Enterome

DELIVERING THE PROMISE OF *IMMUNOTHERAPY*

APRIL 2023

Important notice and disclaimers

This presentation is provided by Enterome S.A. (“Enterome”) for informational purposes only. The information contained herein does not purport to be all-inclusive and none of Enterome, any of its affiliates, any of its or their respective officers, directors, employees or representatives makes any representation or warranty, express or implied, as to the accuracy, completeness or reliability of the information contained herewith.

Forward-looking statements. This presentation and accompanying oral commentary contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “may,” “will,” “expect,” “plan,” “anticipate,” “target,” “estimate” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Such forward-looking statements are subject to risks, uncertainties, and many other factors which could cause actual results to differ materially from those expressed or implied by such forward-looking statements. These forward-looking statements are based upon estimates and assumptions that, while considered reasonable by Enterome and its management, are inherently uncertain. New risks and uncertainties may emerge at any time, and it is not possible to predict all risks and uncertainties. Nothing in this presentation should be regarded as a representation by any person that the forward-looking statements set forth herein will be achieved or that any of the contemplated results of such forward-looking statements will be achieved. You should not place undue reliance on forward-looking statements, which speak only as of the date they are made. Enterome undertakes no duty to update these forward-looking statements.

No Offer or Solicitation. This communication does not constitute, or form a part of, an offer to sell or the solicitation of an offer to sell or an offer to buy or the solicitation of an offer to buy any securities, and there shall be no sale of securities, in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction.

Industry and Market Information. Information regarding market share, market position and industry data pertaining to Enterome's business contained in this presentation consists of estimates based on data and reports compiled by industry professional organizations and analysts and Enterome's knowledge of their industry. Although Enterome believes the industry and market data to be reliable, this information could prove to be inaccurate. You should carefully consider the inherent risks and uncertainties associated with the market and other industry data contained in this presentation. Forward-looking information obtained from third-party sources is subject to the same qualifications and the additional uncertainties as the other forward-looking statements in this presentation

Advancing a portfolio of novel immunotherapies against cancer

Enterome

EMPLOYEES	76	HEAD OFFICE	Paris	INCEPTION	2012

CLINICAL STAGE COMPANY DEVELOPING A NEW GENERATION OF IMMUNOMODULATORY DRUGS

Bacterial Effector-based drug discovery platform

Therapeutic Proteins & Peptides / Small Molecules / Synthetic Antigens

3 Programs in **Phase 2**

2 Programs entering the clinic in 2023

Numerous PC assets

Multiple strategic partnerships

€100M in upfront payments to date from partners

Profit sharing US (25%) & Royalties row on partnered program

Nestlé HealthScience

Leading international venture and corporate investors

Equity **€116M** raised to date

Nestlé HealthScience · Bristol Myers Squibb · Takeda · seventure · HealthForLife · Lundbeckfonden · OMNES · xYence · SymBiosis · SIGNET

Our management team has the expertise and the drive to deliver

Pierre Belichard, PhD

CEO & co-founder

Pierre brings 25 years' experience in the biopharmaceutical industry having founded and sold Fovea pharmaceuticals and held various leadership positions at Sanofi, Ethypharm and UroGene.

Marie-Laure Bouttier

CCO & co-founder

Marie-Laure has 20 years' experience in business management and development in the biopharmaceutical industry. She held various leadership positions at Sanofi, Urogene and Fovea pharmaceuticals.

Christelle Dumoussaud

Chief Financial Officer

Christelle has more than 20 years' experience in senior finance roles from various industries including 10 years in the pharmaceutical industry at Fournier/Solvay Pharma

Anne Dagallier, PhD

Chief Business Officer

Anne brings over 20 years of experience in global business and drug development. She joined Enterome in 2021 after having held several scientific and senior business development positions at Sanofi

Jan Fagerberg MD, PhD

Chief Medical Officer

Jan has more than 30 years' experience in immuno-oncology. He joined Enterome in 2019 after an extensive career in industry and academia.

Christophe Bonny, PhD

Chief Scientific Officer

Christophe has more than 20 years' experience in the field of molecular biology and signaling pathways and 15 years in the field of computational hit identification to candidate selection.

Laurent Chene, PhD

Head of Drug Discovery

Laurent brings 25 years of experience in target identification, screening and drug discovery, with responsibility for advancing several preclinical targets across diverse therapeutic area.

Lucie Rouch

Head of Clinical Operations

Lucie has a strong track record of delivering successful clinical programs, having worked for more than 20 years with global CROs, pharma and biotech companies.

Industry-Leading Scientific Advisors

Scientific Advisory Board

Pedro Romero

Specializing in translational tumor immunology, with a highly valued expertise in immune and tumoral responses, Pr. Romero is deputy scientific director of the Ludwig Institute for Cancer Research and honorary professor of the University of Lausanne.

David Klatzmann

World-renowned immunologist and co-discoverer of the HIV, Pr. David Klatzmann is Professor of Immunology Sorbonne University, Head service of Biotherapies at La Pitié-Salpêtrière Hospital (AP-HP). He brings Enterome his unique expertise in T cell-based therapies.

Justin Eyquem

Assistant Professor, Microbiology and Immunology at UCSF, co-founder of Mnemo Tx, Pr. Eyquem has a unique knowledge of the engineering of T lymphocytes to improve antitumor activity.

Medical Advisory Group

Alexander Zukiwski

Serving as Chief Medical Officer at CASI Pharmaceuticals, Alexander Zukiwski brings over 25 years of experience in global oncology drug development. Having held several leadership roles at pharmaceutical companies such as Hoffmann-LaRoche, Glaxo Wellcome, Johnson & Johnson, MedImmune, and Arno Therapeutics, he has supported the clinical evaluation and registration of many successful oncology treatments, including Taxotere, Xeloda, Procrit/Eprex, Velcade, Yondelis, and Doxil.

Peter Kiener

Peter Kiener is a biotechnology industry leader with experience across multiple organizations, including Sucampo, Ambrx, Zyngenia, MedImmune and Bristol-Myers Squibb. He is currently a Venture Partner at ICG LifeSciences. Peter has published over 120 papers in peer-reviewed journals and holds more than 40 patents and patent applications.

Zuzana Jiráková Trnkova

Dr. Jiráková is currently Chief Medical Officer of Highlight Therapeutics. She holds over 20 years of industry experience with broad level of clinical development expertise, with focus on immuno-oncology and medical affairs at global blue-chip Life Science companies as well as leading biotech including Bayer Pharmaceuticals and BioNTech.

