immutep
LAG-3 IMMUNOTHERAPY

# The global leader in developing LAG-3 therapeutics

*(ASX: IMM, NASDAQ: IMMP)*

## *Extraordinary General Meeting*
## *CEO Presentation*

*26 July 2021*

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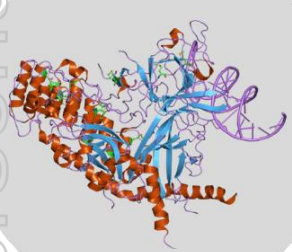
*This presentation is authorised for release by Marc Voigt, CEO of Immutep Limited.*

# Overview





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

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# LAG-3 Overview

# - Landscape-

# LAG-3 Acceleration & Validation



## LAG-3 is an exciting and promising immune checkpoint for cancer treatment

**Accelerating interest in LAG-3:**

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

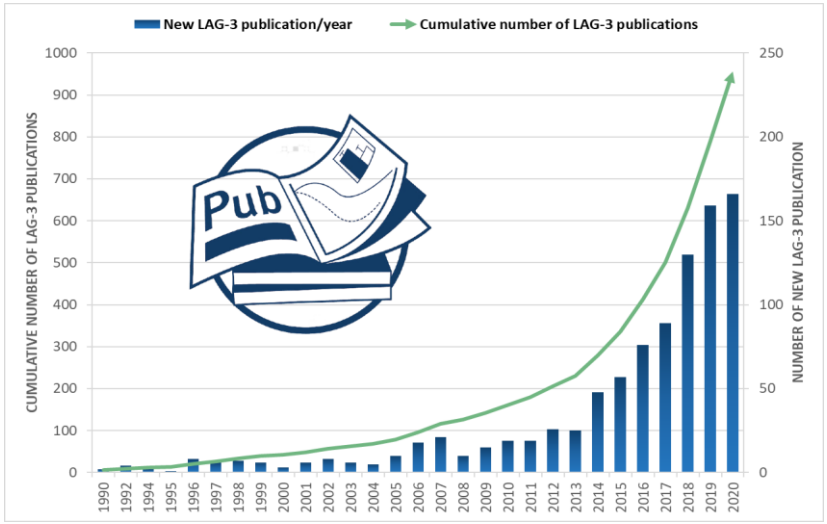
**Recent LAG-3 validation:**

- Interaction between LAG-3 and MHC class II was recently validated by pharma company Bristol Myers Squibb with Phase III data
- Its anti-LAG-3 antibody is helping patients with melanoma to live significantly longer without disease progression (PFS)

**Immutep is the leading LAG-3 immunotherapy biotech**

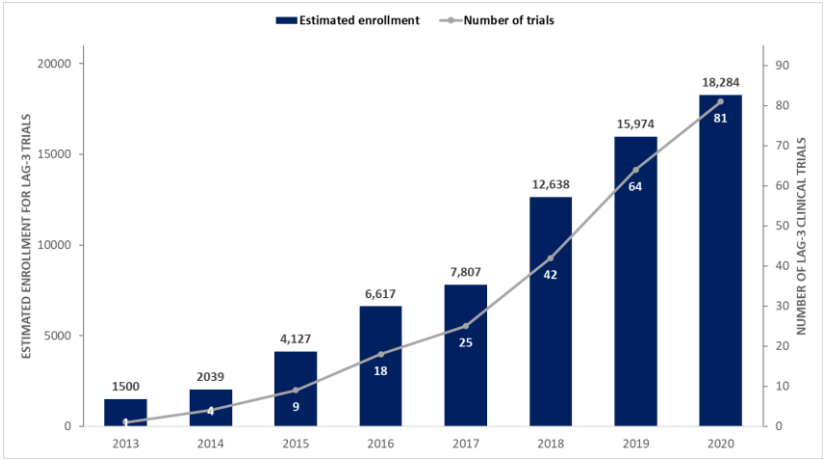
**It is the only company with four LAG-3 related compounds each with a different mechanism of action.**

