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LAG-3 IMMUNOTHERAPY

# The global leader in developing LAG-3 therapeutics

***Corporate Presentation***
***September 2021***

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

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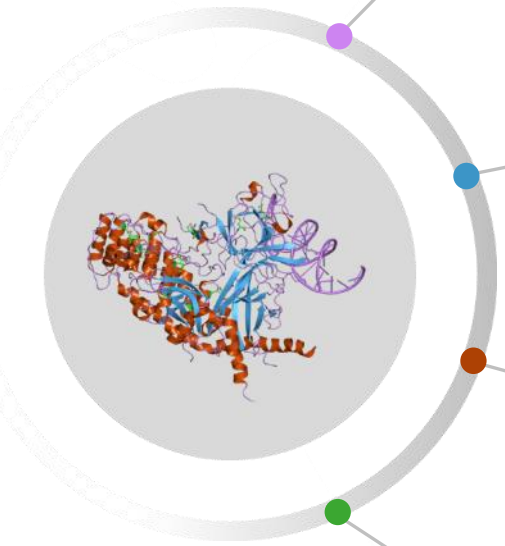
*This presentation was authorised for release by the CEO, Marc Voigt.*

# 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

NOVARTIS · Pfizer · gsk GlaxoSmithKline · Merck KGaA, Darmstadt, Germany · MERCK INVENTING FOR LIFE · EOC · CYTLIMIC Cytotoxic T Lymphocyte Immunotherapy in Cancer · LabCorp

## 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 | immutep | Eftilagimod Alpha[5] | | 10 | 4 | | 14 | 967 |
| Oncology | Antagonist | BMS | Relatlimab | | 7 | 32 | 2 | 41 | 9,706 |
| Oncology | Antagonist | NOVARTIS | Ieramilimab | | 1 | 4 | | 5 | 960 |
| Oncology | Antagonist | Merck & Co. Inc. | Favezelimab | | 1 | 5 | | 6 | 1066 |
| Oncology | Antagonist | Macrogenics | Tebotelimab | | 3 | 3 | | 6 | 1422 |
| Oncology | Antagonist | H-L Roche | RO7247669 | | 1 | 2 | | 3 | 538 |
| Oncology | Antagonist | B.I. | BI754111 | | 4 | 1 | | 5 | 649 |
| Oncology | Antagonist | Regeneron[1] | Fianlimab | | 1 | 1 | | 2 | 836 |
| Oncology | Antagonist | Tesaro[3] | TSR-033 | | 1 | 1 | | 2 | 139 |
| Oncology | Antagonist | Incyte | INCAGN02385 | | 1 | 1 | | 2 | 74 |
| Oncology | Antagonist | Symphogen[2] | SYM022 | | 3 | | | 3 | 169 |
| Oncology | Antagonist | F-star | FS-118 | | 2 | | | 2 | 102 |
| Oncology | Antagonist | Innovent | IBI110 | | 1 | | | 1 | 268 |
| Oncology | Antagonist | Xencor | XmAb-22841 | | 1 | | | 1 | 242 |
| Autoimmune | Agonist | immutep | IMP761 | | | | | -- | -- |
| Autoimmune | Depleting AB | gsk[4] | GSK2831781 (IMP731) | | 2 | 1 | | 3 | 207 |

PDUFA meeting March 19, 2022

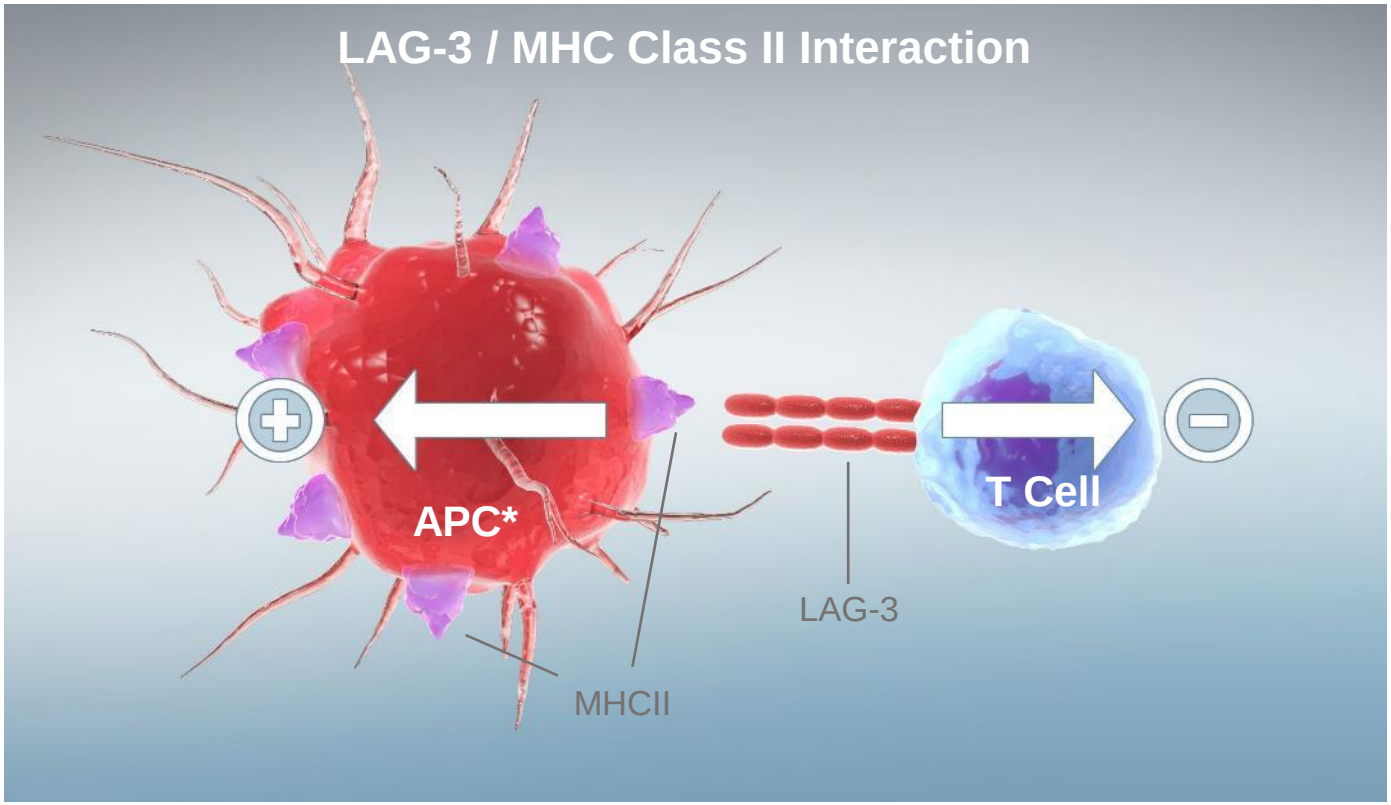
Sources: GlobalData, Company websites, clinicaltrials.gov, and sec.gov, as of **September 2021.** The green bars above represent programs conducted by Immutep &/or its partners. Total trials includes all active, completed &/or inactive trials. Patient totals are based on estimated total enrolled &/or 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 (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/ )
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**




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

**Negative regulation** of LAG-3⁺ 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 → 3rd validated checkpoint in immuno-oncology

*The PDUFA date refers to the date the Food and Drug Administration (FDA) are expected to deliver their decision whether or not a approve a companies New Drug Application (NDA) or Biologics License Application (BLA).