Deep and diversified pipeline of immunomodulatory drug candidates

Enterome

Product	Indication	Discovery	Preclinical	Phase 1	Phase 2	Next Steps
Memory T cell Therapy / CANCER						
EO2401 + nivolumab (Bristol Myers Squibb)	**OncoMimics™**	Recurrent glioblastoma				Phase2 readout Q4 2023
		Adrenal tumors				Pivotal Study initiated
EO2463	**OncoMimics™**	B cell malignancies				Interim data H2 2023
EO2040	**OncoMimics™**	CRC with ctDNA MRD				Phase 2 initiated
EO4010	**OncoMimics ™**	mCRC				FIH Q3 2023
T Reg Therapy / AUTOIMMUNE DISEASES						
EB1010 (Nestlé HealthScience)	**EndoMimics™**	IBD, Food Allergy				FIH Q1 2024
EA300 (Nestlé HealthScience)	**AllerMimics™**	Food Allergy				Preclinical Candidate Selection Q3 2024

Enterome

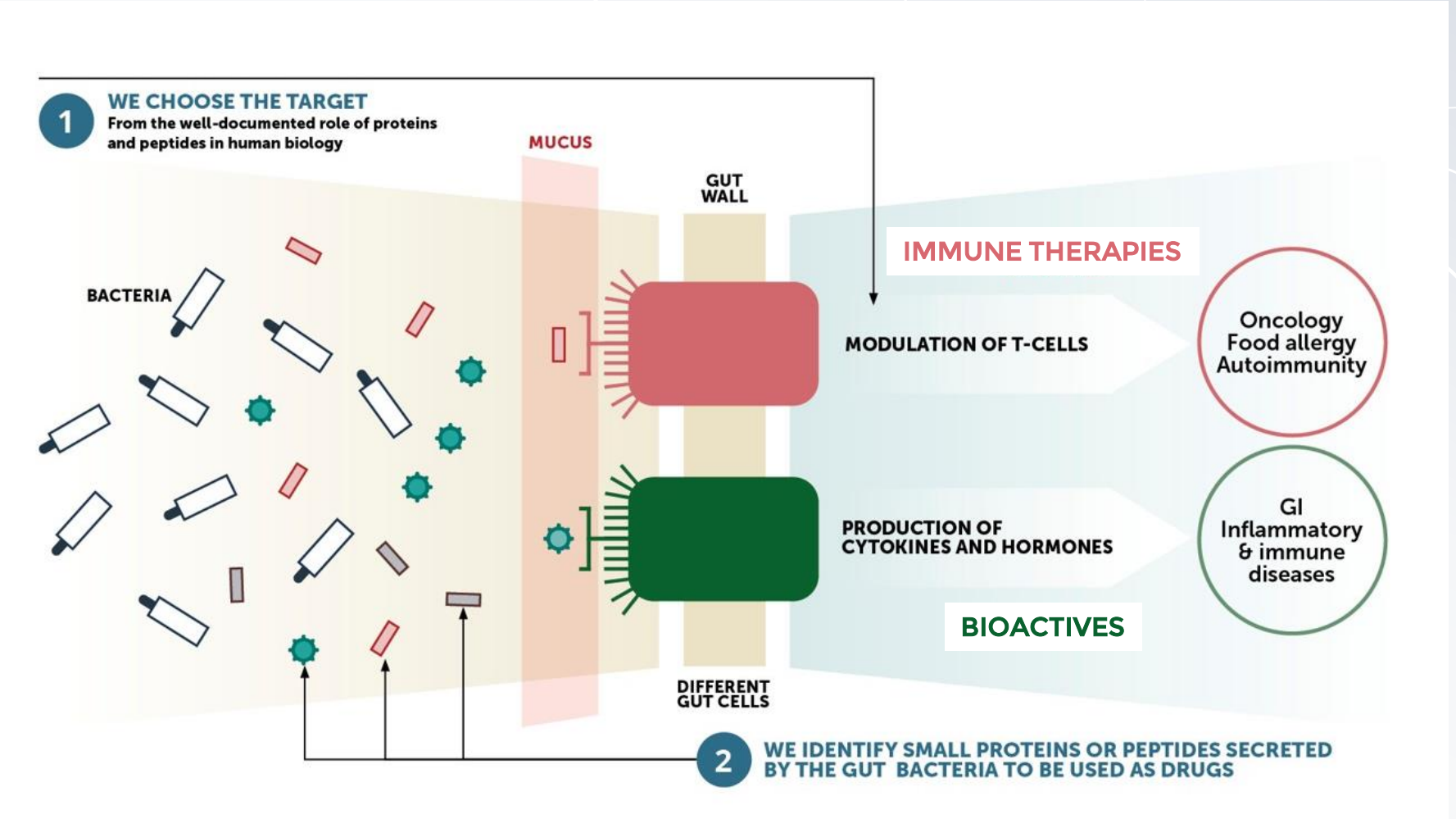
Drug Discovery Platform

DELIVERY OF
NEXT GENERATION IMMUNOTHERAPIES

Unique ability to uncover new biological insights

Our database contains 23 million bacterial proteins in constant cross-talk with human body

