



# The global leader in developing LAG-3 therapeutics

Corporate Presentation  
January 2020

*(ASX: IMM, NASDAQ: IMMP)*

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# Company Snapshot

- Global leadership position in **LAG-3**
- Four **LAG-3** related candidates in **immuno-oncology** and **autoimmune diseases**
- Partnerships with five of the world's largest pharmaceutical companies – **Novartis, GSK, Merck (MSD), Pfizer & Merck KGaA**
- **Decisive data (from two Phase II trials) in Q1 2020** from lead program

## Financial Snapshot

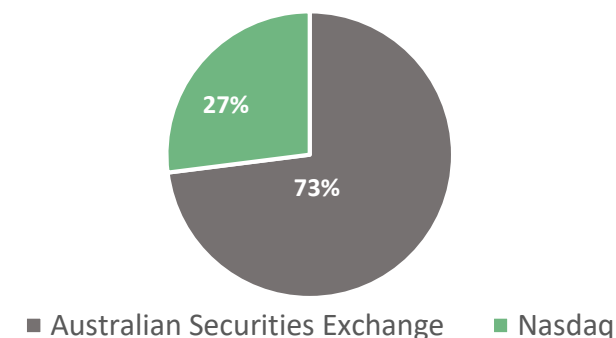
<b>Ticker symbols</b>	IMM (Australian Securities Exchange) IMMP (NASDAQ)
<b>Securities on issue<sup>(1)</sup></b> (as at 6 January 2020)	391.6 million ordinary shares
<b>Cash &amp; Term Deposits</b> (as at 31 December 2019)	~A\$20.5 million (US\$14.4 million)
<b>Market Cap<sup>(2)</sup></b> (as at 6 January 2020)	A\$103 million (US\$71.6 million)

*Notes:*

(1) Currently ~27% of the ordinary shares are represented by ADSs listed on NASDAQ where 1 ADS represents 10 ordinary shares.

(2) Market capitalization based on ASX share price. For a detailed summary of all securities on issue refer to latest Appendix 3B released on ASX.

## Shareholder Base



# Directors & Officers



**Russell J. Howard, PhD, Non-Executive Chairman**

Scientist, executive manager and entrepreneur; previously CEO of Maxygen & Oakbio, positions at NIH, DNAX, Affymax

**Pete A Meyers, Non-Executive Director & Deputy Chairman**

Current Chief Financial Officer of Eagle Pharmaceuticals, Inc.; previously CFO of Motif Bio; previously Co-Head of Global Health Care Investment Banking at Deutsche Bank



**Grant Chamberlain, Non-Executive Director**

20+ years in investment banking; current principal of One Ventures; previously Head of Mergers and Acquisitions and Financial Sponsors Australia at Bank of America Merrill Lynch

**Marc Voigt, Executive Director & Chief Executive Officer**

20+ years in leading positions in finance, venture capital and biotech industry, multiple financing & licensing transactions



**Prof. Frédéric Triebel, MD PhD, Chief Scientific Officer & Chief Medical Officer**

Clinical haematologist, and PhD in immunology (Paris University) and successfully developed several research programs in immunogenetics and immunotherapy, leading to over 144 publications and 16 patents