# Targeting LAG-3 / MHC II:

## Immutep has multiple therapeutics in numerous diseases

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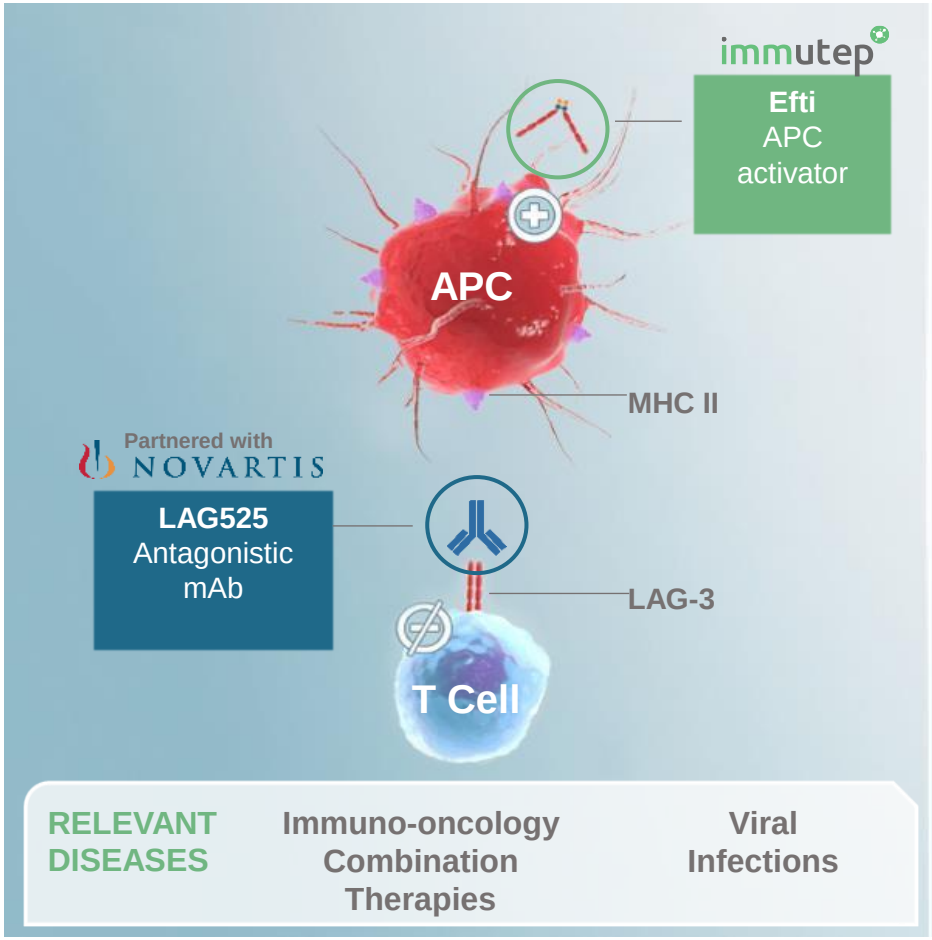
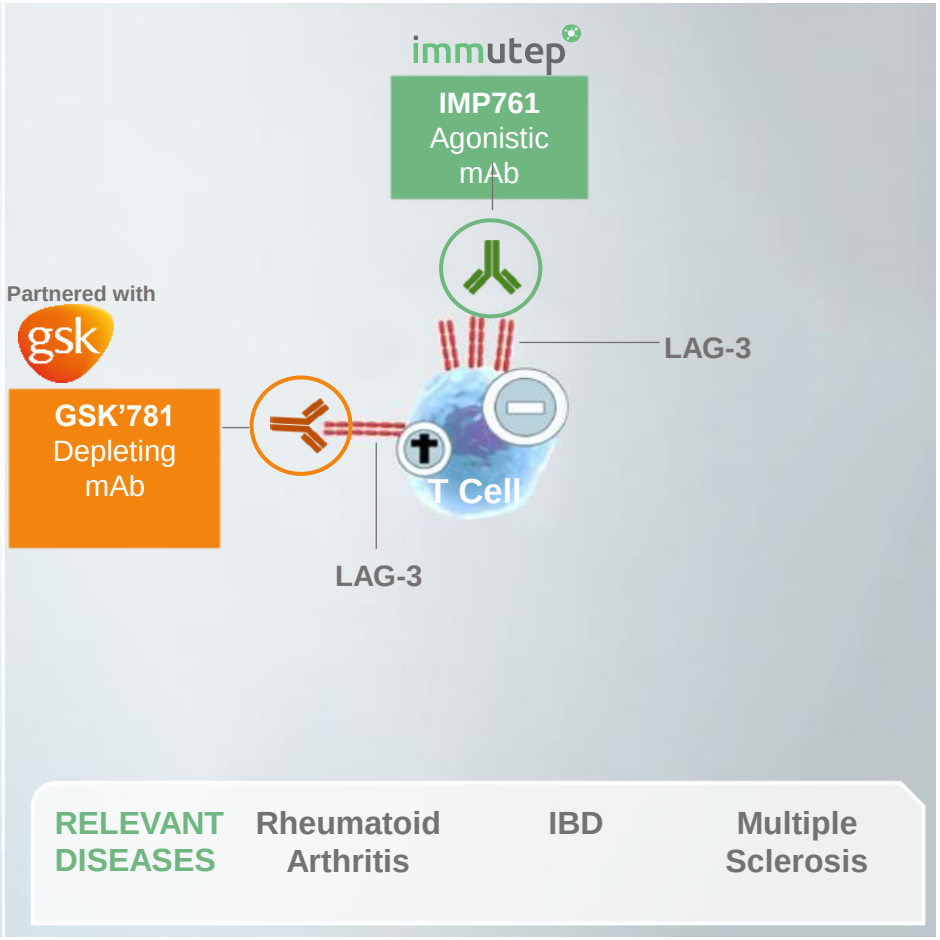
### IMMUNOSTIMULATION




**RELEVANT DISEASES**: Immuno-oncology Combination Therapies; Viral Infections

### IMMUNOSUPPRESSION




**RELEVANT DISEASES**: Rheumatoid Arthritis; IBD; Multiple Sclerosis

- ✓ 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



*Notes:*
* APC: antigen presenting cell

# Immutep's LAG-3 Trial Pipeline*

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

Notes

* Information in pipeline chart current as at September 2021

(1) In combination with KEYTRUDA® (pembrolizumab) (1b) Planned new trial for 1st 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/)

(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[1] | Commercial Rights/Partners | Updates |
|---|---|---|---|---|---|---|
| Oncology | LAG525 (Antagonist AB) | Solid Tumors + Blood Cancer (IO-IO Combo) | | | Global Rights NOVARTIS | Novartis currently has five clinical trials ongoing for LAG525 in multiple cancer indications for approx. 1,000 patients[4] |
| | | 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) | | | | |
| Autoimmune | GSK'781 (Depleting AB) | Ulcerative Colitis[6] | | | Global Rights gsk | Two successful Phase I studies. Phase II clinical study in up to 242 ulcerative colitis patients was discontinued. |
| | | Healthy Japanese and Caucasian Subjects[2] | | | | |
| | | Psoriasis[3] | | | | |

Notes

* Information in pipeline chart current as at September 2021

(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

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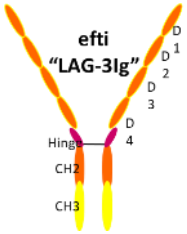
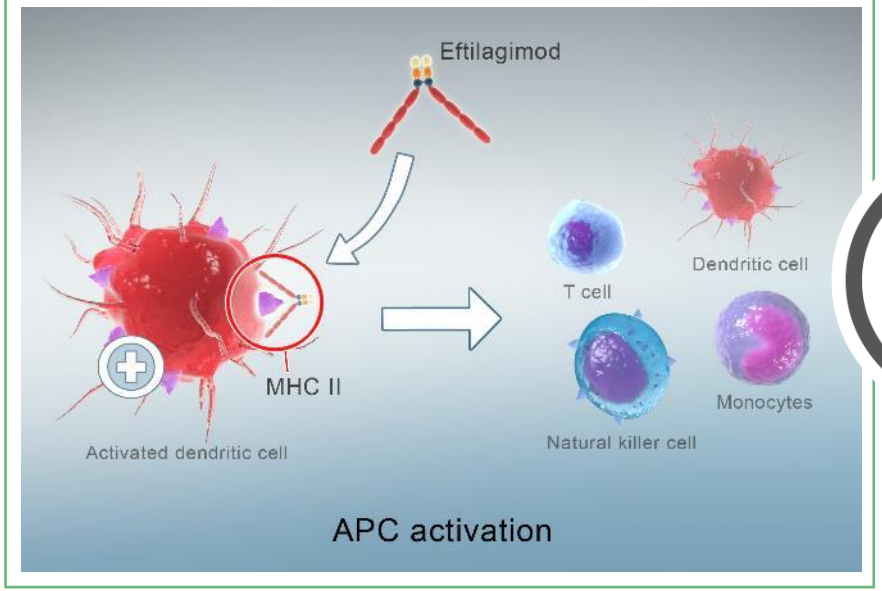
# Eftilagimod Alpha (efti or IMP321)

# 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 & chemotherapies

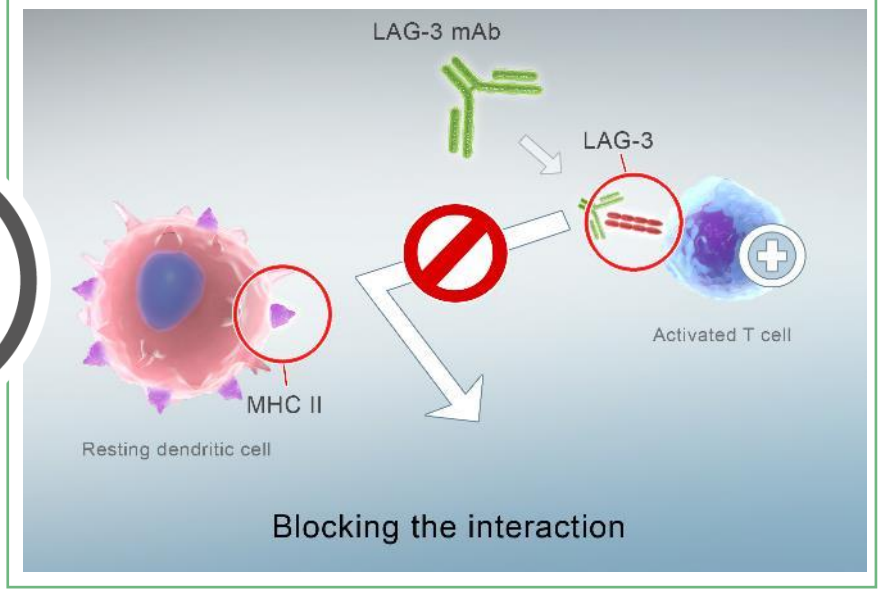
**"PUSHING THE ACCELERATOR ON IMMUNE RESPONSES"**




