OSE IMMUNO THERAPEUTICS

Breaking through the therapeutic ceiling with first-in-class immunotherapies

May 2023

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Our Vision

Breaking through the therapeutic ceiling

with First-in-Class immunotherapies

OSE Immunotherapeutics' **strategic foundations**

Fully integrated biotech company

- Mastering complex biology & pharmaceutical/clinical development
- 60+ qualified employees (30+ PhDs/MDs)

Diversified First-in-Class product pipeline

From Phase 1 to Phase 3, multiple indications

Innovative Research Engine

Next-Generation Immunotherapies
Multi-Platform technologies

>450 patents granted

Specific T-cell

Myeloid cells

Collaborations with strategic leaders

Building a sustainable business with strategic, industry & academic partners

Boehringer Ingelheim

Veloxis PHARMACEUTICALS an Asahi Kasei company

Microsoft

Memorial Sloan Kettering Cancer Center

HARVARD UNIVERSITY

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
Clinical	Proprietary	**Tedopi®**	Neoepitopes Vaccine (OSE IMMUNO THERAPEUTICS)	NSCLC Mono post-ICI					
				NSCLC Combo 2L post-ICI *(IIS)*					
				PDAC Combo maintenance *(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	**FR-104/VEL-101**	Anti-CD28 (Veloxis)	Kidney Transplant					
		OSE-172/BI 765063	Anti-SIRPα (Boehringer Ingelheim)	HNSCC 2L and HCC 1L/2L					
				MSS Endometrial / MSS CRC					
R&D Engine Platform	Proprietary	**OSE-230** & Future undisclosed targets (field resolution)	ChemR23 agonist mAb	Inflammation diseases					
		BiCKI® IL-7v & Next undisclosed BiCKI ®	PD1 x IL-7 bsAb	Immuno-Oncology					
		Myeloid Checkpoint & Future undisclosed targets (field CLEC)	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

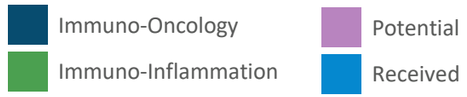
FR-104/VEL-101
Kidney transplant

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 and option of license with J&J and Servier

Our plan to build a leading immunotherapy company

OSE IMMUNO THERAPEUTICS

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

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

Confirm FR-104/VEL-101 benefit as maintenance therapy in kidney transplantation

Advance proprietary early-stage assets from our research platforms
3 pre-IND programs to enter the clinic in 2023-25

Multiple short-term anticipated catalysts

2023

Readouts
- **TEDOPI®**
  Regulatory update (Europe, US)
- **Lusvertikimab/OSE-127**
  Phase 2 trial in UC
- **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
- **OSE-230**
  IND

2024

Readouts
- **TEDOPI®**
  Phases 2 combination update
- **OSE-172/BI 765063 (partnered)**
  Phase 1/2 update
- **OSE-279**
  Phase 1/2 update
- **FR104/VEL-101 (partnered)**
  Phase 1/2 in Kidney Transplantation

Progress
- **Lusvertikimab/OSE-127**
  Phase 3 start
  Phase 1/2 T-ALL under exploration
- **OSE-172/BI 765063 (partnered)**
  Phase 2 start
- **OSE-230**
  Phase 1 start
- **BiCKI-IL7v**
  IND

2025-2026

Readouts
- **TEDOPI®**
  Phase 3 trial in NSCLC 2L
- **Lusvertikimab/OSE-127**
  Phase 1/2 acute Leukemia update
- **OSE-172/BI 765063 (partnered)**
  Phase 2 update
- **FR104/VEL-101(partnered)**
  Phase 2 in Kidney Transplantation
- **OSE-230**
  Phase 1
- **BiCKI-IL7v**
  Phase 1/2 update

Progress
- **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-partnerships Strategy
>€1.4bn milestones: Boehringer Ingelheim, Veloxis

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®:** FDA/EMA regulatory update, preparing confirmatory pivotal phase 3 NSCLC 2L, Phase 2 combination trials
- **Lusvertikimab (OSE-127):** Top-line results Ulcerative Colitis Phase 2
- **OSE-172/BI 765063:** Phase 1b results update in solid tumors
- **VEL-101/FR104:** Phase 2 start in Kidney Transplantation
- **OSE-230** & **BiCKI®IL7v:** 2xIND in the next 12 months

Financial Position

Cash visibility beyond Q2 2024
25.6 M€ available cash as of December 31st, 2022

The OSE team

An experienced executive leadership committee supported by an expert team

Nicolas Poirier, PhD
CEO, CSO

- 15+ years experience in biotech/immunotherapy
- Advanced 5 novel therapies to clinic
- 4 pharma deals
- Global Management, INSEAD

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

Sophie Fay
Chief External Affairs

- 15+ years leadership experience in Pharma/Biotech
- Corporate strategy, Access Go to Market
- MBA, ESSEC

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

Jean-Patrick Demonsang
Director
- President & Managing Director of Seventure Partners (private equity fund)
- Support activites 150+ IT & Life Science companies
- Corporate strategy, Access Go to Market
- MBA HEC

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

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

Alexandre Lebeaut, MD
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
Director
- Former Hematology Professor
- Strategic functions within the French Ministry of Higher Education and Research
- Advised international pharma in R&D strategies.

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

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

Wolfe-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

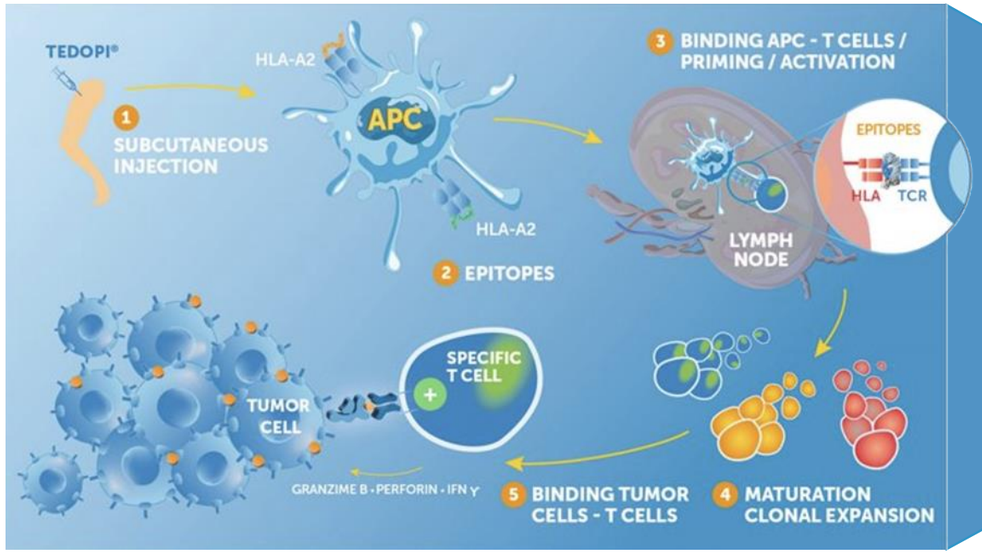
Sophie Brouard, PhD
Immunologist and Director in Vetinary Sciences, Director of Research at the Institut National de la Santé et Recherche Médicale (inserm, National Institute for Health and Medical Research) in Nantes