**Deanne Miller, Chief Operating Officer, General Counsel & Company Secretary**

Lawyer; previous positions at RBC Investor Services, Westpac, Macquarie and ASIC

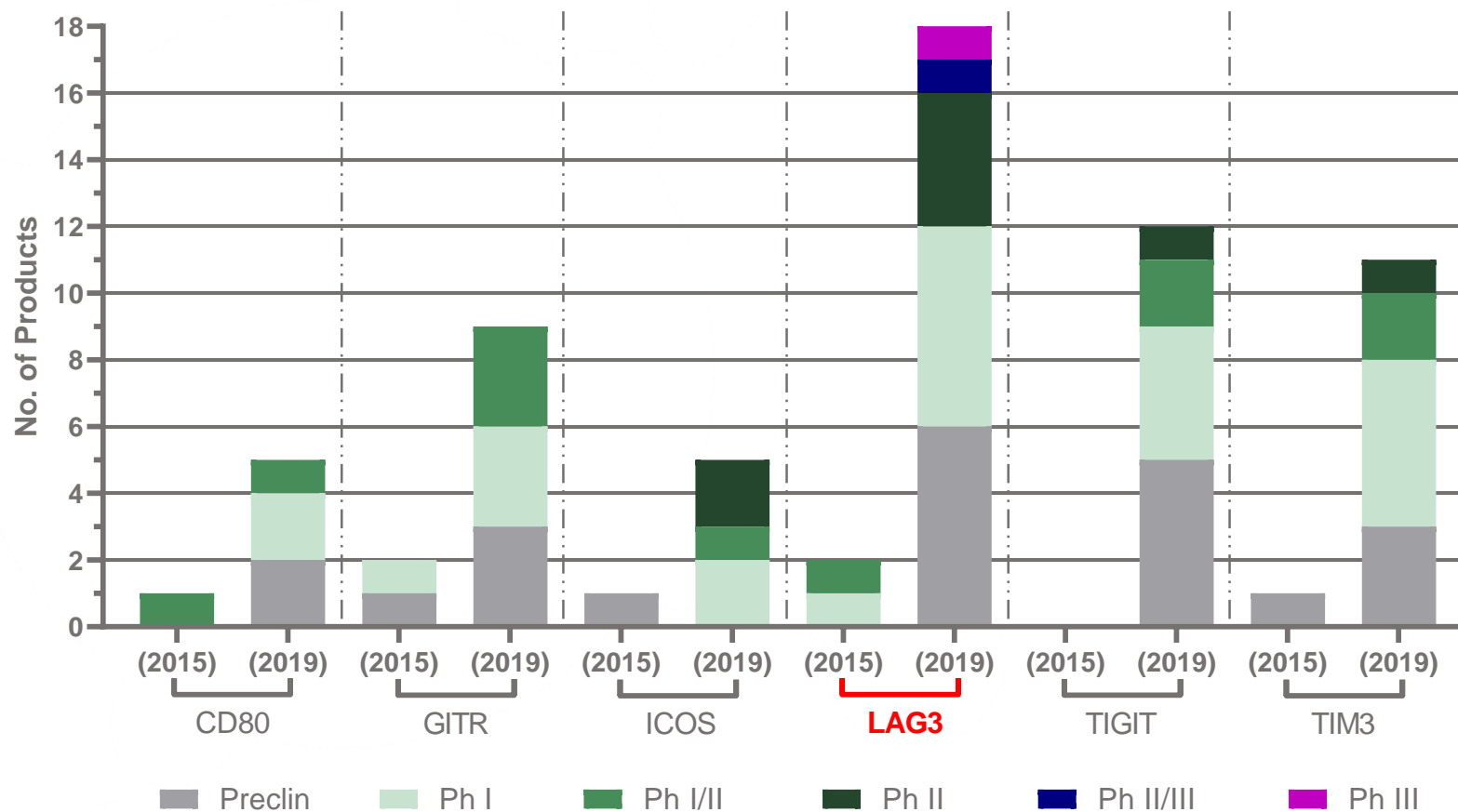


# LAG-3 Overview

- the most promising immune checkpoint -

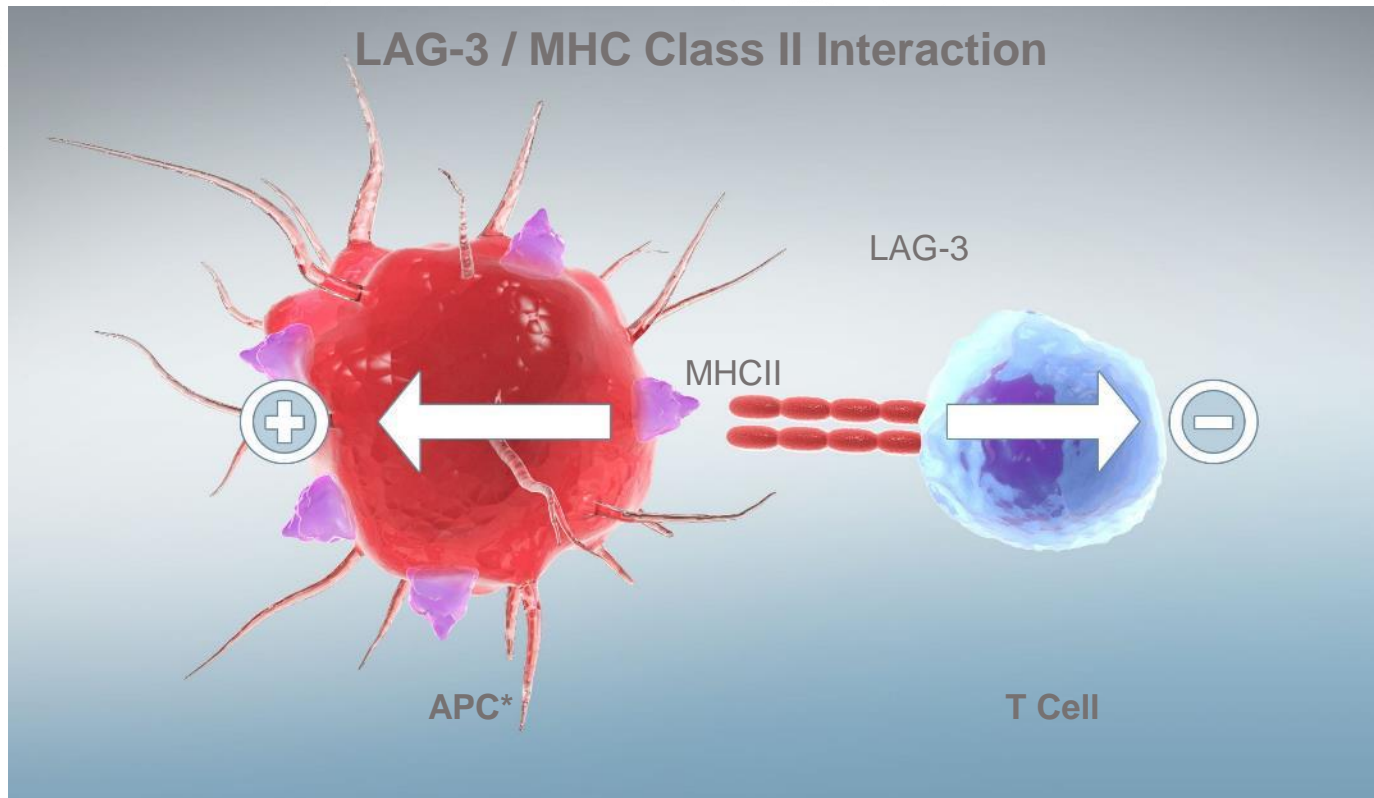
# Immune Checkpoint Landscape beyond PD-1 and CTLA-4

2015 and 2019



# LAG-3 as a Therapeutic Target

LAG-3, an immune checkpoint, is widely expressed on tumor infiltrating lymphocytes (TILs) and cytotoxic T cells → **Prime target for immune therapy**



