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LAG-3 IMMUNOTHERAPY

# The global leader in developing LAG-3 therapeutics

**BioCentury 25th Annual NewsMakers in the Biotech Industry Conference**
**New York**
**7th September 2018**

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

# Notice: Forward Looking Statements

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# Company Snapshot

- Globally active biotechnology company with operations in Australia, Europe and U.S.
- Four LAG-3 related product candidates in development in immuno-oncology and autoimmune disease
- Committed partnerships with three of the world's largest pharmaceutical companies - Merck (MSD), Novartis and GSK, along with Eddingpharm in China
- Backed by high profile institutional healthcare investors: Platinum Asset Management and Australian Ethical in Australia, along with Ridgeback Capital in the U.S.
- Meaningful clinical, regulatory, and corporate news flow throughout calendar 2018 and 2019

## Capital Structure

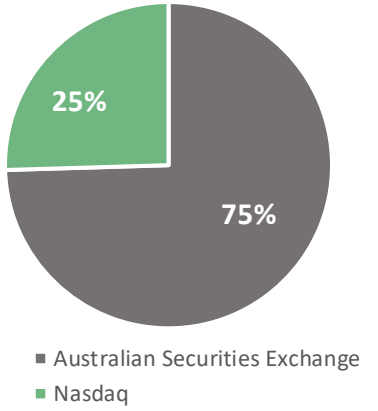
| | |
|---|---|
| **Ticker symbols** | IMM (Australian Securities Exchange)<br>IMMP (NASDAQ - ADRs) |
| **Securities on issue**<br>(as at 17 August 2018) | 3.0 billion ordinary shares<br>7.7 million issued ADRs |
| **Cash & Term Deposits**[1]<br>(as at 30 June 2018) | A$23.5 million (~US$17.4 million) |
| **Market Cap**<br>(as at 17 August 2018) | A$105.9 million (~US$77.1 million) |
| **Avg. Vol.** (3 months)<br>(as at 30 June 2018) | 5.2 million ordinary shares on ASX<br>77 k ADRs on NASDAQ |

*Notes:*

*(1) Cash balance does not include the A$1.9mm (US$1.4mm) R&D rebate received from the French government (21 August 2018)*

*Market capitalisation based on ASX ordinary share price. For a detailed summary of all securities on issue refer to latest Appendix 3B released on ASX. Each ADR represents 100 ordinary shares*