### LAG-3 Scientific Publications




Source: PubMed

### LAG-3 Clinical Trials




Source: GlobalData, May 2021

# Immutep's LAG-3 Trial Pipeline*

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| Program | Preclinical | Phase I | Phase II | Late Stage[5] | Commercial Rights | Market Size[6] |
|---|---|---|---|---|---|---|
| **Oncology** — Eftilagimod Alpha (efti or IMP321); 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 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 LAG-3 Trial Pipeline*



| Program | Preclinical | Phase I | Phase II | Late Stage[1] | Commercial Rights/Partners | Updates |
|---|---|---|---|---|---|---|
| Oncology<br>LAG525 (Antagonist AB) | Solid Tumors + Blood Cancer (IO-IO Combo)<br>Triple Negative Breast Cancer (Chemo-IO Combo)<br>Melanoma (IO-IO-Small Molecule Combo)<br>Solid Tumors (IO-IO Combo)<br>Triple Negative Breast Cancer (Chemo-IO-Small Molecule Combo) | | | | Global Rights<br>NOVARTIS | Novartis currently has five clinical trials ongoing for LAG525 in multiple cancer indications for over 1,000 patients.[4] |
| Autoimmune<br>GSK'781 (Depleting AB) | Ulcerative Colitis[6]<br>Healthy Japanese and Caucasian Subjects[2]<br>Psoriasis[3] | | | | Global Rights<br>gsk | Two successful Phase I studies, but the Phase II clinical study in up to 242 ulcerative colitis patients was discontinued.[5] |

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

# TACTI-002 (Phase II)

## Design & Status

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**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. |

**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

**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) |

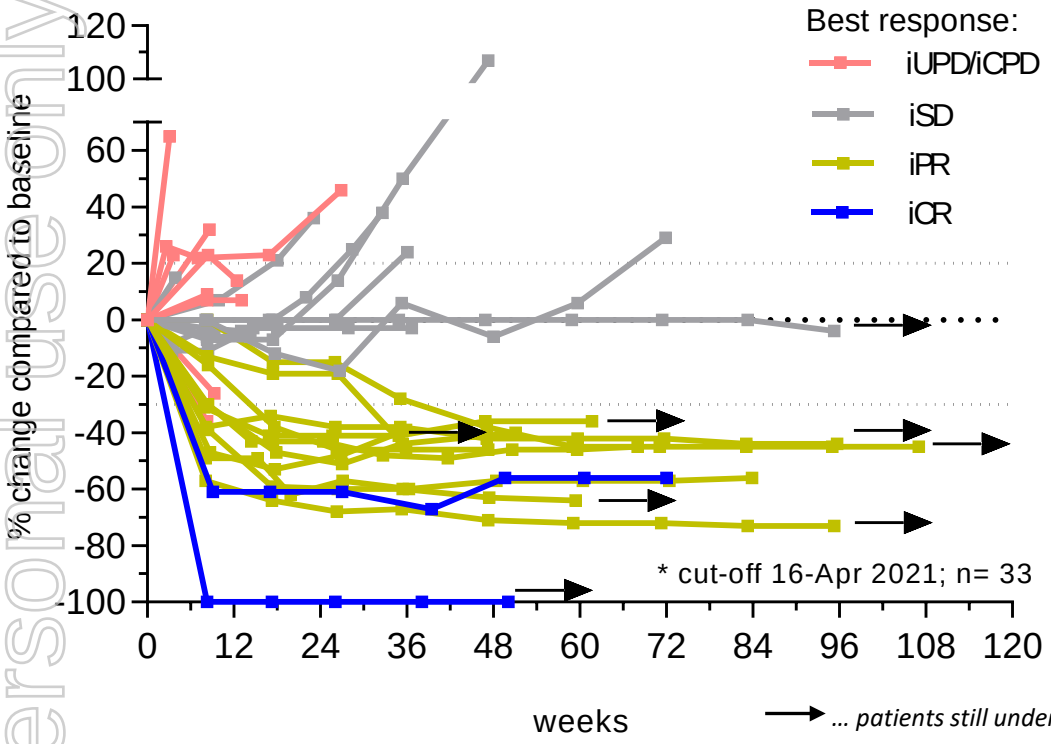
| Best overall response, iRECIST, N = 36 | Local Read (investigator) N (%) | Blinded Read (BICR) N (%) |
|---|---|---|
| **Complete Response** | **2 (5.6)** | **2 (5.6)** |
| Partial Response | 11 (30.6) | 13 (36.1) |
| Stable Disease | 11 (30.6) | 10 (27.8) |
| Progression | 8 (22.2) | 6 (16.7) |
| Not Evaluable** | 4 (11.1) | 5 (13.9) |
| Disease Control Rate | 24 (66.7) | 25 (69.4) |
| **Overall Response Rate* [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]** |