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

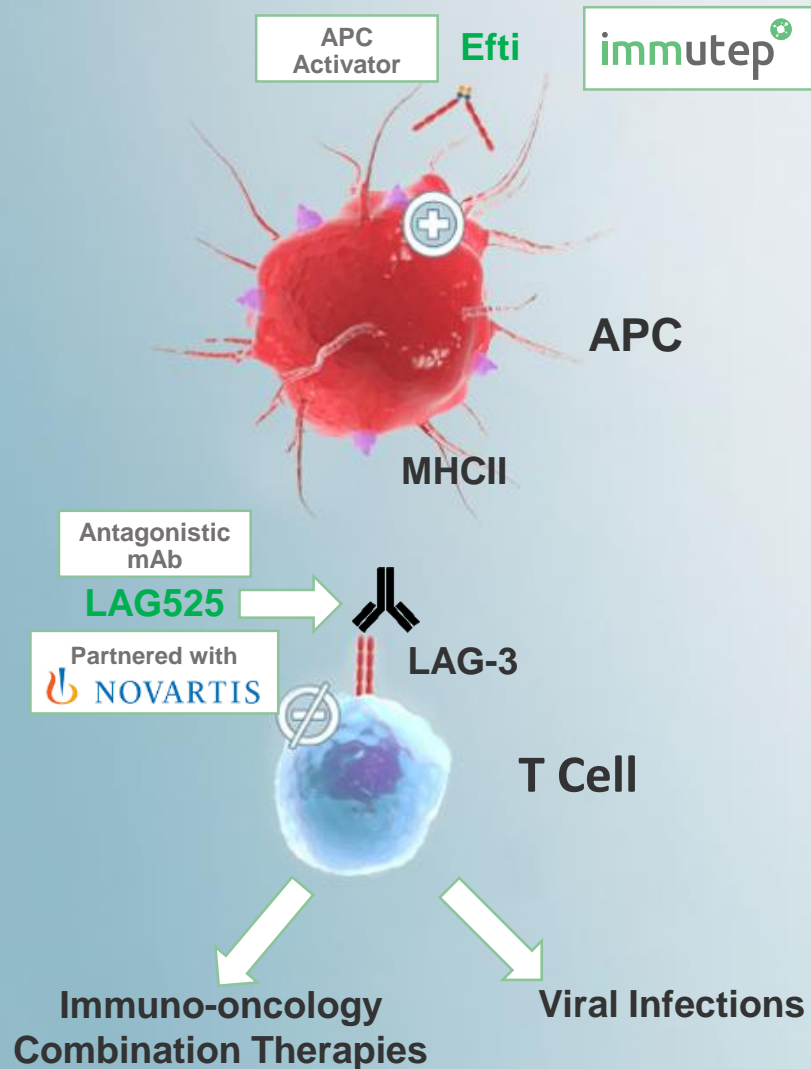


→ **Negative regulation** of LAG-3<sup>+</sup> T Cells

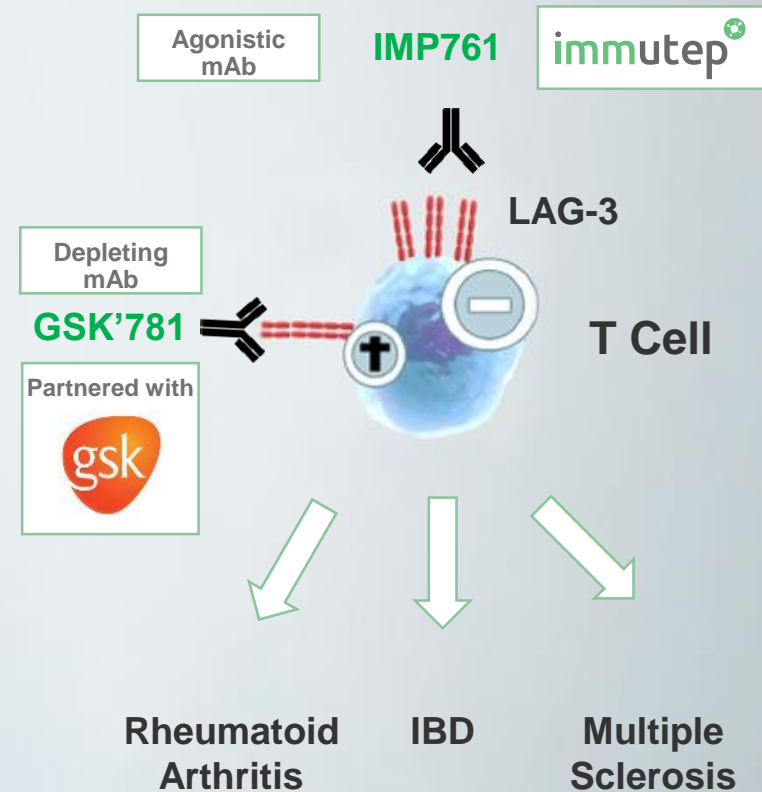


# Targeting LAG-3 / MHC II may lead to multiple therapeutics in numerous indications

## IMMUNOSTIMULATION



## IMMUNOSUPPRESSION





# Immutep Controlled Immunotherapy Pipeline\*

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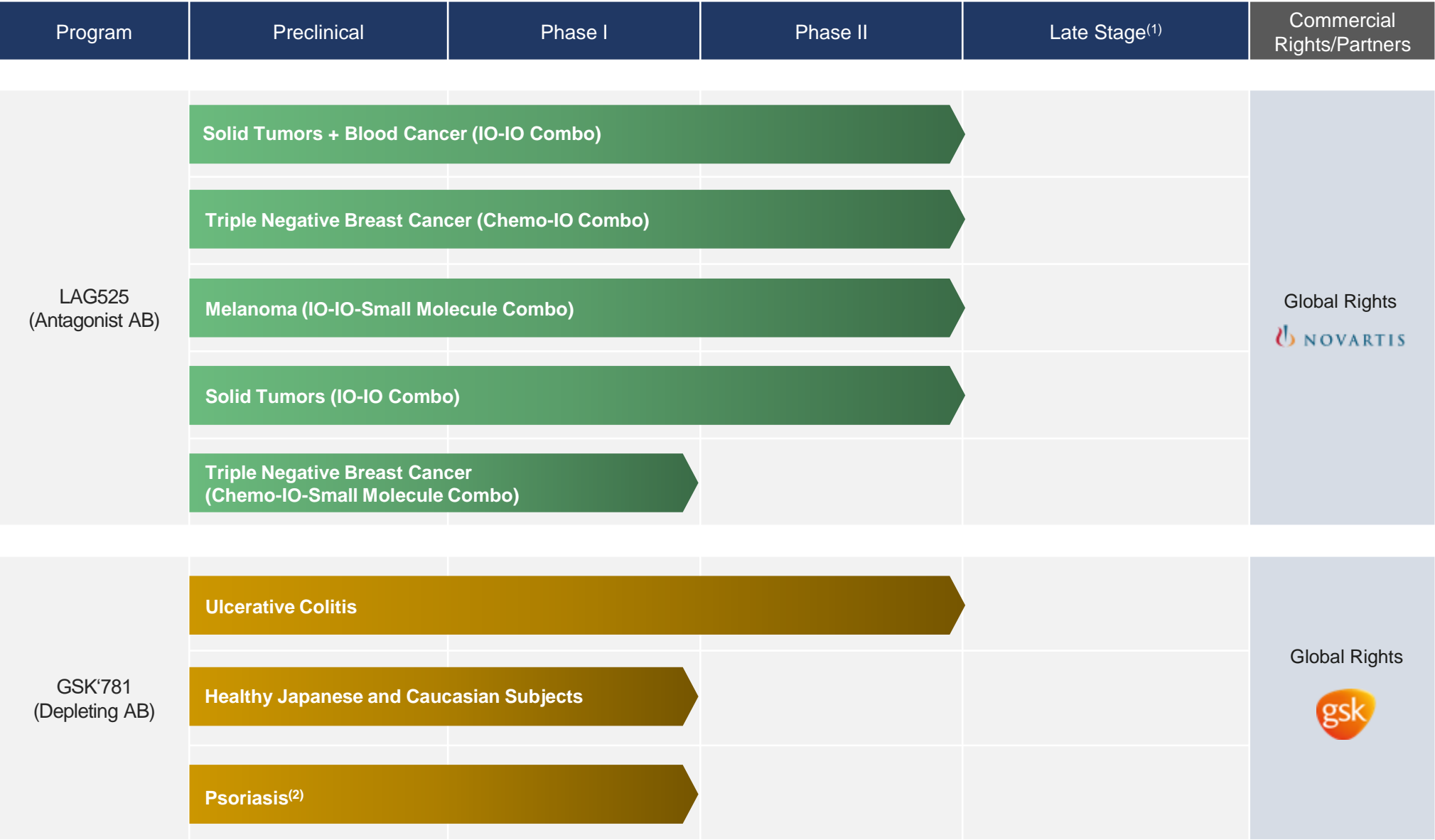
	Program	Preclinical	Phase I	Phase II	Late Stage <sup>(4)</sup>	Commercial Rights	Market Size <sup>(5)</sup> (by)
Oncology	<b>Eftilagimod Alpha (IMP321)</b>  APC activating soluble LAG-3 protein	Metastatic Breast Cancer (Chemo – IO) AIPAC				Global Rights <b>immutep</b> LAG-3 IMMUNOTHERAPY	US\$12.7 billion (2024)
		Non-Small-Cell Lung Carcinoma (IO – IO) <sup>(1)</sup> TACTI-002			 <b>MERCK</b> INVENTING FOR LIFE		US\$33.9 billion (2026)
		Head and Neck Squamous Cell Carcinoma (IO – IO) <sup>(1)</sup> TACTI-002			 <b>MERCK</b> INVENTING FOR LIFE		US\$2.8 billion (2026)
		Solid Tumors (IO – IO) <sup>(2), (3)</sup> INSIGHT-004			 <b>Merck KGaA</b> , Darmstadt, Germany		
		Melanoma (IO – IO) TACTI-mel				Chinese Rights  <b>EOC</b>	US\$7.8 billion (2026)
		Solid Tumors (In situ Immunization) <sup>(2)</sup> INSIGHT					
		Metastatic Breast Cancer (Chemo – IO)					
Autoimmune	<b>IMP761 (Agonist AB)</b>					Global Rights <b>immutep</b> LAG-3 IMMUNOTHERAPY	

## Notes

- 9 (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  
 (5) Estimation of Datamonitor Healthcare, Informa Pharma Intelligence for US, Jap, EU (5)

# Immutep Out-Licensed Immunotherapy Pipeline\*



Notes  
\* Information in pipeline chart current as at 30 September 2019  
(1) Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials  
(2) Reflects completed Phase I study in healthy volunteers and psoriasis

# Lead Program Eftilagimod Alpha (efti or IMP321) - APC activation -

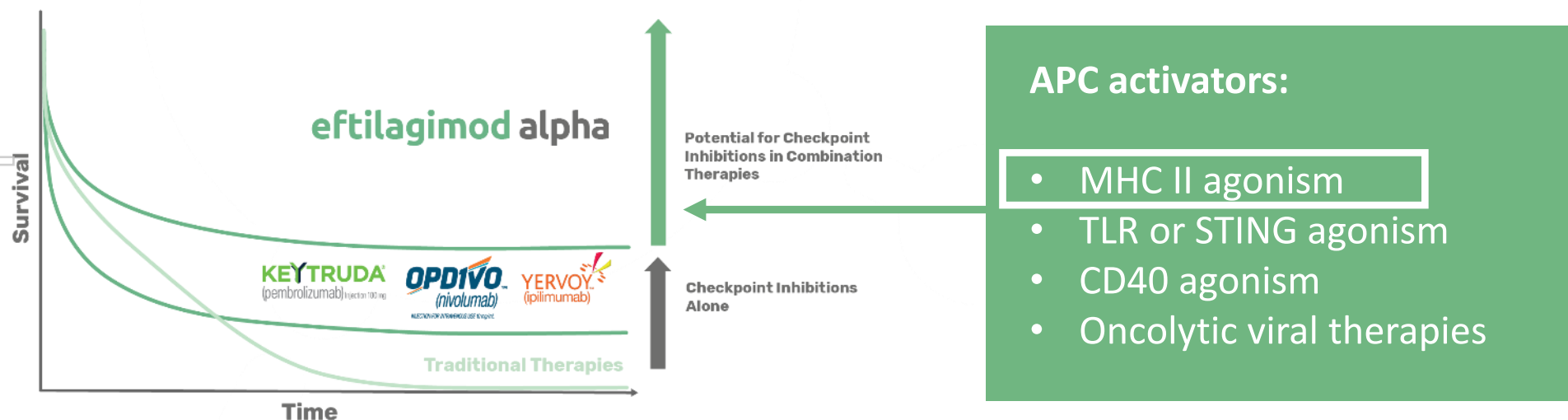
# Efti: IO Therapy Response Rates

Approximately 70-80% of patients do not respond to anti-PD-1 monotherapy<sup>(1)</sup>

