Results from Two Phase 3 Clinical Trials of Chronic Constipation Treatment "GOOFICE® 5mg Tablet" Published in The Lancet Gastroenterology & Hepatology

This material is an English translation of the press release issued on July 9, 2018 in Japanese, and the Japanese release is given priority regarding content and interpretation.

July 9, 2018

Mochida Pharmaceutical Co., Ltd.
EA Pharma Co., Ltd.
Eisai Co., Ltd.

Mochida Pharmaceutical Co., Ltd. (President: Naoyuki Mochida; Headquarters: Shinjuku-ku, Tokyo, Japan) (hereinafter "Mochida") and Eisai Co., Ltd. (CEO: Haruo Naito; Headquarters: Bunkyo-ku, Tokyo, Japan) (hereinafter "Eisai"), Eisai's subsidiary for gastrointestinal diseases EA Pharma Co., Ltd. (President & CEO: Yuji Matsue; Headquarters: Chuo-ku, Tokyo, Japan) (hereinafter "EA Pharma") announce that results from two phase 3 clinical trials (a 2-week double-blind placebo-controlled phase 3 trial and an open-label single-arm 52-week long-term phase 3 trial) for the bile acid transporter inhibitor "GOOFICE® 5mg Tablet" (nonproprietary name: elobixibat hydrate; development code: AJG533, hereinafter "elobixibat") have been published in *The Lancet Gastroenterology & Hepatology*,[1)] a journal of *The Lancet* which is one of the world's most influential medical journals.

The 2-week double-blind clinical trial was a placebo-controlled, randomized, double-blind trial with 133 Japanese patients with chronic constipation. Patients were orally administered 10 mg of elobixibat or placebo once daily for 2 weeks. The elobixibat group demonstrated statistically significant improvements in the primary endpoint of change in spontaneous bowel movement[2)] frequency, as well as in secondary endpoints including change in complete spontaneous bowel movement[3)] frequency (the secondary endpoint), length of time between dosing and the first spontaneous bowel movement, compared to the placebo group. The major side effects were abdominal pain, diarrhea and other gastrointestinal symptoms. There were no serious side effects.

The 52-week open-label phase 3 clinical trial was a single arm trial to evaluate the efficacy and safety of long-term administration of elobixibat in 341 Japanese patients with chronic constipation. The initial dose was 10 mg once daily orally for 7 days. The dose was increased or decreased in the range of 5, 10 and 15 mg per day appropriately depending on the symptoms and given for 52 weeks. As a result, constipation-related improvements including spontaneous bowel movement frequency, complete spontaneous bowel movement frequency and stool consistency were observed as early as 1 week of administration, and the effects were maintained favorably through 52 weeks. The longer the dosing period, the higher patients' satisfaction relating to defecation tended to be. In addition, in all the JPAC-QOL[4)] scores, there were statistically significant declines[5)] compared to baseline. The major side effects were abdominal pain, diarrhea, lower abdominal pain and other gastrointestinal symptoms. A serious side effect (inguinal hernia) was observed in 1 patient.

The above clinical trial results were presented at Digestive Disease Week (DDW) 2018, June 2-5 in Washington D.C., USA.

Elobixibat was jointly developed by Mochida and EA Pharma. Mochida and EA Pharma distribute elobixibat under the same brand name “GOOFICE® 5mg Tablet”, respectively, in Japan. EA Pharma and Eisai jointly provide proper use information of “GOOFICE® 5mg Tablet” under a co-promotion agreement.

Mochida, EA Pharma and Eisai strive to make a further contribution to improve QOL for patients with chronic constipation through maximization of the product value of “GOOFICE® 5mg Tablet”.

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1) Atsushi Nakajima et al. “Safety and efficacy of elobixibat for chronic constipation: results from a randomised, double-blind, placebo-controlled, phase 3 trial and an open-label, single-arm, phase 3 trial” *The Lancet Gastroenterology & Hepatology; 2018; 3: 537-547*
https://www.thelancet.com/journals/langas/article/PIIS2468-1253(18)30123-7/abstract
2) Defecation that occurs without a laxative, enema or manual disimpaction
3) Spontaneous bowel movement without a feeling of incomplete evacuation
4) Japanese version of the Patient Assessment of Constipation Quality of Life questionnaire （PAC-QOL）
5) Lower scores mean better quality of life

More Information

1. About elobixibat（Nonproprietary name: elobixibat hydrate; development code AJG533; brand name "GOOFICE® 5 mg Tablet"）

Elobixibat is a once-daily, orally available chronic constipation* treatment with a novel action mechanism. EA Pharma in-licensed this product from Albireo AB (Headquarters: Sweden) and obtained manufacture and marketing approval in Japan. Elobixibat inhibits the bile acid transporter that regulates reabsorption of bile acids thereby increasing the flow of bile acids to the colon. Elobixibat is the world's first pharmaceutical product approved for marketing with the above action mechanism. The dual action of moisture secretion and bowel movement promotion by bile acids can facilitate defecation.

*Excluding structural disease-caused constipation

2. About *The Lancet Gastroenterology & Hepatology*

The Lancet Gastroenterology & Hepatology is a journal of The Lancet journals, focusing on the gastroenterology and hepatology. The Lancet is one of the 5 most-impacting medical journals in the world.

3. About Mochida Pharmaceutical Co., Ltd.

Mochida Pharmaceutical Co., Ltd. has been committed to research and development of innovative pharmaceutical products since its establishment thereby providing distinctive medicines to the medical field. Currently, the core pharmaceutical business focuses resources on the targeted areas of cardiovascular, obstetrics and gynecology, dermatology, psychiatry and gastroenterology, while also providing medicine for intractable disease as well as generics including biosimilars, to meet medical needs.

For more information on Mochida Pharmaceutical Co., Ltd., please see http://www.mochida.co.jp/english/

4. About EA Pharma Co., Ltd.

EA Pharma Co., Ltd., a subsidiary of Eisai Co., Ltd. for gastrointestinal disease area, was established in April 2016 by integration of the gastrointestinal business unit with more than 60 years' history of the Eisai Group and the gastrointestinal business unit of the Ajinomoto Group having amino acid as its business core. EA Pharma is a gastrointestinal specialty pharma with a full value chain covering R&D, logistics and sales & marketing.

For more information on EA Pharma Co., Ltd., please see http://www.eapharma.co.jp/en/

5. About Eisai Co., Ltd.

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our human health

care (*hhc*) philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products to address unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.
For more information on Eisai Co., Ltd., please see https://www.eisai.com/