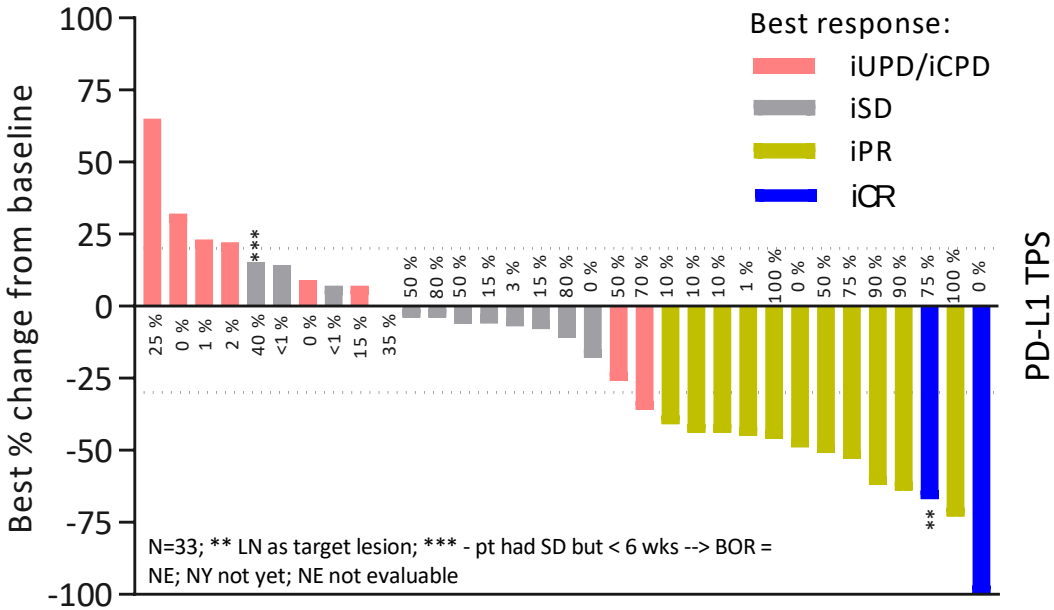
** - All patients stage 1 and 2 (N=36) with* ≥ 1 treatment
*** - dropped off prior to first staging or were not evaluable post-baseline for any reason*
**** - Evaluable for efficacy meaning* ≥ 1 treatment and ≥ 1 post baseline tumor staging

*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)

## 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]** |

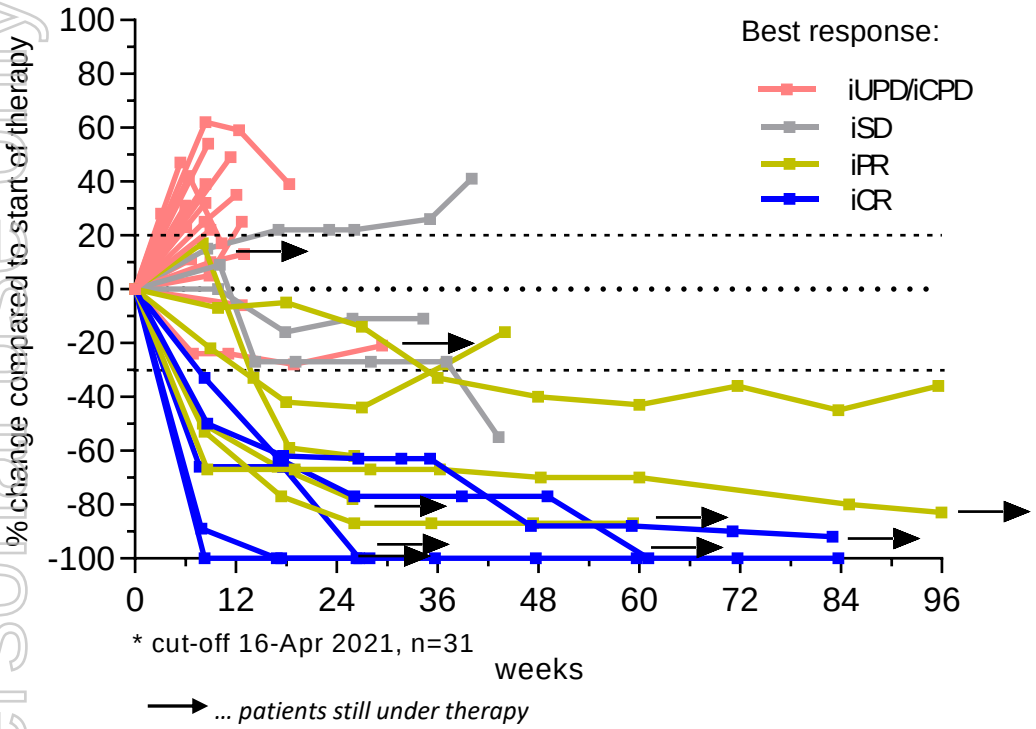
* - *All patients (N=37) with* ≥ 1 treatment and no death due to COVID-19 prior to first post-baseline staging
** - *dropped off prior to first staging or were not evaluable post-baseline for any reason*
*** - *evaluable patients (N=31):* ≥ 1 treatment and ≥ 1 post baseline tumor staging