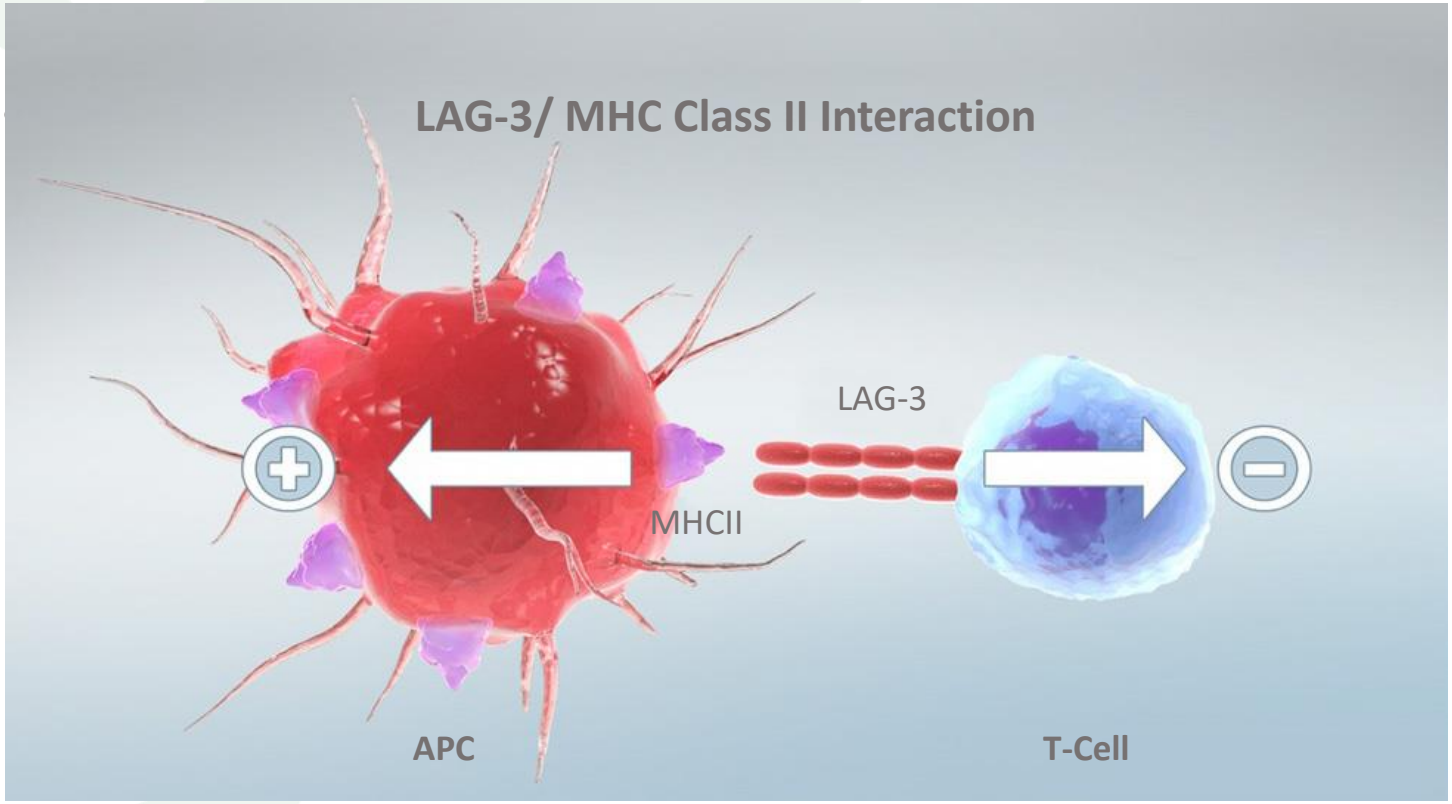
## Shareholders



# LAG-3 Overview & Product Candidates

# LAG-3 as a Therapeutic Target

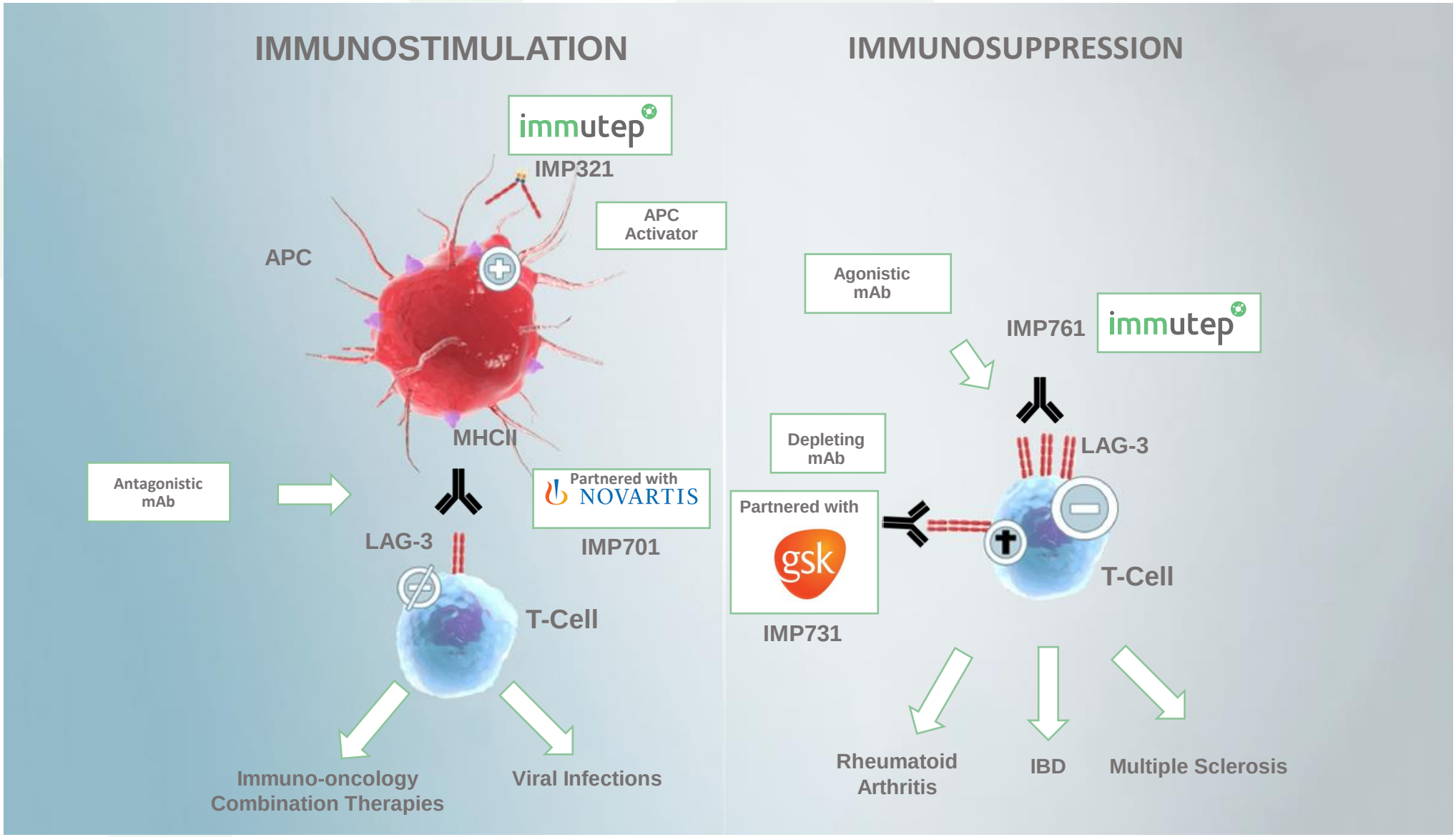
- LAG-3 is widely expressed on tumor infiltrating lymphocytes (TILs) and cytotoxic T cells → **Prime target for an immune checkpoint blocker**
- Functionally similar to CTLA-4 (targeted by Yervoy®) and PD-1 (targeted by Keytruda®)
- There are currently no approved therapeutics targeting LAG-3



