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Eisai Co., Ltd.

U.S. FDA GRANTS PRIORITY REVIEW STATUS TO sNDA FOR ANTICANCER AGENT HALAVEN® AS TREATMENT FOR SOFT TISSUE SARCOMA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that the U.S. Food and Drug Administration (FDA) has accepted for review the supplemental New Drug Application (sNDA) for Eisai's in-house developed anticancer agent Halaven® (eribulin mesylate) as a treatment for soft tissue sarcoma, and granted the sNDA Priority Review status.

The FDA's Priority Review designation is assigned to applications for drugs that treat serious conditions and would, if approved, provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. Through this process, the FDA has assigned a Prescription Drug User Fee Act (PDUFA) action date (proposed review deadline) of January 29, 2016, six months after the sNDA was submitted.

Eisai submitted applications seeking approval for the additional indication of soft tissue sarcoma in the United States and Europe (EU) respectively on July 29, 2015, and in Japan on July 30, 2015.

Soft tissue sarcoma is a collective term for a diverse group of malignant tumors that occur throughout the soft tissue (fat, muscle, nerves, fibrous tissues and blood vessels) in the body. Approximately 12,000 patients in the United States and 29,000 patients in Europe are diagnosed with soft tissue sarcoma each year. According to a patient survey conducted by the MHLW, there are approximately 4,000 patients with soft tissue sarcoma in Japan. Meanwhile, Halaven has been designated as an orphan drug for the treatment of soft tissue sarcoma in the United States and Japan.

Halaven is a halichondrin class microtubule dynamics inhibitor with a novel mechanism of action. It was first approved for the treatment of metastatic breast cancer in the United States in November 2010, and is currently approved in approximately 60 countries including Japan and countries in Europe, the Americas and Asia.

Eisai remains committed to providing further clinical evidence for Halaven aimed at maximizing value of the drug as it seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families, and healthcare providers.

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[Notes to editors]

1. About Halaven (eribulin mesylate)

Halaven, a halichondrin class microtubule dynamics inhibitor with a novel mechanism of action, belongs to a class of antineoplastic agents, the halichondrins, which are natural products isolated from the marine sponge *Halichondria okadai*. It is believed to work by inhibiting the growth phase of microtubule dynamics without affecting the shortening phase and sequestering tubulin into nonproductive aggregates.

Halaven was first approved as a treatment for breast cancer in the United States in November 2010, and is now approved in approximately 60 countries worldwide, including Japan and countries in the Europe, Americas and Asia. In Japan, Halaven has been approved to treat inoperable or recurrent breast cancer and was launched in the country in July 2011. Halaven has also been approved in countries in Europe and Asia indicated as a treatment for patients with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting, unless patients were not suitable for these treatments. In addition, Halaven has been designated as an orphan drug for soft-tissue sarcoma in the United States and Japan.

2. About Soft Tissue Sarcoma

Soft tissue sarcoma is a collective term for a diverse group of malignant tumors that occur throughout the soft tissue (fat, muscle, nerves, fibrous tissues and blood vessels) in the body. As the structures where the tumors originate are diverse, there are various types of soft tissue sarcoma, and the most common types include leiomyosarcoma, adipocytic and malignant fibrous histiocytoma.

While treatment of soft tissue sarcoma is focused on curative surgery, if the degree of malignancy is high, treatment then becomes a combination of chemotherapy and radiation therapy. As outcomes are poor for patients with advanced disease, it remains a disease with significant unmet medical needs.

3. About Study 309[1]

Conducted primarily in Europe and the United States, Study 309 was a multicenter, open-label, randomized Phase III study comparing the efficacy and safety of Halaven versus dacarbazine in 452 patients (aged 18 or over) with locally advanced or recurrent and metastatic soft tissue sarcoma (one of two subtypes: leiomyosarcoma or adipocytic sarcoma) who had disease progression following standard therapies which must have included an anthracycline and at least one other additional regimen. Patients received either Halaven (1.4 mg/m^2 administered intravenously on Day 1 and Day 8) or dacarbazine (850–1200 mg/m^2 administered intravenously on Day 1) every 21 days until disease progression.

From the results for the study, Halaven demonstrated a statistically significant extension in the study's primary endpoint of overall survival (OS) over the comparator treatment dacarbazine (Halaven median OS: 13.5 months vs dacarbazine median OS: 11.5 months, Hazard Ratio (HR) 0.768 [95% CI=0.618-0.954], p=0.017). Furthermore, in the study's secondary endpoint of progression-free rate at 12 weeks ($PFR12_{wks}$), while there was a numerical difference in $PFR12_{wks}$ between the Halaven and dacarbazine arms (33% vs 29%), this was not statistically significant. Median progression-free survival was 2.6 months in both arms.

In this study, the most common treatment-emergent adverse events observed in the Halaven arm were fatigue or asthenia, neutropenia, nausea, alopecia, and peripheral neuropathy, which was consistent with the known side-effect profile of Halaven.

[1] Schöffski P, et al. "Randomized, open-label, multicenter, phase 3 study of eribulin versus dacarbazine in patients (pts) with leiomyosarcoma (LMS) and adipocytic sarcoma (ADI)." Abstract. *American Society of Clinical Oncology Annual Meeting*, 2015; #LBA10502