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

- boost and sustain the $CD8^+$ T cell responses
- activate multiple immune cell subsets

**"RELEASING THE BRAKE ON THE T CELL"**



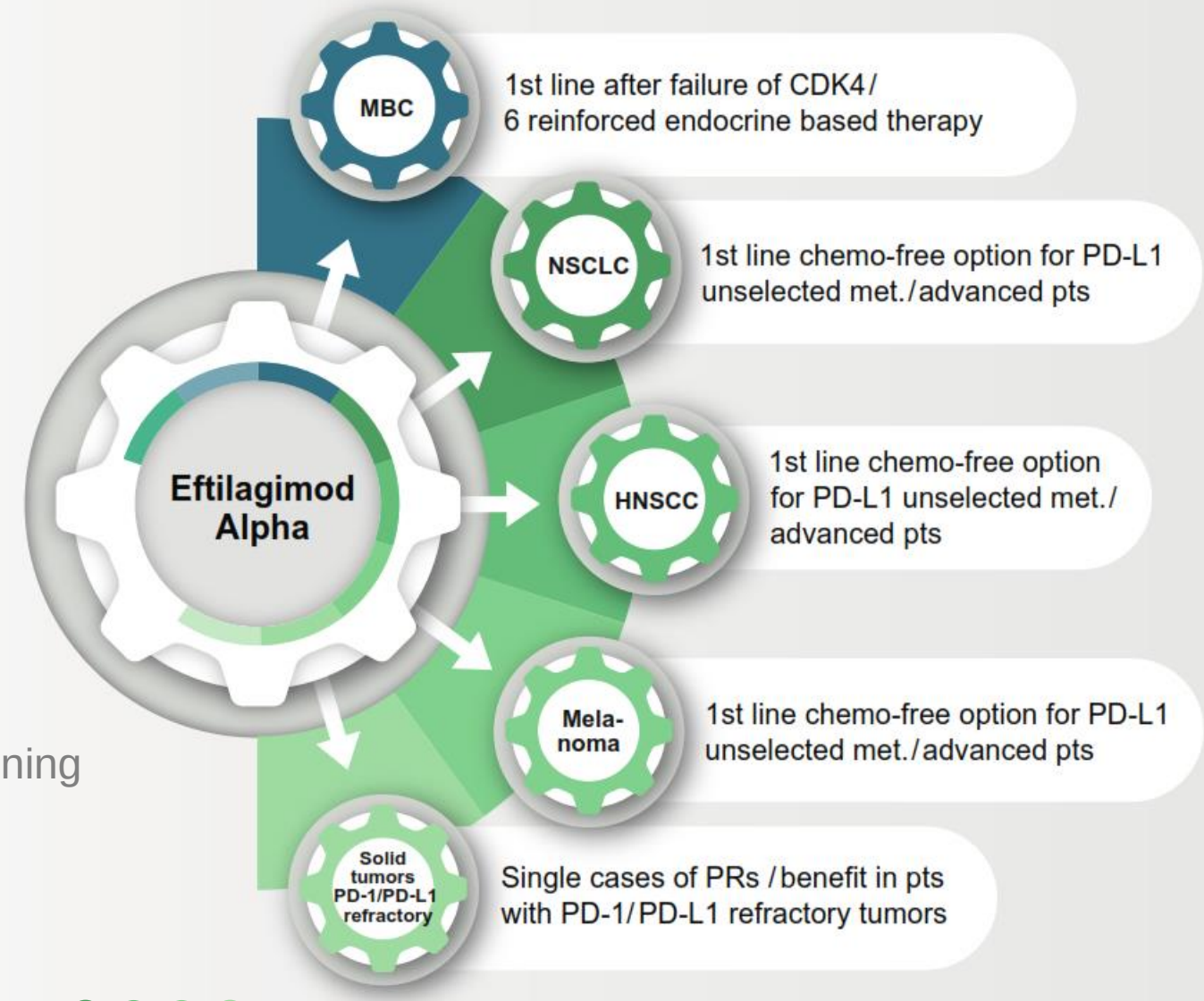

**LAG-3 antagonist** (blocking) antibodies:
**Immune checkpoint inhibitor**

- 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

SCREENING

**UNSELECTED FOR PD-L1**

**PART A:**
1ST LINE MET. NSCLC

**PART B:**
2ND LINE MET. NSCLC, REFRACTORY TO PD-1/PD-L1 TARGETING THERAPY

**PART C:**
2ND LINE MET. HNSCC AFTER PLATINUM THERAPY

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

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

**In collaboration with**

MERCK
INVENTING FOR LIFE

| | |
|---|---|
| **Treatment** | 30 mg efti (IMP321) s.c.<br>200 mg pembrolizumab (Keytruda®) i.v. |

**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**

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

# TACTI-002 Results(1)

## 1st line NSCLC (Part A)

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

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

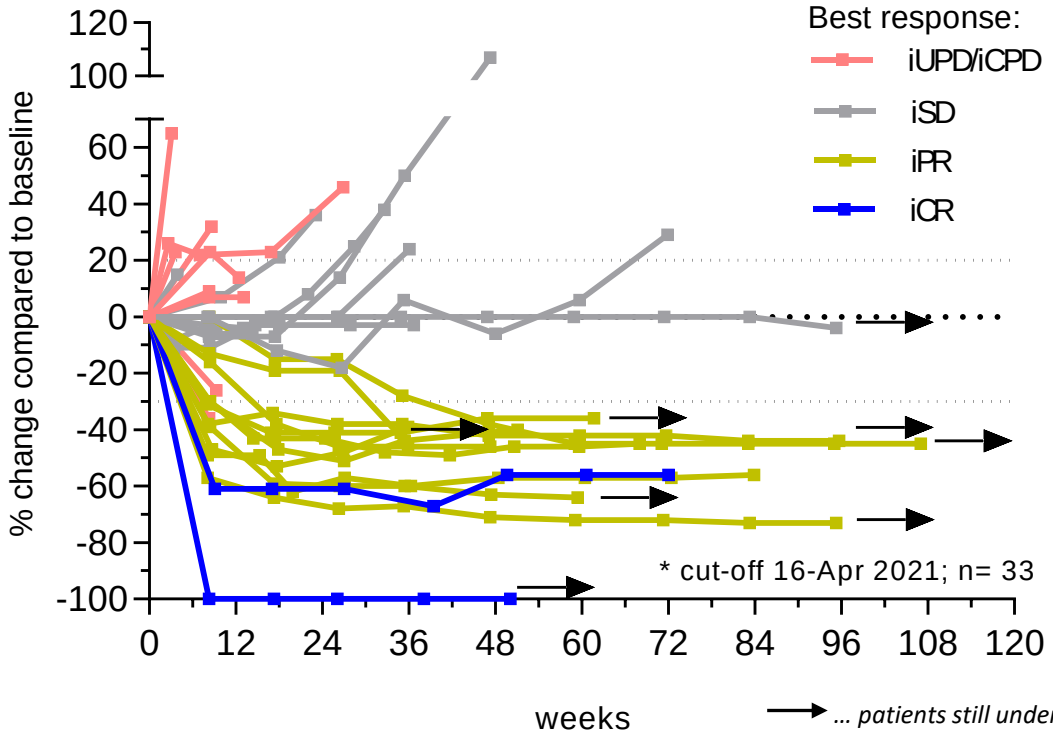
| Best overall response, iRECIST, N = 36 | Local Read (investigator) N (%) | Blinded Read (BICR) N (%) |
|---|---|---|
| **Complete Response** | **2 (5.6)** | **2 (5.6)** |
| Partial Response | 11 (30.6) | 13 (36.1) |
| Stable Disease | 11 (30.6) | 10 (27.8) |
| Progression | 8 (22.2) | 6 (16.7) |
| Not Evaluable** | 4 (11.1) | 5 (13.9) |
| Disease Control Rate | 24 (66.7) | 25 (69.4) |
| **Overall Response Rate*<br>[95% CI interval]** | **13 (36.1)<br>[20.8-53.8]** | **15 (41.7)<br>[25.5-59.2]** |
| **Overall Response Rate – Evaluable pts***<br>[95% CI interval]** | **13 (40.6)<br>[23.7-59.4]** | **15 (48.4)<br>[30.1-60.9]** |

