News Release

FDA Approves Eisai's LENVIMA™ (lenvatinib) for the Treatment of Patients with Locally Recurrent or Metastatic, Progressive, Radioactive Iodine-Refractory Differentiated Thyroid Cancer

- *New Therapy Demonstrated a Dramatic Improvement in Progression-Free Survival and a Statistically Significant Overall Response Rate in Some Patients with RAI-Refractory Differentiated Thyroid Cancer*
- *File Submission and Approval Based on Data from Phase 3 SELECT Study Published in New England Journal of Medicine on February 12, 2015*
- *Approval Granted Two Months Ahead of FDA Priority Review PDUFA Date*

Woodcliff Lake, NJ – February 13, 2015 – Eisai Inc. announced today that the U.S. Food and Drug Administration (FDA) approved the company's receptor tyrosine kinase inhibitor LENVIMA™ (lenvatinib) for the treatment of locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (RAI-R DTC). LENVIMA was approved following a priority review by the FDA, which is designated for drugs the FDA believes have the potential to provide a significant improvement in the treatment of a serious condition. LENVIMA demonstrated a statistically significant progression-free survival (PFS) prolongation and response rate in patients with progressive, differentiated thyroid cancer who had become refractory to radioactive iodine (RAI) therapy.

"In the pivotal Phase 3 SELECT clinical trial, recently published in the *New England Journal of Medicine*, treatment with LENVIMA resulted in a highly statistically significant improvement in progression-free survival and a high overall response rate in patients with locally recurrent or metastatic, progressive, RAI-refractory DTC," said Lori J. Wirth, M.D., study investigator and medical director of the Center for Head and Neck Cancers at the Massachusetts General Hospital. "The thyroid cancer community welcomes an agent that offers a significant, effective option for the treatment of differentiated thyroid cancer in patients who have progressed after becoming refractory to RAI therapy."

"The incidence of thyroid cancer has been increasing globally over the last 50 years and for patients with thyroid cancer that progresses following surgery and radioactive iodine treatment, the prognosis is often poor," said Gary Bloom, Executive Director of ThyCa: Thyroid Cancer Survivors' Association, Inc. "We are excited about the approval of LENVIMA, which may help address an unmet need as there are limited treatment options for patients with this type of thyroid cancer."

In the Phase 3 SELECT trial, which included 392 patients, LENVIMA demonstrated a highly statistically significant improvement in PFS in patients with RAI-R DTC compared with placebo. The median PFS, or delay in the length of time during and after treatment in which the disease did not worsen, with LENVIMA and placebo was 18.3 months and 3.6 months, respectively (HR 0.21; 95% CI: 0.16-0.28; $p<0.001$). In addition, an overall response rate, the sum of partial and complete response rates, of 65% was seen in patients treated with LENVIMA versus 2% with placebo, which included a complete response achieved in 2% of patients treated with LENVIMA versus 0% with placebo. Based on RECIST v1.1 criteria, a partial response is defined as a minimum 30% decrease in the sum of diameters of target lesions and a complete response is defined as a complete disappearance of tumors.

Serious risks seen in patients in the Phase 3 SELECT clinical trial were hypertension, cardiac dysfunction, arterial thromboembolic events, hepatotoxicity, proteinuria, renal failure and impairment,

gastrointestinal perforation and fistula formation, QT interval prolongation, hypocalcemia, reversible posterior leukoencephalopathy syndrome, hemorrhagic events, impairment of exogenous thyroid suppression and embryofetal toxicity. The most common adverse reactions observed in greater than or equal to 30% of LENVIMA-treated patients, in order of decreasing frequency, were: hypertension, fatigue, diarrhea, arthralgia/myalgia, decreased appetite, weight decreased, nausea, stomatitis, headache, vomiting, proteinuria, palmar-plantar erythrodysesthesia (PPE) syndrome, abdominal pain, and dysphonia. The most common serious adverse reactions (at least 2%) were pneumonia (4%), hypertension (3%), and dehydration (3%).

It is important for doctors to know that when treating with LENVIMA, they may modify the dose as needed according to the recommendations provided in the prescribing information. Management of some adverse reactions may require the dose of LENVIMA to be withheld, reduced or discontinued. Upon resolution/improvement of an adverse reaction, treatment may be resumed at a reduced dose as suggested in the prescribing information. In the clinical trial, adverse events led to dose reductions in 68% of patients who received LENVIMA and 5% of patients who received placebo. Some patients will need to discontinue treatment for serious adverse reactions. In the trial, 18% of patients treated with LENVIMA and 5% who received placebo discontinued treatment. The most common adverse reactions (at least 10%) that resulted in dose reductions of LENVIMA were hypertension (13%), proteinuria (11%), decreased appetite (10%), and diarrhea (10%). The most common adverse reactions (at least 1%) resulting in discontinuation of LENVIMA were hypertension (1%) and asthenia (1%).

