

A Global Leader in LAG-3 Therapeutics in Oncology and Autoimmune Disease

Corporate Presentation – September 2022 (ASX: IMM, NASDAQ: IMMP)



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Immutep Overview



Pioneering LAG-3 Portfolio in Oncology & Autoimmune Disease

Immutep is a pure-play LAG-3 clinical-stage company with four product candidates that address significant market opportunities in oncology & autoimmune disease



Compelling Clinical Data

Clinical trials of lead candidate eftilagimod alpha (efti) with immunotherapy & chemotherapy have shown compelling results in NSCLC, HNSCC, HR+/HER2- BC, melanoma and other solid tumors

Immutep LAG-3 Pipeline







Immune system's role in controlling cancer has led to regulatory approval of immunotherapies targeting CTLA-4, PD-1, and now LAG-3 checkpoints



LAG-3 is unique in that its inhibition on T cells & activation of dendritic cells engages the adaptive & innate immune systems against cancer offering significant potential to: (1) improve responses to standard-of-care immunotherapy & chemotherapy, (2) limit emergence of resistance, (3) offer chemotherapy-free options in select indications.



LAG-3 Therapeutics for Oncology





• Immutep developed the first anti-LAG-3 antibody and licensed it to CoStim Pharmaceuticals in 2012, which was acquired by Novartis in 2014

Novartis' anti-LAG-3 mAb, LAG525, activates effector T cells & inhibits regulatory T cells (removing two brakes on the immune system to
respond to and kill cancer cells) and has been tested in multiple clinical trials combined with spartalizumab (anti-PD-1) and chemotherapy**

• IP estate for LAG525 continues to strengthen with patent grants in key markets including US, Europe, Japan and China





Broad activation of immune system

- Efti capitalizes on LAG-3's unique ability to drive adaptive & innate immune systems against cancer
- Efti has high affinity for a subset of MHC II ligand on APCs and their activation drives broad stimulation of multiple anti-tumor cells

Compelling pairing capabilities

- Excellent safety profile drives high suitability for combination partnering
- Synergistic activity & encouraging clinical results with multiple agents including anti-PD-1, anti-PD-L1, and chemotherapy
- Enhances clinical activity of anti-PD-1 across PD-L1 status, including low & negative PD-L1 tumors



LAG-3's unique characteristics

Eftilagimod alpha

(Efti)

LAG-3



M Internal of Immunology

A Soluble Form of Lymphocyte Activation Gene-3 (IMP321/Efti) Induces Activation of a Large Range of Human Effector Cytotoxic Cells

Chrystelle Brignone, Caroline Grygar, Manon Marcu, Knut Schäkel and Frédéric Triebel The Journal of Immunology September 15, 2007, 179 (6) 4202-4211; DOI: 10.4049/jimmunol.179.6.4202

nature medicine

A potential biomarker for anti-PD-1

immunotherapy - A recent study identifies an immune cell type known as classical monocytes in the peripheral blood as a potential biomarker for response to anti-PD-1 immune checkpoint therapy in metastatic melanoma. Goswami, S., Basu, S. & Sharma, P. Nat Med 24, 123–124 (2018). https://doi.org/10.1038/nm.4489

Science Immunology

CXCL9 and CXCL10 bring the heat to tumors Robin Reschke, Thomas F. Gajewski

SCIENCE IMMUNOLOGY - 22 Jul 2022, Vol 7, Issue 73 DOI: 10.1126/sciimmunol.abq6509



Monocyte-derived APCs are central to the response of PD1 checkpoint blockade & provide a therapeutic target for combination therapy Schetters STT, Rodriguez E, Kruijsen LJW, et al Journal for ImmunoTherapy of Cancer 2020;8:e000588. doi: 10.1136/jitc-2020-000588

Pipeline in a Product with Broad Potential





- Combination approaches comprise ~90% of all anti-PD-1/PD-L1 trials to enable more efficacious therapies as up to 80% of patients do not respond to monotherapy
- Opdualag, the first LAG-3 therapeutic candidate to receive FDA approval, is an IO-IO combination of relatlimab (anti-LAG-3) and nivolumab (anti-PD-1)







TACTI-002/KEYNOTE-798: 1st Line Non-Small Cell Lung Cancer (Part A)



