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LAG-3 IMMUNOTHERAPY

Immutep TACTI-002 Clinical Results & Update Global Webcast Slides

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

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

Register: Interested parties can join the webcast by registering via FNN.

A replay of the webcast will also be available at www.immutep.com from the day after the event.

(ASX: IMM, NASDAQ: IMMP)

Notice: Forward Looking Statements

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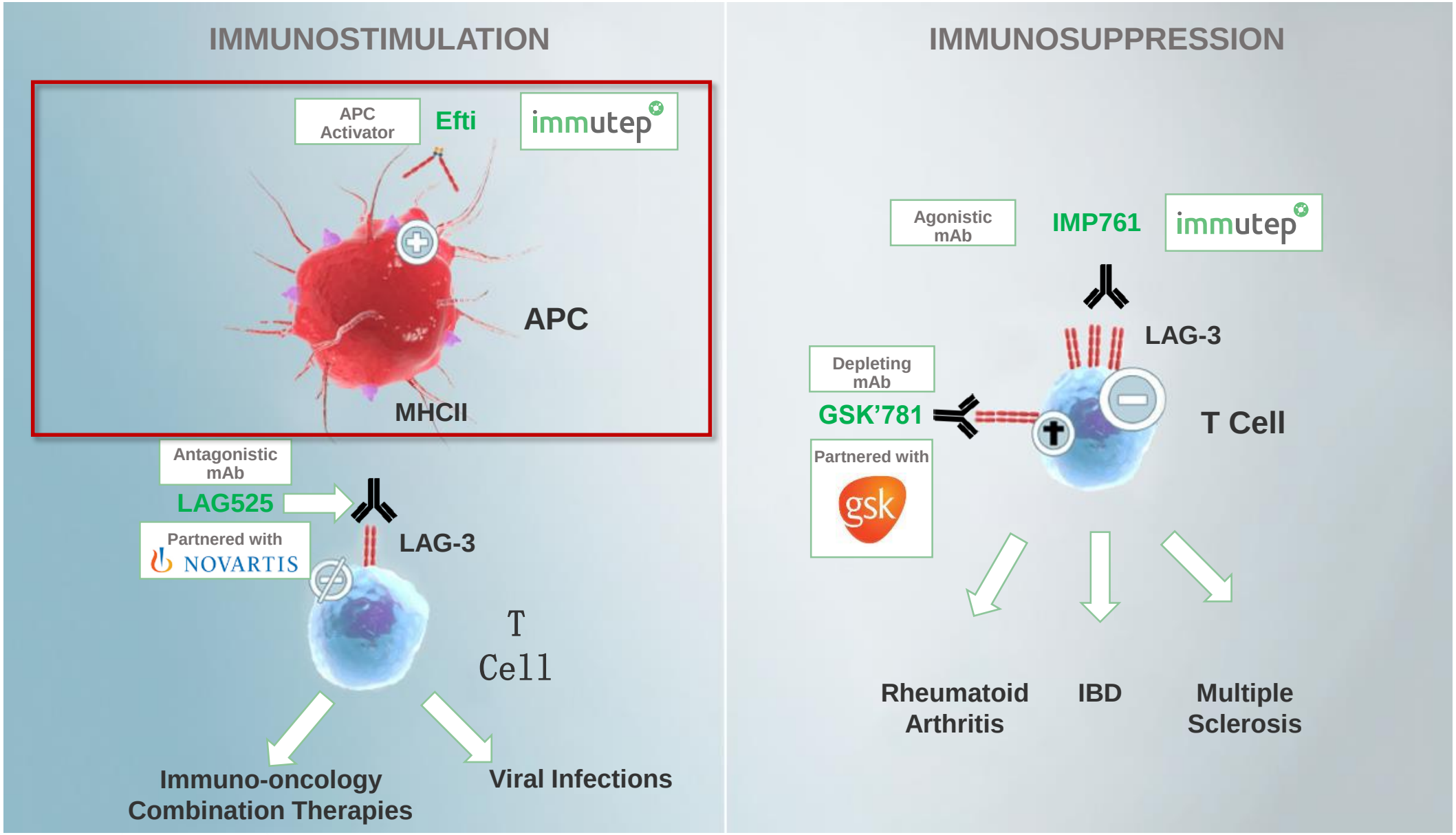
Eftilagimod Alpha (efti or IMP321)

