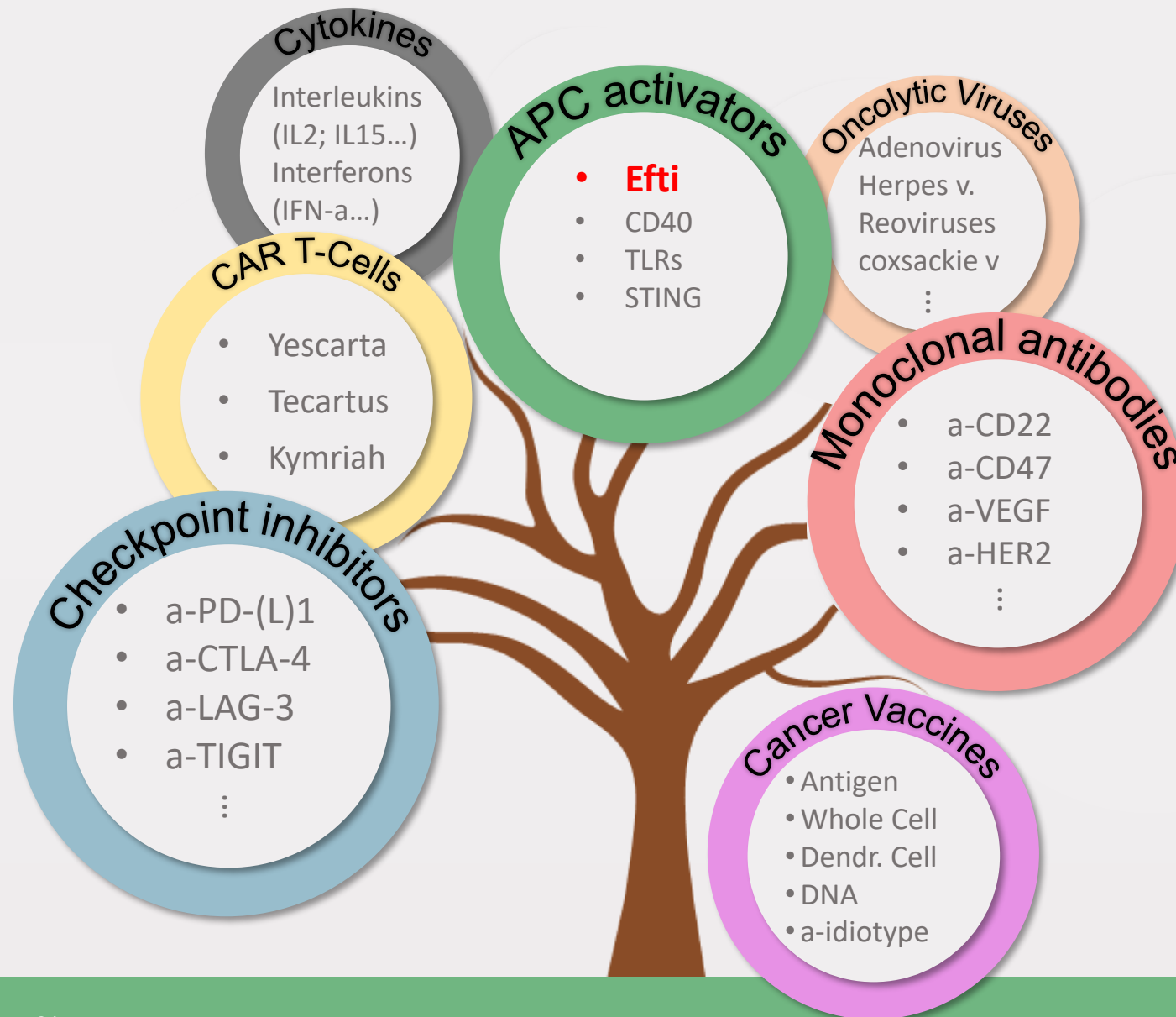
Triangles at the end of the chart represents the survival status



# Competition

# Eftilagimod Alpha

## Leader in its Class of Oncology Products



### Efti:

- No direct competition in Mechanism of Action
- No other MHC-II agonist under development
- Protected by comprehensive patent estate
- Proven in randomized, placebo controlled setting
- Excellent safety profile
- Low cost of goods