Proprietary clinical programs

TEDOPI®

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

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



- **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

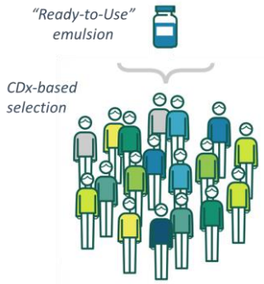
Orphan Drug Designation (FDA) **>1,000 injection** in clinical trials

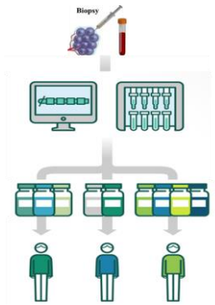
Strong IP position until **2038**[1] (US / EU / Asia)

1: *OSE Immunotherapeutics Receives New European Patent*

Tedopi®, the most advance neoepitopes cancer vaccine

The only one leveraging on a first positive phase 3 (randomized versus chemotherapy active arm)

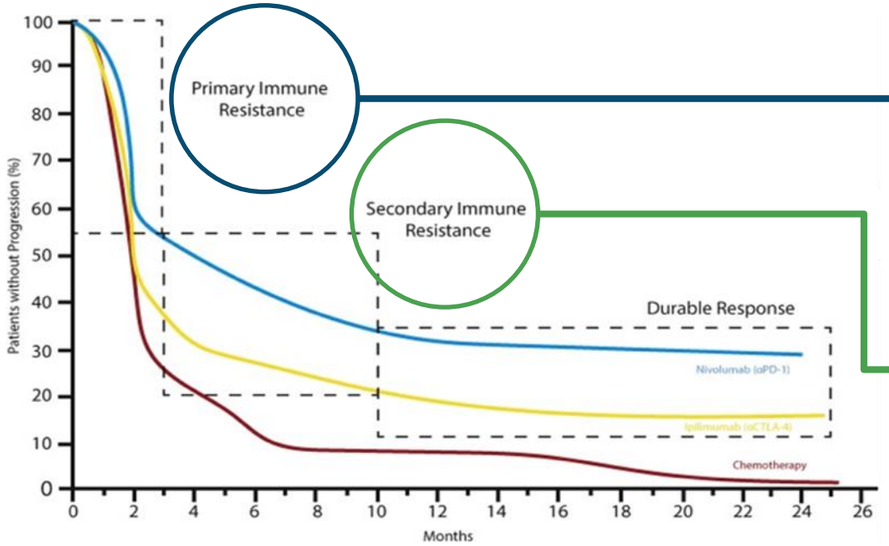




	Company	Product Name	Platform	Indication	Stage	Combo	NCT
off-the-shelf vaccine	OSE IMMUNOTHERAPEUTICS	Tedopi®	Peptide-based	NSCLC 2L	3	n.a.	NCT02654587
	Northwest	DCVax-L	Dendritic-based	Glioblastoma	3	n.a.	NCT00045968
	UbiVac	DPV-001		NSCLC	2	n.a.	NCT02234921
	BioNTech	FixVac (BNT113)	mRNA	HPV16+ head and neck cancer	2	n.a.	NCT03418480
		FixVac (BNT111)		Advanced Melanoma	2	n.a.	NCT02410733
	NuGenerex	AE37	Peptide-based	Breast Cancer	2	Pembrolizumab	NCT04024800
	Ultimovacs	UV1		Melanoma	2	n.a.	NCT04382664
				NSCLC	2	n.a.	NCT01789099
				Mesothelioma	2	nivolumab	NCT04300244
				HNSCC	2	Pembrolizumab	NCT05075122
	Thaio Pharma	TAS0313		Urothelial Carcinoma	2	pembrolizumab	JapicCTI-183824
	Vaccitech	VTP800/850	Viral/bacterial vector	Prostate cancer	2	nivolumab	NCT03815942
	Advaxis	ADXS-503		NSCLC	1/2	Pembrolizumab	NCT03847519
	Gritstone Bio	Slate		KRASmut-driven tumor types	1/2	nivolumab + ipilumab	NCT03953235
	Aston Sci	AST-301	DNA-based	TNBC	1	Pembrolizumab	NCT05163223
	Innovio	INO-5401		glioblastoma	1	cemiplimab	NCT03491683
	BioNTech	FixVac (BNT112)	mRNA	Prostate	1	n.a.	NCT04382898
		FixVac (BNT116)		NSCLC 2L	1	cemiplimab	NCT05142189
	Moderna	mRNA-5671		KRAS mutant tumors	1	Pembrolizumab	NCT03948763
	Aston Sci	AST-021p	Peptide-based	Solid tumors	1	n.a.	NCT04864418
	Ultimovacs	UV1		Prostate	1	n.a.	NCT04701021
	OncoPep	PVX-410		MM	1	Pembro / atezo	NCT02886065
	Nouscom	NOUS-209	Viral/bacterial vector	dMMR/MSI tumours	1	Pembrolizumab	NCT04041310
	Vaccitech	VTP-600		NSCLC	1	pembrolizumab	NCT04908111
	Bavarian Nordic	TAEK-VAK		HER2 cancers	1	traztuzumab	NCT04246671
Personalized vaccine	BioNTech / Roche	Autogene cevumeran	mRNA	mCRC	2	n.a.	NCT04486378
				1L Melanoma	2	Pembrolizumab	NCT03815058
				Solid tumors	2	atezolimab	NCT03289962
	Moderna / Merck	mRNA-4157/PCV		Melanoma	2	Pembrolizumab	NCT03897881
	Curevac / Frame	FRAME-001	Peptide-based	NSCLC	2	Pembrolizumab	NCT04998474
	Gritstone Bio	Granite	Viral/bacterial vector	MSS-CRC	2	atezolimab + ipilumab	NCT05456165
	Nykode/ Roche / Vaccibody	VB10.NEO	DNA-based	Solid tumors	1/2	atezolimab	NCT05018273
						bempegaldesleukin	NCT03548467
	Geneos T/ Innovio	GNOS-PV02		HCC	1	IL-12 + pembrolizumab	NCT04251117
	Moderna / Merck	mRNA-4157/PCV	mRNA	Melanoma	1	Pembrolizumab	NCT03313778
	BioNtech / Neon Therapeutics	NEO-PTC-01 / BNT221	Peptide-based	Melanoma	1	n.a.	NCT04625205
	Nouscom	NOUS-PEV	Viral/bacterial vector	1L NSCLC (TPS > 50%), 1L melanoma	1	Pembrolizumab	NCT04990479
	Transgene	TG4050		HNSCC	1	n.a.	NCT04183166
				OC	1	n.a.	NCT03839524
	Stermina Therapeutics	SW1115C3	mRNA	Solid tumors	1	n.a.	NCT05198752

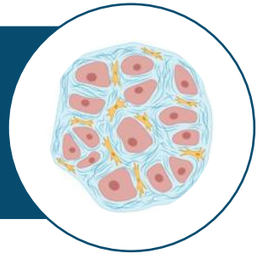
Tedopi® is a **novel cancer vaccine** with a strong biological rationale in post-ICI **secondary resistance**

Shifting paradigms with cancer vaccine immunotherapy



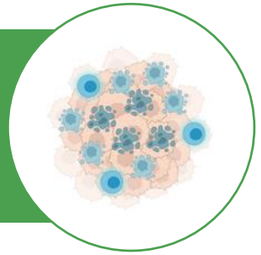
Primary (intrinsic) resistance
Patients who do not respond to ICIs with a rapid disease progression
→ **Immune refractory tumors**

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.