We decode the gut bacteria effector's interaction with the human body



Enterome

OncoMimics™ Platform

DELIVERY OF
NEXT GENERATION IMMUNOTHERAPIES
AGAINST CANCER

Enterome

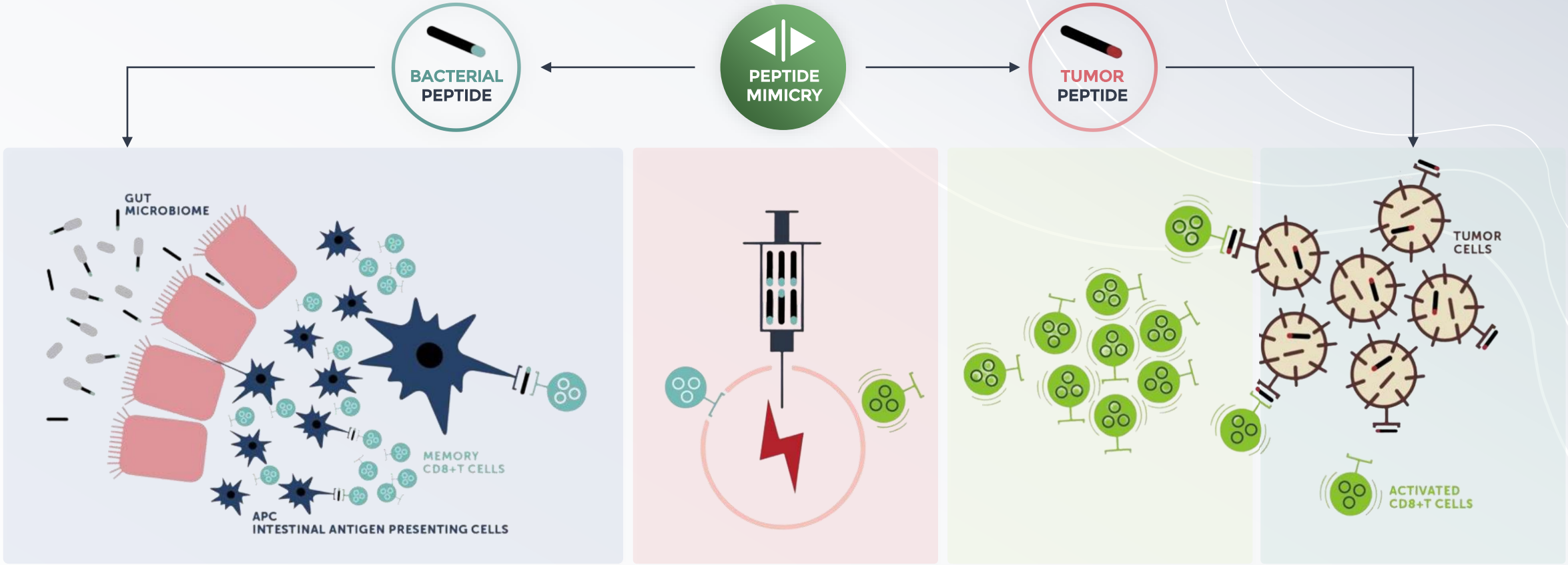
Why are we more comparable to cell therapies than to conventional cancer vaccines ?

A new way of generating high T Cell loads directly in patients

150+ patients treated to date with promising clinical outcome and good safety

- ☑ Break tolerance of Immune System against human tumor associated antigens
- ☑ Boost endogenous and pre-existing effector memory T cells, specifically recognizing several tumor-inducing antigens or B cell markers
- ☑ Induce levels of peripheral T lymphocytes comparable to those obtained by exogenous T cell therapies with cytotoxic and polyfunctional capacity and without exhaustion, up to several months after initiation of treatment
- ☑ Off the shelf – easy to produce – patent protected
- ☑ Strong systemic immune response generated with EO2463 (monotherapy iNHL) and EO2401 (+nivolumab) in line with clinical efficacy:
    - rGBM: median survival 14.5 months (vs 8 months SOC)

OncoMimics™: prevalent, high affinity, non-self bacteria-derived peptides mimicking tumor antigens…



…to generate potent anti-tumor immune responses through expanding pre-existing memory cytotoxic T cells

Enterome

Factors that limit the efficacy and clinical applicability of T cell-based therapies in solid tumors

- Efficacy against self-antigens (thymic deletion)
- T cell functional persistence
- Tumor escape mechanisms
- Manufacturing cost and complexity

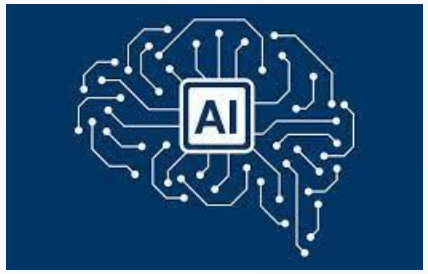
Enterome

Factors that limit the efficacy and clinical applicability of T cell-based therapies in solid tumors

- **Efficacy against self-antigens (thymic deletion)**
- T cell functional persistence
- Tumor escape mechanisms
- Manufacturing cost and complexity

OncoMimics™ peptides are identified through a proprietary bioinformatic pipeline and validated in human

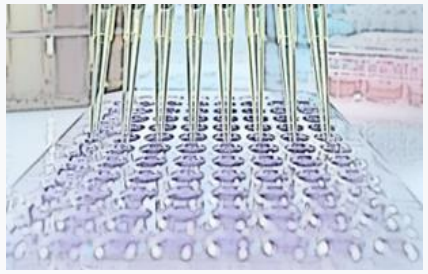
Billions of microbiome antigens



In silico Identification

- ✓ TAA selection
- ✓ Identification of bacterial mimics of selected TAAs
- ✓ MHC affinity / stability / prevalence

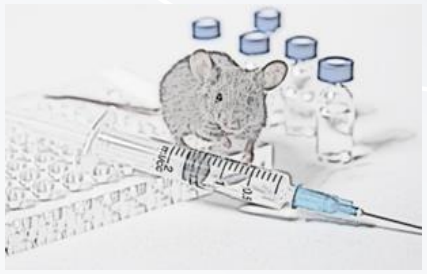
Hundreds of selected antigen mimics



In vitro validation

- ✓ MHC affinity / stability

Tens of in vivo data



In vivo validation

- ✓ Immunogenicity
- ✓ Cross-reactivity against TAAs
- ✓ Ability to generate cytotoxic CD8+ T cells

3-5 OncoMimics™ peptides selected for human trials

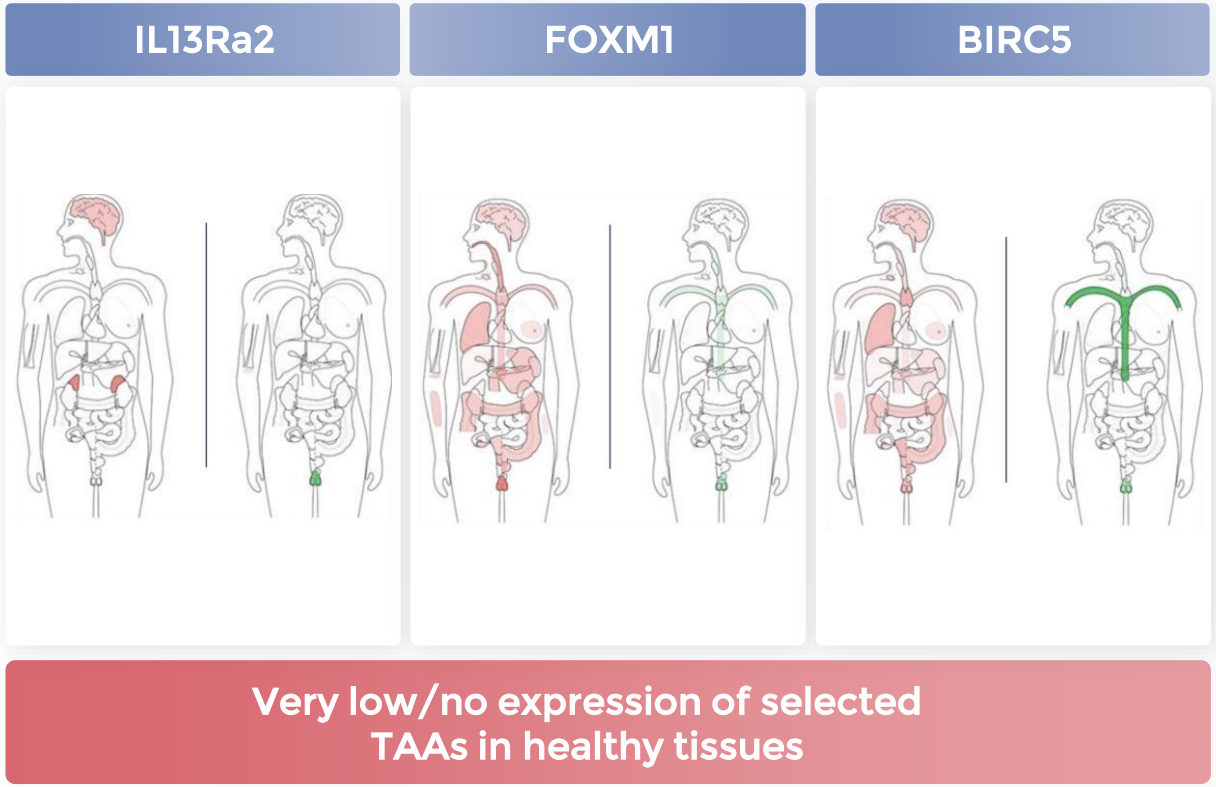
Ex vivo validation (human)

