

**Unlocking the power of
the immune system
to fight cancer and
autoimmune disease**

Forward-Looking Statements

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Leader in LAG-3 immunotherapy



Four clinical-stage assets and one preclinical program designed to fight cancer and autoimmune diseases.

First-in-class lead clinical candidates



Efti is a novel MHC II agonist showing strong efficacy with favourable safety profile in multiple cancers and expanding/enhancing responses to world's top selling drug. *IMP761* is LAG-3 agonist antibody to treat autoimmune disorders.

Phase III in Lung Cancer with MSD



Phase III in collaboration with MSD evaluating *efti* + KEYTRUDA + chemo with potential to establish new standard-of-care in first line non-small cell lung cancer (blockbuster potential). Immutep retains full commercial rights to *efti* and freedom to operate. Additional programs with data readouts in 2025 & beyond.

Validation via collaborations



Multiple partnerships and collaborations with large pharma and leading institutions.

Strong IP and balance sheet



Strong IP portfolio and 12+ years of potential exclusivity for biologics. Cash & cash equivalents of ~A\$159 million provide runway to end of CY2026.#

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Deep Pipeline in Oncology & Autoimmune Diseases

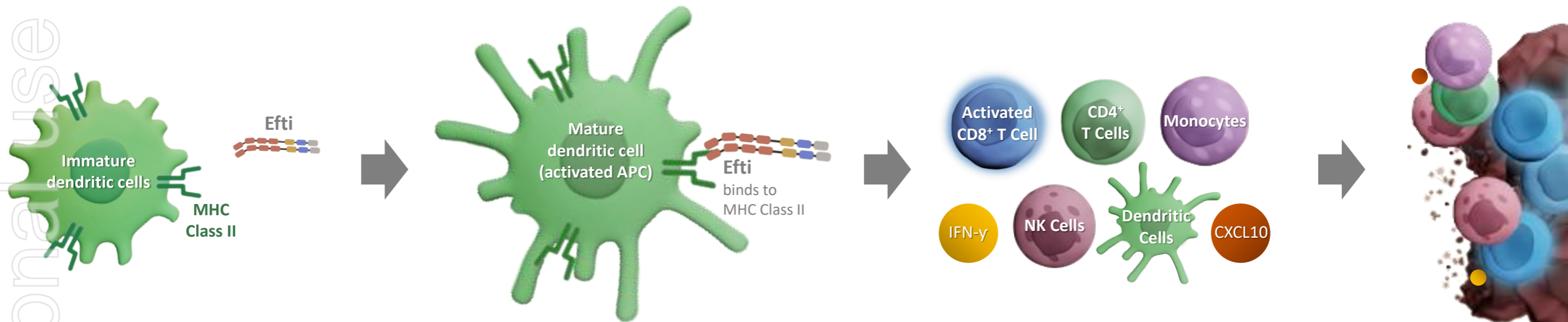
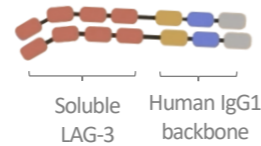
Program	Indication(s)	Preclinical	Phase I	Phase II	Phase III	Collaborations	Commercial Rights
Eftilagimod Alfa Soluble LAG-3 Protein & MHC Class II agonist	1L Non-Small Cell Lung Cancer (NSCLC)	TACTI-004 Efti + Pembrolizumab + Chemo ^a				MERCK MERCK MERCK IKF Merck KGaA Darmstadt, Germany IKF Marekowsky Instytut Onkologii EOC CARDIFF UNIVERSITY	 Global Rights ex-China
	1L Head & Neck Squamous Cell Carcinoma (HNSCC)	TACTI-003 Efti + Pembrolizumab ^a					
	1L NSCLC, 2L HNSCC, PD-X Refractory 2L NSCLC	TACTI-002 Efti + Pembrolizumab ^a					
	1L Non-Squamous NSCLC	INSIGHT-003 Efti + Pembrolizumab + Chemo [§]					
	Urothelial Cancer	INSIGHT-005 Efti + Avelumab ^{§, b}					
	Soft Tissue Sarcoma	EFTISARC-NEO Efti + Pembro + Radiotherapy [§]					
	HR+/HER2- Metastatic Breast Cancer & TNBC	AIPAC-003 Efti + Paclitaxel					
Metastatic Breast Cancer & Solid Tumors	Efti + Paclitaxel and Efti + Pembrolizumab ^{###}						
Anti-LAG-3 Small Molecule	Undisclosed						
LAG525 Anti-LAG-3 Antibody	Solid Tumors, Blood Cancer, TNBC, Melanoma [#]					NOVARTIS	NOVARTIS Global Rights
IMP731* Depleting LAG-3 Antibody	Psoriasis & Ulcerative Colitis						 Global Rights
	Undisclosed						
IMP761 Agonist LAG-3 Antibody	Undisclosed						

Information current as of February 2025. For EOC's China rights, Immutep may receive undisclosed milestones plus royalties. For Novartis' global rights to LAG525 (ieramilimab), Immutep may receive milestones plus royalties. [#] To date Novartis has conducted five separate clinical trials with LAG525. [§] Investigator-initiated trials controlled by lead investigator and Immutep has no control over these clinical trials. ^a In combination with KEYTRUDA[®]. ^b In combination with BAVENCIO[®]. ^{###} Conducted by EOC in China. * Three trials for IMP731 were conducted by GSK (two Phase I studies in healthy volunteers and psoriasis and a Phase II study in ulcerative colitis), which transitioned this clinical-stage asset back to Immutep in 2024.

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

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 activates powerful immune cells called dendritic cells by binding to MHC Class II. This activates a broad, sustained adaptive/innate immune response to fight cancer.*

* In clinical trials, including monotherapy and in combination with anti-PD-(L)1 therapies and with chemotherapy, efti has led to significant and sustained increases in anti-tumor cells and chemokines / cytokines including those listed in the graphic.
MHC Class II = Major Histocompatibility Complex Class II.

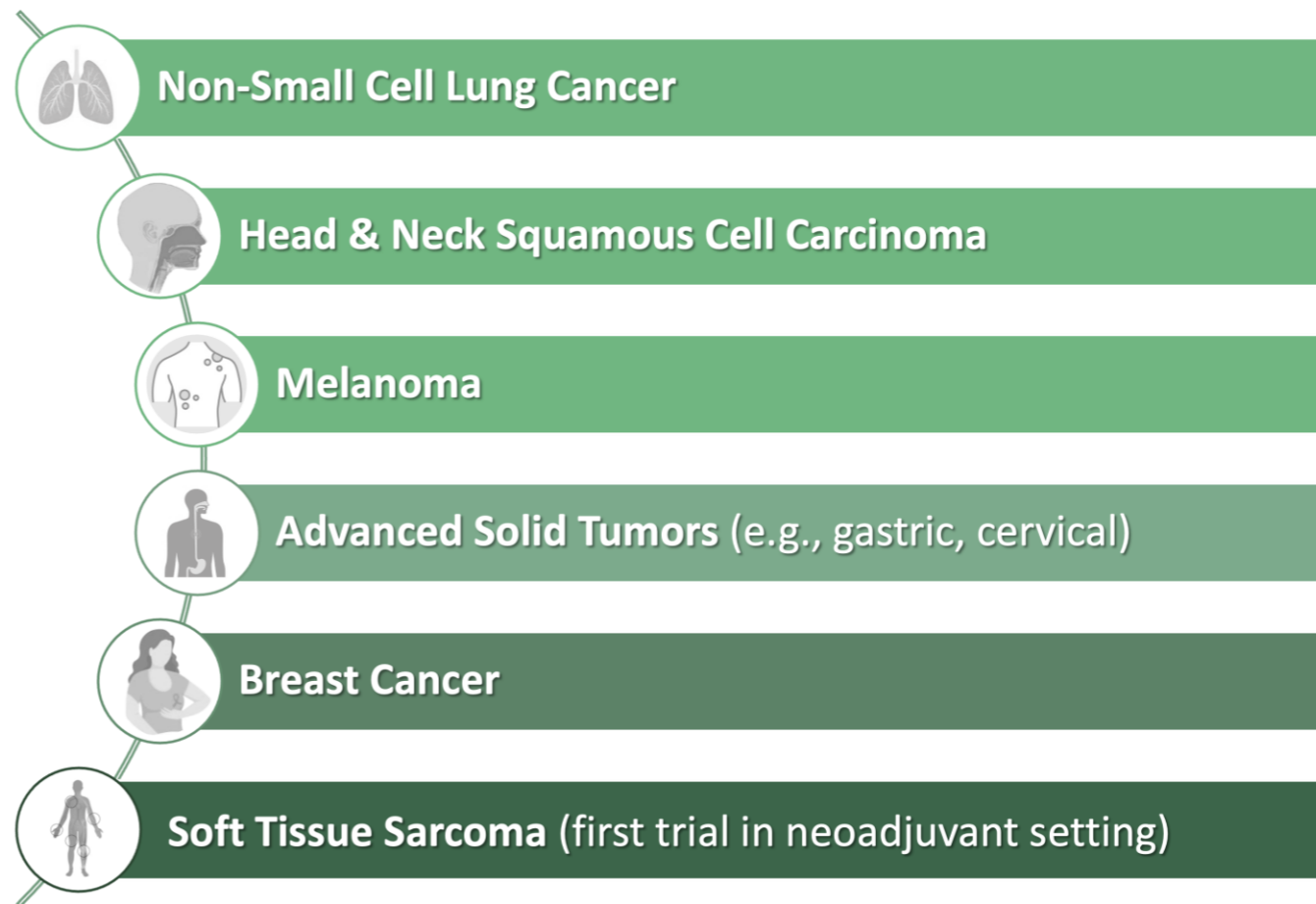
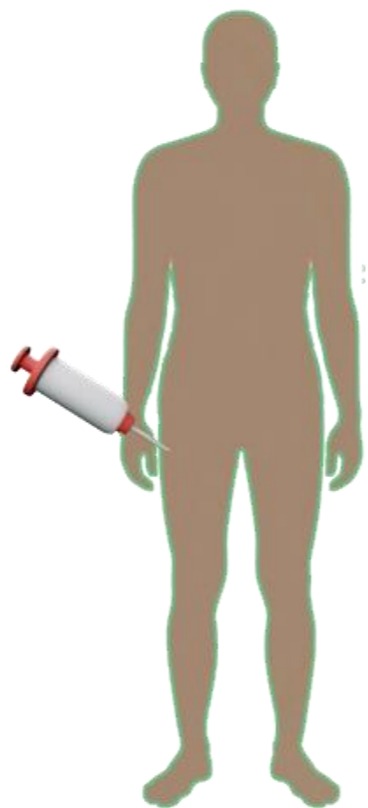
Systemic Immune Effect Leading to Positive Clinical Outcomes

Encouraging data from *efti* in combination with IO, chemotherapy, radiotherapy across multiple indications

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Efti's subcutaneous delivery:

- Generates systemic anti-cancer immune response
- Improves patient experience vs. intravenous (IV) administration
 - ✓ Less invasive
 - ✓ Easier to administer
 - ✓ More flexible
- Potentially increases patient access to treatments



- Efti + Anti-PD-1 Therapy
- Efti + Anti-PD-L1 Therapy
- Efti + Chemotherapy
- Efti + Anti-PD-1 + Radiotherapy

**Efti and Anti-PD-1 Therapy:
A Unique, Complementary Combination**

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Limitations of Anti-PD-1 Therapy

PD-1 inhibitors have reshaped cancer treatment yet alone they're effective in just ~20% of patients and their efficacy often depends on patients' PD-L1 expression levels.

