OSE IMMUNO THERAPEUTICS

Breaking Through the Therapeutic Ceiling with First-In-Class Immunotherapies

October 2023

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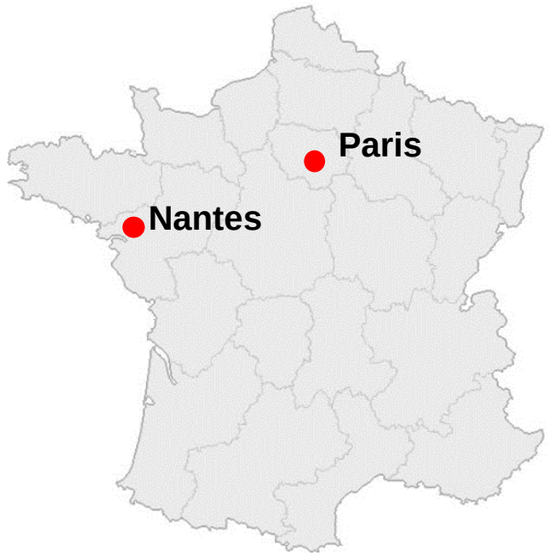
Delivering first-in-class immunotherapies from Target to Clinic

Key In-house expertise and capabilities to identify and develop *First-In-Class* immunotherapies

- Founded in **2012**
- IPO/Euronext in **2015**
- Merged with Effimune in **2016**

- **50+ FTEs**
- **480+ granted patents**
- **Nantes** Headquarters
- **Paris** offices



121 M€ : Partnerships

20 M€ : Grants

28 M€ : R&D Tax credit

52 M€ : Equity

1 **Phase 3 asset:** Tedopi® in NSCLC
Most advanced cancer vaccine

- **TEDOPI** is the first cancer vaccine to show efficacy phase 3 results post-ICI **NSCLC** as monotherapy vs active comparator.

5 **Clinical stage assets**

- 3 **Fully** owned
- 2 **Partnered** with Boehringer Ingelheim and Veloxis

3 **Pre-clinical** assets approaching the clinic

- **Innovative MoA & Targets** to address critical unmet need
- International Research Collaboration

OSE Immunotherapeutics **pipeline**

Combining a clinical portfolio of first-in-class assets with unique, highly productive R&D platforms

		Product candidate	Target	Indication	Research	IND-enabling	Phase I	Phase II	Phase III	Market
Clinical	Proprietary	**Tedopi®**	Neoepitopes Vaccine (OSE IMMUNO THERAPEUTICS)	**NSCLC Mono post-ICI 3L**						*Compassionate (EU)*
				New NSCLC Mono post-ICI 2L						
				PDAC Combo maintenance *(IIS)*						
				NSCLC Combo 2L post-ICI *(IIS)*						
				OC Mono or Combo *(IIS)*						
		OSE-127 Lusvertikimab	Anti-IL-7R (OSE IMMUNO THERAPEUTICS)	Ulcerative Colitis						
				ALL						
		OSE-279	Anti-PD-1 (OSE IMMUNO THERAPEUTICS)	Solid tumors						
	Partnered	**VEL-101**	Anti-CD28 (Veloxis PHARMACEUTICALS)	Kidney Transplant						
		BI 765063	Anti-SIRPα (Boehringer Ingelheim)	HNSCC 2L and HCC 1L/2L						
		BI 770371	Anti-SIRPα (Boehringer Ingelheim)	Solid tumors						
R&D Engine Platform	Proprietary	**OSE-230** & Future targets (field resolution)	ChemR23 agonist mAb *other targets*	Auto-Inflammatory Diseases						
		BiCKI® IL-7v & Next undisclosed BiCKI®	PD1 x IL-7 bsAb *other anti-PD1 Bispe*	Immuno-Oncology						
		Myeloid Checkpoint	Anti-CLEC-1	Immuno-Oncology						

Immuno-Oncology
Immuno-Inflammation

ALL: acute lymphoblastic leukemia. **CRC:** colorectal cancer. **HNSCC:** head and neck squamous cell carcinoma. **MSS:** microsatellite stable cancer. **NSCLC:** non small cell lung cancer. **OC:** ovarian cancer
PDAC: pancreatic ductal adenocarcinoma. **UC:** ulcerative colitis. **IIS:** Investigator Initiated Study. **IND:** Investigational New Drug Application.

Strategic partners provide industry-leading clinical support and strong financial foundations

Over €1.4bn in potential milestones; €121m* already received since 2016

OSE-172/BI 765063
HNSCC and HCC
MSS Endometrial / MSS CRC

Boehringer Ingelheim

€65.3m received

Up to **€1.1bn** in milestones

+ High-single digit to low teens royalties on Global Sales

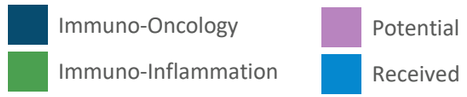
FR-104/VEL-101
Kidney transplant

Veloxis PHARMACEUTICALS
an Asahi Kasei company

€13.9m received

Up to **€315m** in milestones

+ Tiered royalties on Global Sales



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* Including upfront, milestones and reinvoiced R&D costs + previous license agreement with J&J and Servier

Multiple short-term anticipated catalysts

2023

Readouts
- **TEDOPI®**
  Regulatory update (Europe, US)
- **Lusvertikimab/OSE-127**
  Phase 2 UC: completion enrolment
- **OSE-279**
  Phase 1 update
- **OSE-172/BI 765063 *(partnered)***
  Phase 1/2 update

Progress
- **TEDOPI®**
  Phase 3 start in NSCLC 2L
- **FR104/VEL-101 *(partnered)***
  Phase 2 start in Kidney Tx
- **R&D programs**
  New Partnering Opportunities

2024

Readouts
- **Lusvertikimab/OSE-127**
  Phase 2 results in UC
- **TEDOPI®**
  Phase 2 results in PDAC
  Phases 2 NSCLC & OC update
- **OSE-172/BI 765063 *(partnered)***
  Phase 1/2 results in solid tumors
- **FR104/VEL-101 *(partnered)***
  Phase 1/2 results in Kidney Transplantation
- **OSE-279**
  Phase 1 results

Progress
- **Lusvertikimab/OSE-127**
  New Partnering Opportunities
- **OSE-172/BI 765063 *(partnered)***
  Phase 2 start
- **OSE-230**
  Phase 1 start

2025-2026

Readouts
- **TEDOPI®**
  Phase 3 results in NSCLC 2L
- **Lusvertikimab/OSE-127 *(to partner)***
  Phase 3 start
- **OSE-172/BI 765063 *(partnered)***
  Phase 2 update
- **FR104/VEL-101 *(partnered)***
  Phase 2 results in Kidney Transplantation
- **OSE-230**
  Phase 1 results

Progress
- **OSE-230**
  Phase 2 start
- **BiCKI® -IL7v/CLEC-1**
  IND
- **New R&D programs/platforms**

Investment Highlights

Compelling product

Promising clinical data from the lead asset Tedopi®
- Met primary overall survival endpoint in monotherapy in PoI pivotal NSCLC post-ICI study
- Significant better Safety profile & Quality of Life with positive Net Treatment Benefit versus SOC

Large market opportunities

Focus on multi-billion $ markets
- **I/O:** NSCLC (2L, 3L), HCC (1L, 2L), HNSCC (2L), Leukemia
- **I&I:** IBD (Ulcerative colitis), Kidney Transplantation

Strong pharma partnerships

Sustainable business through multi-partnership strategy
>€1.4bn milestones: Boehringer Ingelheim, Veloxis + New Partnership Opportunities

Long duration IP portfolio

IP extends to 2040's
I/O: Tedopi® (>2038), OSE-172 (>2037), OSE-279 (>2039), CLEC-1 (>2040) **I&I:** OSE-127 (>2037), FR104 (>2035), OSE-230 (>2040)

Multiple upcoming catalysts

Multiple key clinical and regulatory milestones expected in next 18 months
- **Tedopi®:** preparing confirmatory pivotal phase 3 NSCLC 2L, Phase 2 in PDAC
- **Lusvertikimab (OSE-127):** Top-line results Ulcerative Colitis Phase 2
- **BI 765063/BI 770371:** Phase 1b results in solid tumors
- **VEL-101:** Phase 1/2 results and Phase 2 start in Kidney Transplantation
- **OSE-230** & **BiCKI®IL7v:** 2xIND in the next 18 months

Financial Position

Cash visibility until Q4 2024
15 M€ available cash as of June 30, 2023, + **5.4 M€** R&D tax credit & + for almost **14 M€** additive financing secured post H1-2023

Our plan to build a leading immunotherapy company

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First-in-class strategy

Position Tedopi® as the best treatment option after ICI-failure in cancer patients

Leverage the clinical advantage of anti-SIRPα in the DON'T Eat Me landscape in Solid Tumors

Boehringer Ingelheim

Demonstrate Lusvertikimab (OSE-127) clinical activity Phase 2 in Ulcerative Colitis

Confirm VEL-101 benefit as maintenance therapy in kidney transplantation

Veloxis PHARMACEUTICALS

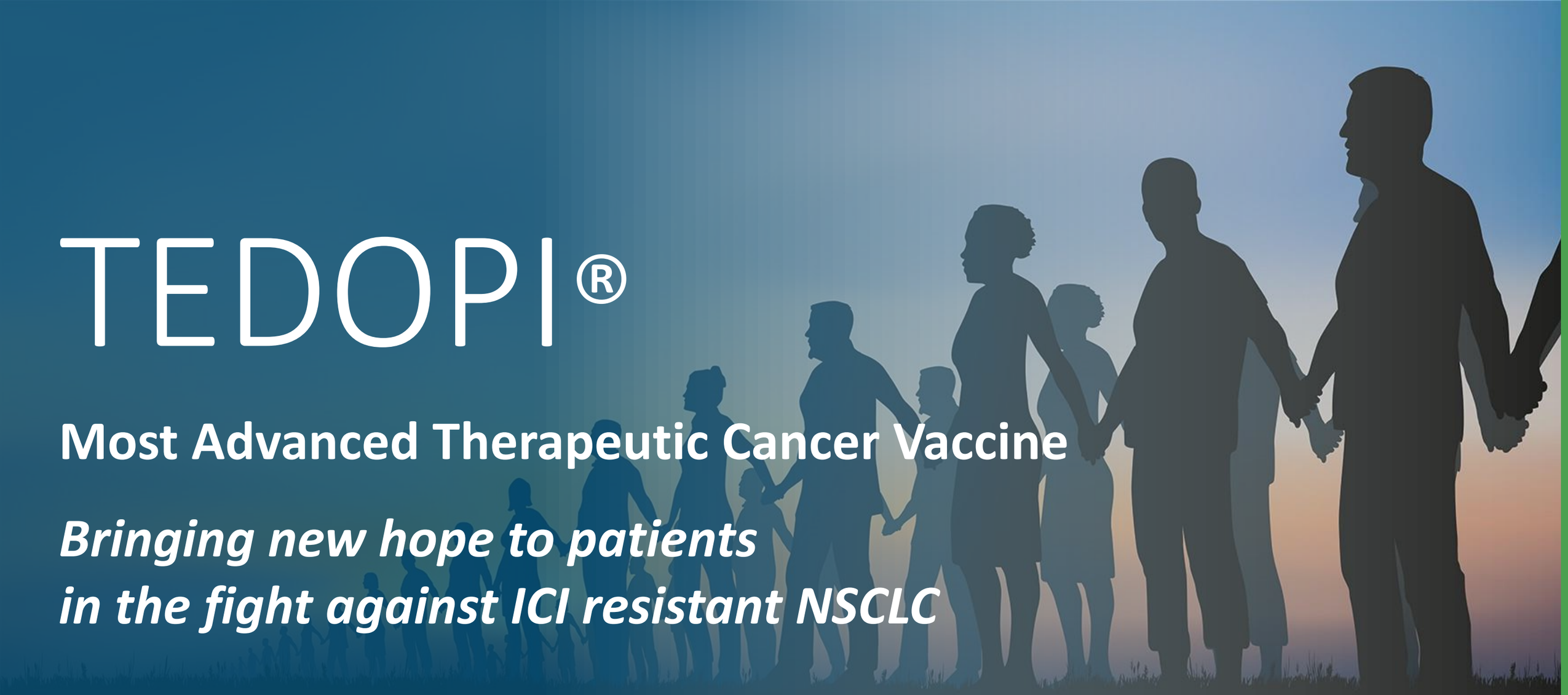
Advanced proprietary early-stage assets from OSE's research platforms
3 programs to enter the clinic in 2023-25 with *New Partnering Opportunities*

