No.16-58

August 5, 2016
Eisai Co., Ltd.

CHINA FOOD AND DRUG ADMINISTRATION ACCEPTS NDA FOR ANTICANCER AGENT HALAVEN®

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that the China Food and Drug Administration (CFDA) has accepted for review a New Drug Application (NDA) submitted for Eisai's in-house developed anticancer agent eribulin mesylate ("eribulin", product name: Halaven®) for use in the treatment of patients with locally advanced or metastatic breast cancer in China.

The NDA was based on Study 304, a multicenter, open-label, randomized, parallel group Phase III clinical study conducted in China to evaluate the efficacy and safety of eribulin and vinorelbine in 530 female subjects with locally recurrent or metastatic breast cancer, previously treated with at least two and a maximum of five prior chemotherapy regimens, including an anthracycline and a taxane. In this study, the primary objective was to assess progression-free survival (PFS) in both treatment groups. From the results for the study, eribulin demonstrated a statistically significant extension in PFS over the comparator treatment vinorelbine.
In addition, the most common adverse events observed in the eribulin group were neutropenia, anaemia, pyrexia, and fatigue/asthenia, which was consistent with the known side-effect profile of eribulin.

The number of women diagnosed with breast cancer in China has been increasing in recent years,[1] with an estimated 272,400 new cases of invasive breast cancer and 70,700 related deaths in 2015.[2] Breast cancer is now the most frequently diagnosed cancer in Chinese women.[1]

Halaven is a halichondrin class microtubule dynamics inhibitor with a distinct binding profile. Recent non-clinical studies showed that Halaven is associated with increased vascular perfusion and permeability in tumor cores.[3] Halaven promotes the epithelial state and decreases the capacity of breast cancer cells to migrate.[4] First approved in the United States for use in the treatment of breast cancer in November 2010, Halaven is currently approved in over 60 countries worldwide, including Japan and countries in Europe, the Americas and Asia.

Eisai positions oncology as a key therapeutic area, and is aiming to discovery revolutionary new medicines with the potential to cure cancer. Eisai remains committed to maximizing the clinical value as well as exploring the potential clinical benefits of Halaven 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 in China and around the world.

Media Inquiries:
Public Relations Department,
Eisai Co., Ltd.
+81-(0)3-3817-5120

[Notes to editors]

1. About Halaven (eribulin mesylate)

Halaven is a halichondrin class microtubule dynamics inhibitor 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, recent non-clinical studies showed that Halaven is associated with increased vascular perfusion and permeability in tumor cores.[3] Halaven promotes the epithelial state and decreases the capacity of breast cancer cells to migrate.[4]

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 60 countries worldwide, including Japan 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 countries including Japan and in Europe. Applications seeking approval for use in the treatment of soft tissue sarcoma are currently under review throughout the world including Switzerland, Australia, Brazil, and countries in 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 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.
- Unresectable liposarcomas who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease.

2. About Study 304

Conducted in China, Study 304 was a multicenter, open-label, randomized, parallel group Phase III clinical study to evaluate the efficacy and safety of eribulin and vinorelbine in 530 female subjects with locally recurrent or metastatic breast cancer, previously treated with at least two and a maximum of five prior chemotherapy regimens, including an anthracycline and a taxane. Patients received either eribulin (1.4 mg/m^2 administered intravenously on Day 1 and Day 8) or vinorelbine (25 mg/m^2 administered intravenously on Day 1, Day 8 and Day 15) every 21 days until disease progression.

From the results for the study, eribulin demonstrated a statistically significant extension in the study's primary endpoint of progression-free survival (PFS) over the comparator treatment vinorelbine. The study's secondary endpoints were overall survival (OS) and objective response rate (ORR).

The most common adverse events observed in the eribulin arm were neutropenia, anaemia, pyrexia, and fatigue/asthenia, which was consistent with the known side-effect profile of eribulin.

Detailed results of the study will be presented at an upcoming academic conference.

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

[2] Chen W et al. Cancer Statistics in China, 2015. *CA CANCER J CLIN,* 2016; 66, 115-132

[3] 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

[4] 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