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Eisai Co., Ltd.

HALAVEN™ (ERIBULIN) RECEIVES EUROPEAN COMMISSION APPROVAL FOR ADVANCED BREAST CANCER

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that it has received approval from the European Commission for Halaven™ (eribulin) for the treatment of patients with locally advanced or metastatic breast cancer who have progressed after at least two chemotherapeutic regimens for advanced disease. Prior therapy should have included an anthracycline and a taxane unless patients were not suitable for these treatments. Halaven™ is a new class of agent which provides statistically significant overall survival improvements compared with current treatment options.

The European Commission approval of Halaven™ was granted through a centralised procedure, which means that the treatment has now been granted marketing authorisation in the 27 EU member states. Eisai plans to launch Halaven™ first in the United Kingdom, followed by other countries such as Germany and Nordic countries.

The approval of European Commission is based on the results of the global Phase III EMBRACE study (Eisai Metastatic Breast Cancer Study Assessing Treatment of Physician's Choice (TPC) Versus Eribulin E7389), which demonstrated a statistically significant increase in overall survival (OS) for patients treated with Halaven™ when compared with TPC. The protocol prespecified analysis at the point of 422 events demonstrated a median OS of 13.1 and 10.6 months, respectively (Hazard Ratio [HR] 0.81; p=0.041)[1)]; the updated analysis requested by European and US regulatory authorities including 589 events demonstrated a median OS of 13.2 and 10.5 months, respectively (HR 0.81; nominal p=0.014)[2)].

Halaven™ is the first single-agent therapy to demonstrate a significant overall survival benefit in patients with advanced breast cancer. The European Commission approval means that patients across the EU will soon be able to benefit from this treatment, which offers them an average of more than 2 months longer life.

Halaven™ was approved in the USA in November 2010 and Singapore in February 2011, and has already been launched in USA. The approval by European Commission is the third in the world, other applications are currently under review in Japan, Switzerland and Canada.

Eisai's commitment to meaningful progress in oncology research, built on scientific expertise, is supported by a global capability to conduct discovery and preclinical research, and develop small molecules, biologic and supportive care agents for cancer across multiple indications. Through these efforts, Eisai will make further contributions to addressing the diversified needs of and increasing the benefits provided to patients and their families as well as healthcare professionals as it seeks to fulfill its human health care (*hhc*) mission.

[Please refer to the following notes on the EMBRACE study, Halaven™ and metastatic breast cancer]

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[Notes to editors]

1. Global Phase III Clinical Study (EMBRACE Study)

EMBRACE was an open-label, randomized, global, multi-center, parallel two-arm study designed to compare overall survival in patients treated with Halaven™ versus a Treatment of Physician's Choice (TPC arm). TPC was defined as any single-agent chemotherapy, hormonal treatment or biologic therapy approved for the treatment of cancer; or palliative treatment or radiotherapy administered according to local practice. The study included 762 patients with metastatic breast cancer who previously had been treated with at least two and a maximum of five prior chemotherapies, including an anthracycline and a taxane. The vast majority (97%) of patients in the TPC arm received chemotherapy. (overall survival for patients treated with Halaven™ when compared with TPC, median OS 13.1 and 10.6 months respectively; HR 0.81; p=0.041)[1)]

An updated analysis of overall survival (not protocol prespecified) of EMBRACE study was performed under the request of European and US regulatory authorities. The results confirmed the significant increase in overall survival for Halaven™ compared with TPC, and no change in safety profile, which was presented in San Antonio Cancer Symposium in 2010. (median OS 13.2 and 10.5 months respectively; HR 0.81; p=0.014)[2)]

The most common adverse reactions (incidence greater than or equal to 25%) among patients treated with Halaven™ were asthenia (fatigue), neutropenia, anemia, alopecia (hair loss), peripheral neuropathy (numbness and tingling in arms, legs and 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%).

2. Halaven™ (eribulin mesylate)

Halaven™ is a non-taxane, microtubule dynamics inhibitor, 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.

Synthesizing Halaven™ is an extremely difficult and complex process, involving some 62 steps to achieve total synthesis. Halaven™ has a molecular weight of 826, including 19 chiral carbons, which means the theoretical number of stereoisomers is 2^{19}, or a possible 524,000, making stereocontrol potentially extremely difficult. However, due to the advanced technological capabilities and strategies of the Eisai discovery and process research teams, it was possible to stereoselectively control all synthetic reactions and commercially synthesize Halaven™.

Eisai is currently conducting late stage clinical trials investigating the potential of Halaven™ as a single-agent therapy in the treatment of other types of cancer such as breast cancer with fewer prior treatments, non-small cell lung cancer, sarcoma, and prostate cancer with the aim of expanding the range of indications for which the agent can be used to treat.

3. Metastatic Breast Cancer (MBC)

Worldwide, more than one million women a year are diagnosed with breast cancer, including 421,000 women in Europe. Approximately 30 percent of women initially diagnosed with earlier stages of breast cancer eventually develop recurrent or metastatic disease, and while around 9 out of 10 of women diagnosed with early stage breast cancer survive beyond five years, this drops to around 1 in 10 among women first diagnosed with MBC. Most MBC patients have a limited survival time of approximately 18 to 24 months.

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1) Cortes J, O'Shaughnessy J, Loesch D, et al. Eribulin monotherapy vs. treatment of physician's choice in patients with metastatic breast cancer. The Lancet. 377, 914 (2011)

2) C. Twelves et al. Updated Survival Analysis of a Phase III Study (EMBRACE) of Eribulin Mesylate vs Treatment of Physician's Choice in Subjects with Locally Recurrent or Metastatic Breast Cancer Previously Treated with an Anthracycline and a Taxane. 33rd Annual San Antonio Breast Cancer Symposium, San Antonio, TX, December 8-12, 2010, P6-14-08