**How can we enable more efficacious T-cell responses?**

- immunogenic cell death to liberate/uncover tumor antigens
- cross-presentation of those antigens
- recruitment of T cells into the tumor microenvironment
- reversing the pathways driving a repressive tumor environment

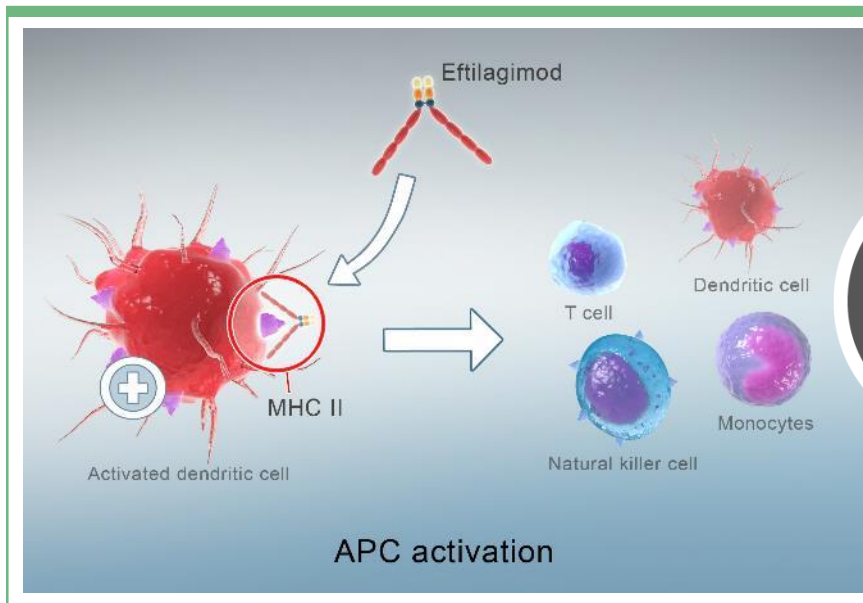
**This could be achieved through the right APC activation**



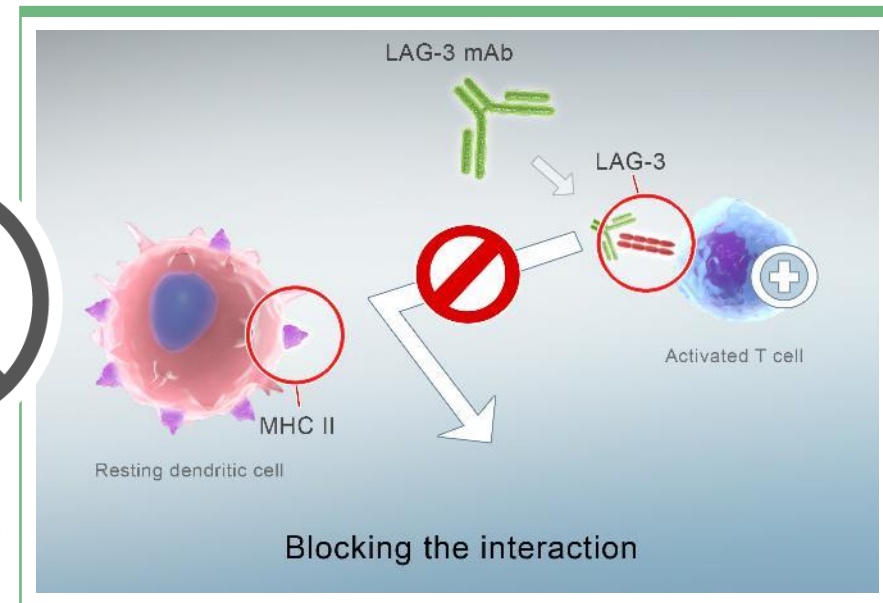
# Efti: an Innovative LAG-3 IO Product Candidate

- the only APC targeting LAG-3 product candidate currently in clinical development
- a unique approach (“turning cold tumors into hot tumors” with LAG-3)
- synergistic with other therapeutic agents and modalities e.g. IO agents or chemotherapy

## “PUSHING THE ACCELERATOR ON IMMUNE RESPONSES”



## “RELEASING THE BRAKE ON THE T CELL”



Efti is an **MHC II agonist**

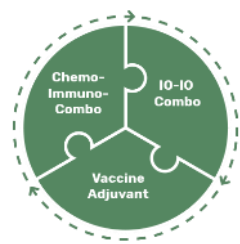
### APC activator

- boost and sustain the CD8<sup>+</sup> T cell responses
- activate multiple immune cell subsets

LAG-3 antagonist, or blocking, antibodies:

### Immune checkpoint inhibitor

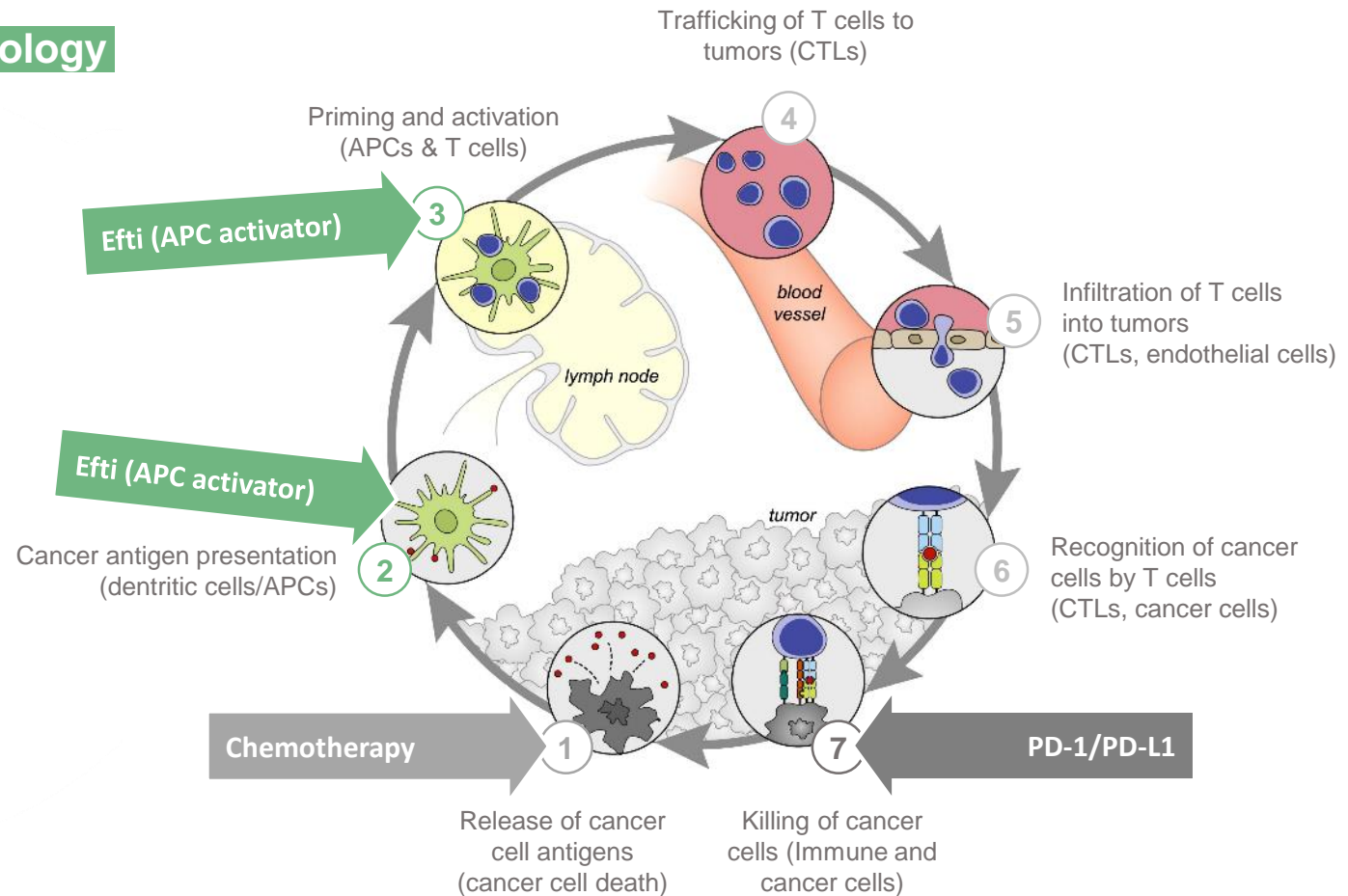
- increase cytotoxicity of the pre-existing CD8 T cell response

