Enterome presents proof-of-concept immune response data and first clinical data from Phase 1/2 trial with EO2401, a first-in-class OncoMimics™ therapeutic cancer vaccine for glioblastoma, at ASCO 2022

Clinical data highlight strong immune responses (proof-of-concept) and early signs of possible clinical benefit in recurrent glioblastoma

Triple combination of EO2401, nivolumab and bevacizumab demonstrated Objective Response Rate of 54.5% and Disease Control Rate of 81.8%

Paris, France – June 6, 2022

Enterome, a clinical stage biopharmaceutical company developing first-in-class immunomodulatory drugs based on its bacterial Mimicry drug discovery platform, today announces proof-of-concept immune response data and first clinical data from its Phase 1/2 clinical trial of EO2401 in combination with an immune checkpoint inhibitor (nivolumab, Opdivo®) +/- an anti-VEGF therapy (bevacizumab, Avastin®), for the treatment of patients with first progression/recurrence of glioblastoma (the ROSALIE trial, EOGBM1-18, NCT04116658). The data[1] were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting, on June 5, 2022 in Chicago and virtually.

EO2401 is Enterome's first-in-class off-the-shelf OncoMimics™ cancer immunotherapy. It combines three OncoMimics™ peptides that closely mimic IL13Ra2, BIRC5 and FOXM1, all of which are known driver antigens present on aggressive solid tumors. In addition, EO2401 contains a CD4 helper peptide UCP2. Enterome selected these OncoMimics™ using its Mimicry platform, which applies best-in-class biocomputational tools and bioassays to identify novel therapeutics from its proprietary database of 20+ million bioactive gut microbiome peptides and proteins.

Key highlights from the EO2401 poster presentation covering the Phase 1/2 ROSALIE trial were:

Proof-of-concept immune response data

Immune monitoring demonstrated the ability of the individual microbiome-derived peptides that comprise EO2401 to induce a strong CD8+ T cell response in patients with strong cross-reactivity against the human tumor antigens that they mimic.

Positive responses against the three OncoMimics™ peptides were demonstrated for 26 of the 27 patients investigated, and sustained for more than 44 weeks in the longest-followed patient.

Promising clinical outcomes

The combination of EO2401 plus nivolumab in study part 1 (Cohorts 1/2a/2b, n=29), despite short treatment durations, showed promising survival with a possible plateau at around 30% after 1 year. The short treatment durations were thought to be a result of a higher than expected rate of "pseudoprogression" leading to neurological symptoms (infiltration of tumor by immune cells and edema).

In study part 2, the addition of time-limited, low-dose bevacizumab as a symptom-driven anti-edema treatment (to counteract edema due to tumor infiltration of immune cells) supported prolonged treatment durations, which could also potentially impact efficacy (efficacy not yet presented due to short follow-up).

The triple combination of EO2401 plus nivolumab and bevacizumab (Cohort 3, n=11) demonstrated interesting directly measurable anti-tumor efficacy (objective tumor shrinkage) as compared with that observed in Cohort 1/2a/2b from study part 1 (EO2401 plus nivolumab without any bevacizumab) (below), and also with previous results shown with a checkpoint inhibitor (pembrolizumab or nivolumab) plus bevacizumab in contemporary trials[2,3]:

- **Objective response rates (ORR) – Cohort 3: 54.5%** (95% CI 23.4; 83.3) vs **Cohorts 1/2a/2b: 10.3%** (95% CI 2.2; 27.4)
- **Disease control rates (DCR) – Cohort 3: 81.8%** (95% CI 48.2; 97.7) vs **Cohorts 1/2a/2b: 34.5%** (95% CI 17.9; 54.3)

The encouraging efficacy seen with the triplet, including longer treatment durations, supports the hypothesis that the addition of symptomatic anti-edema treatment with time-limited, low-dose bevacizumab to the EO2401 plus nivolumab combination might influence efficacy positively.

