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Eisai Co., Ltd.

LAUNCH OF ANTICANCER AGENT HALAVEN® IN CHINA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has launched the in-house developed anticancer agent Halaven® (product name in China: 海乐卫®, generic name: eribulin mesylate) in China.

Halaven is a halichondrin class microtubule dynamics inhibitor with a distinct binding profile. In addition to its mechanism of action of inhibiting the growth of microtubule dynamics, non-clinical studies showed Halaven's unique actions on the tumor microenvironment such as increasing vascular perfusion and permeability in tumor cores,[1] promotion of the epithelial state and decrease in the capacity of breast cancer cells to migrate.[2] In a Phase III clinical study (EMBRACE) 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 showed an extended overall survival compared to TPC.[3] For use in the treatment of breast cancer, Halaven is currently approved in over 70 countries worldwide, including the United States, Japan and countries in Europe and Asia. The most common adverse events (incidence 25% and higher) in the Halaven arm of this study were asthenia (fatigue), neutropenia, alopecia, peripheral neuropathy, nausea and constipation.

In China, Halaven received New Drug Approval for the use in the treatment of patients with locally advanced or metastatic breast cancer, previously treated with at least two prior chemotherapy regimens, including and an anthracycline and a taxane in July 2019 based on the results of Study 304,[4] which was a Phase III clinical study in 530 women with locally recurrent or metastatic breast cancer, previously treated with chemotherapy regimens, including an anthracycline and a taxane. Halaven demonstrated a statistically significant extension of progression-free survival over the comparator treatment vinorelbine. The five most common adverse events observed in the Halaven arm of this study were white blood cell count decreased, neutrophil count decreased, increased aspartate aminotransferase, increased alanine aminotransferase and anemia.

The number of women diagnosed with breast cancer in China has increased in recent years,[5] with an estimated 370,000 new cases of breast cancer and 100,000 related deaths in 2018.[6] Breast cancer is now the most frequently diagnosed cancer in Chinese women.[6]

Eisai positions oncology as a key therapeutic area, and is aiming to create revolutionary new medicines with the potential to cure cancer. Lenvima® has been available in China as a treatment of patients with unresectable hepatocellular carcinoma who have not received prior systematic therapy since November 2018.* With this approval of Halaven, Eisai seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families, and healthcare providers in China.

*Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A's Chinese subsidiary MSD China have been providing information about Lenvima in China.

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<Notes to editors>

1. About Halaven (generic name: eribulin mesylate)

Halaven is in the halichondrin class of microtubule dynamics inhibitors with a novel mechanism of action. Structurally, Halaven is a simplified and synthetically produced version of halichondrin B, a natural product isolated from the marine sponge *halichondria okadai*. Halaven is believed to work by inhibiting the growth phase of microtubule dynamics which prevents cell division. In addition, non-clinical studies showed Halaven's unique actions in the tumor microenvironment such as an increase in vascular perfusion and permeability in tumor cores,[1] promotion of the epithelial state, decrease in capacity of breast cancer cells to migrate,[2] and etc.

Halaven was first approved as a treatment in the United States in November 2010 for patients with metastatic breast cancer. Halaven is currently approved for use in the treatment of breast cancer in over 70 countries worldwide, including Japan, China and countries in Europe, the Americas and Asia. Furthermore, Halaven was first approved as a treatment for soft tissue sarcoma in the United States in January 2016, and is approved in over 65 countries including Japan and in Europe and Asia. Furthermore, Halaven has been designated as an orphan drug for soft tissue sarcoma in the United States and Japan.

Specifically, Halaven is approved for the following indications.

In the United States for the treatment of patients with:

- Metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
- Unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

In Japan for the treatment of patients with:

- Inoperable or recurrent breast cancer, soft tissue sarcoma

In Europe for the treatment of adult patients with:

- Locally advanced or metastatic breast cancer who have received a prior anthracycline-containing 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.
- Unresectable liposarcomas who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.

[1] Funahashi Y et al., Eribulin mesylate reduces tumor microenvironment abnormality by vascular remodeling in preclinical human breast cancer models. *Cancer Sci.*, 2014; 105, 1334-1342

[2] Yoshida T et al., Eribulin mesilate suppresses experimental metastasis of breast cancer cells by reversing phenotype from epithelial-mesenchymal transition (EMT) to mesenchymal-epithelial transition (MET) states. *Br J Cancer*, 2014; 110, 1497-1505

[3] Cortes J et al., Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study *Lancet,* 2011; 377, 914-23

[4] Yuan P et al., Eribulin mesilate versus vinorelbine in women with locally recurrent or metastatic breast cancer: A randomized clinical trial *Eur J Cancer,* 2019; 112, 57-65

[5] Lei F et al., Breast cancer in China. *The Lancet Oncology*, 2014; 15(7), e279–e289

[6] Ferlay J, et al., (2018). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. https://gco.iarc.fr/today, As of January 10, 2020