

March 31, 2022

EA Pharma Co., Ltd.
Kissei Pharmaceutical Co., Ltd.
(Code 4547, Tokyo Stock Exchange 1st Section)

**Results of Phase III Clinical Study of “CAROGRAM[®] Tablets”
Conducted in Japan for Treatment of Ulcerative Colitis (AJM300/CT3)
Published in The Lancet Gastroenterology & Hepatology**

EA Pharma Co., Ltd. (President, Hidenori Yabune; Headquarters, Chuo-ku, Tokyo, Japan; “EA Pharma”) and Kissei Pharmaceutical Co., Ltd. (Head Office: Matsumoto, Nagano; Chairman and CEO: Mutsuo Kanzawa; “Kissei”) announced that results of Phase III clinical study (AJM300/CT3) conducted in Japan for CAROGRAM[®] (nonproprietary name, carotegrast methyl; development code AJM300; hereinafter “CAROGRAM[®]”), of which EA Pharma obtained the manufacturing and marketing approval as of March 28, 2022 indicated for treatment of ulcerative colitis, published in *The Lancet Gastroenterology & Hepatology**, a sister journal of The Lancet. The Lancet is one of the most influential medical journals in the world.

This study was a randomized, double-blind, placebo-controlled study in 203 patients with moderate active ulcerative colitis who had inadequate response or intolerance to the standard treatment with 5-aminosalicylic acid in 82 medical facilities in Japan. The patients were randomized to the groups treated with CAROGRAM[®] or placebo and received oral administration 3 times daily for 8 weeks to investigate the efficacy and safety of CAROGRAM[®]. As a result of the study, in clinical response rate by Mayo Score at 8 weeks of administration (the primary endpoint), the superiority of CAROGRAM[®] group to placebo group was demonstrated. In addition, statistically significant improvements were observed in the secondary endpoints including endoscopic remission rate. The adverse event incidences were similar between CAROGRAM[®] group and placebo group. The major adverse events observed in CAROGRAM[®] group were nasopharyngitis, headache and nausea.

CAROGRAM[®] is a small molecule that was originated by EA Pharma (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.) and is the world-first orally available $\alpha 4$ -integrin antagonist. In Japan, Kissei distributes CAROGRAM[®] with copromotion by EA Pharma. EA Pharma and Kissei strive to increase treatment options for ulcerative colitis to contribute to QOL (Quality of Life) of patients and their families.

*Katsuyoshi Matsuoka et al. AJM300 (carotegrast methyl), an oral antagonist of $\alpha 4$ -integrin, as induction therapy for patients with moderately active ulcerative colitis: a multicentre, randomised, double-blind, placebo-controlled phase 3 study
The Lancet Gastroenterology & Hepatology, Published: March 30, 2022
<https://www.thelancet.com/journals/langas/onlineFirst>

Media Inquiries	
EA Pharma Co., Ltd. Corporate Planning Dept. TEL: +81(0)3-6280-9802	Kissei Pharmaceutical Co., Ltd. Public Relations Dept. TEL: +81(0)263-25-9523

《More Information》

1. 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 year's history of the Eisai Group and the gastrointestinal business unit of the Ajinomoto Group having amino acid as its business core. EA Pharma Co., Ltd., is a gastrointestinal specialty pharmaceutical company with a full value chain covering R&D, production & logistics and sales & marketing.

For further information on EA Pharma Co., Ltd., please visit <https://www.eapharma.co.jp/en/>

2. About Kissei Pharmaceutical Co., Ltd.

Under the management philosophy “contribute to society through high-quality, innovative pharmaceutical products” and “serve society through our employees”, Kissei Pharmaceutical Co., Ltd. provides unique innovative pharmaceutical products as a drug discovery and R&D-oriented company for patients in the world with a special focus on urology, nephrology, dialysis, diabetes, gastroenterology and rare diseases.

For more details about Kissei Pharmaceutical Co., Ltd., please visit <https://www.kissei.co.jp/>

3. About CAROGRA[®] (nonproprietary name: carotegrast methyl)

CAROGRA[®] is an orally available small molecule $\alpha 4$ -integrin antagonist that was originated by EA Pharma (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.). CAROGRA[®] acts on both $\alpha 4\beta 1$ and $\alpha 4\beta 7$ integrins expressed on the surface of inflammatory cells to exert an anti-inflammatory effect by inhibiting the cell adhesion and suppressing excessive aggregation and invasion of inflammatory cells into the inflamed site in the colonic mucosa in ulcerative colitis.

4. About Ulcerative Colitis

Ulcerative colitis is an inflammatory disease that causes ulcers and erosions in the colonic mucosa. The major symptoms are abdominal pain, diarrhea, bloody stools and so on. In many cases, the “remission” stage where the symptoms improve and the “relapse” stage where the symptoms deteriorate repeat over time, and patients suffer from the decline of QOL. The mechanism of onset is unknown up to the present. In Japan, ulcerative colitis is one of the “designated intractable disease” by Ministry of Health, Labour and Welfare. The registered patient number in Japan was nearly 220,000 in 2019, and the patient number has a tendency to increase in recent years.¹⁾

1) Basic treatment guidance for patients with ulcerative colitis” (revised March 2020), Research group for intractable inflammatory bowel diseases, Research project on rare and intractable diseases, Health and Labour Sciences Research Grants.

5. About Mayo Score

Mayo Score is a disease activity index to rate the activity level of ulcerative colitis most frequently used in clinical study in these years. Mayo Score comprises of 4 sub-scores (stool frequency, rectal bleeding, mucosal appearance at endoscopy and physician's global assessment). Each score ranges between 0 to 3 points, and the disease activity is rated by the total of the points (0-12 points). The disease activity is regarded mild with the points between 3-5, moderate between 6-10 and severe between 11-12.