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Eisai Co., Ltd.

**EISAI PRESENTS LATEST PHASE I/II DATA ON
IN-HOUSE DEVELOPED ANTI-FRACTALKINE ANTIBODY E6011**
*RESULTS SUGGEST SAFETY, TOLERABILITY AS WELL AS CLINICAL ACTIVITY
IN RHEUMATOID ARTHRITIS AND CROHN'S DISEASE*

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that interim analyses on the latest data for the world's first anti-fractalkine monoclonal antibody E6011, discovered by Eisai's research subsidiary KAN Research Institute Inc. (Headquarters: Hyogo, President and Representative Director: Toshio Imai), from two respective Phase I/II clinical studies in Crohn's disease and rheumatoid arthritis (Study 101 and Study 103) showed positive results for safety and tolerability, and exploratory assessment suggested clinical activity for E6011. These data have been presented at a number of recent academic conferences.

Study 101 is a multicenter, open-label study to evaluate mainly the safety and tolerability of E6011 in 21 Japanese patients with Crohn's disease who respond inadequately to conventional therapy which includes anti-tumor necrosis factor (TNF) therapies. The results of Study 101 were presented at Digestive Disease Week 2016¹ in May.

Study 103 is a multicenter, open-label study to evaluate mainly the safety and tolerability of E6011 in 27 Japanese patients with rheumatoid arthritis who respond inadequately to methotrexate or anti-TNF therapy. The results of study 103 were presented at the American College of Rheumatology (ACR) Annual Meeting² in November 2015, the Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology³ in April 2016 and the Annual European Congress of Rheumatology EULAR 2016⁴ in June. Additionally, the presentation on the results of Study 103 was accepted as a late-breaking abstract for the ACR Annual Meeting 2015.

Fractalkine is expressed on the surface of vascular endothelial cells in patients with inflammatory diseases including rheumatoid arthritis and inflammatory bowel diseases, and is involved in inflammatory response when bound to fractalkine receptors (CX3CR1) expressed in immune cells. E6011 is an antibody therapy with a novel mechanism of action, and is believed to exhibit an anti-inflammatory effect by suppressing the migration and invasion of CX3CR1-positive immune cells.

Eisai is striving to accelerate the development of E6011 as a key product to contribute to improving the benefit for a greater number of patients and their families.

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[Notes to editors]

1. About E6011

Discovered by Eisai Group subsidiary KAN Research Institute Inc., E6011 is the world's first humanized anti-fractalkine monoclonal antibody. Differing from conventional cytokine therapies, E6011 is an antibody therapy with a novel mechanism of action that neutralizes fractalkine activity, suppressing cell invasion. Fractalkine is a chemokine that is induced on vascular endothelial cells during inflammation, and have the two functions of cell migration factor and cell adherent. The fractalkine receptor CX3CR1 selectively appears in mainly macrophages and killer lymphocytes, and plays an important role in effectively accumulating at cell inflammation sites. It is suggested that the fractalkine/CX3CR1 system has an influence on the pathogenesis of many chronic inflammatory diseases such as inflammatory bowel disease, rheumatoid arthritis, liver disease, diseases of the central nervous system, arteriosclerosis and dermatosis. E6011 is being investigated in respective Phase I/II clinical studies of patients with Crohn's disease and rheumatoid arthritis in Japan. Furthermore, EA Pharma Co., Ltd. (Headquarters: Tokyo) has been responsible for the clinical development of E6011 for the indication of Crohn's disease since April 2016.

2. About Study 101

Study 101 is a Phase I/II multicenter, open-label clinical study to evaluate mainly the safety and tolerability of repeated intravenous administration of E6011 (2 mg/kg or 5 mg/kg administered every 2 weeks up to Week 10 with a double dose at Week 0, or 10 mg/kg or 15 mg/kg administered at Weeks 0,1 and 2, then every 2 weeks up to Week 10) in 21 Japanese patients with Crohn's disease who respond inadequately to anti-tumor necrosis factor (TNF) therapy. Clinical activity was assessed as an exploratory objective. From the results of the study, the incidence rate of treatment-emergent adverse events was 71.4% and the most commonly observed adverse events (two or more cases observed) were nasopharyngitis, headache, nausea and anal abscess. Regarding exploratory assessment of clinical activity, of the 18 patients who had a CDAI (Crohn's Disease Activity Index*) of over 220, the number of patients who experienced an improvement in CDAI over 70 were 1 out of 5 patients in the 2 mg/kg group, 2 out of 7 patients in the 5 mg/kg group, and 4 out of 6 patients in the 10 mg/kg group. In addition, in the 10 mg/kg group, clinical remission (CDAI below 150) was observed in 3 out of 6 patients.

*Index that quantifies the symptoms of Crohn's disease, calculated based on eight factors including number of liquid or soft stools each day, severity of abdominal pain, and an assessment of general well-being for seven days. Lower scores reflect mild symptoms, while higher scores reflect strong symptoms. A CDAI score below 150 indicates stability of symptoms (definition of remission), while a score over 450 indicates severe disease.