Baseline characteristics for	Part A (N=114)		
Age, median (range), years		67 (44-85)	
Sex, n (%)	Female / Male	30 (26.3) / 84 (73.7)	
ECOG PS score, n (%)	0/1	43 (37.7) / 71 (62.3)	
Smoking status, n (%)	Current or Ex-smoker / Non-smoker	108 (94.7) / 6 (5.3)	
Histology, n (%)	Squamous / Non-squamous / Unknown 40 (35.1) / 72 (63		
Metastatic disease, n (%)	Yes / No 106 (93.0) / 8		
PD-L1 expression TPS ¹ , n (%)	< 1% 1-49% ≥ 50% Not evaluable	37 (32.5) 40 (35.1) 31 (27.2) 6 (5.3)	
Previous therapy, n (%)	Radiotherapy Surgery Systemic therapy for non-metastatic disease	38 (33.3) 23 (20.2) 25 (21.9)	

All-comer trial for patients with all levels of PD-L1 expression

Encouraging Clinical Results; Primary Objective Achieved



TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)

- Primary objective achieved (ORR >35%)
 - 38.6% ORR (iRECIST) & 37.7% (RECIST 1.1) in ITT population
 - 42.7% ORR (iRECIST) and 41.8% (RECIST 1.1) in evaluable¹ population
 - 35% ORR (iRECIST) in squamous & 38.9% in non-squamous tumors
- Superior ORR/PFS across all PD-L1 levels
- Comparable disease control rate (69-79%) across all PD-L1 levels
- Sustained, durable responses; median DoR not yet reached
- Combination safe, well tolerated & discontinuation rate of 9.6% in line with pembro monotherapy^{##}

	Efti + Keytruda Combination*	Keytruda Monotherapy	Keytruda Monotherapy
Clinical Trial & Phase	P2 (TACTI-002/KEYNOTE-798)	P3 (KEYNOTE-042)	P3 (KEYNOTE-024)
Patient Number / tumor type	114 / 1L NSCLC	637 vs. 637 / 1L NSCLC	154 vs. 151 / 1L NSCLC
PD-L1 Status	All comer PD-L1 TPS ≥0%	PD-L1 TPS ≥1%	PD-L1 TPS ≥50%
Complete Response (CR) %	1.8% (TPS ≥ 0%)	0.5% (TPS ≥ 1%)	3.9% (TPS ≥ 50%)
Partial Response (PR) %	36.8% (TPS ≥ 0%)	26.8% (TPS ≥ 1%)	40.9% (TPS ≥ 50%)
Stable Disease (SD) %	35.1% (TPS ≥ 0%)	38.6% (TPS ≥ 1%)	24.7% (TPS ≥ 50%)
Overall Response Rate (ORR) %	38.6% (TPS ≥ 0%)	27% (TPS ≥ 1%)	44.8% (TPS ≥ 50%)
ORR in PD-L1 TPS <1%	28.1%	n/a	n/a
ORR in PD-L1 TPS ≥1%	45.5%	27%	n/a
ORR in PD-L1 TPS 1-49%	41.7%	16.6%	n/a
ORR in PD-L1 TPS >50%	52.6%	39%	44.8%
Median PFS (months)	6.9 ^{**} (TPS ≥ 0%)	5.4 (TPS ≥ 1%)	10.3 (TPS ≥ 50%)
mPFS in PD-L1 TPS<1%	4.2#	n/a	n/a
mPFS in PD-L1 TPS ≥1%	8.4#	5.4	n/a
mPFS in PD-L1 TPS 1-49%	9.3#	4.2	n/a
mPFS in PD-L1 TPS ≥50%	11.8#	7.1	10.3

32.5% 1L NSCLC patients in TACTI-002 have TPS <1% and ~68% patients have PD-L1 TPS <50%

*Efti+Keytruda combination data: iRECIST by PD-L1 (central only); **Interim median PFS in the ITT (unselected for PD-L1); #PFS by PD-L1 status (N=108) using central assessment for 87 patients. For 21 patients, local assessment was used due to non evaluable central assessment results; Data cut-off April 16, 2021. Keytruda KN-042 & KN-042 mono data: The Lancet https://doi.org/10.1016/S0140-6736(18)32409-7, Oral Presentation 2018 ASCO Annual Meeting, PP-L1; #N-024 J Clin Oncol 2019, KN-024 J Clin Oncol 2019, https://doi.org/10.1016/S0140-6736(18)32409-7, Oral Presentation 2018 ASCO Annual Meeting, https://doi.org/10.1016/S0140-6736(18)32409-7, Oral Presentation 2018 ASCO Annual Meeting, https://doi.org/10.1016/S0140-6736(18)32409-7, Oral Presentation 2018 ASCO Annual Meeting, https://doi.org/10.1016/S0140-6736(18)32409-7, Oral Presentation 201

Robust ORR/PFS Across Entire PD-L1 Spectrum vs Pembrolizumab

TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)



Pembrolizumab ('pembro') mono efficacy used for benchmarking:

Total: calculation based on KN-001; KN-042 and on adjustment for the same PD-L1 subgroup distribution as in TACTI-002.