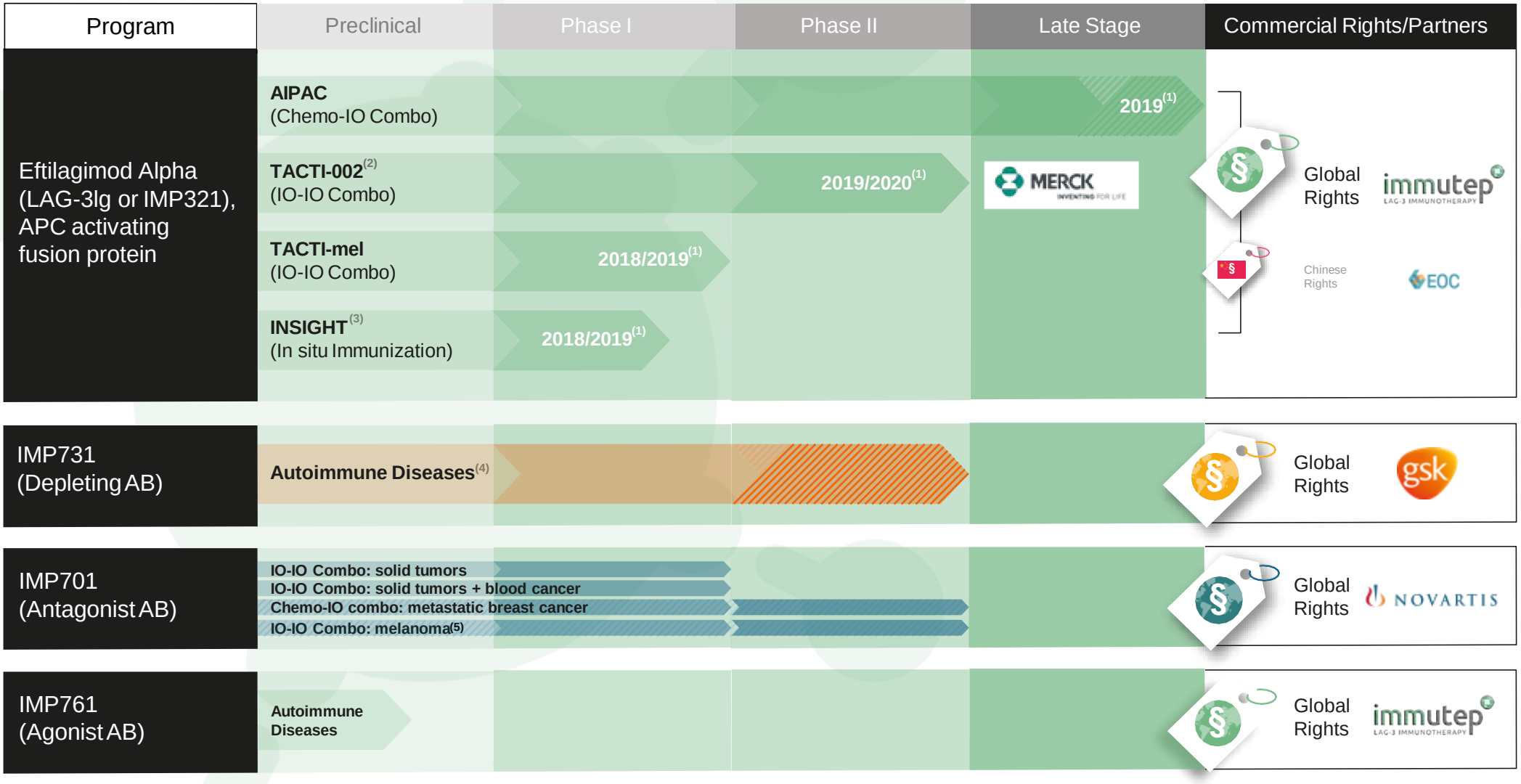

→ **Positive regulation** of antigen presenting cells (APC) → increase in antigen presentation to cytotoxic $CD8^+$ T cells

→ **Negative regulation** of $LAG\text{-}3^+$ T Cells

# Targeting LAG-3 May Lead to Multiple Therapeutics in Numerous Indications



# Oncology and Autoimmune Pipeline*




Notes

(1) Expected timing of data readouts and actual results and timing may differ
(2) In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC"); clinical trial is currently planned and not active
(3) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial
(4) Reflects completed study in psoriasis
(5) Clinical trial is currently planned and not active
* Cell Therapy: CVac™ - divested to and controlled by Sydys Corporation

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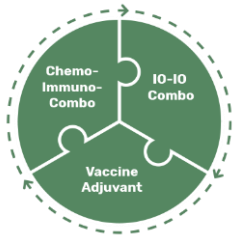
# Lead Program
# Eftilagimod Alpha (IMP321)




# Opportunity for Eftilagimod Alpha

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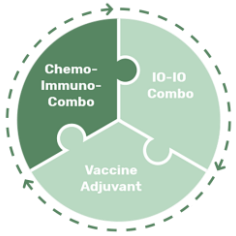
**Eftilagimod has the potential to be an ideal combination candidate in oncology therapy that could improve the prognosis for patients**

**Eftilagimod Key Characteristics (based on current data):**

- Excellent safety profile and encouraging efficacy data thus far
- Potential for use in various combination settings (e.g. IO, chemo, vaccines or in situ immunization)
- Antigen presenting cell activation mechanism of action, that results in t-cell cascade and thereby enhances the immune system response
- Potentially favorable (low) cost of goods based on current flat dosing regimen and manufacturing process

**Opportunity for Eftilagimod:**

- ✓ Potential synergistic effect with current IO, cancer vaccines, or chemo therapies
- ✓ Unique Mode of Action and potential therapeutic synergies
- ✓ European Phase IIb trial of efti + chemo in breast cancer
- ✓ Dose escalation Phase I of efti + Keytruda (TACTI-mel) in melanoma → extension to other indications possible




# Eftilagimod Alpha in MBC (AIPAC) (chemo-immunotherapy)

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## AIPAC trial (Phase IIb): Active Immunotherapy PAClitaxel, MBC patients, different EU countries

Safety-run in, 15 (6+9) patients, 2 cohorts<<

Stage 2

Arm 1, *113* patients: paclitaxel + IMP321

Arm 2, *113* patients: paclitaxel + placebo

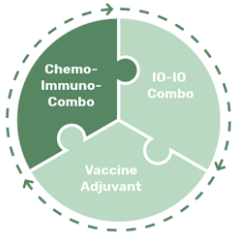
Phase IIb, multinational, randomized, double-blind

Run-in: recommended Phase II dose (RP2D)
Stage 2: Efficacy (PFS)

| | |
|---|---|
| **Primary Objective** | Run-In: Recommended Phase II dose (RP2D)<br>Stage 2: Efficacy (PFS) of paclitaxel + IMP321 vs. paclitaxel + placebo |
| **Other Objectives** | Anti-tumor activity, safety and tolerability, pharmacokinetic and immunogenic properties, quality of life of IMP321 plus paclitaxel compared to placebo |
| **Patient Population** | Advanced MBC indicated to receive 1st line weekly paclitaxel |
| **Treatment** | Run-in: Paclitaxel + IMP321 (6 or 30 mg)<br>Arm 1: Paclitaxel + IMP321 (30 mg)<br>Arm 2: Paclitaxel + Placebo |
| **Countries** | NL, BE, PL, DE, HU, UK, FR → overall 30+ sites |

## Status Report (August 2018)

- ✓ Safety run-in completed successfully
- ✓ Randomized phase started early 2017 with the RP2D (30 mg)
- ✓ Interim-data of safety run-in presented at ASCO 2017
- ✓ To-date, efficacy and safety data in-line with historical control group/ prior clinical trials (Brignone et al Journal Translational Medicine 2010, 8:71)
- ✓ Regulatory approval to conduct trial in 7 EU countries
- ✓ Over 30 sites actively recruiting patients
- ✓ Mid-point of patient enrolment reached (June 2018)
- • Primary read out expected in 2019