Safety

The combination of EO2401, administered sub-cutaneously with the adjuvant Montanide ISA 51 VG, with nivolumab +/- bevacizumab was well tolerated. The safety profile was consistent with the profile of nivolumab, and, when applicable, the profile of bevacizumab, except the addition of local administration site reactions (occurring in 48% of patients, all Grade 1-2).

Professor Wolfgang Wick, Universitätsklinikum Heidelberg and German Cancer Research Center, Heidelberg, Germany commented, "*I am pleased to be part of the ROSALIE trial, the first clinical study to evaluate Enterome's novel therapeutic vaccine EO2401, which is based on the OncoMimics™ concept. In contrast to tumor antigens, the OncoMimic™ peptides in EO2401 are recognized by the immune system as "non-self" and, as we have seen in this study, generate strong human cytotoxic CD8+ responses. Based on the immune response and early clinical data that we have seen so far in this extremely challenging patient propulation, I am hopeful that more mature data from the trial might support further development steps in glioblastoma.*"

Jan Fagerberg, Chief Medical Officer of Enterome said**, "***I am very pleased that we have been able to present these very encouraging data from the ROSALIE trial, evaluating EO2401 in combination with checkpoint blockade, and checkpoint blockade plus anti-VEGF therapy. Most importantly, this first presentation of data from a clinical trial of EO2401 show proof-of-concept with regard to immune response, and also encouraging clinical data. We are looking forward to sharing a more mature set of data from ROSALIE at ESMO in September, which we hope will reinforce the positive findings that we have communicated at ASCO."*

EO2401 in adrenal malignancies

At ASCO, and separately announced today, Enterome presented the first clinical data from its Phase 1/2 clinical trials of EO2401 in combination with nivolumab for the treatment of patients with adrenal tumors (the SPENCER trial, EOADR1-19). View press release **here**.

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About ROSALIE

ROSALIE (EOGBM1-18, NCT04116658) is a multicenter, open-label, Phase 1/2 trial investigating EO2401 in combination with nivolumab, and in combination with nivolumab/bevacizumab in patients with glioblastoma at first progression/recurrence after surgery and adjuvant radiotherapy/temozolomide. The trial is assessing safety, tolerability, immunogenicity and preliminary efficacy in approximately 80 patients at centers in the US and Europe

References

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2. Nayak, L. et al. Randomized Phase II and Biomarker Study of Pembrolizumab plus Bevacizumab versus Pembrolizumab Alone for Patients with Recurrent Glioblastoma. Clin Cancer Res (2021) 27:1048–57 doi: 10.1158/1078-0432.CCR-20-2500
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About Enterome

Enterome is a clinical-stage biopharmaceutical company focused on 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 discovery platform allowing to uncover new biological insights from millions of gut bacteria proteins in constant cross-talk with the human body.

Enterome's potentially 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.

Enterome is presently advancing two pipelines of drug candidates, OncoMimics™ and EndoMimics™, which have the potential to address cancer, inflammatory and autoimmune diseases, respectively:

- OncoMimics™ peptides, a pipeline of therapeutic cancer vaccines. The lead candidate EO2401 is in Phase 1/2 clinical trials in patients with glioblastoma and adrenal tumors and has demonstrated clinical proof of concept. A second OncoMimics™ candidate, EO2463 is in a Phase 1/2 clinical trial for indolent non-Hodgkin lymphomas. Clinical proof-of-concept data are expected in H1 2023. EO4010 is in development for colorectal cancer and targeted to enter clinical trials in 2023.
- EndoMimics™ peptides, a pipeline of next generation bioactives acting like human hormones or cytokines for the treatment of immune diseases. EB1010, the lead candidate, is a potent local inducer of IL-10 designed to provide improved therapeutic outcomes for patients with IBD. EB1010 is expected to enter the clinic in 2023.

Enterome employs 65 people and is headquartered in Paris, France. Since its inception, the company has raised a total of €96 million from Europe- and US-based life science investors and more than €120 million from pharmaceutical partnerships.

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