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Eisai Co., Ltd.

**PHASE III TRIAL OF ANTICANCER AGENT LENVIMA®
AS FIRST-LINE TREATMENT FOR UNRESECTABLE HEPATOCELLULAR
CARCINOMA MEETS PRIMARY ENDPOINT**

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that a Phase III clinical trial (Study 304) of its in-house discovered and developed anticancer agent Lenvima® (lenvatinib mesylate, "lenvatinib") against the comparator sorafenib as a first-line treatment for patients with unresectable hepatocellular carcinoma has achieved its primary endpoint.

Study 304 is a multicenter, randomized, open-label, global Phase III study comparing the efficacy and safety of lenvatinib versus sorafenib, a standard treatment for advanced hepatocellular carcinoma, as a first-line treatment for patients with unresectable hepatocellular carcinoma. In the study, 954 patients were randomized in a 1:1 ratio to receive lenvatinib 12 mg or 8 mg once a day, depending on baseline body weight (n= 478) or sorafenib 400 mg twice a day (n= 476). Treatment was continued until disease progression or unacceptable toxicity.

The primary endpoint of the study was overall survival (OS), with the goal of demonstrating non-inferiority. Other factors including progression free survival (PFS), time to progression (TTP) and objective response rate (ORR) were assessed as secondary endpoints.

According to the results of the study, lenvatinib met the statistical criteria for non-inferiority of OS compared to sorafenib, and showed statistically significant and clinically meaningful improvement for PFS, TTP and ORR. In this study, the five most common adverse events observed in the lenvatinib arm were hypertension, diarrhea, decreased appetite, weight loss and fatigue, which is consistent with the known side-effect profile of lenvatinib. Analyses of the remaining secondary endpoints of quality of life and plasma PK parameters as well as safety are ongoing.

Eisai plans to hold discussions with regulatory authorities for submission in Japan, the United States, Europe and Asia, including China. Eisai will also present the details at an upcoming academic conference.

Liver cancer is the second leading cause of cancer related deaths, and is estimated to be responsible for approximately 700,000 deaths per year in the world¹. The majority of cases occur in Asia, including China, and Africa. Hepatocellular carcinoma accounts for 85% to 90% of primary liver cancer cases. Early stage hepatocellular carcinoma is treatable by a wide variety of means, including surgery, radiofrequency ablation, ethanol injection, chemoembolization therapy, but treatment opinions for unresectable hepatocellular carcinoma are limited and the prognosis is very poor, meaning that this is an area of high unmet medical need.

Eisai positions oncology as a key therapeutic area, and is aiming to discover revolutionary new medicines with the potential to cure cancer. Eisai remains committed to providing further clinical evidence for lenvatinib aimed at maximizing value of the drug 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.

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

[Notes to editors]

1. About lenvatinib mesylate (generic name, product name: Lenvima, “lenvatinib”)

Discovered and developed in-house, lenvatinib is an orally administered multiple receptor tyrosine kinase (RTK) inhibitor with a novel binding mode that selectively inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors (VEGFR1, VEGFR2 and VEGFR3) and fibroblast growth factor (FGF) receptors (FGFR1, FGFR2, FGFR3 and FGFR4) in addition to other proangiogenic and oncogenic pathway-related RTKs (including the platelet-derived growth factor (PDGF) receptor PDGFR α ; KIT; and RET) involved in tumor proliferation.

Currently, Eisai has obtained approval for lenvatinib as a treatment for refractory thyroid cancer in over 50 countries including in the United States, Japan, in Europe, Korea, Mexico, and Brazil, and is undergoing regulatory review in the countries including South Africa and Indonesia. Specifically, Eisai has obtained approval for the agent indicated in the United States for the treatment of locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer, in Japan for the treatment of unresectable thyroid cancer, and in Europe for the treatment of adult patients with progressive, locally advanced or metastatic differentiated (papillary, follicular, Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine, respectively.

Lenvatinib was also approved in the United States in May 2016 for an additional indication in combination with everolimus for the treatment of patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy. Furthermore, lenvatinib was approved in combination with everolimus for the treatment of adult patients with advanced RCC following one prior vascular endothelial growth factor (VEGF) targeted therapy in Europe in August 2016. Lenvatinib has been launched in Europe under the brand name Kisplyx[®] for this indication.

Meanwhile, Eisai is conducting clinical studies of lenvatinib in several other tumor types such as biliary tract cancer (Phase II), and in combination with pembrolizumab for various types of cancer (Phase Ib/II). In addition, Eisai has initiated a Phase III clinical study of lenvatinib in combinations with both pembrolizumab and everolimus in renal cell carcinoma (first-line therapy).

2. About Hepatocellular Carcinoma

Liver cancer is the second-leading cause of cancer deaths, with an estimated approximately 800,000 new cases diagnosed every year in the world. It is estimated to be the cause of approximately 700,000 deaths per year.¹ There is a large regional difference, with the majority of cases occurring in Asia, including China, followed by Africa. Hepatocellular carcinoma accounts for 85% to 90% of primary liver cancer cases. Hepatocellular carcinoma is associated with chronic liver disease, in particular cirrhosis. Major causes of cirrhosis include hepatitis B virus and hepatitis C virus. However, according to a recent investigation, non-B/non-C hepatocellular carcinoma is on the rise. Surgery is the first option for treatment, however, in many cases of recurrence after resection or when the cancer is deemed advanced at diagnosis, surgery is not applicable due to the disease having already metastasized throughout the body, and so it remains a condition with significant unmet medical needs. The only medicine approved for systemic therapy is sorafenib, making this a disease with unmet medical needs.

¹ GLOBOCAN2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. <http://globocan.iarc.fr/>