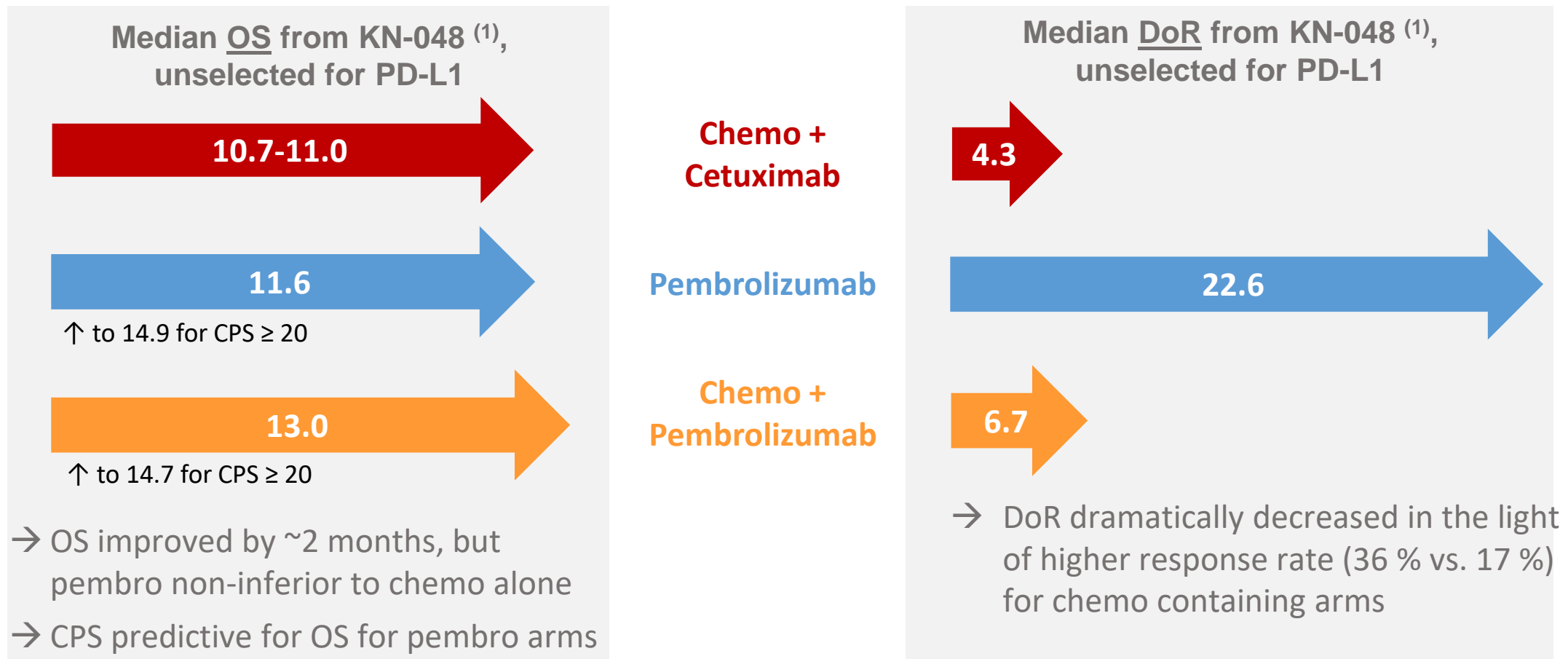
**Efti is well positioned to potentially become “the next big thing” in oncology**

The background features a solid green horizontal band across the middle. Above and below this band are several semi-transparent circles of varying sizes in shades of green and white, some with small stems, resembling bubbles or abstract shapes.