Proprietary clinical programs

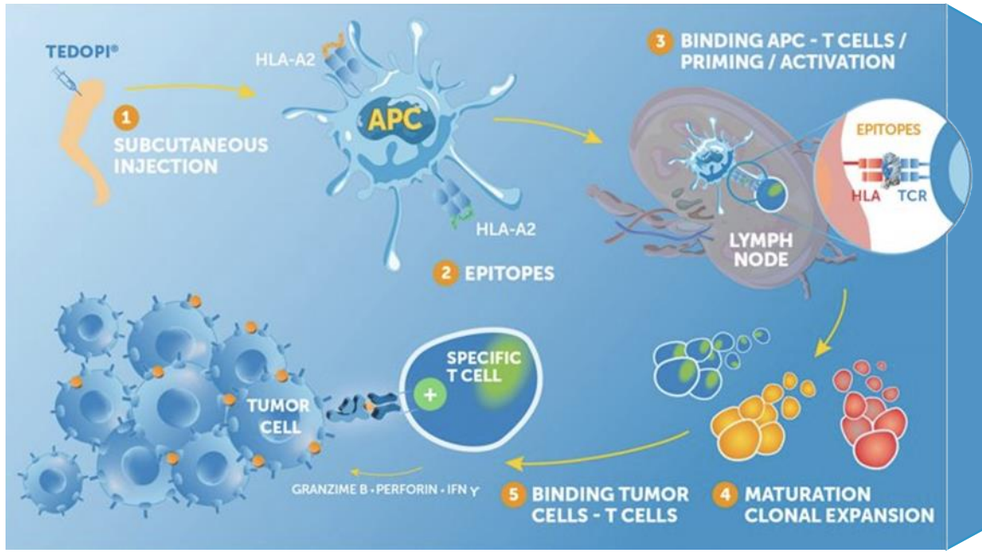
TEDOPI®

Most Advanced Therapeutic Cancer Vaccine

Bringing new hope to patients
in the fight against ICI resistant NSCLC



An **immunotherapy activating specific T-cells** to revive anti-tumor response



Most advanced Cancer Vaccine in clinical development

- **Unique** combination of **neoepitopes**: small peptides deriving from **tumor specific** antigens* expressed in various cancers
- Strong **binding to HLA-A2** receptor (45% population)
- Direct activation of tumor specific T-cells **differs from checkpoint inhibitors** releasing the break of immune response

Proprietary combination (9 **optimized neoepitopes** + 1 epitope giving universal T helper response)	Induces early T cell **memory** responses + **Migration** in tissues	**Ready to Use subcutaneous** formulation with Q3W injection	**Orphan Drug** Designation (FDA) **>1,000 injection** in clinical trials	Strong IP position until **2038**[1] (US / EU / Asia)

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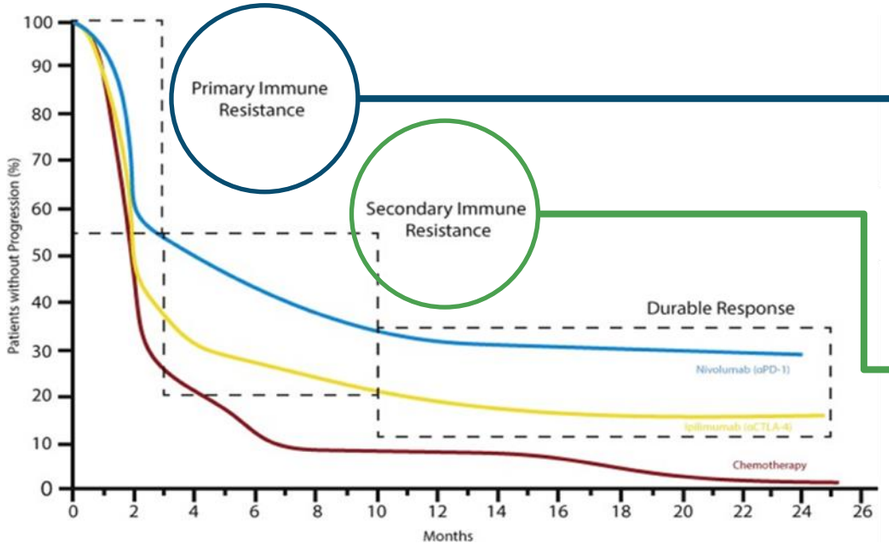
1: *OSE Immunotherapeutics Receives New European Patent*

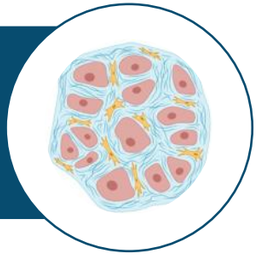
Tedopi® is a **novel cancer vaccine** with a strong biological rationale in post-ICI **secondary resistance**

Shifting paradigms with cancer vaccine immunotherapy



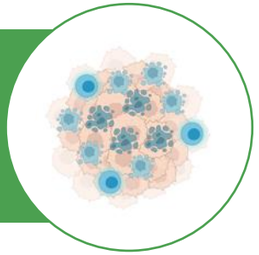
Primary (intrinsic) resistance
Patients who do not respond to ICIs with a rapid disease progression
→ **Immune refractory tumors**

No T-cell refractory tumors



Secondary (acquired) resistance[1]
Patients who have a period of initial ICI therapy benefit followed by disease progression
→ **Immuno-sensitive tumors**

T-cell exhausted & dying



TEDOPI® has the **potential to rejuvenate & refresh specific TILs** in immuno-sensitive tumors.
Neoepitope-specific T cells have tumor killing potential and limited side effects.

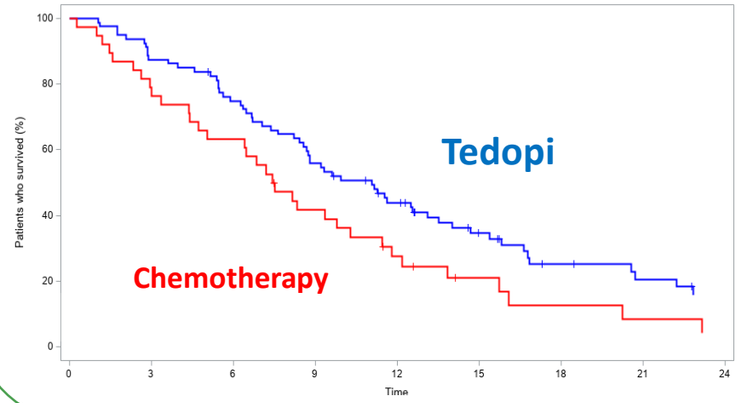
Figure: Schoenfeld AJ, Hellman MD. Cancer Cell 2020. Baxter MA, et al Br J Cancer 2021. **1:** After at least 12 weeks of ICI treatment in monotherapy (Task force SITC 2020 - Kluger H et al 2020).
ICI: immune checkpoint inhibitor. **TILs:** Tumor-infiltrating lymphocytes.

Clinically meaningful benefit of Tedopi®

First randomized Phase 3 with positive results vs. standard of care (SOC)

Overall Survival

secondary resistance post anti-PD(L)1



OS rate at 12 months
44%
in **Tedopi®** vs.
27.5%
in SoC

Delta OS: **3.6** months

Tedopi® 11.1 months
vs
SoC 7.5 months

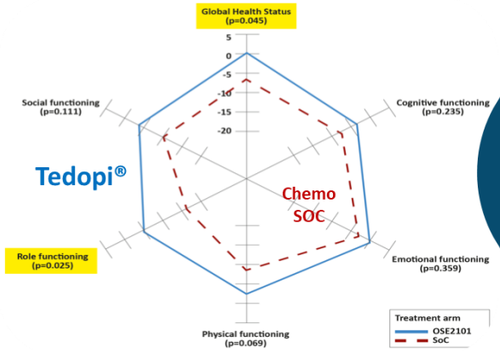
HR 0.59 /
p-value=0.017

Risk of Death reduced by 41% *versus chemo.*

Significantly safer than Chemo.

11% *vs* **35%** *grade 3-5 AEs*

Better Quality of Life



Positive Net Treatment Benefit vs SOC: P=0.032

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Besse et al. Annals of Oncology 2023

ANNALS OF ONCOLOGY driving innovation in oncology

Position Tedopi® as the best treatment option after ICI-failure in cancer patients

Awaited and **innovative mechanism** of action post-IO

Confirmed MoA in patients (T-cell response **correlated with survival**)

Identification of **population with significant benefit**

Increased **Survival**

Decreased **Toxicity** versus SOC

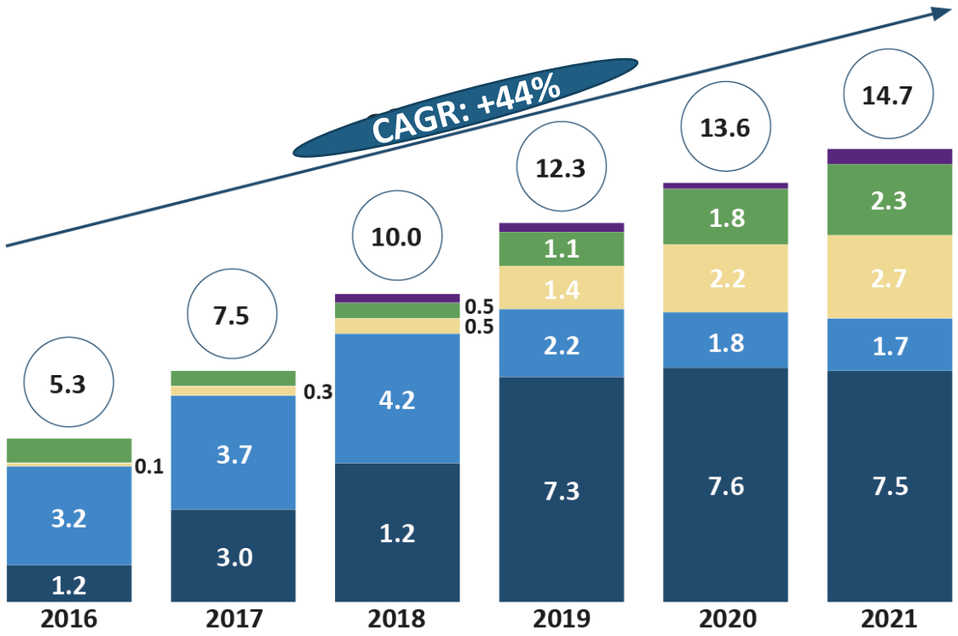
Agencies granted **Early Access/ Compassionate Access Authorisation** (France, Italy, Spain)

OBJECTIVES

- Early access and compassionate use in 3L NSCLC
- FDA/EMA optimal regulatory paths for the new confirmatory pivotal phase 3 trial and CDx for potential approval in 2L NSCLC after ICI-failure
- Additional Phase 2 clinical trials in combination (NSCLC, Pancreatic, Ovarian)

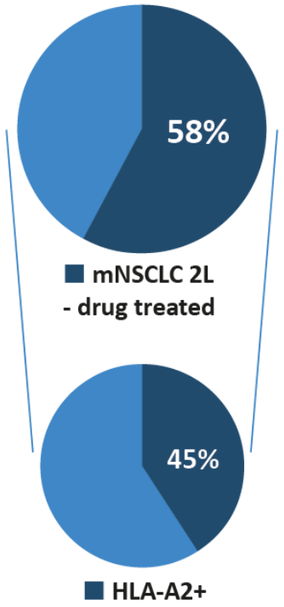
Target population estimated at **100k patients/year** in NSCLC post-ICI (2nd line)

PD-(L)1 NSCLC market is growing (US$bn)[1]



LIBTAYO® (cemiplimab-rwlc) Injection, 350 mg
IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL
TECENTRIQ® atezolizumab
OPDIVO® (nivolumab)
KEYTRUDA® (pembrolizumab) Injection 100 mg

Expending the potential in 2L post-ICI in G7 years



- Lung cancer is the leading cause of cancer mortality worldwide, accounting for about 1.8m deaths each year.[2]
- NSCLC is the most common type of lung cancer, accounting for 85% of all lung cancers.[3]
- ~60% of 1L patients progress within 18 months.
- HLA-A2 phenotype in about 45% of the population.
- Target NSCLC population: **~10%**