 $\underline{<$ 1 % TPS: calculation based on a very limited data set from KN-001. 1st and 2nd line altogether.

1-49 % TPS: calculation based on KN-001, KN-042.

 \geq 50 % TPS: calculation based on KN-001, KN-042.

 \geq 1 % TPS: calculation based on KN-001, KN-042.

Efti + Pembro ORR by iRECIST, unconfirmed, Total (N=114) and PD-L1 TPS subgroups (N=87). Data cut-off date: April 15, 2022 95 % CIs are internal calculations using Clopper-Pearson: https://epitools.ausvet.com.au/ciproportion



Pembrolizumab ('pembro') mono efficacy used for benchmarking: 1.49 % TPS: calculation based on KN-042 $\ge 50 \%$ TPS: calculation based on KN-042 $\ge 1 \%$ TPS: calculation based on KN-042

Deep and Durable Responses



TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)



Tumor Burden Reduced in Majority of Patients

Change in Tumor Size Over Time



- Responses are deep & long-lasting; median DoR not yet reached
- 80% (35) of responses¹ already confirmed & 11.4% (5) pending confirmation
- 95% of patients having a response < 4 months after study start
- Only 8.6% of patients with confirmed response² progressed ≤ 6 months until data cut-off
- 66% (68) of patients with post-baseline assessment had decrease in target lesions

Benchmarking against IO & IO-Chemo Combinations



TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)

	TPS	Treatment		Efficacy ⁽¹⁾	Toxicity: AEs leading to disc.
		Efti + Pembro	ORR 45.5%	PFS 8.4 mos	< 10%
	≥1%	Pembro mono	ORR 27.5%	PFS 5.4 mos	1-14%
		lpi + Nivo ⁽²⁾	ORR 36%	PFS 5.1 mos	18%
		Efti + Pembro	ORR 41.7%	PFS 9.3 mos	< 10%
	1-49%	Doublet Chemo + Pembro	ORR 49.2% (NSQ) & 50% (SQ)	PFS 7.2 (SQ) & 9.2 (NSQ) mos	14%
CLC		Pembro mono	ORR 16.8%	PFS 4.1 mos	1-14%
NSO	> 50%	Efti + Pembro	ORR 52.6%	PFS 11.8 mos	< 10%
	≥ 50%	Pembro/Atezo/Libtayo mono	ORR 35-45%	PFS 7-10 mos	1-14%
		Efti + Pembro	ORR 38.6%	PFS 6.9 mos	< 10%
I	0-100%	Doublet Chemo	ORR 19-30%	PFS 5-9 mos	8-22%
		Doublet Chemo + Pembro	ORR 48% (NSQ) & 63% (SQ)	PFS 6 (sq) & 9 (Nsq) mos	14%
		Doublet Chemo + Atezo + Beva	ORR 56%	PFS 8.4 mos	33%
		Doublet Chemo + Ipi + Nivo	ORR 38%	PFS 6.7 mos	19%

- ✓ Low efficacy of anti-PD-(L)1 monotherapy for patients with TPS <50% (~70% of total population)
- ✓ Double chemo + anti-PD-(L)1 → increased ORR & OS but shorter DoR due to chemo & more toxic; Ipi & Beva combos → high burden in terms of toxicity & high number of patients discontinuing
- Efti addresses both issues as shown with TACTI-002 results; INSIGHT-003 trial also exploring efti + pembro + chemo combination

Arrow lengths are not proportional representations of efficacy data. Data for Efti + Pembro derived from ASCO22 oral presentation. Data cut-off: April 15, 2022. Data for pembro derived from KN-001, KN-042, KN-189, KN-407 publications. ⁽¹⁾ ORR and PFS results taken from respective publications of registrational trials. ⁽²⁾ Only approved by FDA not by EMA for TPS ≥ 1%.



