

Immutep Corporate Presentation – August 2024 (ASX: IMM; NASDAQ: IMMP)

Forward-Looking Statements



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Immutep Highlights





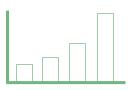
Leader in LAG-3 immunotherapy

LAG-3 pure play with four clinical-stage assets and one preclinical program designed to fight cancer & autoimmune diseases.



First-in-class lead candidate

Eftilagimod alfa (efti) is a unique immune system activator that has shown strong efficacy with a favourable safety profile in multiple cancer indications.



Multiple catalysts ahead; Phase III in 1L NSCLC

Phase III program with MSD in first line non-small cell lung cancer (1L NSCLC) with efti & KEYTRUDA, the top selling drug globally. Laterstage clinical programs in additional large markets* with data readouts in 2024 and beyond.



Validation through partnerships

Multiple partnerships and collaborations with large pharma and institutions.



Global presence; strong IP and balance sheet

Global presence and strong IP across LAG-3 portfolio. Well-funded with cash, cash equivalent, & term deposit of ~\$182 million (US\$ ~119 million)# providing runway to end of CY2026.

Company Overview

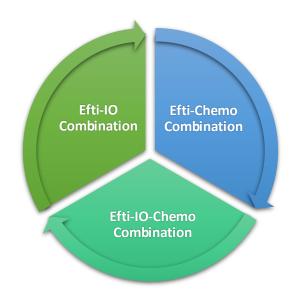


Pure-play LAG-3 company with deep pipeline in oncology & autoimmune diseases:

- Multiple LAG-3 Programs Four clinical-stage assets and one preclinical program
- **Upcoming Milestones** Multiple data updates from clinical programs

Lead candidate Efti addressing therapeutic gaps across the solid tumor treatment landscape:

- First-in-class MOA As unique MHC Class II agonist, efti activates innate and adaptive anti-tumor immunity
- Activity across PD-L1 spectrum Activity in hot/tepid/cold tumors addressing high unmet needs
- **Consistent Outcomes** Improved survival across multiple indications with mature data
- **Favourable Safety** Well-tolerated profile with standard-of-care IO and/or chemotherapy
- Manufacturing Achieved 2000L commercial scale production; authorization for clinical trial use granted in Sept '23



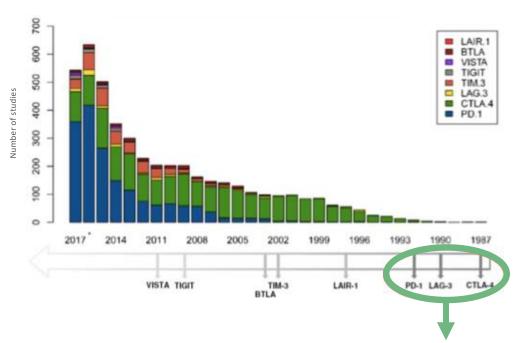
Strong IP/Balance Sheet:

- Intellectual Property Comprehensive IP portfolio; innovative biologics also potentially entitled to test data exclusivity (e.g., up to 12 years in US)
- Well-Financed Cash, cash equivalent and term deposit position totalling ~A\$181.8 million (~US\$118.7 million)¹ providing runway to end of 2026

LAG-3 Newest Entrant to Immuno-Oncology (IO) Landscape

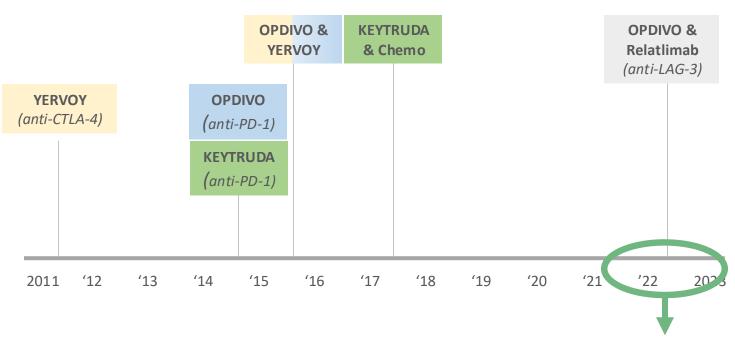


Immune Checkpoint Discovery and Clinical Studies*



LAG-3 discovered in 1990 by Immutep's Chief Scientific Officer, Dr. Frédéric Triebel

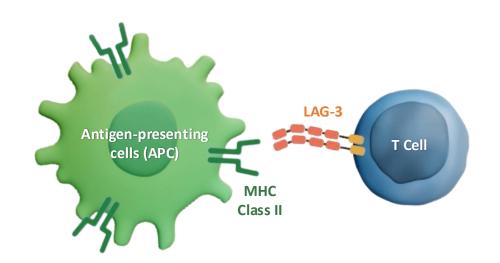
Regulatory Approval Timeline of Immuno-Oncology (IO) Therapies**



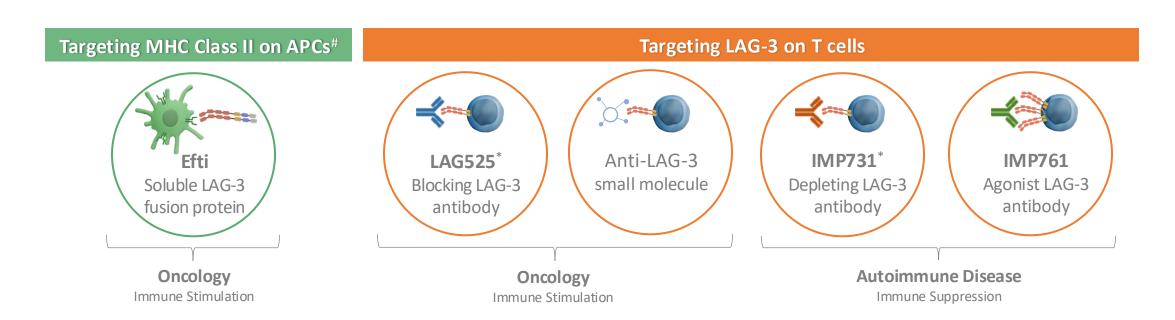
The immune system's ability to fight cancer has led to regulatory approval of IO therapies targeting the immune checkpoints CTLA-4, PD-1, and most recently LAG-3

Pioneering LAG-3 Immunotherapy Portfolio





Immutep has designed multiple first-in-class therapeutics targeting either MHC Class II molecules on antigen-presenting cells (APC) or LAG-3 on T-cells to fight cancer & autoimmune disease



Deep LAG-3 Pipeline in Oncology & Autoimmune Diseases



	Program		Indication	Preclinical	Phase I	Phase II	Late Stage#	Collaborations	Commercial Rights
ONCOLOGY	Eftilagimod Alfa Soluble LAG-3 Protein & MHC Class II agonist	n st	1L Non-Small Cell Lung Cancer (NSCLC) 1L Head & Neck Squamous Cell Carcinoma (HNSCC)	TACTI-004 Efti + Pemb				MERCK MERCK	inmutep Global Rights ex-China
			1L NSCLC, 2L HNSCC, PD-X Refractory 2L NSCLC	TACTI-002 Efti + Pemb				MERCK	
			1L Non-Squamous NSCLC Urothelial Cancer	INSIGHT-003 Efti + Pe				Merck KGaA Darmstadt, Germany	
			Soft Tissue Sarcoma	EFTISARC-NEO Efti + P				Narodowy Instytut Onkologii on Not Stommended on Pattern North Salmon	
			HR+/HER2- Metastatic Breast Cancer & TNBC Metastatic Breast Cancer & Solid Tumors	Efti + Paclitaxel and Efti +				∳ E□C	♦E□C Efti China Rights
	Anti-LAG-3 Small Molecule	X.	Undisclosed					CARDIFF	Global Rights
	LAG525 Anti-LAG-3 Antibody	人	Solid Tumors & Blood Cancer Triple Negative Breast Cancer Melanoma Solid Tumors Triple Negative Breast Cancer					NOVARTIS	NOVARTIS Global Rights
AUTOIMIMUNE DISEASE	IMP731* Depleting LAG-3 Antibody	人	Ulcerative Colitis Psoriasis Healthy Subjects						immutep®
	IMP761** Agonist LAG-3 Antibody	人	Undisclosed						Global Rights

Efti

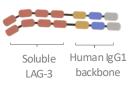
A proprietary soluble LAG-3 protein and first-in-class MHC Class II agonist

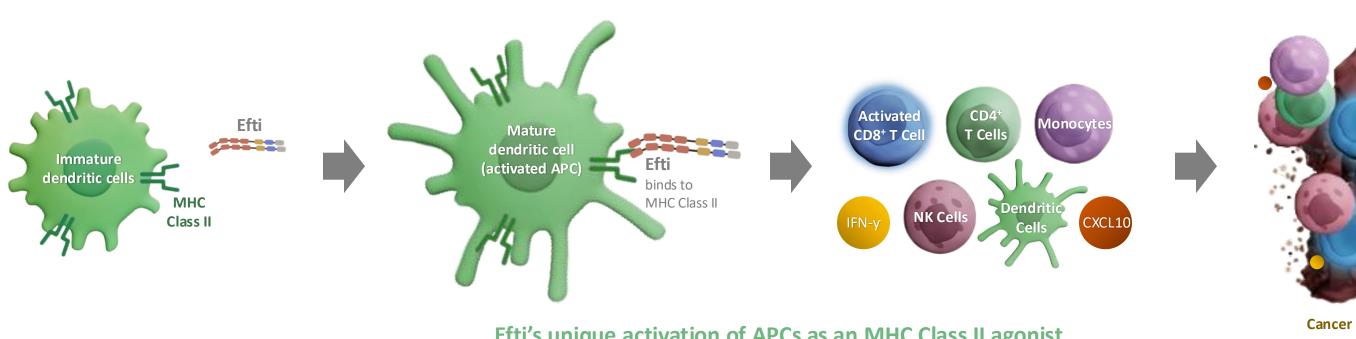
Efti: A Soluble LAG-3 'Key' to Stimulate Immune System via MHC II immutep



Eftilagimod alfa (efti)

A first-in-class soluble LAG-3 fusion protein with high affinity for a subset of MHC Class II molecules on antigen-presenting cells (APCs)