- ✓ Pre-existing memory repertoire
- ✓ Strong immunogenicity
- ✓ Cross-reactivity against TAAs
- ✓ Ability to generate cytotoxic CD8+ T cells

Pick the right TAAs: highly tumor-specific antigens made highly immunogenic by OncoMimics technology

EO2401 is a mix of 3 non-self peptides mimicking three driver antigens involved in glioblastoma and adrenal tumors

Selected TAAs are main tumor development drivers, specifically expressed in glioblastoma and adrenal tumors



Very low/no expression of selected TAAs in healthy tissues

(mRNA expression in organs. Red: tumors; green: healthy tissues)

Specific OncoMimics™ mix

Bacterial peptides (OncoMimics)

EO2317 EO2318 EO2316

BIRC5 FOXM1 IL13Ra2

Human TAAs

- Synthetic bacteria-derived peptides (HLA-A2 restricted epitopes)
- TAAs selectively expressed in GBM and ACC
- Selection of bacterial peptides with outstanding immunogenicity

POC for Enterome flagship project EO2401

Positive clinical outcome in 2 different Phase 2 clinical trials (cold tumors)

Glioblastoma (GBM), patients with 1st recurrence (ROSALIE trial, NCT04116658)

- Specific CD8+ memory T cell response (confirmed in 96% of evaluated pts)
- EO2401/nivolumab was well tolerated with a safety profile consistent with the safety profile of nivolumab monotherapy, except the addition of local administration site reactions
- In our study, pts treated with EO2401 + nivolumab + bevacizumab have a median survival of 14.5 months vs. 8 to 9 months for SOC (lomustine+/-bevacizumab)
  - Nivolumab is not active in GBM and used to support T cell expansion and infiltration of tumor
  - Bevacizumab is used here for its anti-edema properties to counteract pseudo-progression seen in treated patients. 1
- Enrollment completed December 2022 with a total of 100 patients

Enterome

Factors that limit the efficacy and clinical applicability of T cell-based therapies

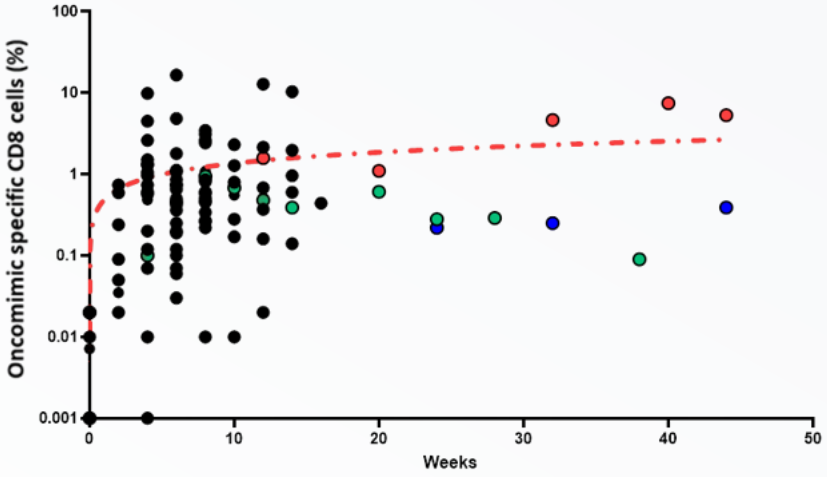
- Efficacy against self-antigens (thymic deletion)
- **T cell functional persistence**
- Tumor escape mechanisms
- Manufacturing cost and complexity

EO2401 induces strong, extended immune response

Robust CD8+ T cell responses detected in treated patients with or without in vitro stimulation

Strong Immune response

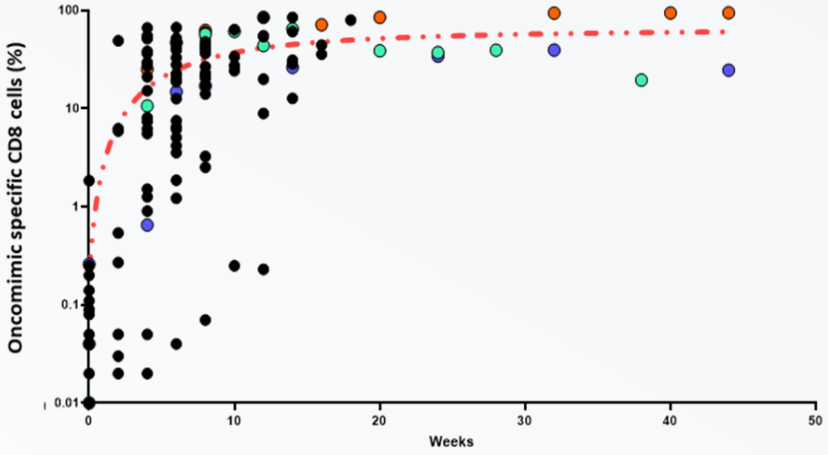
detected in 31/32 patients as early as 2 weeks following first immunization



% of CD8 + T cells specific for EO2401 as assessed by tetramer analysis **ex vivo** on all investigated available timepoint and patient's samples