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



Immutep Controlled Immunotherapy Pipeline (Oncology)*

Notes

* Information in pipeline chart current as at 25 February 2020

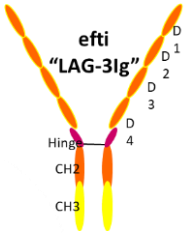
(1) In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC")

(2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

(3) In combination with BAVENCIO® (avelumab)

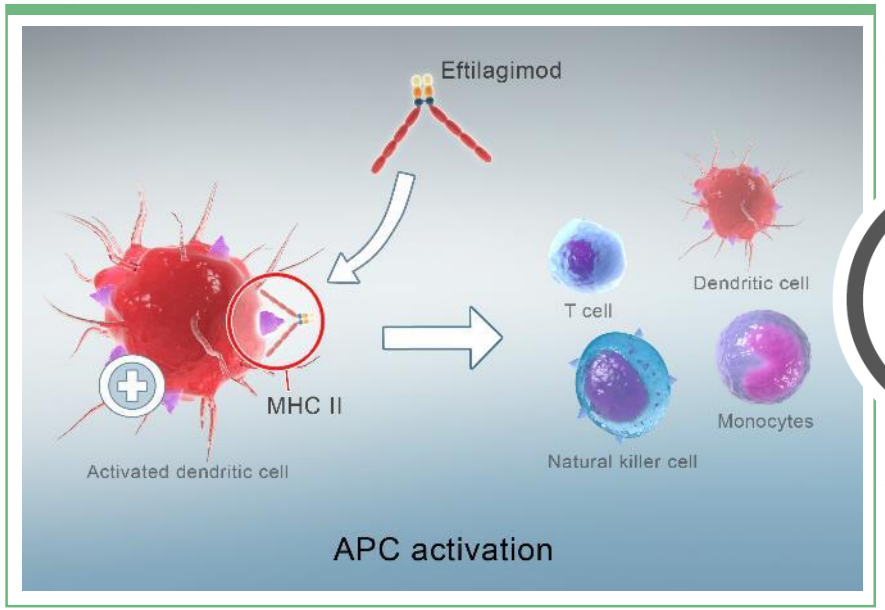
(4) Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials

Efti: an innovative LAG-3 I-O product candidate



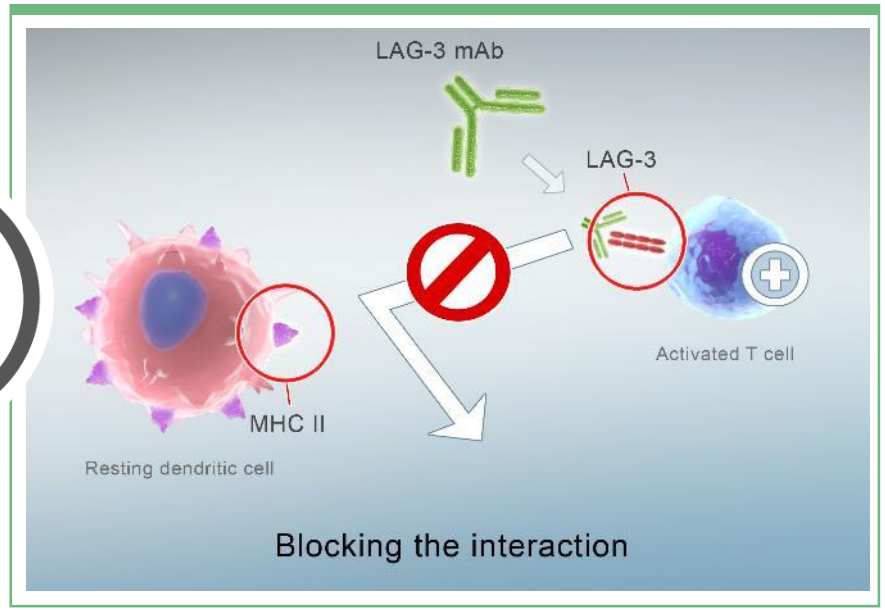
- Efti is a soluble LAG-3 protein targeting a subset of MHC class II on APC
- Potentially synergistic with other therapeutic agents, e.g. I-O agents or chemotherapies