Suboptimal performance in patients with low or no PD-1 expression

	High PD-L1 (TPS \geq 50%)		Low PD-L1 (TPS 1-49%)		No PD-L1 (TPS<1%)	
	US	EU	US	EU	US	EU
KEYTRUDA Monotherapy	✓	✓	✓	✗	✗	✗
OPDIVO & YERVOY	✓	✓	✓	✗	✗	✗
LIBTAYO Monotherapy	✓	✓	✗	✗	✗	✗
TECENTRIQ Monotherapy	✓	✓	✗	✗	✗	✗

Approved PD-(L)1 inhibitors in First Line Metastatic Non-Small Cell Lung Cancer

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Efti's Differentiated, Complementary Approach with KEYTRUDA®



COMPLEMENTARY IMMUNITY

Efti's direct activation of dendritic cells initiates a complementary immune response with KEYTRUDA (anti-PD-1) to fight cancer

EXPANDS/ENHANCES RESPONSES

Efti + KEYTRUDA drives high-quality responses regardless of PD-L1 levels including in patients who typically don't respond well to anti-PD-1

FAVORABLE SAFETY PROFILE

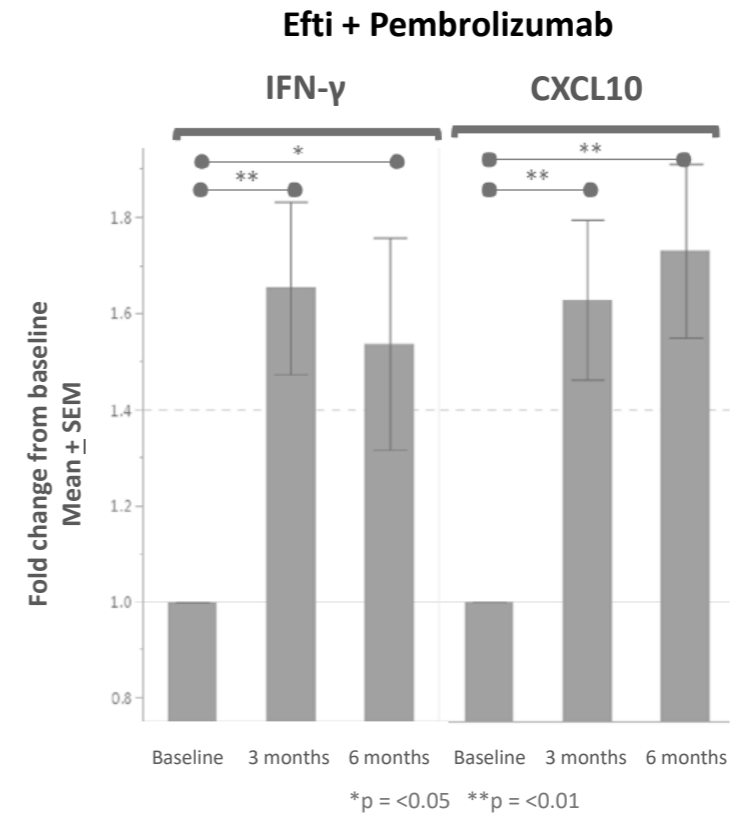
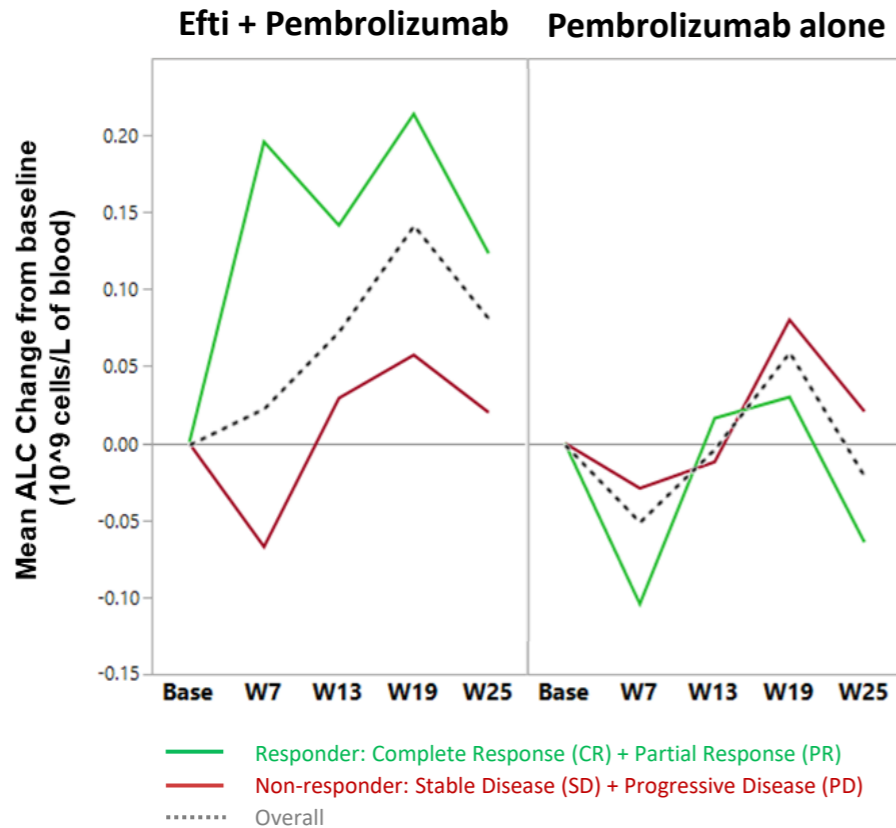
Efti + KEYTRUDA has similar toxicity profile to KEYTRUDA alone yielding sought-after alignment of stronger efficacy & favourable safety

Significant Immune Activity with Efti + KEYTRUDA

Biomarker analyses of blood from multiple trials shows efti's positive impact on immune system

Significant increase in absolute lymphocyte count (ALC) linked to improved responses & shows efti's biological activity in randomised setting¹

Significant increases in Th1 biomarkers (IFN- γ & CXCL10) and absolute lymphocyte count driven by efti led to improved clinical outcomes²



1. Data from TACTI-003 Phase IIb trial in randomised Cohort A. 2. Data from TACTI-002 Phase II trial; increases in Th1 biomarkers as well as absolute lymphocyte count (not pictured here for TACTI-002) were also seen in randomised AIPAC Phase IIb trial in which efti was combined solely with chemotherapy.

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Efti's Potential to Extend Exclusivity for PD-1 Inhibitors

~\$34 Billion of the pharma patent cliff in 2028 stems from PD-1 inhibitors¹

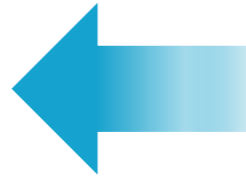
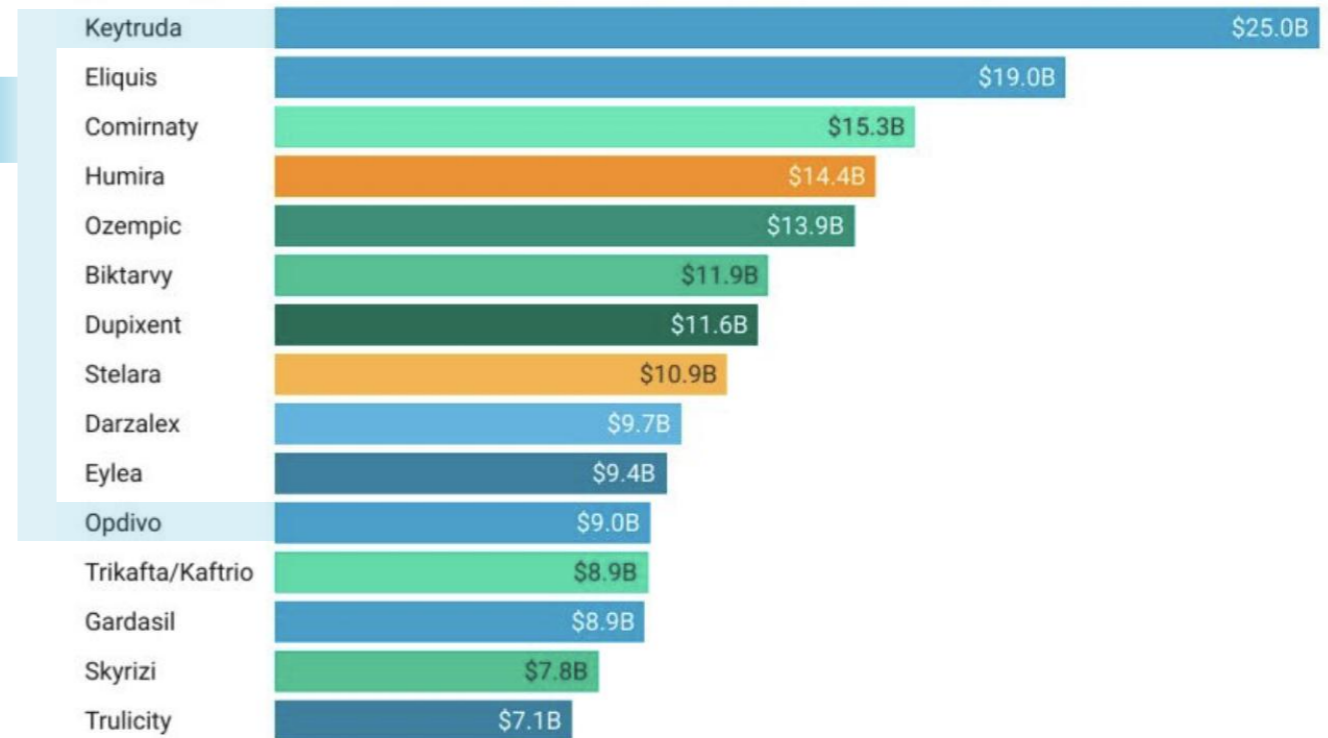