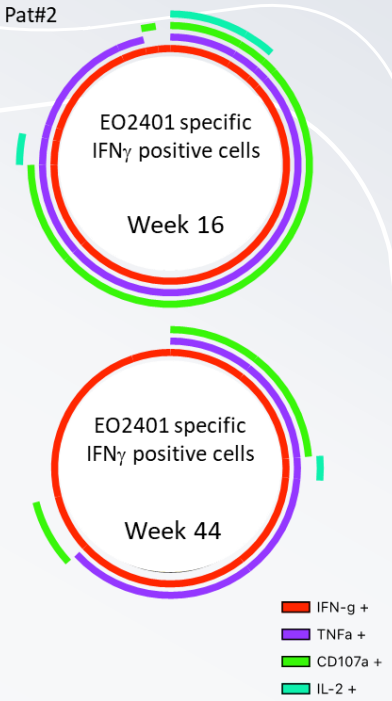
No exhaustion

very long-lasting responses observed in 3 evaluated patients



% of CD8 + T cells specific for EO2401 as assessed by tetramer analysis **after IVS** (Cumulative percentage of EO2316, EO2317 and EO2318 tetramer positive CD8 cells)

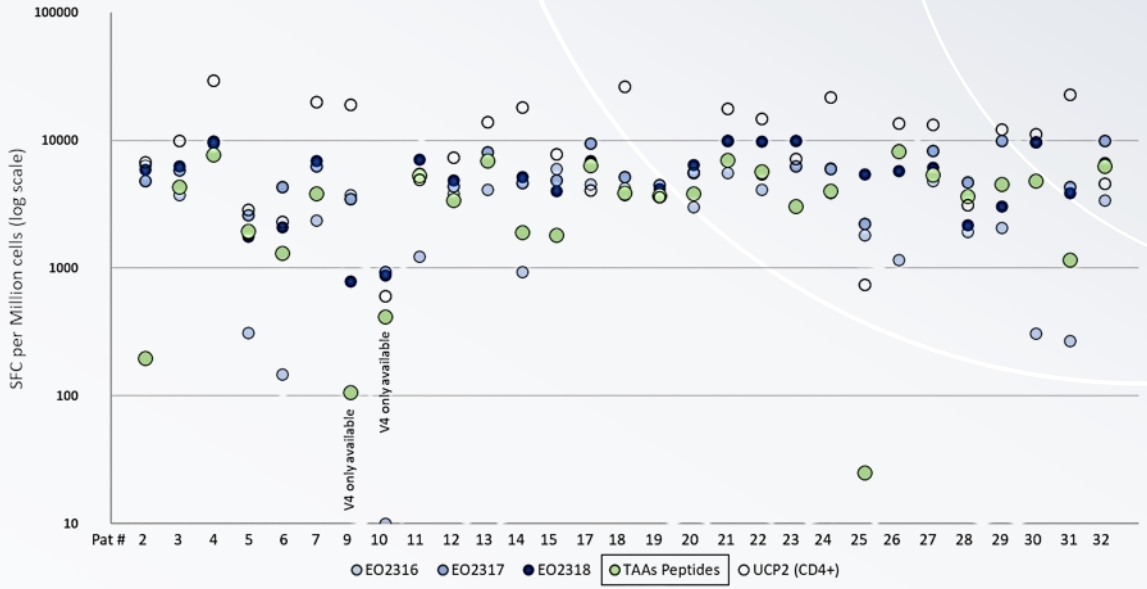
Sustained functionality



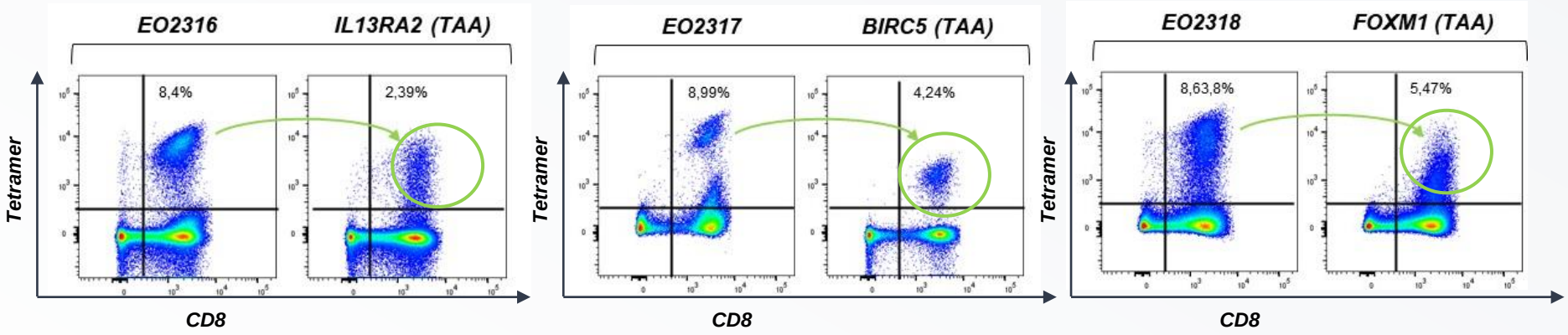
Polyfunctionnality of EO2401 reactive cells **after 12 days IVS**, assessed using intracellular cytokine staining and CD107 expression

Cross-reactivity between OncoMimics™ peptides and TAAs

Observed in 27/28 patients



IFN-γ ELISpot assay after 12 days in vitro stimulation with OncoMimics™ pool and restimulation with either EO2316, EO2317, EO2318 or cross-reactive human peptide pool for all investigated patients.

