



The global leader in developing LAG-3 therapeutics

Jefferies Virtual Healthcare Conference
June 1 – June 4, 2021

(ASX: IMM, NASDAQ: IMMP)

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Overview

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LAG-3

Immute^p

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



Global leadership position

in LAG-3 with four product candidates in immuno-oncology and autoimmune diseases



Clinical Potential

Immute^p'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



Corporate Strategy:

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



LAG-3 Overview

- The most promising immune checkpoint -

LAG-3 Therapeutic Landscape Overview

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

Sources: GlobalData, Company websites, clinicaltrials.gov, and sec.gov, as of 1 June 2021. The green bars above represent programs conducted by Immute^p &/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 Acquires 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/)

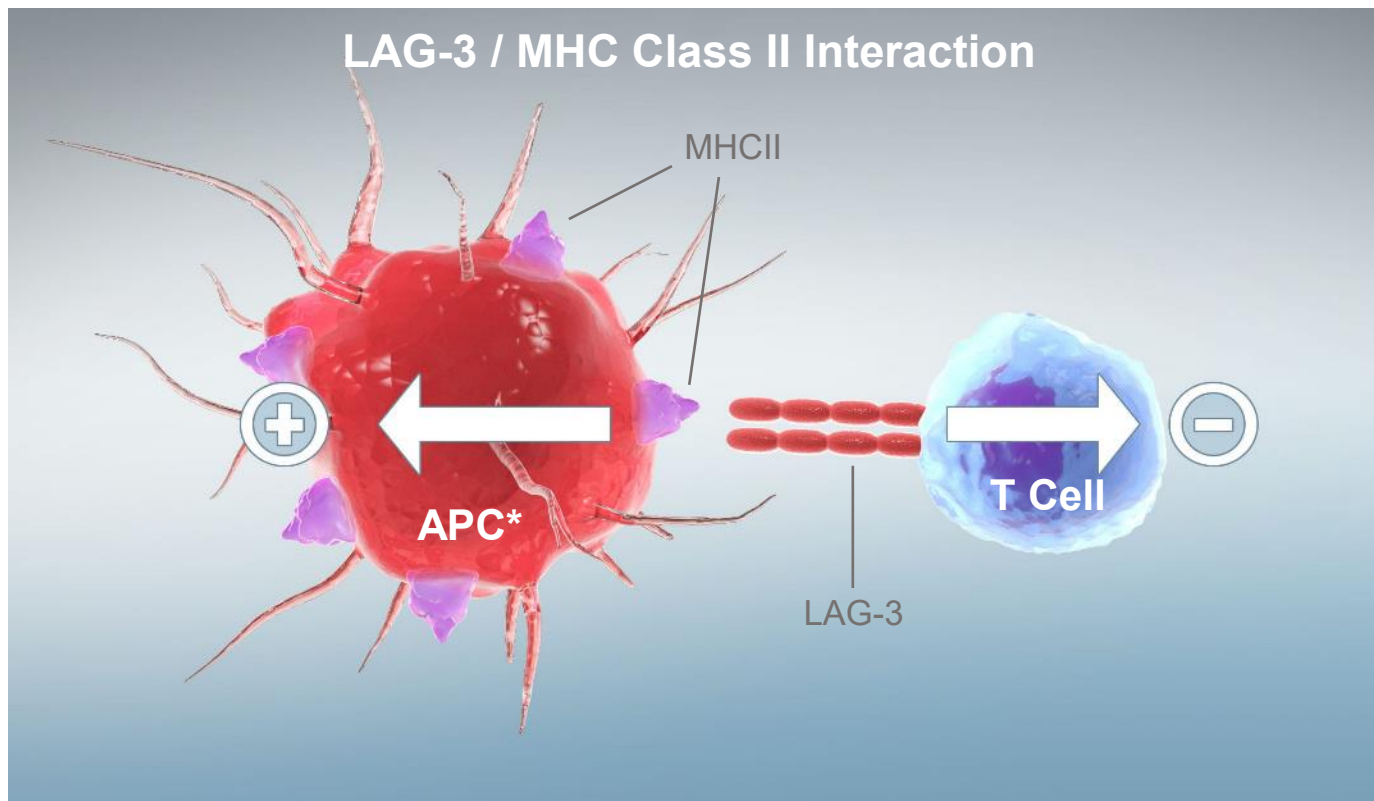
4) Includes two completed Phase I studies and one discontinued Phase 2 study (see slide 9)

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>)

LAG-3 as a Therapeutic Target

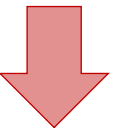
LAG-3, an immune checkpoint, is widely expressed on tumor infiltrating lymphocytes (TILs) and cytotoxic T cells → **LAG-3 / MHC II interaction is a validated target for IO**



→ **Positive regulation** of antigen presenting cells (**APCs**) → increase in antigen presentation to cytotoxic CD8⁺ T cells



