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Eisai Co., Ltd.

EISAI SUBMITS MARKETING APPROVAL APPLICATIONS FOR ANTICANCER AGENT LENVATINIB SIMULTANEOUSLY IN EUROPE AND U.S.

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has submitted applications to regulatory authorities in the U.S. and Europe (the FDA and EMA respectively) for marketing approval of its novel in-house developed anticancer agent lenvatinib mesylate (lenvatinib) as a treatment for progressive radioiodine-refractory differentiated thyroid cancer (RR-DTC).

An application seeking marketing approval of lenvatinib for the indication of thyroid cancer was submitted in Japan on June 26, 2014. Lenvatinib was granted Orphan Drug Designation for thyroid cancer in Japan, Europe and the U.S. Lenvatinib was also granted an accelerated assessment in Europe by the EMA, as it is a new medicine expected to be of major public health interest, particularly from the viewpoint of therapeutic innovation.

Lenvatinib is an oral multiple receptor tyrosine kinase (RTK) inhibitor with a novel binding mode that selectively inhibits the kinase activities of several different RTKs including VEGFR, FGFR, PDGFRα, KIT and RET, involved in angiogenesis and tumor proliferation. This potentially makes lenvatinib a first-in-class treatment in thyroid cancer, especially given that it simultaneously inhibits the kinase activities of FGFR as well as VEGFR.

The applications submitted were based on a Phase III clinical study, known as the SELECT (Study of (E7080) LEnvatinib in Differentiated Cancer of the Thyroid) trial, which was a multicenter, randomized, double-blind, placebo-controlled study of lenvatinib in 392 patients with RR-DTC and radiographic evidence of disease progression within the prior 13 months (patients may have received ≤1 prior VEGFR-targeted therapies). The study was conducted by Eisai in cooperation with SFJ Pharma Ltd.

Compared to placebo, lenvatinib achieved a statistically significant improvement (Hazard Ratio (HR) 0.21, $p<0.0001$) in progression free survival (PFS), which was the primary objective of the study. The most common lenvatinib treatment-related adverse events (events with an incidence rate of at least 40%) were hypertension, diarrhea, decreased appetite, weight loss and nausea.

The number of patients newly diagnosed with thyroid cancer in 2012 in the U.S. and Europe was estimated to be approximately 52,000 and 53,000, respectively. Although treatment is possible for most types of thyroid cancer, there are few treatment options available once thyroid cancer has progressed, therefore it remains a disease with significant unmet medical needs.

Eisai is committed to exploring the potential clinical benefits of lenvatinib in order to further contribute to patients with cancer, including patients with thyroid cancer, and their families.

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[Notes to editors]

1. About Lenvatinib (E7080)

Lenvatinib, discovered and developed by Eisai, is an oral 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 (FLT1), VEGFR2 (KDR) and VEGFR3 (FLT4)), in addition to other proangiogenic and oncogenic pathway-related RTKs (including fibroblast growth factor (FGF) receptors FGFR1, 2, 3 and 4; the platelet-derived growth factor (PDGF) receptor PDGFRα; KIT; and RET) involved in tumor proliferation. This potentially makes lenvatinib a first-in-class treatment in thyroid cancer, especially given that it simultaneously inhibits the kinase activities of FGFR as well as VEGFR. An application seeking marketing approval of lenvatinib for the indication of thyroid cancer was submitted in Japan on June 26, 2014. Lenvatinib was granted Orphan Drug Designation in Japan for thyroid cancer in August 2012, in the United States for the treatment of follicular, medullary, anaplastic, and metastatic or locally advanced papillary thyroid cancer in December 2012, and in Europe for follicular and papillary thyroid cancer in April 2013. It is currently under development as a potential treatment for hepatocellular carcinoma (Phase III), non-small cell lung cancer (Phase II) and other solid tumor types.

2. About the Accelerated Assessment by the European Medicines Agency (EMA)

The EMA's accelerated assessment procedure is granted for new medicines that are expected to be of major public health interest, particularly from the viewpoint of therapeutic innovation.

3. About the SELECT Trial

The SELECT (Study of (E7080) LEnvatinib in Differentiated Cancer of the Thyroid) trial was a multicenter, randomized, double-blind, placebo-controlled Phase III study of lenvatinib in patients with RR-DTC and radiographic evidence of disease progression within the prior 13 months (patients may have received ≤1 prior VEGFR-targeted therapies). Patients were randomized 2:1 to either receive once-daily, oral lenvatinib (24 mg) or placebo therapy. The study enrolled 392 patients 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.

Compared to placebo, lenvatinib achieved a statistically significant improvement (Hazard Ratio (HR) 0.21; 99% CI: 0.14-0.31; $p<0.0001$) in progression free survival (PFS), which was the primary objective of the study. The median PFS with lenvatinib and placebo was 18.3 months and 3.6 months respectively. Secondary endpoints included overall response rate*, overall survival (OS) and safety. The results for overall response rate were 64.8% in the lenvatinib group and 1.5% in the placebo group. Complete response was observed in 1.5% (4 patients) of the lenvatinib group and zero in the placebo group. The median time to response for lenvatinib was 2.0 months. Median OS has not been reached yet in both groups. The most common lenvatinib treatment-related adverse events (TRAEs) (events with an incidence rate of at least 40%) were hypertension (67.8%), diarrhea (59.4%), decreased appetite (50.2%), weight loss (46.4%) and nausea (41.0%). The most common TRAEs (events with an incidence rate of at least 5%) of Grade 3 or higher (Common Terminology Criteria for Adverse Events) included hypertension (41.8%), proteinuria (10.0%), weight loss (9.6%), diarrhea (8.0%), and decreased appetite (5.4%).

*Overall response rate: Sum of complete response and partial response

4. About Thyroid Cancer

Thyroid cancer refers to cancer that forms in the tissues of the thyroid gland, located at the base of the throat near the trachea. It is more common in women than in men. The most common types of thyroid cancer, papillary and follicular (including Hürthle cell), are classified as differentiated thyroid cancer and account for approximately 95% of all cases. The remaining cases are classified as either undifferentiated (3-5% of cases) or medullary carcinoma (1-2% of cases). While most differentiated thyroid cancer patients are curable with surgery and radioactive iodine treatment, a small percentage of patients do not respond to therapy.

5. About the SFJ Pharmaceuticals Group

The SFJ Pharmaceuticals Group, which includes SFJ Pharma Ltd., is a global drug development company, which provides a unique co-development partnering model for some of the world's top pharmaceutical and biotechnology companies. SFJ uses its financial strength and core team of pharmaceutical development experts to provide highly customized partnering models in which SFJ provides the funding and clinical development supervision, necessary to obtain regulatory approval for some of the most promising drug development programs of pharmaceutical and biotechnology companies.