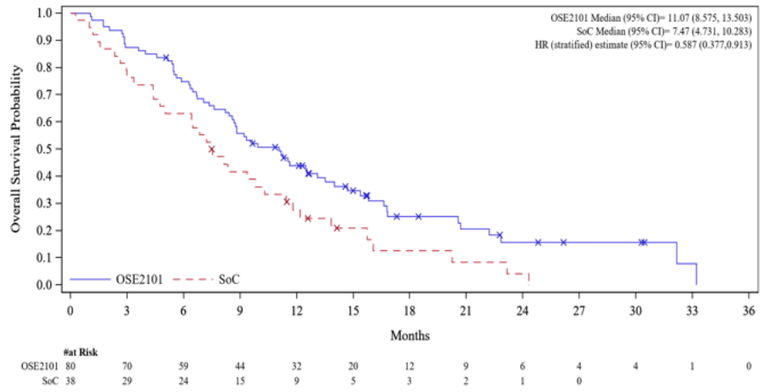
Figure: Schoenfeld AJ, Hellman MD. Cancer Cell 2020. Baxter MA, et al Br J Cancer 2021. **1:** After at least 12 weeks of ICI treatment in monotherapy (Task force SITC 2020 - Kluger H et al 2020).
ICI: immune checkpoint inhibitor. **TILs:** Tumor-infiltrating lymphocytes.

Clinically meaningful benefit of Tedopi® in monotherapy in NSCLC secondary resistance post-ICI

First randomized Phase 3, in this setting, with positive results vs. standard of care (SOC)

Overall Survival in PoI[1]

with 2d resistance in sequential chemotherapy-ICI



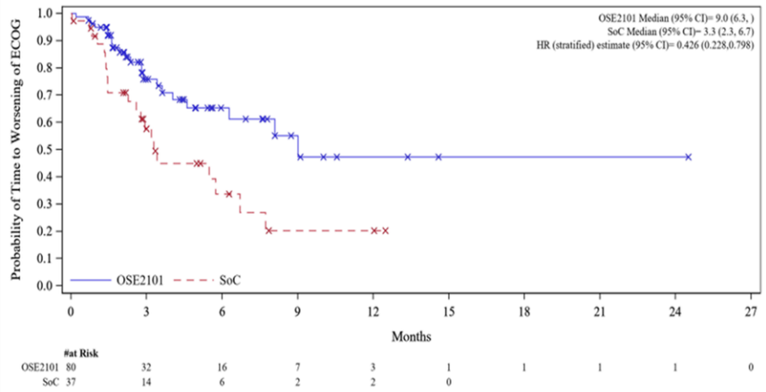
OS rate at 12 months
44%
in **Tedopi®** vs.
27.5%
in SoC

Delta OS:
3.6 months
Tedopi® 11.1 months
vs
SoC 7.5 months
HR 0.59 /
p-value=0.017

Time to worsening ECOG PS ≥ 2 in PoI[2]

delay from randomization to earliest ECOG PS ≥ 2

2022 ASCO ANNUAL MEETING
ADVANCING EQUITABLE CANCER CARE THROUGH INNOVATION



Time to worsening ECOG PS ≥ 2
Tedopi® 9.0 months
vs
SoC 3.3 months
HR 0.43 /
p-value < 0.01

Risk of Death reduced by 41% *versus chemotherapy*

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1: OSE Immunotherapeutics Presented Positive Final Results of Tedopi® Phase 3 **2:** Four Poster Presentations at 2022 ASCO Annual Meeting
B Besse et al; #47LBA ESMO 2021 -Annals of Oncology (2021). Cut-off 15JAN2021; median follow-up 25 months.
PoI: Population of Interest. **SoC:** Standard of care. **OS:** Overall survival. **HR:** Hazard ratio. **CI:** Confidence interval. **ICI:** Immune Checkpoint Inhibitor

Tedopi® demonstrated better safety and quality of life profile

in patients with secondary resistant to ICI vs chemotherapy

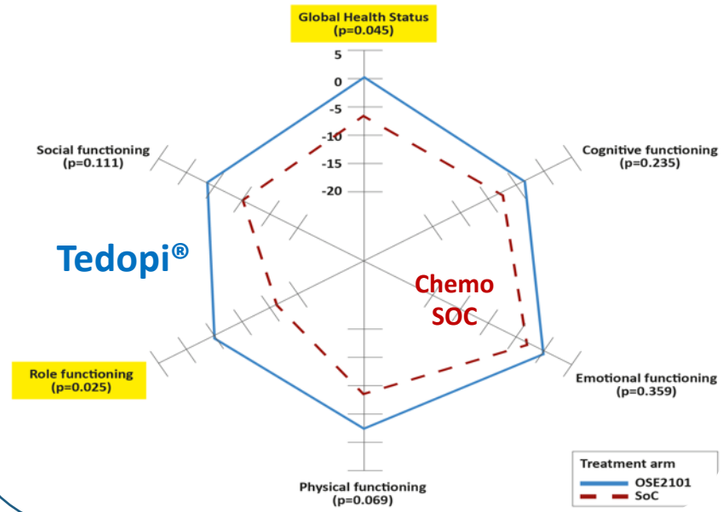
Significantly safer than SOC[1]

	Arm A Tedopi® (N=79)		Arm B SoC (N=37)	
Number of patients with at least one AE	All N (%)	Related N (%)	All N (%)	Related N (%)
All AE	76 (96)	60 (76)	37 (100)	29 (78)
Severe G3-5 AE	**28 (35)[2]**	**9 (11)[2]**	**24 (65)[2]**	**13 (35)[2]**
Fatal G5 AE	4 (5)	0 (0)	5 (14)	0 (0)
Serious AE	26 (33)	9 (11)	18 (49)	3 (8)
AE leading to permanent discontinuation	2 (3)	0 (0)	4 (11)	0 (0)

Quality of life (EORTC QLQ-LC13)[3]

PARIS 2022 ESMO congress

Better Patient reported Outcomes for Global Health Status, Role Functioning, Physical Functioning vs SoC



Positive Net Treatment Benefit vs SOC: P=0.032

OSE IMMUNO THERAPEUTICS

1: B Besse et al; #47LBA ESMO 2021 in Annals of Oncology (2021) 32 (suppl_5): S1283-S1346. 0.1016/annonc/annonc741 median follow-up 25 months
2: p< 0.001
3: B Besse et al; #9094 ASCO 2022 - Quality of Life (QoL) of OSE2101 in HLA-A2+ Non-Small Cell Lung Cancer (NSCLC) patients