"PUSHING THE ACCELERATOR ON IMMUNE RESPONSES"



Efti is an **MHC II agonist:**
APC activator
- boost and sustain the $CD8^+$ T cell responses
- activate multiple immune cell subsets

"RELEASING THE BRAKE ON THE T CELL"

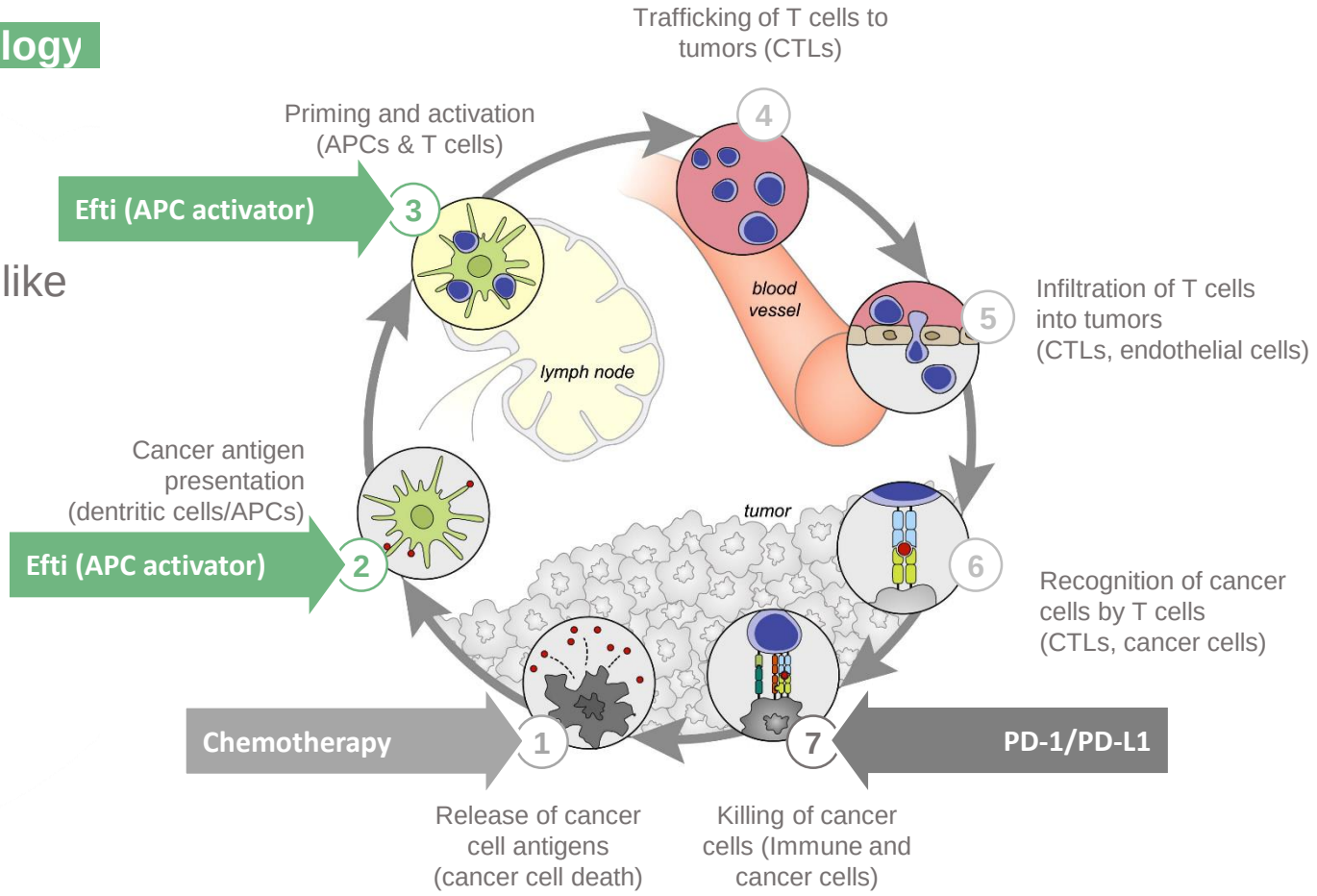


LAG-3 antagonist, or blocking, antibodies:
Immune checkpoint inhibitor
- increase cytotoxicity of the pre-existing CD8 T cell response

