SCOHIA PHARMA, Inc.
June 3, 2019

Publication regarding preclinical studies of SCO-792, a novel enteropeptidase inhibitor

Our research achievement using SCO-792, a novel enteropeptidase inhibitor, was published online in *Diabetes, Obesity and Metabolism* on May 30, 2019. The research group of SCOHIA PHARMA, Inc. and Takeda Pharmaceutical Co., Ltd. elucidated the anti-diabetic and anti-obese effects of SCO-792 in preclinical mouse models in this study.

Paper Title
SCO-792, an enteropeptidase inhibitor, improves disease status of diabetes and obesity in mice
https://onlinelibrary.wiley.com/doi/10.1111/dom.13799

Enteropeptidase is a serine protease localized on the duodenal brush border that catalyzes the conversion of inactive trypsinogen into active trypsin, thereby regulating protein breakdown in the gut. Although proteins contain the same number of calories (4 calories/g) as carbohydrates (4 calories/g), drugs that inhibit dietary protein absorption have not been developed for treating metabolic diseases, unlike carbohydrates and fats.

A new study by the SCOHIA PHARMA, Inc. and Takeda Pharmaceutical Company, ltd. has shown that enteropeptidase inhibition is highly effective to treat diabetes and obesity in preclinical studies.

A single oral administration of SCO-792 inhibited plasma branched-chain amino acids (BCAAs) in an oral protein challenge test in mice, indicating *in vivo* inhibition of enteropeptidase. Repeated treatment with SCO-792 induced food intake reduction and body weight decrease in diet-induced obese (DIO) and obese and diabetic *ob/ob* mice. Plasma FGF21 levels were increased in SCO-792-treated DIO mice—an observation that was likely to be independent of food intake reduction. Hyperglycemia was markedly improved in SCO-792-treated *ob/ob* mice. A hyperinsulinemic-euglycemic clamp study revealed improved muscle insulin sensitivity in SCO-792-treated *ob/ob* mice. SCO-792

also improved plasma and liver lipid profiles and decreased plasma alanine transaminase, suggesting a potential treatment for liver diseases. Dietary supplementation with essential amino acids attenuated the effect of SCO-792 on food intake reduction and body weight decrease in normal mice, suggesting a pivotal role for enteropeptidase in these biological phenomena.

In conclusion, SCO-792 inhibited enteropeptidase *in vivo*, decreased food intake and body weight, increased insulin sensitivity, improved glucose and lipid control, and ameliorated liver parameters in mouse models with obesity and/or diabetes. SCO-792 may exhibit similar effects in patients.

Contact for inquiries : info@scohia.com