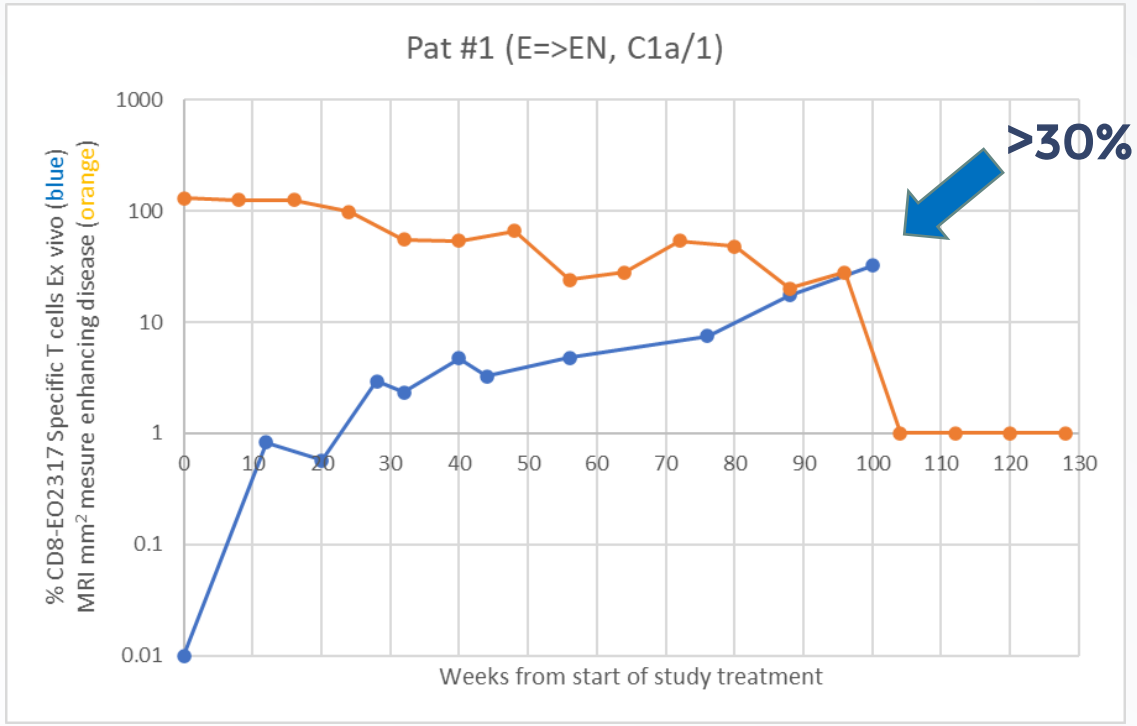


Detection of cross-reactive T CD8 cells after vaccination. PBMCs from patient were stained with specific tetramers after 12 days in vitro amplification in the presence of bacterial peptides. CD8 cells specific for bacterial and human corresponding peptides were quantified using specific tetramers staining and flow cytometry

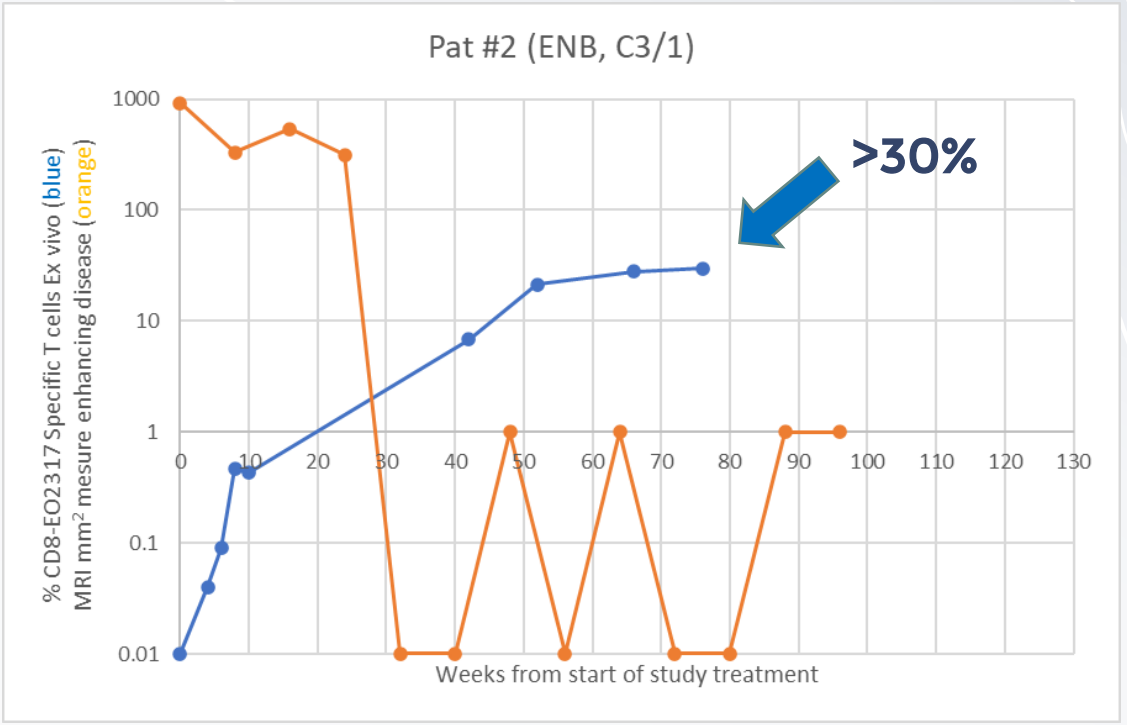
Strong and sustained Immune response associated with Tumor Shrinkage

In some patients >30% of all T cells circulating in the peripheral blood are directed against oncomimics – lasting and not exhausting and associated with tumor shrinkage

