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Eisai Co., Ltd.

EISAI ANNOUNCES PRECLINICAL RESEARCH FINDINGS SUGGESTING NOVEL INHIBITORY EFFECT ON TUMOR METASTASIS FOR ANTICANCER AGENT HALAVEN® AT AACR 104TH ANNUAL MEETING

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that it has presented preclinical research findings suggesting a potential inhibitory effect on tumor metastasis as a possible novel mechanism of action for anticancer agent Halaven® (eribulin mesylate, "eribulin") at the American Association for Cancer Research (AACR) 104th Annual Meeting ("AACR 2013").

Among the research findings presented by Eisai at AACR 2013 were gene expression profiling (GEP) analyses of multiple cancer cell lines, which confirmed that eribulin altered expression in epithelial-mesenchymal transition (EMT) gene sets. EMT was first recognized in the early 1980s and was long assumed to be a feature of embryogenesis in which embryonic epithelial cells acquire mesenchymal characteristics that lead to cell migration[1]; however, EMT has in recent years also been reported[2] to perform a role in numerous disease states in adult stages and, particularly in the acquisition of EMT phenotypes in epithelial cancer cells, to be highly relevant to the infiltration and metastasis of cancer.

Eisai also presented a dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) analysis of human breast xenograft tumors in rats, which confirmed that eribulin improved blood perfusion in the core of tumor tissues ("tumor core"). These findings indicated that eribulin reduces hypoxia by improving blood perfusion in the tumor core. Based on reports[3] that cancer cells inside hypoxic tumor tissues acquire highly metastatic phenotypes, eribulin is expected to potentially prevent hypoxia in the tumor core by improving blood perfusion and thus work to inhibit metastasis.

Eisai remains committed to delivering further scientific evidence aimed at maximizing the value of eribulin, including on the agent's main effect as a non-taxane microtubule dynamics inhibitor and in regard to its potential inhibitory effect on tumor metastasis as suggested in the preclinical research findings presented at AACR 2013. Through this and other endeavors, the company seeks to make further contributions to meet the diverse needs of, and increase the benefits provided to, patients with cancer and their families as well as healthcare providers.

[Please refer to the following notes for further information on Halaven.]

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[Notes to editors]

1. About Halaven® (eribulin mesylate)

Halaven, a non-taxane, 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.

In a Phase III clinical study (EMBRACE) conducted overseas of Halaven versus treatment of physician's choice (TPC) in 762 patients with locally recurrent or metastatic breast cancer previously treated with an anthracycline and a taxane, Halaven indicated an extended overall survival (OS) of 2.5 months (OS of 13.1 months versus 10.6 months, respectively; Hazard Ratio (HR) 0.81; p=0.041) when compared to TPC. An updated analysis of OS (not protocol-specified) in the EMBRACE study was also performed at the request of European and U.S. regulatory authorities. These results demonstrated an increase of 2.7 months in OS for Halaven compared with TPC (OS of 13.2 months versus 10.5 months, respectively; HR 0:81; p=0.014). The most common adverse reactions (events with an incidence rate of at least 25%) among patients treated with Halaven were asthenia (fatigue), neutropenia, anemia, alopecia (hair loss), peripheral neuropathy (numbness and tingling in arms, legs and/or other parts of the body), nausea and constipation. The most common serious side effects reported in patients receiving Halaven were neutropenia with or without fever (4% and 2%, respectively). The most common adverse reaction resulting in discontinuation of treatment with Halaven was peripheral neuropathy (5%). Furthermore, in a Phase II clinical study conducted in Japan, Halaven was found to possess excellent anticancer effects and tolerability in patients with advanced or recurrent breast cancer who had previously undergone treatment.

Halaven was first approved as a treatment for breast cancer in the United States in November 2010, and is currently approved in more than 40 countries worldwide, including European Union member states, Japan, Singapore and Switzerland. In Japan, the drug has been approved to treat inoperable or recurrent breast cancer and was launched in the country in July 2011. Furthermore, with the aim of maximizing value of the drug, Eisai is currently conducting late-stage clinical developments investigating the potential of Halaven as a therapy in the treatment of breast cancer with fewer prior treatments as well as soft-tissue sarcoma and non-small cell lung cancer.

[References]

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[3] Sullivan R, Graham CH. "Hypoxia-driven selection of the metastatic phenotype" *Cancer Metastasis Rev*. 2007; 26(2): 319-331.