FOR IMMEDIATE RELEASE
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Eisai Co., Ltd.
MSD K.K.

LENVIMA®（LENVATINIB） APPROVED FOR ADDITIONAL INDICATION OF UNRESECTABLE THYMIC CARCINOMA IN JAPAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and MSD K.K. (Headquarters: Tokyo, President: Kyle Tattle, "MSD"), a subsidiary of Merck & Co., Inc., Kenilworth, N.J., U.S.A., announced today that LENVIMA® (generic name: lenvatinib mesylate), the multiple receptor tyrosine kinase inhibitor discovered by Eisai, has been approved in Japan for the additional indication of treatment of unresectable thymic carcinoma. This marks the first approval for LENVIMA for unresectable thymic carcinoma in Japan.

The approval was based on the results of an open-label, single-arm, multicenter, investigator-initiated clinical phase II study (REMORA study) conducted in 8 centers across Japan including the National Cancer Center Hospital, evaluating LENVIMA as a single agent in 42 patients with thymic carcinoma previously treated with at least one platinum-based regimen.
LENVIMA met the study's primary endpoint of objective response rate (ORR) as assessed by independent imaging review, demonstrating an ORR of 38.1% (90% confidence interval (CI): 25.6-52.0). The lower value of the CI exceeded the pre-specified statistical criteria with a threshold ORR of 10%. The most common three treatment-related adverse events were hypertension (88.1%), proteinuria (71.4%), and palmar-plantar erythrodysesthesia syndrome (69.0%), which is consistent with the safety profile observed in the previously approved indications.

Thymic carcinoma is an extremely rare disease with low prevalence. It is estimated that there are about 140 patients in Japan. For unresectable thymic carcinoma, platinum-based first-line therapy is recommended. However, since the standard treatment has not yet been established for second-line or later therapy, this is an area of high unmet medical need. In June 2020, LENVIMA received orphan drug designation in Japan for unresectable thymic carcinoma.

Eisai and MSD have been collaborating through the provision of information on LENVIMA in Japan since October 2018, and will work together to expedite the maximization of LENVIMA's contribution to patients with cancer.

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<Notes to editors>

1. About LENVIMA (generic name: lenvatinib mesylate)

LENVIMA, discovered and developed by Eisai, is a kinase inhibitor that inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4). LENVIMA inhibits other kinases 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 FGFR1-4, the platelet derived growth factor receptor alpha (PDGFRα), KIT, and RET. In syngeneic mouse tumor models, lenvatinib decreased tumor-associated macrophages, increased activated cytotoxic T cells, and demonstrated greater antitumor activity in combination with an anti-PD-1 monoclonal antibody compared to either treatment alone. Currently, LENVIMA has been approved for monotherapy as a treatment for thyroid cancer in over 70 countries including Japan, in Europe, China and in Asia, and in the United States for radioiodine-refractory differentiated thyroid cancer. In addition, LENVIMA has been approved for monotherapy as a treatment for unresectable hepatocellular carcinoma in over 65 countries including Japan, the United States, in Europe, China and in Asia. It is also approved in combination with everolimus as a treatment for renal cell carcinoma following prior antiangiogenic therapy in over 60 countries, including the United States, in Europe and in Asia. In Europe, the agent was launched under the brand name Kisplyx® for renal cell carcinoma. In addition, it is approved in combination with KEYTRUDA as a treatment for advanced endometrial cancer that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation in over 10 countries including the United States, Canada and Australia. Continued approval for this indication is contingent upon verification and description of clinical benefit in the confirmatory trials.

2. About REMORA study (NCCH1508 study)[1]

This study is an open-label, single-group, multicenter, investigator initiated clinical phase II study (8 centers across Japan including the National Cancer Center Hospital). Forty-two patients with unresectable advanced or metastatic thymic carcinoma were enrolled who had progressed after at least one prior platinum-based therapy. The primary endpoint is Objective Response Rate (ORR) by independent image review using RECIST1.1, and secondary endpoints include Progression Free Survival (PFS), Disease Control Rate (DCR), Overall Survival (OS) and safety. Lenvatinib was administered at a starting dose of 24 mg once daily in 4-week cycles, and the dose was appropriately reduced according to the patient's condition until the disease progressed or unacceptable adverse events was observed.