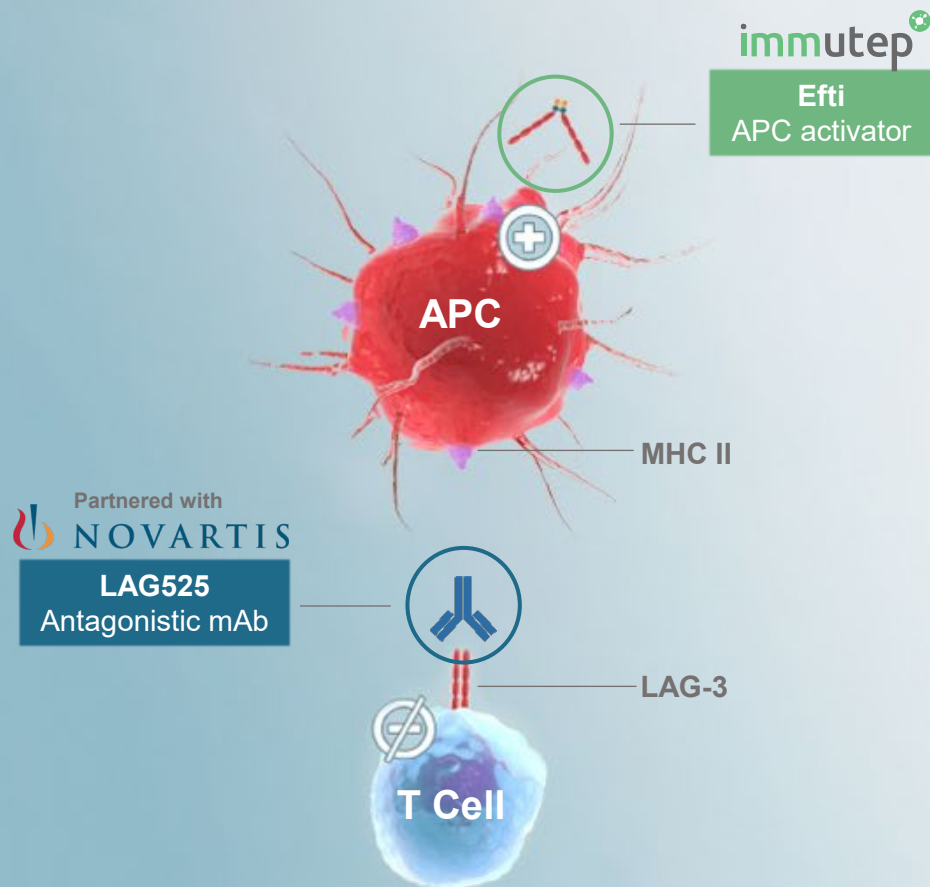
→ **Negative regulation** of LAG-3⁺ T Cells



Targeting LAG-3 / MHC II:

Multiple Therapeutics in Numerous Diseases

IMMUNOSTIMULATION

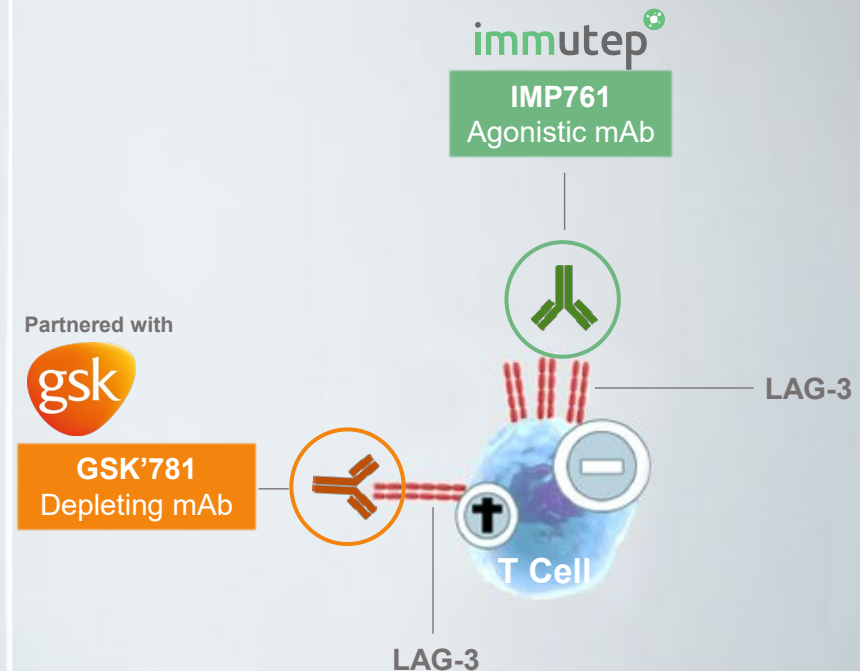


RELEVANT DISEASES

Immuno-oncology
Combination Therapies

Viral Infections

IMMUNOSUPPRESSION



RELEVANT DISEASES

Rheumatoid
Arthritis

IBD

Multiple
Sclerosis

Immunotherapy Pipeline*

Program	Preclinical	Phase I	Phase II	Late Stage ⁽⁵⁾	Commercial Rights	Market Size ⁽⁶⁾
Eftilagimod Alpha (efti or IMP321) APC activating soluble LAG-3 protein	Metastatic Breast Cancer (Chemo – IO) AIPAC				Global Rights 	US\$29.9 billion
	Non-Small-Cell Lung Carcinoma (IO – IO) ⁽¹⁾ TACTI-002					US\$22.6 billion
	Head and Neck Squamous Cell Carcinoma (IO – IO) ⁽¹⁾ TACTI-002					US\$1.9 billion
	Head and Neck Squamous Cell Carcinoma (IO – IO) ^(1b) TACTI-003					
	Solid Tumors (IO – IO) ^{(2), (3a)} INSIGHT-004		 Merck KGaA, Darmstadt, Germany			
	Solid Tumors (IO – IO) ^{(2), (3b)} INSIGHT-005		Merck KGaA, Darmstadt, Germany 			
	Melanoma (IO – IO) ⁽¹⁾ TACTI-mel					US\$4.5 billion
	Solid Tumors (In situ Immunization) ⁽²⁾ INSIGHT					
	Solid Tumors (Cancer Vaccine) ^(4a) YNP01 / YCP02 / CRESCENT 1					
	Metastatic Breast Cancer (Chemo – IO) ^(4b)				Chinese Rights 	US\$2.3 billion
Int. Dis.	Efti	COVID-19 disease (Monotherapy) ⁽⁷⁾ EAT-COVID			Global Rights ⁽⁸⁾ 	
Autoimm.	IMP761 (Agonist AB)				Global Rights 	US\$149.4 billion (2025)

Notes

* Information in pipeline chart current as at June 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*

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Program	Preclinical	Phase I	Phase II	Late Stage ⁽¹⁾	Commercial Rights/Partners	Updates
LAG525 (Antagonist AB)	Solid Tumors + Blood Cancer (IO-IO Combo)				Global Rights 	Novartis currently has five clinical trials ongoing for LAG525 in multiple cancer indications for over 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)					
GSK'781 (Depleting AB)	Ulcerative Colitis ⁽⁶⁾				Global Rights 	Two successful Phase I studies, but the 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 June 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