Immutep's comprehensive patent portfolio for efti provides an opportunity to enhance and substantially extend established or new PD-(L)1 franchises

Patent Expirations for Top 15 Drugs by Sales in 2023

Expiration dates of key patents related to US market

2023 2025 2027 2028 2029 2031 2032 2033 2037 2041



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Efti in First Line Non-Small Cell Lung Cancer: The Key Value Driver

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NSCLC Overview

- Lung cancer is leading cause of cancer death and 80-85% of lung cancers are non-small cell lung cancer (NSCLC)^{1,2}
- ~2.0 million NSCLC diagnoses annually
- Despite advances, Overall Survival still under 2 years for most patients
- Total addressable NSCLC drug market expected to reach US\$48 billion in 2031 with >50% sales from ICIs (e.g. anti-PD-1)³

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

Part A: Large Phase II trial in advanced/metastatic first line non-small cell lung cancer (1L NSCLC)

TACTI-002 (Part A) Phase II: Overview & Trial Design

Overview

- **Status:** Completed
- **Enrolment:** 114 patients
- **Locations:** 18 centers across six countries: US, UK, ES, PL, UA, and AU

Screening incl. PD-L1 testing

- Advanced/metastatic 1L NSCLC
- 0-100% PD-L1 expression
- EGFR/ALK negative

Treatment Phase

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 Q3W for 16 cycles

Up to 1 year

Follow Up Phase

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

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Baseline patient characteristics		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%	Central only ¹ 32 (35.6)	Central + local ² 37 (34.3)
	1-49%	38 (42.2)	42 (38.9)
	≥ 50%	20 (22.2)	29 (26.9)
Previous therapy, n (%)	Radiotherapy	38 (33.3)	
	Surgery	23 (20.2)	
	Systemic therapy for non-metastatic disease	26 (22.8)	

TACTI-002 enrolled 1L NSCLC patients regardless of PD-L1 expression and ~25% had high PD-L1 (TPS ≥50%), a lower proportion than typically would be expected.

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

Tumor Response by PD-L1 Expression Level¹

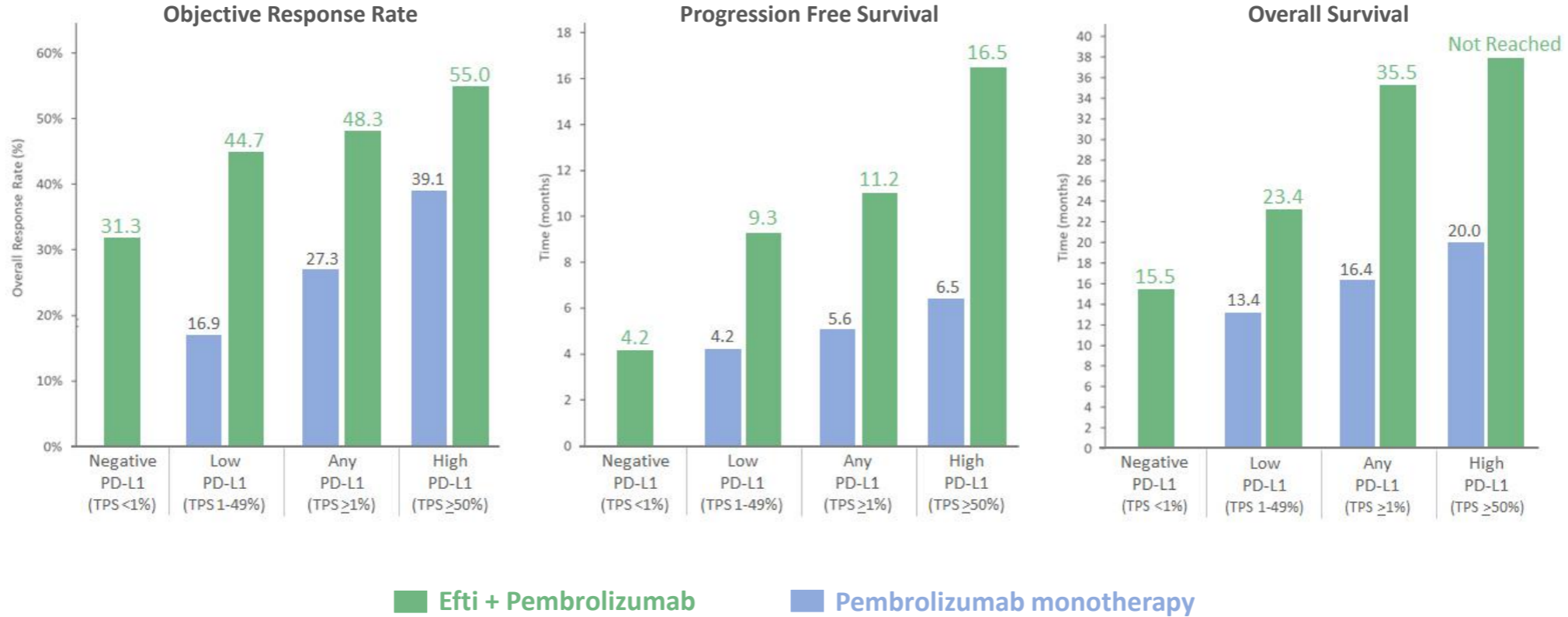
	All-Comer	Negative PD-L1	Low PD-L1	Any PD-L1	High PD-L1
	TPS 0-100% N=114	TPS <1% N=32	TPS 1-49% N=38	TPS ≥1% N=58	TPS ≥50% N=20
ORR^{2,3,4}	40.4%	31.3%	44.7%	48.3%	55.0%
mPFS², months	6.6	4.2	9.3	11.2	16.5
mDoR², months	21.6	20.7	NR	24.2	18.7
mOS, months	20.2	15.5	23.4	35.5	Not Reached

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

- Results offer compelling evidence of efti’s unique stimulation of patients’ immune systems and its potential to fight cancer
- Strong efficacy across all PD-L1 levels differentiates efti + anti-PD-1 (KEYTRUDA) from other chemotherapy-free combinations in 1L NSCLC
- Excellent Overall Survival, the gold standard benchmark in oncology, with exceptional durability, quality of responses, and favorable safety profile

Benchmarking TACTI-002 to KEYTRUDA

Robust response rates, durability, and progression free survival from **efti plus pembrolizumab** across all PD-L1 expression levels translate into compelling overall survival

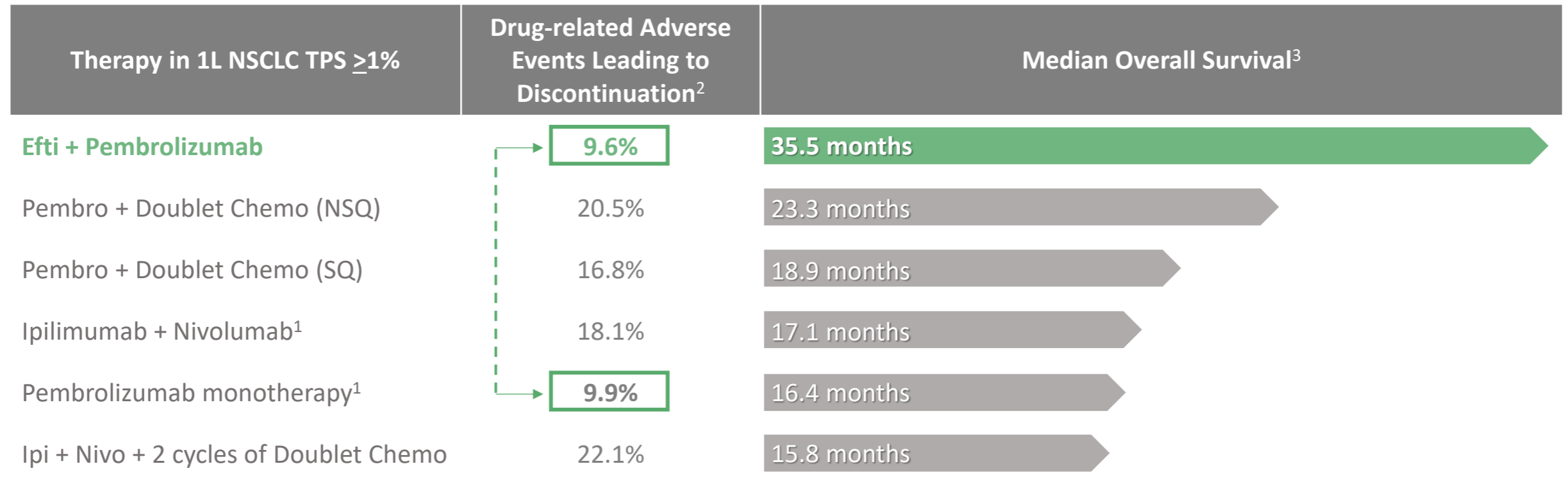


Comparison of data is from different clinical trials. Pembrolizumab monotherapy data from publications/EPAR assessment report of KN-042 registrational trial. Given the lack of historical results in negative PD-L1 expressing 1L NSCLC patients who received pembrolizumab monotherapy in KN-042 and other trials, the chart only has data from patients in TACTI-002 with negative PD-L1 expression (TPS <1%). In 1L NSCLC patients with TPS ≥1%, TACTI-002 has 66% patients with TPS 1-49% and 34% with TPS ≥50%, which compares to KN-042 with ~53% patients with PD-L1 and ~47% patients with PD-L1 TPS ≥50%.

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Favorable Safety and Compelling Overall Survival

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



NSQ = Non-squamous; SQ = Squamous

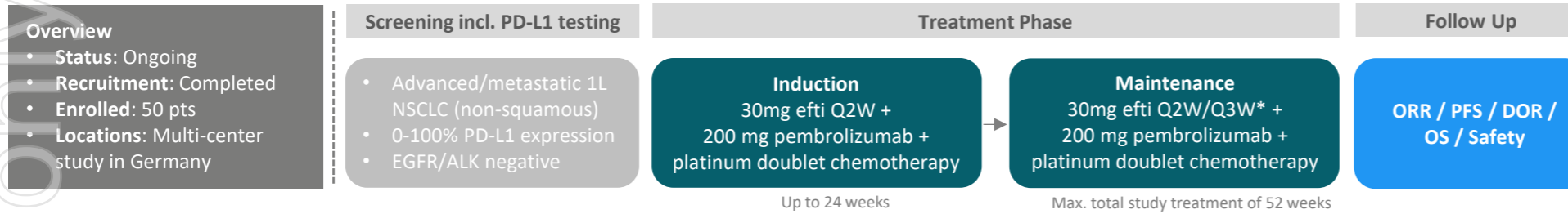
17 Comparison of data is from different clinical trials. 1. Ipilimumab + Nivolumab approved in US for 1L NSCLC PD-L1 TPS >1% but not in EU; Pembro mono not approved in Europe for TPS 1-49%. 2. Treatment related adverse events leading to discontinuation taken from publications/EPAR assessments of respective trials (KN-042, KN-024, KN-189, KN-021, KN-407, CM-227, CM-9LA). 3. Arrow lengths are proportional representations of Overall Survival data. Data for standard-of-care therapies taken from publications of respective registrational trials (e.g., KN-042, KN-189, KN-407, CM-227, CM-9LA).