For efficacy analysis[2], ORR was 38.1% (90% Confidence Interval (CI): 25.6-52.0) and the best overall response was 38.1% for partial response, 57.1% for stable disease, and 4.8% for disease progression. PFS (median) was 9.3 months (95% CI: 7.7-13.9), DCR was 95.2% (95% CI: 83.8-99.4), and the median OS was not reached (95% CI: 16.1-NR (not reached)) at the data cutoff date (Feb 22, 2019). The major treatment-related adverse events[3] (more than 30%) were hypertension (88.1%), proteinuria (71.4%), palmar-plantar erythrodysesthesia syndrome (69.0%), hypothyroidism (64.3%), diarrhea (57.1%), thrombocytopenia (54.8%), decreased appetite (42.9%), weight loss (40.5%), dysphonia (40.5%), increased aspartate aminotransferase (33.3%), malaise (33.3%), and stomatitis (33.3%).

[1] Jun Sato, Miyako Satouchi, Shoichi Itoh, Yusuke Okuma, Seiji Niho, Hidenori Mizugaki, Haruyasu Murakami, Yasuhito Fujisaka, Toshiyuki Kozuki, Kenichi Nakamura, Yukari Nagasaka, Mamiko Kawasaki, Tomoaki Yamada, Ryunosuke Machida, Aya Kuchiba, Yuichiro Ohe, Noboru Yamamoto; Lenvatinib in patients with advanced or metastatic thymic carcinoma (REMORA): a multicenter, phase 2 trial. *The Lancet Oncology,* 2020, Vol.21, No. 6, p843-850

[2] Based on the package insert.

[3] The adverse event data has been updated from the data in the paper.

3. About the Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A. Strategic Collaboration

In March 2018, Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A., known as MSD outside the United States and Canada, through an affiliate, entered into a strategic collaboration for the worldwide co-development and co-commercialization of LENVIMA. Under the agreement, the companies will jointly develop, manufacture and commercialize LENVIMA, both as a monotherapy and in combination with Merck & Co., Inc., Kenilworth, N.J., U.S.A.'s anti-PD-1 therapy KEYTRUDA® (generic name: pembrolizumab).

In addition to ongoing clinical studies evaluating the LENVIMA plus KEYTRUDA combination across several different tumor types, the companies have jointly initiated new clinical studies through the LEAP (LEnvatinib And Pembrolizumab) clinical program and are evaluating the combination in 14 different tumor types (endometrial carcinoma, hepatocellular carcinoma, melanoma, non-small cell lung cancer, renal cell carcinoma, squamous cell carcinoma of the head and neck, urothelial cancer, biliary tract cancer, colorectal cancer, gastric cancer, glioblastoma, ovarian cancer, pancreatic cancer and triple-negative breast cancer) across 20 clinical trials.

4. About Eisai Co., Ltd.

Eisai is a leading global research and development-based pharmaceutical company headquartered in Japan, with approximately 10,000 employees worldwide. Eisai defines our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. We strive to realize our *hhc* philosophy by delivering innovative products in therapeutic areas with high unmet medical needs, including Oncology and Neurology. In the spirit of *hhc*, Eisai takes that commitment even further by applying our scientific expertise, clinical capabilities and patient insights to discover and develop innovative solutions that help address society's toughest unmet needs, including neglected tropical diseases and the Sustainable Development Goals.

For more information about Eisai, please visit www.eisai.com (for global), us.eisai.com (for U.S.) or www.eisai.eu (for Europe, Middle East, Africa), and connect with us on Twitter (U.S. and global) and LinkedIn (for U.S.).

5. About MSD

For 130 years, MSD has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. MSD is a trade name of Merck & Co., Inc., with headquarters in Kenilworth, N.J., U.S.A. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, MSD continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit www.msd.co.jp and connect with us on Facebook, Twitter and YouTube.