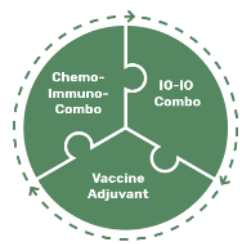


# Efti: a pipeline in a product

## Efti has disruptive potential for oncology

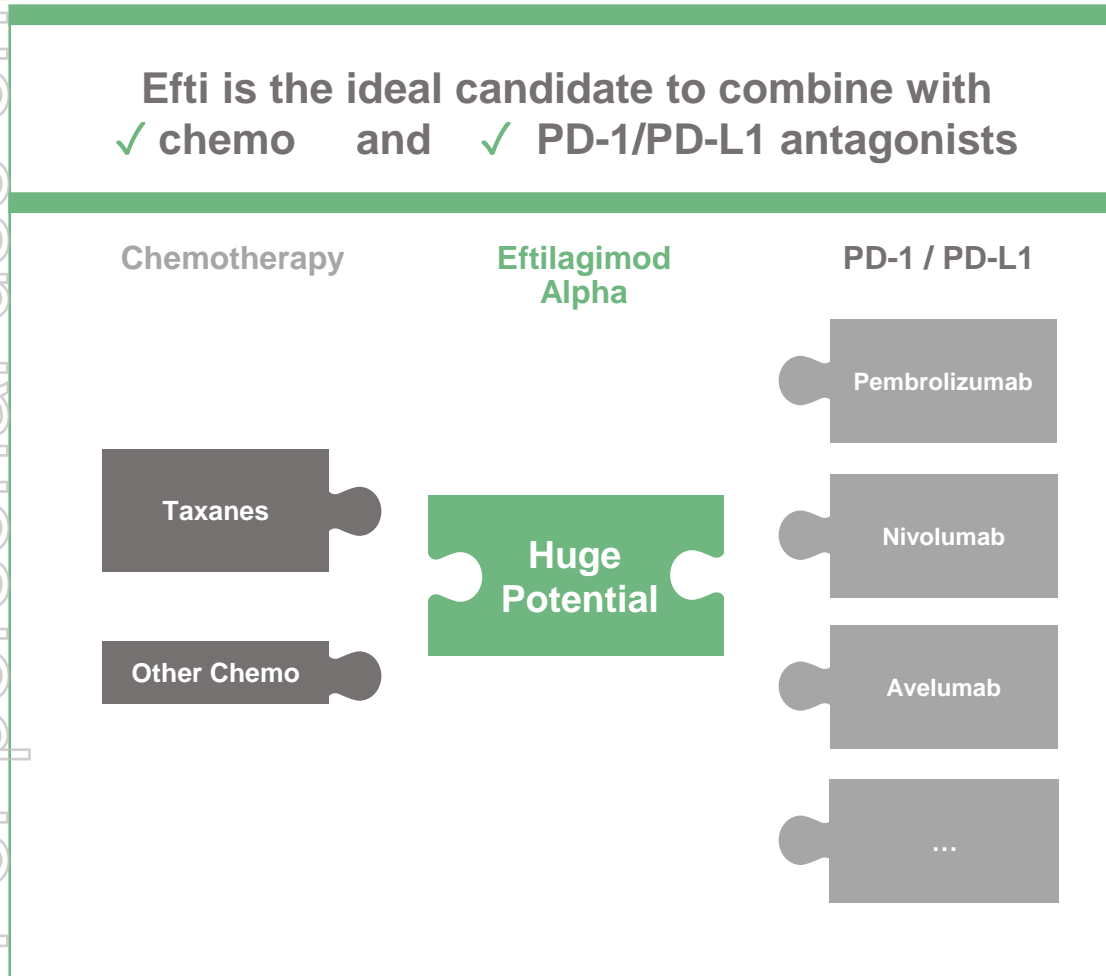
- ✓ **First-in-Class** MHCII agonist
- ✓ good safety profile
- ✓ encouraging efficacy data
- ✓ low cost of goods
- ✓ potential for use in various combination settings →  
**efti is a “pipeline in a product”**





# Efti: a pipeline in a product

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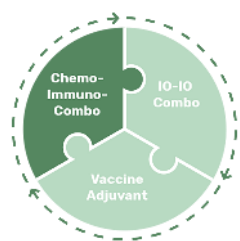


## Which kind of combinations were successful in the past?

- **Different MoA** to hit virus/cancer simultaneously

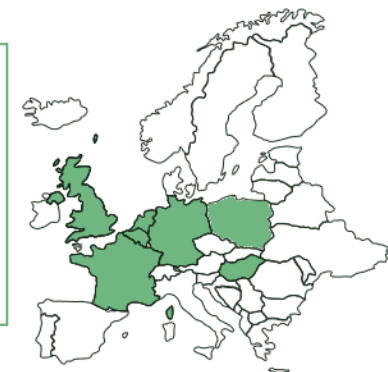
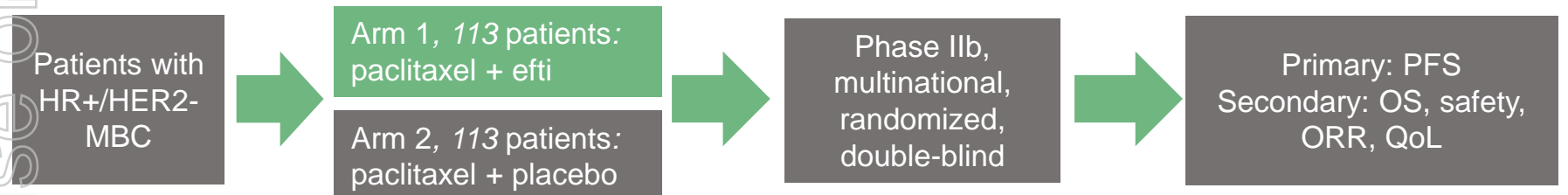
## Historical examples:

- **Pembrolizumab + Chemo** in 1st line NSCLC
- **CHOP + rituximab** in large B-cell lymphoma
- **Tritherapy** in HIV