# Eftilagimod Alpha Prelim. Efficacy Metastatic Breast Cancer

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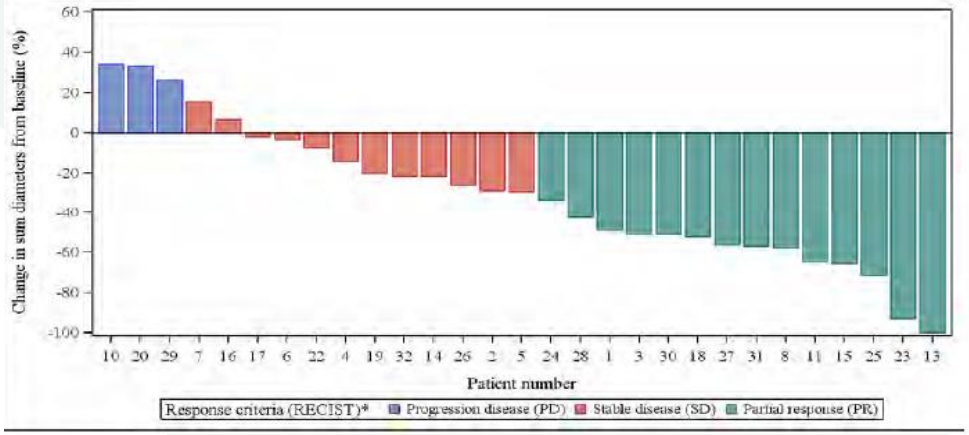
## Observed response rates are substantially better than the 22-33% response rates seen in historical control groups with paclitaxel monotherapy

### Phase I (n=30)




- **ORR* of 47% and DCR** of 83%**
- Responders had further tumor shrinkage between months 3 and 6

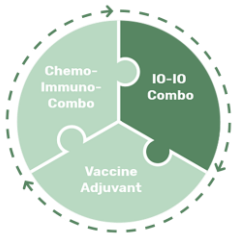
### AIPAC – Safety Run Phase (n=15)

| Response Parameter | Paclitaxel + IMP321 (n = 15) |
|---|---|
| Complete Response (CR) | 0/15 (0%) |
| Partial Response (PR) | 7/15 (47%) |
| Stable Disease (SD) | 6/15 (40%) |
| Progressive Disease (PD) | 2/15 (13%) |
| Overall Response Rate (ORR) | 7/15 (47%) |
| Disease Control Rate (DCR) | 13/15 (87%) |

- **ORR of 47% and DCR of 87%**
- Two of the responses occurred relatively late (after ~6 months)

**Overall Response Rate **Disease Control Rate*

*Preliminary data, status Interim CSR April 2018, best response acc. To RECIST 1.1*




# Efti (IMP321) in Melanoma

## TACTI-mel (IO combination) – Trial Design

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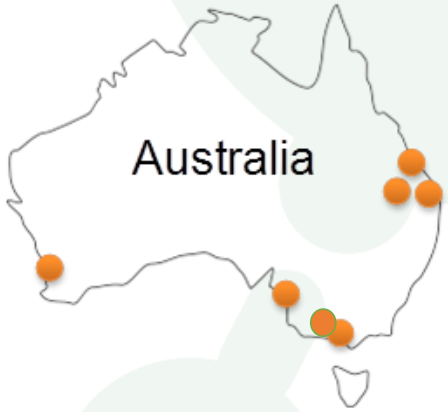
**TACTI-mel = Two ACTive Immunotherapeutics in melanoma**

24 patients, 4 cohorts of 6 patients → Efti (IMP321) + anti-PD-1 (Keytruda®) → Phase I, multicenter, open label, dose escalation → Recommended Phase II dose, safety and tolerability

| | |
|---|---|
| **Primary Objective** | Recommended dose for Phase II with efti (IMP321) + pembrolizumab<br><br>Safety + tolerability |
| **Other Objectives** | PK and PD of IMP321, response rate, time to next treatment, PFS |




**7 sites in Australia**

- Part A: efti (IMP321) at 1, 6 and 30 mg s.c. every 2 weeks starting with cycle 5 of pembrolizumab

→ Status: recruitment completed; interim results on next slides

- Part B: efti (IMP321) at 30 mg s.c. every 2 weeks starting with cycle 1 of pembrolizumab

→ Status: recruitment completed; data expected Q4

- Pembrolizumab (Keytruda®) 2 mg/kg every 3 weeks i.v. part A and B

*preliminary data, status 17th August 2018*

# Efti (IMP321) in Melanoma

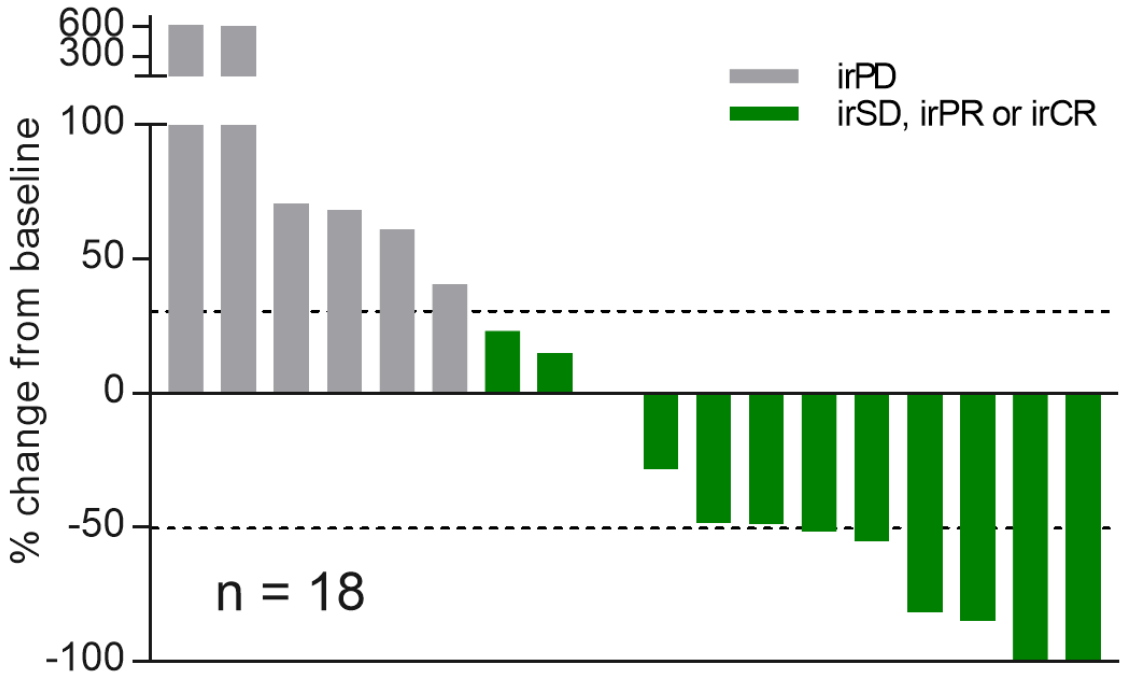
## TACTI-mel (IO combination) – Results after Start of Combo (1)