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1: EvaluatePharma - OSE Internal analysis based on publicly available data. **2:** World Health Organization. Globocan 2020 Fact Sheet. Available at: https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed November 2022. **3:** https://www.cancer.org/cancer/lung-cancer/about/what-is.html. Accessed November 2022

Tedopi® delivers important clinical benefits vs competition

Better Safety profile and QoL in current landscape of late-stage drug development post CT-IO

Company	OSE IMMUNO THERAPEUTICS	MIRATI THERAPEUTICS	Roche / IPSEN / EXELIXIS	MERCK / Eisai	gsk	BIONTECH / OncoC4	AstraZeneca / Daiichi-Sankyo	SANOFI	abbvie
Target	**Multi-epitopes vaccine**	**TKIs (anti-angiogenic)**			**Checkpoint Inhibitors**		**ADCs**		
					TIM-3	CTLA-4	TROP2	CEACAM5	c-MET
Current Study	**ATALANTE-1**	SAPPHIRE	CONTACT-01	LEAP-008	COSTAR Lung	PRESERVE-003	Tropion-LUNG1	CARMEN-LC03	NCT04928846
n	**219** **118 (secondary resistant)**	500	350	405	750	600	604	554	698
Therapy	**Tedopi® vs docetaxel**	Sitra + Opdivo vs. docetaxel	Cabo+Tecentriq vs. docetaxel	Lenvi + Keytruda vs. docetaxel	Cobolimab + Jemperli vs. docetaxel	Gostistobart vs. docetaxel	datopotamab deruxtecan vs docetaxel	SAR408701 vs. docetaxel	Telisotuzumab Vedotin vs. Docetaxel
Primary endpoints	**OS**	OS	OS	PFS and OS	OS	OS	PFS and OS	PFS and OS	PFS and OS
Initiation	**2017**	Q3 2019	Q3 2020	Q2 2019	Dec 2020	Q2 2023	Q4 2020	Q1 2020	Q1 2022
Read-out	**2022**	**Failed**	**Failed**	Delayed	2024+	2027+	**Failed OS** (interim analysis)	2024+	2025+
		Efficacy/safety data from early-stage trials in NSCLC post-ICI							
- Design	**Active comparator (vs. docetaxel)**	**No active comparator**							
- mOS (months)	**11.1 (8.6 Sq & 12.5 non-Sq)**	Phase II: 14.9 (non-Sq)	Phase II: 13.8 (non-Sq)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
- TEAEs G3/4	**11%**	**60%**	**39%**	**78%**	n.a.	**43%**	**25-30%**	**36%**	**36%**
Source	**Besse et al. 2023**	Leal, et al ESMO 2021	Neal et al, ASCO 2022	Taylor et al, J. Clin. Oncol. 38, 1154–1163.	Davar et al, SITC 2018	He et al, ASCO 2023	Lisberg et al, ESMO 2023	Gazzah et al, ASCO 2020	Camidge DR, et al. WCLC 2021

1 - OSE internal analysis based on publicly available information. **2** - World Health Organization. Globocan 2020 Fact Sheet. Available at: https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed December 2021. OSE Internal analysis based on publicly available data. Note: No direct head-to-head data available. Caution advised when comparing across studies

Further additional potential clinical value in combination in NSCLC, PDAC and OC

Phase 2 ISS trials in combination with immunotherapy or chemotherapy treatments

2nd line post 1st line chemo IO

Combi-TED - NSCLC
In combination with nivolumab

Tedopi® Plus Docetaxel or Tedopi Plus Nivolumab as 2nd line Therapy in Metastatic NSCLC failing standard 1st line Chemo-immunotherapy[1]

Sponsored by FoRT
PI: Federico CAPPUZZO
(Roma Cancer Institute)
Italy /Spain/ France

Readout expected 2025

Maintenance setting post standard of care

TEDOVA - Ovarian Cancer
In combination with pembrolizumab

Tedopi® Alone or in Combination With Pembrolizumab vs Best Supportive Care as Maintenance in Patients with Platinum-Sensitive Recurrent Ovarian Cancer[2]

Sponsored by ARCAGY GINECO
PI: Alexandra LEARY
(Gustave Roussy Institute)
France/ Germany/ Belgium

Readout expected in 2025

TEDOPaM - Pancreatic Cancer
In combination with FOLFIRI

Tedopi® plus FOLFIRI vs FOLFIRI as Maintenance Treatment in Controlled Advanced or Metastatic Pancreatic Ductal Adenocarcinoma after 8 Cycles of Folfirinox[3]

Sponsored by GERCOR PRODIGE
PI: Cindy NEUZILLET
(Curie Institute)
France

Recruitment completed Q2 2023

Readout expected in 2024

1 - NCT04884282 105 Patients planned
2 - NCT04713514 180 Patients
3 - NCT03806309 136 patients -recruitment completed

OSE-279: Proprietary PD-1 - Value generator

High affinity PD-1 antibody, recent patent granted in US, Europe, China, Japan*

Potential of combo with internal asset

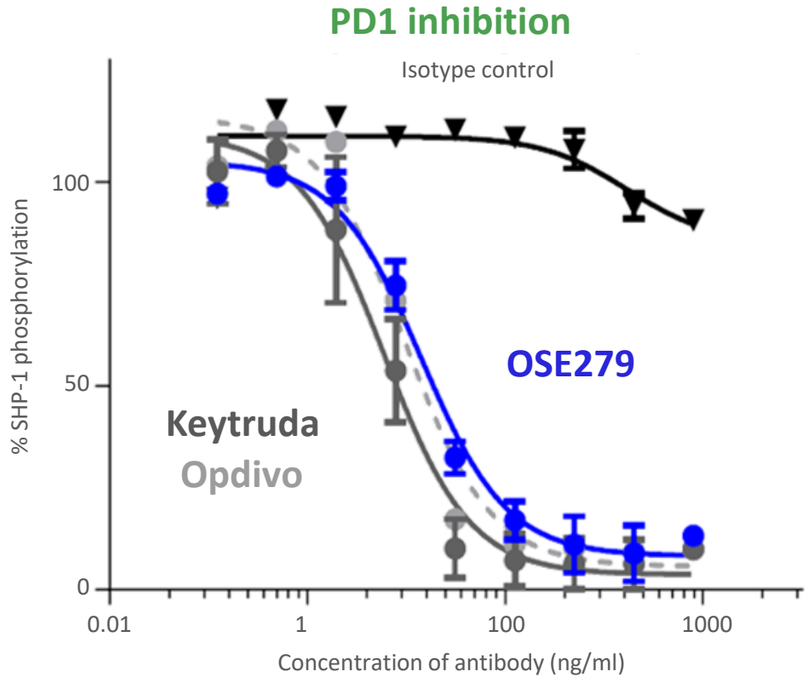
- **First positive clinical efficacy signals in solid tumors (Oct. 2023)**
- Evaluate OSE-279 in combination with in-house molecules to obtain proprietary treatment options

Backbone of the BiCKI® platform

- Develop first-in-class monovalent bispecific antibodies from our proprietary bispecific platform BiCKI® using OSE-279 as backbone therapy

Potential for partnership with biotech/biopharma in combo with external assets

Potential future development and approval in niche indications with strong unmet medical needs



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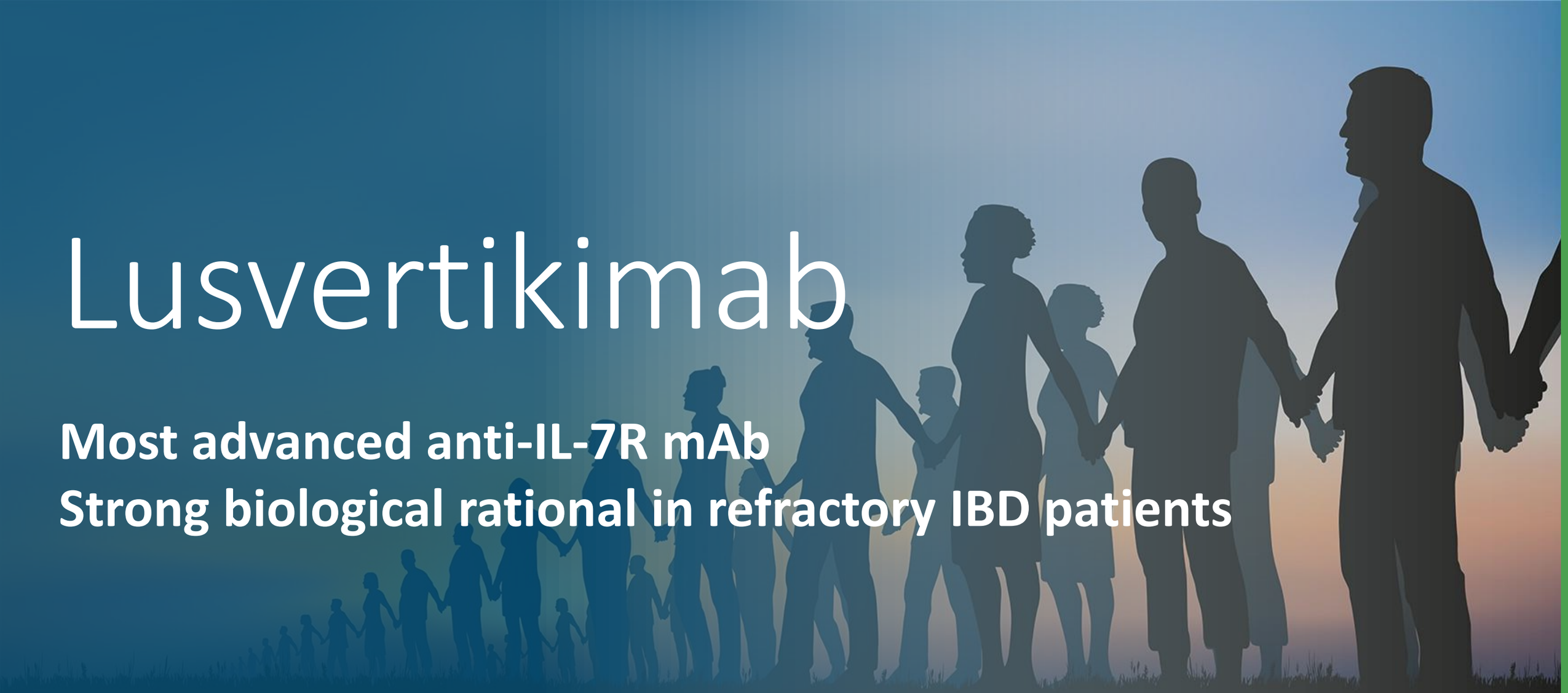
OSE Immunotherapeutics Receives First Notice of Allowance for a US Patent Covering Anti-PD1 Monoclonal Antibody OSE-279 And its Use in Cancer Treatment