**All four pathologies enrolled**

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

# TACTI-002 Results(1)

## 2nd line HNSCC (Part C)



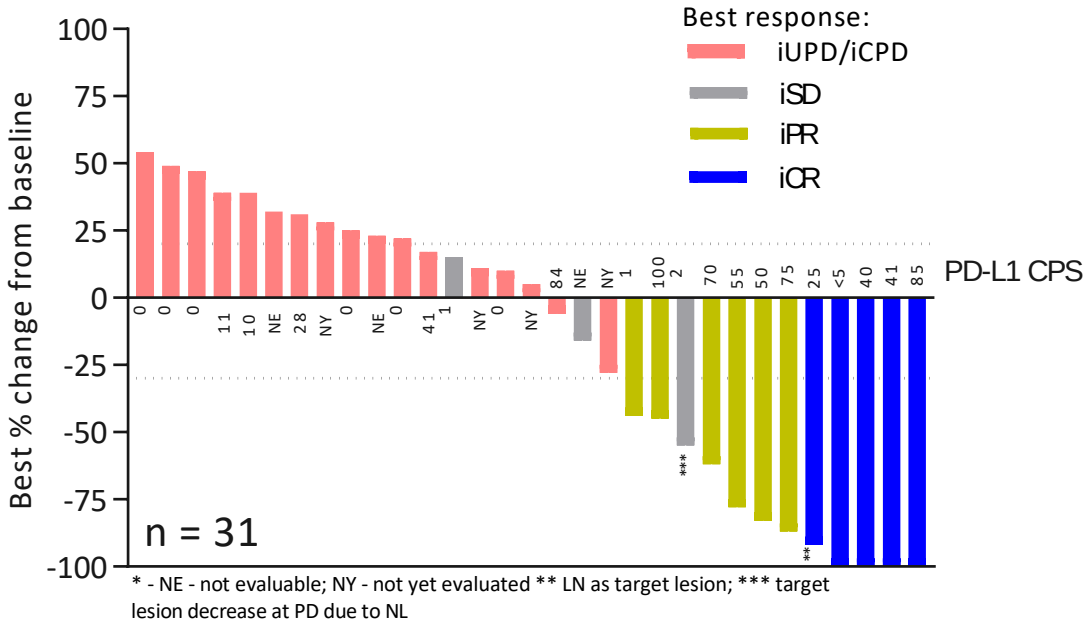
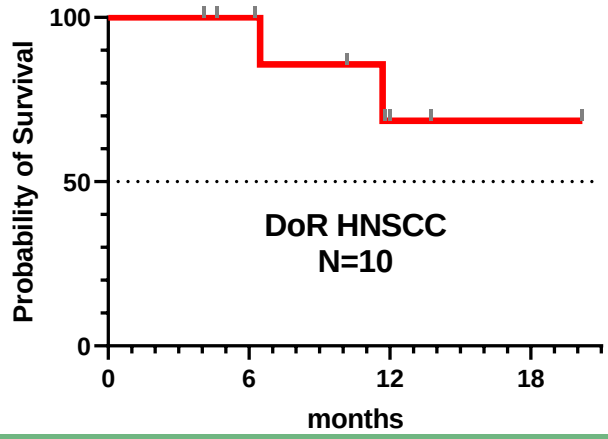