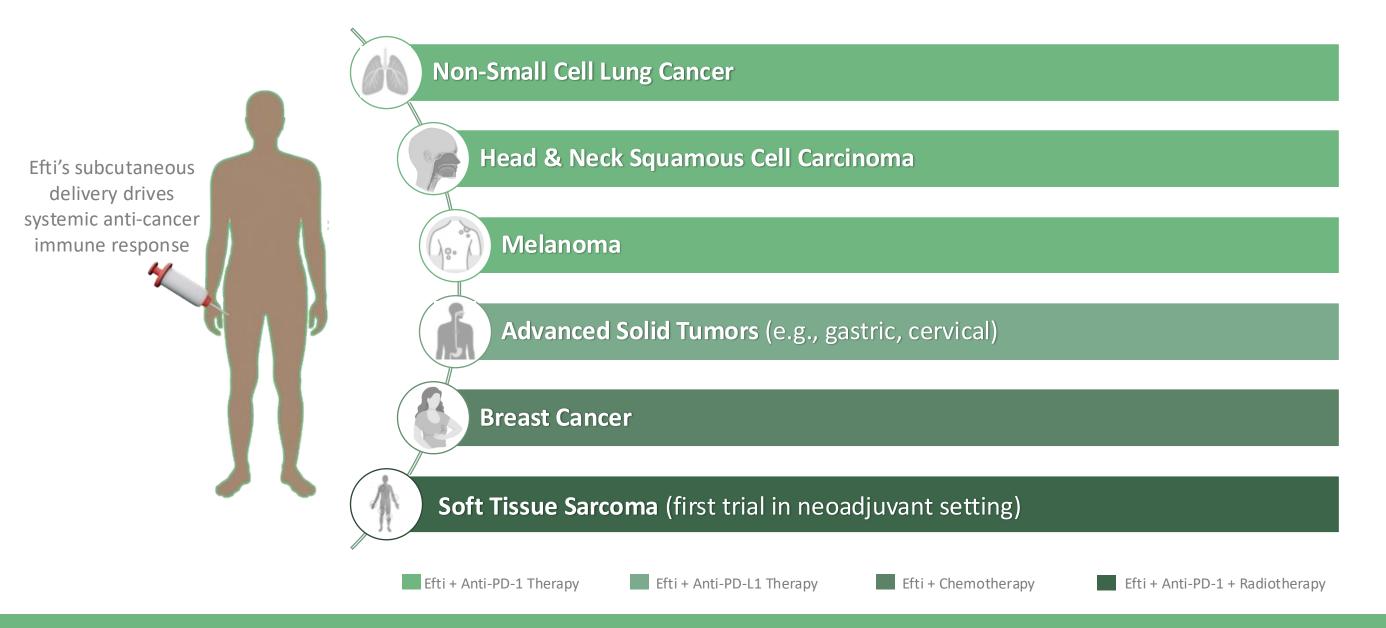


Efti's unique activation of APCs as an MHC Class II agonist drives a broad, sustained adaptive/innate immune response to fight cancer*

Systemic Immune Effect Leading to Positive Clinical Outcomes



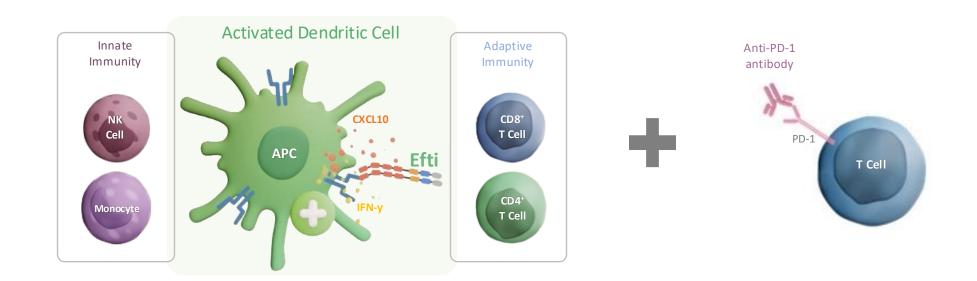
Encouraging data from efti in combination with IO, chemotherapy, radiotherapy across multiple indications LAG-3 IMMU



Differentiated Approach in Oncology



Efti has complementary action with immune checkpoint inhibitors (ICIs) like anti-PD-(L)1 therapy



Efti's unique activation of antigen-presenting cells (e.g. dendritic cells, monocytes) engages the adaptive and innate immune system, which complements anti-PD-(L)1 therapy to fight cancer

- Efficacy across "hot", "tepid", "cold" tumours in patients with high, low, and negative PD-L1 expression
- Additionally, efti in combination with anti-PD-(L)1 has a favourable safety profile

Substantial Commercial Opportunity in Combination with ICIs



Encouraging Clinical Data from Efti in Combination with Anti-PD-(L)1 Therapy including KEYTRUDA® & BAVENCIO®

- More than double Overall Survival of KEYTRUDA® (anti-PD-1) monotherapy and well above other standard-of-care IO-IO and/or IO-chemotherapy combinations in first line non-small cell lung cancer (1L NSCLC) with any PD-L1 expression
- More than double Progression Free Survival of KEYTRUDA® monotherapy in 1L
 NSCLC patients across varying levels of PD-L1 expression
- Double the Overall Response Rate of KEYTRUDA® monotherapy in 1L NSCLC and higher response rates in 1L & 2L head & neck cancer (HNSCC)
- Deep, durable responses in negative & low PD-L1 expressing patients with both KEYTRUDA® and with BAVENCIO® (anti-PD-L1) across multiple indications

KEYTRUDA® became the world's top selling drug in 2023 with sales exceeding \$25 billion

Anti-PD-1**







\$35+ Billion in 2023 sales

Anti-PD-L1**

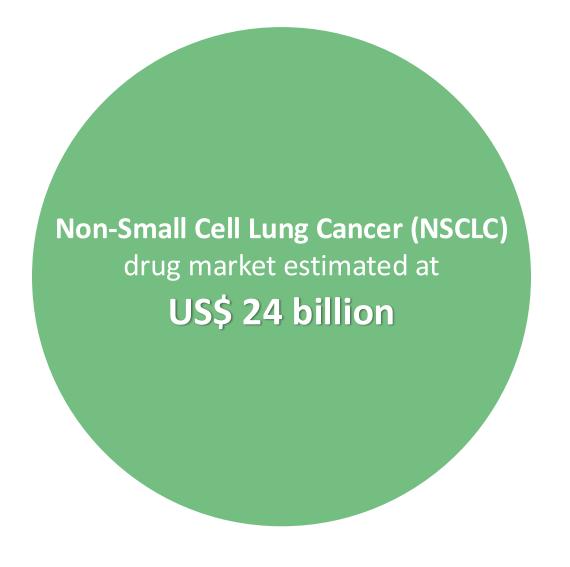


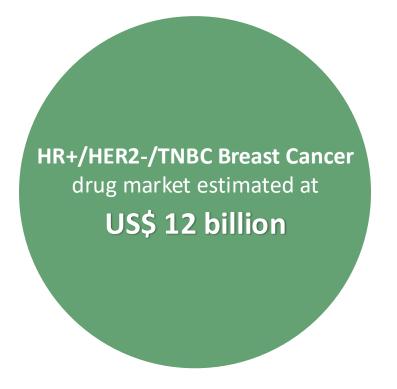


\$9+ Billion in 2023 sales

Clinical Trials Target Large Addressable Markets









*Efti has FDA Fast Track designation in 1L NSCLC and 1L HNSCC

Lead Indication

First Line Non-Small Cell Lung Cancer (NSCLC)



ASCO 2022 - Dr. Enriqueta Felip presenting 1L NSCLC data from TACTI-002/KN-798 in Oral Presentation



SITC 2022 - Dr. Wade lams presenting 1L NSCLC data from TACTI-002/KN-798 in Late Breaking Abstract Oral Presentation



ESMO 2023 - Dr. Enric Carcereny presenting Overall Survival data in 1L NSCLC from TACTI-002/KN-798



NSCLC Overview

- Lung cancer is a leading cause of cancer death^{1,2}
- 80 85% of lung cancers are non-small cell lung cancer (NSCLC)
- There are ~2.0 million NSCLC diagnoses worldwide annually
- Only ~20% of patients respond to immune checkpoint inhibitor (ICI) monotherapy
- Despite treatment advances, Overall Survival is still under 2 years for most NSCLC patients

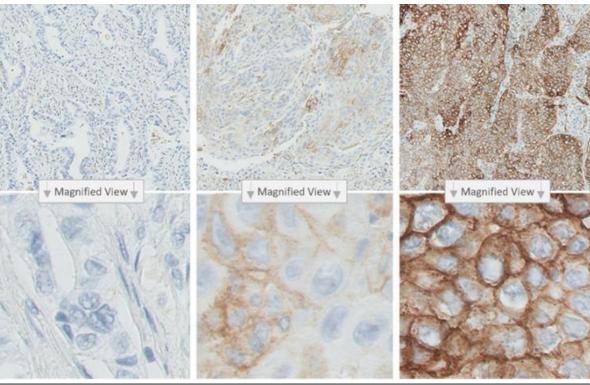
Total addressable NSCLC drug market expected to nearly double to US\$48 billion in 2031 and ICIs (including anti-PD-1 therapy) are expected to generate \$26 billion in sales³

PD-L1 Expression Levels and Why They Matter in 1L NSCLC



- PD-L1 expression as measured by Tumor Proportion Score (TPS) is an FDA approved predictive biomarker in 1L NSCLC for ICIs including anti-PD-(L)1 therapy
- Patients are grouped by high (TPS ≥50%), low (TPS 1-49%), and negative (TPS <1%) PD-L1 expression
- Generally, high expressors (who have a strong preexisting local anti-tumor T cell response) respond best, low expressors respond sub-optimally, and negative expressors have negligible responses to ICI therapies
- Mixed clinical responses to anti-PD-(L)1 therapy across these three PD-L1 levels are reflected in the regulatory landscape of approved chemo-free ICI therapies (as shown in the graphic to the right)

High PD-L1 (TPS >50%) **Negative PD-L1** (TPS < 1%) **Low PD-L1** (TPS 1-49%)



Approvals of Chemotherapy-free ICI Therapies in 1L NSCLC by PD-L1 Levels

None approved in Europe or the US for patients with negative PD-L1 expression

None approved in Europe and two approved in US for patients with low PD-L1 expression*

Three approved in both Europe and US for patients with high PD-L1 expression**

Targeting Entire 1L NSCLC Population Regardless of PD-L1 Status



Strength of clinical data from *Efti in combination with KEYTRUDA* in high, and particularly negative & low PD-L1 expressing patients, positions this novel combination to potentially establish a new standard of care in 1L NSCLC, one of the largest indications in oncology and the main revenue driver for KEYTRUDA today

1L NSCLC Patient Population by PD-L1 Tumor Proportion Score (TPS)¹





















TPS $<1\% = ^35\%$ population

Negligible responses to anti-PD-(L)1 therapy in these "cold" tumors

TPS 1-49% = ~35% population

Suboptimal responses to anti-PD-(L)1 therapy in these "tepid" tumors

TPS ≥50% = ~30% population

Best responses in these "hot" tumors (strong preexisting local anti-tumor T cell response)

+US\$24 billion TAM

TACTI-002 / KN-798 Trial Overview and Baseline Characteristics



Part A: Large Phase II trial (N=114) in metastatic 1st Line non-small cell lung cancer (1L NSCLC)

TACTI-002 (Part A) in 1L NSCLC

- Phase II, open label, Simon's two stage design
- Six countries (US, UK, ES, PL, UA, AU)
- 114 patients enrolled across 18 sites

PD-L1 Expression in TACTI-002

- TACTI-002 enrolled 1L NSCLC patients regardless of PD-L1 expression
- ~75% patients have PD-L1 TPS <50%, with ~35% having negative expression (TPS <1%)
- ~25% patients have high PD-L1 (TPS ≥50%); this is lower proportion than would typically be expected

TACTI-002 (Part A) Trial Design

 Advanced/metastatic 1L NSCLC

0-100% PD-L1 expression

EGFR/ALK negative

Combination Therapy 30mg efti Q2W + 200 mg pembrolizumab Q3W for 8 cycles, followed by 30mg efti + 200mg pembrolizumab for 9 cycles

200 mg pembrolizumab Q3W for 16 cycles

Up to 1 year —

Monotherapy

Primary endpoint: ORR by iRECIST Secondary Endpoints: ORR by RECIST 1.1, PFS, OS, DOR, safety, PK/PD

In collaboration with



Patients were recruited according to Simon's optimal two-stage design: during the first stage, 17 pts were recruited; second stage recruitment (n=19) was opened only after the number of responses was above 4. An extension stage (n=78) could be added if there were above 12 responses. In total, 114 pts were enrolled.