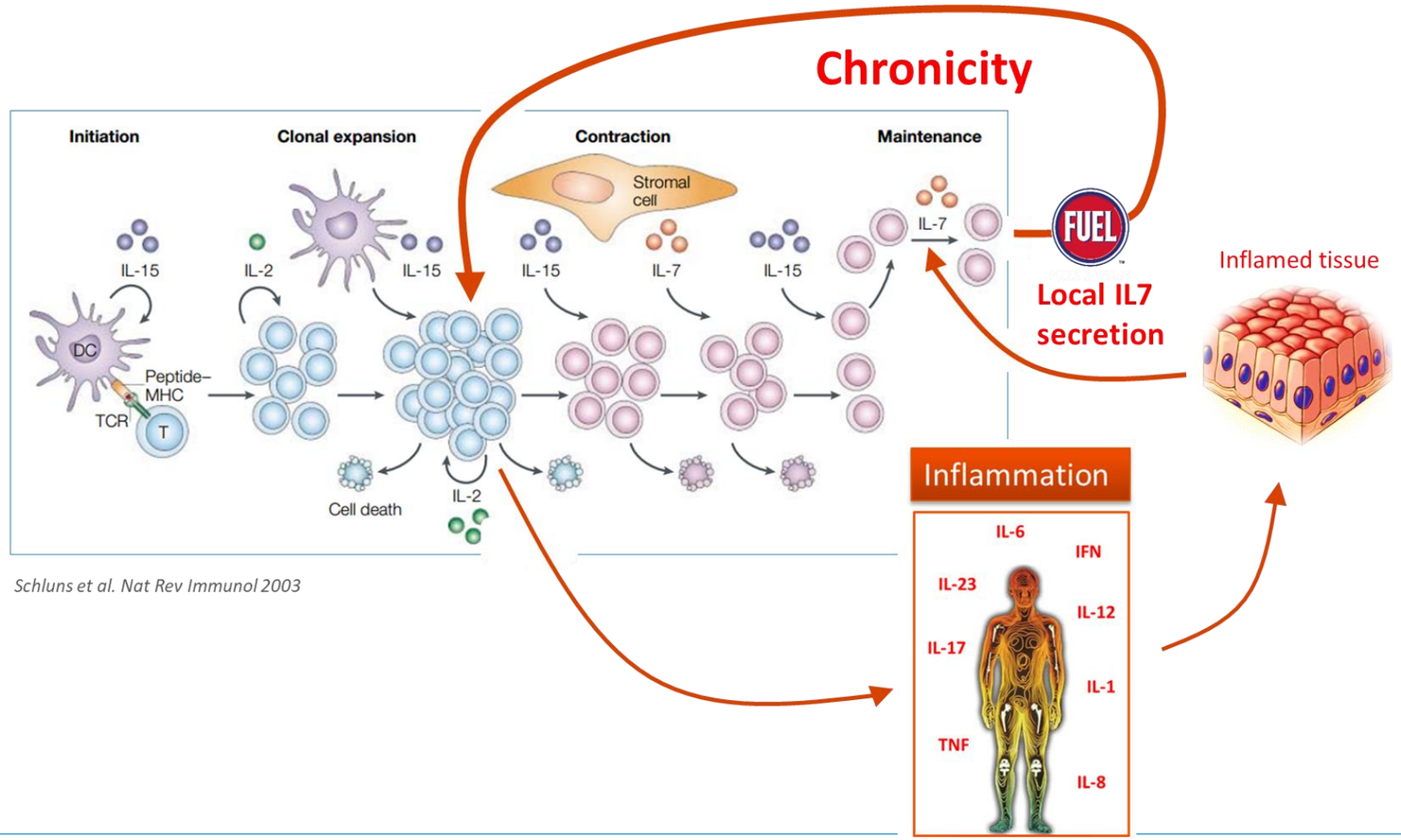
Lusvertikimab

Most advanced anti-IL-7R mAb
Strong biological rational in refractory IBD patients



IL-7 fuels chronic inflammation in tissues

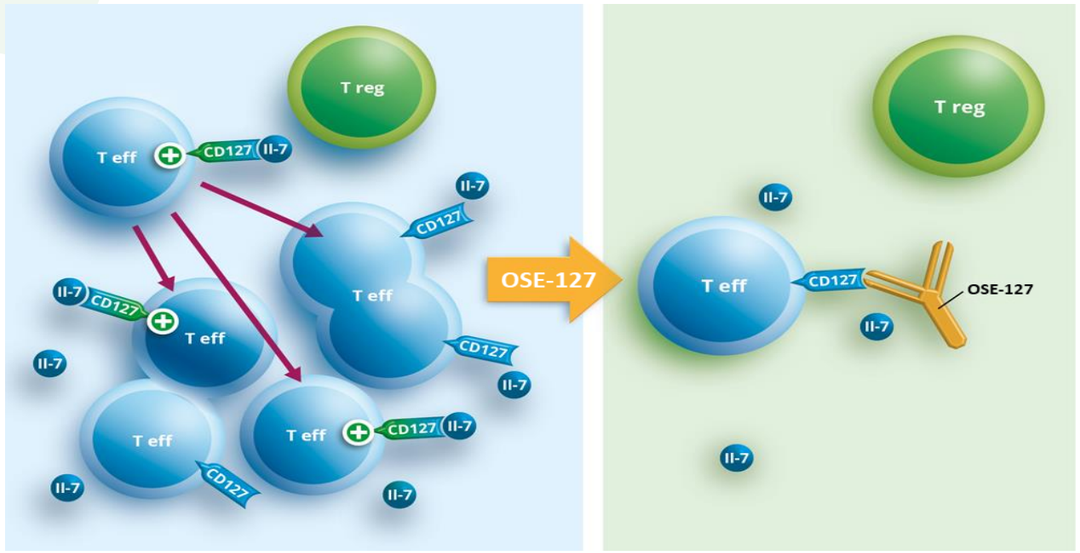
Lusvertikimab controls pathogenic memory T-cell persistence



Schluns et al. Nat Rev Immunol 2003

Lusvertikimab/OSE-127 - Differentiated MoA as full IL-7 receptor antagonist

Tackling the fuel of memory T-lymphocytes while sparing Tregs



A differentiated and highly qualified candidate

- Lusvertikimab, first non-internalizing (fully antagonist) anti-IL7R mAb[1] and **most advanced** IL-7R antagonist in clinic
- IL7 produced by inflamed tissues sustain **T-cell survival and chronicity**
- IL-7R pathway overexpression in anti-TNF IBD non-responders[2]
- Good safety, PK/PD profile in Phase 1[3], no cytokine release, confirmed target-engagement
- High preclinical activity in acute leukemia (T and B-ALL)[4] **ASH Merit Award**

- **On-going Phase 2 study in UC with clinical readout H1-2024**

1: Belarif et al. Nature Communication (2018). **2:** Belarif et al. JCI 2019. **3:** Poirier et al. In revision. **4:** https://www.ose-immuno.com/wp-content/uploads/2022/11/EN_221103_ASH_OSE-127.pdf

Lusvertikimab most advanced First-in-Class anti-IL7R mAb

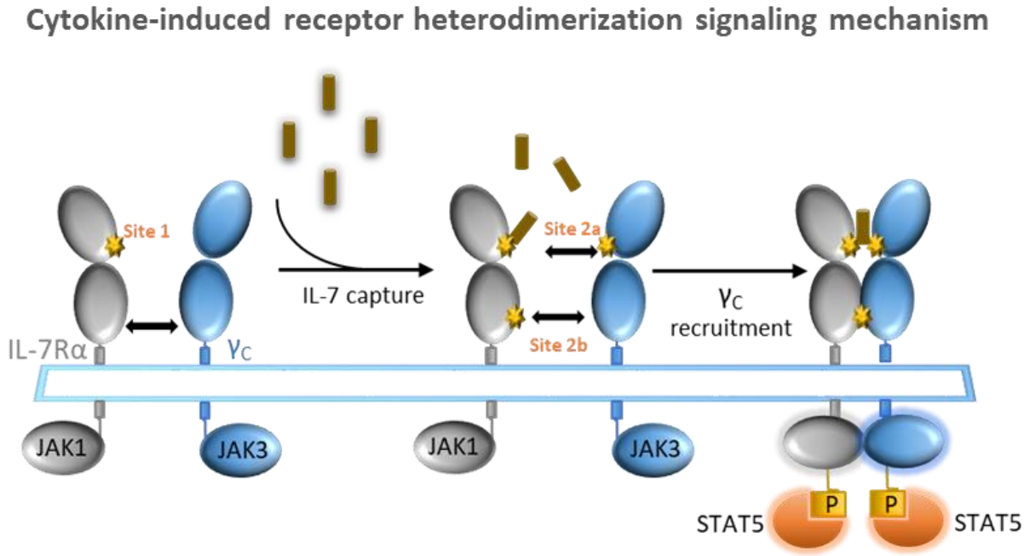
Differentiated by its Mechanism of Action

	OSE IMMUNO THERAPEUTICS	zurabio / Pfizer	Q32 BIO / HORIZON / Bristol Myers Squibb	gsk
Isotype	**IgG4**	**IgG1**	**IgG1**	**IgG1**
MoA	- **Non-Internalizing**[1] - **Full Antagonist IL-7R**	- Internalizing - Antago + Partial Agonist IL-7R - TSLP Antago - T-cell Depletion[2]	- Internalizing - TSLP Antago	- Internalizing - Antago + Partial agonist IL-7R
Phase	**2**	**1b**	**2a**	**1**
Indication	**Ulcerative Colitis (IBD)** ***(Results expected Q4 2023)***	Alopecia Areata *(not initiated)*	Atopic Dermatitis *(Initiated Q4 2022)* Alopecia Areata *(Initiated Q3 2023)*	Multiple Sclerosis *(Discontinued, High Immunogenicity[3,4])*

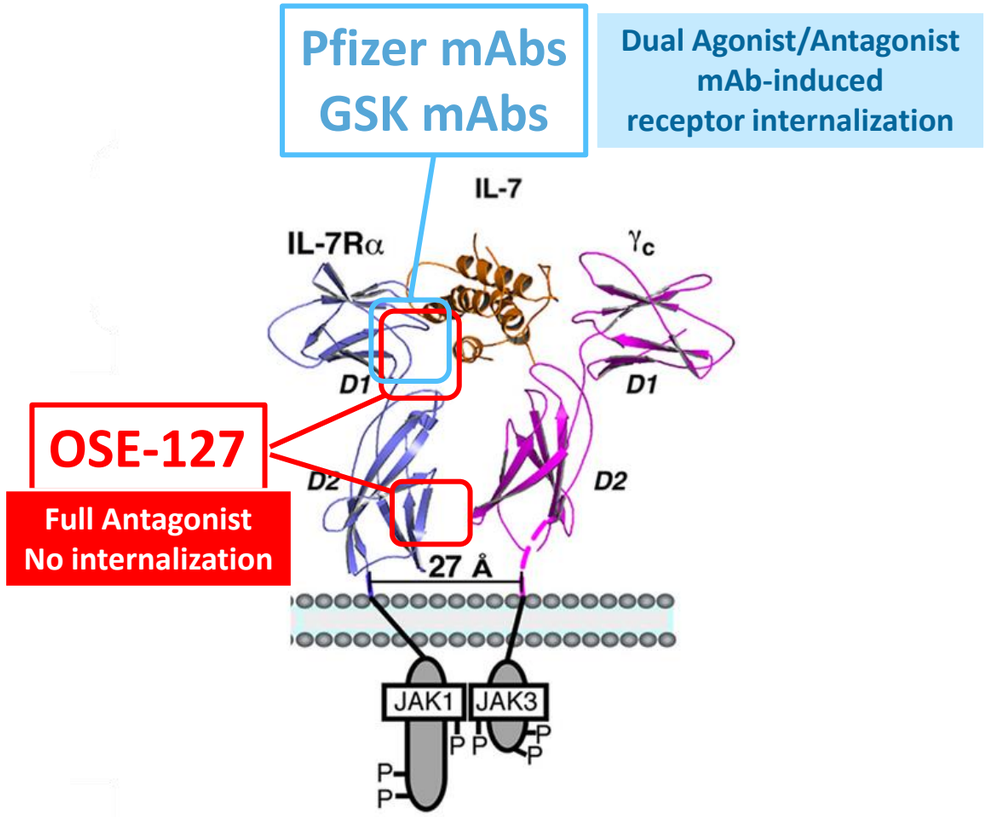
1. Belarif et al. Nature Com 2018; 2. Herold et al. JCI Insight 2019; 3. Ellis et al. Br J Clin Pharmacol 2019; 4. Liao et al. PlosOne 2021