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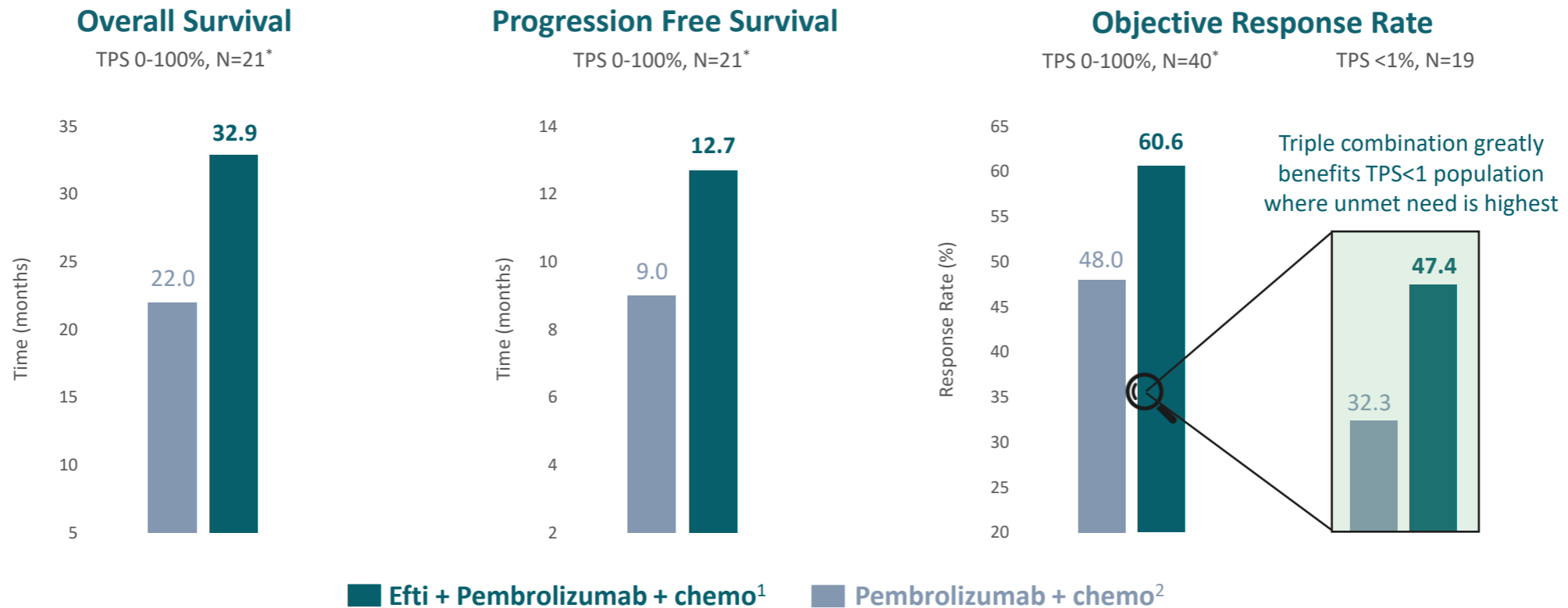
INSIGHT-003: Excellent Mature Survival Data

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

INSIGHT-003 (Stratum C) Phase I: Overview & Trial Design



INSIGHT-003 is an investigator-initiated, multi-centre Phase I trial led by Frankfurt Institute of Clinical Cancer Research (IKF)



Comparison of data is from different clinical trials. 1. Data cut-off date is 15 October 2024 for INSIGHT-003. * Objective Response Rate (N=40) and Overall Survival & Progression Free Survival data from patients with mature follow up of at least 22 months (N=21). Of note, INSIGHT-003 has ~19% patients with high PD-L1 who typically respond better to anti-PD-1 vs ~32% patients in historical control. 2. Shirish Gadgeel et al., Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non-Small-Cell Lung Cancer. JCO 38, 1505-1517(2020). DOI:10.1200/JCO.19.03136. * After 24 weeks, efti is injected every 3 weeks when combined with the SOC therapy or every 2 weeks as monotherapy.

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Immutep & MSD (Merck) Phase III Trial in 1L NSCLC

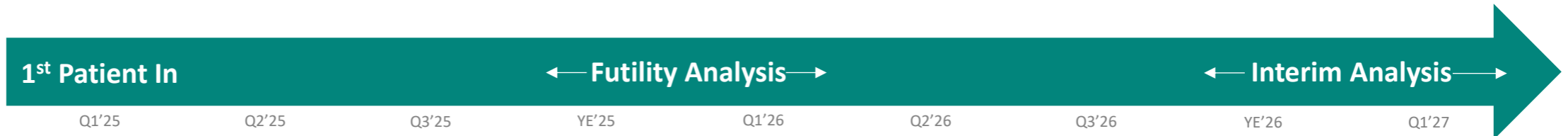
TACTI-004 / KEYNOTE-PNC-91 Phase III: Overview & Trial Design



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Upcoming Milestones



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Global Phase III 1L NSCLC Trials with KEYTRUDA in Treatment Arm

TACTI-004 addresses the broadest 1L NSCLC patient population eligible for anti-PD-1 therapy

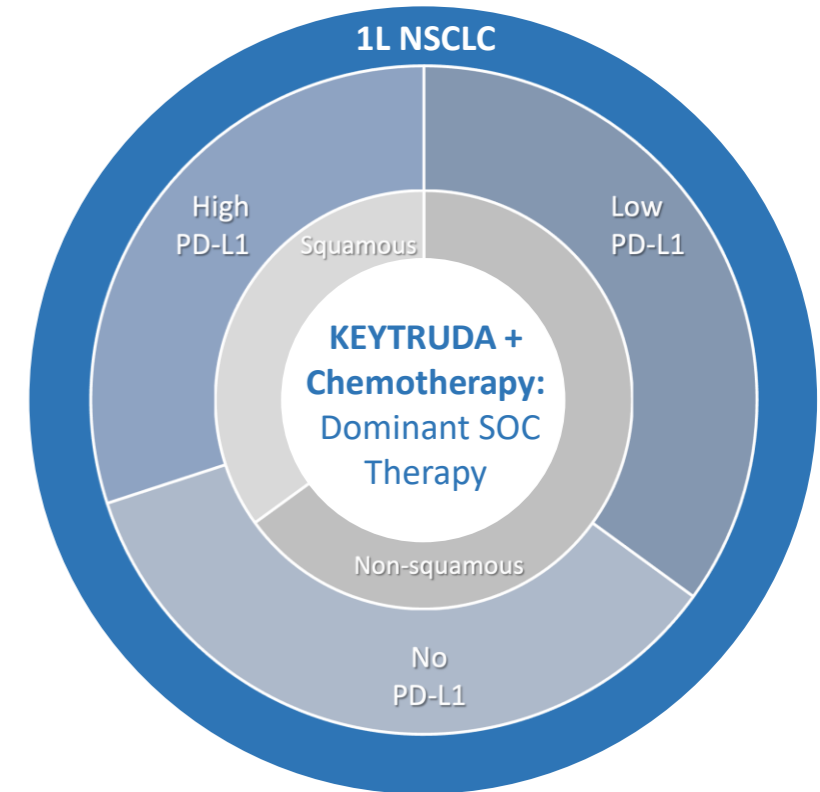


	PD-L1 TPS <1	PD-L1 TPS 1-49	PD-L1 TPS ≥50	Non-squamous	Squamous	Total Population
1L NSCLC patient population*	35%	35%	30%	70%	30%	Up to 100%
TACTI-004 (ImmuteP) Efti + KEYTRUDA + Chemo	✓	✓	✓	✓	✓	100%
TROPION-Lung07 (Daiichi Sankyo) DatoDXd + KEYTRUDA	✓	✓	✗	✓	✗	49%
EVOKE-03 (Gilead) Sacituzumab Govitecan + KEYTRUDA	✗	✗	✓	✓	✓	30%
TROPION-Lung08 (Daiichi Sankyo) DatoDXd + KEYTRUDA	✗	✗	✓	✓	✗	21%

Potential Blockbuster Commercial Opportunity

If TACTI-004 is successful it presents a potential multi-billion US\$ opportunity for Immutep as efti will be positioned as a safe, effective addition to KEYTRUDA & chemo, the standard-of-care therapy most often chosen by physicians in 1L NSCLC:

- KEYTRUDA has revolutionized treatment landscape and MSD (Merck) captures between 7 to 8 of every 10 patients with metastatic lung cancer*
- Estimates are ~US\$9 billion or +35% of KEYTRUDA's overall sales in 2023 from lung cancer**
- Potential peak sales for efti can be reached faster vs. typical therapeutic launch given KEYTRUDA + chemo's dominant position in 1L NSCLC market



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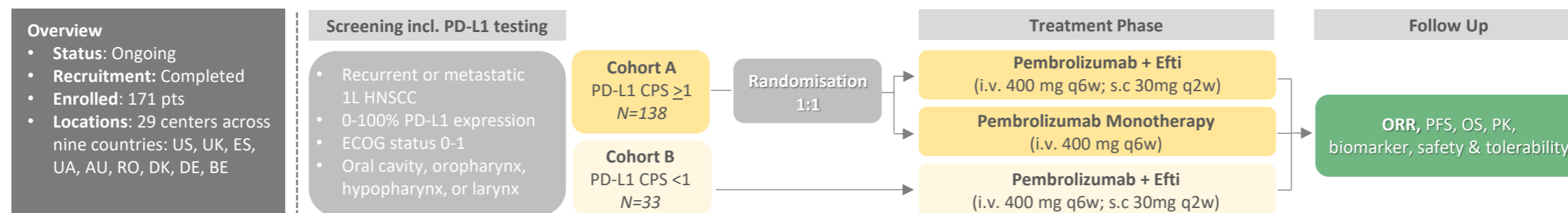
**Additional Oncology Indications &
Small Molecule Anti-LAG-3 Oncology Program**

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TACTI-003 / KN-C34 Trial Overview

