PRESS RELEASE
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Enterome highlights *Microbiome* publication describing sibofimloc's novel mechanism of action for the treatment of Crohn's disease

• The mechanism of action of the investigational medicine sibofimloc positions it as a potential novel and important treatment option for Crohn's disease

• Oral sibofimloc is a first-in-class gut-restricted small molecule FimH-blocker designed to treat the underlying cause of Crohn's disease and maintain patients in a non-inflammatory disease state

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

Paris, France – September 16, 2021

ENTEROME SA, a clinical stage biopharmaceutical company developing novel drugs based on its unique ability to decode molecular interactions in the gut microbiome impacting human health, announces the publication of a new paper describing the novel mechanism of action of its investigational medicine sibofimloc (also called TAK-018) for the treatment of Crohn's disease (CD) in the high impact peer-reviewed journal *Microbiome*. Sibofimloc is currently in Phase 2a clinical trial and is being developed under a global licensing, co-development and co-commercialization agreement with Takeda Pharmaceutical Company Limited ("Takeda").

Sibofimloc is a first-in-class, orally administered, gut-restricted small molecule FimH-blocker designed to treat the underlying cause of CD and maintain patients in a non-inflammatory disease state.

In the paper, the authors showed that blocking the adhesion of overabundant FimH-expressing bacteria to the gut wall is a promising therapeutic mechanism that effectively disarms these virulent bacteria without killing them. This mechanism represents a highly selective strategy to suppress the potentially critical trigger of intestinal inflammation in CD patients without disturbing the overall composition of the gut microbiota.

Sibofimloc was shown to selectively bind and aggregate FimH-expressing bacteria in 65%-85% of ileal biopsies from CD patients. Aggregation of bacteria to sibofimloc led to a strong decrease in inflammation and a general improvement of gut integrity. Furthermore, when used at therapeutically relevant doses, sibofimloc preserved normal gut tissue integrity.

Dr Vijay Yajnik, Senior Medical Director of the Gastroenterology Therapeutic Area Unit at Takeda, said: "Current therapies for the treatment of Crohn's disease target the patient's immune system, but there still remains a significant unmet medical need to develop new therapies targeting novel pathways including the gut microbiome. The published research on sibofimloc shows a very

promising finding that it exerts its local anti-inflammatory action by blocking pathogenic bacteria without disrupting the commensal gut microbiome."

Dr Christophe Bonny, Chief Scientific Officer at Enterome, said: "It is a great achievement for the Enterome team that we have been able to publish such promising data. Sibofimloc's innovative mechanism of action targets the virulence factor FimH expressed on pathogenic gut bacteria from the Enterobacteriaceae family. This target has been validated by the application of Enterome's unique and proprietary technologies. Sibofimloc, which is currently the only drug candidate targeting the underlying cause of the disease, is in a Phase 2 trial in post-operative Crohn's disease and a data readout is expected in H1 2023. 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 as a maintenance therapy with an attractive safety profile."

The Phase 1b trial evaluating sibofimloc in active CD patients was well tolerated, demonstrated minimal systemic exposure and decreased several inflammatory biomarkers.

Reference

Chevalier*, Laveissière*, *et al.* Blockage of bacterial FimH prevents mucosal inflammation associated with Crohn's disease. *Microbiome* (2021) DOI: 10.1186/s40168-021-01135-5 **[Link]**

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About Enterome

Enterome is a clinical stage biopharmaceutical company developing novel drugs based on its unique ability to decode molecular interactions in the gut microbiome impacting human health. Enterome's success is based on its unique ability to identify small proteins and peptides from gut bacteria that can deliver a therapeutic benefit in humans.

Enterome is leveraging this unique ability to develop two highly promising pipelines of clinical and pre-clinical candidates with a focus on cancer and inflammatory diseases:

- **OncoMimics™**: innovative, off-the-shelf, microbiome peptide powered cancer vaccines (EO2401, EO2463). EO2401 is in Phase 1/2 clinical trials in patients with glioblastoma and adrenal tumors. EO2463 is in a Phase 1/2 clinical trial for indolent non-Hodgkin B-cell lymphomas.

- **EndoMimics™**: a new generation of biologics targeting inflammatory diseases (EB1010).

These pipelines have been created using Enterome's highly efficient proprietary drug discovery platform that uses machine learning and lab assays to interrogate and decode the world's largest database of gut bacterial proteins, a unique source of novel precision drugs.

In addition, Enterome's clinical candidate sibofimloc (also referred to as TAK-018) is advancing through Phase 2 clinical trial in Crohn's disease. Sibofimloc has been partnered with Takeda globally, with Enterome retaining a significant profit share in the US.

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

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

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 disorders.

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 plan to 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.