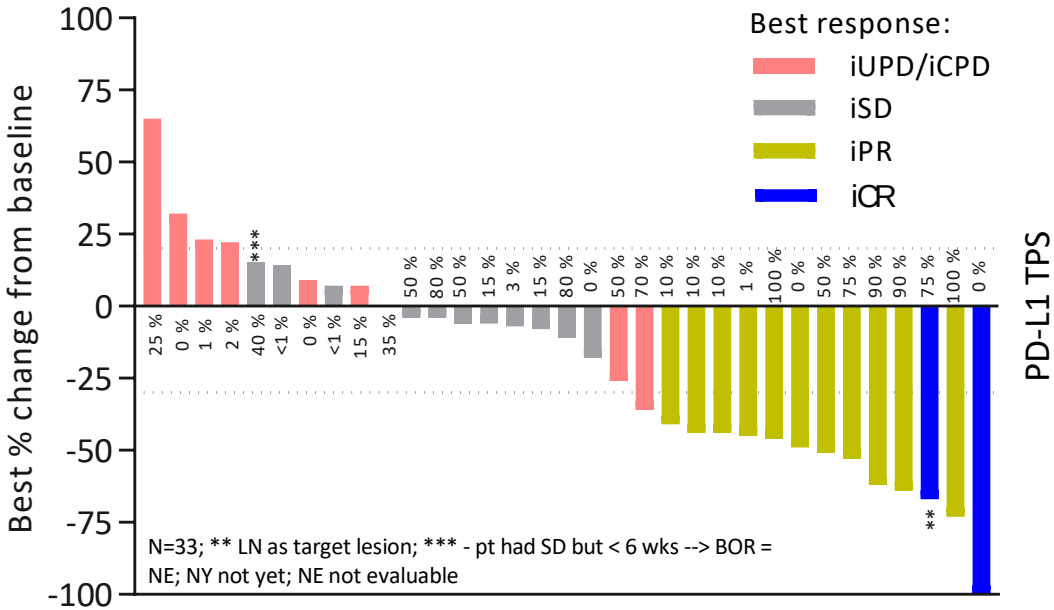
** - All patients stage 1 and 2 (N=36) with ≥ 1 treatment*
*** - dropped off prior to first staging or were not evaluable post-baseline for any reason*
**** - Evaluable for efficacy meaning ≥ 1 treatment and ≥ 1 post baseline tumor staging*

*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(1)

## 1st 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*

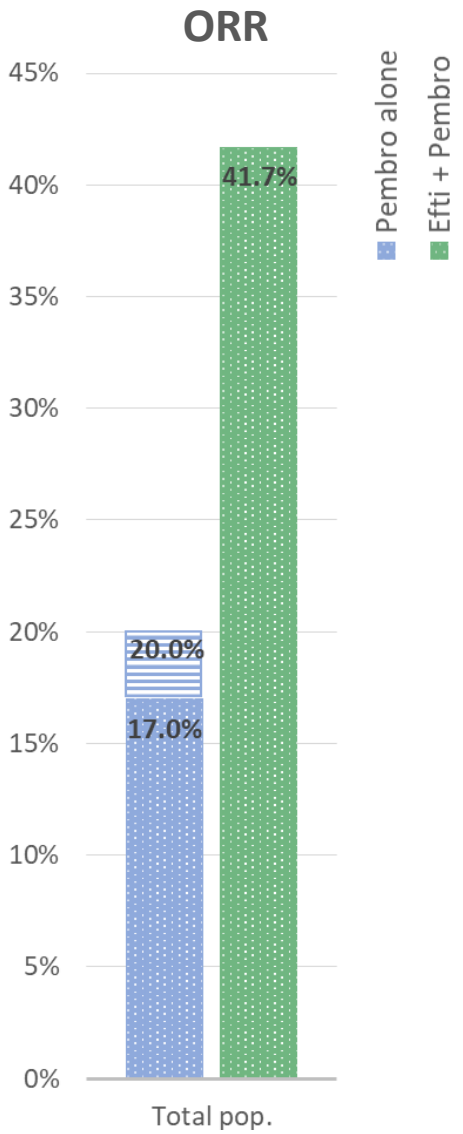
# TACTI-002 Results(1)

## 1st 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[2][3][4]; *** 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[2][5]




(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
(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 Leighl et al, The Lancet 2019, http://dx.doi.org/10.1016/S2213-2600(18)30500-9

# TACTI-002 Results(1)

## 2nd line HNSCC (Part C)

- 2nd 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<br>Male | 4 (10.3)<br>35 (89.7) |
| ECOG 0<br>ECOG 1 | 13 (33.3)<br>26 (66.7) |
| Current / Ex-smokers<br>Non-smokers | 33 (84.6)<br>6 (15.4) |
| Previous chemotherapy | 39 (100) |
| Previous cetuximab | 16 (41.0) |
| Lung lesions<br>Liver lesions | 19 (48.7)<br>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 (%) |
|---|---|
| **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**<br>**[95% CI interval]** | **11 (29.7)**<br>**[15.9-47.0]** |
| **Overall Response Rate – Evaluable pts*****<br>**[95% CI interval]** | **11 (35.5)**<br>**[19.2-54.6]** |

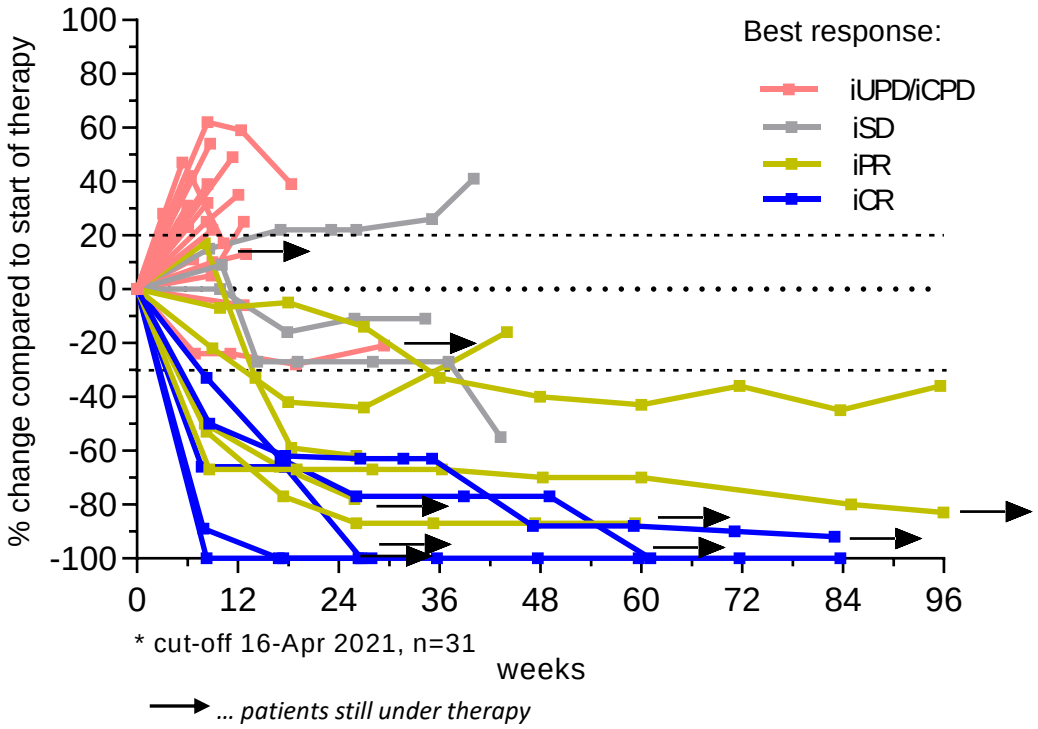
* - *All patients (N=37) with* ≥ 1 treatment and no death due to COVID-19 prior to first post-baseline staging
** - *dropped off prior to first staging or were not evaluable post-baseline for any reason*
*** - *evaluable patients (N=31):* ≥ 1 treatment and ≥ 1 post baseline tumor staging