Alive, ongoing EO2401 mono



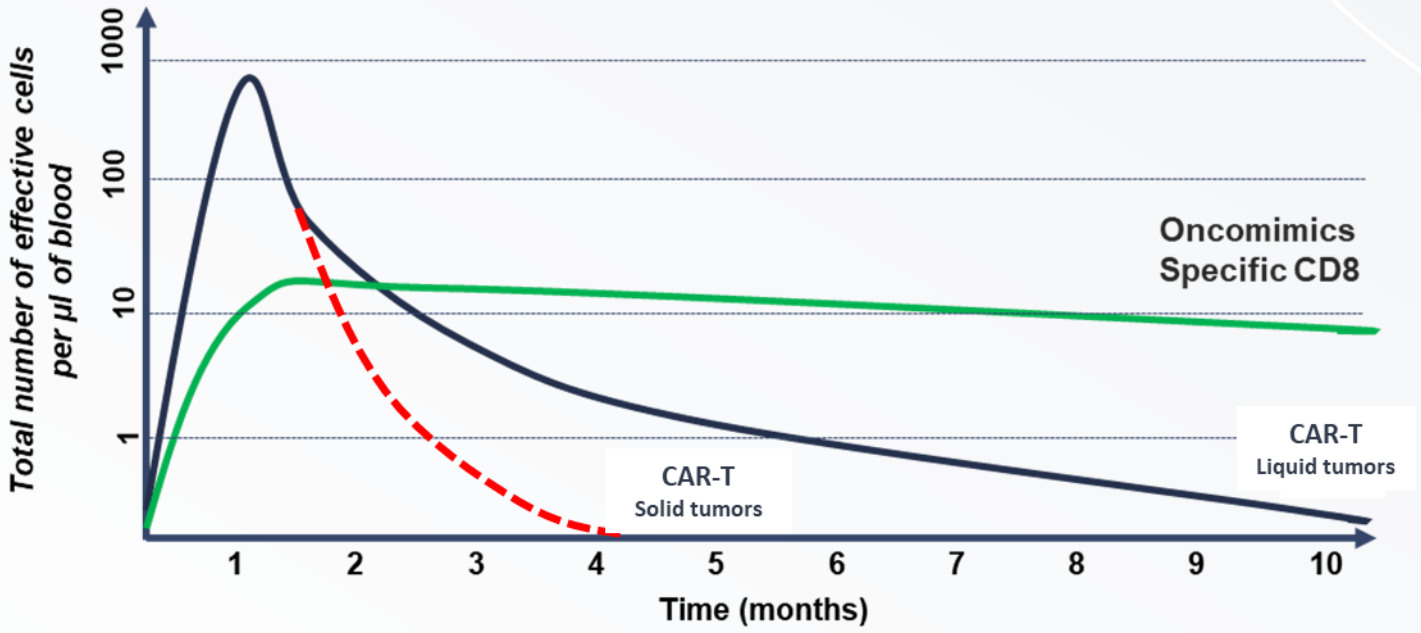
Alive, ongoing EO2401 + Nivo



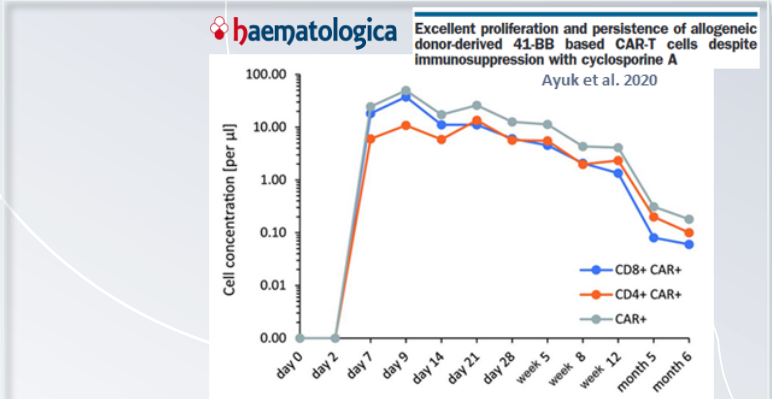
Stable response over time with OncoMimics vs. CAR-T

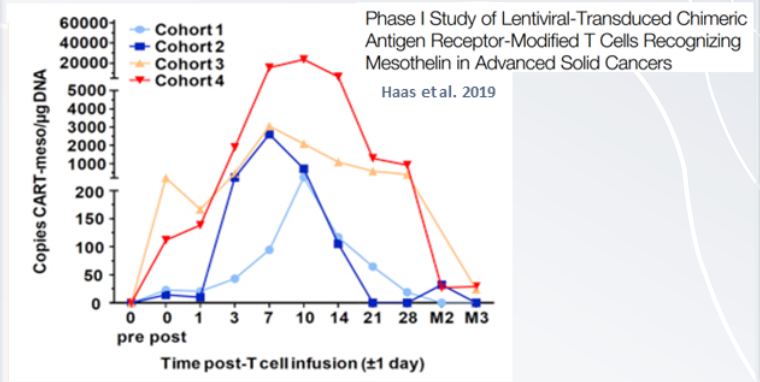
Enterome

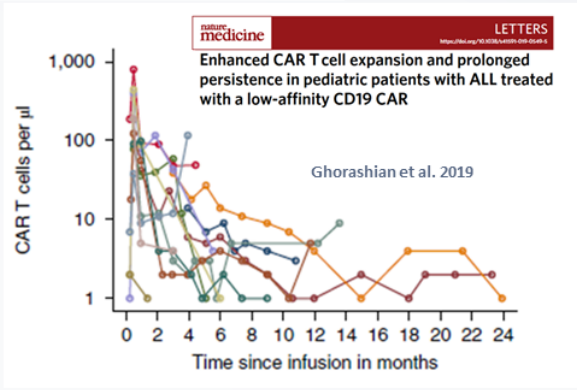
Schematic representation of the number of Oncomimic-specific cells versus the number of CART cells detected in patients



Note : 1% of specific CD8 correspond to around 5 specific T CD8 cells / µl of blood
*CART cell number was extrapolated from available literature studies (*Ayuk et al. 2020 PMID: 32241845; Ghorashian et al. 2019 PMID: 31477906; Kimmel et al. 2021 PMID: 33757357; Mueler et al. 2021 PMID: 28935694; Penelt et al.2022 PMID: 35309367; Kiem et al. 2022 PMID: 34064196 ...)







Example of classical CART kinetic

Enterome

Factors that limit the efficacy and clinical applicability of T cell-based therapies

- Efficacy against self-antigens (thymic deletion)
- T cell functional persistence
- **Tumor escape mechanisms**
- Manufacturing cost and complexity

EO2463 - novel OncoMimics™ candidate for MZL and FL

Quadruple targeting designed for better killing & prevent escape

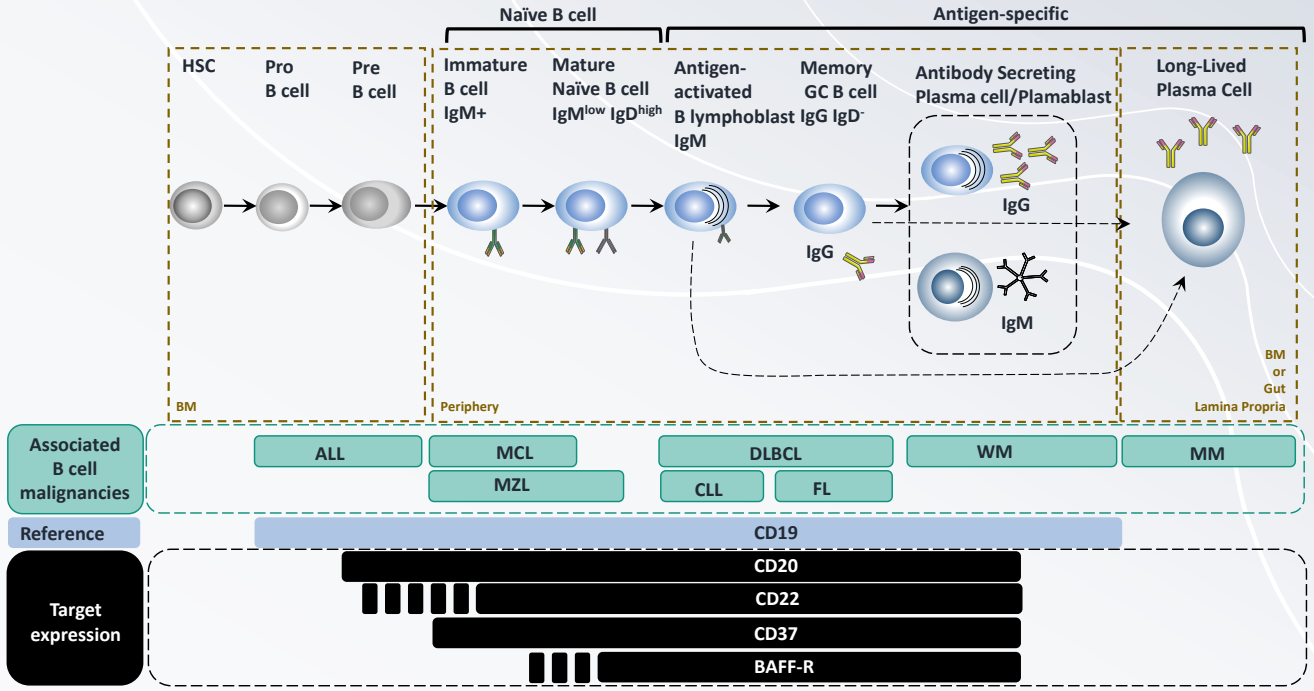
Targeted B-cells markers in Marginal Zone Lymphoma (MZL) and Follicular Lymphoma (FL):