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

TACTI-003 / KEYNOTE-C34 Phase IIb: Overview & Trial Design



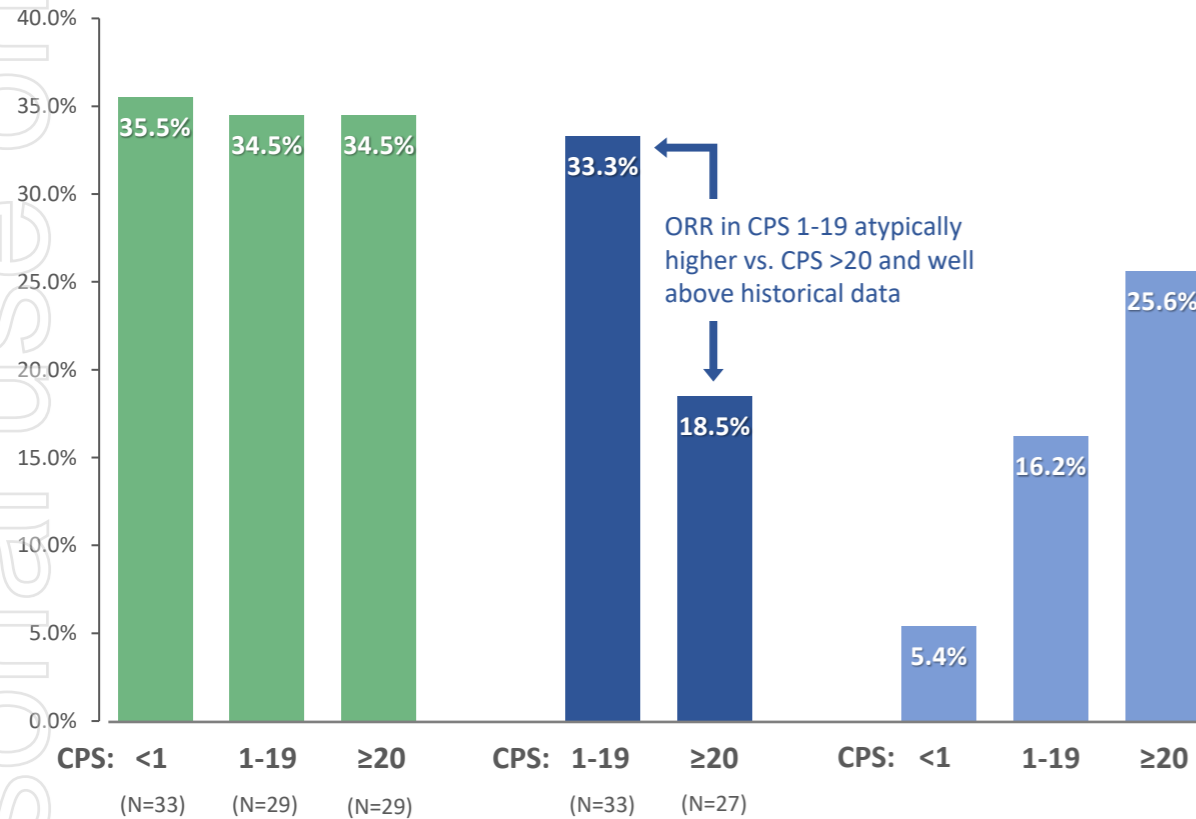
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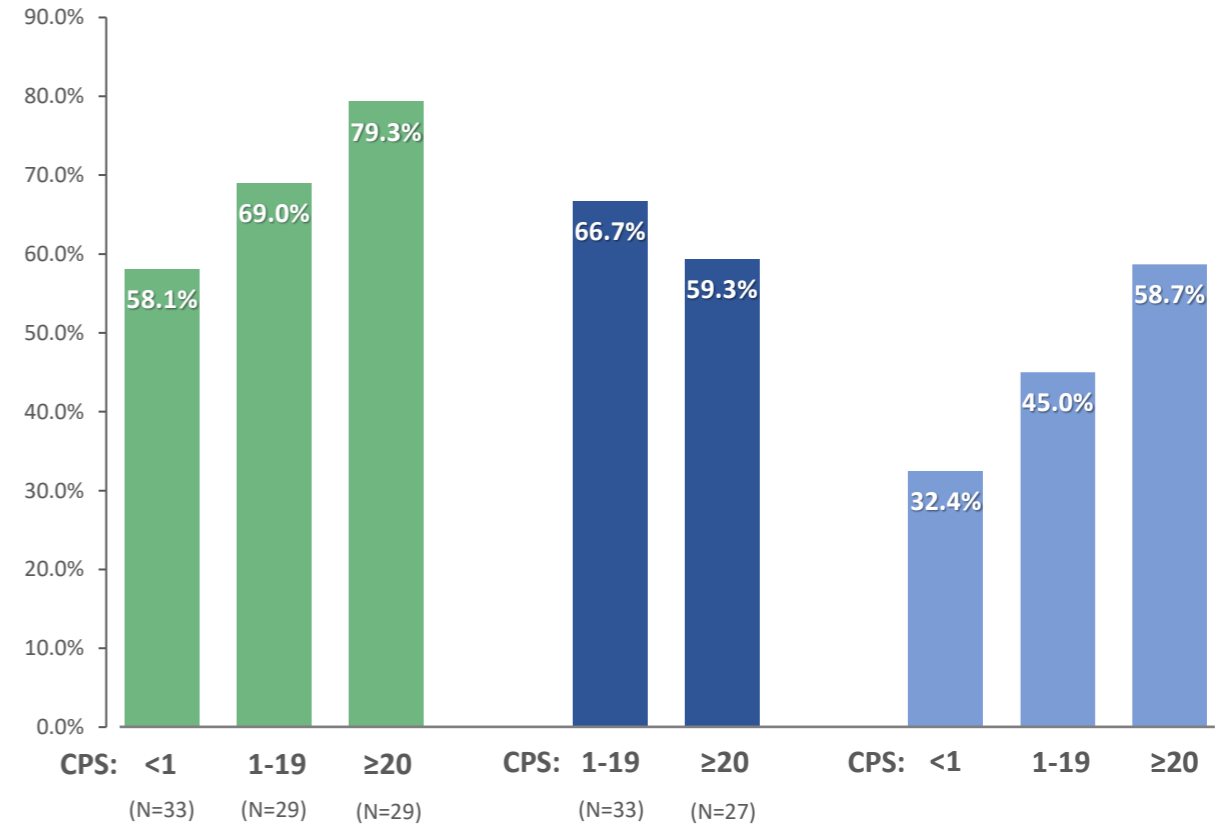
- Randomised, multicenter Phase IIb trial evaluating efti in combination with pembrolizumab (KEYTRUDA[®]) in first line recurrent or metastatic head and neck squamous cell carcinoma (1L R/M HNSCC):
 - Cohort A (N=138) - Patients with any PD-L1 expression (CPS ≥ 1) randomised 1:1 evaluating efti + KEYTRUDA[®] vs. KEYTRUDA monotherapy
 - Cohort B (N=33) - Patients with no PD-L1 expression (CPS < 1), which could not be randomised as KEYTRUDA monotherapy 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

Cohorts A/B: High Response Rates Regardless of PD-L1 Expression

Objective Response Rate (ORR)



Disease Control Rate (DCR)



■ Efti + KEYTRUDA (TACTI-003)
 ■ KEYTRUDA mono (TACTI-003)
 ■ KEYTRUDA mono (KN-048)*

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Cohorts A/B: Favourable Safety Profile

Safety Parameter	KEYTRUDA alone (Cohort A, n=68) n (%)	Efti + KEYTRUDA (Cohort A, n=69) n (%)	Efti + KEYTRUDA (Cohort B, n=33) n (%)
Any TEAR Leading to Discontinuation of Study Treatment	3 (4.4%) ¹	3 (4.3%) ²	3 (9.1%) ³

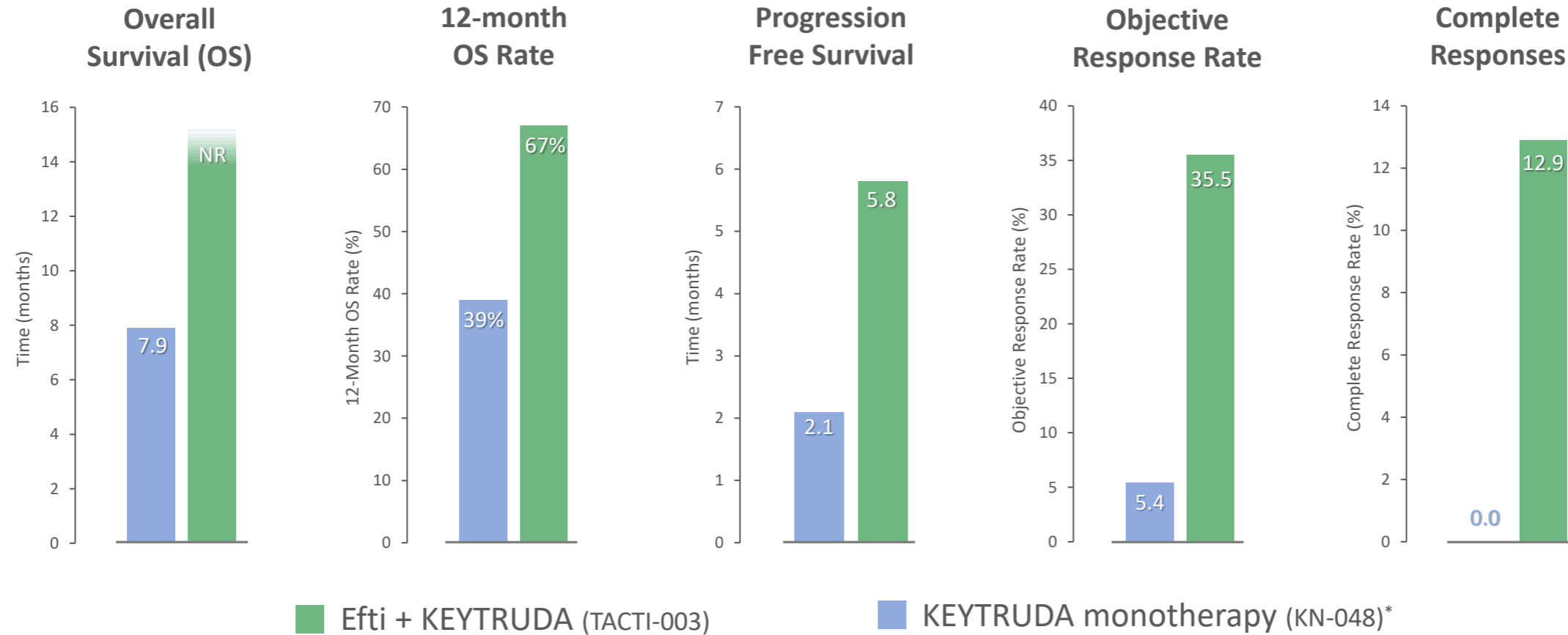
TEAR: Treatment-emergent adverse reaction

