PRESS RELEASE
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Enterome announces first patient dosed in Phase 2a trial of sibofimloc in Crohn's disease

• Sibofimloc (EB8018/TAK-018) is a first-in-class, orally administered, gut-restricted small molecule designed to reduce inflammation underlying Crohn's disease

• Sibofimloc binds FimH, a novel microbiome-derived therapeutic target validated by Enterome, to selectively disarm virulent bacteria in the gut that can cause inflammation without disrupting the local microbiome

• Sibofimloc is advancing through clinical development under a global licensing, co-development and co-commercialization partnership with Takeda

Paris, France and Cambridge, MA, USA – September 23, 2020

ENTEROME SA, a clinical-stage biopharmaceutical company leveraging its unique knowledge of the microbiome-immunoinflammation axis to develop next-generation therapeutics, today announced that the first patient has been dosed in a Phase 2a clinical trial of sibofimloc (EB8018/TAK-018) in patients with Crohn's disease. Sibofimloc is advancing through clinical development under a 2018 global licensing, co-development and co-commercialization partnership with Takeda Pharmaceutical Company Limited ("Takeda").

Sibofimloc is a first-in-class, orally administered small molecule specifically designed to reduce the inflammatory cascade underlying Crohn's disease and remain gut-restricted, to minimize absorption into the bloodstream.

Sibofimloc binds FimH, a novel microbiome-derived therapeutic target validated by Enterome, to selectively disarm virulent bacteria in the gut that can cause intestinal inflammation without disrupting the local microbiome. It acts by inhibiting FimH-mediated inflammation induced by the interaction of pathogenic pro-inflammatory bacteria expressing FimH to human TLR4 receptors in the gut wall, thereby reducing the production of inflammatory cytokines including TNF alpha.

Sibofimloc was found to be well tolerated in healthy volunteers and in patients with Crohn's disease in Phase 1 studies, which also generated first indications of target engagement.

Based on these data, sibofimloc has been advanced into a randomized, double-blind, placebo-controlled, multicenter, Phase 2a study ("SYMMETRY"; NCT03943446) to evaluate its safety, tolerability and proof of concept for the prevention of recurrence of intestinal inflammation in up to 96 postoperative participants with Crohn's disease.
The primary endpoint of the study is the percentage of participants with endoscopic recurrence of Crohn's disease as assessed by Rutgeerts grading scale* at week 26. The trial will take place in the US and Europe and results are expected in 2022.

Vijay Yajnik, Global Clinical Lead, Microbiome and Senior Medical Director, GI Therapeutic Area Unit at Takeda, commented: "*We are delighted with the progress being made with sibofimloc. The clinical and translational data have been encouraging for what could be a truly novel approach to treating inflammation in Crohn's disease patients. We look forward to advancing patient enrollment into the trial as quickly as possible.*"

Jan Fagerberg, Chief Medical Officer of Enterome, added: "*Sibofimloc blocks a virulence factor on pathogenic gut bacteria that Enterome has validated by the application of our metagenomic technologies and that is currently not targeted by any available therapies. We believe that its novel anti-inflammatory mechanism of action could also be applicable in other serious inflammatory bowel diseases (IBD) and in different therapeutic settings of IBD, such as chronic active disease. The progress we are making in collaboration with Takeda is very exciting and we hope this new trial will demonstrate the clinical potential of sibofimloc.*"

*Endoscopic recurrence is defined as a Rutgeerts' score greater than or equal to (>=) i2. The Rutgeerts scoring is a 5-point scale used to assess endoscopic recurrence at the ileocolonic anastomosis and preanastomotic ileum. The scale ranges from i0 to i4; where i0 equal to (=) no lesions, i1= less than or equal to (<=) 5 aphthous ulcers, i2= greater than (>) 5 aphthous ulcers with normal mucosa between lesions or lesions are confined to the anastomosis, i3= diffuse aphthous ileitis with diffusely inflamed mucosa and i4= diffuse inflammation with larger ulcers, nodules, and/or narrowing.

About the Enterome-Takeda agreement

Enterome entered into a global licensing, co-development and co-commercialization agreement with Takeda in October 2018 for sibofimloc in patients with Crohn's disease, with the potential to expand to other gastrointestinal (GI) disorders and liver diseases.

Enterome received a $50 million upfront payment on signing as well as a commitment from Takeda to make further investments in the Company, including in Enterome's Series E financing in June 2020. Enterome is also eligible to receive up to $640 million for achieving specified clinical development, regulatory and commercial milestones with sibofimloc. In addition, Enterome and Takeda will co-develop sibofimloc under the joint agreement and, if approved, the product will be co-promoted in the US under a profit/cost sharing structure. Takeda will receive an exclusive license to commercialize sibofimloc outside of the US, and Enterome will be eligible to receive royalties on net sales generated in these territories.

Sibofimloc was discovered by Vertex Pharmaceuticals, Inc. and in-licensed by Enterome in 2016.

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About Enterome

Enterome is a world leader in the discovery and development of novel pharmaceuticals based on its unrivalled understanding of the interaction between the gut microbiome and the immune system (the 'microbiome-immunoinflammation axis'). Enterome is leveraging this expertise to develop a pipeline of clinical and pre-clinical candidates (small molecules, proteins and peptides) with a focus on cancer, autoimmune, inflammatory and metabolic diseases.

Enterome has two unique platforms that are generating highly promising drug candidates:

- **OncoMimics:** highly effective, off-the-shelf immunotherapies against cancers (EO2401, EO2463). EO2401 is in Phase 1/2 clinical trials in patients with glioblastoma and adrenal tumors. EO2463, is being prepared as a clinical candidate for B-cell malignancies (lymphomas and leukemias).
- **EndoMimics:** a new generation of biologics for inflammatory diseases (EM101), Type 2 diabetes and inflammatory bowel disease.

These highly productive platforms have been created using Enterome's world-leading Metasecretome technology, which gives it an unrivalled ability to generate precision drugs by using the natural reservoir of thousands of safe and tolerized effector proteins that are produced by the gut bacteria.

In addition, Enterome's clinical candidate EB8018 (also referred to as sibofimloc/TAK-018), which selectively blocks the virulence factor FimH, is advancing through Phase 2 clinical trials in Crohn's disease. EB8018 has been partnered with Takeda globally, with Enterome retaining a significant profit share in the US.

Enterome is headquartered in Paris (France) with operations in Boston (US) and is backed by leading venture capital investors.

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