



Enterome's new OncoMimics™ immunotherapy, EO2463, demonstrates early efficacy and favorable safety in Phase 1/2 trial for indolent non-Hodgkin lymphoma

EO2463 uniquely targets four distinct B cell markers to maximize tumor killing and prevent immune escape, generating fast, strong and durable CD8+ T cell activation against malignant B cells

Initial data from EONHL1-20/SIDNEY study presented at the 17th International Conference on Malignant Lymphoma (ICML) in Lugano

Beneficial clinical responses observed following 6 weeks of treatment with EO2463 as monotherapy; preliminary complete response rate of 50% in evaluable patients for EO2463 in combination with lenalidomide + rituximab

EO2463 is well tolerated as monotherapy, without additional safety signals when combined with lenalidomide + rituximab

Paris, France – June 14, 2023

Enterome, a clinical-stage company developing first-in-class immunomodulatory drugs for solid and liquid malignancies and inflammatory diseases based on its unique Mimicry platform, today announces first clinical results from the Phase 1/2 (EONHL1-20/SIDNEY) trial of EO2463, an experimental treatment for indolent non-Hodgkin B cell lymphoma (iNHL). The initial data, presented at the 17th International Conference on Malignant Lymphoma (ICML), show that EO2463, as monotherapy and in combination with the standard of care (lenalidomide and rituximab), is well tolerated and generates strong immune responses associated with early clinical activity. ICML is taking place June 13-17, 2023 in Lugano, Switzerland.

EO2463 is an innovative, off-the-shelf immunotherapy candidate that combines four synthetic OncoMimic™ peptides. These non-self, microbial-derived peptides correspond to CD8 HLA-A2 epitopes that exhibit molecular mimicry with the B lymphocyte-specific lineage markers CD20, CD22, CD37 and CD268 (BAFF receptor). EO2463 also includes the helper peptide (CD4+ epitope) universal cancer peptide 2 (UCP2).

The unique ability of EO2463 immunotherapy to selectively target multiple B cell markers enables the destruction of malignant B lymphocytes that are abundant in iNHL. By ensuring broad target coverage across malignant B cells while avoiding a detrimental impact on normal peripheral B cells, this novel approach aims to simultaneously improve safety and maximize efficacy, reducing the tumor cells' capacity to develop immune-resistance mechanisms.

Dr. Jan Fagerberg, Chief Medical Officer of Enterome said, "EO2463 was designed to expand pre-existing memory cytotoxic T cells recognizing specific protein sequences from gut bacteria that cross-react with B cell specific proteins to drive targeted anti-tumor activity against B cell



malignancies. We are very encouraged that EO2463 is showing promising efficacy with a good safety profile in indolent non-Hodgkin B cell lymphomas, confirming the validity of our approach and the ability of OncoMimics™ -based immunotherapies to target liquid tumors. We now look forward to continuing the trial with multiple expansion cohorts.”

Key highlights from the EONHL1-20/SIDNEY trial poster presentation, entitled ‘Phase 1 trial of EO2463 peptide-based immunotherapy as monotherapy and in combination with lenalidomide and rituximab in indolent non-Hodgkin lymphoma’:

- EO2463 appears well tolerated as a monotherapy, and without additional safety signals when combined with lenalidomide and rituximab.
- Clinical activity (metabolic marker/tumor size reduction) observed in 4 of 9 (44%) patients after 6 weeks on EO2463 monotherapy and encouraging preliminary complete response rate on EO2463 combination therapy (50% in patients evaluable after 19 weeks).
- Expansion of specific CD8+ T cells against the OncoMimic™ peptides and targeted B cell antigens was detected in 6 of 8 tested patients, including in 2 patients with no measurable B cells at baseline.
- EO2463 generated fast, strong, and durable on-target immune activation with cytotoxic T cells with the ability to kill malignant HLA-A2 B cell lines in vitro.
- Study on-going with opening of 3 extension cohorts:
 - EO2463 monotherapy in patients with newly diagnosed, previously untreated follicular lymphoma (FL) or marginal zone lymphoma (MZL), not in need of therapy ("watch-and-wait" setting)
 - EO2463 + rituximab (from week 7) in patients with newly diagnosed, previously untreated, FL/MZL and low tumor burden, in need of therapy, and
 - EO2463 + lenalidomide (from week 1) + rituximab (from week 19) in patients with relapsed/refractory, previously treated FL/MZL