Baseline characteristics for	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 (63.2) / 2 (1.8)		
Metastatic disease, n (%)	Yes / No	113 (99.1) / 1 (0.9)		
PD-L1 expression TPS, n (%)	< 1% 1-49% ≥ 50%	Central only ¹ Central + local ² 32 (35.6) 37 (34.3) 38 (42.2) 42 (38.9) 20 (22.2) 29 (26.9)		
Previous therapy, n (%)	Radiotherapy Surgery Systemic therapy for non-metastatic disease	38 (33.3) 23 (20.2) 26 (22.8)		

Strong Efficacy Data across All PD-L1 Expression Levels in 1L NSCLC immutep



Tumor Response by PD-L1 Expression Level¹

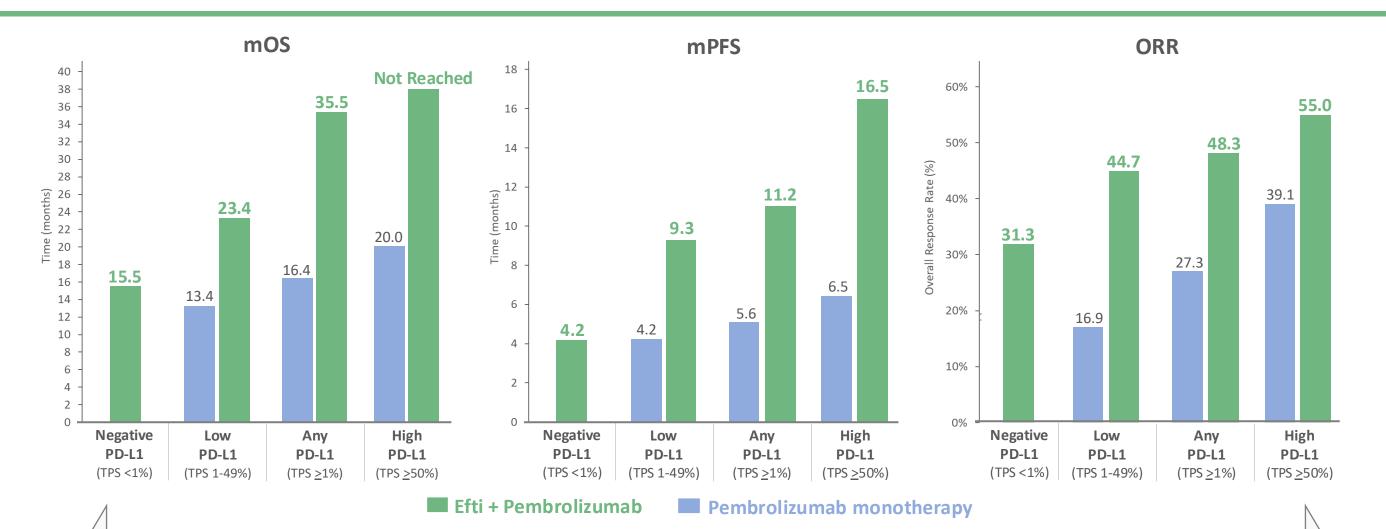
	All-Comer	Negative PD-L1	Low PD-L1	High PD-L1	Any PD-L1
	TPS 0-100% N=114	TPS <1% N=32	TPS 1-49% N=38	TPS ≥50% _{N=20}	TPS ≥1% _{N=58}
ORR ^{2,3,4}	40.4%	31.3%	44.7%	55.0%	48.3%
mPFS ² , months	6.6	4.2	9.3	16.5	11.2
mDoR ² , months	21.6	20.7	NR	18.7	24.2
mOS, months	20.2	15.5	23.4	Not Reached	35.5

ORR - Overall Response Rate mPFS – median Progression Free Survival mDOR - median Duration of Response mOS - median Overall Survival

- Strong efficacy across all patients, including negative & low expressors (~75% of patients in TACTI-002), differentiates efti with anti-PD-1 from other chemotherapy-free IO combinations in 1L NSCLC
- Excellent Overall Survival, the gold standard benchmark in oncology
- Exceptional durability and quality of responses with favorable safety profile
- Results offer compelling evidence of efti's unique stimulation of patients' immune systems and the positive impact that has in fighting cancer

Benchmarking to Pembrolizumab (KEYTRUDA®) Monotherapy





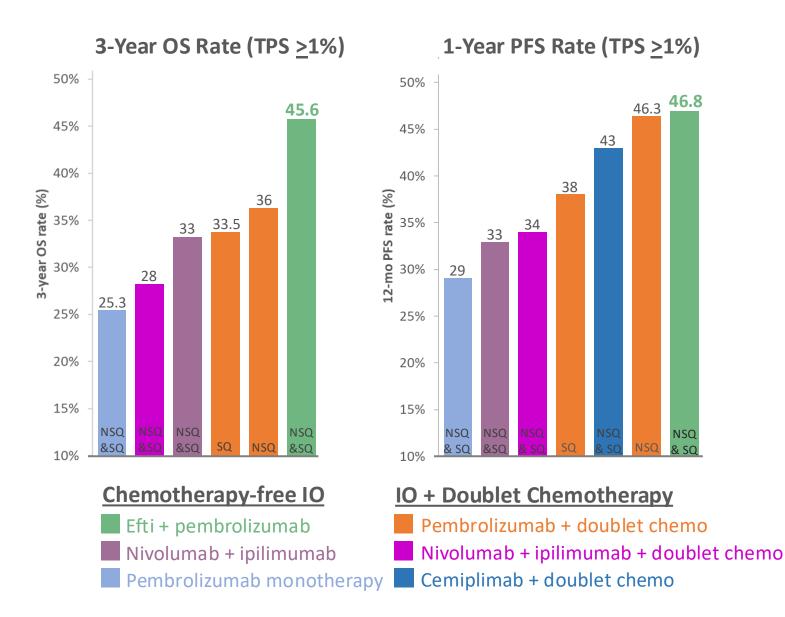
Robust median overall survival (mOS), median progression free survival (mPFS), and response rates (ORR) from efti plus pembrolizumab

Strength of efti plus pembrolizumab in TPS 1-49% contributes significantly to TPS ≥1% results, unlike other IO + anti-PD-1 combinations

OS/PFS/ORR in negative PD-L1 (TPS <1%) patients compares well to pembrolizumab monotherapy in low PD-L1 (TPS 1-49%) patients

Exceptional Durability and Quality of Responses



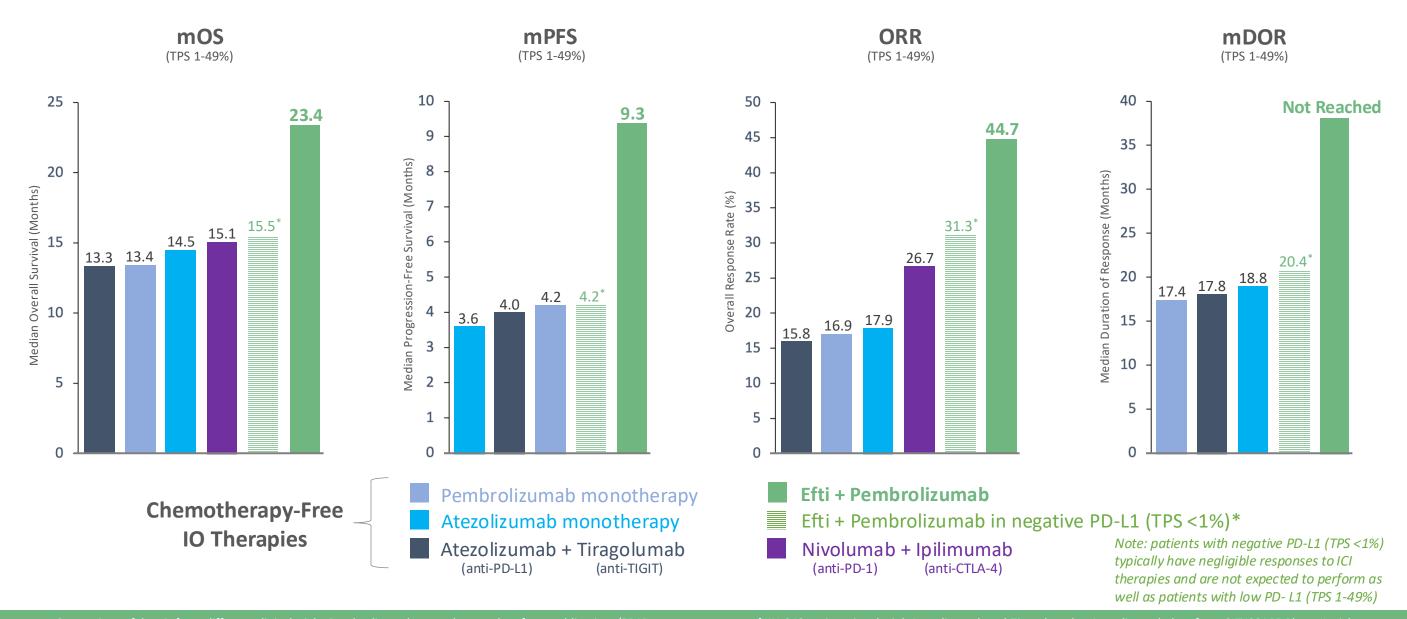


- Exceptional 3-year Overall Survival rate of 45.6% in 1L
 NSCLC, superior to pembrolizumab monotherapy and standard-of-care chemo-free & chemo-containing regimens
- Positive 12-month PFS rate of 46.8%, superior to pembro monotherapy and inline/above chemo-containing regimens
- Efti + pembro may be in a unique position to lift the tail of the survival curve in patients that express PD-L1

Differentiated Efficacy in Low & Negative PD-L1 Patients



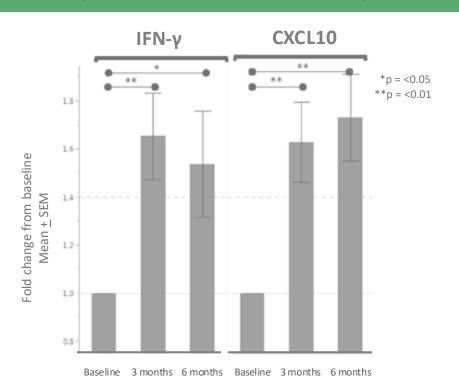
Efti + pembro results in <u>low & negative PD-L1 patients</u> compare favorably to other therapies <u>in low PD-L1</u>



Th1 Biomarker Data Linked to Improved Clinical Outcomes



Significant, sustained increases in CXCL10 & IFN-y in TACTI-002 Phase II trial in 1L NSCLC tied to efti's unique stimulation of immune system



* Similar increase in Th1 biomarkers also seen in randomized AIPAC Phase IIb trial in metastatic breast cancer, which combined efti solely with chemotherapy

- **IFN-γ** After first efti dosing, 86% (6/7) of responders* showed a ≥1.4-fold change and 86% (6/7) of non-responders# had less than a 1.4-fold change.
- **CXCL10** After first efti dosing, 100% (7/7) of responders* showed a ≥1.4-fold change and 100% (5/5) of non-responders# had less than a 1.4-fold change.