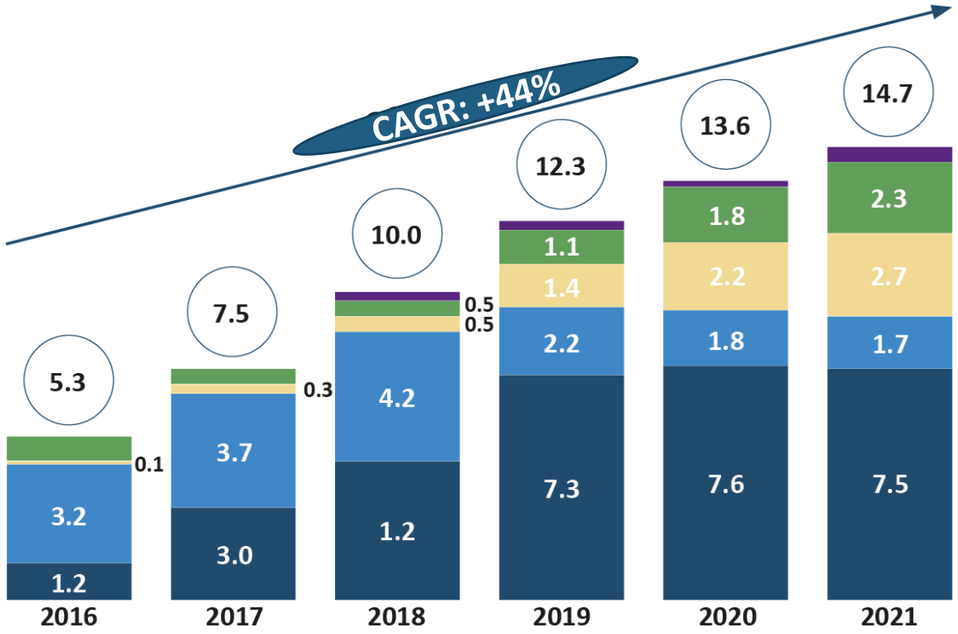
Position Tedopi® as the best treatment option after ICI-failure in cancer patients

OBJECTIVES

- ✓ Early access and compassionate use in 3L NSCLC
- ✓ Positive FDA/EMA discussion (confirmatory pivotal Phase-3 2L NSCLC after ICI-failure (*secondary resistance*)
- ✓ Additional Phase-2 clinical trials in combination (NSCLC, Pancreatic, Ovarian)

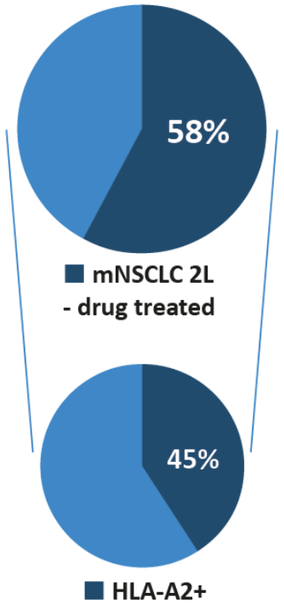
Target population estimated at **100k patients/year** in NSCLC post-ICI (2nd line)

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.
- ~70% of patients receive 2L in Western Countries.
- HLA-A2 phenotype in about 45% of the population.

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

Company	OSE IMMUNO THERAPEUTICS	MIRATI THERAPEUTICS	Roche / IPSEN / EXELIXIS	MERCK / Eisai	gsk	AstraZeneca / Daiichi-Sankyo	SANOFI	abbvie
Target	**Multi-epitopes vaccine**	TKIs			Immunotherapy	ADC		
					TIM-3	TROP2	CEACAM5	c-MET
Current Study	**ATALANTE-1**	MRTX-500	CONTACT-01	LEAP-008	COSTAR Lung	Tropion-LUNG1	CARMEN-LC03	NCT04928846
n	**219** **118 (secondary resistant)**	500	350	405	250	590	554	698
Therapy	**Tedopi® vs docetaxel**	Sitra + Opdivo vs. docetaxel	Cabo+Tecentriq vs. docetaxel	Lenvi + Keytruda vs. docetaxel	Cobolimab + Jemperli vs. docetaxel	datopotamab deruxtecan vs docetaxel	SAR408701 vs. docetaxel	Telisotuzumab Vedotin vs. Docetaxel
Primary endpoints	**OS**	OS	OS	PFS and OS	OS and ORR	PFS and OS	PFS and OS	PFS and OS
Initiation	**2017**	Q3 2019	Q3 2020	Q2 2019	Dec 2020	Q4 2020	Q1 2020	Q1 2022
Read-out	**2022**	2023 (delayed)	**Failed**	2023 (Achieved LPI)	2024+	H2 2022	2023e	2025e
		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.
- TEAEs G3/4	**11%**	**66%**	**53%**	**48%**	**n.a.**	**30-58%**	**51%**	**44%**
Source	**B.Besse et al, ESMO 21**	Leal, et al ESMO 2021	Neal et al, ASCO 2022	Taylor et al, J. Clin. Oncol. 38, 1154–1163.	Davar et al, SITC 2018	Garon et al, WCLC 2021	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-ICI

CombiTED[1] – NSCLC
in combination with nivolumab or docetaxel

- 3 groups (n=105)
  - Tedopi® plus docetaxel
  - Tedopi® plus nivolumab
  - docetaxel alone
- In 2nd line treatment in metastatic NSCLC, after 1st line chemo-immunotherapy

Study Sponsor FoRT

Maintenance treatment after standard treatment

TEDOVA[2] – Ovarian cancer
in combination with pembrolizumab

- 3 groups (n= 180)
  - Tedopi® monotherapy
  - Tedopi® in combination with pembrolizumab
  - Best supportive care
- Maintenance treatment in platinum-sensitive recurrent OC patients

Study Sponsor ARCAGY GINECO ENGOT European Network of Gynaecological Oncological Trial groups

TEDOPaM[3] – Pancreatic cancer
in combination with FOLFIRI

- 2 groups (n=106)
  - Tedopi® plus FOLFIRI
  - FOLFIRI
- Maintenance treatment in advanced or metastatic PDAC with no progression after 8 cycles of FOLFIRINOX
- Initial positive data presented at ASCO'22
  - Maintenance with Tedopi® monotherapy showed a favorable safety profile and encouraging time to failure of strategy

Study Sponsor GERCOR

1 - NCT04884282 Abstract #TPS9140: Combi-TED: A Multicenter, Phase II, Open Label, Randomized
2 - NCT04713514 TEDOVA/GINECO-OV244b/ENGOT-ov58 trial: Neo-epitope based vaccine OSE2101 alone
3 - NCT03806309 A randomized non-comparative phase II study of maintenance OSE2101 vaccine alone or in combination with nivolumab (nivo), or FOLFIRI after induction with

OSE-279: Proprietary PD-1 - value generator

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

Potential of combo with internal asset

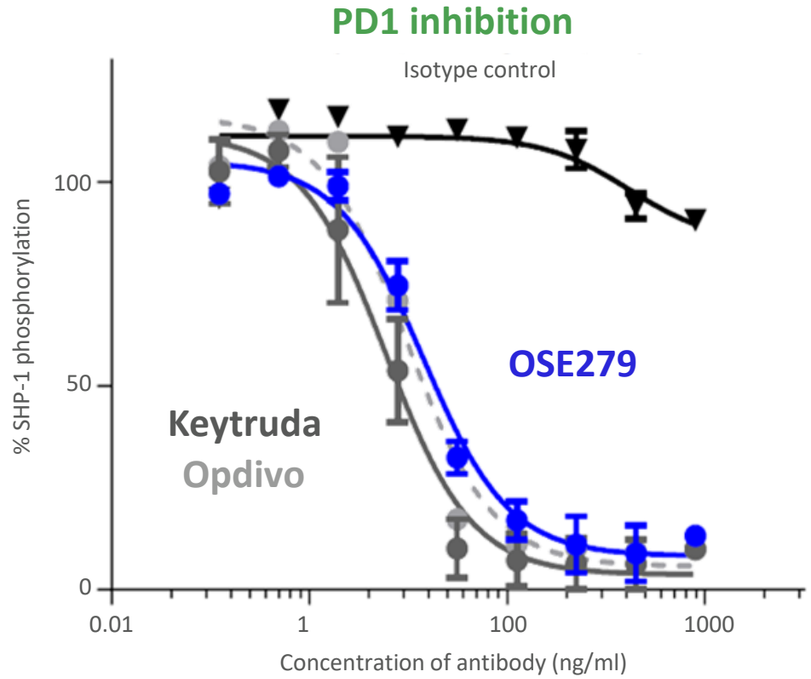
- Evaluate OSE-279 in combination with in-house molecules to obtain proprietary treatment options
- Tedopi®, CLEC-1