| Baseline Characteristics | N = 18 (%) |
|---|---|
| Elevated LDH | 7 (39%) |
| Metastasis stage M1c | 15 (83 %) |
| Pre-treated with BRAF/MEK/ipilimumab | 4 (22 %) |
| irPD/irSD to pembro after 3 cycles | 12 (67 %) |

| Best Overall Response acc. to irRC | N = 18 (%) |
|---|---|
| irCR | 1 (6 %) |
| irPR# | 5 (28 %)# |
| irSD | 6 (33 %) |
| irPD | 6 (33 %) |
| **Best overall response rate (ORR)** | **6 (33 %)** |
| **Patients with tumor shrinkage** | **9 (50 %)** |
| **Disease control rate** | **12 (66 %)** |

# - incl. 1 pt with complete disappearance of all target lesions; CR acc. to RECIST 1.1

**Waterfall Plot* (starting after 4 cycles of pembrolizumab)**




* - acc to irRC

- Patients very late stage of disease (M1c, elevated LDH)
- Majority not responding to pembrolizumab

→ Tumor shrinkage in 50 % of these patients incl. 2 pts with complete disappearance of all target lesions

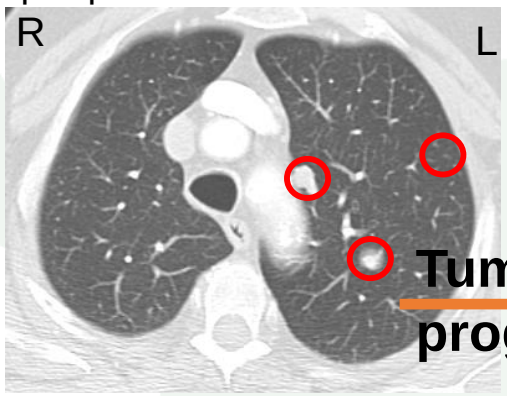
*preliminary data, status 9th May 2018*

# Efti (IMP321) in Melanoma

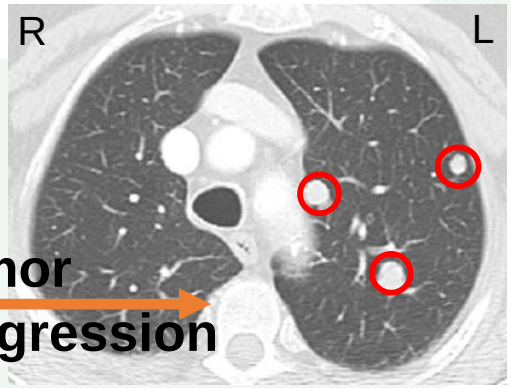
## TACTI-mel (IO combination) – Single Case at 1 mg efti

## Efficacy: Metastatic Melanoma

pre-pembro

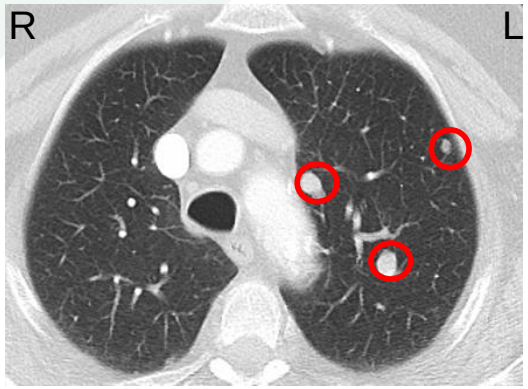



week 9 (pembro)

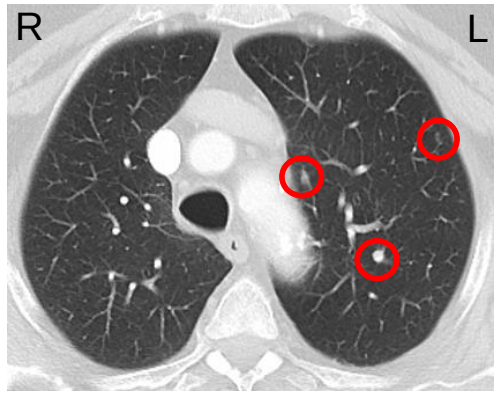



**Tumor progression**

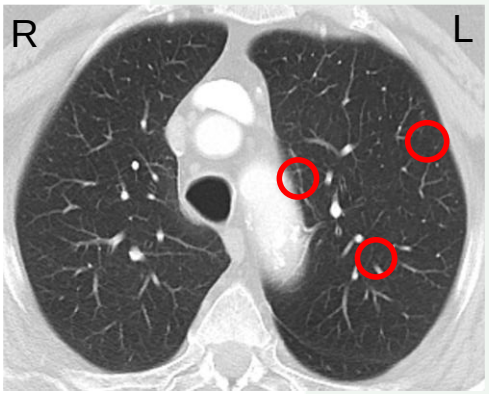
week 25 (combo)



