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

# Results of Phase III Clinical Study of AJM300 (Nonproprietary Name: Carotegrast Methyl) for Treatment of Ulcerative Colitis Conducted in Japan (AJM300/CT3 Study) – Primary Endpoint Achieved -

EA Pharma Co., Ltd. (President, Yuji Matsue; Headquarters, Chuo-ku, Tokyo, Japan) and Kissei Pharmaceutical Co., Ltd. (Head Office: Matsumoto, Nagano; Chairman and CEO: Mutsuo Kanzawa; "Kissei") announced that the primary endpoint was achieved in Phase III clinical study (AJM300/CT3) of AJM300 (nonproprietary name: carotegrast methyl), which the two companies have developed for treatment of ulcerative colitis.

Ulcerative colitis is an inflammatory bowel disease that causes ulcers and erosions in the colonic mucosa with symptoms of 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 (quality of life). 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).

AJM300 is an orally available low molecular weight alpha-4 integrin antagonist that was originated by EA Pharma (formerly known as Ajinomoto Pharmaceuticals Co., Ltd.). AJM300 acts on both alpha-4 beta-1 integrin and alpha-4 beta-7 integrin to exert an anti-inflammatory effect by suppressing excessive invasion of lymphocytes into the inflamed site. EA Pharma and Kissei have jointly developed AJM300 since 2015.

The above clinical study was conducted in 203 patients with moderately active ulcerative colitis who had inadequate response to the existing basic treatment with 5-aminosalicylic acid in 82 study sites located in Japan. Patients were randomized in a double-blind manner into the groups treated with AJM300 or given placebo and received oral administration 3 times daily for 8 weeks to evaluate the efficacy and safety.

As a result, statistically significant difference of AJM300 group to the placebo group in the response rate based on Mayo Score at 8 weeks, which is the primary endpoint of the study, was demonstrated. In addition, statistically significant improvements were observed in the secondary endpoints including mucosal remission rate and rectal bleeding disappearance rate. The major adverse events observed in AJM300 group were nasopharyngitis, headache and nausea. Details of the results will be presented in an international scientific conference in a near future.

EA Pharma and Kissei are now preparing for filing the marketing approval of AJM300 in Japan with the data of the above study. The two companies strive to quickly provide AJM300 for clinical practice in addition to "RECTABUL® 2 mg Rectal Foam 14 Doses", which is now available on the market distributed by both companies, to increase treatment options for ulcerative colitis and enhance QOL of patients.


| Media Inquires | |
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(More Information)

### 1. About EA Pharma Co., Ltd. (EA Pharma)

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
http://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, renal diseases dialysis, diabetes, gastroenterology and rare diseases.

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

### 3. About AJM300 (nonproprietary name: carotegrast methyl)

In ulcerative colitis, lymphocytes and other inflammatory cells excessively aggregate and invade into the inflamed site in the colonic mucosa. The series of reactions are mediated by binding of integrin expressed on the surface of inflammatory cells to adhesion molecules (VCAM-1, MAdCAM-1, etc.) excessively expressed on the vascular endothelial cells in the colonic mucosa. AJM300 (nonproprietary name: carotegrast methyl) can antagonize alpha-4 integrin and block the cell adhesion mediated by binding of

alpha-4 beta-1 integrin to VCAM-1 as well as alpha-4 beta-7 integrin to MAdCAM-1 to suppress the antiinflammatory actions. EA Pharma and Kissei aim to launch AJM300 as the first commercial product of orally available low molecular weight alpha-4 integrin antagonist in the world.

## 4. 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 (bowel movement frequency, rectal bleeding, mucosal appearance at endoscopy and physician rating). 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.

Source

(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.