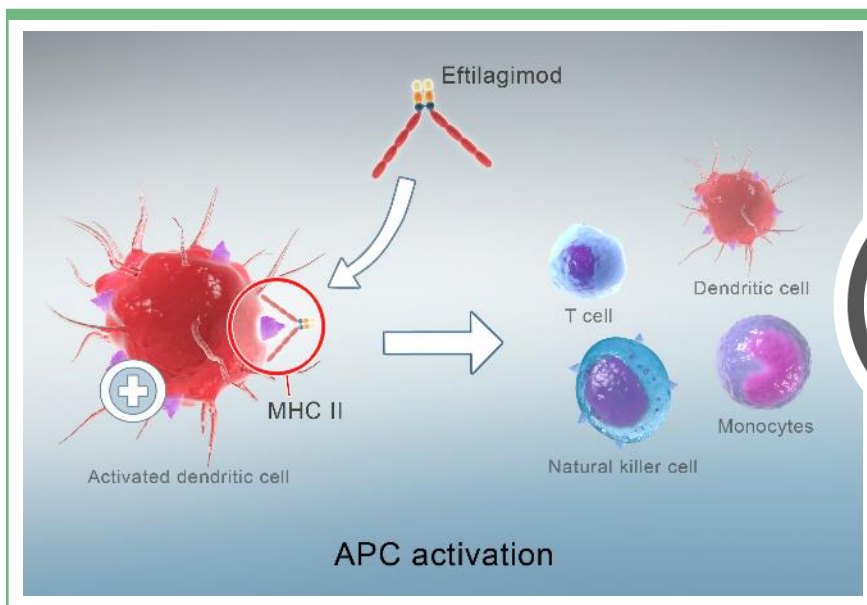
Eftilagimod Alpha (efti or IMP321)

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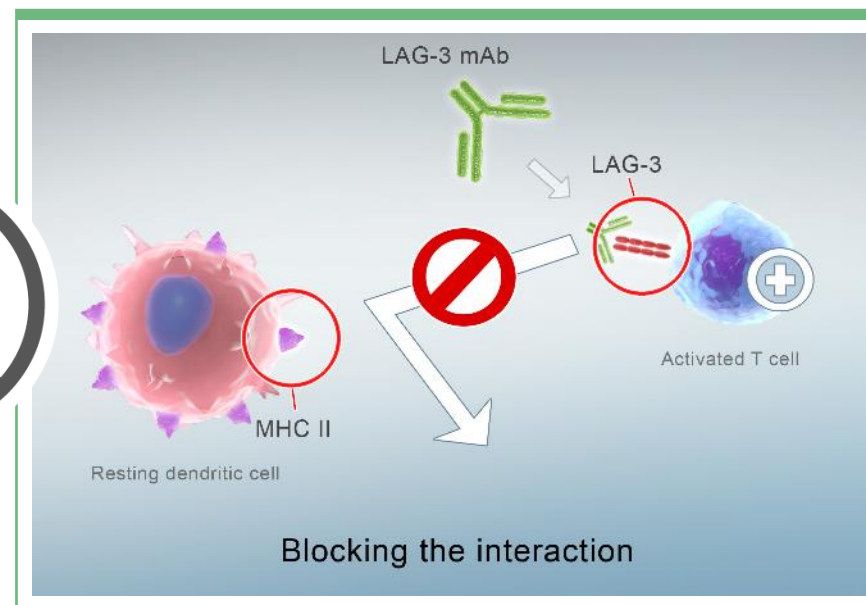
Efti: an Innovative LAG-3 IO Product Candidate

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

“PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”



“RELEASING THE BRAKE ON THE T CELL”