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

Obtain marketing approvals in orphan indications with strong unmet medical needs

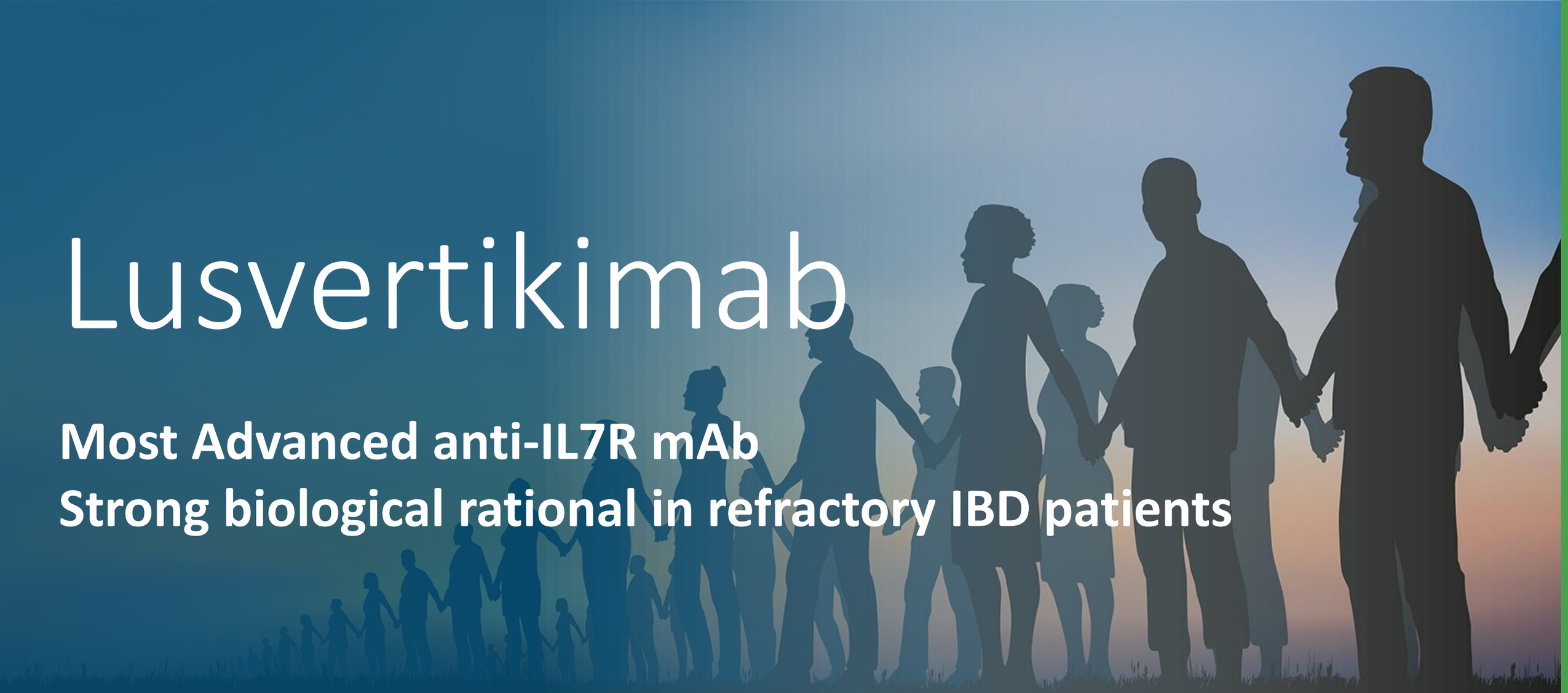


OSE IMMUNO THERAPEUTICS

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

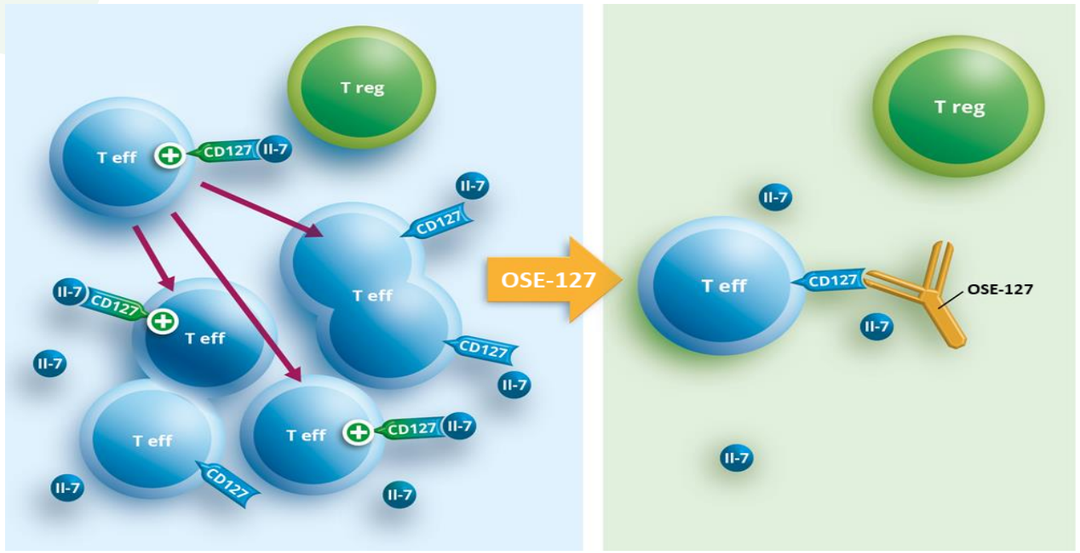
Lusvertikimab

Most Advanced anti-IL7R mAb
Strong biological rational in refractory IBD patients