**All four pathologies enrolled**

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

# TACTI-002 Results(1)

## 2nd line HNSCC (Part C)



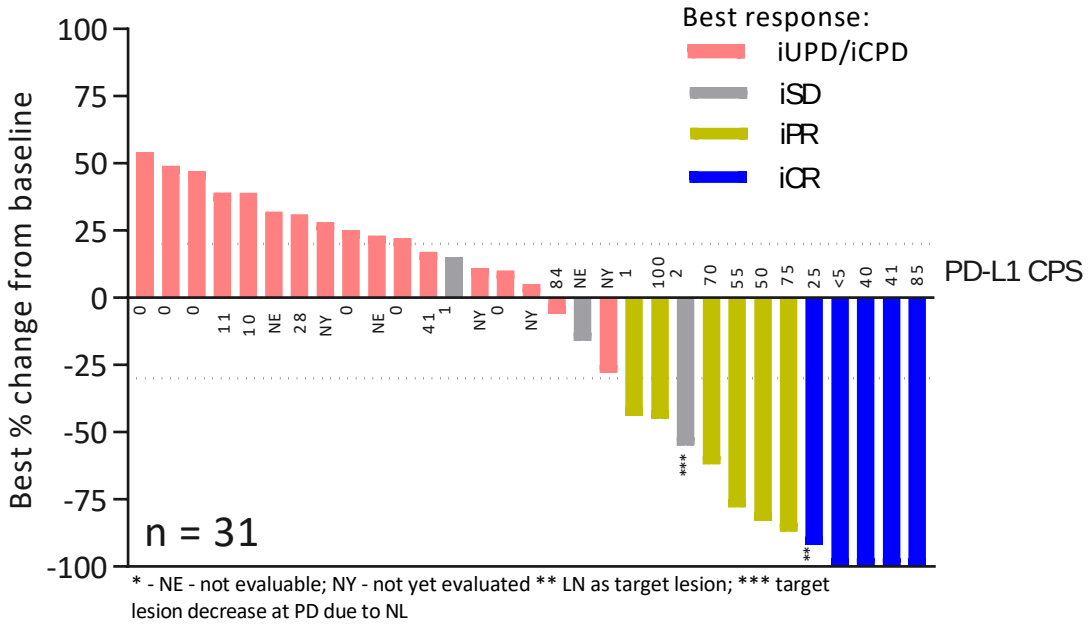
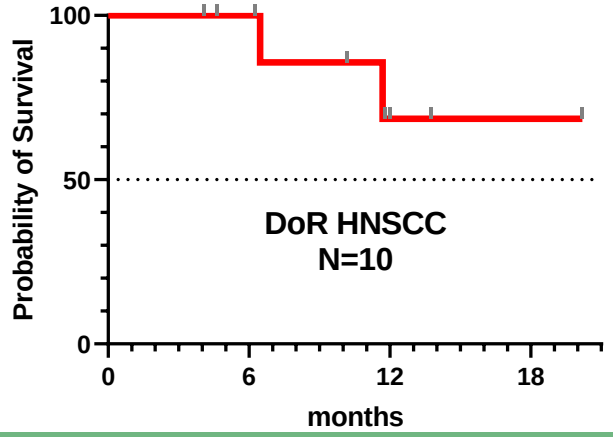




*Figure 3: Duration of response (DOR) for confirmed responders*




**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

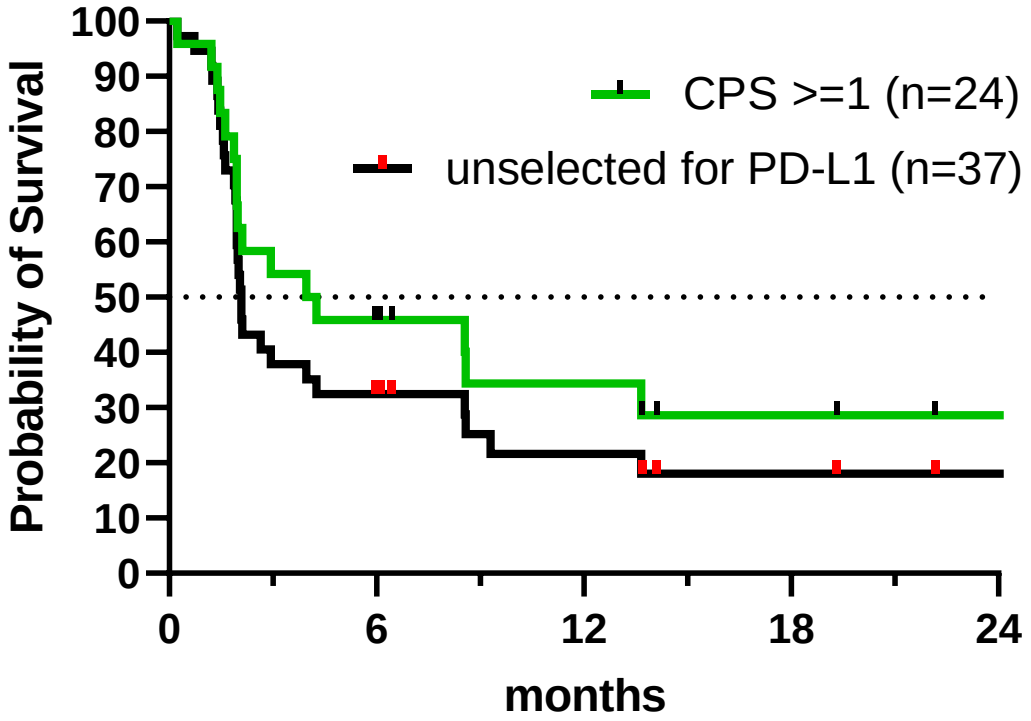
*Note:*

(1) Preliminary data, cut-off 16 Apr 2021
** >= 1 post baseline tumor staging (N=31)

# TACTI-002 Results(1)

## 2nd 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)

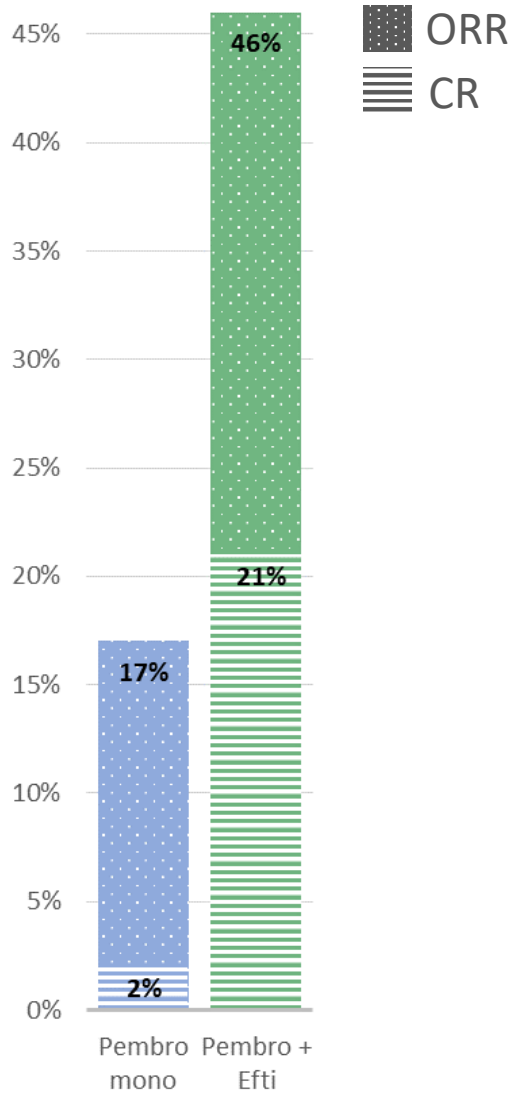
# TACTI-002 Results(1)

## 2nd 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#** |
| **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§** 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§** 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(2)

- ORR of pembro mono generally low → increase to 22% (≥ 20 CPS) and 28% (≥ 50 CPS)(3)
- Duration of response drops dramatically if you add chemo(4) – 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
(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

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# 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 4th 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 | Treatment | Results |
|---|---|---|
| **Solid tumors**<br>• histologically confirmed locally advanced or metastatic<br>• received ≤ 3 prior lines of therapy<br>• no selection for immunogenic markers (e.g. PD-L1 expression levels, msi high or tmb) | **1) Avelumab + Efti (6 mg - 30 mg) s.c.**<br>qw 2 for a maximum of 6 months<br>**2) Avelumab monotherapy (maintenance)**<br>qw 2 for a maximum of further 6 months | **RP2D, Safety,**<br>ORR, PFS, PK, PD |

# **INSIGHT-004** (Stratum-D)

## Results(1)

### 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; 3rd line gastroesophageal junction
- 75% (n=9) are still alive → 66.7% (n=4) of cohort 1 and 83.3% (n=5) of cohort 2