Efti is an **MHC II agonist**

APC activator

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

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

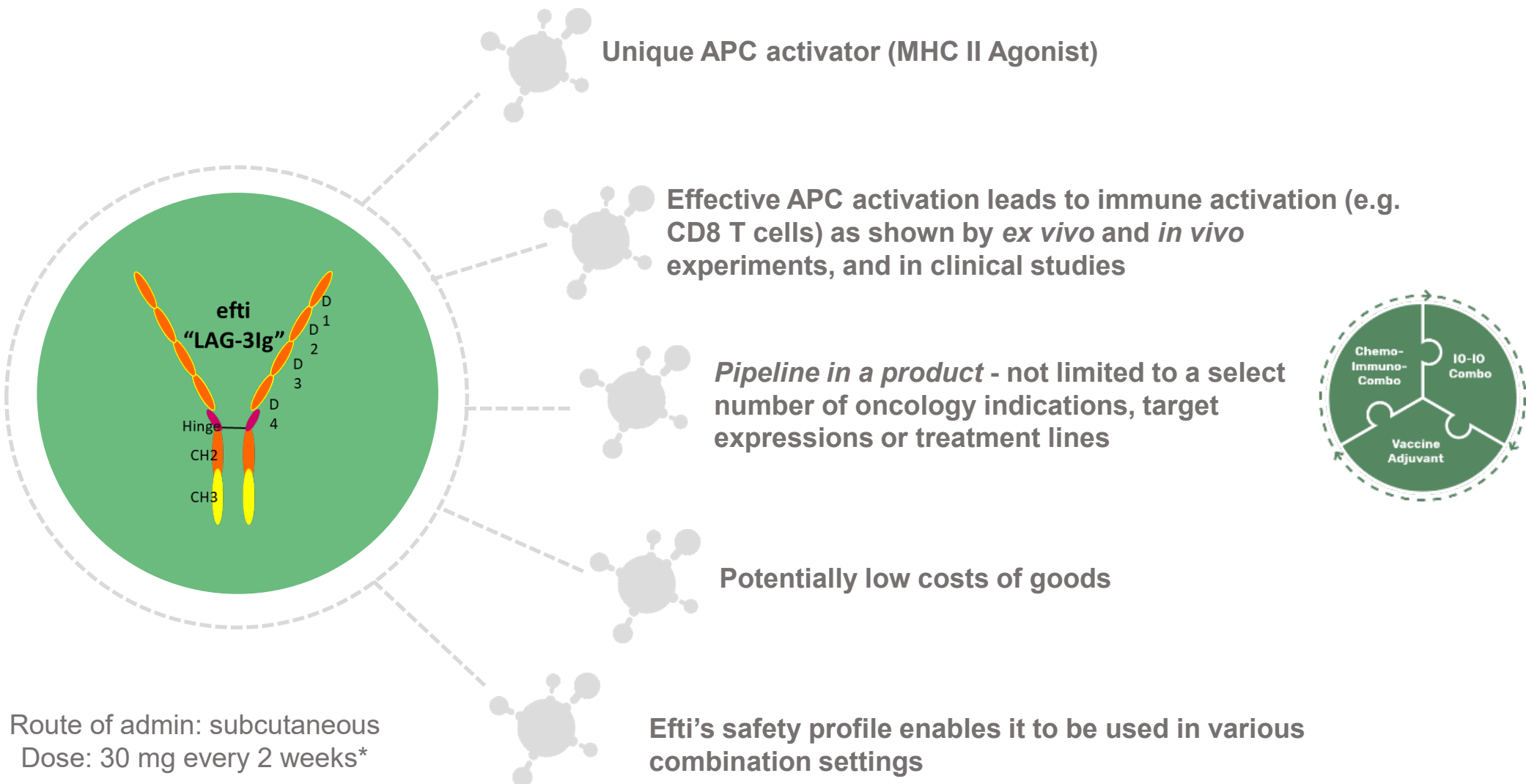
Immune checkpoint inhibitor

- increases cytotoxicity of pre-existing CD8 T cell response

Efti: Potential Pipeline in a Product

High intrinsic value

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

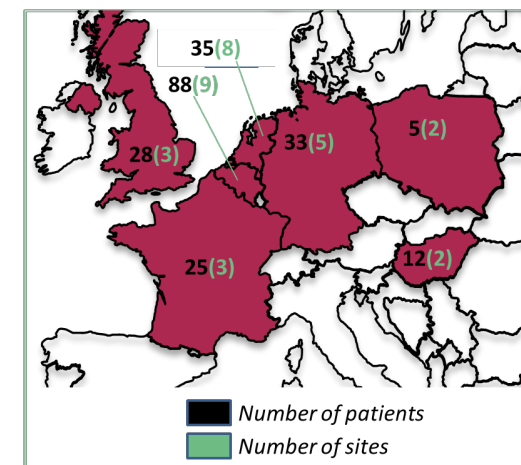
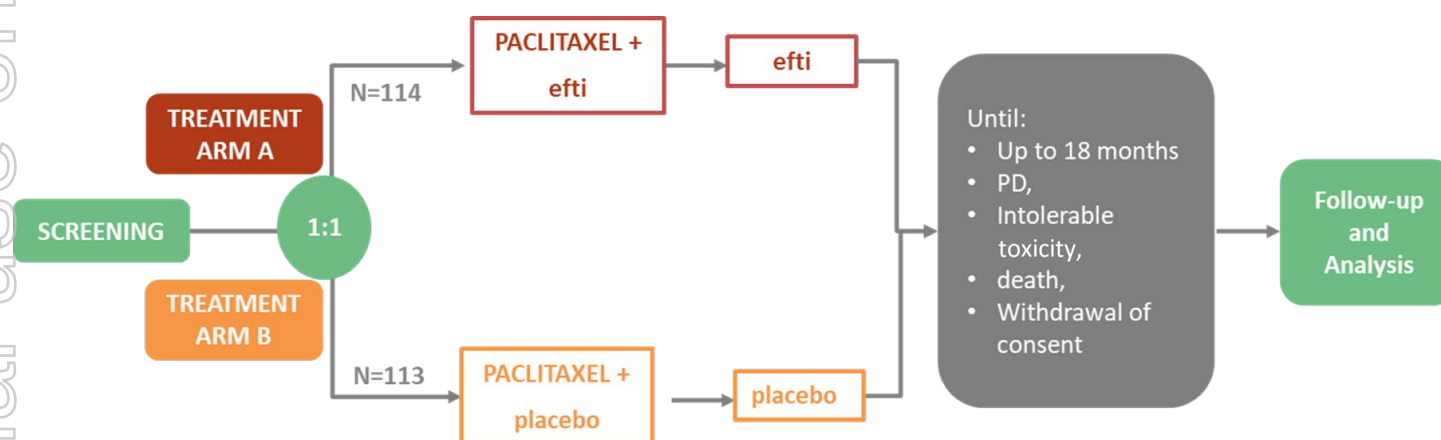
Efti + Chemo Combination:

Exciting interim OS results

Presented at SABCS in December 2020

Efti: AIPAC (Phase IIb) design

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



Primary endpoint^(*) (presented Mar. 2020) included:

- Assessment of Progression-Free Survival (PFS)

Secondary endpoints^(*) (presented Dec. 2020) included:

- Overall Survival (OS)
- Safety and tolerability
- Overall Response Rate (ORR) and other efficacy parameters
- Biomarker and Immune Monitoring

Fact sheet

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

AIPAC Phase IIb Clinical Results

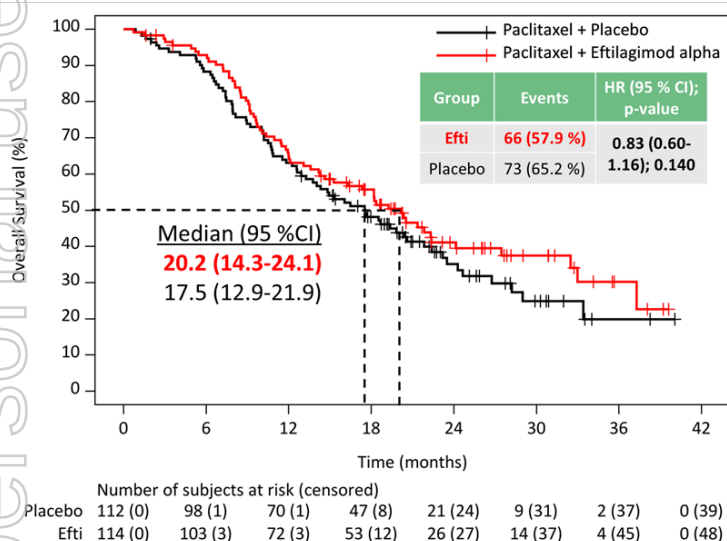
Subgroups: low monocytes and < 65 years – PFS / OS / ORR