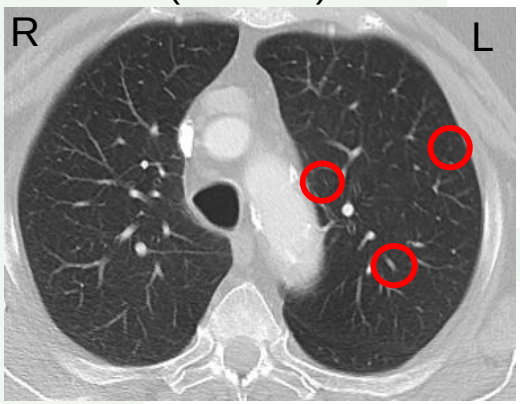

week 37 (combo)

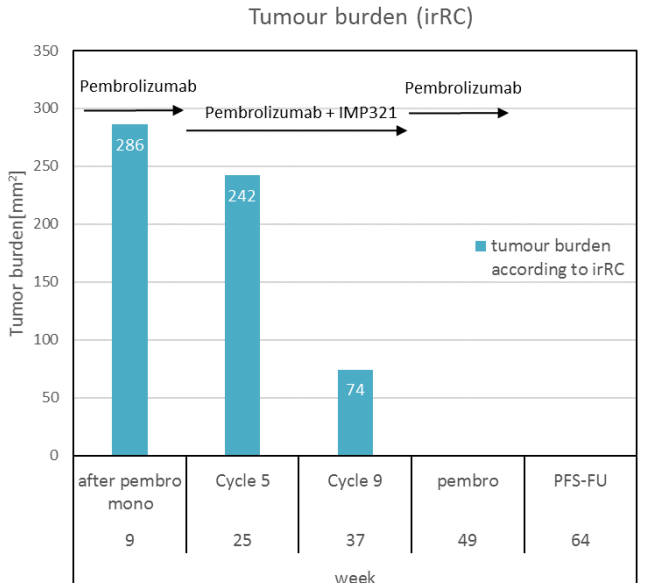



week 49 (Pembro mono)



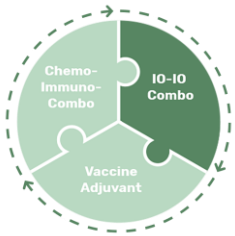

week 64 (PFS-FU)




**All lesions disappeared → CR (confirmed)**
**patient without treatment and disease free**

*preliminary data, status 9th May 2018*




# Efti (IMP321) in Melanoma

## Response Analysis Starting Cycle 1 Day 1 Pembrolizumab

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Trial Design TACTI-mel: Combination treatment of efti and pembrolizumab starts at cycle 5 in patients not responding well or progressing on pembrolizumab → difficult to compare to any historical control

How does the efficacy look from the start of pembrolizumab?
→ Performed analysis of read-outs starting from cycle 1 day 1 of pembrolizumab, including the 4 cycles pembrolizumab monotherapy ("C1/D1 Analysis")

- Overall response rate is 61% and 66% of patients are progression free 6 months after start of pembrolizumab (1)
- 7/12 (58 %) patients with progression (irPD) or stable disease (irSD) have a benefit by adding IMP321(1)

| Best Overall Response acc. to irRC (C1/D1 analysis)(1) | N = 18 (%) |
|---|---|
| irCR | 1 (6%)(1) |
| irPR# | 10 (56%)(1),(2) |
| irSD | 5 (28%)(1) |
| irPD | 2 (11%)(1) |
| **Best overall response rate (ORR)** | **11 (61%)(1)** |
| **Progression free at 6 months** | **12 (66%)(1)** |

Notes
(1) Response rates determined by C1/D1 Analysis
(2) Includes 1 patient with complete disappearance of all target lesions, CR acc to RECIST1.1



*preliminary data, status 9th May 2018*

# Collaboration and Supply Agreement

- In March 2018 Immutep entered into clinical trial collaboration and supply agreement with Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the United States and Canada) to evaluate the combination of eftilagimod alpha with MSD's anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in a new Phase II clinical trial
- The planned Phase II combinatory clinical trial, referred to as TACTI-002, will evaluate the safety and efficacy of this novel immunotherapy combination in patients in different cancer indications such as head and neck small cell carcinoma (“HNSCC”) or two different lines of non small cell lung cancer (“NSCLC”)
- The TACTI-002 clinical trial will be a Phase II, Simon two-stage, non-comparative, open-label, single-arm, multicenter clinical study
- Up to 110 patients across the three indications are planned to be treated in medical centers in Europe and the United States with the trial expected to commence in the second half of 2018

# Efti (IMP321) – Clinical Development

## TACTI-002 Trial Design

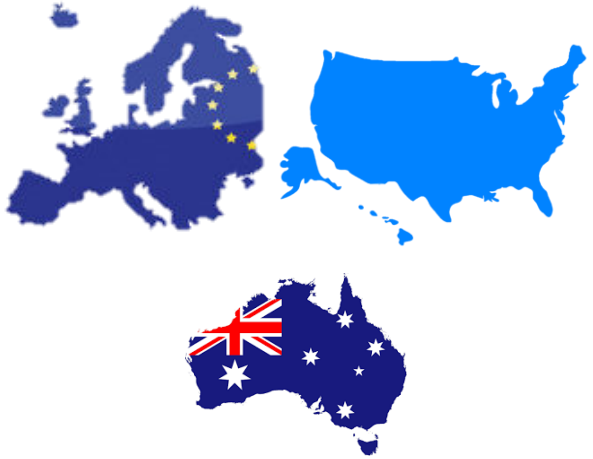
**TACTI-002; a basket trial: Two ACTive Immunotherapeutics in different indications**

Simons 2 stage; 3 indications; up to 110 pts → Efti (IMP321) + Pembrolizumab (Keytruda®) for 12 months + max. of 12 months pembrolizumab monotherapy → Phase II, multi-national (EU + US + AUS), open label → Response rate; PFS, OS, PK, Biomarker; Safety and tolerability

| | |
|---|---|
| **Primary Objective** | Response rate (iRECIST) |
| **Other Objectives** | Safety, PFS+OS, PK, exploratory biomarker analysis |
| **Patient Population** | Part A: 1st line NSCLC PD-X naive<br>Part B: 2nd line NSCLC, PD-X refractory<br>Part C: 2nd line HNSCC, PD-X naive |
| **Treatment** | 30 mg Efti (IMP321) s.c.<br>200 mg Pembrolizumab i.v. |