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

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Cohort B: Exceptional Results for a Chemo-Free Regimen

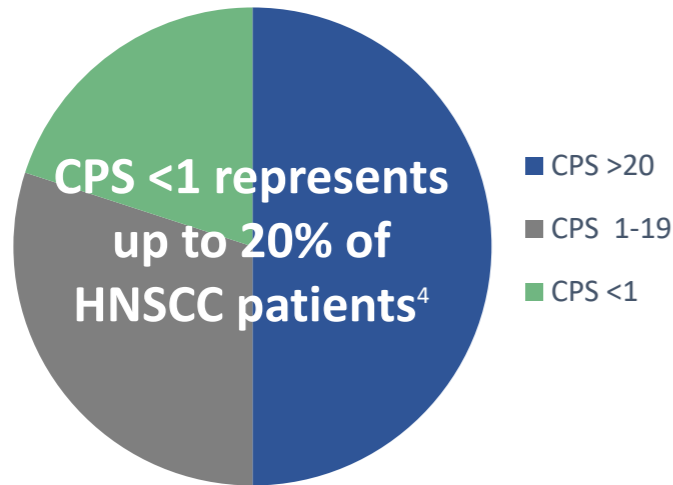
Benchmarking to KEYTRUDA monotherapy in patients with PD-L1 expression below 1 (CPS <1)



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Limited Competition in CPS <1: A Valuable Market

Head & Neck Cancer
\$2.8 billion market¹



>890,000 HNSCC diagnoses per annum worldwide with ~100,000 patients who develop metastatic disease.^{1,2,3}

No chemo-free therapies for 1L HNSCC patients with PD-L1 CPS <1

Standard-of-Care (SOC) Therapies include Chemo

Pembrolizumab /
doublet chemo
US only

Cetuximab /
doublet chemo
US & EU

Ongoing Clinical Trials without Chemo

Efti /
Pembrolizumab

Efti + KEYTRUDA shows superior OS, PFS, and durability with less toxicity as compared to SOC therapies & generates high response rates.

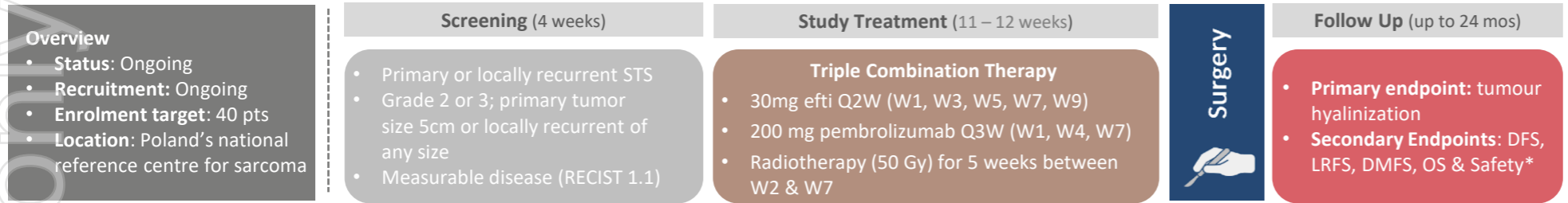
Next Steps

- Discuss the path forward in 1L HNSCC CPS <1 with regulatory agencies
- Discuss results with key stakeholders (investigators etc.)

Positive Data in Soft Tissue Sarcoma Presented at CTOS 2024

Phase II studying novel triple combination of Efti + Radiotherapy + KEYTRUDA in soft tissue sarcoma (STS)

EFTISARC-NEO Phase II: Overview & Trial Design

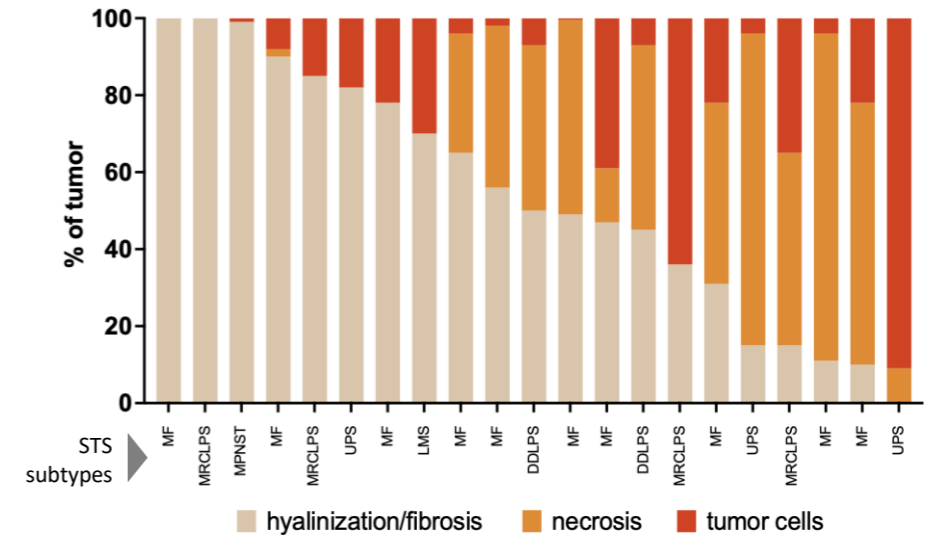
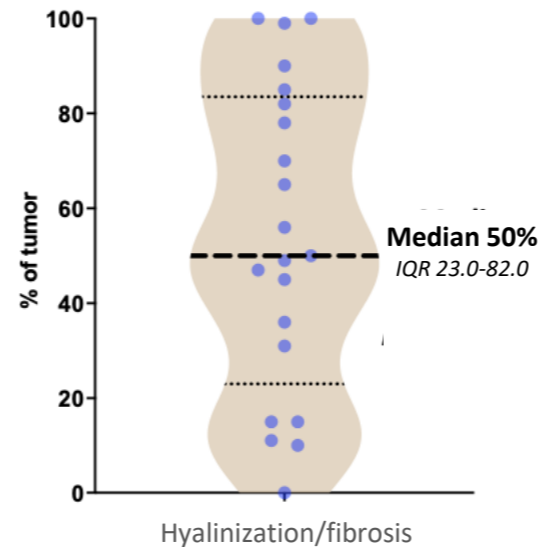
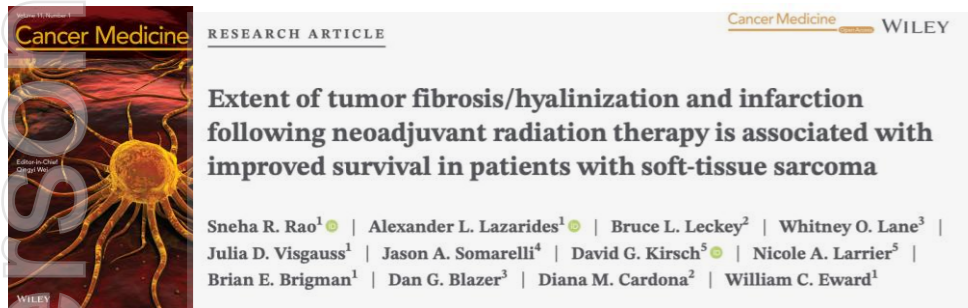


EFTISARC-NEO is an investigator-initiated trial conducted at Poland's national reference centre for sarcoma, the Maria Skłodowska-Curie National Research Institute of Oncology.

Strong efficacy in patients assessed for tumour hyalinization/fibrosis, trial's primary endpoint associated with improved survival in STS patients¹

50% tumour hyalinization/fibrosis vs. 15% from RT alone²

71.4% patients achieved pathologic response (hyalinization \geq 35%) across five STS subtypes

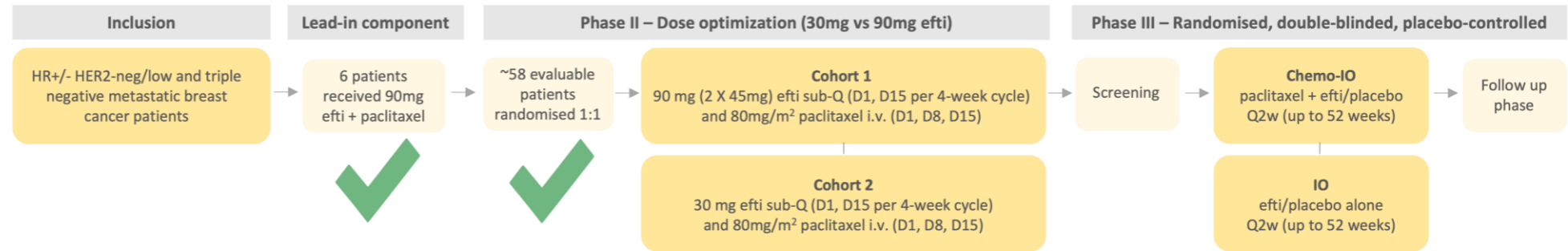


AIPAC-003 Phase II/III Trial in Metastatic Breast Cancer

AIPAC-003: Overview and Trial Design

Overview

- **Status:** Ongoing
- **Recruitment:** Phase II complete
- **Enrolled:** 65 pts in Phase II and 6 pts in lead in component
- **Location:** 22 centres across five countries



- HR+/- HER2-negative/low and triple negative metastatic breast cancer (MBC) patients represent ~78% breast cancer cases¹
- Patients receive efti + paclitaxel on same day; IO-chemo treatment can continue until disease progression
- Trial design incorporates feedback from FDA & EMA and provides risk-balanced approach
- Randomised Phase II dose optimization underway to find optimal biological efti dosing (e.g. 30mg or 90mg)

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

INSIGHT-005 (Stratum E) Phase I: Overview & Trial Design

Overview

- **Status:** Ongoing
- **Recruitment:** Ongoing
- **Enrolment target:** 30 pts
- **Location:** Multi-centre study in Germany

Screening

- Metastatic or unresectable locally advanced urothelial carcinoma (UC)
- 0-100% PD-L1 expression
- Enrolment in 3 subgroups

Treatment Phase

30mg efti s.c. + 800 mg avelumab i.v. on same day
Q2W for a maximum of 24 cycles

Follow Up

Feasibility / Safety /
ORR / DOR / PFS / OS



INSIGHT-005 is an investigator-initiated, multi-centre Phase I trial led by Frankfurt Institute of Clinical Cancer Research (IKF)

In collaboration with

Merck KGaA
Darmstadt, Germany

- INSIGHT-005 evaluating safety & efficacy of efti and avelumab (BAVENCIO®), which has previously shown promising efficacy in solid tumours in Phase I trial
- Jointly funded by Immunotep & 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

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Novel Small Molecule Anti-LAG-3 Preclinical Program in Oncology