For predefined sub-groups:

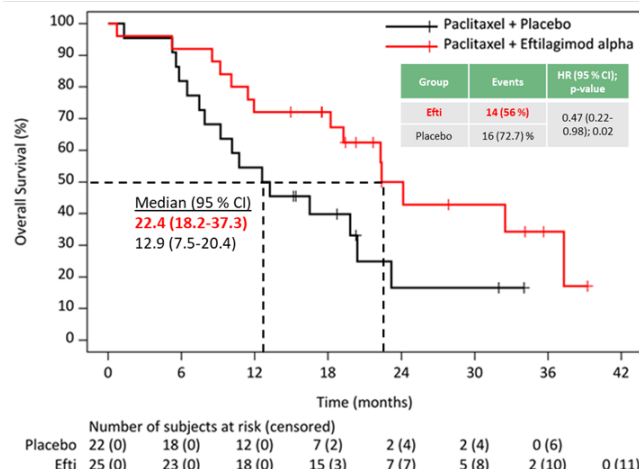
Clinically meaningful absolute and relative improvement for efficacy parameters, significance for OS

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

Overall Survival (Follow-up†) – Total Population

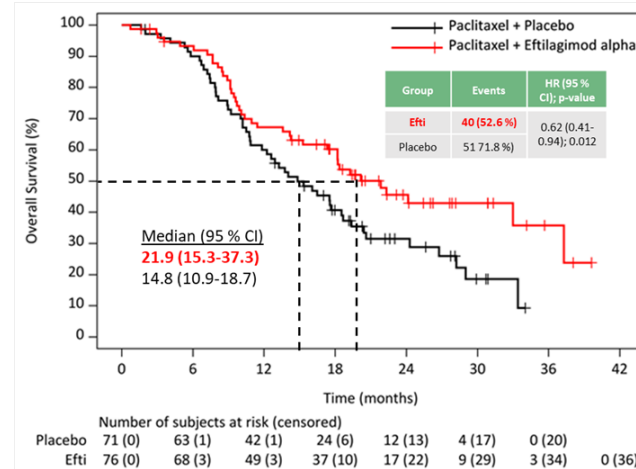


Patients with low monocytes
- OS -



+9.1 months median OS

Patients with age < 65 yrs.
- 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)

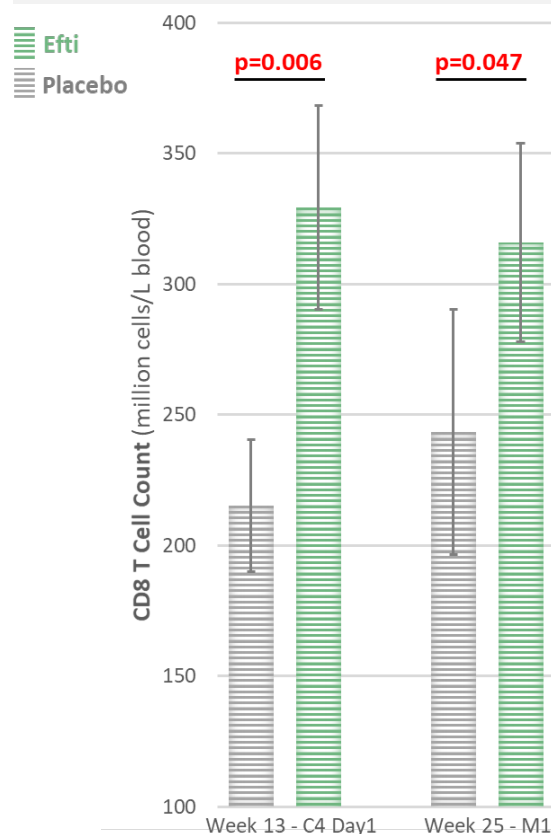
CDK4/6 are now standard, and most patients will have received it in future studies / real world → favorably for efti

AIPAC Phase IIb Clinical Results

Immune Monitoring on Fresh Blood (up to 70 patients)

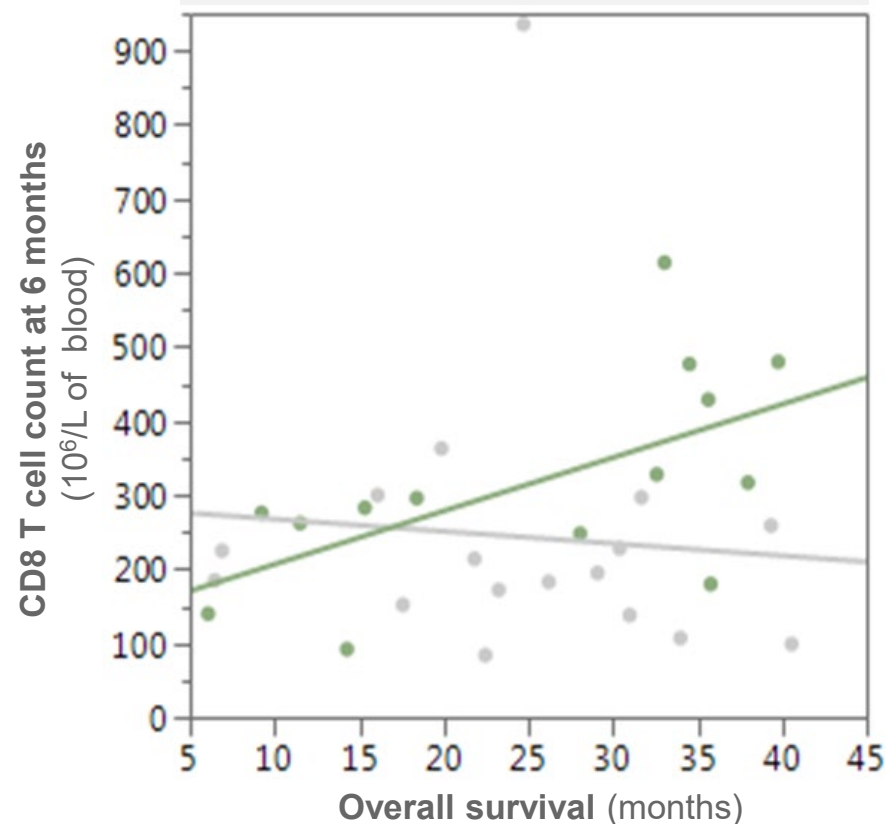
Cytotoxic CD8⁺ T Cell count over time

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



Number of T cells increased in efti group, especially cytotoxic CD8⁺ $\rightarrow$ 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 $\rightarrow$ Proof of Concept.