# Efti Clinical Development AIPAC (Phase IIb)

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



## Results of efti plus paclitaxel in MBC from two Phase I studies :

Antitumor activity acc. to RECIST 1.1	P005 (N=30)	P011 (N=15)
<b>ORR*</b>	47%	47%
<b>DCR**</b>	87%	83%

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

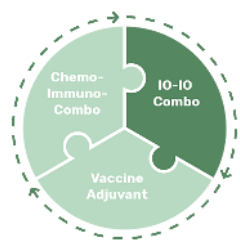
**Observed ORR are substantially better than the 22-33% response rates seen in historical control groups with paclitaxel alone**

## Status Report

- ✓ Regulatory approval in 7 EU countries
- ✓ 227 patients recruited in Stage 2 → LPI Jun 2019
- **PFS & ORR data expected calendar Q1 2020 (March)**

**Key features:** 1. double blinded pivotal trial in MBC patients → potential to seek conditional marketing authorization in the EU, pending positive data  
2. broader perspective: validation of Antigen Presenting Cell activators → a new class of active I-O products after the Immune Checkpoint Inhibitors

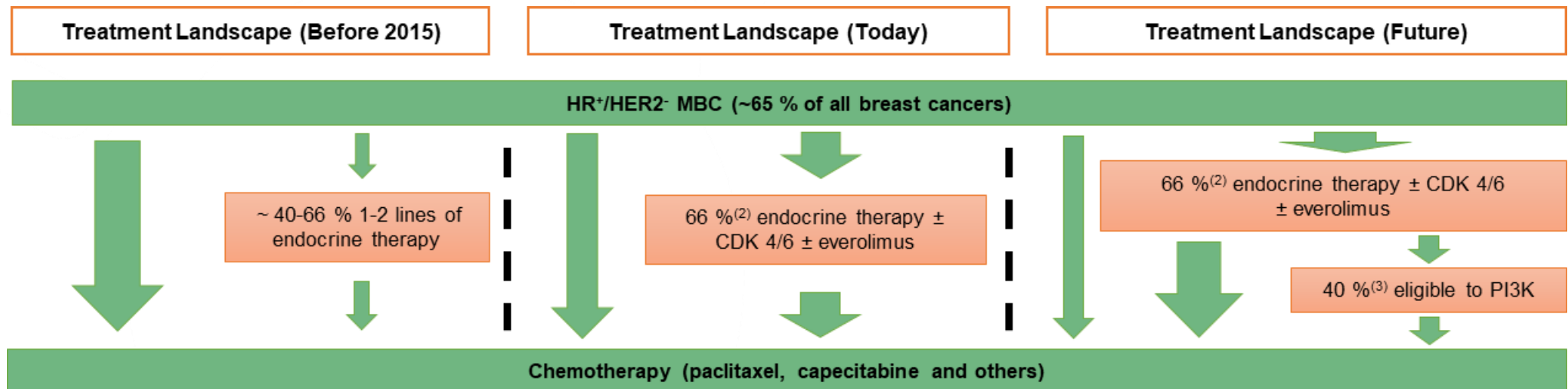




# Treatment Landscape for HR+/HER2- MBC

## Epidemiology:

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

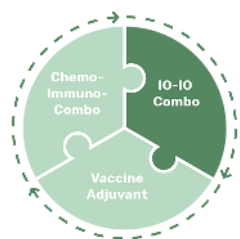


- Despite all changes → no improvement for patients receiving first-line chemotherapy
- Paclitaxel one of the most widely used chemotherapies
- No active IO in this setting thus far
- No active development of any IO agent or other game changer in late stage clinical trials

### Notes

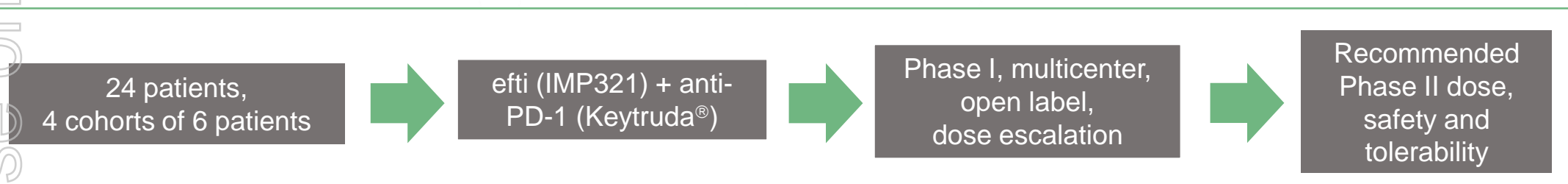
- (1) Source: GlobalData 2019
- (2) Caldeira et al Oncology and therapy 2016; 4:189-197
- (3) <https://www.ascp.org/News/59389> ; Usage to be determined as not yet approved by EMA
- (4) <https://www.onclive.com/insights/mbc-endocrine-partner/role-of-pi3k-inhibitors-in-hr-positive-metastatic-breast-cancer>

MBC – metastatic breast cancer BC – breast Cancer



# Efti Clinical Development TACTI-mel (Phase I)

## TACTI-mel: Two Active Immunotherapeutics in Melanoma



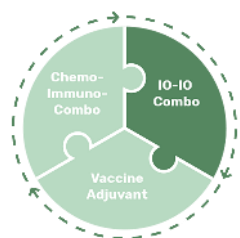
Other objectives	PK and PD of efti, response rate, PFS
Patient Population	Metastatic melanoma

### Status Report

- Part A: 1, 6 and 30 mg efti s.c. every 2 weeks **starting with cycle 5** of pembrolizumab
- Part B: efti at 30 mg s.c. every 2 weeks **starting with cycle 1** of pembrolizumab
- Pembrolizumab (Keytruda®) 2 mg/kg every 3 weeks i.v. Parts A and B
- Recruitment completed
- **Encouraging final efficacy** results presented



