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Eisai Co., Ltd.

ANTICANCER AGENT HALAVEN® SHOWS SIGNIFICANT EXTENSION IN OVERALL SURVIVAL IN PHASE III STUDY ON SOFT TISSUE SARCOMA

Phase III data to be presented in a Soft Tissue Sarcoma oral session at ASCO

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today the results of a Phase III clinical study (Study 309) of its in-house discovered and developed anticancer agent Halaven® (eribulin mesylate, "eribulin") in patients with soft tissue sarcoma. In the study's primary endpoint of overall survival (OS), eribulin demonstrated a statistically significant extension in OS over the comparator treatment dacarbazine (eribulin 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). These data will be presented today at the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO) taking place in Chicago, the United States, as part of the official press program, and also in a soft tissue sarcoma oral session on Monday, June 1.

Study 309 was a multicenter, open-label, randomized Phase III study comparing the efficacy and safety of eribulin 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 eribulin (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.

In addition to the primary endpoint of OS, the secondary endpoints included assessment of progression-free survival (PFS) and progression-free rate at 12 weeks ($PFR12_{wks}$). While there was a numerical difference in $PFR12_{wks}$ between the eribulin and dacarbazine arms (33% vs 29%), this was not statistically significant. Median PFS was 2.6 months in both arms.
In this study, the most frequent treatment-emergent adverse events in the eribulin arm were neutropenia, fatigue, nausea, alopecia and constipation, which was consistent with the known side-effect profile of eribulin.

"This is the first and only randomized controlled trial of a single agent systemic therapy to demonstrate an improvement in overall survival in people previously treated for soft tissue sarcomas," comments Dr. Patrick Schöffski, Head of the Department of General Medical Oncology, University Hospitals Leuven, Belgium. "These results are important in a disease where so few treatment options exist."

Soft tissue sarcoma is a rare form of malignant tumor with approximately 12,000 cases in the United States and 29,000 cases in Europe diagnosed each year. According to a patient survey conducted by the Japanese Ministry of Health, Labour and Welfare, there are approximately 4,000 patients with soft tissue sarcoma in Japan. 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 highly significant unmet medical needs.

Eribulin has been designated as an orphan drug for the treatment of soft tissue sarcoma in the United States and Japan.

Eribulin is a halichondrin class microtubule dynamics inhibitor with a novel mechanism of action. It was first approved for the treatment of 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. Through the results of Study 309, eribulin has demonstrated overall survival benefit as a single agent chemotherapy in soft tissue sarcomas as well as metastatic breast cancer, following two prior regimens in the advanced setting.
Based on the results of Study 309, Eisai intends to submit applications during the first half of fiscal 2015 to the regulatory authorities in multiple countries including Japan, the United States and Europe seeking an expansion of the indication for eribulin to include soft tissue sarcoma.

Eisai remains committed to providing further clinical evidence for eribulin 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 currently approved in approximately 60 countries worldwide, including Japan and countries in the Americas, Europe and Asia. In Japan, Halaven has been approved to treat inoperable or recurrent breast cancer and was launched in the country in July 2011. Since June 2014, Eisai has been obtaining approval in countries in Europe and Asia for the indication expansion of Halaven to contribute earlier treatment of 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 in the body. As the structures where the tumors originate are diverse, there are an extremely large number of types of sarcoma, and the most common types include leiomyosarcoma, adipocytic sarcoma 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 highly significant unmet medical needs.