Enterome presents positive Phase 2 interim results in relapsed/refractory indolent non-Hodgkin lymphoma after EO2463 OncoMimics™ immunotherapy treatment at ICML

- 60% (12/20) complete response rate after treatment with EO2463 in combination with lenalidomide and rituximab (R^2)
- EO2463 plus R^2 was well tolerated in patients with follicular and marginal zone lymphoma
- EO2463 plus R^2 combination treatment resulted in higher-than-expected rates of complete remission so far in this study compared to historical data for R^2 alone

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Enterome SA, a clinical-stage company developing first-in-class OncoMimics™ immunotherapies to treat cancer, presented positive interim results for its OncoMimics™ immunotherapy EO2463 from Cohorts 1 and 4 of the ongoing open label Phase 1/2 SIDNEY trial in patients with indolent non-Hodgkin lymphoma (iNHL), at the International Conference on Malignant Lymphoma (ICML) in Lugano. Interim data including 24 patients with follicular and marginal zone lymphoma (relapsed/refractory iNHL) showed that treatment with EO2463 in combination with lenalidomide and rituximab (R^2) was well tolerated and demonstrated encouraging signs of efficacy that appear better than historical data in similar patients treated with R^2.

Importantly, EO2463 showed direct anti-lymphoma activity, including partial responses to the OncoMimics™ monotherapy, during the first six weeks of the study, a short time period during which just the first three doses of EO2463 were administered, before the protocol called for initiation of treatment with lenalidomide (followed subsequently by adding rituximab). Moreover, once lenalidomide and rituximab were added, the effect of EO2463 appeared to support a deepening of responses, resulting in a complete response rate of 60%, higher than would have been expected with R^2 alone, based on historical data[1].

Pierre Belichard, CEO of Enterome said, "The EO2463 interim results are very encouraging, demonstrating exceptional tolerability for an active immunotherapy, and

[1] https://doi.org/10.1200/JCO.22.00843

showing a clear signal that the combination with R^2 can provide more robust responses in this patient population over R^2 alone. This is consistent with the strong response rate we observed with EO2463 monotherapy in patients with low tumor burden disease, the so-called 'watch-and-wait' population, included in Cohort 2 of SIDNEY. While we plan to focus our near-term efforts on initiating a registrational Phase 3 trial of EO2463 for the watch-and-wait population, this evidence of a complementary effect in combination with R^2 in relapsed/refractory iNHL is very exciting and offers new hope for this patient group, most of whom still see insufficient efficacy with available therapeutics."

EO2463 is designed to expand pre-existing memory $CD8^+$ T cells recognizing non-self-protein sequences from gut bacteria, which mimic several purposefully selected B cell antigens. The interim SIDNEY data from Cohorts 1 and 4 presented at ICML show fast, robust, and durable expansion of the specific $CD8^+$ T cells that were active against EO2463 mimic peptides and the targeted B cell epitopes. Most important, the magnitude of the EO2463-driven expansion of specific $CD8^+$ T cells correlated with the probability of complete remission upon treatment with EO2463 combined with R^2 in the SIDNEY study. EO2463 in combination with lenalidomide and rituximab (R^2) is well tolerated in patients with follicular and marginal zone lymphoma.

Jan Fagerberg, Chief Medical Officer of Enterome, said, "These early efficacy results suggest EO2463 offers additional benefit when used together with the R^2 regimen in patients with relapsed/refractory iNHL. We **previously reported data** from Cohort 2 of SIDNEY, at ASH in December 2024, showing that EO2463 OncoMimics™ monotherapy generated a 46% objective response rate in patients who are usually proposed 'watchful waiting' and no active anti-lymphoma therapy – and also had an excellent tolerability profile. In short, taken together, these SIDNEY data indicate that this well tolerated novel active immunotherapy may well have broad potential across hematological malignancies."

EO2463 is an innovative, off-the-shelf OncoMimics™ active immunotherapy that combines four synthetic 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). It also includes the helper peptide (CD4+ epitope) universal cancer peptide 2 (UCP2).

The unique ability of EO2463 active immunotherapy to selectively target multiple B cell markers enables the destruction of malignant B lymphocytes. By ensuring broad target coverage across malignant B cells, this novel approach aims to simultaneously improve

safety and maximize efficacy, reducing the tumor cells' capacity to develop immune-resistance mechanisms such as antigen escape.

SIDNEY is an ongoing open label Phase 1/2 study that aims to assess safety, tolerability, immunogenicity, and preliminary efficacy of EO2463 monotherapy and combination therapy with lenalidomide/rituximab in up to 55 patients with follicular lymphoma and marginal zone lymphoma including four cohorts of three patient populations:

- Cohort 2: patients with newly diagnosed, previously untreated low tumor burden disease, not in need of standard of care therapy, i.e., the "watch-and-wait" setting; treatment = EO2463 monotherapy
- Cohort 3: patients with newly diagnosed, previously untreated low tumor burden disease, in need of therapy; treatment = EO2463 in combination with rituximab
- Cohorts 1 and 4: patients with relapsed/refractory disease and at least one prior treatment; treatment = EO2463 in combination with lenalidomide and rituximab (R^2)

OncoMimics™ are synthetically produced peptides designed *in silico* using AI and machine learning to mine Enterome's extensive proprietary database of microbial bacteria. Unlike cancer antigens, OncoMimics™ bypass a gating process, known as thymic deletion, that prevents the immune system from mounting an attack against the "self" proteins (e.g. antigen) on tumor and blood cancer cells. Furthermore, that they trigger a more targeted, rapid and robust immune response than would otherwise be possible, because very early in human development the immune system learns to protect the body from microbiome bacteria. This means that OncoMimics™ call up memory CD8+ T cells that selectively target the cancer cells that carry the mimicked antigen(s). This therapeutic strategy takes inspiration from and is de-risked by emulating the gut microbiome's causal role in certain autoimmune diseases.

OncoMimics™ are easy to manufacture, store, distribute and administer as an "off-the-shelf" subcutaneous injection. In clinical testing to date they have been shown to be extremely well tolerated, especially compared to other potent immunotherapies.

Enterome SA (www.enterome.com) is a privately held clinical-stage biopharmaceutical company developing breakthrough OncoMimics™ immunotherapeutics for cancer. The three most advanced product candidates have shown positive early data in Phase 2 clinical development, supporting novel OncoMimics™ modality. The company's pioneering approach to drug discovery is based on the unique and powerful bacterial Mimicry drug discovery platform, which allows it to discover OncoMimics™ with high similarity to tumor

associated antigen (TAA) based on the big-data insights from millions of gut bacterial proteins, that live in humans.

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