*Figure 3: Duration of response (DOR) for confirmed responders*




**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:*

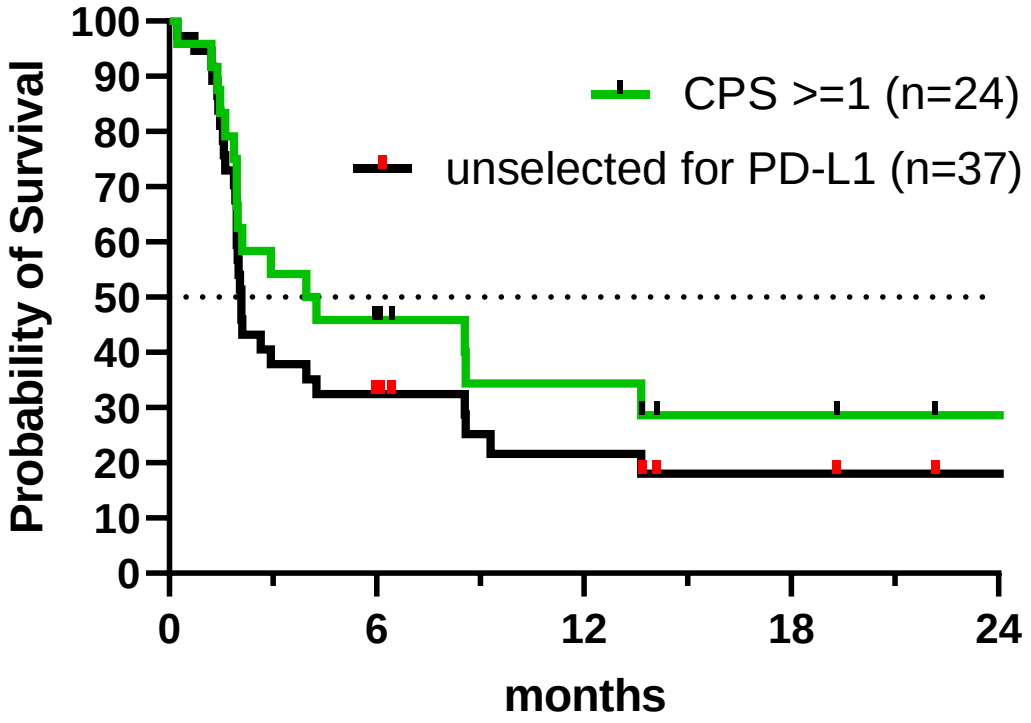
(1) Preliminary data, cut-off 16 Apr 2021
** >= 1 post baseline tumor staging (N=31)

# 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)

# INSIGHT-004 (Stratum D) Results(1)



## 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

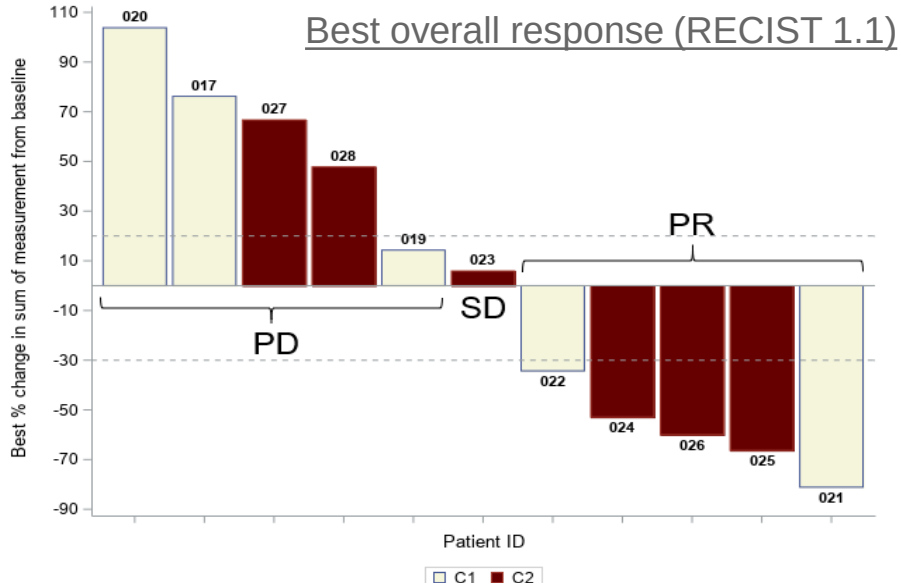
## Safety

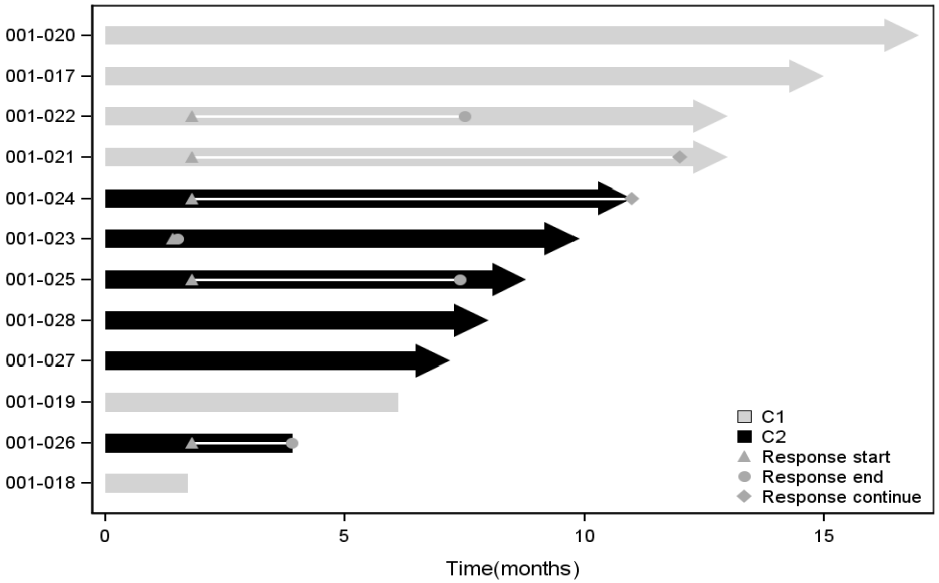
- Combo of avelumab 800 mg + efti 6 mg or 30 mg efti s.c. is feasible and safe
- No unexpected AEs

