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=ebcd827b2f840684111e57730c2b6cccd2c1

A replay of the webcast will also be available at www.immutep.com

*(ASX: IMM, NASDAQ: IMMP)*
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This presentation is authorised for release by the CEO of Immutep Limited.
Immutep 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
Immutep’s product candidates have demonstrated clinical potential in a range of indications with high unmet need.

Collaboration deals executed with industry leaders:
- Novartis
- Pfizer
- GlaxoSmithKline
- Merck KGaA, Darmstadt, Germany
- Merck
- EDOC
- Cytlimic
- LabCorp
LAG-3 Overview & Product Candidates
LAG-3 Pioneer: French immunologist
Frédéric Triebel, PhD, MD
Immutep CMO & CSO

https://en.wikipedia.org/wiki/Fr%C3%A9d%C3%A9ric_Triebel
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

**ASCO 2021:** significant increase in PFS for relatilimab + nivolumab → Target validation

Immutep is the only company with four LAG-3 related compounds each with a different mechanism of action
<table>
<thead>
<tr>
<th>Company</th>
<th>Program</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Total Trials</th>
<th>Patients</th>
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<tr>
<td>immutep</td>
<td>Eftilagimod Alpha</td>
<td></td>
<td>10</td>
<td>4</td>
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<td>BMS</td>
<td>Relatlimab</td>
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<td>7</td>
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<td>NOVARTIS</td>
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<td>Tesaro(3)</td>
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<td>1</td>
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<td>Incyte</td>
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<td>1</td>
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<td>Symphogen(2)</td>
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<td>3</td>
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</table>

Sources: GlobalData, Company websites, clinicaltrials.gov, and sec.gov, as of June 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 [link](https://www.sec.gov/Archives/edgar/data/872589/000110465919000977/a19-1325_18k.htm)
2) On 3 Apr. 2020 Les Laboratoires Servier Acquires Symphogen [link](https://www.sec.gov/Archives/edgar/data/872589/000110465919000977/a19-1325_18k.htm)
3) Tesaro was acquired by and is now part of GSK [link](https://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
Immutep Mission: Targeting LAG-3 / MHC II
Multiple product candidates in numerous diseases

Notes:
* APC: antigen presenting cell

✓ 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
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

**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 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 → 3rd validated checkpoint in immuno-oncology

**Notes:**
* APC: antigen presenting cell
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+ 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)

- **1st line after failure of CDK4/6 reinforced endocrine based therapy**
- **1st line chemo-free option for PD-L1 unselected met./advanced pts**
- **1st line chemo-free option for PD-L1 unselected met./advanced pts**
- **Single cases of PRs /benefit in pts with PD-1/PD-L1 refractory tumors**

**Combination Settings:**
- **Chemo-IO combo**
- **IO-IO combo**
**Clinical Development**

**Efti: Main Trials**

<table>
<thead>
<tr>
<th>Program</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Late Stage</th>
<th>Commercial Rights</th>
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<td>Metastatic Breast Cancer (Chemo – IO)</td>
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<td>AIPAC</td>
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<td>Head and Neck Squamous Cell Carcinoma (IO – IO)</td>
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<td>TACTI-003</td>
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<td>Head and Neck Squamous Cell Carcinoma (IO – IO)</td>
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<td>TACTI-002</td>
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<td>Non-Small-Cell Lung Carcinoma (IO – IO)</td>
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<td>TACTI-002</td>
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<td>Solid Tumors (IO – IO)</td>
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<td>INSIGHT-004</td>
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<td>Solid Tumors (IO – IO)</td>
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<td>INSIGHT-005</td>
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<td>Melanoma (IO – IO)</td>
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<td>TACTI-mel</td>
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<td>Solid Tumors (In situ Immunization)</td>
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<td>INSIGHT</td>
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<td>Solid Tumors (Cancer Vaccine)</td>
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<td>YNP01 / YCP02 / CRESCENT 1</td>
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<tr>
<td>Metastatic Breast Cancer (Chemo – IO)</td>
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</tbody>
</table>

**Notes:**
- Information in pipeline chart current as at June 2021
- In combination with KEYTRUDA® (pembrolizumab)
- INSIGHT Investigator Initiated Trial (IIT) is controlled by lead investigator and therefore Immutep has no control over this clinical trial
- a) Conducted by CYTLIMIC in Japan; b) Conducted by EOC in China; Immutep has no control over either of these trials.
- Late stage refers to Phase Ib clinical trials or more clinically advanced clinical trials
- Metastatic Breast Cancer (Chemo – IO) is not yet recruiting
Combining efti and anti-PD-1 pembrolizumab

TACTI-002
Three types of patient tumors

**Inflamed responder**
- Considerable immune cell infiltration e.g.: CD8+ Tc; Macrophages
- High levels of IFN-γ produced → inducing high PD-L1 expression on tumor cells