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

Tackling the fuel of memory T-lymphocytes while sparing Tregs



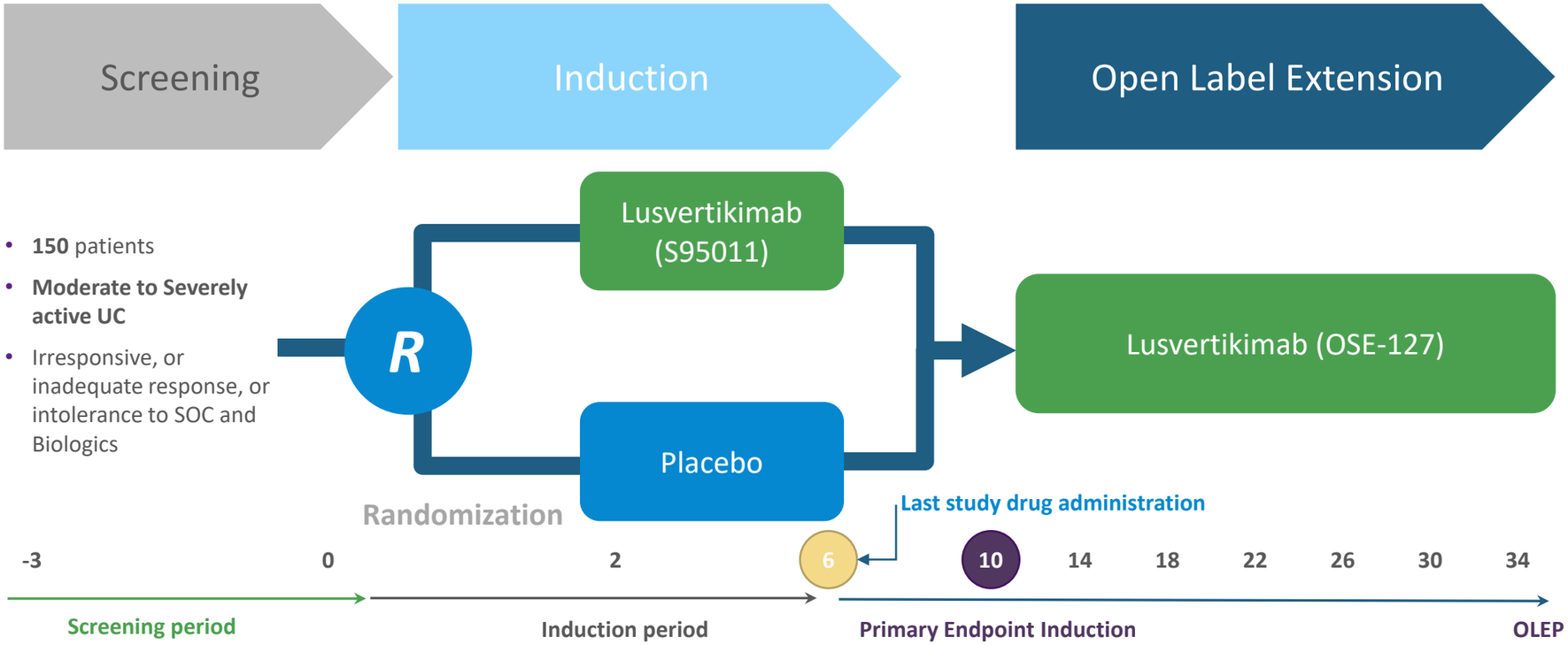
A differentiated and highly qualified candidate

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

- **On-going Phase-2 study in UC with clinical readout Q4 2023**

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

OSE-127 in moderate-to-severe **ulcerative colitis**



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)

OSE IMMUNOTHERAPEUTICS

- 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

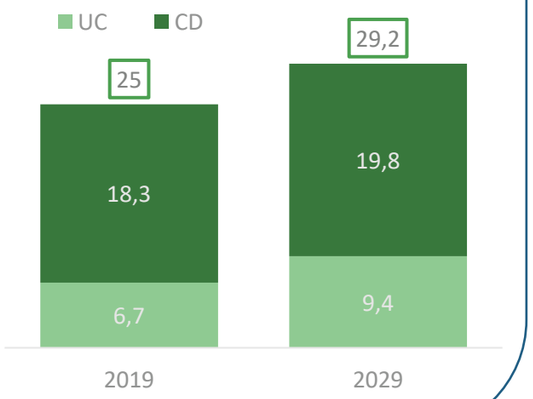
Secondary endpoints at Week 10 include:
1/ Clinical Remission by adapted Mayo score components: a stool frequency score of 0 or 1, a rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1.
2/ Clinical Response by adapted Mayo Score: reduction in adapted Mayo score ≥ 3 and ≥ 30%, with 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 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])

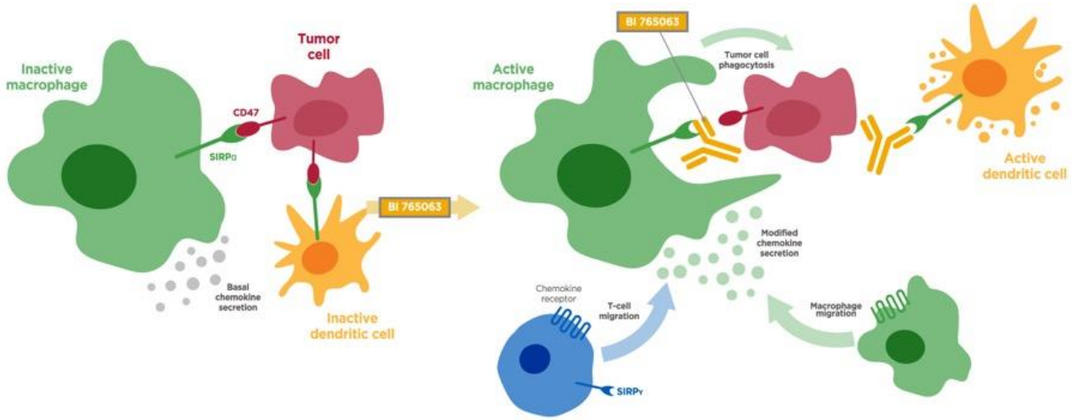
1: DRG UC Disease Landscape & Forecast 2021 **2:** Global Data **3:** Childhood Acute Lymphoblastic Leukemia Treatment (PDQ®)–Health Professional Version, accessed October 2022
4: OSE internal data released at ASH2022 **5:** Researchandmarkets.com/reports/4857889

Partnered clinical programs

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

- Infiltrating **myeloid cells promote 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		Ongoing Accrual Expansion Studies		
Trial number	NCT03990233			NCT04653142	NCT05249426[3]
Phase	Ia	Ia	Ib	Ib	Ib
N	50	18	40	36	150
Treatment	OSE-172	OSE-172 + ezabenlimab	OSE-172 + ezabenlimab	OSE-172 +/- ezabenlimab	OSE-172 + ezabenlimab ± chemotherapy, cetuximab or VEGF/Ang2 inhibitor
Patient population	Solid tumors		MSS CRC (n=30) MSS endometrial (n=10)	Solid tumors	HNSCC HCC
Region	EU	EU	EU	JP	US EU JP

Key takeaways from dose escalation

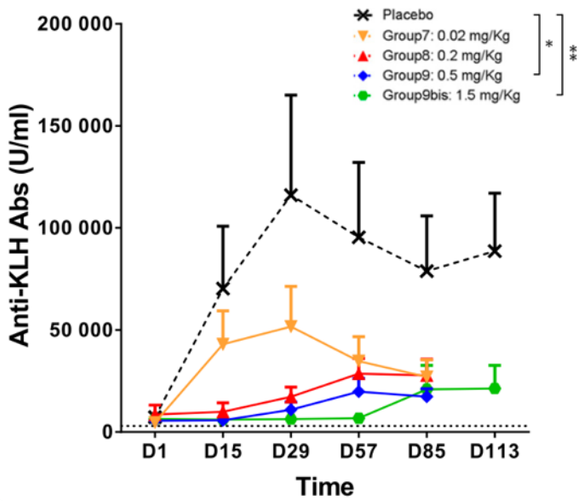
- **Safety**
  No hematotoxicity reported, no DLTs, MTD not reached[1,2]
- **Efficacy**
  - 1 PR in HCC, **45% clinical benefit rate as a single agent**[1]
  - 3 PRs in MSS endometrial cancer and CRC in combination with a checkpoint inhibitor[2]