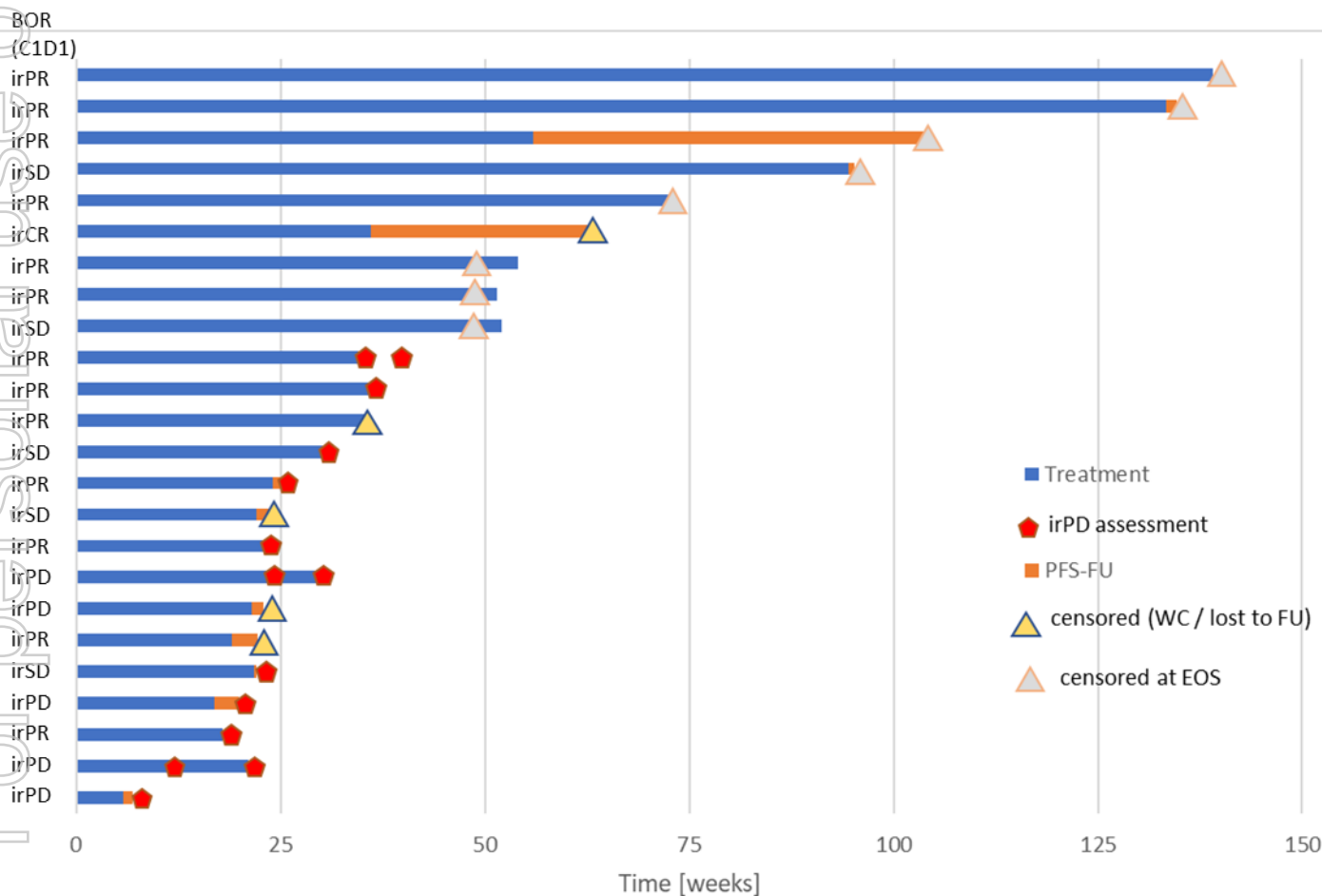
7 sites in Australia



# Efti Clinical Development

## TACTI-mel: Results (Parts A + B)

**Swimmerplot Parts A + B**  
(starting cycle 1 day 1 pembrolizumab)



### Conclusion

- No treatment termination due to safety issues with the combination
- 9 patients (38%) on treatment for ~12 months → durable responses / disease control
- 2 CR according to RECIST 1.1 and 1 metabolic inactive (PET-CT) PR
- 6 patients with complete disappearance of target tumour lesions according to irRC

#### Notes:

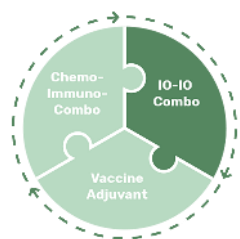
BOR: Best Overall Response per patient with start of pembrolizumab as baseline (cycle 1 day 1)

EOS – end of study

PFS-FU – progression free survival follow-up

irPD – PD according to ir

Data-cut-off: Oct 2019



# Efti Clinical Development TACTI-002 (Phase II)

## TACTI-002: Two Active Immunotherapeutics in different indications

Up to 109 patients  
with NSCLC or  
HNSCC

efti (IMP321) + anti-PD-  
1 (Keytruda®)

Phase II, multi-national,  
open label, Simon's 2  
stage design

ORR, PFS, OS, PK,  
biomarker, safety and  
tolerability

### Patient Population

A: 1<sup>st</sup> line NSCLC, PD-X naïve  
B: 2<sup>nd</sup> line NSCLC, PD-X refractory  
C: 2<sup>nd</sup> line HNSCC, PD-X naïve

### Treatment

30 mg efti (IMP321) s.c.  
200 mg pembrolizumab i.v.

### Status Report

- ✓ Fully approved in all countries (ES, GB, US and AU)
- ✓ Part A (1<sup>st</sup> line NSCLC): 41% initial ORR
- ✓ Stage 2 already opened for Parts A and C
- ✓ 49 patients recruited in total

**Updated results will be presented  
German Cancer Congress in Feb 2020**



13 sites in Europe / US /  
Australia

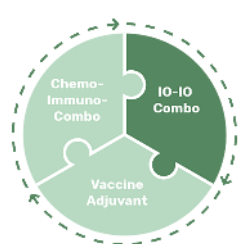
In collaboration with



**MERCK**

INVENTING FOR LIFE

**Key features: PD-X refractory patients (Part B), chemo-free option for NSCLC, first FDA IND for efti, PD-L1 all comers**



# Efti Clinical Development INSIGHT-004 (Phase I)

## INSIGHT-004: dose escalation of efti in combination with avelumab

Dose escalation, solid tumors, 2 cohorts of 6 patients each

efti (IMP321) + avelumab (Bavenico®) for 6 months + 6 months avelumab monotherapy

Phase I, monocenter DE, open label, IIT

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

### Status Report

<b>Patient Population</b>	Solid tumors after failure of standard therapy
<b>Treatment</b>	6 / 30 mg efti (IMP321) s.c. 800 mg avelumab i.v. Both every 2 weeks

- ✓ 1 site in Germany
- ✓ Protocol approved by CA / ED
- ✓ Six patients dosed thus far at 6 mg w/o DLT
- ✓ 1 PR at 6 mg
- ✓ 30 mg cohort opened

### In collaboration with



**Merck KGaA, I.K.F.**  
Darmstadt, Germany

**Key features: safety with a PD-L1 antagonist (avelumab)**

# Eftilagimod Alpha Partnerships



- EOC, an Eddingpharm spin-off holding the Chinese rights for efti, Phase I study in MBC ongoing
- Milestone and royalty bearing partnership



- Spin off from NEC, Japan. Est. December 2016; aims to develop cancer drugs discovered by artificial intelligence → mainly cancer vaccines
- Clinical Trial Collaboration (up to US\$5 million); clinical research ongoing



- Strategic supply partnership for the manufacture of efti
- Through WuXi, Immuteq was the first company to use a Chinese manufactured biologic in a European clinical trial



# Out-Licensed Immunotherapy Pipeline

# LAG525 (IMP701) for Cancer

- Novartis holds an exclusive WW licence to develop and commercialise LAG525 (which is derived from Immutep's antagonist antibody known as IMP701)
- 1st and 2nd milestone payments received by Immutep in August 2015 (undisclosed) and August 2017 (US\$1 million)
- In 2018 Novartis cancelled 90 other R&D programs but continued to invest heavily in progressing the development of LAG525
- Novartis currently has five clinical trials ongoing for LAG525 in multiple cancer indications for over 1,100 patients<sup>(1)</sup>



- **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**



# GSK'781 (IMP731) for Autoimmune Diseases

- GSK holds an exclusive WW licence to develop and commercialise GSK'781 (which is derived from Immutep's depleting antibody known as IMP731)
- Up to £64 million in upfront payments and milestones, plus royalties
- GSK portfolio review in 2017 -> GSK'781 continued despite cancellation of 13 clinical and 20 preclinical programs
- March 2018: Phase I trial in psoriasis completed in 67 subjects/patients<sup>(2)</sup>
- Phase I clinical study ongoing evaluating GSK'781 in 36 healthy Japanese and Caucasian subjects, PK/PD study
- September 2019: 1<sup>st</sup> patient dosed in Phase II trial in ulcerative colitis in 280 patients triggered a £4 million (~US\$5.0 million) milestone payment to Immutep<sup>(1)</sup>

**GSK's investigational product, GSK2831781, which is derived from IMP731 antibody, aims to kill the few activated LAG-3<sup>+</sup> T cells that are auto-reactive in autoimmune disease leading to long term disease control without generalized immune suppression**