**Inflamed non-responder**
- Some infiltrates in the tumor margins but no response.
- Medium levels of IFN-γ produced → inducing low PD-L1 expression on tumor cells

**Non-inflamed non-responder**
- Minimal to no immune cell infiltration on the tumor margins.
- Low levels of IFN-γ produced → no induction of PD-L1 expression on tumor cells

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

Due to low level of TH1 (IFN-γ) driven T-cell activation → unlikely to respond to ICI treatment

Due to low numbers of infiltrating T-cells → unlikely to respond to ICI treatment
TACTI-002 (Phase II)
Design & Status

TACTI-002: Two ACTive Immunotherapeutics in NSCLC and HNSCC

**UNSELECTED FOR PD-L1**

**PART A:**
1\(^{ST}\) LINE MET. NSCLC

**PART B:**
2\(^{ND}\) LINE MET. NSCLC, REFRACTORY TO PD-1/PD-L1 TARGETING THERAPY

**PART C:**
2\(^{ND}\) LINE MET. HNSCC AFTER PLATINUM THERAPY

**COMBINED IMMUNOTHERAPY**
Pembrolizumab+Efti for 12 MONTHS + 12 MONTHS Pembrolizumab MONO

**Status Report**
- Fully approved in all countries
- Up to 183 patients in three indications
  - Part A (N=36) completed; extension (N=74 recruiting)
  - Part C (N=39) completed
  - Part B (N=36); stage 2 recruitment ongoing

**In collaboration with**
Merck

**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
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 ≥ 1 adverse events ≥ grade 3
- No new safety signals of this combination identified until cut-off

Selected safety aspects of other treatment regimens

<table>
<thead>
<tr>
<th>Regimen(2)</th>
<th>Treatment related adverse events leading to discontinuation</th>
<th>Treatment related adverse events leading to death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double Chemo</td>
<td>8-22%</td>
<td>1-6%</td>
</tr>
<tr>
<td>Ipi + Nivo</td>
<td>20%</td>
<td>&lt; 2%</td>
</tr>
<tr>
<td>Chemo + Pembro</td>
<td>23-33%</td>
<td>3-8%</td>
</tr>
<tr>
<td>Pembro alone</td>
<td>10-15%</td>
<td>&lt; 2%</td>
</tr>
</tbody>
</table>

✓ Efti + pembrolizumab combination has a very good safety profile
✓ Favorable compared to any combination which included chemotherapy

Notes:
(1) Preliminary data, cut-off 16-Apr 2021
(2) Source: Calculated from corresponding publications e.g.: Checkmate-227; Keynote-40/189/407/48;
Non-Small Cell Lung Cancer (NSCLC)

Introduction

High unmet medical need for well tolerated and efficacious treatment options

Epidemiology\(^{(1)}\):
- 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

Stage IV NSCLC: Molecular Test Negative (ALK/BRAF/EGFR/ROS1)

PD-L1 expression

PD-L1 ≥ 50 \%

Any PD-L1

1st line:
- anti-PD-1/PD-L1
- anti-PD-1/PD-L1 + Doublet Chemo
- Doublet Chemo

2nd line:
- Chemo
- PD-1 / PD-L1 / Chemo

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**

1st line NSCLC (Part A)

- **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

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

### Best overall response, iRECIST, N = 36

<table>
<thead>
<tr>
<th>Response</th>
<th>Local Read (investigator) N (%)</th>
<th>Blinded Read (BICR) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>2 (5.6)</td>
<td>2 (5.6)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>11 (30.6)</td>
<td>13 (36.1)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>11 (30.6)</td>
<td>10 (27.8)</td>
</tr>
<tr>
<td>Progression</td>
<td>8 (22.2)</td>
<td>6 (16.7)</td>
</tr>
<tr>
<td>Not Evaluable**</td>
<td>4 (11.1)</td>
<td>5 (13.9)</td>
</tr>
<tr>
<td>Disease Control Rate</td>
<td>24 (66.7)</td>
<td>25 (69.4)</td>
</tr>
</tbody>
</table>

- **Overall Response Rate**
  - [95% CI interval]
    - Local Read: 13 (36.1) [20.8-53.8]
    - Blinded Read: 15 (41.7) [25.5-59.2]

- **Overall Response Rate – Evaluable pts***
  - [95% CI interval]
    - Local Read: 13 (40.6) [23.7-59.4]
    - Blinded Read: 15 (48.4) [30.1-60.9]

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* - 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

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Notes:

(1) Preliminary data, cut-off Apr 16, 2021
ECOG...Eastern Cooperative Oncology Group
RECIST...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

Best response:
- iUPD/iCPD
- iSD
- iPR
- iCR

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

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.