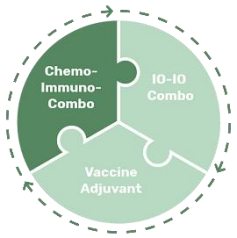
Efti: a pipeline in a product

Efti has disruptive potential for oncology

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



AIPAC update



Efti: Clinical Development AIPAC (Phase IIb)

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

Patients with HR+/HER2- MBC

→ Arm 1, *113* patients: paclitaxel + efti

Arm 2, *113* patients: paclitaxel + placebo

→ Phase IIb, multinational, randomized, double-blind

→ **Primary: PFS**
Secondary: OS, safety, ORR, QoL

Primary endpoint will include:

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

Status Report

✓ Fully recruited in 7 EU countries (227 pts)

- PFS & ORR data expected by end of March 2020

Key features:

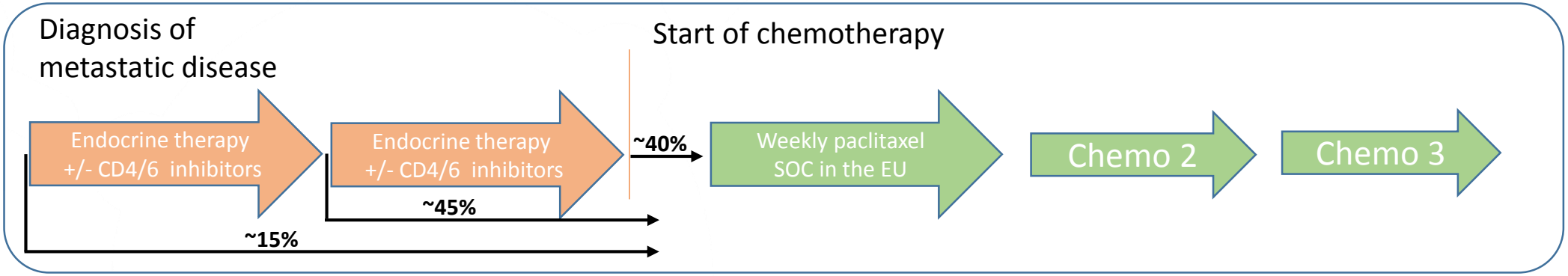
1. **double blinded potentially pivotal trial in MBC patients → conditional marketing authorization in the EU depending on data**
2. **broader perspective: validation of Antigen Presenting Cell activators → a new class of active I-O products after the Immune Checkpoint Inhibitors**

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

Efti positioning in HR+/HER2- MBC

Epidemiology:

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



Current Status:

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

Typical Patient Population in MBC:

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

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

Notes
(1) Source: GlobalData 2019

MBC – metastatic breast cancer BC – breast Cancer

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

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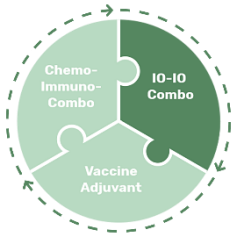
Approval status	Drug	Indication	Trial	Results		
				PFS T+nP	**PFS Pl-nP**	**HR**
APPROVED (2019)	Tecentriq (atezolizumab)	1st line in combo with nab-paclitaxel for mTNBC	**Impassion130**: Tecentriq + nP vs. Placebo + nP	7.5	5.3	**0.63**
				PFS piqr.+fulv.	**PFS Pl+fulv.**	**HR**
APPROVED (2019)	Piqray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

Notes
(1) Source: FDA and EMA, published data

Combining efti and anti-PD-1:

TACTI-002



Rationale for combining efti with PD-1 antagonists

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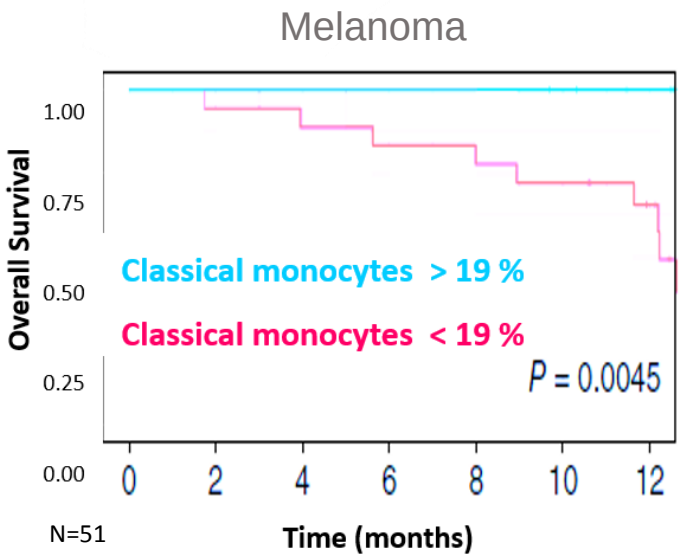
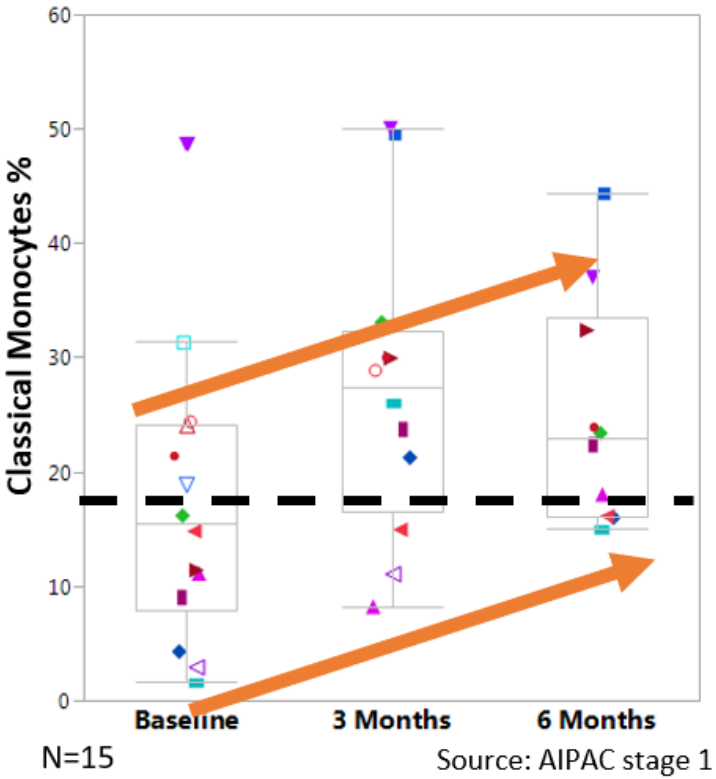
Efti increases monocyte number in cancer patients

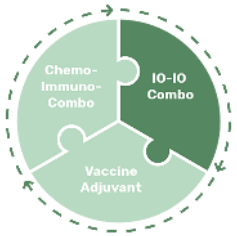


Source: Krieg et al., Nat. Med. 24, 2018.

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



Source: AIPAC stage 1



Efti: Clinical Development TACTI-002 (Phase II)

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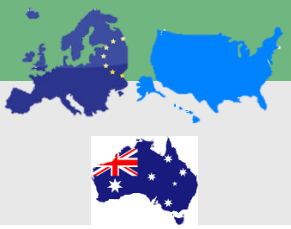
Trial Design + Introduction



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

Eligiblity

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

Part A:
1st line met. NSCLC

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

Part C:
2nd line met. HNSCC after platinum

→

30 mg efti SC
+
200 mg pembrolizumab IV

Up to 12 months then pembrolizumab alone for another 12 months

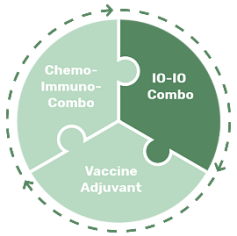
→

Primary endpoint: iORR (iRECIST)

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

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

Notes:
NSCLC – non-small-cell lung cancer, HNSCC – head and neck squamous cell cancer, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK –pharmacokinetics, PD-X – any PD-1 or PD-L1 treatment
*as of Feb 20th 2020



Efti: Clinical Development
TACTI-002 - Safety

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TACTI-002: Preliminary results – Safety, all parts

