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Eisai Co., Ltd.

## **EISAI RECEIVES COMPLETE RESPONSE LETTER FROM U.S. FDA FOR DNA METHYLATION INHIBITOR DACOGEN® FOR INJECTION sNDA IN ACUTE MYELOID LEUKEMIA**

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito) announced today that its U.S. subsidiary Eisai Inc. has received a complete response letter from the U.S. Food and Drug Administration (FDA) stating that the FDA cannot approve the company's supplemental New Drug Application (sNDA) for the DNA methylation inhibitor DACOGEN® (decitabine) proposed for the treatment of acute myeloid leukemia (AML) in adults 65 years of age or older who are not considered candidates for induction therapy.

FDA declined to approve the application because it said that the primary study (DACO-016) did not provide convincing evidence of the safety and effectiveness of DACOGEN for the proposed AML indication. Eisai will give careful consideration to the issues raised in the complete response letter before determining next steps.

DACOGEN was approved by the FDA in 2006 as a treatment for myelodysplastic syndromes (MDS) and has been marketed in the United States by Eisai Inc. since 2008. In 2010, a new five-day dosing regimen with a shorter administration time was approved as an alternative to the existing three-day dosing regimen in which DACOGEN is administered by continuous intravenous infusion over three hours repeated every eight hours for three consecutive days. The approval of the five-day regimen provides MDS patients with a new dosing option that takes into consideration their quality of life.

**[Please refer to the following notes for further information on DACOGEN  
and the DACO-116 study]**

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## [Notes to editors]

### 1. About DACOGEN® (U.S. Product Outline)

1) Product Name

DACOGEN® for Injection

2) Generic Name

decitabine

3) Formulation Type

Injectable

4) Indications and Usage:

Dacogen for Injection is indicated for treatment of patients with myelodysplastic syndromes (MDS) including previously treated and untreated, *de novo* and secondary MDS of all French-American-British (FAB) subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, chronic myelomonocytic leukemia) and Intermediate-1, Intermediate-2, and High-Risk International Prognostic Scoring System (IPSS) groups.

5) Dosage and Administration

- Dacogen is administered at a dose of 15mg/m<sup>2</sup> by continuous intravenous infusion over 3 hours repeated every 8 hours for 3 days. This cycle should be repeated every 6 weeks.
- Dacogen is administered at a dose of 20mg/m<sup>2</sup> by continuous intravenous infusion over 1 hour repeated daily for 5 days. This cycle should be repeated every 4 weeks.

6) Major Adverse Events

- In Phase III clinical trials in MDS patients, the highest incidence of Grade 3 or Grade 4 adverse events was neutropenia (87%), thrombocytopenia (85%), febrile neutropenia (23%) and leukopenia (22%).
- In the single-arm study in MDS patients (N=99), the highest incidence of Grade 3 or Grade 4 adverse events when DACOGEN was administered at a dose at 20mg/m<sup>2</sup> by intravenous infusion over 1 hour daily for 5 consecutive days was neutropenia (37%), thrombocytopenia (24%) and anemia (22%).

### 2. About the DACO-116 Study

DACO-016 was a Phase III randomized open-label, multi-center trial comparing DACOGEN versus patient's choice with physician's advice of either supportive care or low-dose cytarabine in patients 65 years and older with newly diagnosed *de novo* or secondary acute myeloid leukemia (AML) and with poor- or intermediate-risk cytogenetics.

Of the 485 patients, 242 were randomized to DACOGEN and 243 to patient's choice of supportive care or low-dose cytarabine. DACOGEN was administered at 20 mg/m<sup>2</sup> for one hour by intravenous infusion once daily for five consecutive days repeated every four weeks, continued as long as the patient derived benefit. Patients treated with cytarabine received 20 mg/m<sup>2</sup> subcutaneously once daily for 10 consecutive days every four weeks. The median duration of treatment for patients on DACOGEN was 4.4 months, compared with 2.4 months in the cytarabine group.