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Eisai Co., Ltd.

EISAI PRESENTS ADDITIONAL ANALYSIS FINDINGS ON HALAVEN® (ERIBULIN) AT EUROPEAN CANCER CONGRESS 2013

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that it has presented *post hoc* analysis findings regarding a Phase III trial (Study 301) of Halaven® (eribulin mesylate; below, "eribulin"), an anticancer agent being developed in-house, versus capecitabine in patients with metastatic breast cancer at the European Cancer Congress (ECC) 2013.

Improved progression-free survival (PFS) in patients receiving therapy for metastatic breast cancer often fails to translate into overall survival (OS) benefit. Previous results from Study 301 found no difference in PFS but demonstrated a trend for improved OS in patients who received eribulin ("Group E"), though not statistically significant, versus patients who received capecitabine ("Group C"). With the aim of investigating the discordance between OS and PFS, the *post hoc* analysis presented at the congress compared median OS in patient subsets by stratifying patients who had been confirmed with disease progression during the trial into two groups: patients with a newly detected metastasis (Group E: 271 patients, Group C: 285 patients) and patients who progressed with an increase in the size of pre-existing lesions (Group E: 147 patients, Group C: 129 patients). The analysis results showed that the median OS of these subsets was similar among patients who progressed with an increase in the size of pre-existing lesions (Group E: median OS of 17.4 months, Group C: median OS of 17.4 months; HR 1.13; 95% CI 0.87, 1.46; nominal p-value=0.35). In comparison, among patients confirmed to have a newly detected metastasis, Group E recorded a trend favoring extended OS, with a nominal p-value of 0.02 (Group E: median OS of 15.5 months, Group C: median OS of 12.9 months; HR 0.81; 95% CI 0.68, 0.97).

Dr. Christopher Twelves, Professor of Clinical Cancer Pharmacology and Oncology, University of Leeds and St James' University Hospital and investigator for Study 301, comments: "These results suggest that the conventional PFS definition may not be adequate and that clinically meaningful differences may exist among different subsets of patients with metastatic breast cancer depending on how and where their disease progresses. The importance in this *post hoc* analysis of the emergence of 'new' metastases is intriguing and warrants further study."

Furthermore, the *post hoc* analysis compared new metastasis-free survival (nMFS), which indicates the time until a new metastasis was first confirmed. This comparison showed an nMFS of 5.8 months in Group E (554 patients) and 5.2 months in Group C (548 patients), indicating a trend favoring extended nMFS in Group E by a difference of 0.6 months (HR 0.90; 95% CI 0.77, 1.05; nominal p-value=0.17).

Eisai will continue its efforts to translate in a clinical setting the main effect of eribulin as a non-taxane microtubule dynamics inhibitor as well as its experimental inhibitory effect on tumor metastasis as suggested in preclinical research findings to date. Through these endeavors, the company seeks to maximize the value of the agent in order to make further contributions to patients with cancer and their families.

[Please refer to the following notes for further information on Halaven, Study 301, and preclinical research findings on eribulin presented at the AACR 104th Annual Meeting.]

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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 advanced or recurrent 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 approved in more than 50 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 moving ahead with 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.

2. About Study 301

Study 301 was an open-label, randomized, two-parallel-arm, multicenter study designed to evaluate Halaven versus capecitabine in 1,102 women with locally advanced or metastatic breast cancer who had up to three prior chemotherapy regimens in the (neo)adjuvant setting, and no more than two prior regimens for locally advanced and/or metastatic disease. The regimens must have included an anthracycline and a taxane. Although eribulin did not achieve a statistically significant result when compared to capecitabine in terms of overall survival (OS) and progression-free survival (PFS), the co-primary endpoints of the study, eribulin did demonstrate a trend favoring improved OS (eribulin median OS: 15.9 months, capecitabine median OS: 14.5 months; HR 0.879; 95% CI: 0.770-1.003; p=0.056). Additionally, a later PFS assessment carried out by an independent evaluation body concluded that there was no significant difference between the two drugs (eribulin median PFS: 4.1 months, capecitabine median PFS: 4.2 months, HR 1.079; 95% CI: 0.932-1.250; p=0.305). In regard to safety, adverse events (AEs) were consistent with the known side-effect profiles of both drugs. The most common AEs (events with an incidence rate of at least 20%) for Halaven and capecitabine were, respectively, neutropenia (54.2% vs. 15.9%), hand-foot syndrome (0.2% vs. 45.1%), alopecia (34.6% vs. 4.0%), leukopenia (31.4% vs. 10.4%), diarrhea (14.3% vs. 28.8%), and nausea (22.2% vs. 24.4%).

3. About the Preclinical Research Findings on Eribulin Presented at the AACR 104th Annual Meeting

At the American Association for Cancer Research (AACR) 104th Annual Meeting ("AACR 2013"), Eisai presented new preclinical research findings confirming that eribulin altered expression in epithelial-mesenchymal transition (EMT) gene sets and, in a dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) analysis, that the agent also improved blood perfusion in the tumor core. Existing studies report that the acquisition of EMT phenotypes in epithelial cancer cells is highly relevant to the infiltration and metastasis of cancer and that cancer cells inside hypoxic tumor tissue have been observed to acquire highly metastatic phenotypes. Given this background, the findings presented on eribulin at AACR 2013 suggest that the agent may potentially work to inhibit metastasis. For more information on these findings, please refer to Eisai's news release issued on April 10, 2013, which can be accessed via the following link: http://www.eisai.com/news/news201321.html.