Lusvertikimab – Targets a specific "site 1/2b" Epitope

Full antagonist, preventing receptor internalization & signaling



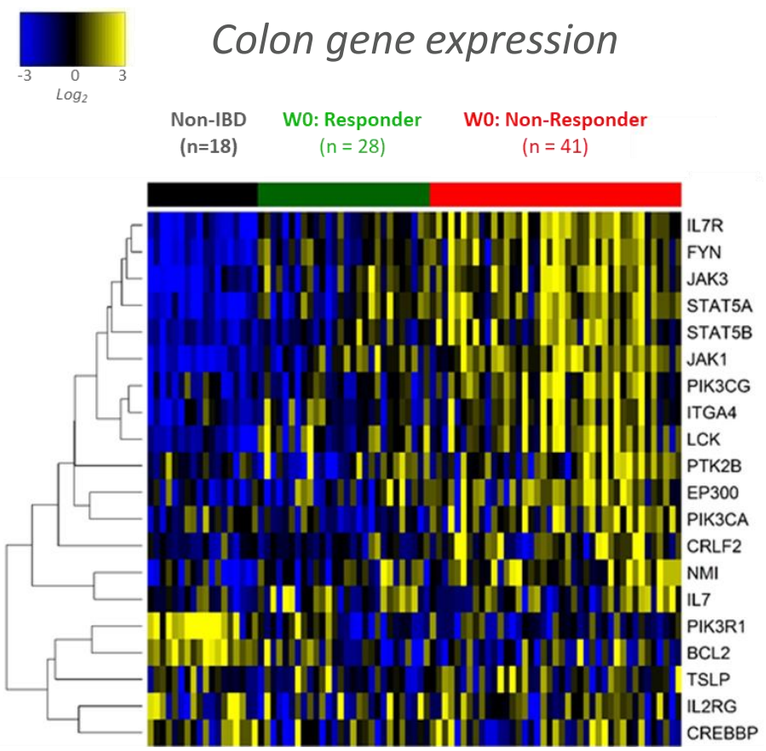
Walsh ST et al Immunol. Rev. 2012

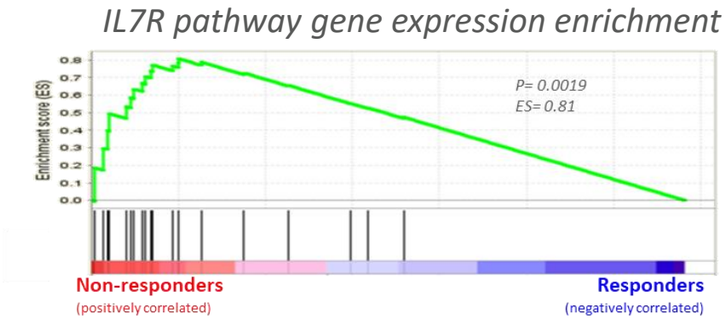


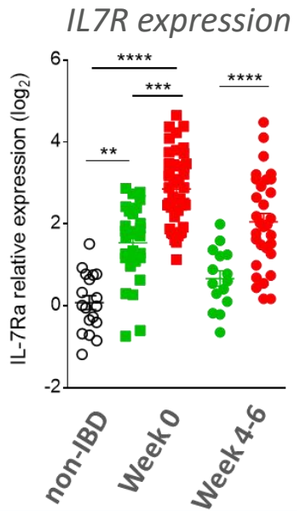
Belarif et al. Nature Com 2018

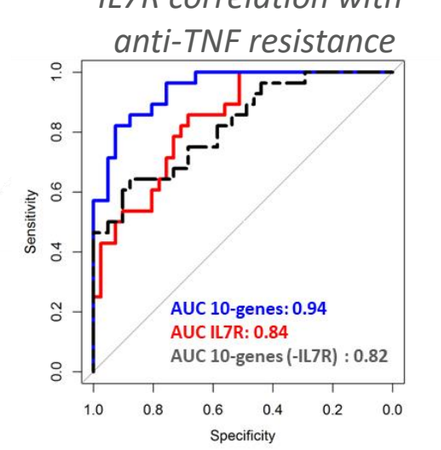
Mucosal IL-7R pathway over-expression in IBD tissues

High IL-7R expression in anti-TNF refractory patients









Anti-TNF Responder patients
Anti-TNF Refractory patients

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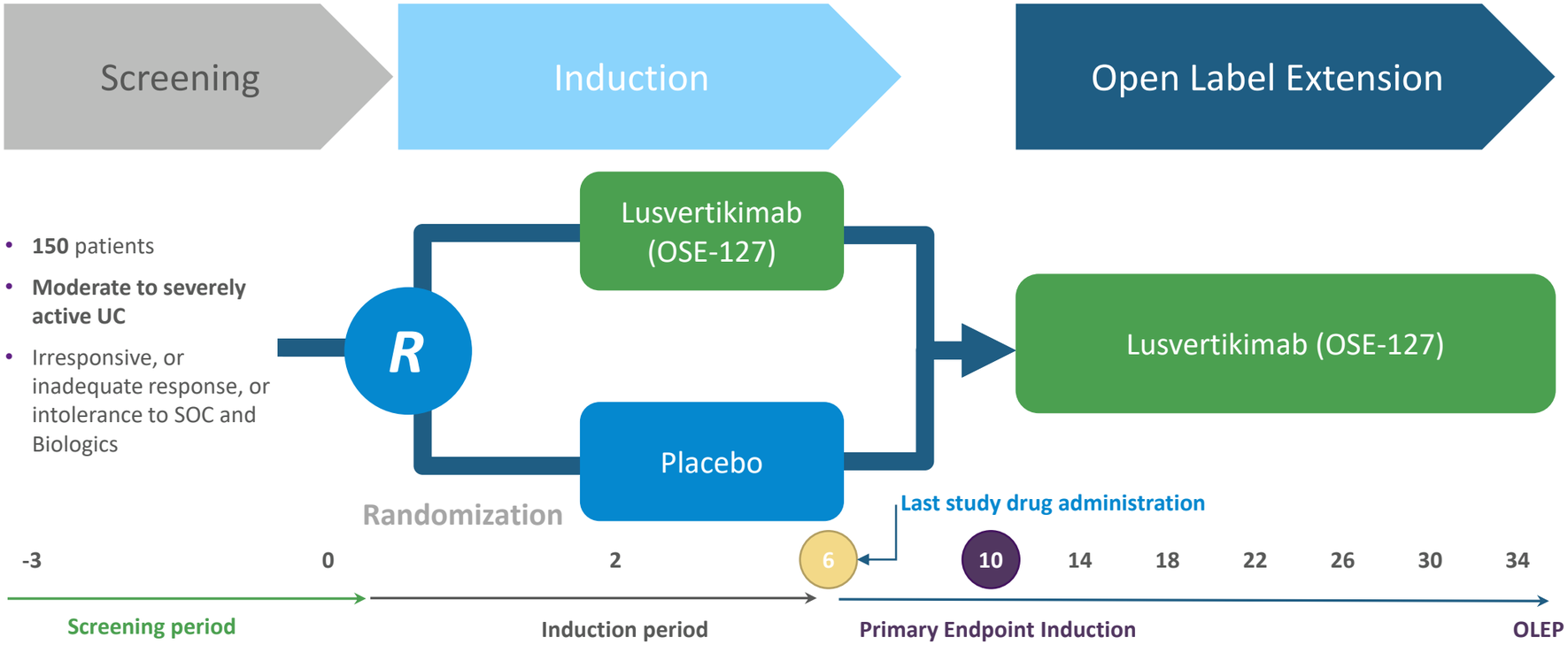
Belarif et al. JCI 2019

JCI The Journal of Clinical Investigation

Lusvertikimab in moderate-to-severe **ulcerative colitis**



- **150** patients
- **Moderate to severely active UC**
- Irresponsive, or inadequate response, or intolerance to SOC and Biologics

Positive Recent Futility Analysis[1]

- Futility analysis conducted on 33% of the total patient enrolment (n=150)
- Primary endpoint is the efficacy assessment of Lusvertikimab vs. placebo on the reduction of the modified Mayo Score at W10
- 24 weeks open-label extension study planned (NCT04605978)

End of enrollment expected in 2023

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- OSE Immunotherapeutics is Pleased to Announce the Continuation of its Phase 2 Trial Testing Anti-IL-7 Receptor Antagonist OSE-127/S95011 in Ulcerative Colitis after the Interim Futility Analysis

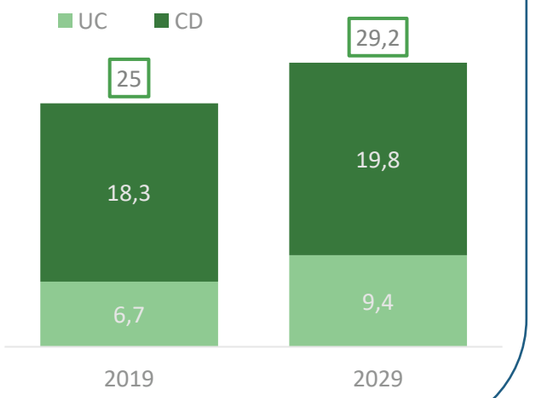
Secondary endpoints at Week 10 include:
1/ Clinical Remission by adapted Mayo score components: a stool frequency score of 0 or 1, a rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1.
2/ Clinical Response by adapted Mayo Score: reduction in adapted Mayo score ≥ 3 and ≥ 30%, with a reduction in the rectal bleeding subscore ≥ 1 or an absolute subscore ≤ 1
3/**Endoscopic Remission**: Mayo endoscopic subscore = 0; 4/**Endoscopic Healing**: Mayo endoscopic subscore ≤1

Significant opportunity in Ulcerative Colitis and Acute Lymphoblastic Leukemia targeted markets

Ulcerative Colitis (UC)

- UC affects 3.3 million patients in US, Europe and Japan
- ~50% UC patients "moderate to severe", requiring methotrexate, corticosteroids, anti-TNFa, JAK etc.
- Despite broad options, remission rates are of only 25-30% leaving most patients without satisfactory treatment

IBD Global market projections for G7 major markets (USDbn[1])



Acute Lymphoblastic Leukemia (ALL)

- ALL is a rare disease with a diagnosed incident cases in EU, US, China, Japan estimated to achieve 26,482 in 2029[2].
- 40% cases of ALL diagnosed are in adults and among them about 50% present refractory disease or undergo relapse under current conventional therapies[3].
- IL-7R expression in >84% of B-ALL and T-ALL samples[4]

ALL Global market projections for G7 major markets (USDbn[5])

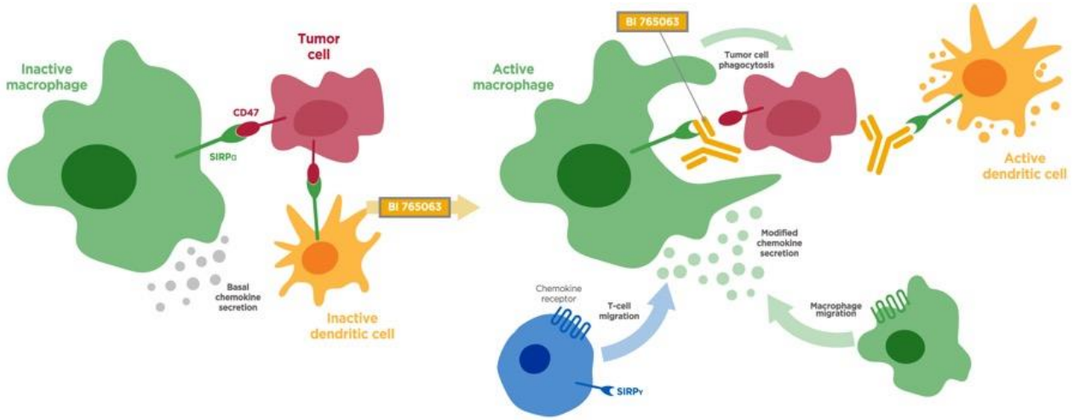
1: DRG UC Disease Landscape & Forecast 2021 **2:** Global Data **3:** Childhood Acute Lymphoblastic Leukemia Treatment (PDQ®)–Health Professional Version, accessed October 2022
4: OSE internal data released at ASH2022 **5:** Researchandmarkets.com/reports/4857889

Partnered clinical programs

SIRPα inhibition may have a synergistic antitumour effect when combined with ICIs

- Infiltrating **myeloid cells promotes immune evasion**, and this has generated interest in **myeloid-immune targets**[1,2]
  - The CD47–SIRPα interaction transduces inhibitory signals on macrophages and other myeloid cells[2]
- Preclinical studies have indicated that **CD47 or SIRPα blockade in combination with ICIs** may have a synergistic antitumour effect[3]

The use of SIRPα antagonists to enhance antitumour immunity is currently being explored[4]



	Anti-CD47	Anti-SIRPα	
Broad/restricted expression	Broad	Restricted to cells of the myeloid lineage	Limited **side effects** expected and less frequent dosing
Safety signals	Acute anemia, Thrombocytopenia	**No hematotoxicity**	Higher therapeutic window expected
Interaction CD47/SIRPγ	**Inhibit human T cells**	OSE-172 is SIRPα specific	Favors T cell responses in solid tumors

CD: cluster of differentiation; ICI: immune checkpoint inhibitor; SIRPα: signal regulatory protein-α.

1: Khair DO, et al. Front Immunocol 2019;10:453; **2:** Weiskopf K, et al. Eur J Cancer 2017;76:100-9; **3:** Murata Y, et al. Cancer Sci 2018;109(8):2349-57; **4:** Boehringer Ingelheim. Data on file.