INSIGHT-003: Phase I in Solid Tumors Focusing on NSCLC Adenocarcinomas

INSIGHT-003 - Third arm (Stratum C) of ongoing Investigator-initiated study focusing on NSCLC adenocarcinomas

Status:

- Recruiting (over 50% enrolled^{*}; reported good safety from initial five patients in Dec 2021)
- Initial results to be reported by year end^{*}

Design:

- Evaluating triple combination therapy consisting of efti in conjunction with carboplatin and anti-PD-1 therapy with solid tumors
- Trial will assess safety, tolerability and initial efficacy of the combination



Triple Combination Approach to Capitalize on Efti's Synergistic Effects with Chemotherapy & Immunotherapy





TACTI-002/KEYNOTE-798: 2nd Line Head & Neck Squamous Cell Carcinoma (Part C)



Responses	at	all	PD-L1	levels	inc	luding	5	iCRs
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	Efti + Keytruda Combination*	Keytruda Monotherapy [#]
Clinical Trial & Phase	P2 (TACTI-002/KN-798)	P3 (KN-040)
Patient Number / tumor type	39 / 2L HNSCC	247 vs. 248 / 2L HNSCC
PD-L1 Status	PD-L1 All comer	PD-L1 All comer
Complete Response (CR) %	13.5%	1.6%
Partial Response (PR) %	16.2%	13%
Stable Disease (SD) %	8.1%	22.7%
ORR in evaluable patients %	35.5%	n/a
Overall Response Rate (ORR) %	29.7%	14.6%
PD-L1 CPS ≥1% group	40.7%	17.3%
PD-L1 CPS ≥20% group	64.3%	21.9%
Median PFS (months)	2.1	2.1
PD-L1 CPS ≥1% group	4.1	2.2
Median OS (months)	12.6	8.4
PD-L1 CPS ≥1% group	12.6	8.7

Robust ORR, CR and DoR for Efti + Pembro vs Pembro



TACTI-002/KEYNOTE-798: 2L HNSCC (Part C)



Fast Track Designation in 1L HNSCC



TACTI-003: Phase IIb in 1st Line Head and Neck Squamous Cell Carcinoma (HNSCC)





Status:

- Recruiting (~30% enrolled; recruitment accelerating as further sites have been activated*)
- FDA Fast Track designation on strength of TACTI-002 data in 2L HNSCC

Design:

- Randomised trial with ORR as primary endpoint
- Sites worldwide (AU, US, Europe)
- Approximately 154 patients: either to be randomised to have sufficient patients in each group or in an experimental arm



Efti + Anti-PD-L1 (Avelumab) in Advanced Solid Tumors



INSIGHT-004: Phase I in Various Advanced Solid Tumors



P Merck KGaA, Darmstadt, Germany





Dose escalation study evaluating efti in combination with BAVENCIO (avelumab)

Key Takeaways*:

- Combination safe with promising signals of efficacy including durable responses
- 5/12 (42%) partial responses in different indications:

 1st line MSI high colorectal cancer; (2) 1st line pleural mesothelioma; (3) after radio-chemo in squamous anal cell; (4) pre-treated squamous cervical cancer (PD-L1 TPS < 1%) carcinoma; (5) 3rd line gastroesophageal junction
- Activity also observed in pre-treated non-immunogenic tumors



AIPAC Phase IIb: Significant OS Improvement Across Multiple Pre-Specified Subgroups with Superior QoL



AIPAC: Active Immunotherapy PAClitaxel in HER2–/ HR+ metastatic breast cancer Phase IIb Trial

AIPAC: Multicenter, placebo-controlled, double-blind, 1:1 randomized Phase IIb study; 226 patients randomized to efti (N=114) or placebo (N=112)

Subgroup Analysis	Median Overall Survival	Hazard Ratio	P-value
Low Monocytes	+19.6 months mOS	HR 0.44	p=0.008
<5 Years Since Diagnosis [#]	+9.4 months mOS	HR 0.57	p=0.008
Under 65 Years	+7.5 months mOS	HR 0.66	<i>p=0.017</i>
High NLR Ratio [#]	+6.9 months mOS	HR 0.61	p=0.012
Luminal B	+4.2 months mOS	HR 0.67	p=0.049
No Prior Taxanes	+4.8 months mOS	HR 0.74	p=0.076

- Efti + paclitaxel had ORR & DCR of 48.3% and 85.1% vs placebo ORR & DCR of 38.4% and 75.9%, respectively
- Efti + paclitaxel led to +2.9 month increase in median OS to 20.4 months, and +0.46 month increase in PFS to 7.12 months^{**} (Effect on PFS observed until paclitaxel discontinued at 6 months under European trial design)