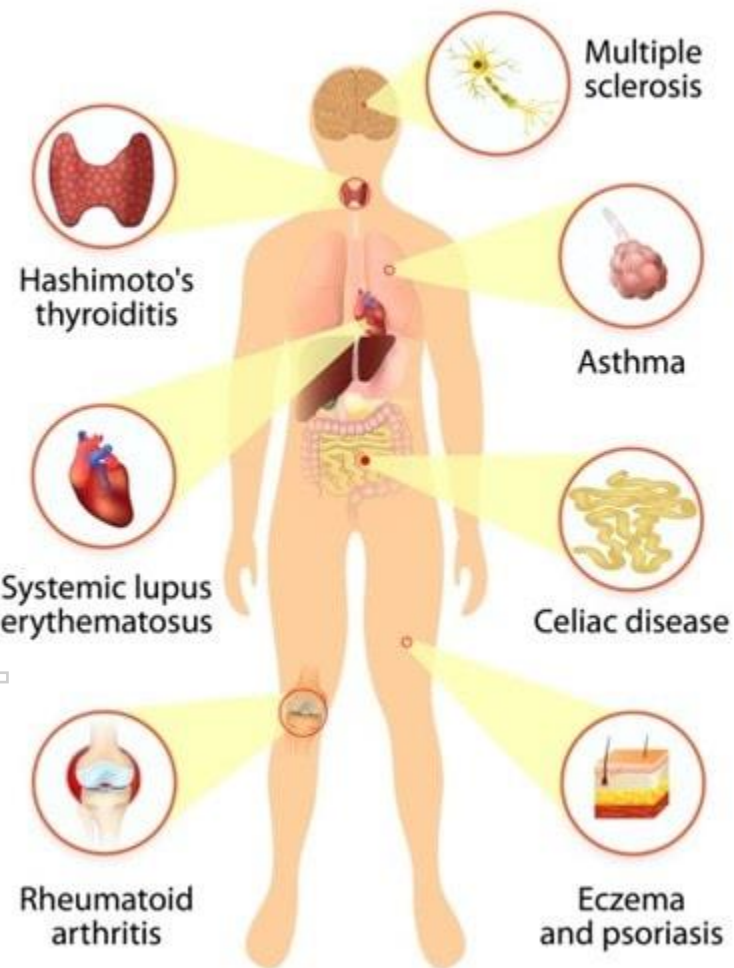


# IMP761

## (Autoimmune Diseases)

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

## AUTOIMMUNE DISEASES



## THE PRESENT: FIGHTING THE SYMPTOMS

Treating general inflammation:

corticoids, methotrexate,  
anti-TNF- $\alpha$ , -IL-6, -IL-17, -IL-23 mAbs

## THE FUTURE: FIGHTING THE CAUSE

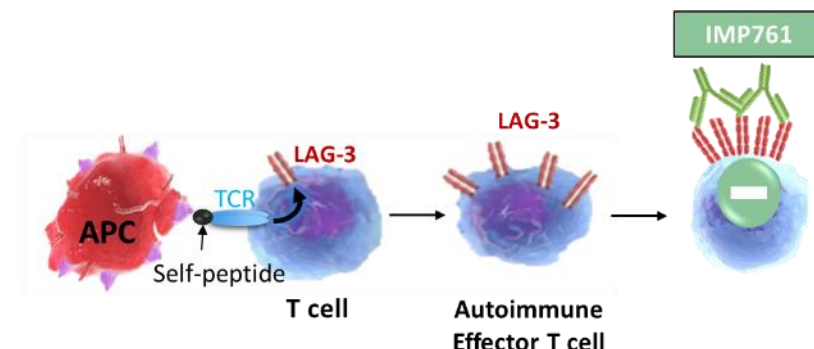
Treating the disease process:

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

# IMP761 Overview





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- **The Concept:** treating the cause of autoimmune diseases, not just the symptoms
- **The Target:** the self-peptide specific memory T cells harboring LAG-3
- **The Tool:** an agonistic LAG-3-specific mAb down-modulating self-peptide-induced TCR signaling
- **The Evidence (1)\*:** *in vitro* down-modulation of peptide-induced human T cell proliferation and activation
- **The Evidence (2)\*:** *in vivo* down-modulation of peptide-induced T cell infiltration / inflammation at the tissue site in a NHP model
- **IP:** 1 family - composition of matter & methods of treatment, expiry 2036
- **The Status:** cell line development ongoing and GMP manufacturing preparations underway in order to progress to clinical development



# LAG-3 Landscape and Outlook

# LAG-3 Therapeutic Landscape Overview

	Company	Program	Preclinical	Phase I	Phase II	Phase III	Total Trials	Patients on Trials
Agonist		Eftilagimod Alpha		2	2		4	424
Antagonist	BMS	Relatlimab		6	19	2	27	9,422
		LAG525 (IMP701)		1	4		5	1,100
	B.I.	BI754111		4	1		5	849
	Merck & Co. Inc.	MK4280		2	1		3	910
	Macrogenics	MGD013		1	1		2	1,105
	Tesaro <sup>(1)</sup>	TSR-033		1			1	260
	Regeneron <sup>(2)</sup>	REGN3767		1			1	589
	Xencor	XmAb-22841		1			1	242
	Symphogen A/S	SYM022		2			2	132
	Incyte	INCAGN02385		1			1	40
	F-Star	FS-118		1			1	51
Agonist		IMP761					--	--
Depleting AB		GSK2831781 (IMP731)		2	1		3	383

## Notes:

Sources: Company websites, clinical trials.gov, and sec.gov, as of September 27, 2019

(1) Tesaro was acquired by and is now part of GSK

(2) As of January 7, 2019 Regeneron is in full control of program and continuing development (Sanofi discontinued)

(3) Includes the Phase I study in psoriasis (completed March 2018)

Note: The green bars above represent programs conducted by Immute<sup>te</sup>p &/or its partners..

# 2020 Clinical Guidance\*

## Reported 2019:

- ✓ TACTI-002 to commence, Phase II trial in collaboration with MSD: H1 2019
- ✓ IMP761 program update: 2019
- ✓ INSIGHT-004 to commence, IIT Phase I trial in collaboration with Pfizer and Merck KGaA: Q2 2019
- ✓ AIPAC fully recruited: Q2 2019
- ✓ TACTI-002 first data in September 2019
- ✓ TACTI-mel final efficacy data: Q4 2019
- ✓ TACTI-002 data update: Q4 2019
- ✓ INSIGHT-004 update: Q4 2019

## Upcoming Data 2020 (est):

- MBC - mature, robust PFS & ORR data from AIPAC: Q1 2020 (March)
- NSCLC 1st line - more data from Stages 1 and 2 from TACTI-002 throughout 2020 (e.g. German Cancer Congress February 2020)
- HNSCC 2nd line - initial data from Stages 1 and 2 from TACTI-002 throughout 2020 (e.g. AACR April 2020)
- NSCLC 2nd line - initial data from Stage 1 from TACTI-002 throughout 2020
- Combination with avelumab - initial data from Phase I trial throughout 2020

\*The actual timing of future data readouts may differ from expected timing shown above. These dates are provided on a calendar year basis.

# Highlights

Global Leader in  
Development of LAG-3  
Therapeutics

First-in-Class /  
Potential Pipelines in  
Product Candidates

Near-Term Phase II  
Clinical Data Expected  
for Eftilagimod Alpha

Leading Industry  
Partners

- More clinical-stage LAG-3 programs than any other company
- Dr. Frédéric Triebel, MD Ph.D., Immutep's Chief Scientific Officer and Chief Medical Officer, discovered the LAG-3 gene
- LAG-3 fusion protein that is a MHC II agonist and APC activator for oncology
- LAG-3 agonist mAb for autoimmune diseases
- Significant data updates from Phase II clinical study in combination with Keytruda<sup>(1)</sup> expected in **2020**
- PFS data from Phase IIb double blind placebo-controlled study of 227 patients with HER2-negative / HR positive MBC expected in **Q1 2020 (March)**
- Relationships with multiple industry partners including Novartis, GSK, Merck (MSD), Pfizer & Merck KGaA



# Thank you!