Clinical development overview

Most advanced clinically-tested SIRPα

	Dose Escalation & Expansion studies		ONGOING Studies	
Trial number	**NCT03990233**	**NCT04653142**	**NCT05249426**	**NCT05327946**
Phase	Ia + Ib	Ib	Ib	Ia
N	108	36	150	42
Treatment	**BI 765063** +/- Ezabenlimab	**BI 765063** +/- Ezabenlimab	**BI 765063** + Ezabenlimab ± chemotherapy, cetuximab or VEGF/Ang2 inhibitor	**BI 770371** +/- Ezabenlimab
Patient population	Solid tumors	Solid tumors	HNSCC HCC	Solid tumors
Region				

Key takeaways from dose escalation

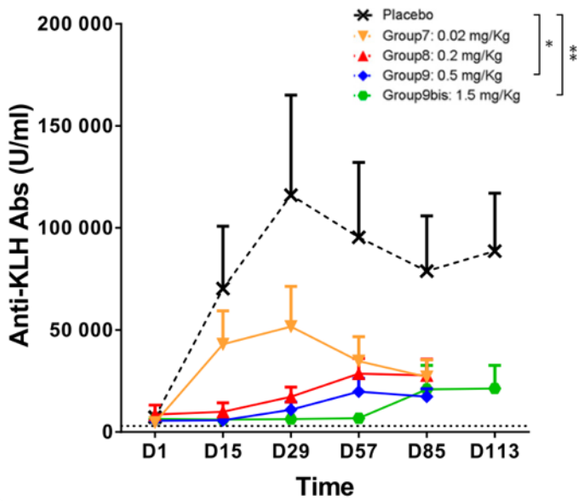
- **Safety**
  No hematotoxicity reported, no DLTs, MTD not reached[1,2]
- **Efficacy BI765063**
  - **1 PR** in HCC, **45% clinical benefit rate as a single agent**[1]
  - **3 PRs** in MSS endometrial cancer and CRC in combination with a checkpoint inhibitor[2]

MSS: Microsatellite stable. **HNSCC:** Head and Neck Squamous Cell Carcinoma. **CRC:** Colorectal Cancer. **1:** Champiat S, et al. J Clin Oncol 2021;39(Suppl15) #2623. **2:** Kotecki N. et al. ESMO 2021; #983. **3:** Boehringer Ingelheim and OSE Immunotherapeutics Announce First Patient Dosed in a Phase 1 Expansion Trial of SIRPα Antagonist Monoclonal Antibody BI 765063, Targeting Myeloid Cells in Immuno-Oncology Initiation of the Phase 1 clinical expansion trial triggers a €10 million milestone payment from Boehringer Ingelheim to OSE Immunotherapeutics

FR104/VEL-101
CD28 antagonist in transplantation

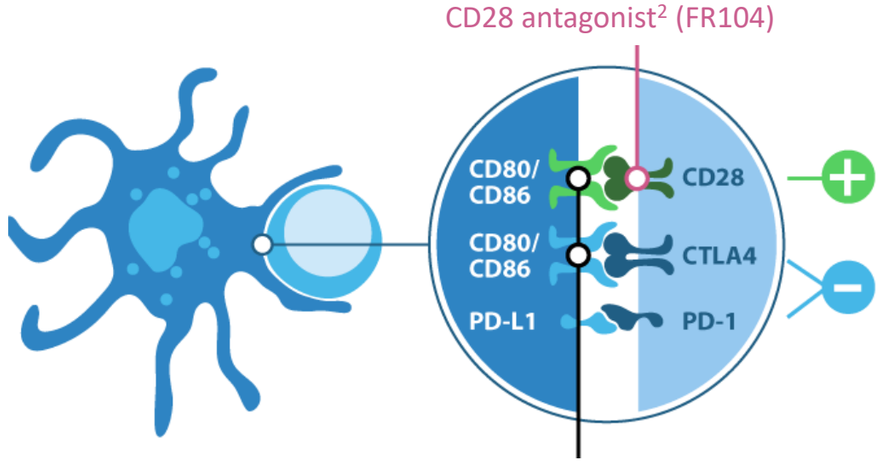
Veloxis PHARMACEUTICALS
an Asahi Kasei company

Phase 1 results: Selective CD28 antagonist FR104 persistently reduces antibody responses



- **Good safety**[1] - demonstrated
  - Absence of clinical or biological events
  - No change in total lymphocyte counts
- No cytokine elevation
- Controls model IgG (anti-KLH) response for up to 57 days
- Controls T follicular helper and IgG responses
- Tfh cells correlated with autoimmune diseases activity

Ongoing Phase 1/2 trial in kidney transplantation



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1: Poirier N. et al, Journal of Immunol, (2016), doi: 10.4049/jimmunol.1601538. **2:** Watkins, BK et al. J Clin Invest. 2018

FR104/VEL-101 – Transforming kidney transplant management

Ambitious Partnership with Veloxis

- Deal value: EUR 315m[1] and tiered royalties on sales
  - **Veloxis** is a global leader in transplantation with leading product Envarsus XR (tacrolimus) realizing **c. USD 140m[2]** turnover
  - Joined **Asahi Kasei** in FY2019[3], a **USD 17bn** annual turnover conglomerate with healthcare representing 17% of sales
  - First patient dosed by Veloxis[4]
- **Phase 1 / 2 in kidney transplantation**, sponsored and conducted by the Nantes University Hospital, patient enrolment completed

Kidney Transplant Market Opportunity

- **40k+** new kidney transplant annually for an estimated **500k+** people living with a functioning kidney graft in G7 countries
- Chronic exposure to **CNIs** is associated with **renal toxicity**, cardio-metabolic complications, **insufficient** graft protection as well as **cancer** and **infections**
- FR104 seeks to address challenges associated with current immunosuppressive transplantation regimens using CNI-based therapies
- Potential to provide “One Transplant for Life” with improved patient and graft survival and become the new SoC in transplant

1 – OSE Immunotherapeutics and Veloxis Pharmaceuticals Enter Into Global License Agreement to Develop, Manufacture, and Commercialize FR104, a CD28 Antagonist, in the Organ Transplantation Market
2 – https://www.asahi-kasei.com/ir/library/presentation/pdf/211005.pdf
3 – https://www.asahikasei.com/ir/library/presentation/pdf/191125eng.pdf
4 - OSE Immunotherapeutics Announces Dosing of the First Participant in a Phase 1 Study of VEL-101/FR104, a Novel Investigational Drug for Kidney Transplant Immunosuppression

Our Innovative Discovery Engines

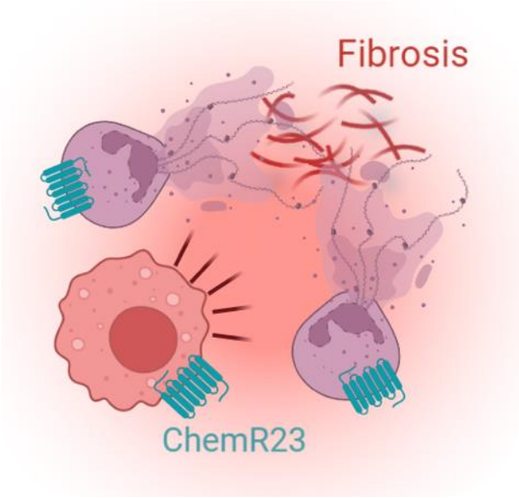
Designed to deliver next generation first-in-class immunotherapies

OSE-230 - Resolving inflammation is an active immune process

Pro-resolutive mAb

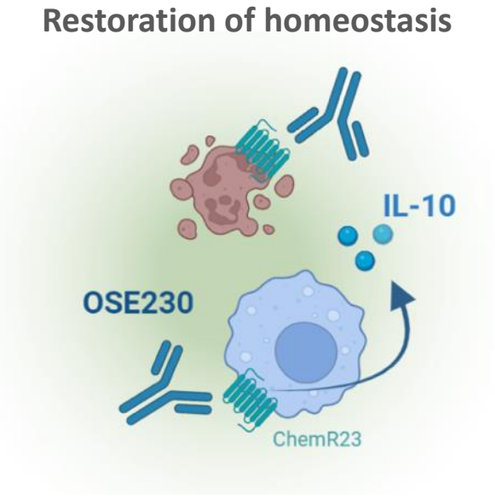
During chronic inflammation

Dying neutrophils **send out inflammatory signals (e.g. NETosis)** that are important in maintaining chronic inflammation & fibrosis



With ChemR23 agonistic mAbs

OSE-230 limits recruitment, survival & NETosis of inflammatory neutrophils & reprograms macrophages, **removing further chronic inflammatory signals**



First-in-class pre-IND candidate

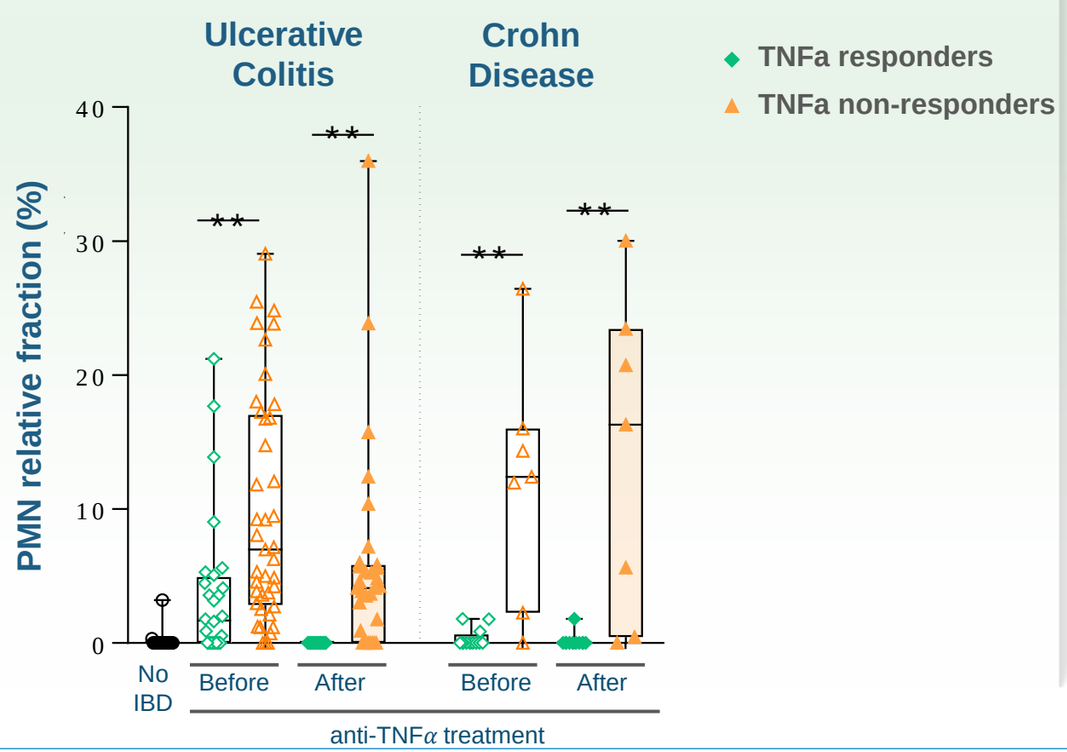
Published in Science Advances AAAS

OSE IMMUNO THERAPEUTICS

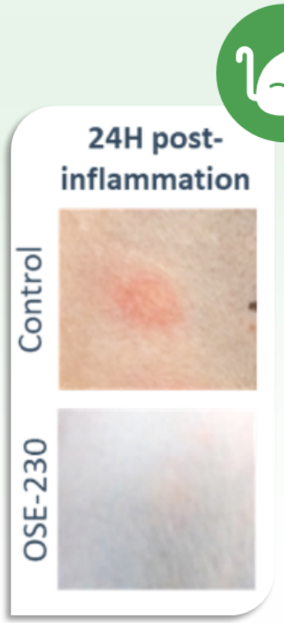
Trilleaud et al; Science advances 2021

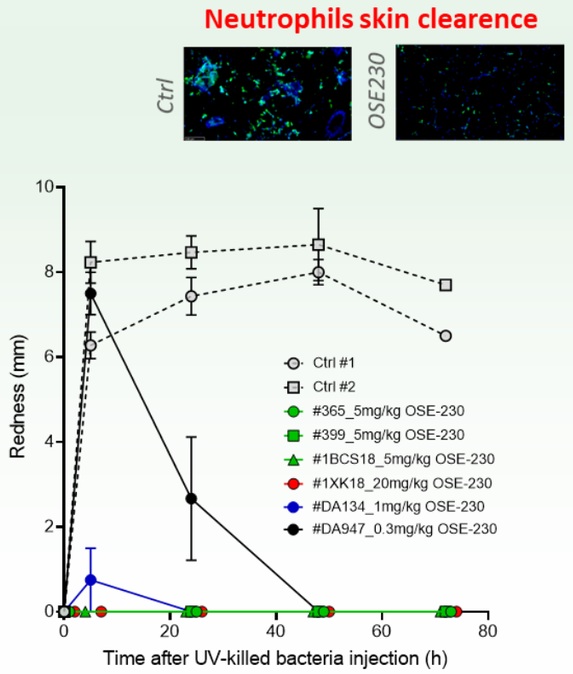
OSE-230 – Preclinical data demonstrate strong effect on neutrophils and leucocytes

