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Eisai Co., Ltd.

LENVIMA®（LENVATINIB）IN COMBINATION WITH KEYTRUDA®（PEMBROLIZUMAB） APPROVED IN TAIWAN FOR THE TREATMENT OF PATIENTS WITH ADVANCED ENDOMETRIAL CARCINOMA WHO HAVE DISEASE PROGRESSION FOLLOWING PRIOR SYSTEMIC THERAPY IN ANY SETTING AND ARE NOT CANDIDATES FOR CURATIVE SURGERY OR RADIATION

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that LENVIMA® (generic name: lenvatinib mesylate), the multiple receptor tyrosine kinase inhibitor discovered by Eisai, in combination with Merck & Co., Inc., Kenilworth, N.J., U.S.A. (known as MSD outside the United States and Canada)'s KEYTRUDA® (generic name: pembrolizumab) has been approved in Taiwan for the treatment of patients with advanced endometrial carcinoma who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

The approval is based on results from the pivotal Phase 3 Study 309/KEYNOTE-775 trial. These results were presented at the Society of Gynecologic Oncology (SGO) 2021 Annual Meeting on Women's Cancer in March 2021, and published in the *New England Journal of Medicine* in January 2022.[1] In this trial, LENVIMA plus KEYTRUDA demonstrated statistically significant improvements in overall survival (OS), reducing the risk of death by 38% (HR=0.62 [95% CI, 0.51-0.75]; p<0.0001), and progression-free survival (PFS), reducing the risk of disease progression or death by 44% (HR=0.56 [95% CI, 0.47-0.66]; p<0.0001), versus chemotherapy (investigator's choice of doxorubicin or paclitaxel). The median OS was 18.3 months for LENVIMA plus KEYTRUDA versus 11.4 months for chemotherapy. The median PFS was 7.2 months for LENVIMA plus KEYTRUDA versus 3.8 months for chemotherapy. The objective response rate (ORR) was 32% (95% CI, 27-37) for patients treated with LENVIMA plus KEYTRUDA versus 15% (95% CI, 11-18) for patients treated with chemotherapy (p<0.0001). Patients treated with LENVIMA plus KEYTRUDA achieved a complete response (CR) rate of 7% and partial response (PR) rate of 25% versus a CR rate of 3% and a PR rate of 12% for patients treated with chemotherapy.[2] In this trial, the five most common adverse reactions (any grade) observed in the LENVIMA plus KEYTRUDA combination arm were hypothyroidism, hypertension, fatigue, diarrhea and musculoskeletal disorders.[2]

LENVIMA plus KEYTRUDA was previously approved under accelerated approval process in Taiwan, for the treatment of patients with advanced endometrial carcinoma 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 based on data from the Study 111/KEYNOTE-146 trial. In accordance with accelerated approval regulations, continued approval was contingent upon verification and description of clinical benefit; these accelerated approval requirements have been fulfilled with the data from Study 309/KEYNOTE-775.

Endometrial cancer is the most common type of uterine body cancer. It is considered that more than 90% of uterine body cancers occur in the endometrium.[3] Worldwide, it was estimated there were more than 417,000 new cases and more than 97,000 deaths from uterine body cancers in 2020.[4] In Taiwan, there

were more than 2,700 new cases of uterine body cancer and nearly 400 deaths from the disease in 2018.[5] The five-year relative survival rate for metastatic endometrial cancer (stage IV) is estimated to be approximately 17%.[6]

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 lenvatinib for cancer treatment, as it seeks to contribute to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families and healthcare professionals.

*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 lenvatinib, both as monotherapy and in combination with the anti-PD-1 therapy pembrolizumab from Merck & Co., Inc., Kenilworth, N.J., U.S.A.

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[Notes to editors]

1. About LENVIMA® (lenvatinib mesylate)

LENVIMA, discovered and developed by Eisai, is an orally available 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.