* cut-off 16-Apr 2021; n= 33

PD-L1 TPS

(1) Preliminary data, cut-off Apr 16, 2021
### TACTI-002 Results

1\textsuperscript{st} line NSCLC (Part A) - Benchmarking

<table>
<thead>
<tr>
<th>ORR (%)</th>
<th>PD-L1 (TPS)</th>
<th>Pembro alone** (NSQ+SQ)</th>
<th>Pembro + Efti*** (NSQ+SQ)</th>
<th>Pembro + Chemo NSQ</th>
<th>Pembro + Chemo SQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 50</td>
<td>39.5</td>
<td>53.8*</td>
<td>62.1</td>
<td>60.3</td>
<td></td>
</tr>
<tr>
<td>≥ 1</td>
<td>27.3</td>
<td>44.0*</td>
<td>~ 55.8</td>
<td>~ 55.1</td>
<td></td>
</tr>
<tr>
<td>&lt; 50</td>
<td>--</td>
<td>31.6*</td>
<td>~ 40.7</td>
<td>~ 57.1</td>
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<table>
<thead>
<tr>
<th>PFS (mths)</th>
<th>Overall pop.</th>
<th>-</th>
<th>Pembro alone** (NSQ+SQ)</th>
<th>Pembro + Efti*** (NSQ+SQ)</th>
<th>Pembro + Chemo NSQ</th>
<th>Pembro + Chemo SQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall pop.</td>
<td>--</td>
<td>-</td>
<td>8.2</td>
<td>9.0</td>
<td>6.4</td>
<td></td>
</tr>
<tr>
<td>≥ 50</td>
<td>7.1</td>
<td>-</td>
<td>11.8</td>
<td>11.1</td>
<td>8.0</td>
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</tr>
</tbody>
</table>

**ORR & PFS comparable**

**Improved DoR**

**Less toxicity**

- Increased ORR & median PFS
- Responses in PD-L1 low expressors
- Comparable safety profile

* Pts with PD-L1 results available and ≥ 1 post baseline RECIST assessments (32/36); ** Data for pembrolizumab derived from KN042, KN189, and KN-407\textsuperscript{(2)(3)(4)}; *** According to investigator read

### Toxicity

- Pembro alone: Well tolerated
- Pembro + Efti: No significant add. toxicity
- Pembro + Chemo: + toxicity

- Co-med: No add. co-med required
- Pembro + Efti: + cost of chemo co-med

### References

1. Preliminary data, cut-off 16 Apr 2021 for TACTI-002
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\(^{(1)}\)
- 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\(^{st}\) line barely exceeds 12 months
- ORR of 10-18% in 2\(^{nd}\) line regardless of therapy

Notes:
(3) FDA and EMA approval differences. Pembrolizumab approval by the European Medicines Agency is for patients whose tumours express PD-L1 with a ≥ 50% TPS, which differs from FDA approval.
# 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) &nbsp;&nbsp; N (%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (years)</td>
<td>62 (37-84)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (10.3)</td>
</tr>
<tr>
<td>Male</td>
<td>35 (89.7)</td>
</tr>
<tr>
<td>ECOG 0</td>
<td>13 (33.3)</td>
</tr>
<tr>
<td>ECOG 1</td>
<td>26 (66.7)</td>
</tr>
<tr>
<td>Current / Ex-smokers</td>
<td>33 (84.6)</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>6 (15.4)</td>
</tr>
<tr>
<td>Previous chemotherapy</td>
<td>39 (100)</td>
</tr>
<tr>
<td>Previous cetuximab</td>
<td>16 (41.0)</td>
</tr>
<tr>
<td>Lung lesions</td>
<td>19 (48.7)</td>
</tr>
<tr>
<td>Liver lesions</td>
<td>6 (17.6)</td>
</tr>
</tbody>
</table>

## Best overall response*, iRECIST

<table>
<thead>
<tr>
<th>Status</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>5 (13.5)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>6 (16.2)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>3 (8.1)</td>
</tr>
<tr>
<td>Progression</td>
<td>17 (45.9)</td>
</tr>
<tr>
<td>Not Evaluable**</td>
<td>6 (16.2)</td>
</tr>
<tr>
<td>Disease Control Rate</td>
<td>14 (37.8)</td>
</tr>
</tbody>
</table>

## Investigator assessment N (%)

### Overall Response Rate

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Response Rate</td>
<td>11 (29.7)</td>
</tr>
<tr>
<td>[95% CI interval]</td>
<td>[15.9 – 47.0]</td>
</tr>
</tbody>
</table>

### Overall Response Rate – Evaluable pts***

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Response Rate</td>
<td>11 (35.5)</td>
</tr>
<tr>
<td>[95% CI interval]</td>
<td>[19.2 – 54.6]</td>
</tr>
</tbody>
</table>

---

* - 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\(^{(1)}\)
2\(^{nd}\) 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