CXCL10 may be an important biomarker with anti-PD-1 therapies**

"Strategies that support effector T cell recruitment via induction of CXCL10 should be considered as a mechanism-based intervention to expand immunotherapy efficacy."1



"CXCL9 and CXCL10 bring the heat to tumors"3

Science Immunology

"...Chemokines CXCL9/10 are indispensable for robust responses to immune checkpoint inhibitors (anti-PD-1 and anti-CTLA-4)..."2

CLINICAL CANCER RESEARCH

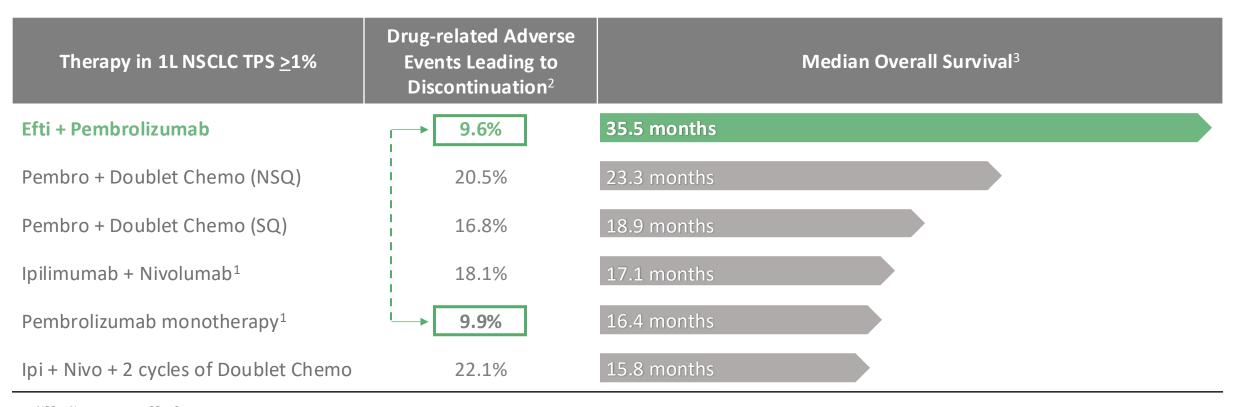
"Circulating CXCL10 at baseline appeared to be a robust predictor of response."4



Favorable Safety



Differentiated OS from Efti + Pembrolizumab achieved with a favorable safety profile



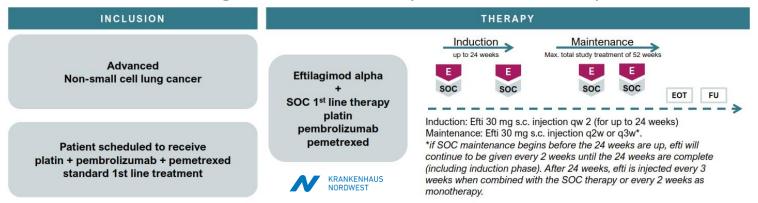
NSQ = Non-squamous; SQ = Squamous

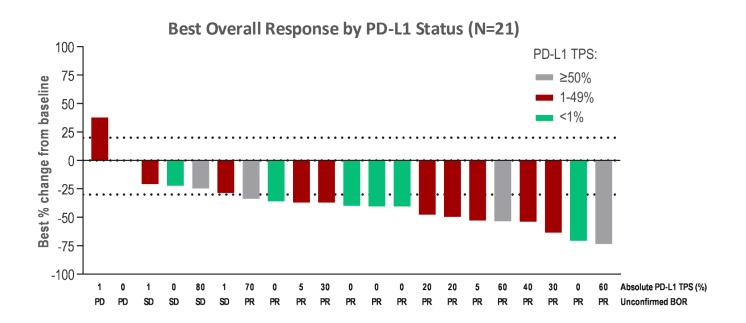
INSIGHT-003: IO-IO-Chemo Combination Trial in 1L NSCLC



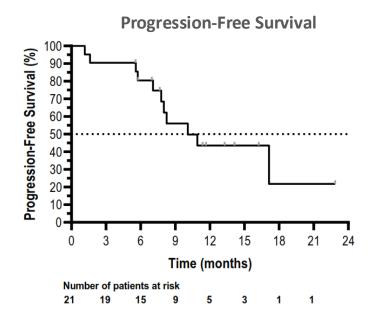
Promising initial efficacy & safety from first-in-human study evaluating Efti + KEYTRUDA + doublet chemo

INSIGHT-003 - Investigator-initiated study in first line non-squamous NSCLC





- Triple combination well tolerated and appears safe
- ~81% of patients have negative or low PD-L1
- At data cut-off, unconfirmed ORR of 71.4% (confirmed ORR of 66.7%)
- mPFS of 10.1 months and mOS not reached in ITT population (median follow up 12.4 months)



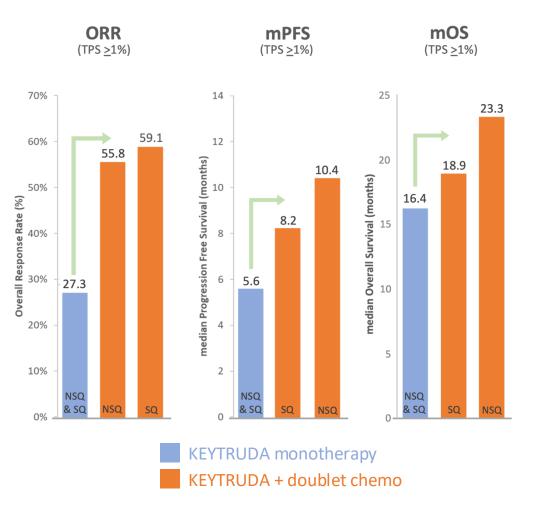
Chemotherapy is Additive to KEYTRUDA's Efficacy in 1L NSCLC

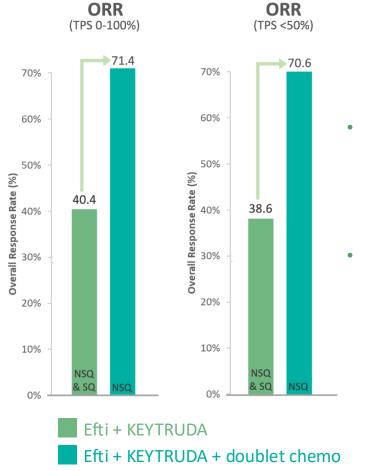


KEYTRUDA with Chemotherapy has Superior Efficacy versus **KEYTRUDA** Monotherapy in 1L NSCLC



Same Additive Benefit from Chemotherapy to Efti + KEYTRUDA Observed in INSIGHT-003 trial in 1L NSCLC





- Without chemo... Efti +
 KEYTRUDA has higher ORR,
 PFS, OS vs KEYTRUDA
 monotherapy in 1L NSCLC
 across all PD-L1 levels
- With chemo added... Efti + KEYTRUDA sees large ORR boost and OS/PFS trending favorably in INSIGHT-003

Registration Strategy in First line Non-Small Cell Lung Cancer (1L NSCLC)

Evolution of Efti + KEYTRUDA® in Clinical Trials





TACTI-mel



- First in human study of efti in combination with KEYTRUDA
- No collaboration or supply agreement with MSD for KEYTRUDA
- All patients enrolled had suboptimal responses or progressive disease after KEYTRUDA monotherapy
- Efti with KEYTRUDA led to encouraging responses, including disappearance of all target tumor lesions in patients

TACTI-002

Phase II





- 1st clinical trial collaboration & supply agreement with MSD (March '18)
- 109 patients treated in two indications NSCLC (1L and 2L) and HNSCC (2L)
- Excellent initial efficacy and favorable safety in 1L NSCLC, and strong results in 2L HNSCC & 2L NSCLC
- Fast Track designation for 1L HNSCC based on trial data

TACTI-002 Expansion Phase II



- Expansion of 1L NSCLC cohort to 114 patients from 36 patients in 2020 post initial results and to test robustness.
- Excellent overall survival along with very high response rates, progression free survival, and duration of response achieved in 1L NSCLC
- Fast Track designation for
 1L NSCLC based on trial data

TACTI-003 Phase IIb



- 2nd clinical trial collaboration
 & supply agreement with MSD
 (March '21)
- Prompted by strong results in 2L HNSCC patients in TACTI-002
- 171 patients treated in total with sole focus on 1L HNSCC
- Efti with KEYTRUDA led to response rates exceeding KEYTRUDA alone across all levels of PD-L1 expression with largest differential in CPS ≥20 and CPS <1

TACTI-004

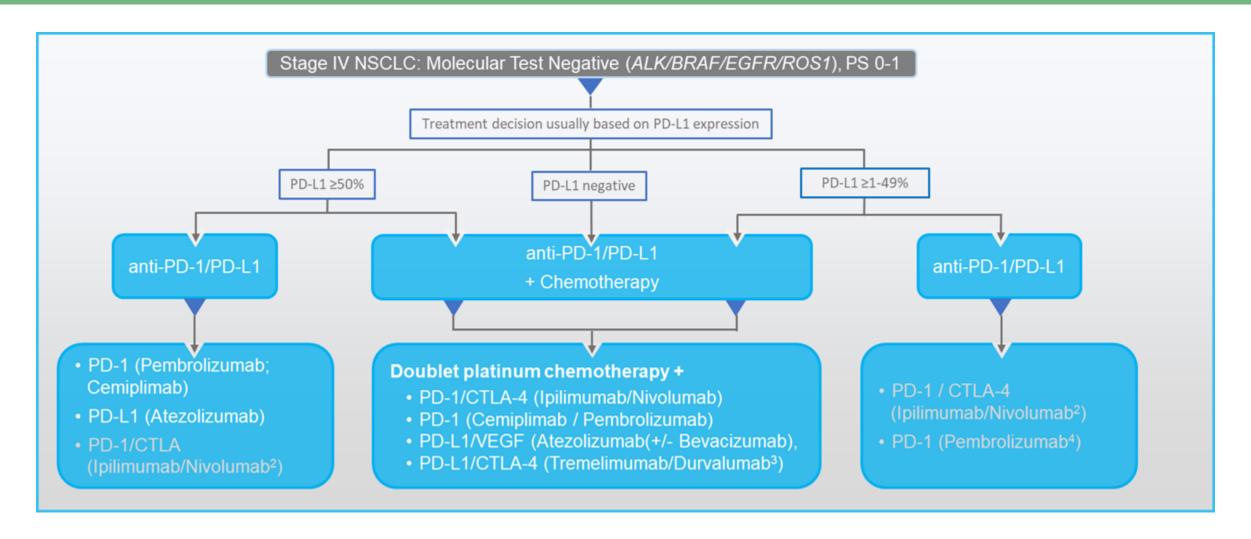
Phase III



- Third and most important collaboration & supply agreement with MSD (June '24)
- Registrational Phase III trial in 1L NSCLC with ~750 patients
- Immutep to conduct trial & retains commercial rights to efti
- Potential to establish new standard of care in NSCLC, one of largest oncology indications and revenue drivers for KEYTRUDA
- Planned KEYTRUDA supply has significant value (typical ICI drug supply for such a PIII trial is approx. US\$100m)