Currently, LENVIMA has been approved for monotherapy as a treatment for thyroid cancer in over 75 countries including Japan, in Europe, China and in Asia, and in the United States for locally recurrent or metastatic, progressive, radioiodine-refractory differentiated thyroid cancer. In addition, LENVIMA has been approved for monotherapy as a treatment for unresectable hepatocellular carcinoma in over 70 countries including Japan, in Europe, China and in Asia, and in the United States for first-line unresectable hepatocellular carcinoma. LENVIMA has been approved for monotherapy as a treatment for unresectable thymic carcinoma in Japan. It is also approved in combination with everolimus as a treatment for renal cell carcinoma following prior antiangiogenic therapy in over 60 countries, including in Europe and Asia, and in the United States the treatment of adult patients with advanced renal cell carcinoma following one prior anti-angiogenic therapy. In Europe, the agent was launched under the brand name Kisplyx® for renal cell carcinoma. LENVIMA has been approved in combination with KEYTRUDA (generic name: pembrolizumab), for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC) in the United States and in Europe. LENVIMA has been approved in combination with KEYTRUDA as a treatment for advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation in the United States, and has been approved for the similar indication (including conditional approval) in over 10 countries such as Canada and Australia. In some regions, continued approval for this indication is contingent upon verification

and description of clinical benefit in the confirmatory trials. In Europe, it has been approved in combination with KEYTRUDA as the treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum containing therapy in any setting and who are not candidates for curative surgery or radiation. In Japan, it has been approved in combination with KEYTRUDA as the treatment of patients with unresectable advanced or recurrent endometrial carcinoma that progressed after cancer chemotherapy and with radically unresectable or metastatic renal cell carcinoma.

2. About Study 309/KEYNOTE-775 Trial

The approval was based on data from Study 309/KEYNOTE-775 (ClinicalTrials.gov, NCT03517449), a Phase 3 multicenter, open-label, randomized, active-controlled study conducted in 827 patients with advanced endometrial carcinoma who had been previously treated with at least one prior platinum-based chemotherapy regimen in any setting, including in the neoadjuvant and adjuvant settings. The primary efficacy outcome measures were OS, and PFS as assessed by blinded independent central review (BICR) according to RECIST v1.1.

Patients were randomized 1:1 to receive LENVIMA (20 mg orally once daily) plus KEYTRUDA (200 mg intravenously every three weeks) or investigator's choice, consisting of either doxorubicin (60 mg/m^2 every three weeks) or paclitaxel (80 mg/m^2 given weekly, three weeks on/one week off). Treatment with LENVIMA plus KEYTRUDA continued until RECIST v1.1-defined progression of disease as verified by BICR, unacceptable toxicity, or for KEYTRUDA, a maximum of 24 months. Administration of LENVIMA plus KEYTRUDA was permitted beyond RECIST-defined disease progression if the treating investigator considered the patient to be deriving clinical benefit and the treatment was tolerated.

3. About the Merck & Co., Inc., Kenilworth, N.J., U.S.A. and Eisai 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 monotherapy and in combination with KEYTRUDA, the anti-PD-1 therapy from Merck & Co., Inc., Kenilworth, N.J., U.S.A.

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 more than 10 different tumor types across more than 20 clinical trials.

In Taiwan, Eisai's pharmaceutical sales subsidiary Eisai Taiwan Inc. is marketing Lenvima and is co-commercializing it with a local branch of Merck & Co., Inc., Kenilworth, N.J., U.S.A.

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2. The information listed in Taiwanese Package insert
3. American Cancer Society, "Causes, Risks, Prevention." Endometrial Cancer. https://www.cancer.org/content/dam/CRC/PDF/Public/8610.00.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. Taiwan Cancer Registry 2018 Report.
6. American Cancer Society, "Survival Rates for Endometrial Cancer." https://www.cancer.org/content/dam/CRC/PDF/Public/8611.00.pdf .