Higher ChemR23 expression in anti-TNFα refractory patients



OSE-230 significantly reduces skin erythema & Neutrophils infiltrates in cynomolgus monkeys





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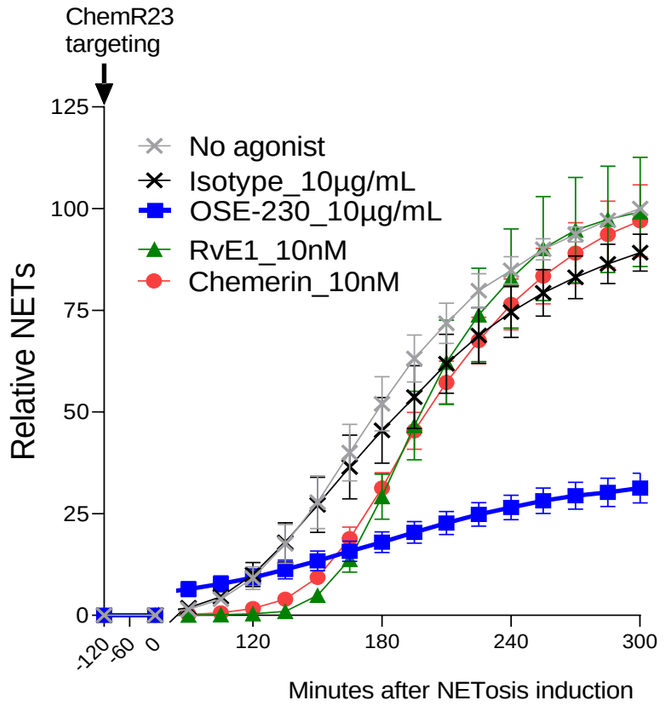
Trilleaud et al. Science Advances 2021

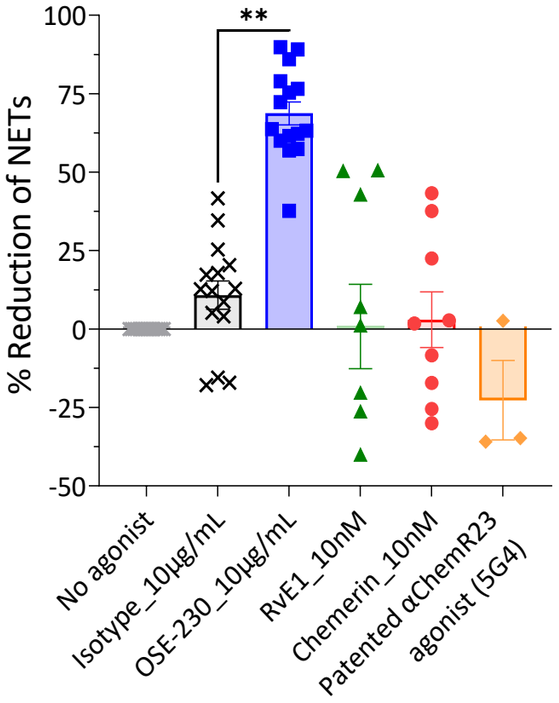
Science Advances AAAS

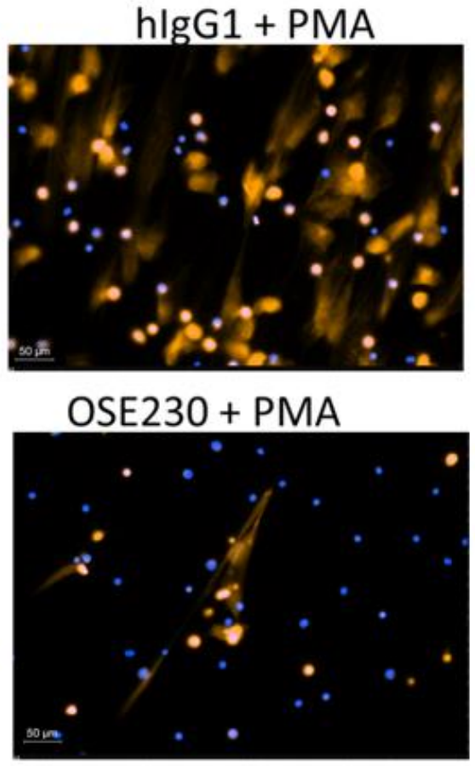
OSE-230 significantly inhibits human neutrophils NETosis

NETosis time-course



NETosis inhibition

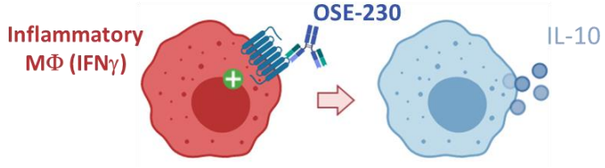


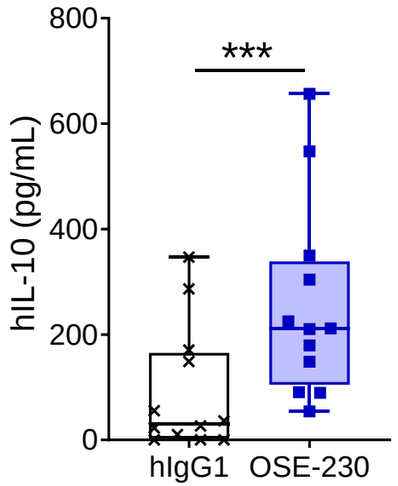


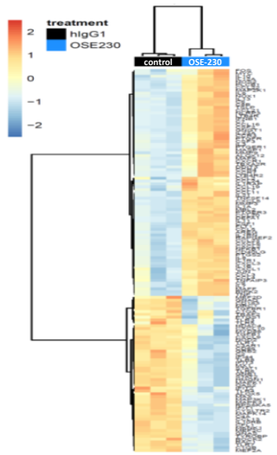
OSE-230 promotes pro-resolutive human Macrophages reprograming

Deep macrophage transcriptomic reprograming, Increases IL-10 secretion

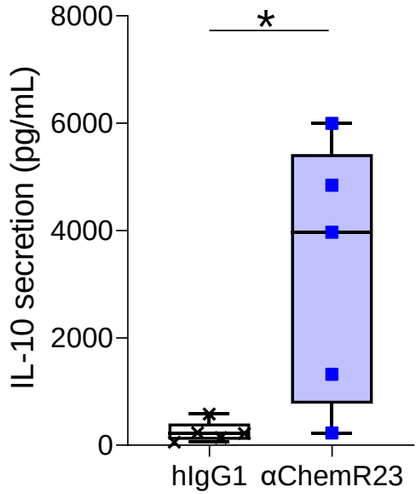
Inflammatory Macrophages

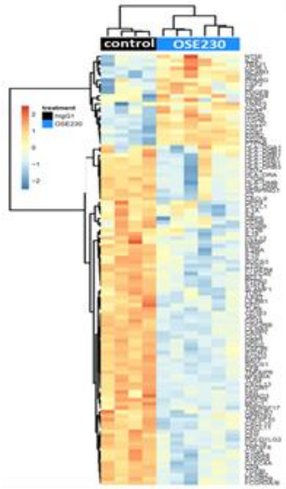


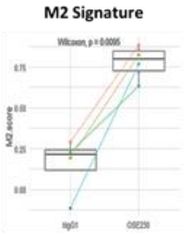


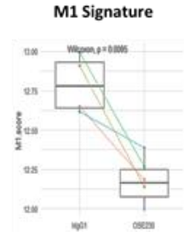


Pro-resolutive Macrophages









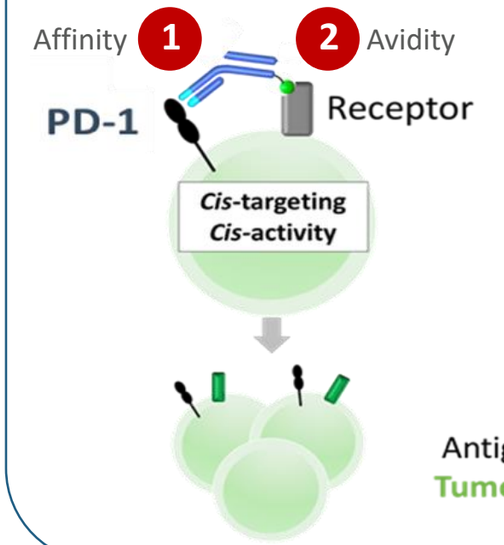
Next-generation anti-PD1 bispecifics

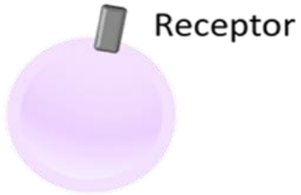
Improving the quality of tumor-specific T-cell responses both in TME & Lymph Nodes

Anti-PD1 bispecifics

Targeting the RIGHT T-cells…

Selective targeting of Tumor-specific PD1+ T cells





Non experienced
NaîveT cells

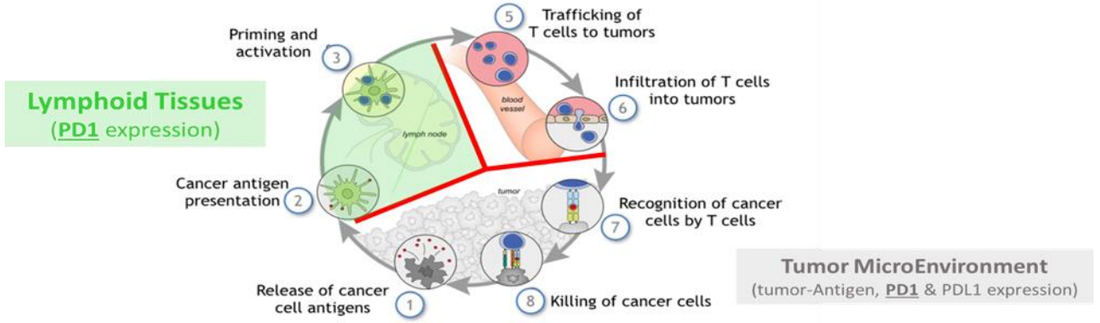
Antigen experienced
Tumor specific T cells

↗ Survival, Migration

↘ Exhaustion, Immunosuppression

…at the right place

Selective Biodistribution in TME + Lymphoid tissues



BiCKI®-IL7v* candidate highlighted at AACR 2022*

OSE IMMUNO THERAPEUTICS

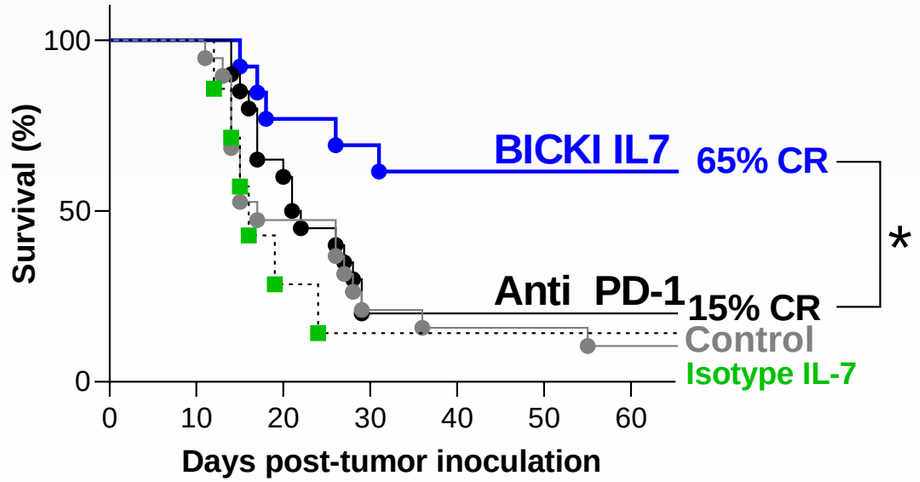
OSE Immunotherapeutics Invited to Present Preclinical Data on its PD-1/IL-7 Bifunctional Program BiCKI®-IL-7 Cancer Immunotherapy (AACR 2022, Morello et al)