Treatment Landscape in 1L NSCLC (US/EU)





KEYTRUDA (pembrolizumab) and chemotherapy utilized across entire 1L NSCLC landscape, regardless of PD-L1 expression, which is the same patient population the efti + pembrolizumab + chemotherapy combination will be evaluated in

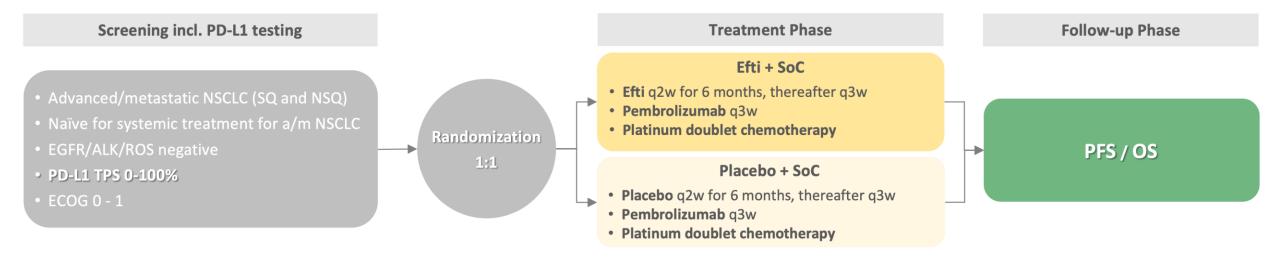
⁾ Simplified based on ESMO and NCCN Guidelines: DOI:https://doi.org/10.1016/j.annonc.2022.12.013 and https://www.ncn.org/guidelines/guidelines-detail?category=1&id=1450
) Ipilimumab/Nivolumab without chemotherapy is not approved in the EU, although recommended in the ESMO guidelines; approved in the US, only indicated in special circumstances in the NCCN guidelines for PD-L1 ≥ 50 %
) Not all options available for all histologies and all regions and PD-L1 negative patients, number of cycles and components of chemotherapy varies. Please see the guidelines for more detail.

Immutep & Merck (MSD) to Undertake Phase III Trial in NSCLC



Opportunity to set a new standard of care across entire NSCLC population regardless of PD-L1 expression

TACTI-004 / KEYNOTE-PNC-91 Trial Design



Trial Overview:

- TACTI-004 will be a 1:1 randomized, double-blind, multinational, controlled clinical study with ~750 patients
- Trial will enroll first line squamous and non-squamous NSCLC patients who are unselected for PD-L1 expression
- Dual primary endpoints will be Progression-Free and Overall Survival with both being adequately powered

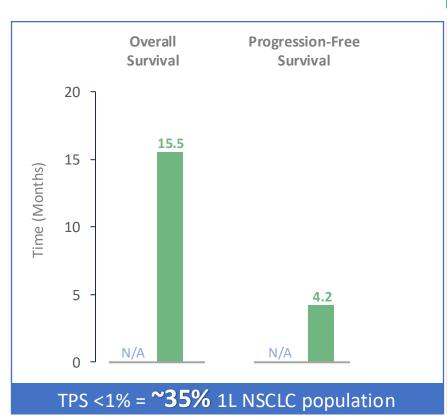
Key Milestones:

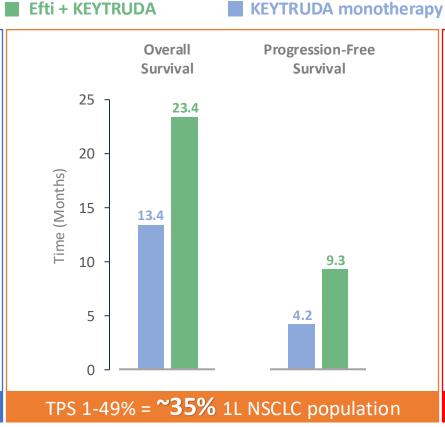
- First patient expected to be enrolled in Q4 2024 / Q1 2025
- Futility analysis expected in late 2025 / early 2026 and interim analysis in late 2026 till mid-2027 (event driven)

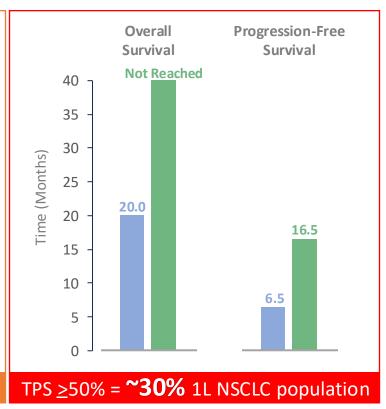
Strong Results in Dual Primary Endpoints (OS/PFS) Across All PD-L1 Expression Levels Drives Confidence in TACTI-004



TACTI-004's large trial design will effectively capture 1L NSCLC patient populations with negative (TPS <1%), low (TPS 1-49%), and high (TPS >50%) PD-L1 expression. The strength of efti + KEYTRUDA results in TACTI-002 & INSIGHT-003 trials across all three levels, including negative & low PD-L1, drives confidence in a potential positive outcome.



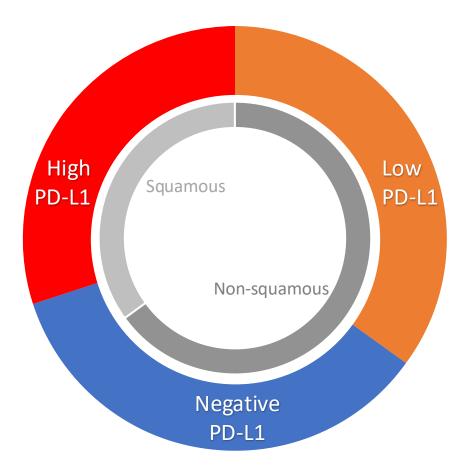




Uniquely Positioned Phase III in 1L NSCLC Landscape



- KEYTRUDA has revolutionized the treatment landscape in lung cancer, and as a result MSD (Merck) captures between 7 to 8 of every 10 metastatic lung cancer patients today*
- Of KEYTRUDA's ~US\$25 billion in sales in 2023, it is estimated that ~US\$9 billion or +35% are from lung cancer**
- Efti in combination with KEYTRUDA and chemotherapy is uniquely positioned to potentially drive a new standard of care for 1L NSCLC patients eligible for anti-PD-(L)1 therapy



TACTI-004 among the few global Phase III trials evaluating combination therapies with KEYTRUDA that addresses almost the entire 1L NSCLC patient population eligible for anti-PD-(L)1 therapy

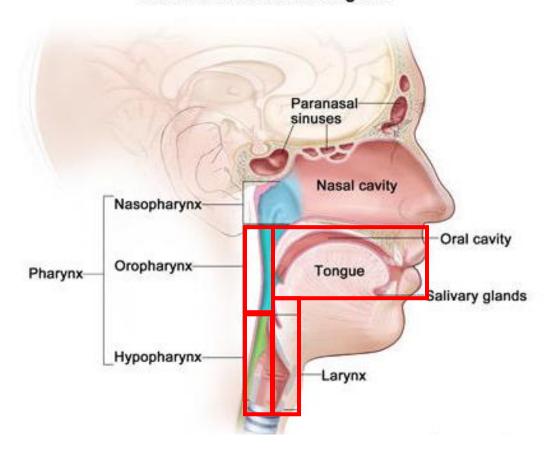


Efti + Anti-PD-1 in Head & Neck Cancer

Head and Neck Squamous Cell Carcinoma



Head and Neck Cancer Regions



TACTI-003 included cancers that originate from the areas delineated by red boxes

Overview:

- Head and neck squamous cell carcinoma (HNSCC) encompasses a spectrum of heterogeneous diseases originating in the oral cavity, pharynx, and larynx
- HNSCC is a complex disease involving distinct anatomical sites and with varying etiological factors including smoking, alcohol consumption and infection with Human Papilloma Virus (HPV)

Epidemiology:

- More than 890,000 HNSCC diagnoses and 450,000 deaths per annum worldwide¹
- Up to ~100,000 estimated to develop metastatic disease in 8MM countries²
- 5-year survival for metastatic HNSCC is 39.3%³ and varies depending on the anatomical site of cancer origin

Treatment Landscape in 1L HNSCC

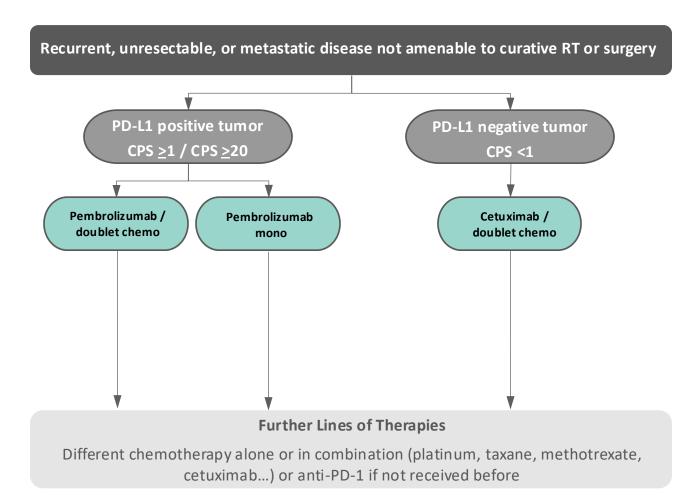


High unmet need:

Overall Survival in first line HNSCC is ~12 months.

PD-L1 expression:

- PD-L1 expression as measured by Combined Proportion Score (CPS) is an FDA approved predictive biomarker in 1L HNSCC for anti-PD-1 therapy
- Patients are grouped by high (CPS ≥20), low (CPS 1-19), and negative (CPS <1) PD-L1 expression¹. Generally, high PD-L1 expressors respond best, low respond sub-optimally, and negative have negligible responses to anti-PD-1 therapies.
- Currently, there are no effective chemotherapy-free treatments for patients with no PD-L1 expression (CPS <1)

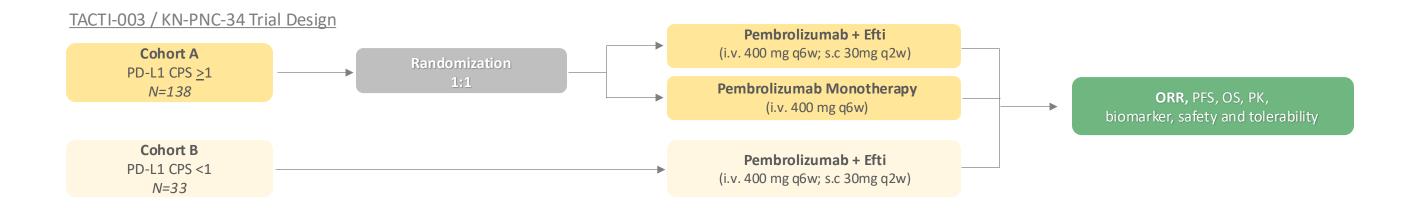


Simplified based on NCCN Guidelines Head and Neck Cancers and EHNS-ESMO-ESTRO Clinical Practice Guidelines