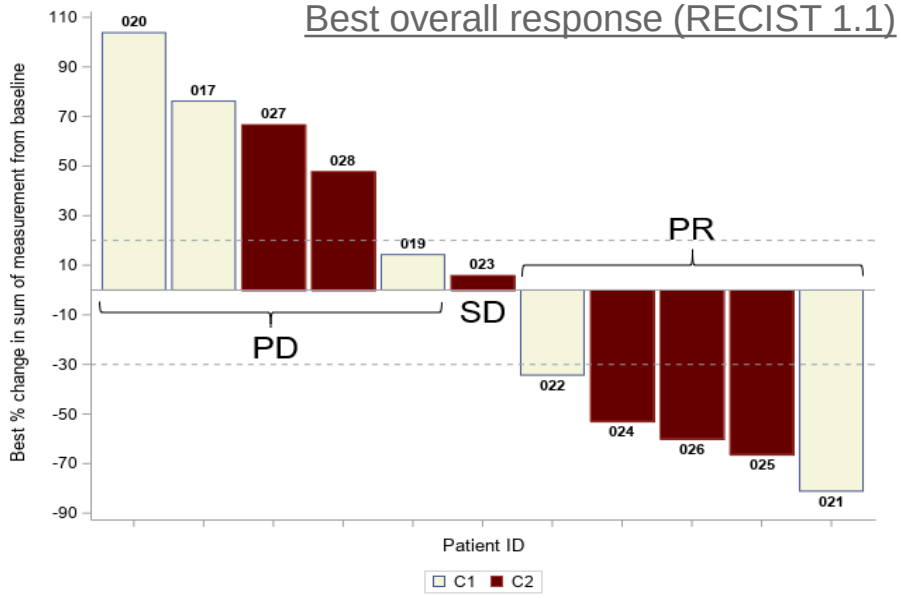
### Safety

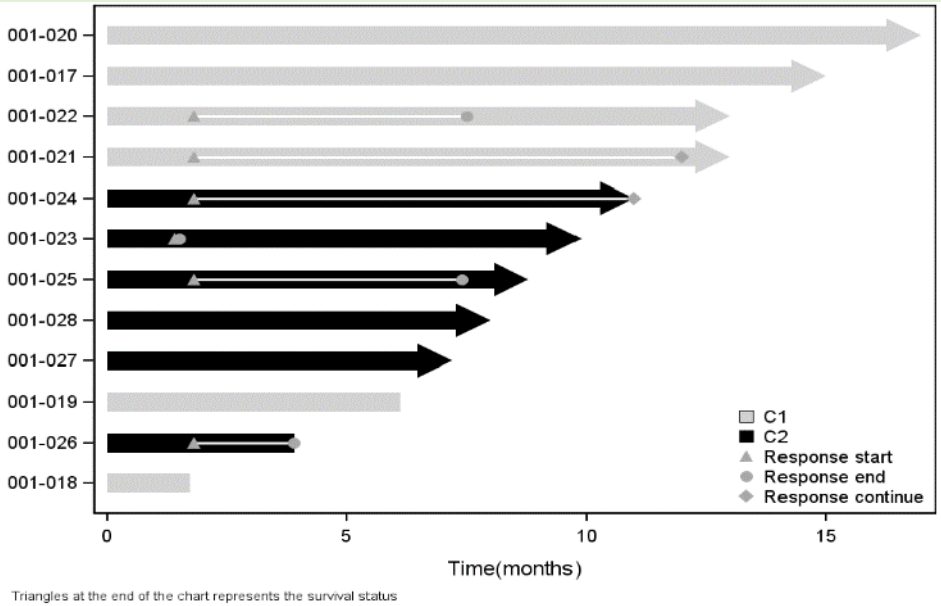
- Combo of avelumab 800 mg + efti 6 mg or 30 mg efti s.c. is feasible and safe
- No unexpected AEs

### 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

Best overall response (RECIST 1.1)






*Note:*

(1) ASCO 2021: J Clin Oncol 39, 2021 (suppl 15; abstr 2518); DOI 10.1200/JCO.2021.39.15_suppl.2518

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# Efti + Chemo Combination

# AIPAC

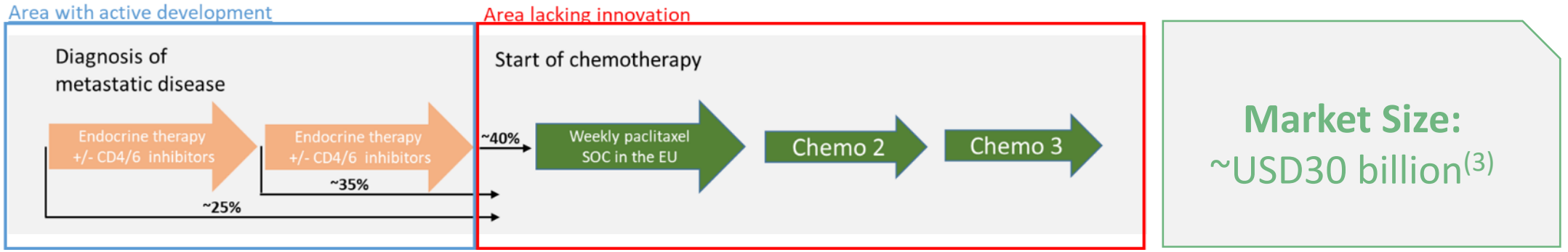
**Exciting interim OS results presented at SABCS in December 2020**

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

# **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[1]
- Highest incidence rate among cancers: ~25% of all new cancer diagnoses among women and ~12% in the total population, including men.[1]
- Up to **350,000 patients younger than 65 develop metastatic disease** and are eligible to receive chemotherapy[1] [2]




**Market Size:**
~USD30 billion[3]

### 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*



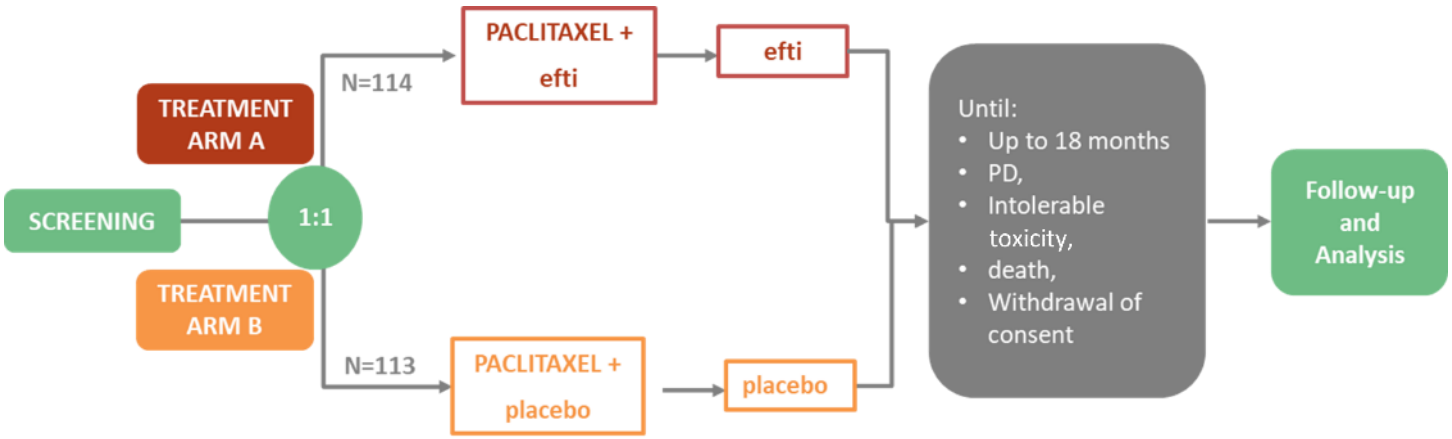
*Notes*

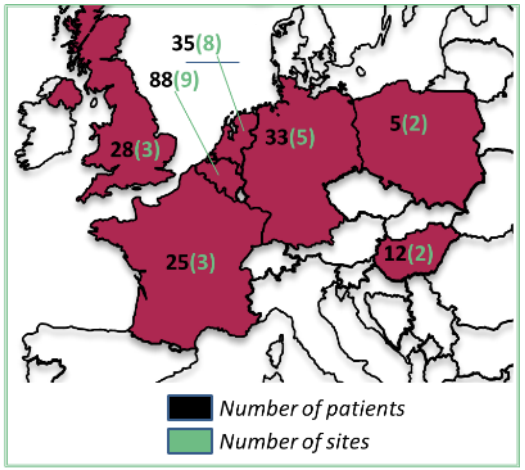
(1) Source: WHO Global Cancer Observatory 2020 and Informa Intelligence October 2020
(2) Wang et al. BMC Cancer (2019) 19:1091
(3) GlobalData Market Size forecast for US, JP, EU5, Urban China and Australia