BiCKI® OSE-279/IL-7 demonstrates high preclinical efficacy

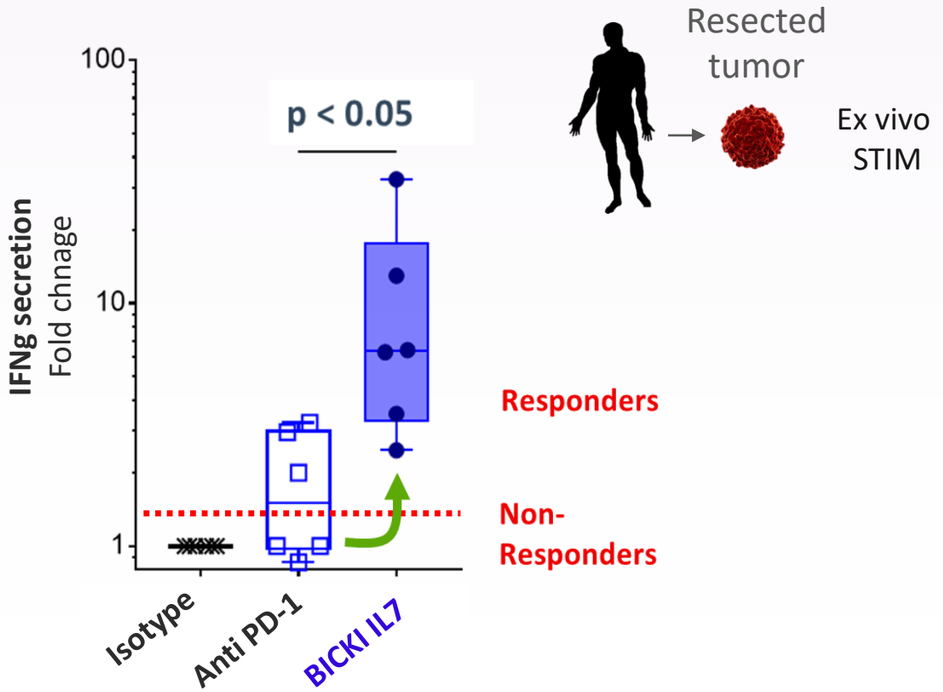
Superior efficacy in PD-1 resistant models

In vivo preclinical efficacy in PD1 resistant mouse model

HCC orthotopic model
hPD1 humanized mice



Ex vivo reactivation of anti-PD1 resistant human TILs



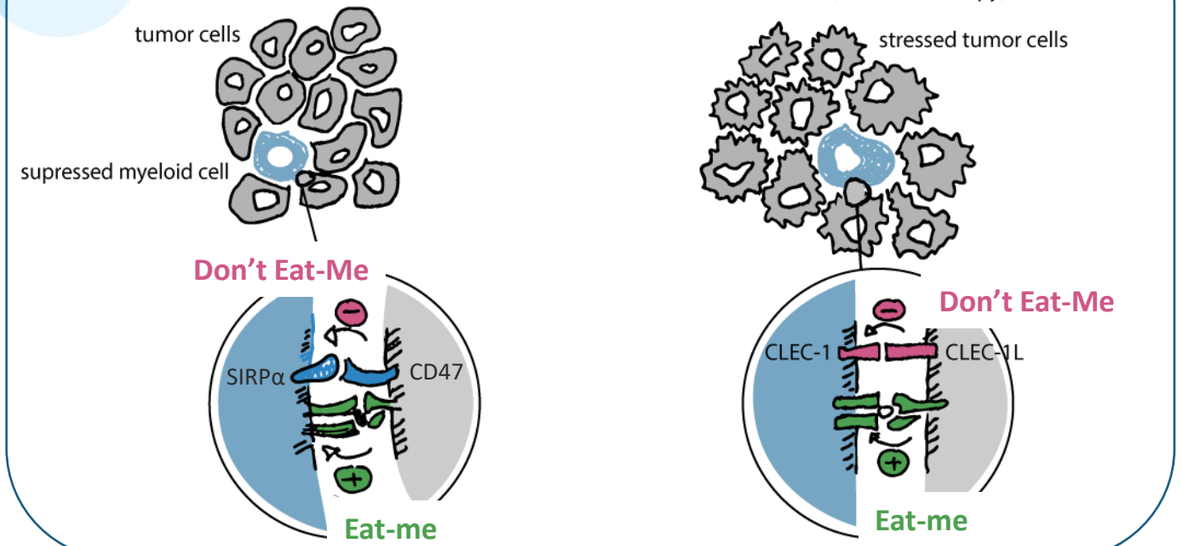
Poster #910 SITC 2020 – *"A novel bifunctional anti-PD-1 / IL-7 fusion protein potentiates effector function of exhausted T cell and disarms Treg suppressive activity"*

CLEC-1 - Another way to not get eaten

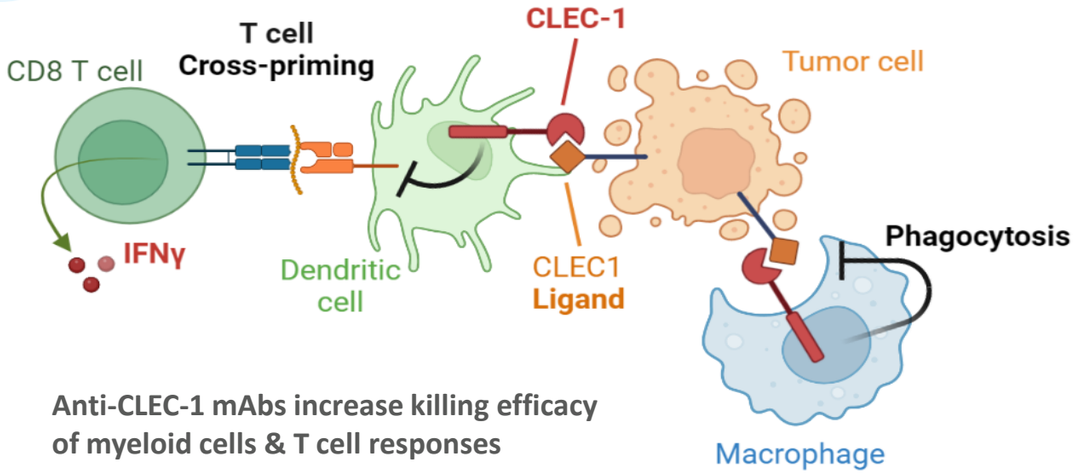
Blocking myeloid immune checkpoint from delivering another “Don’t-eat-me” signal

Myeloid checkpoint

Tumor homeostasis



CLEC-1 mAbs disrupt tumor homeostasis[2]



Anti-CLEC-1 mAbs increase killing efficacy of myeloid cells & T cell responses

First-in-class preclinical LEAD validation[1]

Published in Science Advances AAAS

OSE IMMUNOTHERAPEUTICS

Drouin et al, Science Advance 2022
1: A new protection covering CLEC-1 antagonists until 2037
2: OSE Immunotherapeutics Presented the First Positive Preclinical Efficacy Data on CLEC-1, a Novel Myeloid Immune Checkpoint Target For Cancer Immunotherapy

The OSE team

An experienced executive leadership committee supported by an expert team

Nicolas Poirier, PhD
CEO, CSO

- 18+ years experience in biotech/immunotherapy
- Advanced 5 novel immunotherapies to clinic
- Leading to 4 pharma deals
- Global Management & Finance (INSEAD, HEC)

Anne-Laure Autret-Cornet
Chief Financial Officer

- 15+ years experience in Finance / Biotech
- Graduated from ESSCA Management school
- Corporate Finance, HEC

Dominique Costantini, MD
Chief Development & Strategy

- 30+ years in product development/ marketing
- Chairwoman, Co-founder
- IPO completion in 2015

Jean-Pascal Conduzorgues
Chief Pharmaceutical Officer & QP

- 30+ years in pharmaceutical development
- Large experience as a qualified person (QP)
- PharmD

Aurore Morello, PhD
Head of Research

- 13+ years experience in Immunotherapy
- International Post-doctoral Fellowship (MSKCC, NYC)

Silvia Comis, MD
Head of Clinical

- 30+ years experience in Pharma
- Previously Senior Medical Director IQVIA, and European Head of Early Products Medical Affairs in oncology at Novartis

Jean-Jacques Mention, PhD
Chief Business Officer

- 15+ years of Research in Immunology at King's College London, Institut Pasteur
- 7+ years experience in Business Development

Valérie Gabarre, PharmD
Medico-Marketing Director

- 25+ years of experience in Pharma/Biotech, in Medico-Marketing & Sales - EU & Global, Immunotherapy & Oncology
- Global Network of Leaders & Corporative Groups in Onco
- PharmD

A Board of Directors combining international expertise in drug development, industry & finance & experience in listed biotech companies

Dominique Costantini, MD
Chairwoman, Chief Development & Strategy
- 30+ years in product development/ marketing
- Chairwoman, Co-founder
- IPO completion in 2015

Maryvonne Hiance
Vice Chairwoman
- Founder and CEO of Effimune
- General Manager SangStat Atlantic, DrugAbuse Sciences
- Former President & Vice President of France Biotech

Nicolas Poirier, PhD
Director, CEO & CSO
- 15+ years experience in biotech/immunotherapy
- Advanced 5 novel therapies to clinic
- 4 pharma deals
- Global Management, INSEAD

Elsy Boglioli
Ind. Director
- Founder & CEO of Bio-Up
- Healthcare advisor
- 10+ years Partner & Managing Director at the Boston Consulting Group (BCG)

Eric Leire, MD
Ind. Director
- Genflow Bioscience CEO
- Previously chairman & CEO of several biotech listed in US
- Previous Marketing Director position in Pharma US & EU

Brigitte Dréno, MD
Ind. Director
- Head Depart of Dermatology Nantes
- Director of Biotherapy Clinical Investigation Centre
- Operational functions and research responsibilities

Didier Hoch, MD
Ind. Director
- 25+ years in pharma and vaccine industry
- Several functions incl. commercial, marketing, general management

Alexandre Lebeaut, MD
Ind. Director
- 25+ years experience and leadership in innovation, research and devpt in immunology, oncology, immuno-inflammation
- Global positions in the US (Sanofi, Novartis, IPSEN Schering Plough)

Gérard Tobelem, MD
Ind. Director
- Former Pr. Hematology
- Strategic functions within the French Ministry of Higher Education and Research
- Advised international pharma in R&D strategies.

Anne-Laure Autret-Cornet**
CFO, employee shareholder representative
- 15+ years in Finance & Biotech
- ESSCA Management school
- Finance Corporate, HEC

Nomination and Remuneration Committee: M. Hiance, E. Boglioli, G. Tobelem
Audit Committee: D. Hoch, E. Leire

International SAB - **Renowned experts in IO and I&I**

Wolf-Hervé Fridman, MD
Chairman of the SAB, Professor Emeritus of Immunology at the Université de Paris, France

Myriam Merad, MD, PhD
Director of the Precision Immunology Institute at Mount Sinai School of Medicine in New York and the Director of the Mount Sinai Human Immune Monitoring Center (HIMC)

Charles N. Serhan, PhD, DSc
Professor of Anaesthesia (Biochemistry and Molecular Pharmacology) at Harvard Medical School, Professor of Oral medicine, Infection and Immunity at Harvard School of Dental Medicine

Jennifer Wargo, MD, M.M.Sc
Professor of Genomic Medicine & Surgical Oncology, UT MD Anderson Cancer Center

Bernard Malissen, PhD
Group Leader at Centre D'Immunologie de Marseille-Luminy and Founduing-Director of Center for Immunphenomics, Marseille, France

Sophie Brouard, PhD
Immunologist and Director in Vetinary Sciences, Director of Research at the Institut National de la Santé et Recherche Médicale (inserm, National Institute for Health and Medical Research) in Nantes

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Head Office
22, boulevard Bénoni Goullin
44200 Nantes, France

Paris Office
10, Place de Catalogne
75014 Paris, France

Company Information: http://ose-immuno.com/en/