EISAI LAUNCHES IN-HOUSE DEVELOPED NOVEL ANTICANCER AGENT LENVIMA® (LENVATINIB MESYLATE) AS TREATMENT FOR UNRESECTABLE THYROID CANCER IN JAPAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced that it has launched its in-house developed novel anticancer agent Lenvima® Capsule 4 mg and 10 mg (lenvatinib mesylate, “Lenvima”) as a treatment for unresectable thyroid cancer in Japan on May 20, 2015.

Lenvima is the first molecular targeted treatment in Japan approved with an indication for unresectable thyroid cancer which covers differentiated thyroid cancer as well as medullary thyroid carcinoma and anaplastic thyroid carcinoma. In a global Phase III study (the SELECT study) of Lenvima in differentiated thyroid cancer, Lenvima demonstrated a statistically significant extension in progression free survival and improved response rates compared to placebo[1]. In the SELECT study, the five most common Lenvima treatment-related adverse events of any grade were hypertension, diarrhea, fatigue or asthenia, decreased appetite, and weight loss. Furthermore, a Phase II study (Study 208) conducted in Japan suggested tolerability and efficacy of Lenvima in medullary thyroid carcinoma and anaplastic thyroid carcinoma as well.

The number of patients with thyroid cancer in Japan is estimated to be between 13,000 and 29,000. Although treatment is possible for most types of thyroid cancer, there are few treatment options available for unresectable thyroid cancer and so there is a pressing need for the development of new treatment options. With a high degree of clinical malignancy and a prognosis among the worst of all types of cancer, anaplastic thyroid carcinoma in particular is a disease with significant unmet medical needs. Eisai hopes that Lenvima will make a contribution to patients as a new standard treatment for unresectable thyroid cancer, which has no established standard treatment in Japan at present.

Discovered at Eisai’s Tsukuba Research Laboratories and developed in-house, Lenvima is an orally administered molecular targeted agent that selectively inhibits the activities of several different molecules including VEGFR, FGFR, RET, KIT and PDGFR. In particular, the agent simultaneously inhibits VEGFR, FGFR and also RET which are especially involved in tumor angiogenesis and proliferation of thyroid cancer. Furthermore, Lenvima has been confirmed through X-ray co-crystal structural analysis to demonstrate a new binding mode (Type V) to VEGFR2, and exhibits rapid binding to the target molecule and potent inhibition of kinase activity, according to kinetic analysis[2].

Lenvima was launched in the United States in February 2015, and received a positive opinion from the European Medicines Agency’s Committee for Medicinal Products for Human Use in March 2015. In addition, the agent is currently undergoing regulatory review in Switzerland, South Korea, Canada, Singapore, Russia, Australia and Brazil. Furthermore, Eisai is conducting a global Phase III study of Lenvima in hepatocellular carcinoma as well as Phase II studies of Lenvima in several other tumor types such as renal cell carcinoma and non-small cell lung cancer.

In addition to providing Lenvima as a new treatment option for thyroid cancer, in accordance with the conditions of approval, Eisai will work after launch to carry out a special use investigation (all-case study)

and promote the appropriate use of Lenvima. Eisai is committed to exploring the potential clinical benefits of Lenvima in order to further contribute to, and address the diverse needs of, patients with cancer, and their families.

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

[Notes to editors]

1. Product Details

1) Product name
   Lenvima® Capsule 4 mg, Lenvima® Capsule 10 mg
2) Generic name
   Lenvatinib mesylate
3) Indication

Lenvima was launched in the United States indicated for the treatment of locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer in February 2015, and received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use for treatment of adult patients with progressive, locally advanced or metastatic differentiated (papillary, follicular, Hürthle cell) thyroid carcinoma refractory to radioactive iodine in March 2015. In addition, Lenvima is currently undergoing regulatory review in Switzerland, South Korea, Canada, Singapore, Russia, Australia and Brazil. Furthermore, Eisai is conducting a global Phase III study of Lenvima in hepatocellular carcinoma as well as Phase II studies of Lenvima in several other tumor types such as renal cell carcinoma and non-small cell lung cancer.

3. About Lenvima's Novel Binding Mode (Type V)[2]

Kinase inhibitors are categorized into several types (Type I to Type V) depending on the binding site and the conformation of the targeted kinase in complex with them. Most of the currently approved tyrosine kinase inhibitors are either Type I or Type II, however according to X-ray crystal structural analysis, Lenvima was found to possess a new Type V binding mode of kinase inhibition that is distinct from existing compounds. In addition, Lenvima was confirmed via kinetic analysis to exhibit rapid and potent inhibition of kinase activity, and it is suggested that this may be attributed to its novel binding mode.

4. About the SELECT study[1]

The SELECT (**S**tudy of (**E**7080) **LE**nvatinib in Differentiated **C**ancer of the **T**hyroid) study was a multicenter, randomized, double-blind, placebo-controlled Phase III study to compare the progression-free survival (PFS) of patients with radioactive iodine-refractory differentiated thyroid cancer and radiographic evidence of disease progression within the prior 13 months, treated with once-daily, oral Lenvima (24mg) versus placebo. Patients were randomized 2:1 to either Lenvima or placebo therapy. The primary endpoint was PFS assessed by independent radiologic review. The secondary endpoints of the study included response rate (sum of complete and partial responses), overall survival (OS) and safety. The study enrolled 392 patients (including 40 patients in Japan) in over 100 sites in Europe, North and South America and Asia, including Japan, and was conducted by Eisai in collaboration with SFJ Pharma Ltd. In the study, Lenvima demonstrated a statistically significant extension in PFS compared to placebo ($p<0.001$; median PFS in the Lenvima group: 18.3 months, median PFS in the placebo group: 3.6 months; Hazard Ratio 0.21 [99% CI: 0.14-0.31]). In addition, Lenvima demonstrated a statistically significant improvement in response rate compared to placebo ($p<0.001$; Lenvima: 64.8% vs placebo: 1.5%). In particular, complete response was observed in 1.5% (4 patients) of the Lenvima group and zero in the placebo group. The most common Lenvima treatment-related adverse events of any grade, which occurred in more than 40% of patients in the Lenvima group, were hypertension (67.8%), diarrhea (59.4%), fatigue or asthenia (59.0%), decreased appetite (50.2%), weight loss (46.4%) and nausea (41.0%).

5. About Study 208

Study 208 was a multi-center, open label, non-randomized, single-arm Phase II clinical study to evaluate the safety,