TACTI-003 / KEYNOTE-PNC-34 Trial Overview

immutep LAG-3 IMMUNOTHERAPY

Efti + anti-PD-1 therapy has FDA Fast Track designation in recurrent or metastatic 1L HNSCC



- Randomized, multicenter Phase IIb trial evaluating efti in combination with pembrolizumab (KEYTRUDA®) in first line recurrent or metastatic head and neck squamous cell carcinoma (1L R/M HNSCC). A total of 171 patients enrolled in 29 clinical sites across nine countries (US, UK, ES, UA, AU, RO, UA, DK, DE):
 - Cohort A (N=138) Patients with any PD-L1 expression (CPS ≥1) randomized 1:1 evaluating efti + KEYTRUDA® versus KEYTRUDA monotherapy
 - Cohort B (N=33) Patients with negative PD-L1 expression (CPS <1), which could not be randomized as KEYTRUDA monotherapy is not approved in CPS <1
- Primary endpoint is Objective Response Rate (ORR) among evaluable patients (>= 1 post baseline CT), according to RECIST1.1
- Secondary endpoints include Overall Survival and Progression-Free Survival, ORR (iRECIST), and Disease Control Rate

Favourable Safety Profile



Safety Parameter	Efti + KEYTRUDA (Cohorts A+B) n (%)	KEYTRUDA alone (Cohort A) n (%)
Any TEAE Leading to Discontinuation of Study Treatment	8 (7.8%)	4 (5.9%)
Related to Efti and/or Pembrolizumab	6 (5.9%)	3 (4.4%)

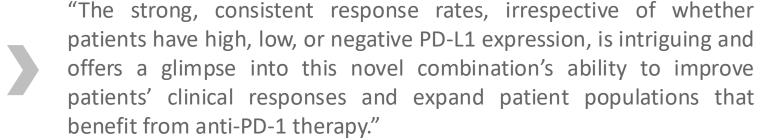
- No new safety signals
- Rate of treatment related discontinuation was low and comparable between treatment regimens
- Safety profile comparable to KEYTRUDA monotherapy

Overall Response Rate in Evaluable Patients



TACTI-003 primary endpoint is objective response rate (ORR) in evaluable patients, according to RECIST1.1

Efti plus KEYTRUDA achieved a ~34% ORR (N=89) regardless of HPV status and PD-L1 levels, including 31 patients with negative PD-L1 expression



- Dr. Martin Forster, UCL Cancer Institute, London, UK

Efti plus KEYTRUDA led to higher ORR across all levels of PD-L1 expression versus KEYTRUDA monotherapy and durability is tracking well



"We are pleased with the quality of responses. Once again, durability is tracking well driven by the complementary nature of these two unique immunotherapies in fighting cancer."

- Dr. Frédéric Triebel, CSO of Immutep

Randomised Cohort A: Patients with Any PD-L1 Expression



TACTI-003		
Efti + KEYTRUDA	KEYTRUDA alone	

High PD-L1 Expression (CPS ≥20)

31.0% ORR (N=29)

18.5% ORR (N=27)

In CPS ≥20, efti + KEYTRUDA shows strongest outperformance with 68% relative increase and 12.5% absolute increase. Patients with CPS ≥20 represent ~50% of the 1L HNSCC patient population.*

Low PD-L1 Expression (CPS 1-19)

34.5% ORR (N=29)

33.3% ORR (N=33)

In CPS 1-19, efti + KEYTRUDA has relatively high 34.5% ORR in CPS 1-19. KEYTRUDA monotherapy's 33.3% ORR is higher than historical published data, including a 14.5% ORR in KN-048*, that may be explained by imbalances including gender, smoking status, HPV+/- status, and location of primary tumour.

Any PD-L1 Expression (CPS ≥1)

32.8% ORR (N=58)

26.7% ORR (N=60)

In CPS ≥1, efti + KEYTRUDA has 23% relative Increase and 6.1% absolute increase against KEYTRUDA monotherapy results that were driven higher by results in CPS 1-19 group. efti + KEYTRUDA 90% CI: 22.6%-44.3%; KEYTRUDA 90% CI: 17.5%-37.6%

- Multiple prognostic markers favor the KEYTRUDA mono arm in Cohort A
 - √ 30.0% female vs 20.7% in combination arm
 - ✓ 16.7% current smokers vs22.4% in combination arm
 - ✓ 13.3% hypopharynx vs 19.0% in combination arm
 - ✓ 65.0% HPV+ vs 29.2% in combination arm
- No prognostic markers favor the Efti + KEYTRUDA combination arm

Cohort B: Response Rate Among Highest Recorded in CPS <1



ESMO VIRTUAL PLENARY

SOUR SCIENCE STITU MUSICALE SKIT PARADICE		
Best objective response ¹ , n (%)	RECIST 1.1 N=31	iRECIST N=31
Complete response	3 (9.7)	3 (9.7)
Partial response	8 (25.8)	9 (29.0)
Stable disease	7 (22.6)	8 (25.8)
Progressive disease	13 (41.9)	11 (35.5)
ORR, [95% CI] ²	11 (35.5) [19.2-54.6]	12 (38.7) [21.8-57.8]
DCR, [95% CI] ²	18 (58.1) [39.1-75.5]	20 (64.5) [45.4-80.8]

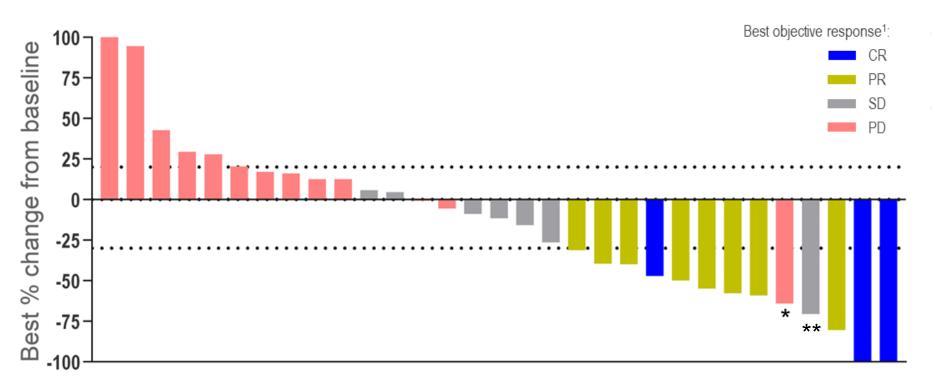
Key Takeaways:

- ORR of 35.5% and DCR of 58.1%, according to RECIST 1.1
- The 35.5% ORR is among the highest recorded for a chemo-free approach in 1L HNSCC patients with no PD-L1 (CPS <1) expression
- ~10% complete responses
- Responses are observed regardless of HPV status*

Cohort B: Tumour Shrinkage in 60% of CPS <1 Patients



Change in Tumour Burden

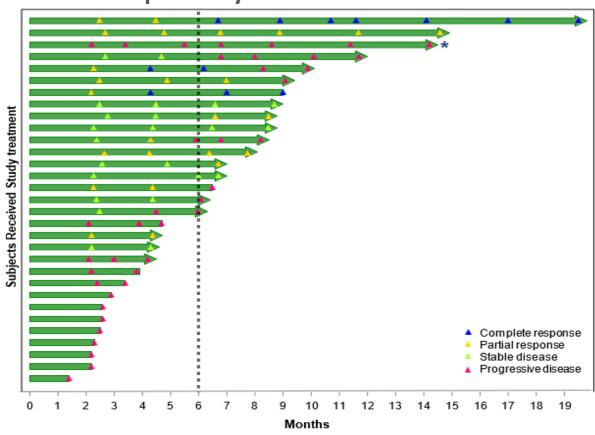


- ~60% of patients experienced tumour shrinkage
- Despite deep responses in target lesions, two patients not counted as responders:
 - One patient (*) with pseudoprogression later had a confirmed partial response (PR) according to iRECIST yet not RECIST 1.1
 - Another patient (**) with -71% shrinkage in target lesion diameters at week 27 had progression in a non-target lesion

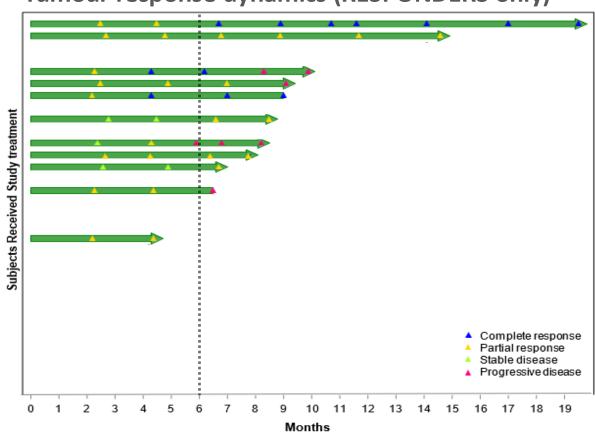
Cohort B: Excellent Duration of Treatment



Tumour response dynamics over time*



Tumour response dynamics (RESPONDERS only)



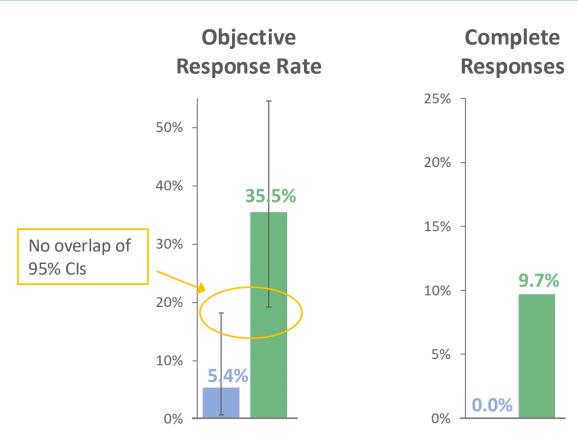
- Durability of treatment / responses tracks very well
- >50% patients remain on treatment 6+ months
- >90% of responders remain on treatment 6+ months

Benchmarking: Exceptional Results for a Chemo-Free Regimen



Key takeaways, Cohort B (CPS <1)

- ✓ ORR of 35.5% and DCR of 58.1% are exceptional for a chemo-free regimen in this patient population
- ✓ Compares favorably to <u>historical results</u> from KEYTRUDA monotherapy (see figures to right)
- ✓ ORR similar to KEYTRUDA + chemo (~31%) and in range of EXTREME regimen (~40%)*, without toxicity of chemo
- ✓ Early trends in durability look favourable (90% responders ongoing treatment at 6 months)
 - → Typically, duration of response (DOR) is much longer with IO-only therapies (e.g., DOR for KEYTRUDA alone is ~23 months vs. ~7 months when it is combined with chemo**)



PD-L1 CPS <1	KEYTRUDA mono (N=37) (KN-048)#	Efti + KEYTRUDA (N=31) (TACTI-003)
ORR, [95% CI]*	2 (5.4%) [0.7-18.2]	11 (35.5%) [19.2-54.6]
Complete Responses	0 (0.0%)	3 (9.7%)
Partial Responses	2 (5.4%)	8 (25.8%)

Efti + Pembro in 2L Head & Neck Squamous Cell Carcinoma



Strong, durable efficacy in second line HNSCC (2L HNSCC)