3. About Study 103

Study 103 is a Phase I/II multicenter, open-label clinical study to evaluate mainly the safety and tolerability of repeated subcutaneous administration of E6011 (100 mg/kg or 200 mg/kg administered repeatedly, subcutaneously at Week 0, 1, 2, followed by every 2 weeks up to 10 weeks) in 27 Japanese patients with rheumatoid arthritis who respond inadequately to methotrexate or anti-TNF therapy. Clinical activity was assessed as an exploratory objective. From the results of the study, the incidence rate of treatment-emergent adverse events was 59.3%, and the most commonly observed adverse events (two or more cases observed) were nasopharyngitis, headache and oropharyngeal pain. Regarding exploratory assessment of clinical activity, the ACR20 response* after 12 weeks of treatment was 75.0% for the 100 mg/kg group and 80.0% for the 200 mg/kg group, respectively. Similarly, ACR50 response was 33.3% for the 100 mg/kg group and 26.7% for the 200 mg/kg group. ACR70 response was 8.3% for the 100 mg/kg group and 20.0% for the 200 mg/kg group.

*Standard for assessing the clinical improvement of rheumatoid arthritis symptoms defined by the American College of Rheumatology. Regarding the seven criteria (1) number of tender joints, 2) number of swollen joints, 3) patient's assessment of pain,

4) patient's assessment of function, 5) physician's global assessment of disease status, 6) patient's global assessment of disease status and 7) acute-phase reaction protein [CRP or ESR] levels), ACR20 response is the proportion of patients who achieve at least a 20% improvement in 1) and 2) and a 20% improvement in at least three of the five criteria from 3) to 7). Similarly ACR50 and ACR70 are the proportion of patients who achieve at least a 50% improvement and 70% improvement in the criteria, respectively.

4. About Crohn's Disease

Crohn's disease is a chronic autoimmune disease of unknown etiology that is characterized by inflammatory lesions mainly in the small and large intestine. The Ministry of Health, Labor, and Welfare has designated Crohn's disease as a specified disease for which financial support is provided for healthcare. Crohn's disease has become increasingly common during recent years. As at the end of fiscal 2013, 39,799 patients were registered in Japan. The prevalence of Crohn's disease is higher in the United States and Europe, it is estimated that there are approximately 200 patients per 100,000 people in the United States compared to approximately 27 patients per 100,000 people in Japan.⁵

Crohn's disease is more prevalent among males, with a male/female ratio of 2:1, and its most common age of onset is 20–29 years. Crohn's disease is characterized by intestinal stenosis, ileus, intestinal abscesses (collections of pus resulting from infection) and perianal fistulas (ulcers in the intestine that form tunnels to surrounding intestinal wall or skin). When signs and symptoms cannot be controlled with drug therapy, patients may require surgical treatment. Since patients with Crohn's disease often exhibit flare-ups and periods of remission, long-term treatment is required to prevent recrudescence (recurrence of gastrointestinal inflammation) and recurrence (occurrence of inflammation in a new region) even after achieving remission.

5. About Rheumatoid Arthritis

Rheumatoid arthritis is a disease that leads to the inflammation of multiple joints throughout the body, causing joint swelling and pain. With joint destruction progressing right from the early stages of the disease, rheumatoid arthritis causes joint deformities and functional impairment over the long term. Rheumatoid arthritis is an autoimmune disease in which synovial cells, which line the inner surface of the joint cavity, proliferate due to an unknown cause. The number of blood vessels in joints also increases, resulting in the migration of lymphocytes, macrophages and other white blood cells from inside blood vessels to the synovial tissue of joints. An immune reaction in localized joints causes an inflammatory reaction and the progression of cartilage and bone destruction due to the effects of cytokines produced by lymphocytes and macrophages. The global prevalence of rheumatoid arthritis varies between 0.3% and 1%.⁶ In Japan, rheumatoid arthritis is said to affect an estimated 700,000 to 800,000 patients.

¹ Matsuoka K, et al., Safety, Tolerability and Efficacy of E6011, Anti-Human Fractalkine Monoclonal Antibody, in the First-Patient Study for Crohn's Disease, *Digestive Disease Week 2016*, Poster Number Mo1890.

² Tanaka Y, et al., Safety and Efficacy of E6011, an Anti-Fractalkine Monoclonal Antibody, in a First-in-Patient Phase 1/2 Study in Rheumatoid Arthritis. *ACR 2015*. Late-breaking Abstract Number 13L

³ Tanaka Y, et al., Safety, Pharmacokinetics and Efficacy of E6011, an Anti-Fractalkine Monoclonal Antibody, in a First-in-Patient Phase 1/2 Study in Japanese Patients with Rheumatoid Arthritis. *60th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2016*. Poster Number ICW-C15-5.

⁴ Tanaka Y, et al., Safety and Efficacy of E6011, an Anti-Fractalkine Monoclonal Antibody, in a First-in-Patient Phase 1/2 Study in Rheumatoid Arthritis. *EULAR Annual European Congress of Rheumatology 2016*, Poster Number FRI0236

⁵ Data from the Japan Intractable Disease Information Center: <http://www.nanbyou.or.jp/entry/81>

⁶ World Health Organization, Chronic Rheumatic Conditions: <http://www.who.int/chp/topics/rheumatic/en>.