“We are excited that LENVIMA was approved today by the FDA following the priority review designation received in October and look forward to offering this new treatment option to patients with progressive, RAI-refractory DTC,” said Takashi Owa, Ph.D., Chief Innovation Officer at Eisai. “Eisai is committed to innovative research and product creation with the goal of helping patients with cancer.”

Eisai is committed to ensuring patients have access to medicines from which they may benefit and is dedicated to working to ensure that our products are available to those who need them. Once LENVIMA is available, Eisai will provide reimbursement support programs for eligible patients.

LENVIMA™ (lenvatinib) will be available to order in the near future through specialty pharmacies Biologics, Inc. and Accredo.

About the LENVIMA™ (lenvatinib) Pivotal Clinical Trial
The SELECT (Study of E7080 LEnvatinib in Differentiated Cancer of the Thyroid) study was a multicenter, randomized, double-blind, placebo-controlled Phase 3 study to compare the PFS of patients with locally recurrent or metastatic RAI-R DTC and radiographic evidence of disease progression within 12 months prior to randomization, treated with LENVIMA (24 mg) once daily or placebo. Other outcome measures of the study included overall response rate (ORR), overall survival (OS) and safety. The study enrolled 392 patients stratified by geographic region, prior VEGF/VEGFR targeted therapy and age and randomized at a ratio of 2:1 to receive treatment with either LENVIMA 24 mg/day (administered orally, once a day) or placebo. The SELECT study was conducted by Eisai in collaboration with the SFJ Pharmaceuticals Group.

The full results of this study were presented at the 2014 ASCO Annual Meeting and recently published in the *New England Journal of Medicine*.

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 and most are in their 40s or 50s at the time of diagnosis. Thyroid cancer is the most common endocrine malignancy and global figures show that its incidence has increased significantly over the last 50 years.

The most common types of thyroid cancer, papillary and follicular (including Hürthle cell), are classified as differentiated thyroid cancer (DTC) and account for approximately 90% of all cases. While most DTC patients are curable with surgery and radioactive iodine treatment, the prognosis for those patients whose cancers persist or recur is poor. There are limited treatment options for this radioactive iodine-refractory form of thyroid cancer.

About LENVIMA™ (lenvatinib)
LENVIMA, discovered and developed by Eisai, is a receptor tyrosine kinase (RTK) inhibitor that inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4). LENVIMA also inhibits other RTKs that have been implicated in pathogenic angiogenesis, tumor growth, and cancer progression in addition to their normal cellular functions, including fibroblast growth factor (FGF) receptors FGFR1, 2, 3, and 4; the platelet derived growth factor receptor alpha (PDGFRα), KIT, and RET. It is currently under investigation in hepatocellular, renal cell carcinoma, endometrial, anaplastic thyroid cancer, non-small cell lung cancer and other solid tumor types. LENVIMA was granted Priority Review designation by the FDA in October 2014. Eisai was granted Orphan Drug Designation (ODD) for lenvatinib in various types of thyroid cancer in the United States, Japan, and Europe.

LENVIMA™ (lenvatinib) Important Safety Information

Warnings and Precautions

Hypertension was reported in 73% of LENVIMA-treated patients (of which 44% were ≥ Grade 3) and 16% of patients in the placebo group. Control blood pressure prior to treatment and monitor blood pressure after 1 week, then every 2 weeks for the first 2 months, and then at least monthly during treatment. Withhold LENVIMA for Grade 3 hypertension; resume at a reduced dose when hypertension is controlled at ≤ Grade 2. Discontinue LENVIMA for life-threatening hypertension.

Cardiac dysfunction was reported in 7% of LENVIMA-treated patients (2% Grade 3 or greater). Monitor patients for clinical symptoms or signs of cardiac decompensation. Withhold LENVIMA for development of Grade 3 cardiac dysfunction until improved to Grade 0 or 1 or baseline. Resume at a reduced dose or discontinue LENVIMA depending on the severity and persistence of cardiac dysfunction. Discontinue LENVIMA for Grade 4 cardiac dysfunction.

Arterial thromboembolic events were reported in 5% of LENVIMA-treated patients; events of Grade 3 or greater were 3%. Discontinue LENVIMA following an arterial thrombotic event. LENVIMA has not been studied in patients who have had an arterial thromboembolic event within the previous 6 months.

4% of LENVIMA-treated patients experienced an increase in ALT and 5% experienced an increase in AST that was Grade 3 or greater. Monitor liver function before initiation and during treatment with LENVIMA. Withhold LENVIMA for the development of ≥ Grade 3 liver impairment until resolved to Grade 0 to 1 or baseline. Resume at a reduced dose or discontinue LENVIMA depending on the severity and persistence of hepatotoxicity. Discontinue LENVIMA for hepatic failure.

Proteinuria was reported in 34% of LENVIMA-treated patients (of which 11% were Grade 3). Monitor for proteinuria before initiation of, and periodically during treatment. Obtain a 24 hour urine protein if urine dipstick proteinuria ≥2+ is detected. Withhold LENVIMA for ≥ 2 grams of proteinuria/24 hours and resume at a reduced dose when proteinuria is <2 gm/24 hours. Discontinue LENVIMA™ (lenvatinib) for nephrotic syndrome.