# Summary and Outlook

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

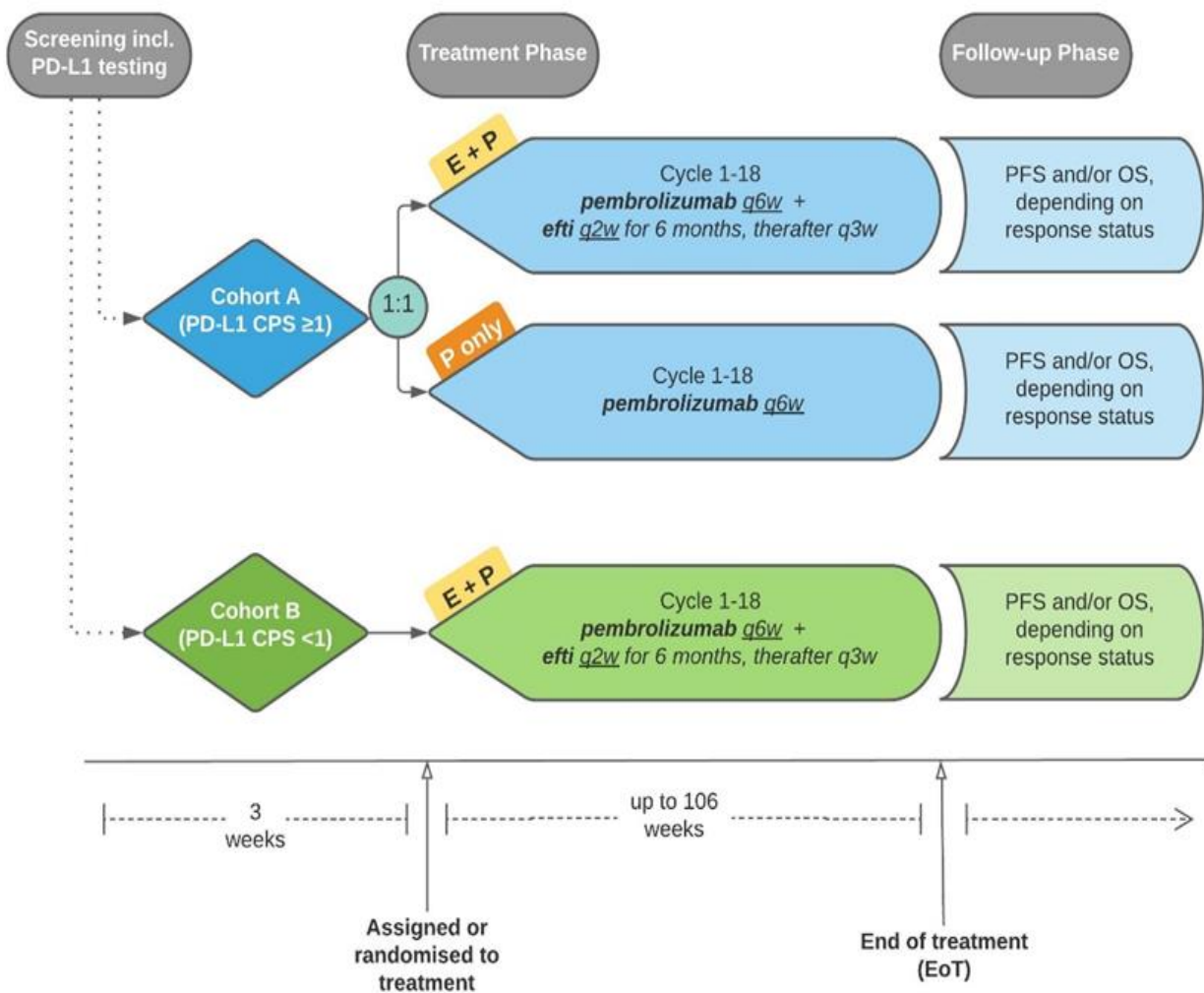
## 1<sup>st</sup> line HNSCC SoC



Despite progress high unmet medical need → therapy with comparable duration of response in combination with a higher ORR and improved OS with a comparable safety profile like pembro alone would be excellent

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

## Current Design + Status



Legend: PD-L1 = programmed cell death ligand 1; CPS= combined positive score; 1 cycle = 6 weeks; q2w = every 2 weeks; q3w = every 3 weeks; q6w = every 6 weeks; E + P = efti + pembrolizumab; P only = pembrolizumab monotherapy

In collaboration with



### 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**

# 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

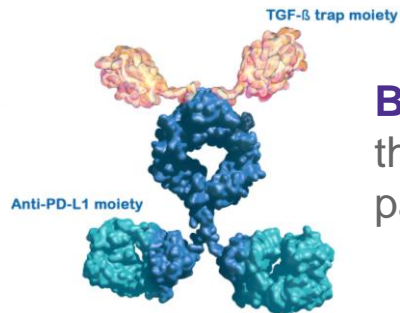
**Merck KGaA,**  
Darmstadt, Germany



Institut für Klinisch-Onkologische Forschung



**KRANKENHAUS  
NORDWEST**



**Bintrafusp alfa:** bifunctional fusion protein that aims to block two immunosuppressive pathways: TGF- $\beta$  and PD-L1



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



### Phase I

Open label trial



**12**

Patients in 3 cohorts



**12 months**

Combination treatment



**Two sites**

Germany

### Solid tumors

- histologically confirmed locally advanced or metastatic
- received  $\leq 4$  prior lines of therapy

### Q2W for maximum of 12 months

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

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

# 2020 & 2021 News Flow\*

2020

- ✓ **AIPAC** – PFS, ORR and OS delivered
- ✓ US **IND** for MBC
- ✓ **TACTI-002** – recruitment & data delivered e.g. at ASCO, EMSO & SITC for
  - ✓ 1<sup>st</sup> 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**

2021

- ✓ Fast Track designation granted for efti in 1<sup>st</sup> line HNSCC from US FDA
- ❑ Final data from **AIPAC**: 2<sup>nd</sup> OS follow up
- ✓ Data from **TACTI-002** & final data from **INSIGHT-004** at ASCO
- ❑ Recruitment & data from **TACTI-002**
- ❑ Start & ongoing recruitment of **new randomized 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 further partnerships & expansion of existing programs

- ✓ Validation of LAG-3/MHC-II interaction through readout of BMS's Phase III data for relatlimab + nivo combination

Notes:

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



# 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 in 2021

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

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



**Thank you!**