MBC – metastatic breast cancer BC – breast Cancer

# **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

❖ **2nd 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*

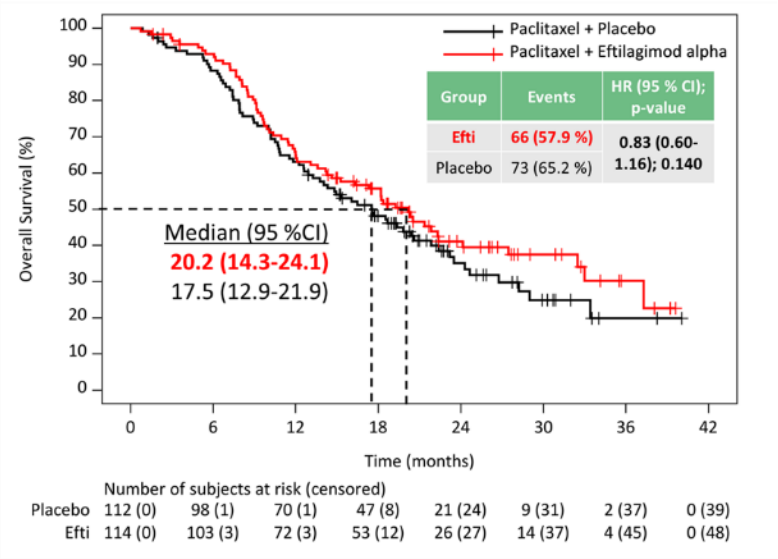
## Subgroups: low monocytes and < 65 years – PFS / OS / ORR

**For predefined sub-groups:**

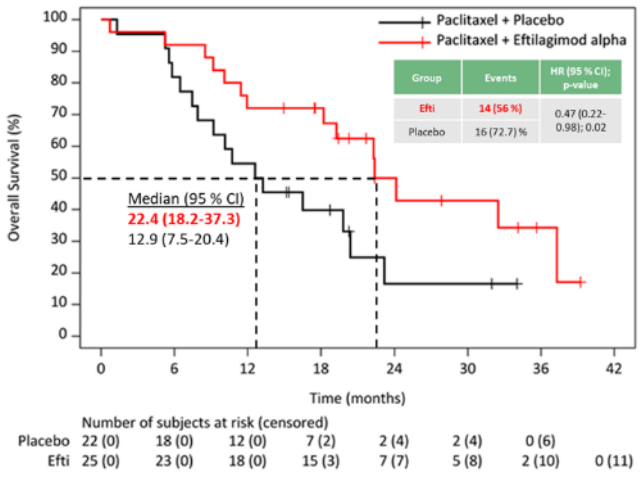
**Clinically meaningful absolute and relative improvement for efficacy parameters, significance for OS**

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

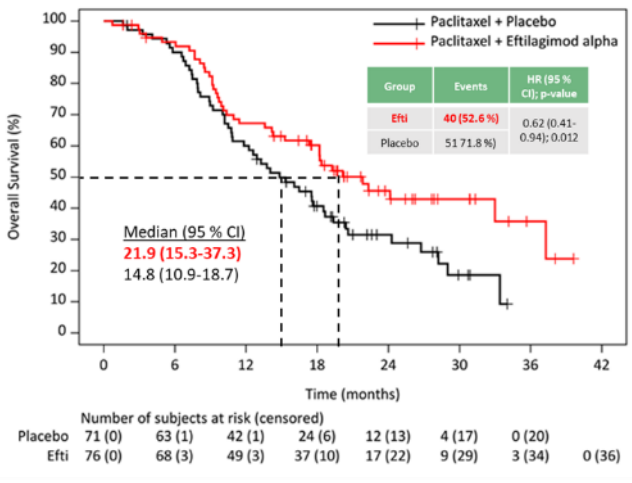
Overall Survival (Follow-up‡) – Total Population




**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

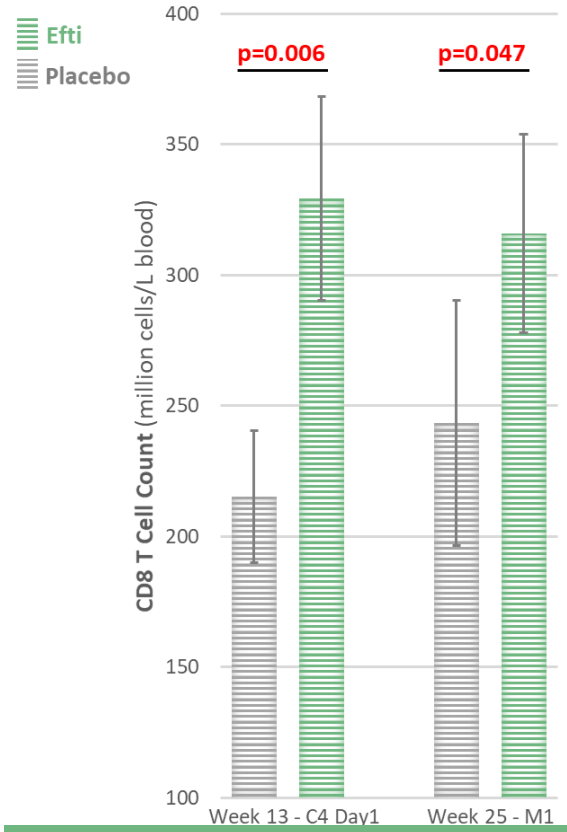
*Notes:*
* These results were presented at SABCS 2020. Data cut-off for interim overall survival results was 24 September 2020.
** used for reimbursement in Europe: https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1

# AIPAC Phase IIb Clinical Results

## Immune Monitoring on Fresh Blood (up to 70 patients)

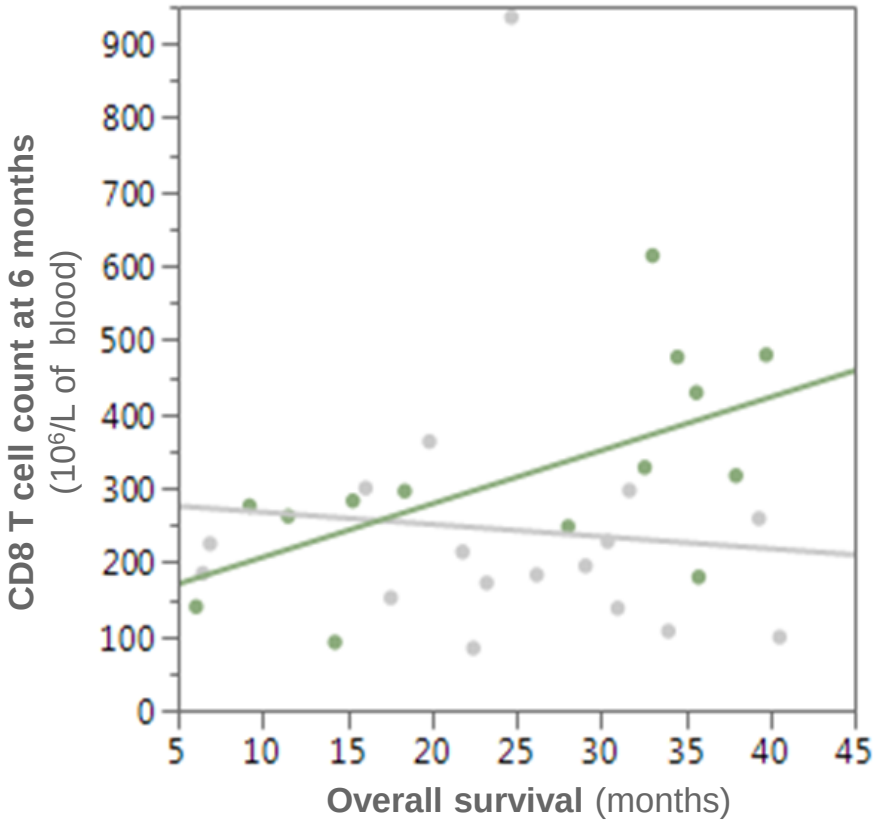
**Cytotoxic CD8⁺ T Cell count over time**

(Mean ± SEM million cells/L of blood; p-value Wilcoxon)




**Number of T cells increased in efti group, especially cytotoxic CD8⁺ → Proof of Principle.**

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




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

# AIPAC Phase IIb Clinical Results

## Summary and Conclusions

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### 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