AIPAC Phase IIb Clinical Results

Summary and Conclusions

First time



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

Proof of Concept



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

Proof of Principle



Significant increase in cytotoxic T cell numbers compared to placebo

Path Forward



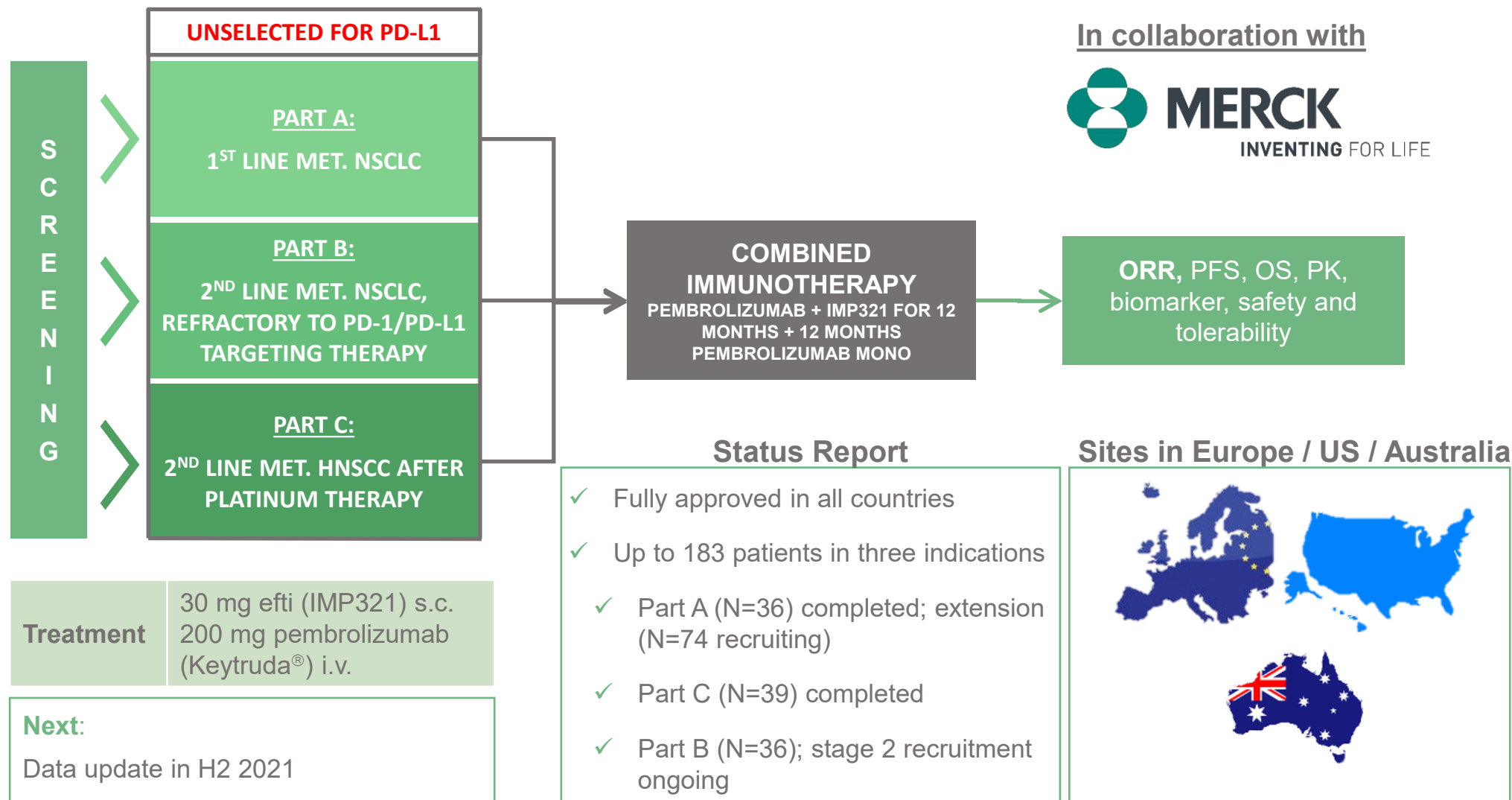
Regulatory (FDA and EMA) discussions are prioritised now

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

Key Clinical Trials

TACTI-002 (Phase II) design & status

TACTI-002: Two ACTIVE Immunotherapeutics in NSCLC and HNSCC



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

BASELINE CHARACTERISTICS & EFFICACY*

Baseline Disease Characteristics*

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

Tumor Response*

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

* - 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

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

EFFICACY

ORR by PD-L1 subgroup*

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

* according to investigator read, evaluable pts only

Overall PFS estimates by PD-L1 subgroup**

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

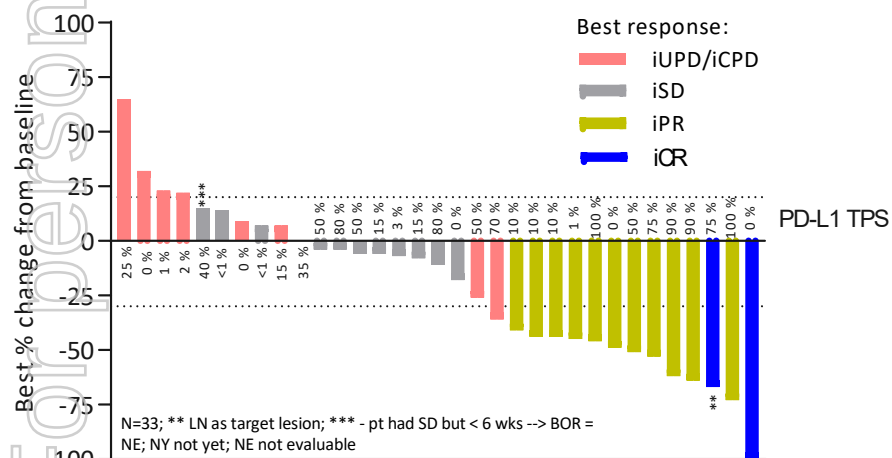
** according to investigator read, minimum follow-up of 8.3 months, all patients stage 1 and 2 with ≥ 1 treatment