Summary

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

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

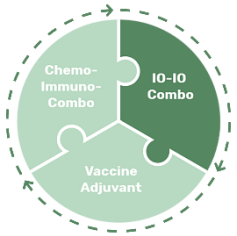
TEAEs occured in > 10% of pts (N=48 in total)*

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

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

*Treatment Emergent Adverse Event

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



Efti: Clinical Development
TACTI-002 - 1st line NSCLC (Part A)

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TACTI-002: Preliminary[1] results 1st line NSCLC – part A, stage 1

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

→ *Patients are typical NSCLC 1st line pts*

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

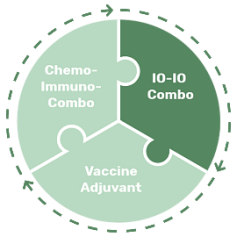
Central assessment of tumor cell PD-L1 expression done post enrollment		
PD-L1 (n=13)[2]	N (%)	Historical[3] Distribution
< 1%	3 (23%)	35%
1-49%	6 (46%)	35%
≥ 50%	4 (31%)	30%

Notes:

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

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

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



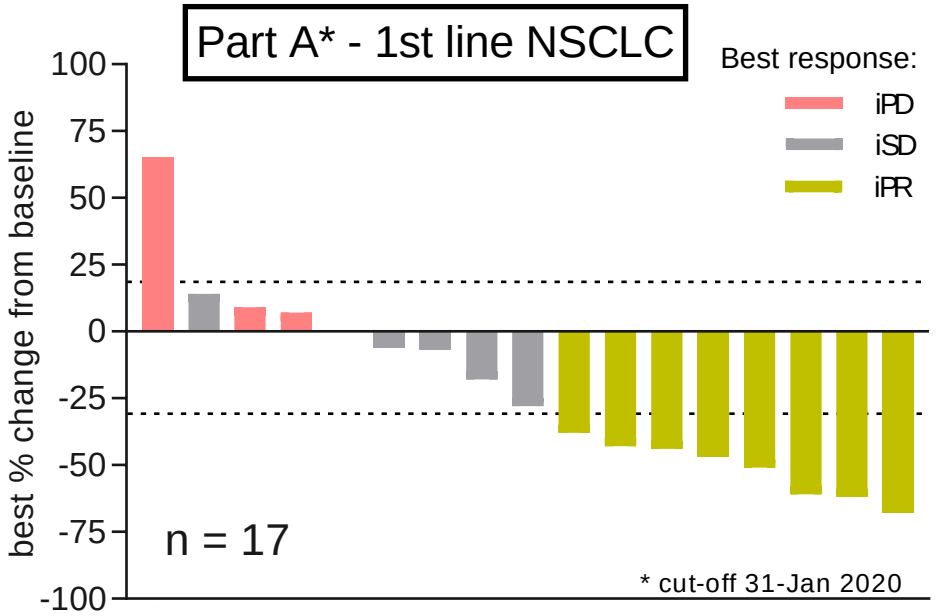
Efti: Clinical Development
TACTI-002 - 1st line NSCLC (Part A, Stage 1) - Results[1]