## 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

Best overall response (RECIST 1.1)




Triangles at the end of the chart represents the survival status



*Note:*

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

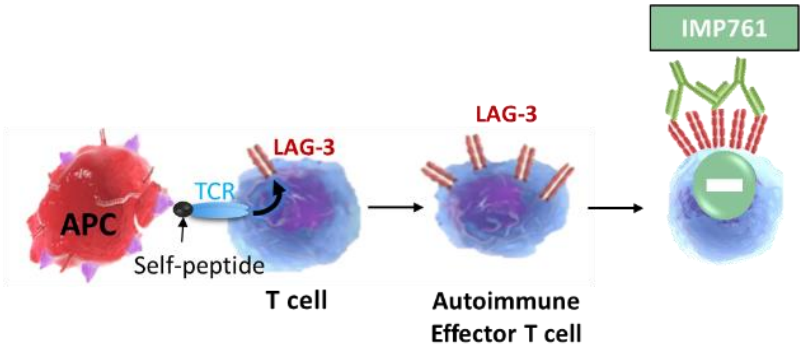
# IMP761 a Potential Game Changer for Autoimmune Diseases



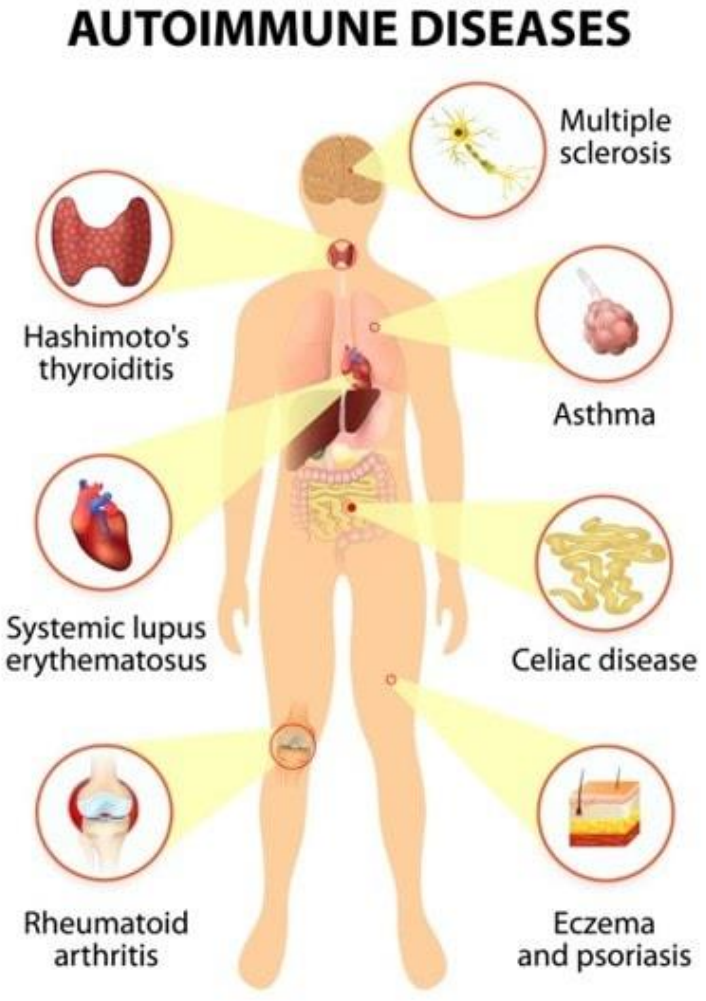
Current autoimmune drugs fight the symptoms, treating general inflammation (corticoids, methotrexate, anti-TNF-α, -IL-6, -IL-17, -IL-23 mAbs)

