March 28, 2022

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

"CAROGRA® Tablets", Approved in Japan for Treatment of Ulcerative Colitis
- The World-First Orally Available α4 Integrin Antagonist -

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 EA Pharma obtained the manufacturing and marketing approval of "CAROGRA® Tablets" (Nonproprietary name, carotegrast methyl; Development code AJM300), hereinafter "CAROGRA®", for treatment of ulcerative colitis as of March 28, 2022 in Japan.

CAROGRA® is a small molecule compound that was originated by EA Pharma (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.) and is the first α4 integrin antagonist drug approved as an orally available dosage form in the world. CAROGRA® acts on both α4β1 and α4β7 integrins expressed on the surface of inflammatory cells to exert anti-inflammatory effects by suppressing excessive aggregation and invasion of inflammatory cells into the inflamed site of colonic mucosa in ulcerative colitis.

EA Pharma and Kissei have jointly developed CAROGRA® since 2015. This approval is based on the results of Phase III clinical study (AJM300/CT3) in patients with moderate active ulcerative colitis who had inadequate response or intolerance to the basic treatment with 5-aminosalicylic acid. CAROGRA® will be distributed by Kissei with co-promotion by EA Pharma in Japan.

EA Pharma and Kissei strive to increase treatment options for ulcerative colitis and contribute to QOL (Quality of Life) of patients and their families by providing CAROGRA® for clinical practice quickly.

Media Inquiries	
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《More Information》

1. CAROGRA® Tablets Product Outline

Brand Name	CAROGRA® Tablets
Nonproprietary Name	Carotegrast Methyl
Date of Manufacturing and Marketing Approval	March 28, 2022
Manufacturer and Marketing Authorization Holder	EA Pharma Co., Ltd.
Distributor	Kissei Pharmaceutical Co., Ltd.
Indication	Moderate ulcerative colitis (limited to those patients who had inadequate response to 5-aminosalicylic acid)
Dose and Administration	Normally in adults, 960 mg of carotegrast methyl per dose should be taken orally after a meal 3 times a day.

2. 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/

3. 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/

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 Phase III Clinical Study of CAROGRA® (AJM300/CT3)

The 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 CAROGRA® or placebo and received oral administration 3 times daily for 8 weeks to investigate the efficacy and safety of CAROGRA®. As a result of the study, in clinical response rate by Mayo Score at 8 weeks of administration (the primary endpoint), the superiority of CAROGRA® 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 CAROGRA® group and placebo group. The major adverse events observed in CAROGRA® group were nasopharyngitis, headache and nausea.

6. 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.