Responses and Waterfall plot

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

→ *Responses in all PD-L1 subgroups*

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



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

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

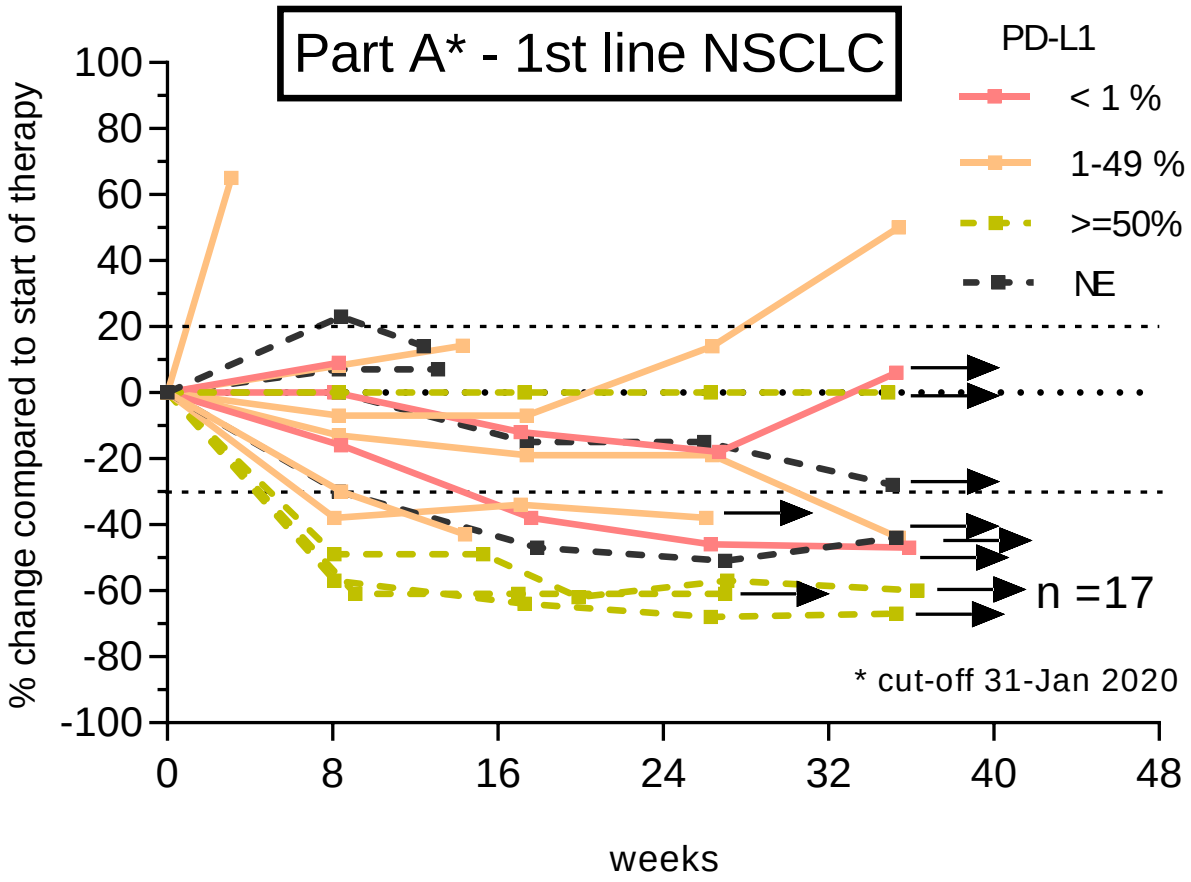
Notes:

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

Efti: Clinical Development
TACTI-002 - 1st line NSCLC (Part A, Stage 1) - Results[1]

Spiderplot

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



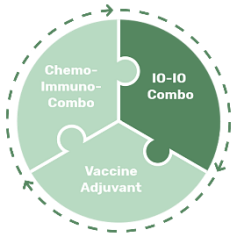
→ Patients continuing treatment

Main reason for discontinuation

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

Notes:

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



Efti: Clinical Development
TACTI-002 - 2nd line HNSCC (Part C, Stage 1) - Results[1]

Responses and Waterfall plot

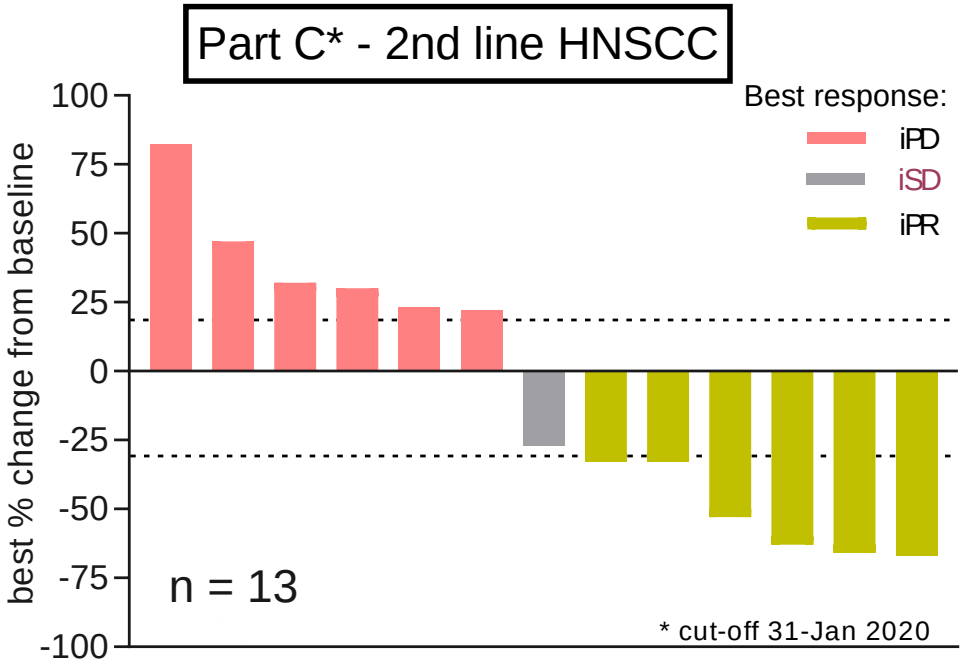
→ *Initial iORR of 33.3% in this PD-L1 all comer HNSCC 2nd line patient*