IMP761 potentially fights the cause, treating the disease process by silencing the few autoimmune memory T cells accumulating at the disease site

Immutep to submit an Investigational New Drug (IND) application with the US FDA to begin clinical trials




**US$153.32 billion market by 2025[1]**




IMP761 has broad potential in targeting auto-reactive memory T cells



Notes

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

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# New Efti Studies

## - TACTI-003, INSIGHT-005 & INSIGHT-003 -

# Positive data driving expansion of clinical program



With the ongoing strength of data reported at leading conferences SITC 2020; SABCS 2020; ASCO 2021), Immutep plans to expand and advance its clinical portfolio(1):

**New Phase III Registration Trial**

Metastatic breast cancer (based on AIPAC)

**New Phase II Trial**

e.g. Triple therapy: anti-PD1 + chemo + efti combination

**Other Trials**

Two new investigator-initiated trials (IITs) with up to 40 pts each

**Manufacturing**

Commence process characterisation and validation for efti commercial manufacturing (2,000 L scale)

**Regulatory**

Ongoing interactions with the FDA and EMA

**Autoimmune Program**

IND package for IMP761

**Strengthen the team**

and research projects

**Immutep expects a range of clinical trials to have significant data read outs in the coming years**



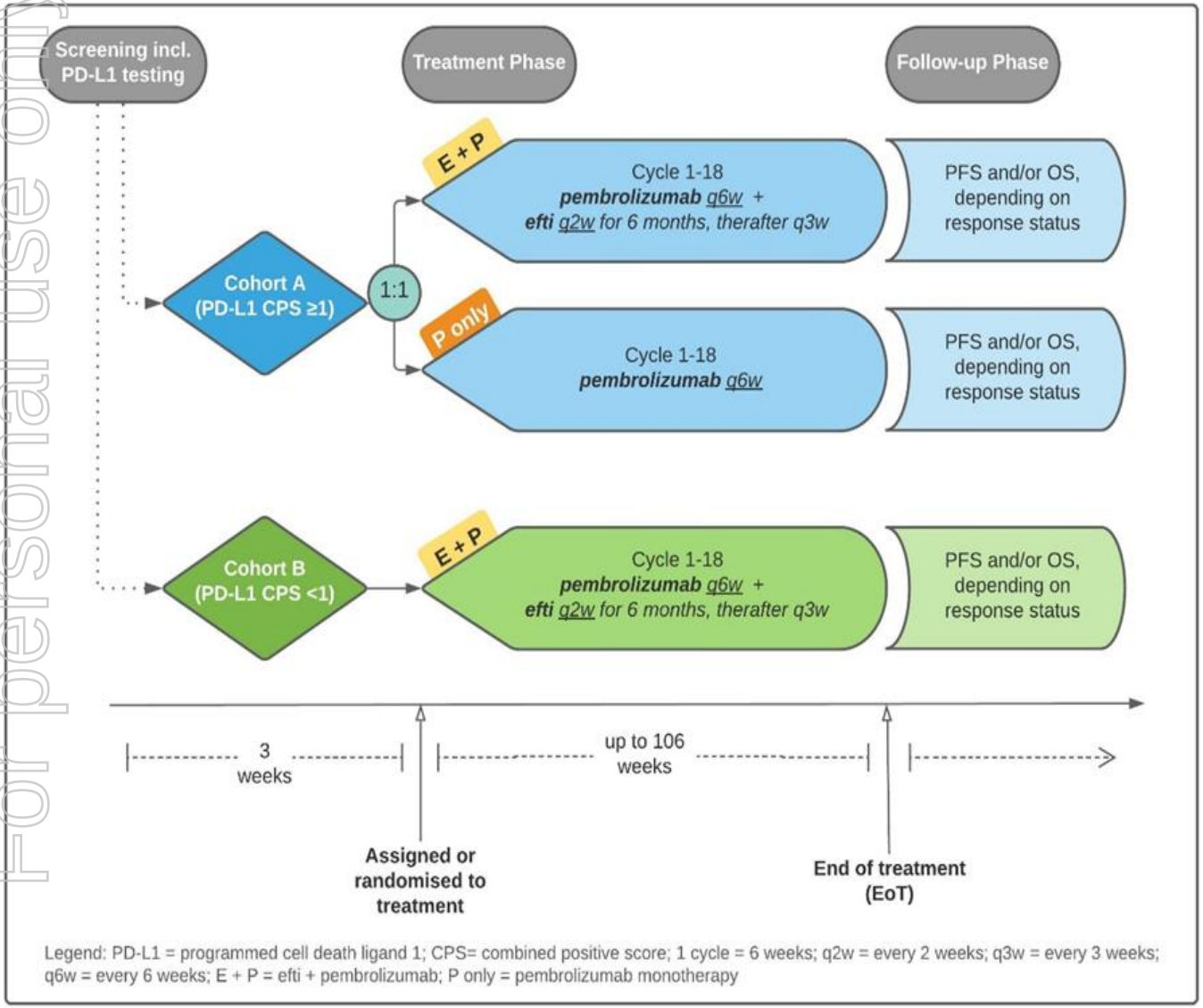
Notes

(1) Expansion and advancement of clinical portfolio is subject to achieving relevant regulatory approvals.

# TACTI-003 Trial in 1st line HNSCC

Current Design + Status






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

**In collaboration with**

MERCK
INVENTING FOR LIFE

**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:**

- Study start up announced on 6 July 2021, with patient recruitment expected to begin within Q3 of calendar year 2021.
- **Fast Track designation granted by FDA in April 2021**

# INSIGHT Platform Trial in Solid Tumours

INSIGHT-005 study arm (Stratum E): Efti + Bintrafusp Alfa combo

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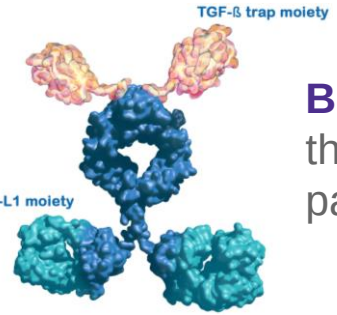
**To evaluate the feasibility and safety of combined treatment with bintrafusp alfa (M7824) and eftilagimod alpha.**

**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

**Phase I/IIa**
Open label trial

**12**
Patients in 3 cohorts

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

**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** 1200 mg i.v.
- **eftilagimod alpha** 30 mg s.c.

→

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