Statistically-significant OS improvement in multiple pre-specified subgroups, with no Quality of Life deterioration observed in efti group at 6 months versus significant deterioration in placebo group

Substantial Increase in Monocytes, CXCL10 & Cytotoxic CD8+ T Cells Correlated to Stronger OS



AIPAC: Active Immunotherapy PAClitaxel in HER2–/ HR+ metastatic breast cancer Phase IIb Trial

Statistically-Significant Increase of Cytotoxic CD8+ T Cell Count



Minimal Residual Effect: samples taken just before next treatment

Statistically-Significant Correlation: OS & Cytotoxic CD8⁺ T cell count



Fold Change of CD8+ & CD4+ T Cells, Monocytes, and CXCL10

Biomarker	Treatment	Fold change mean ± SEM Median (25%Q-75%Q)	p-value*
Monocytes	efti (n=42)	5.81±1.49 2.07 (1.40-5.16)	0.025
	Placebo (n=34)	2.29 ±0.44 1.47 (1.21-2.23)	0.025
Activated CD8 T cells	efti (n=45)	2.54 ±0.35 1.76 (1.10-3.25)	0.027
	Placebo (n=35)	1.86 ±0.40 1.17 (0.79-1.67)	0.027
Activated CD4 T cells	efti (n=42)	2.17 ±0.23 1.56 (1.07-3.14)	0.200
	Placebo (n=34)	1.54 ±0.13 1.31 (1.05-1.84)	0.206
CXCL10	efti (n=32)	2.78 ±0.30 2.39 (1.36-3.93)	0.006
	Placebo (n=22)	1.56 ±0.18 1.40 (0.86-2.18)	0.006



LAG-3 Therapeutics for Autoimmune Disease





Present Approaches Fight the Symptoms of Autoimmune Diseases

Treating general inflammation: Corticoids, methotrexate, anti-TNF-α, -IL-6, -IL-17, -IL-23 mAbs



Future Approaches Target the Causes of Autoimmune Disease

Treating the disease process: Targeting autoimmune memory T cells with depleting or agonist LAG-3 antibodies

IMP761: Broad Potential Targeting Auto-Reactive Memory T Cells



A LAG-3–Specific Agonist Antibody for the Treatment of T Cell–Induced Autoimmune Diseases Mathieu Angin, Chrystelle Brignone and Frédéric Triebel J Immunol January 6, 2020, ji1900823 Deficiency in LAG3 Pathways Linked to Development of Autoimmune Diseases



Epigenetic Reprogramming (DNA methlyation, histone modifications, miRNAs)



(e.g. T1 Diabetes, Rheumatoid Arthritis) (e.g. Allergic (e Asthma) Bov

(e.g. Irritable (e.g. Psoriasis) Bowel Syndrome)

IMP761

Immutep's proprietary humanized IgG4 LAG-3–specific antibody



As the **first LAG-3–specific agonist** acting upstream on activated T cells, the root cause of self-Ag–specific T cell–induced autoimmune diseases, IMP761 is a **potential gamechanger in autoimmune diseases**.

Summary



2022 Milestones

- Clinical data from TACTI-002
 - ✓ 1L NSCLC Oral Presentation at ASCO
 - ✓ 2L NSCLC PD-X refractory data presented at European Lung Cancer Congress 2022
- Additional clinical data updates through year end
 - New data from Phase II TACTI-002 in 1L NSCLC
 - Initial results from INSIGHT-003 (first triple-combo data)
 - Update from Phase IIb TACTI-003 in 1L HNSCC
- Ongoing recruitment & updates from randomized trial in 1L HNSCC (TACTI-003)
- Regulatory updates
- Manufacturing scale up to 2,000L
- Expansion of existing programs
- Updates from IMP761 and partnered programs (e.g. Novartis, GSK, EOC Pharma)

Corporate Snapshot

- Pioneering LAG-3 portfolio in oncology and autoimmune diseases with four product candidates in multiple clinical trials
- First-in-class positioning with eftilagimod alpha (efti)
- Multiple big pharma partnerships & collaborations, while retaining full control of efti (ex-China) & IMP761
- Well funded with ~A\$80 million* in cash
- Cash runway to early CY2024*
- Ticker symbols:
 - IMM (ASX)
 - ✓ IMMP (NASDAQ)
- Market cap ~A\$217M / \$147M US**



Thank You