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

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

* - dropped out prior to first restaging

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

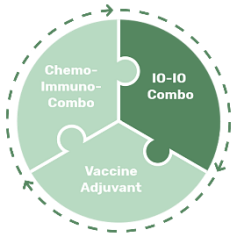


- LPI - Dec 2019 → 3 pts with outstanding imaging
- 7 pts (39%) had a decrease in target lesions
- All pts with iSD or iPR are still under treatment (median 6.4 months)

Note:

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

Comparables and Outlook



Efti: Clinical Development TACTI-002 (Phase II)

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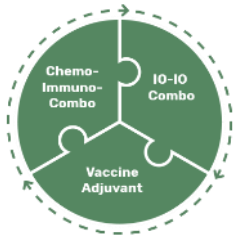
TACTI-002: Trial design/status details

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

Notes:
(1) Preliminary data, cut-off October 2019



Efti: a pipeline in a product

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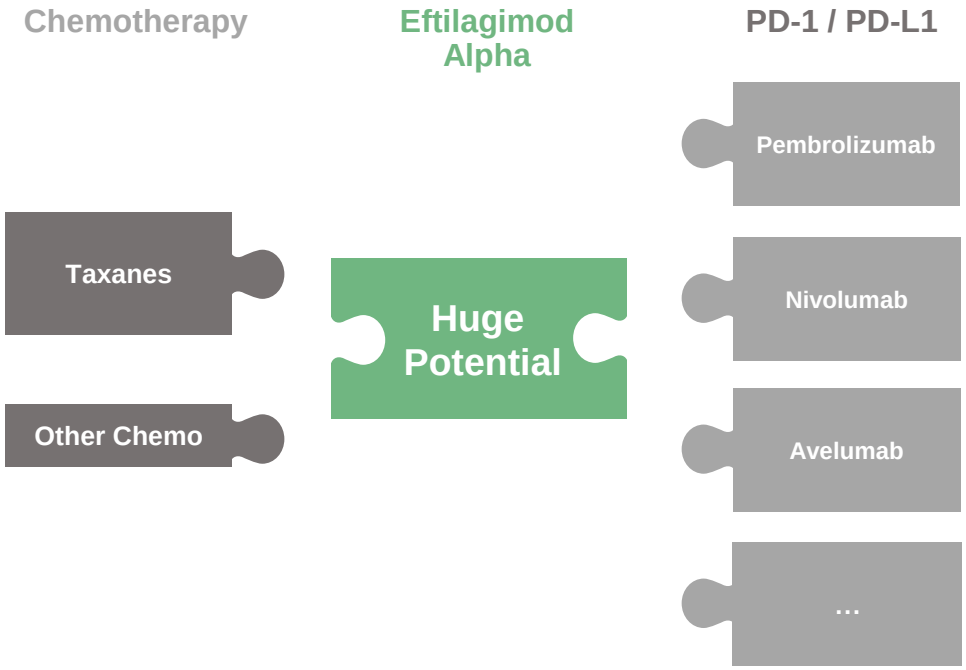
Efti is the ideal candidate to combine with
✓ chemo and ✓ PD-1/PD-L1 antagonists



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

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

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

Thank you!