CD20, first specific B cell marker, is a B cell restricted tetra spanning protein and plays a role in the development, differentiation, and activation of B-lymphocytes.

CD22 is a cell surface adhesion molecule that regulates B cell activation is associated with development, differentiation, and functionality of B cells.

CD37 is one of the tetraspanins restricted to the lymphoid lineage 5 (TSPAN26) and plays a role in many aspects of cell biology and physiology, including cellular migration, adhesion, activation, proliferation and apoptosis.

BAFF-R is the B cell activating factor receptor and is one of the main pro-survival receptors in B cells.



- Four targets are validated in B-cell malignancies
- Strong alternative to CD19 marketed therapies (CD19 negative relapses)
- Potentially prevents resistance due to antigen loss by targeting CD20, CD22, CD37 and BAFF-R simultaneously

Enterome

Factors that limit the efficacy and clinical applicability of T cell-based therapies

- Efficacy against self-antigens (thymic deletion)
- T cell functional persistence
- Tumor escape mechanisms
- **Manufacturing cost and complexity**

A new platform to generate high T cells load directly in patients

OncoMimics™ : Easily manufactured treatments

- ☑ Innovative way to improve T cell reactivity towards tumors **without complex engineering**
- ☑ **Chemically synthetized peptides** following standard manufacturing and regulatory pathways
- ☑ **Off-the-shelf**

A Platform with the potential to generate multiple drug candidates

Enterome

Potential pool of >1,000 patented bacterial peptides for various cancer indications

Tumor type	Composition	Product	Indication	
Solid	EO2317 BIRC5, EO2318 FOXM1, EO2316 IL13RA2	EO2401	+ rGBM + ACC	Ongoing Ph1/2
Solid	EO2317 BIRC5, EO2318 FOXM1	EO2040	+ ctDNA defined MRD in CRC	Ongoing Ph2
Solid	EO2317 BIRC5, EO2318 FOXM1, OPM10 UBE2C, OPM11 CDC20, OPM12 KIF2C	EO4010	+ mCRC	Ph 1/2 Q3 2023
Liquid	OMP64 CD20, OMP65 CD22, OMP66 CD37, OMP72 BAFF-R	EO2463	+ B cell Lymphoma	Ongoing Ph 1/2

Advancing a portfolio of novel immunotherapies against cancer

We strive to help more patients beat cancer by extending the benefits of immunotherapy

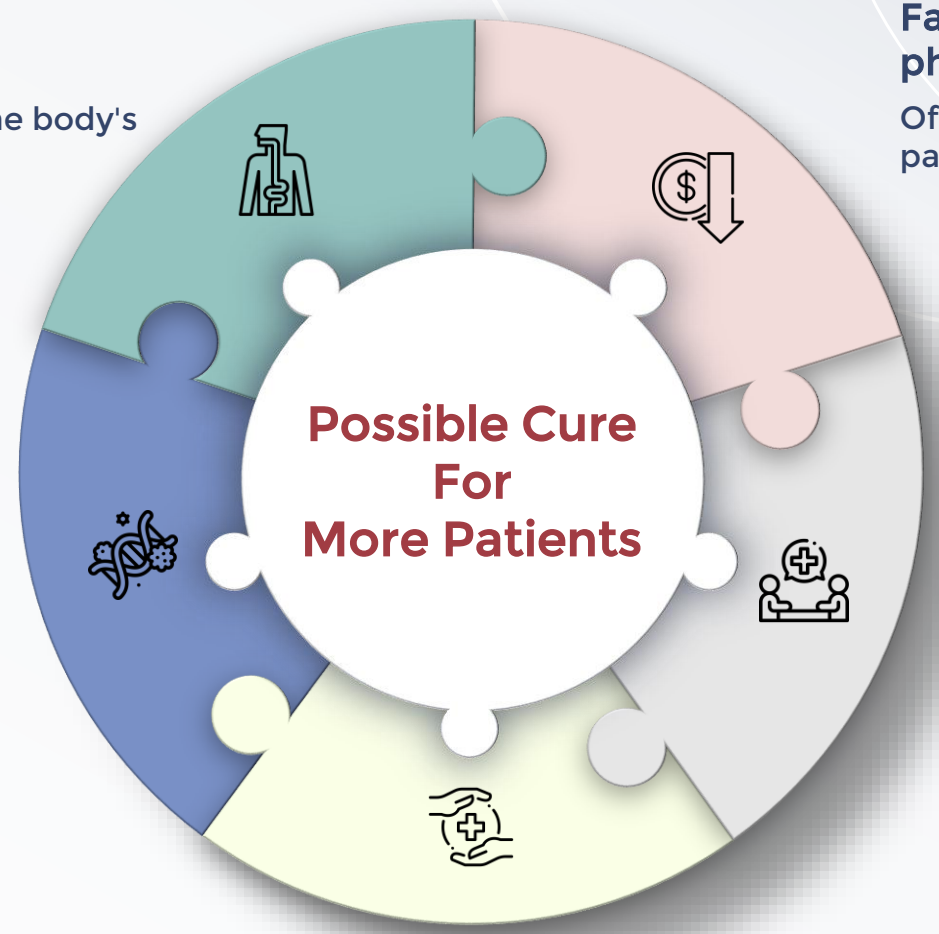
Enterome

Human-centric discovery platform

Therapeutics drawn from the body's most potent immune organ

Favorable pharmacoeconomic profile

Off-the-shelf, easy to produce and patent protected small molecules



Defeat tumor resistance

Strong and long-lasting responses against all immune phenotypes in both solid and liquid tumors

Support from top clinicians and strategic leaders

Collaboration with the most advanced research centers to rapidly deliver clinical results in different settings

Good Safety

No systemic side-effects reported in more than 150 patients treated