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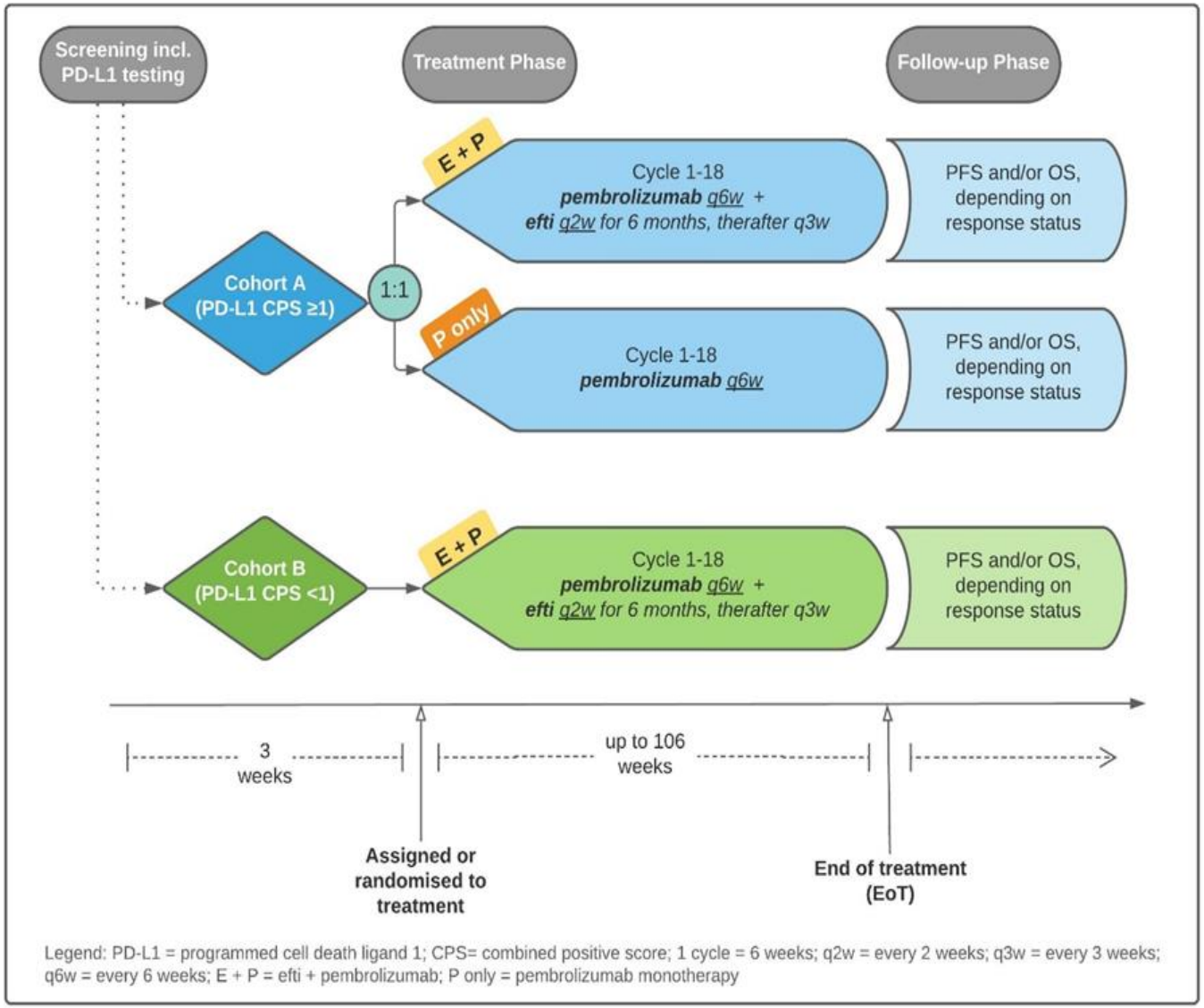
# New Trials

## TACTI-003, INSIGHT-003 and INSIGHT-005

# TACTI-003 Trial in 1st line HNSCC

## 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**

MERCK
INVENTING FOR LIFE

**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

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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 | Treatment | Results |
|---|---|---|
| **Solid tumors**<br>• histologically confirmed locally advanced or metastatic<br>• received no or max. 1 prior lines of therapy<br>• no selection for immunogenic markers (e.g. PD-L1 expression levels, msi high or tmb) | **1) SoC (Chemo + a-PD-1 therapy) + Efti**<br>30 mg s.c., qw 2 for a maximum of 6 mts<br>**2) Maintenance therapy**<br>Dependent on SoC maintenance schedule | **RP2D, Safety,**<br>ORR, PFS, PK, PD |

# INSIGHT Platform Trial in Solid Tumours

## Stratum-005: Efti + Bintrafusp Alfa Combination

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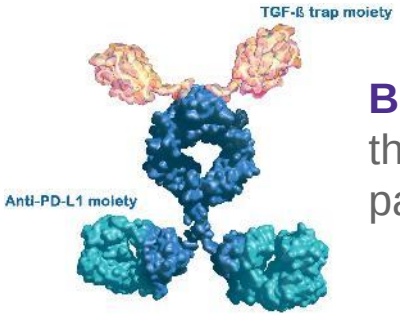
To evaluate the feasibility and safety of combined treatment with bintrafusp alfa (M7824) and eftilagimod alpha. Conducted as the 5th arm of the INSIGHT trial.

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




**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 | Treatment | Results |
|---|---|---|
| **Solid tumors**<br>• histologically confirmed locally advanced or metastatic<br>• received ≤4 prior lines of therapy | **Q2W for maximum of 12 months**<br>• **bintrafusp alfa** 1.200mg i.v.<br>• **eftilagimod alpha** 30mg s.c. | **RP2D, Safety,**<br>ORR, PFS, PK, PD |

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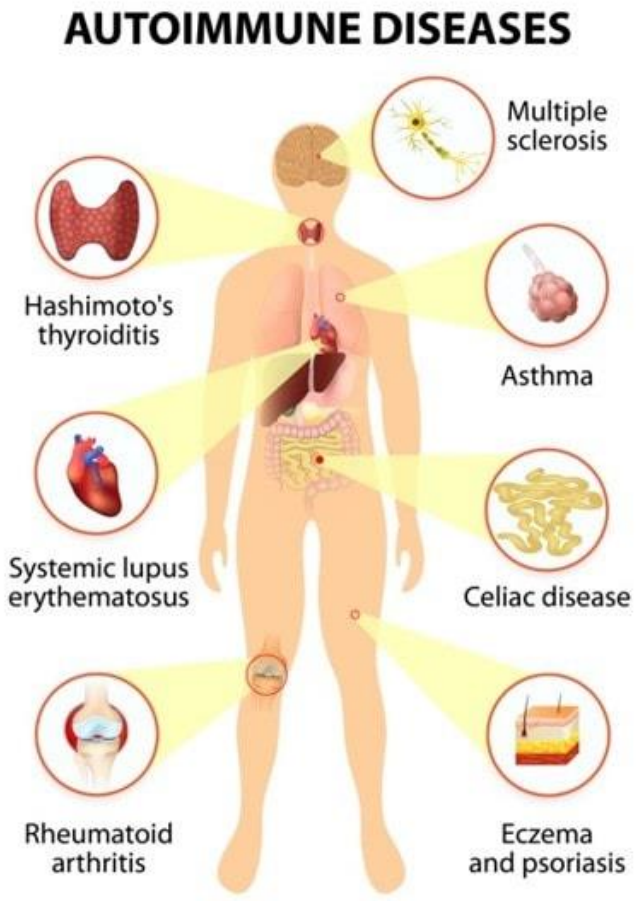
# IMP761
# - Autoimmune Diseases -

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

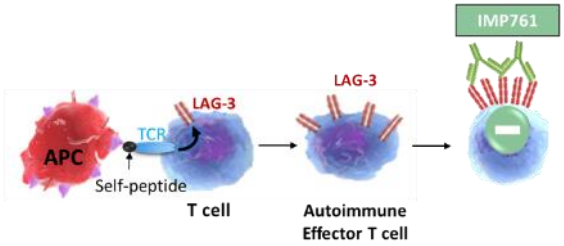



## THE PRESENT: FIGHTING THE SYMPTOMS

**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 (US $153.32 billion by 2025)[1]**



Notes

(1) Source: https://www.researchandmarkets.com/reports/4828880/autoimmune-disease-therapeutics-market-by-drug

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# 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 Immutep's antagonist antibody known as IMP701)
- 1st and 2nd milestone payments received by Immutep 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(1)
- Novartis currently has five clinical trials for Ieramilimab in multiple cancer indications for over 1,000 patients(2)

- **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 Immutep'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(1)
- March 2018: Phase I trial in psoriasis completed in 67 subjects/patients(2)
- September 2019: 1st patient dosed in Phase II trial in ulcerative colitis in 242 patients triggered a £4 million (~US$5.0 million) milestone payment to Immutep(2)
- Phase I clinical study completed, evaluating GSK'781 in 36 healthy Japanese and Caucasian subjects, PK/PD study(2)
- 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+ T cells that are auto-reactive in autoimmune disease leading to long term disease control without generalized immune suppression**



Notes
(1) https://www.biopharmadive.com/news/glaxosmithkline-gsk-rd-pipeline-restructuring-cut-q2-earnings/447924/
(2) For additional information refer https://www.clinicaltrials.gov/ct2/results?cond=&term=GSK2831781&cntry=&state=&city=&dist=

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

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# Outlook

# 2021/2022 News Flow*

## H1 2021

- ✓ **Fast Track designation** granted for efti in 1st 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

- ❑ Final data from **AIPAC**: 2nd 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)

## 2022

*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

| | |
|---|---|
| **Ticker symbols** | IMM (ASX)<br>IMMP (NASDAQ) |
| **Securities on issue**(1) | ~ 850.92 million ordinary shares |
| **Proforma cash balance**(2) | ~ A$114 million (US$85.7 million) |
| **Market Cap**(3) | ~ 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 Immutep'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 efti & 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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# Thank You