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

TACTI-002 (Part C) Trial Design

- Advanced/metastatic recurrent HNSCC- Failed 1L platinum

therapy

Combination Therapy
30mg efti Q2W + 200 mg pembrolizumab
Q3W for 8 cycles, followed by 30mg efti +
200mg pembrolizumab for 9 cycles

Up to 1 year

Monotherapy 200 mg pembrolizumab O3W for 16 cycles

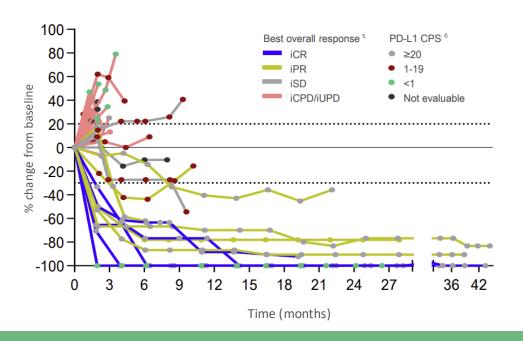
Up to 1 year —

Primary endpoint: ORR by iRECIST **Secondary Endpoints:** ORR by RECIST

1.1, PFS, OS, DOR, safety, PK/PD

- Encouraging ORR of 29.7% in ITT population (all-comer PD-L1) and treatment well-tolerated
- Early onset of responses (median ~2 months) that were deep (13.5% CRs) and durable (median DoR not reached despite a median follow up of ~39 months)
- Promising ORR of 60%, median PFS of 13.6 months and median OS of 15.5 months in patients with CPS ≥20

	ITT N=37	CPS ≥1* _{N=25}	CPS ≥20* _{N=15}
ORR ^{2,3}	29.7%	38.5%	60.0%
mPFS ^{2,4} , months	2.1	2.3	13.6
6-mo PFS rate	32.4%	40.0%	53.3%
mDoR ² , months	NR	NR	NR
mOS ⁴ , months	8.7	12.6	15.5
12-mo OS rate	46.0%	52.0%	66.7%





Efti + Chemotherapy in Metastatic Breast Cancer (MBC)

AIPAC-001: Efti + Chemo in Randomized Phase IIb in MBC



AIPAC-001 Study Design



AIPAC was conducted in 34 sites across: Belgium, France, Hungary, Poland, Netherlands, UK, and Germany



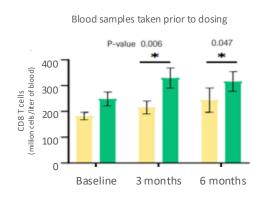




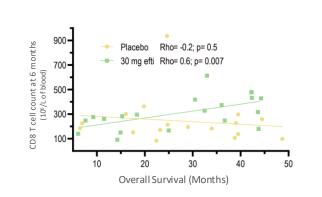


Paclitaxel Efti + paclitaxel N=112 **Overall Response Rate** 38.4% 48.3% 75.9% **Disease Control Rate** 85.1% Median Overall Survival (mOS) 17.5 months 20.4 months mOS in Pre-Specified Subgroups Low Monocytes, <0.25/nl 12.9 months 32.5 months 14.8 months Under 65 Years 22.3 months Luminal B 12.6 months 16.8 months

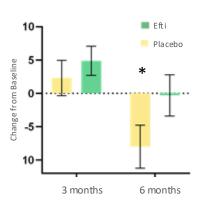
CD8⁺ T cell count increased significantly



Significant correlation between OS & Cytotoxic CD8⁺ T cell count



Sustained Quality of Life (QoL) vs significant decline in placebo grp*



AIPAC-003 Phase II/III Trial Underway in MBC



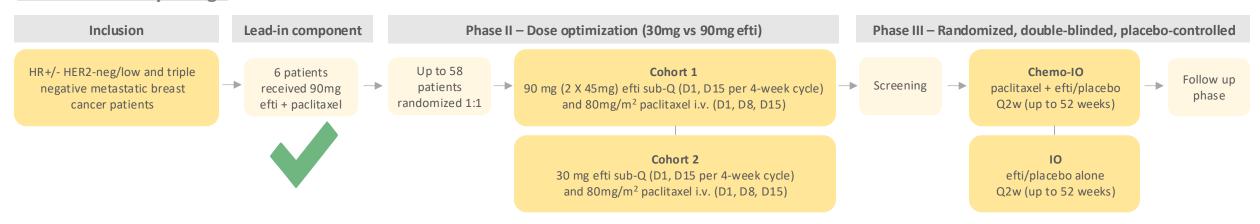
AIPAC-003: Active Immunotherapy (Eftilagimod Alfa) and PAClitaxel



AIPAC-003: Integrated Phase II/III trial in Metastatic Breast Cancer (MBC)

- Trial design incorporates feedback from FDA & EMA and provides risk-balanced approach
- Patient population: HR+/- HER2-negative/low and triple negative MBC (~78% breast cancer cases¹)
- Patients will receive efti + paclitaxel on same day and IO-chemo treatment can continue until disease progression (previous trial administered on different days & ceased paclitaxel at 6 months)
- Randomised Phase II dose optimization underway

AIPAC-003 Study Design



Encouraging Safety and Early Efficacy in AIPAC-003

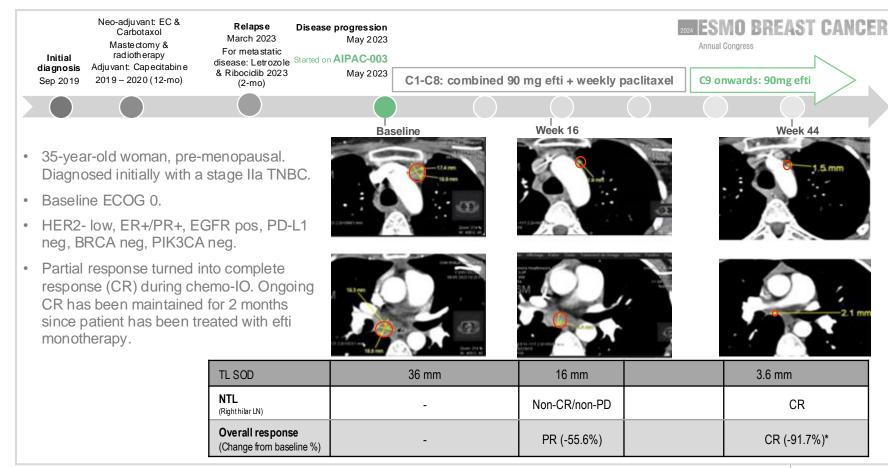


50% Response Rate, 100% DCR, and a Confirmed Complete Response at Higher 90 mg Efti Dosing

AIPAC-003: Active Immunotherapy (Eftilagimod Alfa) and PAClitaxel

- Efti + paclitaxel combination continues to be well tolerated with a favorable safety profile
- Encouraging initial efficacy in six MBC patients, who exhausted all endocrine therapy including CDK4/6 inhibitors, demonstrated by a confirmed 50% ORR and a 100% DCR
- Confirmed complete response (CR) in a patient with metastatic breast cancer refractory to several lines of therapy
 - CR achieved during combination treatment with 90mg efti & paclitaxel has been maintained with efti monotherapy for over 4 months**
- Data from randomized Phase II portion of study expected in CY2024

Case Study: 35-year-old Woman with Confirmed CR that Continues on Efti Monotherapy*





Additional Oncology Indications and Studies

Efti + Anti-PD-L1 (Avelumab) in Metastatic Urothelial Cancer



INSIGHT-004 – Completed Phase I dose escalation study in advanced solid tumors*

- Efti in combination with avelumab (BAVENCIO®) safe with promising signals of efficacy in 12 patients
- 5/12 partial responses (42%) in different solid tumors**
- Encouragingly, durable responses achieved in patients with low
 & negative PD-L1 expression and in non-immunogenic tumors



INSIGHT-005 – Ongoing Phase I study in metastatic urothelial cancer

- Investigator-initiated study evaluating safety & efficacy of efti and avelumab (BAVENCIO®) in up to 30 patients
- Jointly funded by Immutep & Merck KGaA, Darmstadt, Germany
- Targeting area of high unmet need: patients not eligible for platinum-based chemotherapy or who are progressing during/after platinum-based chemotherapy
- Announced first patient enrolled and safely dosed in Jan 2024





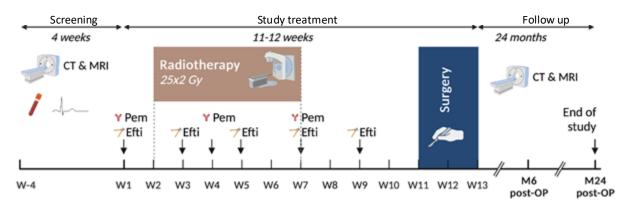


Soft Tissue Sarcoma: Orphan Disease with High Unmet Need



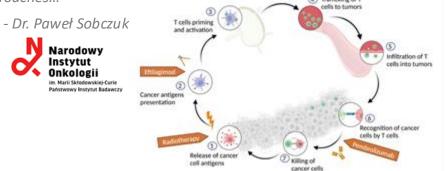
Investigator-initiated trial studying novel triple combination of Efti + Radiotherapy + KEYTRUDA

EFTISARC-NEO Phase II Trial Design*



Rationale for triple combination based on cancer-immune cycle*

"...Given efti's synergistic effects with immune checkpoint inhibitors and its ability to arm, activate, and proliferate cytotoxic T cells with radiotherapy-induced cancer antigens, this combination has a strong foundation to drive effective immunity against soft tissue sarcoma, a rare and aggressive disease in immense need of new therapeutic approaches..."



- First trial studying efti in neoadjuvant, non-metastatic cancer setting and also first to study efti with radiotherapy
- Importantly, study will provide access to tumor tissue prior to and after treatment, so tumor microenvironment can be assessed**
- Cost-efficient Phase II study funded by grant from Polish government
- Up to 40 patients will be enrolled

Positive initial data from EFTISARC-NEO reported in May 2024:

- ✓ Four of six patients treated have very good, near-complete pathologic responses (primary endpoint of study), which are rarely observed with standard therapies
- ✓ Triple combination therapy well tolerated
- ✓ Additional data planned for a medical conference in H2 CY2024

TACTI-mel: Efti plus KEYTRUDA in Metastatic Melanoma

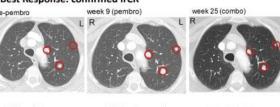


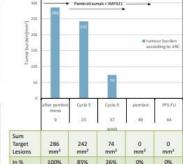
First-in-man study evaluating efti with KEYTRUDA® (pembrolizumab) in metastatic melanoma patients who had suboptimal responses to or progression after **KEYTRUDA** monotherapy:

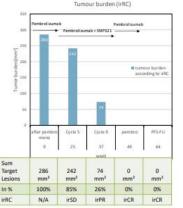
- Patients had very late stage of disease: (a) 75% classified as M1c (associated with lowest probability of survival), (b) 67% lung metastasis, (c) 50% liver metastasis, (d) 50% elevated LDH
- Deep, durable responses observed with tumor shrinkage of 56% and 66% in Part A (efti 1, 6, 30mg; N=18) and Part B (efti 30mg given same day as KEYTRUDA; N=6)
- Part B had 50% ORR, 66% DCR, and twothirds of patients were progression free at six months

Patient Case #1 - Pembrolizumab + 1mg Efti (IMP321)