Duration of Response (DOR)

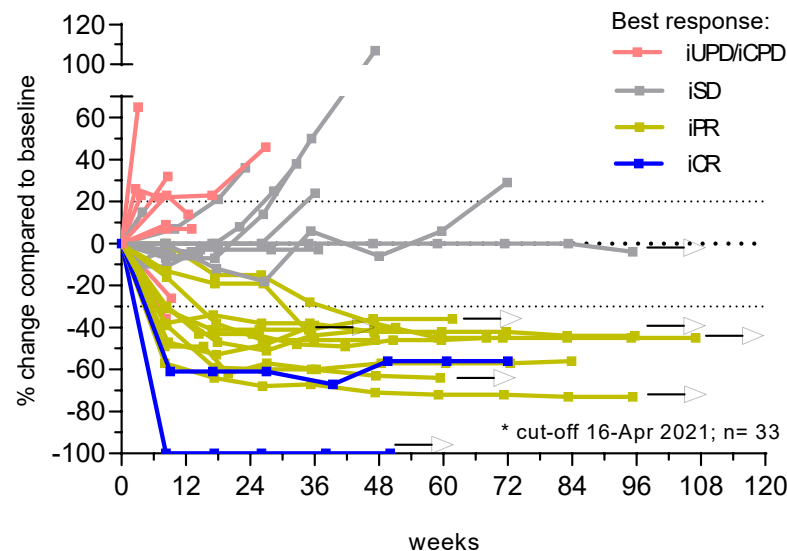
- 92% responses confirmed
- 58% confirmed responses ongoing with 6+ months
- Median DOR estimated 13+ months

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

Waterfall plot



Spider plot



TACTI-002: Phase II of efti and pembro in 2nd line HNSCC (Part C)

BASELINE CHARACTERISTICS & EFFICACY*

Baseline disease characteristics

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

Primary tumor location

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

Tumor response*

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

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

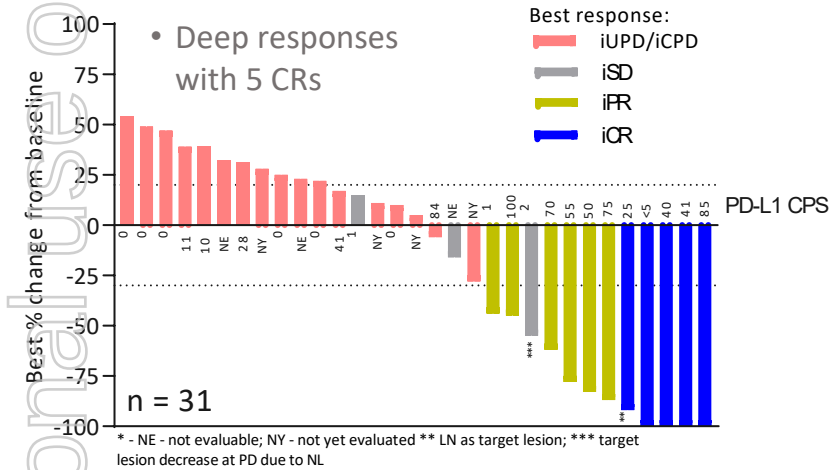
** - dropped off prior to first staging or were not evaluable post-baseline for any reason

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

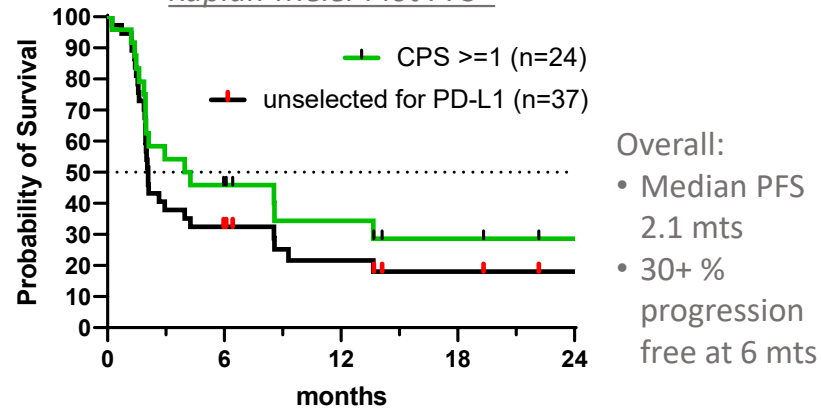
TACTI-002: Phase II of efi and pembro in 2nd line HNSCC (Part C)

EFFICACY*

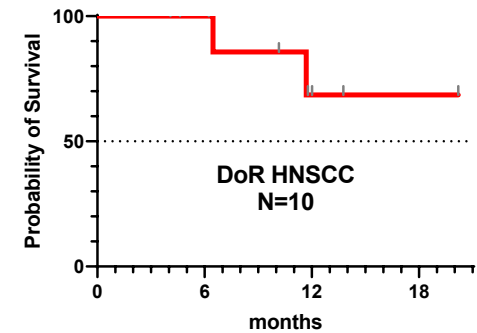
Waterfall plot**



Kaplan-Meier Plot PFS*



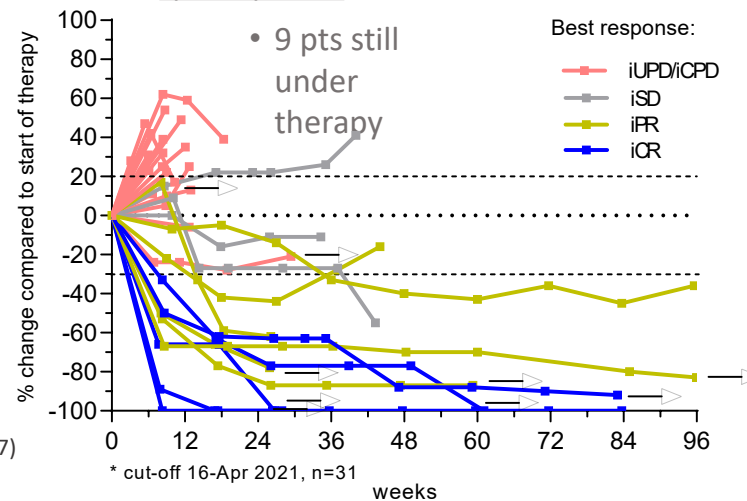
Duration of response (DOR) for confirmed responders