# INSIGHT Platform Trial in Solid Tumours

New INSIGHT-003 study arm (Stratum C): Efti + anti-PD-1 + chemo



## First evaluation of efti in a triple combination therapy

INSIGHT-003 is a new stratum of the investigator-initiated phase I trial, INSIGHT

- Expansion into triple combination therapy of efti, standard of care chemotherapy and anti-PD-1 therapy
- Regulatory and ethical approvals received enabling patient recruitment
- First patient expected to be enrolled in Q3 of calendar year 2021 and first interim results expected in 2022
- Results to inform about safety and activity

Phase I study

Up to 20 patients
with various solid tumours

Safety, tolerability & initial activity

One site
Germany

24 weeks
therapy duration

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# Corporate Snapshot
# &
# Outlook

# Corporate Snapshot

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| | |
|---|---|
| **Ticker symbols** | IMM (ASX)<br>IMMP (NASDAQ) |
| **Securities on issue**(1)<br>(post transaction) | ~ 850.92 million ordinary shares |
| **Proforma cash balance**(2)<br>(post transaction) | ~ A$114.03 million (US$85.73 million) |
| **Market Cap**(3)<br>(post transaction) | ~ A$425.46 million (US$311.61 million) |

*Notes:*
*NB: All above figures are provided on a "post transaction" basis and include new Shares from the completed Share Purchase Plan (SPP) (the details of which were announced to ASX on 21 July 2021) and assumes Tranche 2 Placement Shares are approved by shareholders at today's EGM.*
*(1) As at 30 Jun 2021, 39.04% 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 at 30 June 2021 plus the gross proceeds from the SPP and Tranche 2 share issuance.*
*(3) Market capitalization based on ASX close share price of A$0.50 on 21 July 2021 and basic ordinary shares outstanding on a post transaction basis.*
*US equivalent of amounts above are based on foreign exchange rate for AUD/USD of 0.7324 for market capitalization, and the US cash & cash equivalents amount was calculated using FX rate of 0.7518.*

# 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 in H2 2021
- ❑ Start & ongoing recruitment of **new randomised trial in 1st line HNSCC** (TACTI-003) in Q3 2021
- ❑ Recruitment & further data from **TACTI-002** in 2021 or early 2022
- ❑ **INSIGHT-003** first patient enrolled in Q3 2021 and first interim results in 2022
- ❑ **INSIGHT-005** first patient enrolled in H2 2021
- ❑ Manufacturing scale up to 2,000 L
- ❑ Ongoing **regulatory** engagement
- ❑ Updates from **IMP761**
- ❑ 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.

immutep

LAG-3 IMMUNOTHERAPY

# Thank You