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EA Pharma Co., Ltd.
Eisai Co., Ltd.

Industry-Academia-Government Joint Development Agreement Concerning Anti-Fractalkine Antibody E6011 for Treatment of Crohn's Disease Concluded, Research Activities Commence

Eisai Co., Ltd. (CEO: Haruo Naito; Headquarters: Tokyo, Japan, "Eisai") and Eisai's subsidiary for gastrointestinal diseases EA Pharma Co., Ltd. (President & CEO: Yuji Matsue; Headquarters: Tokyo, Japan, "EA Pharma") announced today that EA Pharma has entered into an industry-academia-government joint research agreement with six related joint research organizations, and that research activities have fully commenced. This joint research project was selected by the Japan Agency for Medical Research and Development (AMED) for its Cyclic Innovation for Clinical Empowerment (CiCLE) grant program.¹

E6011 is a novel anti-fractalkine antibody originally developed by Eisai's research subsidiary KAN Research Institute Inc. Fractalkine (FKN) is expressed in vascular endothelial cells in inflammatory diseases including inflammatory bowel disease and rheumatoid arthritis. FKN induces inflammatory reaction by binding to the immune cells expressing FKN receptors (CX3CR1). E6011 is a biopharmaceutical (antibody preparation) with the novel action mechanism of anti-inflammation by suppressing migration and invasion of CX3CR1 expressing immune cells.

EA Pharma represents the above initiative to "develop biologics and new markers originated in Japan for Crohn's disease by industry-academia collaboration," selected by AMED for CiCLE. In this project, EA Pharma conducts the clinical development of E6011, and the organizations under the joint research agreement (Keio University School of Medicine; Tokyo Medical and Dental University; Kitasato University Kitasato Institute Hospital; Nagoya City University; Kagoshima University and KAN Research Institute, Inc.) conduct the development of new biomarkers.

In addition to the above project, EA Pharma has also participated in the industry-academia-government joint project for commercialization of "acute liver failure treatment by the recombinant human hepatocyte growth factor," which was selected by AMED for Adaptable and Seamless Technology transfer Program through target driven R&D (AMED·A-STEP), as well as another project for "development of self-expanding biodegradable stents for the small intestine available for endoscopic stenting for treatment of benign disease-induced ileus," which was selected by AMED for its Development of Medical Devices through Collaboration between Medicine and Industry program. Further, the joint research project of EA Pharma and the University

of Tsukuba for “treating inflammatory bowel disease using small molecules and biomarkers” has been adopted by the Japan Science and Technology Agency’s Newly extended Technology transfer Program (NexTEP).

EA Pharma and Eisai strive to increase treatment benefits for patients with Crohn’s disease and their families through quicker development of E6011 via industry-academia-government collaboration, taking the advantage of adoption for CiCLE.

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More Information

1. About CiCLE

AMED’s CiCLE is a grant program to promote the establishment of infrastructure (including human resources) to respond to medical needs and the creation of an environment for open innovation and venture development based on industry-academia-government collaboration.

2. About E6011

E6011 is the world’s first humanized anti-fractalkine monoclonal antibody developed by Eisai’s research subsidiary KAN Research Institute, Inc. E6011 is an antibody pharmaceutical with a novel action mechanism inhibiting cell invasion by neutralizing activity of fractalkine (FKN), unlike existing cytokine treatments. FKN is a chemokine that has dual functions of cell migration regulation and cell adhesion. The FKN receptor (CX3CR1) is mostly expressed in macrophages and killer lymphocytes selectively and plays a key role in efficient collection of the cells to the inflamed site. It has been suggested that the FKN/CX3CR1 system relates to various chronic inflammatory diseases including inflammatory bowel disease, rheumatoid arthritis, liver disease, central nervous system disease, arteriosclerosis, dermatosis and others. For E6011, phase II clinical trials in patients with Crohn’s disease, primary biliary cholangitis or rheumatoid arthritis are being conducted. EA Pharma has been conducting the clinical development of E6011 for patients with Crohn’s disease or primary biliary cholangitis since April 2016.

3. About Crohn’s disease

Crohn’s disease (CD) is an inflammatory disease characterized by ulcers and/or inflammatory lesions in the small and/or large intestines. The cause is unknown. Japan’s Ministry of Health, Labour and Welfare designated CD as an intractable

disease. The number of patients with CD has been increasing in recent years. As of 2016, 42,789 patients were registered in Japan². The prevalence is higher in the US and Europe than in Japan: the number of patients is estimated to be about 27 per 100,000 people in Japan, and approximately 200 per 100,000 in the US³. CD is more common in men than women, with the male-female ratio of the patients being 2:1. CD is most commonly seen in adolescents with a peak in their late 10s to early 20s. CD complicates stricture, ileus, abscess (abscess formation in the infected site) and so on. Anal fistula (Pores are formed in the intestinal tract, which allows abnormal communication between the intestinal tracts or the perianal skin) is a characteristic symptom. Surgical procedures are used when nutrition therapy and chemotherapy are insufficient. In CD, active/remission stages repeat over a long period of time. Even though once the disease enters into a remission stage, long-term treatment is needed for prevention of flares/relapses (Inflammation occurs in the intestinal tract again) and recurrence (Inflammation occurs in a new site in the intestinal tract).

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/>

¹ AMED's CiCLE selection related website:

https://www.amed.go.jp/koubo/07/saitaku_00013.html

² Japan Intractable Disease Information Center Number of Recipient Certificates Issued for Specific Disease Treatment: <http://www.nanbyou.or.jp/entry/5354>

³ Japan Intractable Disease Information Center Crohn's disease (Designated intractable disease 96): <http://www.nanbyou.or.jp/entry/81>