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Eisai Co., Ltd.

## **EISAI ANNOUNCES U.S. FDA APPROVAL FOR NEW HIGHER DOSE ARICEPT® 23 MG TABLET FOR THE TREATMENT OF MODERATE-TO-SEVERE ALZHEIMER'S DISEASE**

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito) announced today that its U.S. subsidiary Eisai Inc. has received approval from the U.S. Food and Drug Administration (FDA) for Aricept® (generic name: donepezil hydrochloride) 23 mg once daily tablet for the treatment of moderate-to-severe Alzheimer's disease (AD). Aricept® 23 mg tablet offers another dosing option for patients with moderate-to-severe AD for whom few treatments are available. Approximately 3.6 million Americans age 65 and older suffer with moderate-to-severe AD.

The approval of Aricept® 23 mg tablet is based on data from a large head-to-head study (Study 326) of 1,467 patients with moderate-to-severe AD, which showed that Aricept® 23 mg tablet demonstrated significant improvement in cognition compared to Aricept® 10 mg tablet. Two co-primary endpoints were examined: the Severe Impairment Battery (SIB), which measures cognition, and the Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC plus), which measures global function. While Aricept® 23 mg tablet, as compared to Aricept® 10 mg tablet, demonstrated a statistically significant improvement in SIB, it did not achieve statistically significant improvement in CIBIC plus. The changes in total score in the SIB (higher scores are better) was  $2.6 \pm 0.58$  in the 23 mg group compared to  $0.4 \pm 0.66$  in the 10 mg group, a difference of 2.2 ( $p = 0.0001$ ), and the overall changes in score for the CIBIC plus (lower scores are better) was  $4.23 \pm 1.07$  in the Aricept® 23 mg tablet group compared to  $4.29 \pm 1.07$  in the 10 mg group, a difference of 0.06 ( $p = 0.1789$ ). The most frequently reported adverse events (5 percent or more) with Aricept® 23 mg tablet were digestive symptoms such as nausea, vomiting, diarrhea and anorexia, which are commonly seen in patients taking acetylcholine esterase inhibitors.

AD is a progressive, neurodegenerative disease that affects cognition. Age is the biggest risk factor for AD, as the chances of developing the disease doubles every five years after age 65. By 2050, it is estimated 13.5 million Americans may have AD, and 77 percent (10.4 million) of them may have moderate or severe disease, according to the Alzheimer's Association. With the growing aging population, it is more important than ever to develop valuable therapies for the treatment of AD.

Based upon the submission of the Aricept® 23 mg tablet clinical trial data to the FDA, Aricept® 23 mg tablet is expected to have three years of data exclusivity in the U.S.

Aricept® 23 mg tablet will be marketed in the United States by Eisai Inc. with support from its Aricept® co-promotion partner Pfizer Inc. The approval of Aricept® 23 mg tablet will not only enable Eisai to offer Aricept® in a range of dosing options, which include 5 mg, 10 mg and 23 mg formulations, thereby demonstrating its commitment to delivering new treatment options to patients with all stages of AD (mild to severe) and their caregivers, it will also allow the Company to draw upon its heritage in further improving their quality of life.

**[Please refer to the following notes for further information on Study 326 the pivotal study, SIB, CIBIC plus and Aricept®]**

Media Inquiries:  
Public Relations Department,  
Eisai Co., Ltd.  
+81-(0)3-3817-5120

## **[Notes to editors]**

### **1. About Aricept® Study 326, the pivotal study**

The Aricept® 23 mg NDA submitted to the FDA was based on results of Study 326. Data from the study, including SIB, CIBIC plus and safety data, was presented at the 2010 Alzheimer's Association International Conference on Alzheimer's Disease (ICAD).

#### Study Overview:

- 1) Design: Head-to-head, double-blind, randomized, parallel-group
- 2) Patient Enrollment: 1,467 patients with moderate-to-severe AD who had been treated for three or more months with Aricept® 10 mg tablet
- 3) Drugs compared: Aricept® 23 mg tablet versus the approved Aricept® 10 mg tablet
- 4) Co-primary endpoints: Severe Impairment Battery (SIB), Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC plus)
- 5) Both endpoints calculated the change in the patients' total scores from the study start to week 24

#### Study Results

- 1) Change in total scores in the SIB:  $2.6 \pm 0.58$  in the 23 mg group compared to  $0.4 \pm 0.66$  in the 10 mg group (based on the data from the intent-to-treat (ITT,  $p = 0.0001$ )) (higher scores are better)
- 2) Overall changes in score for the CIBIC plus:  $4.23 \pm 1.07$  in the Aricept® 23 mg tablet group compared to  $4.29 \pm 1.07$  in the 10 mg group (ITT,  $p = 0.1789$ ) (lower scores are better)
- 3) Most frequently observed adverse events (5 percent or more) with Aricept® 23 mg tablet versus Aricept® 10 mg tablet, respectively, included nausea (11.8 percent vs. 3.4 percent), vomiting (9.2 percent vs. 2.5 percent), diarrhea (8.3 percent vs. 5.3 percent), anorexia (5.3 percent vs. 1.7 percent) and other digestive symptoms commonly seen in patients taking acetylcholine esterase inhibitors.

### **2. SIB (Severe Impairment Battery)**

SIB is a validated clinical instrument used to measure cognition. Patients are evaluated in an interview that assesses cognitive function in nine domains: Social Interaction, Memory, Orientation, Attention, Praxis, Visuospatial, Language, Construction, and Name Orientation. Test scores range from 100 (normal) to 0 (severely impaired)

### **3) CIBIC plus (Clinician's Interview-Based Impression of Change plus Caregiver Input)**

CIBIC plus is a validated clinical instrument used to measure change in global function through an interview with patients and their caregivers. Patients are assessed on a 7-point scale, "1. Very much improved" to "7. Marked worsening", or rated "Indeterminable" in four major categories: General, Mental/Cognitive State, Behavior, and Activities of Daily Living.

### **4) About Aricept®**

Aricept® is an acetylcholine esterase inhibitor discovered and developed by Eisai and was approved first in the United States in November 1996. It increases levels of acetylcholine in the brain and slows disease progression by inhibiting acetylcholine esterase, an enzyme that breaks down the neurotransmitter acetylcholine. Currently approved in more than 90 countries around the world, Aricept® is the most widely-used AD treatment. Aricept® is the first and only prescription medication approved in the United States by the FDA for the treatment of all stages of AD—mild, moderate and severe dementia of the Alzheimer's type. Aricept® is currently available in the United States in 5 mg tablet, 10 mg tablet, orally disintegrating tablet (5 mg and 10 mg) and now 23 mg tablet. Aricept® 23 mg tablet is expected to be available in the United States from the start of August, 2010. Aricept® is marketed in the United States by Eisai Inc. with support from its Aricept® co-promotion partner Pfizer Inc.