Events of renal impairment were reported in 14% of LENVIMA-treated patients. Renal failure or impairment ≥ Grade 3 was 3% in LENVIMA-treated patients. Withhold LENVIMA for development of Grade 3 or 4 renal failure/impairment until resolved to Grade 0 to 1 or baseline. Resume at a reduced dose or discontinue LENVIMA depending on the severity and persistence of renal impairment.

Events of gastrointestinal perforation or fistula were reported in 2% of LENVIMA-treated patients. Discontinue LENVIMA in patients who develop gastrointestinal perforation or life-threatening fistula.

QT/QTc interval prolongation was reported in 9% of LENVIMA-treated patients (2% Grade 3 or greater). Monitor ECG in patients with congenital long QT syndrome, CHF, bradyarrhythmias, or patients taking drugs known to prolong the QT interval. Monitor and correct electrolyte abnormalities in all patients. Withhold LENVIMA for the development of ≥ Grade 3 QT interval prolongation. Resume LENVIMA at a reduced dose when QT prolongation resolves to Grade 0 or 1 or baseline.

Hypocalcemia ≥ Grade 3 was reported in 9 % of LENVIMA-treated patients. Monitor blood calcium levels at least monthly and replace calcium as necessary during LENVIMA treatment. Interrupt and adjust LENVIMA dosing as necessary depending on severity, presence of ECG changes, and persistence of hypocalcemia.

Reversible posterior leukoencephalopathy syndrome (RPLS) was reported in 3 patients across clinical studies in which 1108 patients received LENVIMA. Confirm the diagnosis of RPLS with MRI. Withhold LENMIVA for RPLS until fully resolved. Resume at a reduced dose or discontinue LENVIMA depending on the severity and persistence of neurologic symptoms.

Hemorrhagic events occurred in 35% of LENVIMA-treated patients and in 18% of the placebo group. The incidence of Grade 3-5 hemorrhage was similar between arms at 2% and 3%, respectively. The most frequently reported hemorrhagic event was epistaxis (11% Grade 1 and 1% Grade 2). Discontinuation due to hemorrhagic events occurred in 1% of LENVIMA-treated patients. There was one case of fatal intracranial hemorrhage among 16 patients who received LENVIMA and had CNS metastases at baseline. Withhold LENVIMA for the development of Grade 3 hemorrhage until resolved to Grade 0 to 1. Resume at a reduced dose or discontinue LENVIMA depending on the severity and persistence of hemorrhage. Discontinue LENVIMA in patients who experience Grade 4 hemorrhage.

LENVIMA impairs exogenous thyroid suppression. Elevation of TSH level above 0.5 mU/L was observed post baseline in 57% of LENVIMA-treated patients. Monitor TSH levels monthly and adjust thyroid replacement medication as needed.

LENVIMA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LENVIMA and for at least 2 weeks following completion of therapy.

Advise women not to breastfeed during treatment with LENVIMA.

Adverse Reactions

The most common adverse reactions observed in LENVIMA-treated patients vs. placebo treated patients respectively were hypertension (73% vs 16%), fatigue (67% vs 35%), diarrhea (67% vs 17%), arthralgia/myalgia (62% vs 28%), decreased appetite (54% vs 18%), weight decreased (51% vs 15%), nausea (47% vs 25%), stomatitis (41% vs 8%), headache (38% vs 11%), vomiting (36% vs 15%), proteinuria (34% vs 3%), palmar-plantar erythrodysesthesia syndrome (32% vs 1%), abdominal pain (31% vs 11%), and dysphonia (31% vs 5%).

For more information about LENVIMA, click here for the full Product Information or visit www.LENVIMA.com.

LENVIMA™ (lenvatinib) Indication
LENVIMA™ (lenvatinib) is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine refractory differentiated thyroid cancer (DTC).

About Eisai Inc.
At Eisai Inc., *human health care* is our goal. We give our first thoughts to patients and their families, and helping to increase the benefits health care provides. As the U.S. pharmaceutical subsidiary of Tokyo-based Eisai Co., Ltd., we have a passionate commitment to patient care that is the driving force behind our efforts to help address unmet medical needs. We are a fully integrated pharmaceutical business with discovery, clinical, manufacturing and marketing capabilities. Our key areas of commercial focus include oncology and specialty care (Alzheimer's disease, epilepsy and metabolic disorders). To learn more about Eisai Inc., please visit us at www.eisai.com/US.

Eisai Inc. has affiliates that are part of a global product creation organization that includes R&D facilities in Massachusetts, New Jersey, North Carolina and Pennsylvania, as well as a global demand chain organization that includes manufacturing facilities in Maryland and North Carolina. Eisai's global areas of R&D focus include neuroscience; oncology; metabolic disorders; vascular, inflammatory and immunological reaction; and antibody-based programs.

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.

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