Enthera Pharmaceuticals Announces Publication in the *Journal of Clinical Investigation* Supporting the Clinical Development of Ebrasodebart

- *Preclinical data demonstrate crucial role of Transmembrane Protein 219 (TMEM219) in exacerbating inflammatory bowel disease (IBD) by inducing intestinal epithelial stem cell (ISC) death and impairing mucosal healing*
- *Findings support Phase 1 clinical development of Enthera's lead candidate, Ebrasodebart (Ent001), a monoclonal antibody targeting the IGFBP3/TMEM219 pathway*
- *Ebrasodebart is currently being studied in a proof-of-concept Phase 1b clinical trial for the treatment of ulcerative colitis (UC)*

Milan, Italy, May 28, 2025 – Enthera Pharmaceuticals ("Enthera"), a clinical-stage biotech company developing a first-in-class antibody therapeutic targeting the Insulin Growth Factor Binding Protein 3 (IGFBP3)/TMEM219 pathway for IBD and T1D, today announced the publication of preclinical data in *The Journal of Clinical Investigation* that revealed TMEM219's key role in driving ISC apoptosis and impairing mucosal healing in IBD.

The findings support Enthera's clinical development of Ebrasodebart, a monoclonal antibody that targets the IGFBP3/TMEM219 pathway for the treatment of IBD, including UC and Crohn's disease. The company recently completed patient enrollment in the Phase 1b trial with Ebrasodebart in patients with UC.

"Our publication in the prestigious *Journal of Clinical Investigation* is a validation of our scientific approach and testament to our team's commitment to targeting the TMEM219 pathway in IBD," said **Dr. Lisa M. Olson, CEO of Enthera**. "This research sheds light on the complex pathophysiology of IBD and supports the examination of the potential of Ebrasodebart to deliver clinical benefit to those patients who do not respond to existing immunomodulating treatments."

As outlined in the publication, patients with refractory or active Crohn's disease experienced overactive TMEM219 signaling that correlated with a failure to regenerate the mucosal layer, despite immune suppressive therapy, and contributed to increased ISC death. Regulating TMEM219 by blocking the interaction between the protein and its ligand, IGFBP3, restored the self-renewal capabilities *in vitro* in patient-derived organoids (PDOs). These results were further supported by the demonstration of attenuating TMEM219 *in vivo,* which improved colitis symptoms and promoted mucosal healing in mouse models. The preclinical findings suggest the potential of a new therapeutic avenue focused on epithelial repair.

About Enthera Pharmaceuticals

Enthera Srl is a clinical-stage biotech company developing first-in-class antibody therapeutics to transform the treatment paradigm in inflammatory bowel diseases (IBD) and type 1 diabetes (T1D) by re-establishing stem cell capabilities. Enthera's pioneering approach capitalizes on the key discovery of the IGFBP3/TMEM219 pathway, which is dysregulated in IBD and T1D patients and leads to excessive apoptosis of stem cell in the gut and beta cells in the pancreas. Enthera's lead program, Ebrasodebart (Ent001), which is currently in Phase 1 clinical development, has the potential to restore the original intestinal mucosal structure in IBD and the endogenous pancreatic stem cell compartment in T1D, resulting in the restoration of organ function.

Enthera is a private company headquartered in Milan, Italy and founded in 2016 by Prof. Paolo Fiorina and Dr. Francesca D'Addio with BiovelocITA, Italy's first biotech accelerator. Enthera's discovery engine and assets are protected by a broad portfolio of patents. The company is backed by Sofinnova Partners, AbbVie Ventures, T1D Fund, Roche Venture Fund, and several Italian private investors.

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