Pierre Belichard, CEO of Enterome added, *“These very promising data from the SIDNEY trial as well as the positive data from our lead OncoMimics™ candidate, EO2401, being evaluated in recurrent glioblastoma and in adrenal tumors, continue to provide strong support for the potential of Enterome’s Mimicry platform to transform cancer immunotherapy, in particular its unique ability to enable a multi-targeting approach. This growing set of clinical data gives us confidence in our ability to generate OncoMimics™-based immunotherapies targeting unmet needs across a wide range of solid and liquid tumors. Alongside EO2401 and EO2463, we have initiated enrollment for a new clinical study to evaluate EO2040 in patients with colorectal cancer with ctDNA-defined, minimal residual disease. We are also preparing to enter another new OncoMimics™ candidate, EO4010, for the treatment of metastatic colorectal cancer, into clinical development.”*

The abstract #435 is available [here](#) and the presentation will be available on Enterome’s [website](#).

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About OncoMimics™

OncoMimics™ immunotherapies are designed to activate pre-existing effector memory T cells that target bacterial (non-self) peptides, which are strongly cross-reactive against selected Tumor-Associated Antigens (TAAs), or B cell markers expressed on tumoral cells, resulting in a rapid targeted cytotoxic response against cancer.

About EO2463

EO2463 is Enterome's second, clinical-stage off-the-shelf OncoMimics™ peptide-based immunotherapy. It combines four microbial-derived OncoMimics™ peptides that closely mimic specific cytotoxic T cell (CD8+ T cell) epitopes in B cell Tumor-Associated Antigens CD20, CD22, CD37, and CD268 (BAFF receptor), as well as a helper CD4 peptide, UCP2. The EO2463 mimic peptides are non-self, high affinity and stable MHC class I binders.

About SIDNEY

SIDNEY (EONHL1-20/, NCT04669171) is a multicenter, open-label, non-randomized Phase 1/2 trial investigating EO2463 in monotherapy and in combination with standard of care - rituximab and rituximab in combination with lenalidomide – for treatment of patients with indolent Non-Hodgkin's Lymphoma. The trial is assessing safety, tolerability, immunogenicity and preliminary efficacy in 60 patients at centers in the US and Europe. Patient enrollment is ongoing.

About iNHL

Non-Hodgkin lymphoma is the seventh most common cause of new cancer cases among both men and women, accounting for 4% to 5% of new cancer cases, and 3% to 4% of cancer-related deaths. Indolent non-Hodgkin lymphoma (iNHL) constitutes a distinct subset where, even though currently available treatments are efficacious, the main disease subtypes, such as follicular lymphoma (FL) and marginal zone lymphoma (MZL), are considered non-curable in most patients. Thus, novel therapeutic approaches are still needed to enhance treatment outcomes and limit or delay the use of potentially more toxic therapies.

About Enterome

Enterome is a clinical-stage biopharmaceutical company developing breakthrough immunomodulatory drugs for the treatment of cancer and immune diseases. Enterome's pioneering approach to drug discovery is based on its unique and powerful bacterial Mimicry drug

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discovery platform, allowing it to analyze and uncover new biological insights from the millions of gut bacterial proteins in constant cross-talk with the human body. Its first-in-class small protein and peptide drug candidates modulate the immune system by closely mimicking the structure, effect or actions of specific antigens, hormones, or cytokines.

The company's two pipelines of drug candidates include:

- **OncoMimics™** peptides, a pipeline of peptide-based immunotherapies. Lead candidate, EO2401, is in Phase 2 clinical trials in patients with glioblastoma and adrenal tumors and has demonstrated clinical proof of concept. EO2463 is in a Phase 1/2 clinical trial for indolent non-Hodgkin lymphomas, and has demonstrated a good safety profile with first signs of efficacy. EO2040, a new immune therapy, is expected to start a Phase 2 trial in 2023 in patients suffering from colorectal cancer with ctDNA-defined, minimal residual disease. EO4010 is in development for third-line colorectal cancer and targeted to enter clinical trials in 2023.
- **EndoMimics™** peptides, a pipeline of next generation bioactives acting like human hormones or cytokines, are being developed in collaboration with Nestlé Health Science, for food allergies and inflammatory bowel disease (IBD). Lead candidate, EB1010, expected to enter the clinic in 2024, is a potent local inducer of IL-10, designed to improve therapeutic outcomes for patients with IBD.

Enterome employs 70 people and is headquartered in Paris, France. Since its inception, the company has raised a total of €116 million from Europe- and US-based life science investors and more than €100 million from pharmaceutical partnerships.

For more information, please visit the company's website at: www.enterome.com