- Male, Caucasian, 84 years
- stage IV visceral disease (lung and thorax metastases), best response pembrolizumab monotherapy irPD
- · Patient completed study, PFS-FU (incl. Pembrolizumab monotherapy) was stopped due to patient wish after week 64 → PFS censored week 64
- Best Response: confirmed irCR







Patient Case #3 - Pembrolizumab + 30mg Efti (IMP321)

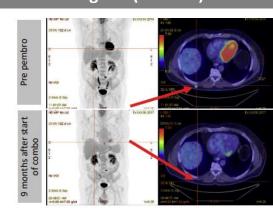
- 61-year-old male patient
- TxNxM1b at study entry in March 2018
- irPR reached by week 12 and maintained until end of study





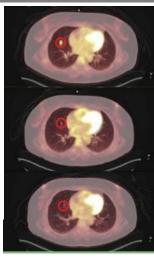
Patient Case #2 - Pembrolizumab + 6mg Efti (IMP321)

- Male, Caucasian, 54 years
- Stage IV skin/superficial disease → best response pembrolizumab monotherapy was irSD
- Target lesion: chest wall; Non-target lesion: Left common iliac LN
- Patient has completed the study treatment, PFS-FU (incl. Pembrolizumab monotherapy) ongoing → PFS 22+ months
- Complete disappearance of target lesions, lymph node normalized
- Best Response: confirmed irPR



Patient Case #4 - Pembrolizumab + 30mg Efti (IMP321)

- 46-year-old female patient
- TxNxM1c at study entry in August 2018
- Deep irPR reached by week 12 and maintained until end of study
- Residual tumor mass not metabolically active (complete metabolic response, CMR)
- PET-scans negative on two occasions, at the time of and after end of study



← June 2018

PET-Scans

← May 2019

← Aug 2019

Novel Small Molecule Anti-LAG-3 Preclinical Program







Immutep aims to develop and commercialize an orally-available small molecule anti-LAG-3 treatment for cancer patients at a lower cost compared with anti-LAG-3 antibodies commercially available or under clinical development today.

"Our collaboration with Immutep has been exciting and fruitful, resulting in a number of small molecules with the potential to fight cancer by blocking the interaction between LAG-3 on T cells and MHC Class II on antigen-presenting cells. Small molecules represent the next generation of anti-LAG-3 therapies and hold tremendous promise, as they can be given to cancer patients as a convenient oral pill."

Professor Andrew Godkin, Theme Lead in Immunology in the College of Biomedical Life Sciences, Cardiff University*



IMP761 & Summary

Targeting Autoimmune Disease with Immune Checkpoint Agonists immutep





Inhibitory receptor agonists: the future of autoimmune disease therapeutics?

"Although critical questions remain, inhibitory receptor agonists represent an underappreciated and untapped opportunity for the treatment of autoimmune and inflammatory diseases"



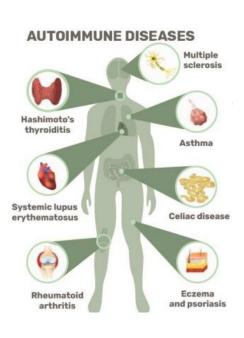
From bench to bedside: targeting lymphocyte activation gene 3 as a therapeutic strategy for autoimmune diseases

"The manipulation of the LAG3 pathway can serve as a promising therapeutic strategy"



Fewer LAG-3⁺ T Cells in Relapsing-Remitting Multiple Sclerosis and Type 1 Diabetes

These findings further support the potential clinical benefits of a LAG-3 agonist in the treatment of human autoimmunity"



Present Approaches Target the Symptoms of Autoimmune Diseases

Corticosteroids, methotrexate, TNF & interleukin inhibitors (anti-TNF-α,-IL-6, -IL-17, -IL-23 mAbs)



Future Approaches Target the Causes of Autoimmune Diseases

Targeting autoimmune effector T cells with immune checkpoint (e.g. LAG-3 and PD-1) agonists

IMP761: First-in-Class LAG-3 Agonist is a Potential Game-Changer



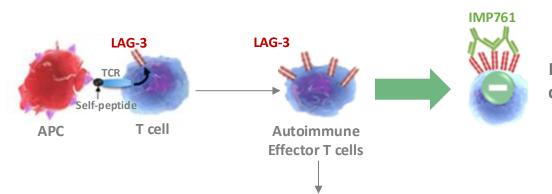


IMP761 - A LAG-3-Specific Agonist Antibody for the Treatment of T Cell-Induced Autoimmune Diseases



IMP761 - Juvenile idiopathic arthritis: LAG-3 is a central immune receptor in children with oligoarticular subtypes

IMP761 is the world's first immunosuppressive LAG-3 agonist antibody that is designed to address the underlying cause of many autoimmune diseases. This potential game-changer in the treatment landscape received regulatory clearance in July 2024 and enrolled its first participant in August 2024.



Epigenetic reprogramming leads to T cell helper (Th) induced Autoimmune Diseases such as Rheumatoid Arthritis (Th1), Allergic Asthma (Th2), IBS (Th17), etc.

IMP761 increases natural LAG-3-mediated down-regulation of auto-reactive memory T cells (root cause of many diseases)

Clinical Development of IMP761

Leading World-Call Research Institute Appointed to Conduct First-in-Human Study



Key aspects:

- Placebo-controlled, double-blind Phase I (N = 49)
- Centre for Human Drug Research (CHDR) has been selected for conduct
- First participant enrolled in August 2024
- First data expected in CY2024; study completion 2025
- Read-out: Safety, PK, Dose response through PD model
- GMP manufacturing process at 200L scale

Single Ascending Dose (SAD): Healthy volunteers

Part A: Healthy N=5

Cohort 1-SAD-A: 3 Subjects 0.0075 mg/kg + 2 placebo

FIH Microdosing

Single IV

Part B: Healthy N=30

Cohort 2-SAD-B : 4 Subjects 0.03 mg/kg + 1 placebo Cohort 3-SAD-B : 4 Subjects 0.1 mg/kg + 1 placebo

Cohort 4-SAD-B: 8 Subjects 0.3 mg/kg + 2 placebo Cohort 5-SAD-B: 8 Subjects 0.9 mg/kg + 2 placebo 3x KLH immunization, DTH

PK/PD

Single IV

Multiple Ascending Dose (MAD): Healthy volunteers

Part C: Healthy N=14. 3 dosing (3 months)

Cohort 6-MAD-C : 5 Subjects 0.3 mg/kg + 2 placebo Cohort 7-MAD-C : 5 Subjects 0.9 mg/kg + 2 placebo PK

Multiple (Q4W)



- World-class institute in Leiden, the Netherlands specializing in cutting-edge early-stage clinical drug research.
- CHDR offers a unique keyhole limpet haemocyanin (KLH) challenge model that allows for the evaluation of IMP761's pharmacological activity at the earliest stages of clinical development.



Board and Management





Dr Russel Howard Non-Executive Chairman

Dr Howard has over 45 years' experience in Australian & US biotech sectors, including the Walter & Eliza Hall Institute, Schering-Plough, GSK and as Maxygen CEO. He currently is Chairman of NeuClone Ptv Ltd and a former Director of Circadian Technologies Ltd.



Deanne Miller COO. General Counsel

Ms Miller has broad commercial Investment Commission. KPMG.



Pete Mevers Deputy Chairman

Mr Meyers spent 18 years in health care investment banking before taking on CFO roles in biotechnology including Eagle Pharmaceuticals, Motif BioSciences and TetraLogic Pharmaceuticals. Most recently he was CFO of Slavback Pharma, a KKR portfolio company acquired in Sept 2023.



Non-Executive Director

Ms Boyce has over 30 years' experience as a corporate lawyer and is a partner at Piper Alderman. She has a strong focus on Life Sciences and Healthcare, and is deputy chair of AusBiotech's AusMedtech Advisory Group, as well as a member of AusBiotech's State Committee for NSW.



Anne Anderson Non-Executive Director

Ms Anderson's executive career of over 35 years spanned the global financial services and energy sectors, holding several Managing Director roles with UBS Asset Mgt, including leading its Asia Pacific Fixed Income business. She is a non-executive director of a leading Australian wealth manager, BTFM.



Marc Voigt Executive Director & CEO

Mr Voigt has over 25 years of experience in the corporate and biotechnology sectors, including Deutsche Life Science, Revotar Biopharmaceuticals AG, Medical Enzymes AG and Allianz. He was appointed as CEO and Executive Director in July 2014. Mr Voigt is based in Berlin.



Prof. Frédéric Triebel, MD, PhD **Executive Director, CSO**

Prof Triebel discovered the LAG-3 gene while working at the Gustave Roussy Institute and is a pioneer in the LAG-3 field of immunooncology. He was the founder of Immutep S.A., which was acquired by the Company in 2014. Based in Paris, he holds a Ph.D. in immunology (Paris University).



experience having held legal, investment banking, regulatory compliance and tax advisory positions at RBC Investor Services, Westpac Group, Macquarie Group, the Australian Securities and



Florian Vogl. MD. PhD **Chief Medical Officer**

Dr Vogl is a board-certified MD and has over 13 years in the biopharmaceutical industry with extensive clinical development expertise in the field of oncology in the Europe and the US through roles at Cellestia Biotech, Rainier Therapeutics, Novartis and Amgen.



Christian Mueller SVP, Strategic Development

Mr Mueller has +10 years of clinical development experience in oncology, including at Medical AG focusing on therapeutic enzymes for cancer treatment and at Ganymed Pharmaceuticals AG developing ideal mAbs in immune oncology.



Claudia Jacoby, PhD **Director of Manufacturing**

Dr Jacoby has +15 years of biotech industry experience with extensive skills in protein expression and purification as well as in analytical and preclinical development from her various positions at preclinical and clinical-stage pharmaceutical companies.



James Flinn, PhD **IP & Innovation Director**

Dr Flinn is an Australian Patent Attorney with +25 years of professional experience in building and managing IP portfolios, including GSK, two US-based pharmaceutical companies, a major Australian retailer, and a Melbourne Patent Attorney firm.



David Fang Finance Director

Joining Immutep in 2018, Mr Fang has over 12 years of accounting and auditing experience across various industries including biotechnology, manufacturing and healthcare including Group Finance Manager of Kazia Therapeutics Limited and auditor at PWC.

Outlook



Milestones & Catalysts Ahead

- Non-Small Cell Lung Cancer TACTI-004 preparations for study start with FPI in late 2024 / early 2025
- Non-Small Cell Lung Cancer Update from triple combo INSIGHT-003 trial
- Head and Neck Squamous Cell Carcinoma Additional data will be presented in H2 CY2024
- **Soft Tissue Sarcoma** Update from investigator-initiated EFTISARC-NEO study
- Metastatic Breast Cancer Update from AIPAC-003 study evaluating 90mg vs 30mg efti dosing
- Metastatic Urothelial Carcinoma Update from investigator-initiated INSIGHT-005 study
- Autoimmune Diseases First participant enrolled in Phase I of IMP761; safety data anticipated by year-end & PK/PD data in H1 CY2025
- Other indications Updates from partnered programs and potential expansion of clinical trial pipeline
- Cash Balance Cash, cash equivalent and term deposit position totalling ~A\$181.8 million (~US\$118.7 million)¹ providing runway to end of calendar year 2026



Thank You