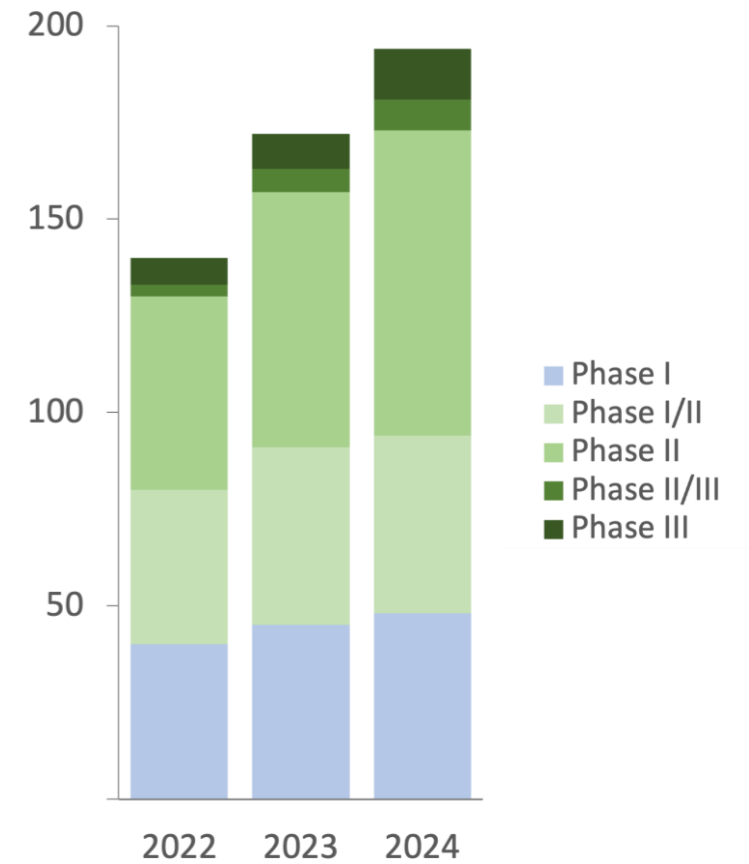


Immutep aims to develop an orally-available small molecule anti-LAG-3 treatment at a lower cost compared with anti-LAG-3 antibodies commercially available (Opdualag; ~\$864 million in TTM sales**) or under clinical development

“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

Anti-LAG-3 Antibody Clinical Trials*



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**IMP761: First-in-class LAG-3 Agonist Antibody
for Autoimmune Diseases**

Targeting Autoimmune Diseases with a LAG-3 Checkpoint Agonist

New paradigm to treat the cause -- as opposed to the symptoms -- of autoimmune disorders



*“These findings further support the potential clinical benefits of a **LAG-3 agonist** in the treatment of human autoimmunity”¹*

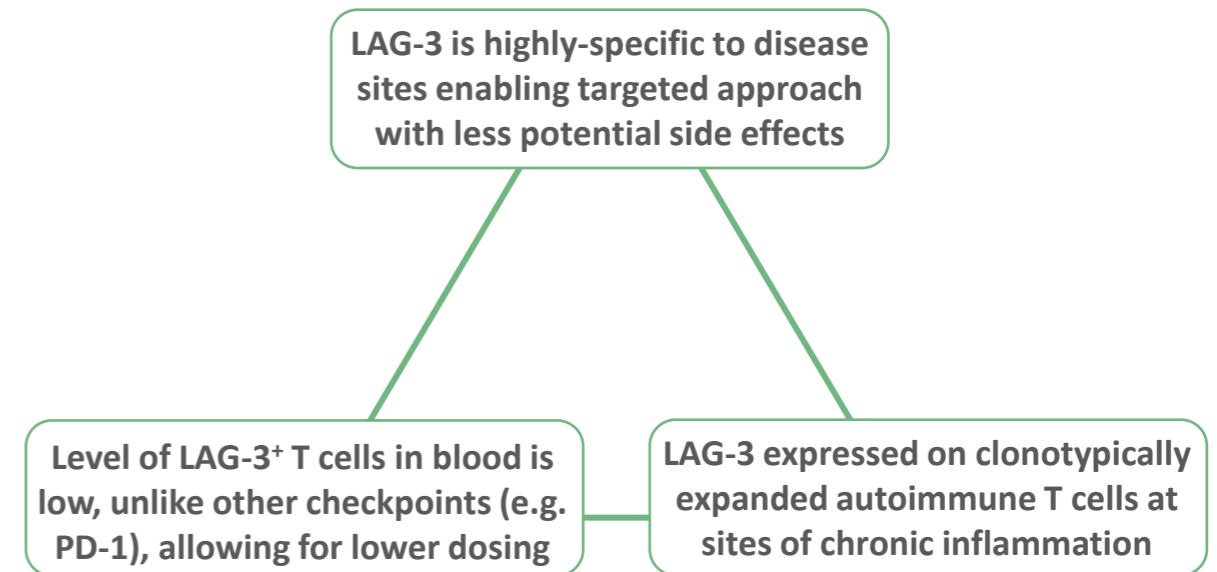


*“**LAG-3 agonism** could be a potential target for future treatment in rheumatoid arthritis”²*



*“The manipulation of the **LAG-3 pathway** can serve as a promising therapeutic strategy”³*

Unique advantages of LAG-3 make it an ideal target for an agonist antibody to treat autoimmune diseases



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1. Britta E. Jones, Megan D. Maerz, Henry T. Bahnson, Ashwin Somasundaram, Lucas H. McCarthy, Cate Speake, Jane H. Buckner; Fewer LAG-3+ T Cells in Relapsing-Remitting Multiple Sclerosis and Type 1 Diabetes. *J Immunol* 1 February 2022; 208 (3): 594–602. <https://doi.org/10.4049/jimmunol.2100850>. 2. Pedersen, J.M., Hansen, A.S., Skejød, C. et al. Lymphocyte activation gene 3 is increased and affects cytokine production in rheumatoid arthritis. *Arthritis Res Ther* 25, 97 (2023). <https://doi.org/10.1186/s13075-023-03073-z>. 3. Zhou, X., Gu, Y., Wang, H. et al. From bench to bedside: targeting lymphocyte activation gene 3 as a therapeutic strategy for autoimmune diseases. *Inflamm. Res.* 72, 1215–1235 (2023). <https://doi.org/10.1007/s00011-023-01742-y>

LAG-3: An Important Immune Checkpoint in Autoimmunity

Learnings from immune checkpoint inhibitors (ICI) in oncology

ICI therapies (e.g. anti-PD-[L]1, anti-CTLA-4, anti-LAG-3) are effective in many oncology indications



Main side effects of ICIs are emergence of autoimmune disorders (e.g. immune-mediated pneumonitis, colitis, hepatitis, thyroiditis, etc.) due to overactivation of the immune system



Immune checkpoints are controlling autoimmunity

Addition of relatlimab (anti-LAG-3) mostly *doubled frequency of immune mediated AEs* vs. nivolumab (anti-PD-1)¹

RELATIVITY-047 Phase III trial in Melanoma

Adverse Events (AE) %	Relatlimab + Nivolumab (N = 355)	Nivolumab alone (N = 359)
Hypothyroidism or thyroiditis	18.0	13.9
Arthralgia	14.4	7.2
Diarrhea or colitis	6.8	3.1
Hepatitis	5.6	2.5
Adrenal insufficiency	4.2	0.8
Pneumonitis	3.7	1.7
Hypophysitis	2.5	0.8
Myocarditis	1.7	0.6

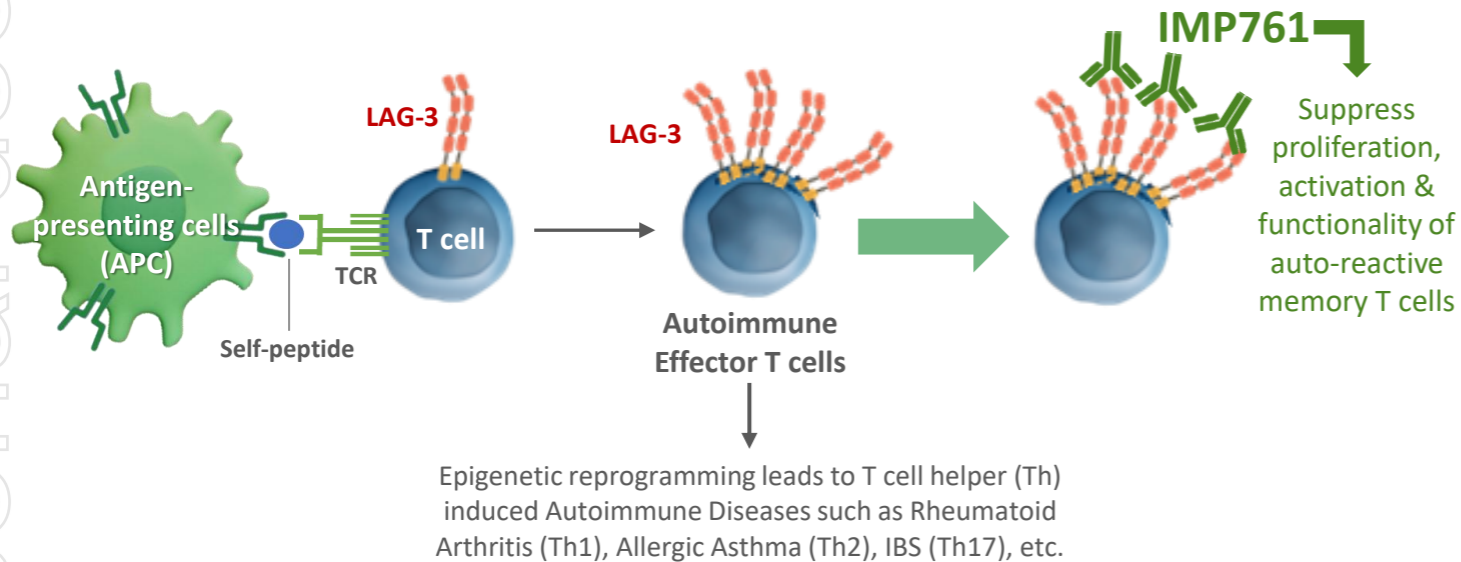


LAG-3 is an important checkpoint in autoimmunity

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

Many autoimmune diseases can potentially be targeted including several large disorders

IMP761 increases “brake” function of the LAG-3 immune checkpoint and its natural down-regulation of auto-reactive memory T cells, which represent the root cause of many diseases