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

FR-104/VEL-101
CD28 antagonist in transplantation

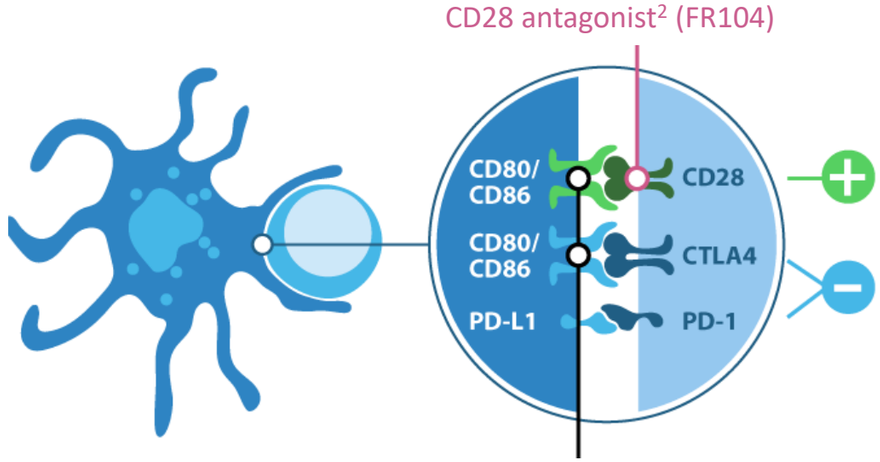
Veloxis PHARMACEUTICALS
an Asahi Kasei company

Phase 1 results: Selective CD28 antagonist FR-104 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



OSE IMMUNO THERAPEUTICS

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 140m²** 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 is on-going

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

Mastering complex biology - Two drug discovery platforms

Fit for purpose design
- Engineered proteins & Antibodies
- Artificial Intelligence (AI)-driven mAb discovery
- Multi-specific / multi-functional therapeutics

Flexible targeting
- Ligands / receptors
- Myeloid lineage
- Leucocyte lineage
- GPCRs

Tunable pharmacology
- Antagonists / inhibitors
- Agonists / activator
- Modulators (cytokines, co-stimulatory, co-inhibitory)

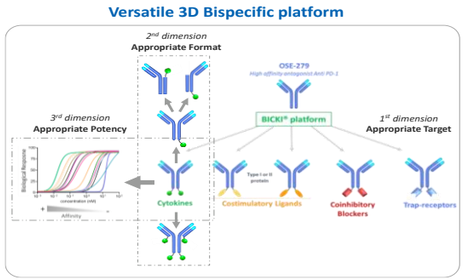
Myeloid platform

Myeloid Checkpoint
- **Releasing the potential of innate immunity**
- CLEC-1 program: LEAD selection

Pro-resolutive mAb
- **Triggering Resolution of inflammation**
- OSE-230 Pre-IND program

BiCKI® Platform

Anti-PD1 bispecifics
- **Tumor-specific T cells rejuveneting**
- First candidate BiCKI®IL7v

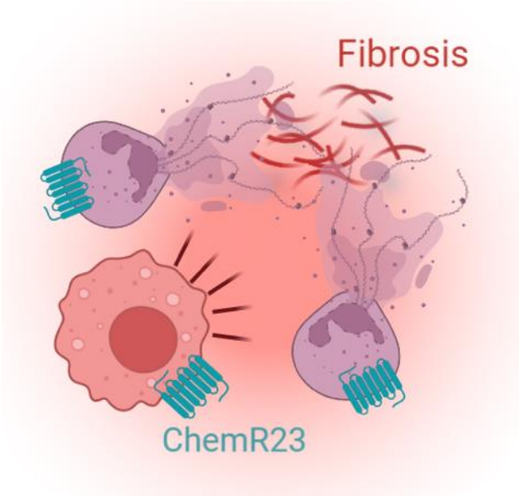


OSE-230 - Resolving inflammation is an active immune process

Pro-resolutive mAb

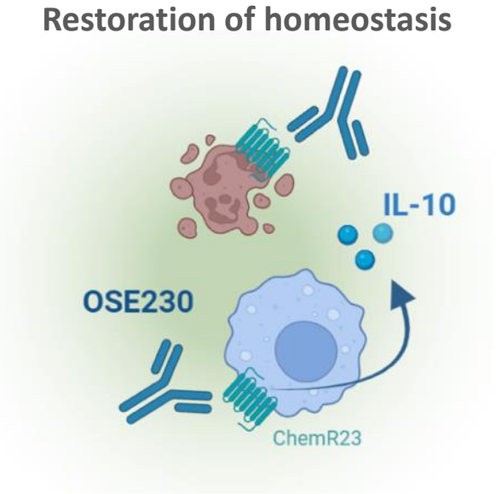
During chronic inflammation

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 acrophages, **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

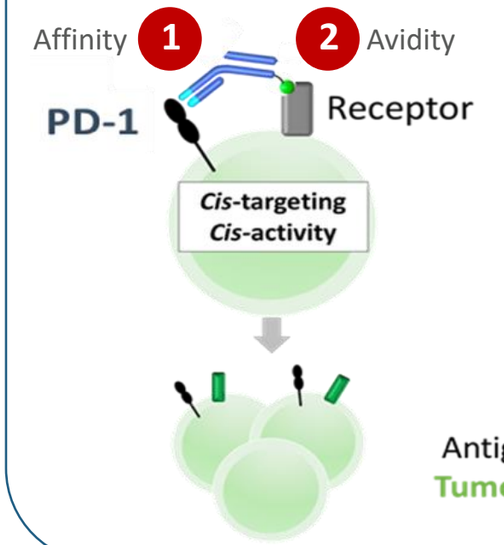
Next-generation anti-PD1 bispecifics

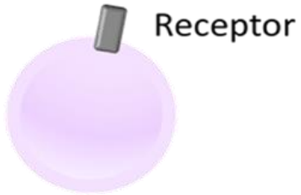
Improving the quality of tumor-specific T-cell responses both in TME & Lymph Nodes

Anti-PD1 bispecifics

Targeting the RIGHT T-cells…

Selective targeting of Tumor-specific PD-1+ T cells





Non experienced
NaîveT cells

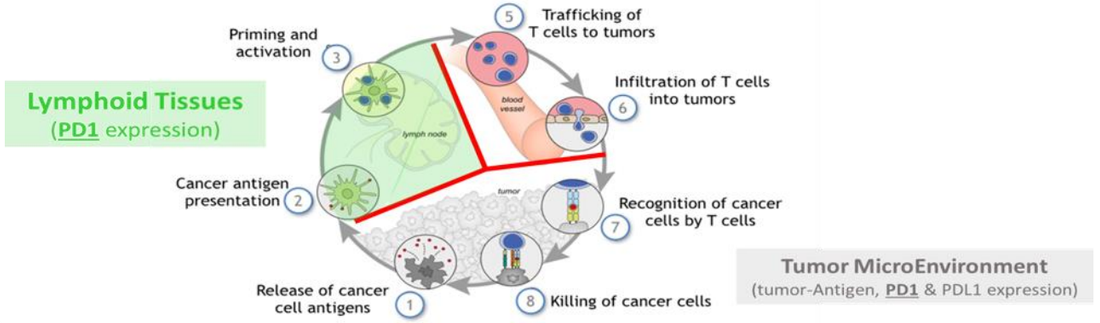
Antigen experienced
Tumor specific T cells

↗ Survival, Migration

↘ Exhaustion, Immunosuppression

…at the right place

Selective Biodistribution in TME + Lymphoid tissues



BiCKI®IL7v* first pre-IND candidate presented at AACR 2022*

OSE IMMUNOTHERAPEUTICS

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)