Note:
\(^{(1)}\) Preliminary data, cut-off 16 Apr 2021
\(^{**}\) >= 1 post baseline tumor staging (N=31)
TACTI-002 Results\(^{(1)}\)
2\(^{nd}\) 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)
(3) ** >= 1 post baseline tumor staging (N=31)
## TACTI-002 Results\(^{(1)}\)

**2nd line HNSCC (Part C) – Benchmarking**

<table>
<thead>
<tr>
<th></th>
<th>PD-L1 (CPS)</th>
<th>Pembro alone(^{**})</th>
<th>TACTI-002</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR (%)</strong></td>
<td>≥ 1</td>
<td>17.3 (2% CR)</td>
<td>45.8* (20.8% CR(^{*}))</td>
</tr>
<tr>
<td></td>
<td>Overall pop.</td>
<td>14.6</td>
<td>35.5(^{#})</td>
</tr>
<tr>
<td><strong>mPFS (mths)</strong></td>
<td>≥ 1</td>
<td>2.2 (28.7% PFS rate at 6 mths)</td>
<td>4.1* (45% PFS rate at 6 mths)</td>
</tr>
<tr>
<td></td>
<td>Overall pop.</td>
<td>2.1 (25.6% PFS rate at 6 mths)</td>
<td>2.1(^{§})</td>
</tr>
<tr>
<td><strong>mOS (mths)</strong></td>
<td>≥ 1</td>
<td>8.7 (40% alive at 12 mths)</td>
<td>12.6* (54% alive at 12 mths)</td>
</tr>
<tr>
<td></td>
<td>Overall pop.</td>
<td>8.4 (37% alive at 12 mths)</td>
<td>12.6(^{§})</td>
</tr>
</tbody>
</table>

* - 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)\(^{(4)}\)
- Duration of response drops dramatically if you add chemo\(^{(5)}\) – 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)

---

**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
5. KN-048: The Lancet, 2019; https://doi.org/10.1016/S0140-6736(19)32591-7
Combining efti and anti-PD-L1 avelumab

INSIGHT-004
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

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
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; 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

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

Cytokines
- Interleukins (IL2; IL15...)
- Interferons (IFN-a...)

CAR T-Cells
- Yescarta
- Tecartus
- Kymriah

APC activators
- Efti
  - CD40
  - TLRs
  - STING

Oncolytic Viruses
- Adenovirus
- Herpes v.
- Reoviruses
- coxsackie v
-...

Monoclonal antibodies
- a-CD22
- a-CD47
- a-VEGF
- a-HER2
-...

Checkpoints inhibitors
- a-PD-(L)1
- a-CTLA-4
- a-LAG-3
- a-TIGIT
- ...

Cancer Vaccines
- Antigen
- Whole Cell
- Dendr. Cell
- DNA
- a-idiotype

Efti: Leader in its Class of Oncology Products
Summary and Outlook
**TACTI-003 Trial in 1st line HNSCC**

1st line HNSCC SoC

<table>
<thead>
<tr>
<th>Median OS from KN-048 (1), unselected for PD-L1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>10.7-11.0</strong></td>
</tr>
<tr>
<td><strong>11.6</strong></td>
</tr>
<tr>
<td><strong>13.0</strong></td>
</tr>
</tbody>
</table>

↑ to 14.9 for CPS ≥ 20
↑ to 14.7 for CPS ≥ 20

→ OS improved by ~2 months, but pembrolizumab non-inferior to chemo alone
→ CPS predictive for OS for pembrolizumab

<table>
<thead>
<tr>
<th>Median DoR from KN-048 (1), unselected for PD-L1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4.3</strong></td>
</tr>
<tr>
<td><strong>22.6</strong></td>
</tr>
</tbody>
</table>

→ DoR dramatically decreased in the light of higher response rate (36 % vs. 17 %) for chemo containing arms

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 pembrolizumab alone would be excellent

**Notes:**
(1) B Burtness et al.: Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. The Lancet 2019, https://doi.org/10.1016/S0140-6736(19)32591-7
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**
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 alpha. Conducted as the 5th arm of the INSIGHT trial.

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

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

**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**

**Phase I**
- Open label trial

**12 months**
- Combination treatment

**12 Patients in 3 cohorts**

**Two sites**
- Germany

**Merck KGaA, Darmstadt, Germany**

In collaboration with

Institut für Klinisch-Onkologische Forschung

Krankenhaus Nordwest
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\textsuperscript{st} line NSCLC
  - 2\textsuperscript{nd} line NSCLC
  - 2\textsuperscript{nd} 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\textsuperscript{st} line HNSCC from US FDA
- Final data from AIPAC: 2\textsuperscript{nd} 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 1\textsuperscript{st} 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

*The actual timing of future data readouts may differ from expected timing shown above. These dates are provided on a calendar year basis.*
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 efti & strong rationale to combine with multiple FDA approved treatments

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