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

Median OS (58% events)	Median PFS (71% events)	ORR iRECIST (95% CI)
12.6 mts 54% alive at 12 mts	4.1 mts 45% PFS free at 6 mts	45.8% (25.6-67.2)

Spider plot**



Duration of response

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

INSIGHT-004*: Phase I of efti and avelumab

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

Key findings

- No DLTs and no new safety signals with standard dose of avelumab
 - 5/12 (**42%**) patients with **partial responses** in:
 - 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
- Efti plus avelumab is safe and well tolerable
 - Encouraging single cases in non ICI sensitive cancers

In collaboration with



Merck KGaA,
Darmstadt, Germany

Institut für Klinisch-Onkologische Forschung
 **KRANKENHAUS
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

INSIGHT-005: Phase I for efti and bintrafusp alfa

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

In collaboration with

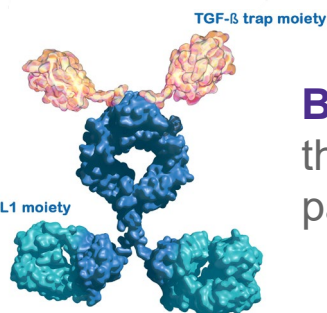
Merck KGaA,
Darmstadt, Germany



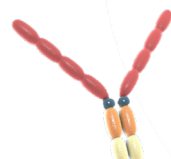
Institut für Klinisch-Onkologische Forschung



**KRANKENHAUS
NORDWEST**



Bintrafusp alfa: bifunctional fusion protein that aims to block two immunosuppressive pathways, TGF- 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



12 months
Combination treatment



Two sites
Germany

Solid tumors

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

Q2W for maximum of 12 months

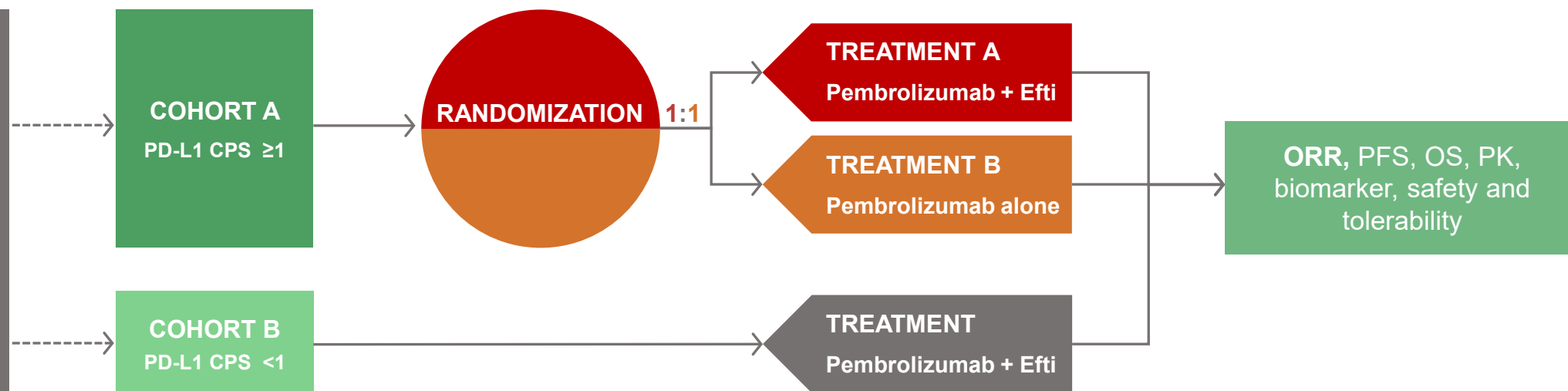
- **bintrafusp alfa** 1.200mg i.v.
- **eftilagimod alpha** 30mg s.c.

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

*INSIGHT is an investigator initiated trial (IIT)

TACTI-003 Trial in 1st line HNSCC

Current Design + Status



Design:

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

Status:

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

In collaboration with



IMP761

- Autoimmune Diseases -

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

AUTOIMMUNE DISEASES

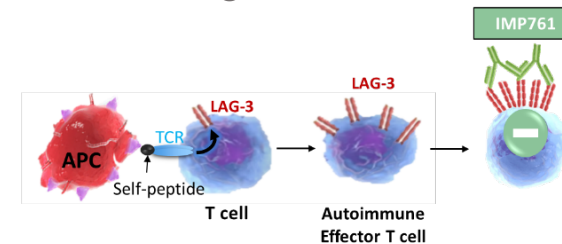


THE PRESENT: FIGHTING THE SYMPTOMS

Treating general inflammation:
corticoids, methotrexate,
anti-TNF- α , -IL-6, -IL-17, -IL-23 mAbs

THE FUTURE: FIGHTING THE CAUSE

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



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

Corporate Snapshot & Outlook

For personal use only

Corporate Snapshot

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

Notes:

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

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

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

2020 & 2021 News Flow*

2020

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

2021

- ❑ Final data from **AIPAC**: 2nd OS follow up
- ✓ Data from **TACTI-002** & final data from **INSIGHT-004** at ASCO
- ❑ Recruitment & first data from **TACTI-002** Part A extension
- ❑ Start & ongoing recruitment of **new trial in 1st line HNSCC** (TACTI-003)
- ❑ Ongoing **regulatory** engagement
- ❑ Updates from **IMP761**
- ❑ Updates from partnered programs (e.g. GSK, Novartis, EAT COVID, CYTLIMIC and EOC Pharma)
- ❑ Potential new partnerships and expansion of existing programs

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

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 four LAG-3 related product candidates in immuno-oncology and autoimmune disease

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

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

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



Thank You