### Status Report

- IND in the U.S. granted in July 2018
- Study start expected Q.4 ‘18
- First DMC meeting planned mid ’19
- First data expected mid ‘19



12-15 sites in Europe / US / Australia

Notes
NSCLC – non-small-cell lung cancer, HNSCC – head and neck squamous cell cancer, DMC – data monitoring comittee, PFS – progression free survival, OS – overall survival, PK – pharmacokinetics, PD-X – any PD-1 or PDL-1 treatment

# Eftilagimod Alpha Partnerships

- Eddingpharm holds Chinese rights
- Chinese IND for IMP321 granted in Dec 2017 -> USD1m milestone paid to Immutep
- EOC, an Eddingpharm spin-off holding the Chinese rights for IMP321, Phase I study in MBC expected to start Sep 2018
- Milestone and royalty bearing partnership for Immutep

- Spin off from NEC, Japan. Est. Dec 2016; aims to develop cancer drugs discovered by artificial intelligence
- Multiple Material Transfer Agreements
- Preclinical and clinical research ongoing

- Strategic supply partnership for the manufacturing of eftilagimod alpha
- Through WuXi, Immutep was first company ever to import and use a Chinese manufactured biologic in a European clinical trial

# IMP731
# (Autoimmune Diseases)

# GSK‘781 for Autoimmune Diseases

**GSK2831781, which is derived from IMP731 antibody, aims to kill the few activated LAG-3$^{+}$ T cells that are auto-reactive in autoimmune disease leading to long term disease control without generalized immune suppression**

- GSK holds exclusive WWW rights
- Jan 2015: Immutep received a single-digit million US$ milestone payment
- Up to £64m in total upfront payments and milestones, plus royalties if all objectives are achieved
- GSK2831781 in Phase Ib trials
- Phase 1 study completion date: March 2018
  (see http://www.gsk-clinicalstudyregister.com/study/200630#ps)

# IMP701
# (Cancer)

# IMP701 (LAG525) for Cancer

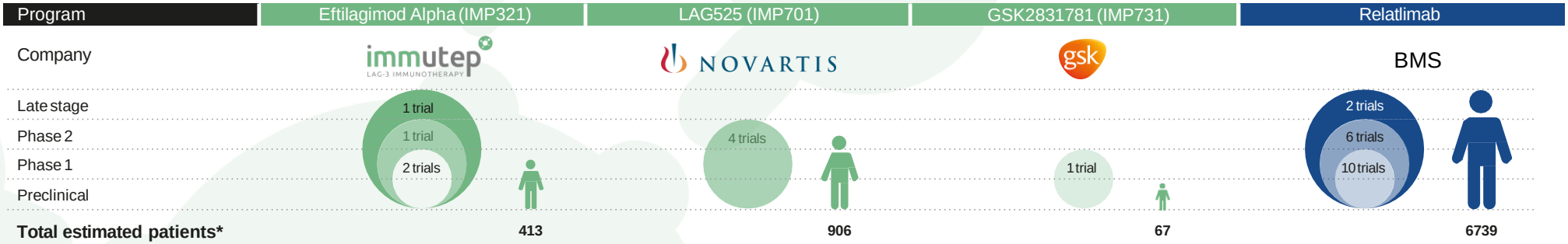
- Novartis holds exclusive WW rights
- August 2015: Start of Phase I study of IMP701 in combination with PDR001 (anti-PD-1 mAb) in 13 different cancer indications in 240 patients
- 1st and 2nd Milestone payments received in Aug 2015 and August 2017, respectively
- Estimated study completion date is April 2019
- December 2017: new Phase II study of IMP701 in combination with PDR001 in advanced solid and hematologic malignancies in 160 patients made public
- April 2018: two new Phase II combination studies made public that planned to begin in June/ July 2018 in triple-negative breast cancer (126 patients) and metastatic melanoma (160 patients)

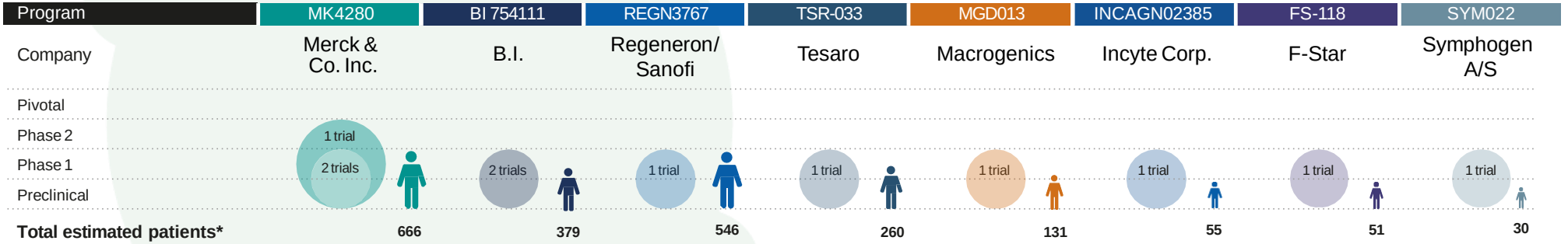
- **IMP701 is an anti-LAG-3 mAb that blocks LAG-3-mediated immune down-regulation**
- **LAG-3 is a prime target for immune checkpoint blockade as it is readily expressed at a high level in many human tumors**