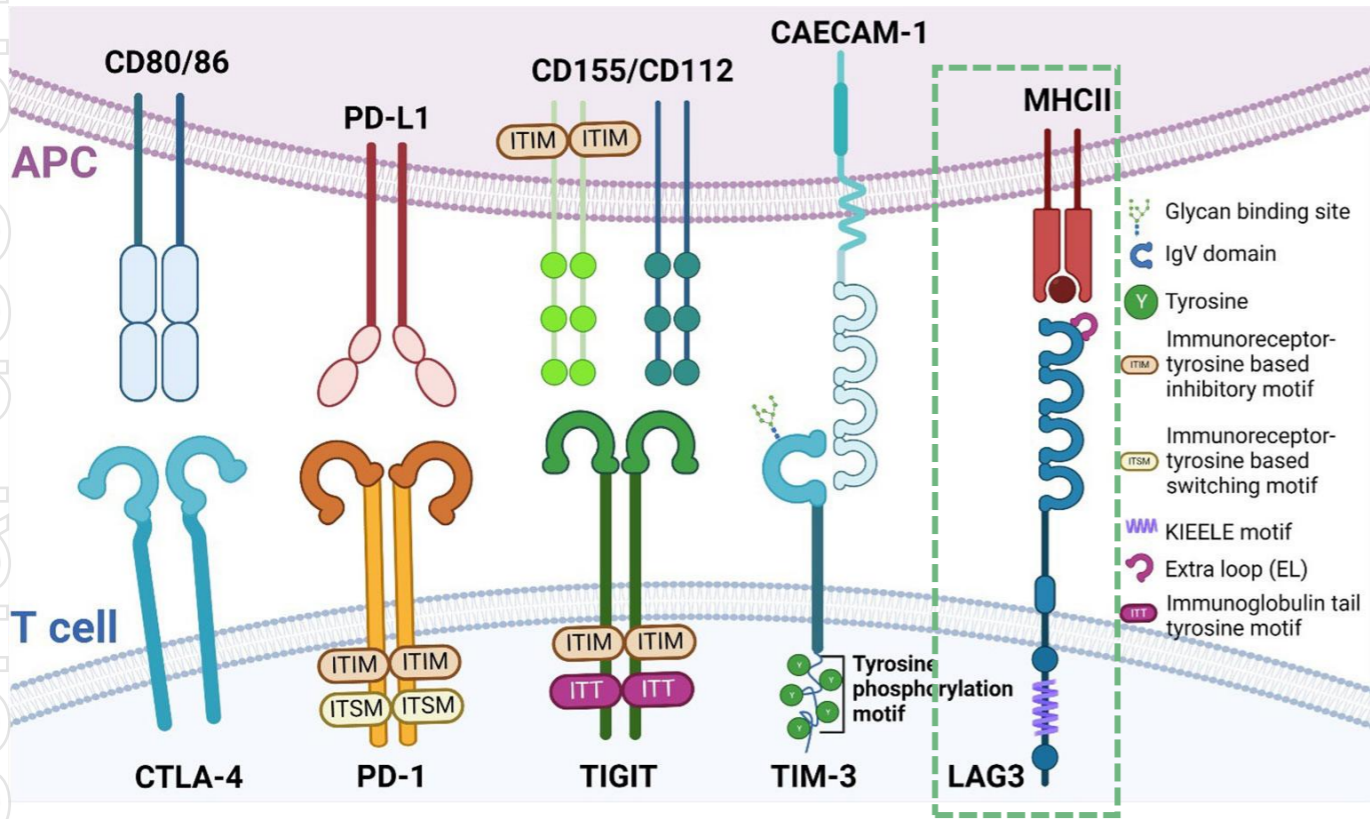
IMP761 as a LAG-3 agonist can target numerous autoimmune diseases including:

- Rheumatoid arthritis: market size est. \$29.6 billion*
- Type 1 diabetes: market size est. \$9.9 billion*
- Multiple sclerosis: market size est. \$32.9 billion*

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IMP761: Strong Inhibition of TCR Signalling & T cell Activation

Unique LAG-3 Signalling Pathway



- Unlike 100+ inhibitory receptors (including PD-1, TIGIT, BTLA), LAG-3 has no tyrosine-based ITIM motif¹ in its cytoplasmic domain
- The inhibitory motifs unique to LAG-3² explain in part **clear & rapid inhibition of T cell receptor (TCR) signalling** induced by IMP761 in preclinical studies
- IMP761 also **strongly blocks T cell activation** via the TCR in preclinical studies

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1. ITIM motif (S/I/V/LxYxxI/V/L). 2. Three unique inhibitory motifs (KIEELE, repeated EP, FXXL). Lui, Y., Davis, S.J. LAG-3: a very singular immune checkpoint. Nat Immunol 19, 1278–1279 (2018) <https://doi.org/10.1038/s41590-018-0257-1>. N Jantz-Naem et al, Front. Oncol., 17 February 2023, Sec. Cancer Metabolism, Vol 13 -<https://doi.org/10.3389/fonc.2023.1060112>. Maeda, Takeo K. et al. Atypical motifs in the cytoplasmic region of the inhibitory immune co-receptor LAG-3 inhibit T cell activation Journal of Biological Chemistry, April 2019, Volume 294, Issue 15, 6017 - 6026

Clinical Development of IMP761

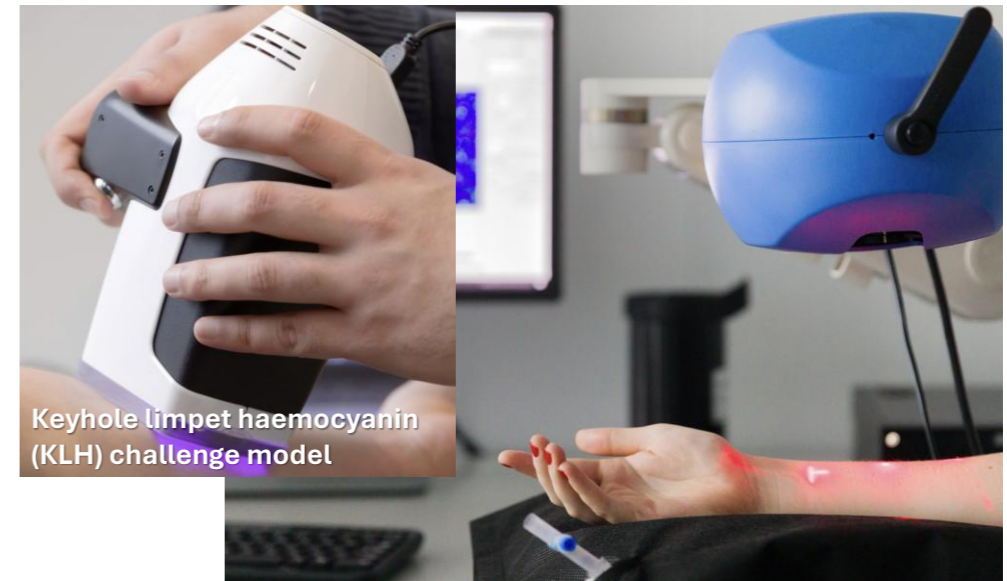
Leading world-class research institute appointed to conduct first-in-human study

Overview / Key Milestones:

- Placebo-controlled, double-blind Phase I (N = 49)
- Centre for Human Drug Research (CHDR) has been selected to conduct
- First participant enrolled in August 2024
- Favourable initial safety data reported in December 2024
- Additional data and study completion expected in 2025



- World-class research institute in Leiden, the Netherlands
- CHDR offers a unique KLH challenge model allowing for evaluation of IMP761's pharmacological activity at early stages of development



Keyhole limpet haemocyanin (KLH) challenge model

Single Ascending Dose (SAD): Healthy volunteers

Part A: Healthy N=5

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

COMPLETED

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

ONGOING

3x KLH
immunization,
DTH

PK/PD

Single IV

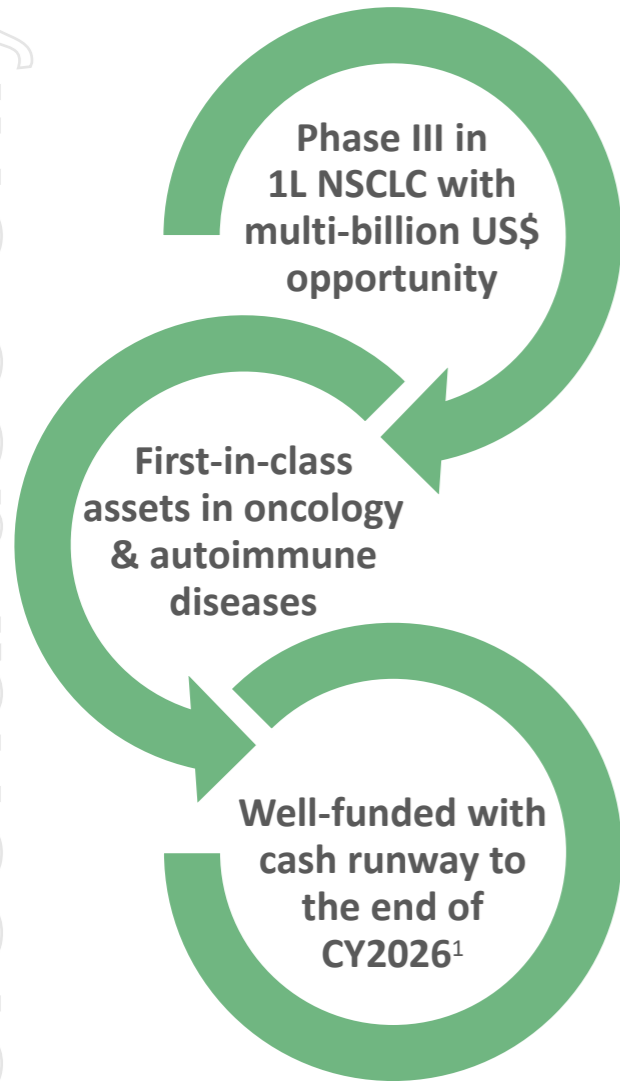
Multiple Ascending Dose (MAD): Healthy volunteers

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)
IV



2025 Milestones

- Non-Small Cell Lung Cancer:
 - FPI in TACTI-004 Phase III in Q1 CY2025
 - TACTI-004 potential futility analysis by year end CY2025 or early 2026*
 - Update from investigator-initiated INSIGHT-003 trial
- Metastatic Breast Cancer – Update from AIPAC-003 trial
- Head and Neck Squamous Cell Carcinoma – Update from TACTI-003 trial
- Soft Tissue Sarcoma – Update from investigator-initiated EFTISARC-NEO trial
- Metastatic Urothelial Carcinoma – Update from investigator-initiated INSIGHT-005 trial
- Autoimmune Diseases – Update from IMP761 first-in-human Phase I trial
- Additional Updates – From ongoing clinical trials, partnered programs, and potential expansion of clinical trial pipeline



Thank You

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