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Eisai Co., Ltd.

MINISTRY OF HEALTH, LABOUR AND WELFARE GRANTS ORPHAN DRUG DESIGNATION IN JAPAN TO ANTI-CANCER AGENT LENVIMA® (LENVATINIB) WITH PROSPECTIVE INDICATION FOR UTERINE BODY CANCER

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has received orphan drug designation for LENVIMA® (generic name: lenvatinib mesylate), the orally available multiple receptor kinase inhibitor discovered by Eisai, with a prospective indication for uterine body cancer, by the Ministry of Health, Labour and Welfare (MHLW).

In Japan, the estimated number of patients with uterine body cancer is approximately 30,000.[1] It is estimated that in 2020, there were more than 17,000 new cases of uterine body cancer and more than 3,000 deaths from the disease.[2] It is considered that more than 90% of uterine body cancers occur in the endometrium.[3]

The pivotal Phase 3 Study 309/KEYNOTE-775 evaluated LENVIMA in combination with KEYTRUDA® (generic name: pembrolizumab) in patients with advanced endometrial cancer (advanced uterine body cancer in Japan), following at least one prior platinum-based regimen in Japan, the United States, Europe and other countries. In this study, LENVIMA plus KEYTRUDA met its dual primary endpoints, overall survival (OS) and progression-free survival (PFS), as well as its secondary efficacy endpoint of objective response rate (ORR). Currently, Eisai is preparing to submit an application for additional indications based on these results in various countries around the world including Japan.

In March 2018, Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A., through an affiliate, entered into a strategic collaboration for the worldwide co-development and co-commercialization of LENVIMA.

Eisai positions oncology as a key therapeutic area and is aiming to discover innovative new medicines with the potential to cure cancer. Eisai is committed to expanding the potential clinical benefits of LENVIMA for cancer treatment, as it seeks to contribute addressing the diverse needs of, and increasing the benefits provided to, patients with cancer and their families.

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

[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, LENVIMA 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. The combination of LENVIMA and everolimus showed increased anti-angiogenic and anti-tumor activity as demonstrated by decreased human endothelial cell proliferation, tube formation, and VEGF signaling in vitro and tumor volume in mouse xenograft models of human renal cell cancer greater than each drug 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 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 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 Uterine Body Cancer and Endometrial Cancer

In 2020, it was estimated there were more than 417,000 new cases of uterine body cancer diagnosed and more than 97,000 deaths from the disease worldwide.[4] In Japan, there were more than 17,000 new cases and 3,000 deaths from uterine body cancer in 2020.[2] In Japan alone, it was estimated there were more than 30,000 cases of uterine body cancer diagnosed.[1] It is considered that more than 90% of uterine body cancers occur in the endometrium.[3] The five-year survival rate for metastatic endometrial cancer is estimated to be approximately 17%.[5]

3. About Study 309/KEYNOTE-775

Study 309/KEYNOTE-775 is a multicenter, randomized, open-label, Phase 3 trial (ClinicalTrials.gov, NCT03517449) evaluating LENVIMA in combination with KEYTRUDA in patients with advanced endometrial cancer following at least one prior platinum-based regimen. The dual primary endpoints are OS and PFS, as assessed by Blinded Independent Central Review (BICR) per Response Evaluation Criteria in Solid Tumors Version (RECIST) v1.1. Select secondary endpoints include ORR by BICR per RECIST v1.1 and safety/tolerability. Of the 827 patients enrolled, 697 patients had tumors that were non-MSI-H or pMMR, and 130 patients had tumors that were MSI-H or dMMR. Patients were randomized 1:1 to receive KEYTRUDA (200 mg intravenously [IV] every three weeks) for up to 35 cycles (approximately two years) in combination with LENVIMA (20 mg orally once daily); or Chemotherapy (Treatment of physician's choice [TPC] of either doxorubicin 60 mg/m^2 IV every three weeks for up to a maximum cumulative dose of 500 mg/m^2 or paclitaxel 80 mg/m^2 IV on a 28-day cycle [three weeks of receiving weekly paclitaxel and one week of not receiving paclitaxel])

4. Orphan Drug Designation System in Japan

The orphan drug designation system in Japan aims to support the development of drugs for diseases for which the number of patients is small and research and development is not progressing, despite high unmet medical need. As the requirement for designation based on Article 77-2 of the Pharmaceutical and Medical Device Act (PMD Act) of Japan, a drug must meet the following conditions in order to be considered for orphan drug designation in Japan: the number of people expected to use the drug for its intended use is less than 50,000 people in Japan; there is no suitable alternative drug or treatments in Japan, or the proposed drug is expected to be significantly more effective or safer than drugs already available on the Japanese market; there is a scientific rationale to support the necessity of the drug for the target disease, and the development plan for the drug is appropriate. Specific measures to support the development of orphan drugs include giving prioritized consultation regarding clinical development and conducting priority examinations, reducing application fees, extending registration validity period, granting subsidies for research and development expenditures, and tax incentives.

[1] Patient Survey 2017, e-Stat: Portal Site of Official Statistics of Japan (available for Japanese only)
https://www.e-stat.go.jp/

[2] International Agency for Research on Cancer, World Health Organization. “Japan Fact Sheet.” Cancer Today, 2020.
https://gco.iarc.fr/today/data/factsheets/populations/392-japan-fact-sheets.pdf .

[3] American Cancer Society, “CANCER FACT & FIGURES 2020.”
https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/cancer-facts-and-figures-2020.pdf .

[4] International Agency for Research on Cancer, World Health Organization. “Corpus uteri Fact Sheet.” Cancer Today, 2020.
https://gco.iarc.fr/today/data/factsheets/cancers/24-Corpus-uteri-fact-sheet.pdf .

[5] American Cancer Society website, accessed 2/16/2021:
https://www.cancer.org/cancer/endometrial-cancer/detection-diagnosis-staging/survival-rates.html .