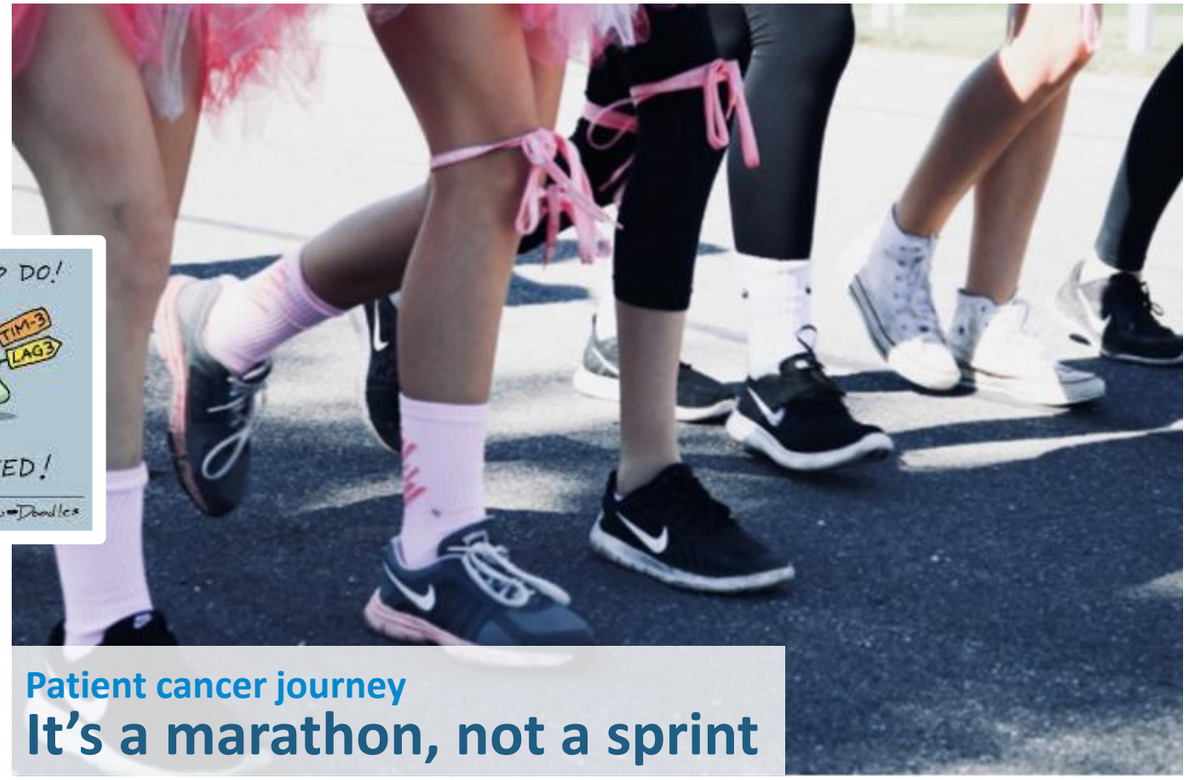
What's wrong with previous cytokine approaches?

Success takes time - it's a marathon, not a sprint

Anti-PD1/IL7 bispecifics

IL2/IL15
Sprinters legs

IL7
Marathon runners legs



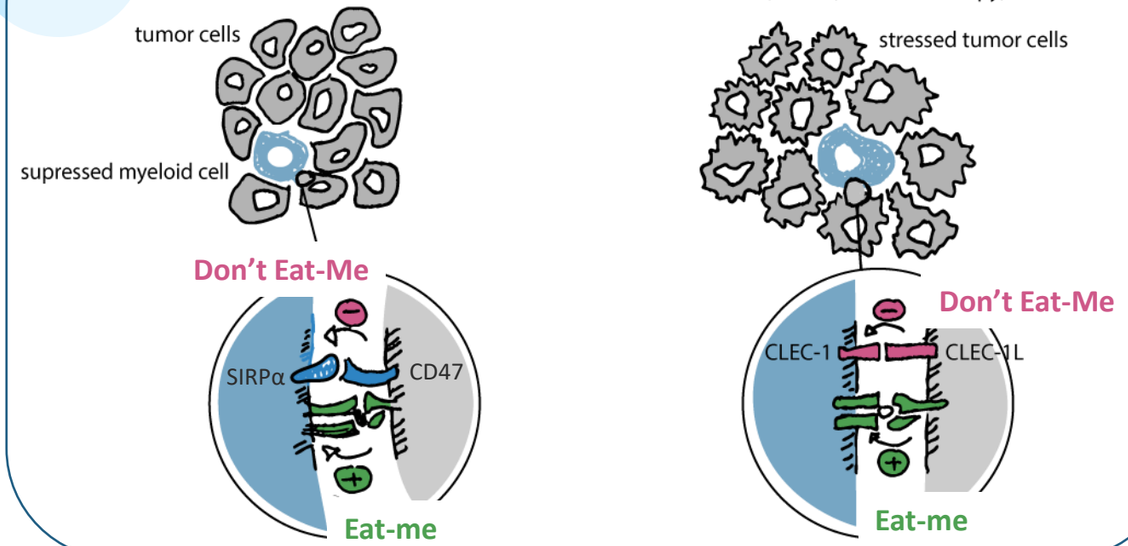
Patient cancer journey
It's a marathon, not a sprint

CLEC-1 - Another way to not get eaten

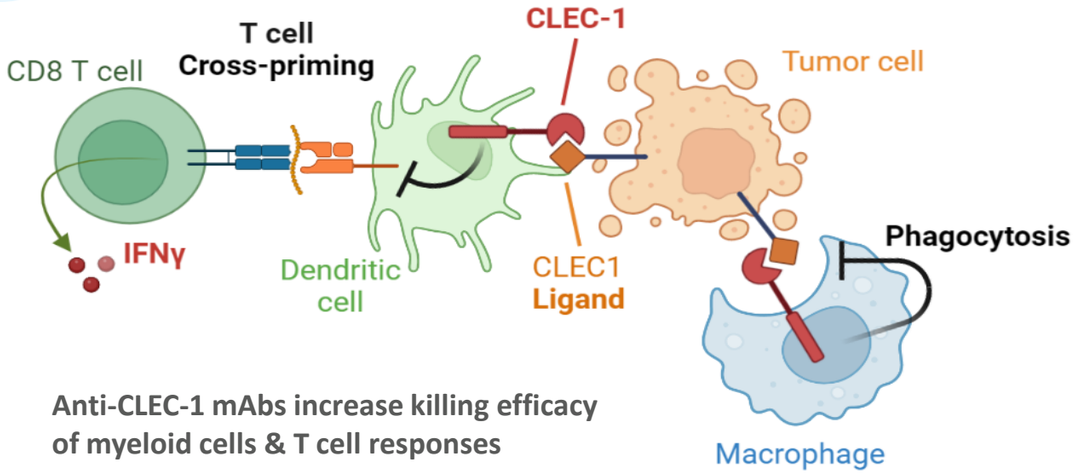
Blocking myeloid immune checkpoint from delivering another “Don’t-eat-me” signal

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

OSE IMMUNO THERAPEUTICS

Breaking through the therapeutic ceiling with first-in-class immunotherapies

Immuno-Oncology & Immuno-Inflammation

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75014 Paris, France

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