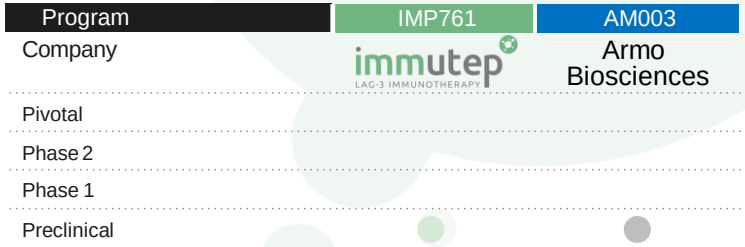
# Market & Competition

# LAG-3 Therapeutic Landscape Overview

## *Immutep is the leader in developing LAG-3 modulating therapeutics*



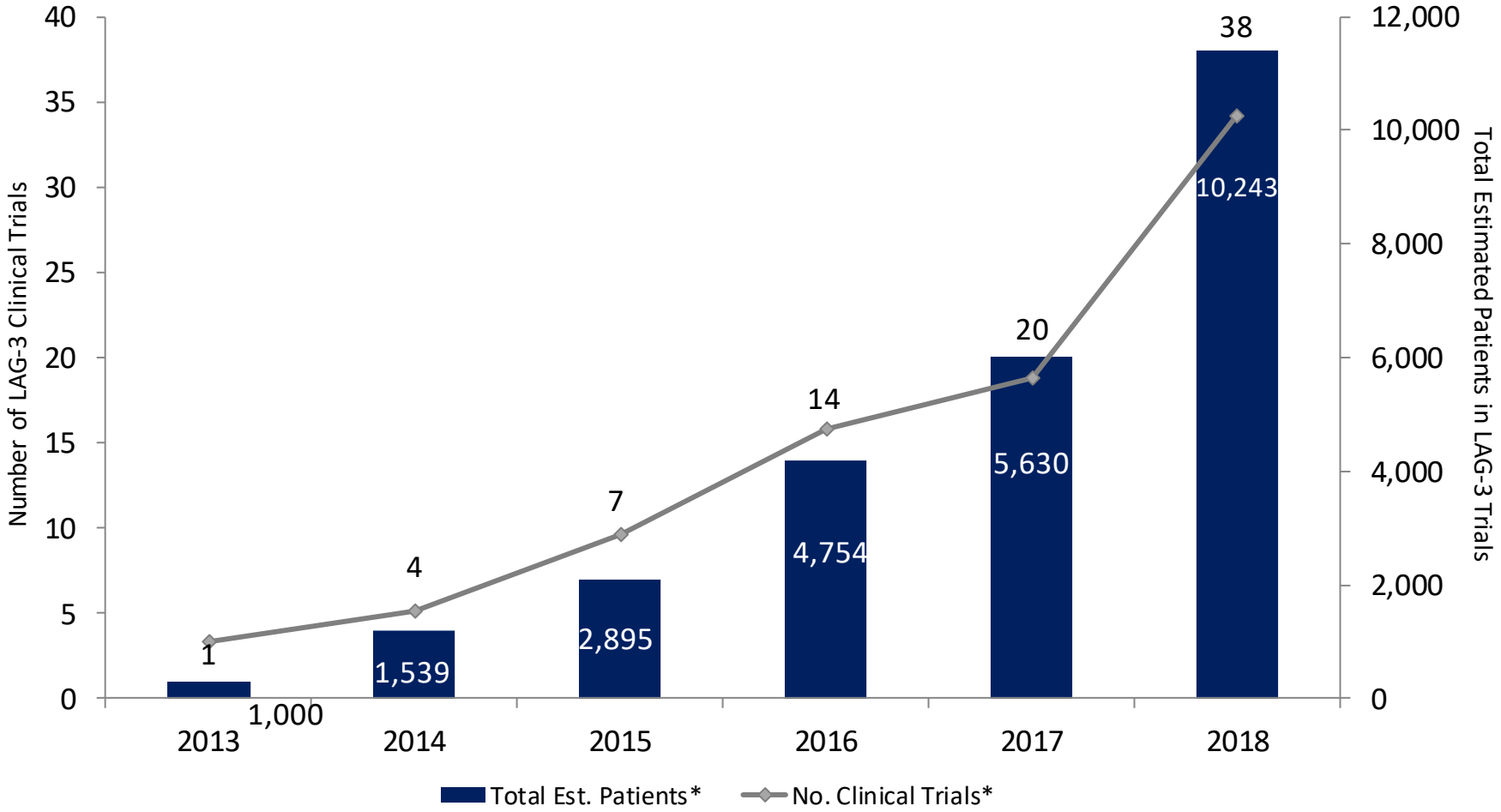

Indicates one product; size indicates stage of development, green = product either developed by Immutep or under license from Immutep

Indicates No. of patients on trials

Sources: GlobalData, company websites, clinical trials.gov, and sec.gov
Information as of August 17, 2018, includes planned and completed trials, includes trials where the company may not be the sponsor

# Increasing Clinical Trials Targeting LAG-3

## Industry increasingly deploying resources to development of LAG-3 therapeutics




Sources: GlobalData, company websites, clinical trials.gov, and sec.gov
Information as of August 17, 2018
*2018 includes planned and completed trials, includes trials where the company may not be the sponsor

# Outlook

# Outlook

Immutep is well funded with a cash runway to calendar Q4 2019, well beyond the final progression free survival data from its Phase IIb AIPAC breast cancer trial.

## Potential News Flow and Milestones

| | |
|---|---|
| **Clinical** | AIPAC fully recruited (226 patients): H2 2018 |
| | TACTI-mel data from fourth patient cohort (30 mg dose at cycle 1): H2 2018 |
| | TACTI-002 to commence, Phase II trial in collaboration with MSD: H2 2018 |
| | IMP761 preclinical data: 2018 |
| | INSIGHT single cases from study: throughout 2018 |
| | AIPAC final progression free survival data (metastatic breast cancer trial): H1 2019 |
| **Other** | Potential milestone payments from clinical partners as trials progress |
| | Continued expansion of patent portfolio |
| | Continued regulatory interaction |
| | Ongoing business development activities |

# Investment Highlights

The global leader in developing LAG-3 therapeutics for immuno-oncology and autoimmune diseases

Deep expertise and IP in the LAG-3 immune control mechanism

Broadest LAG-3 portfolio with four product candidates, three of which are in nine ongoing or planned clinical trials

Multiple industry partnerships including Merck (MSD), GSK and Novartis

Expecting clinical results, regulatory updates, and business development news flow in 2018-2019

# Thank you!