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Eisai and Merck & Co., Inc., Rahway, NJ, USA Provide Update on Phase 3 LEAP-015 Trial Evaluating LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) in Combination with Chemotherapy in Patients with Certain Types of Gastroesophageal Adenocarcinoma

TOKYO and RAHWAY, NJ, Jan. 24, 2025 – Eisai (Headquarters: Tokyo, CEO: Haruo Naito) and Merck & Co., Inc., Rahway, NJ, USA (known as MSD outside of the United States and Canada) today announced results from the Phase 3 LEAP-015 trial evaluating LENVIMA® (lenvatinib), the orally available multiple receptor tyrosine kinase inhibitor (TKI) discovered by Eisai, plus KEYTRUDA® (pembrolizumab), the anti-PD-1 therapy from Merck & Co., Inc., Rahway, NJ, USA, in combination with chemotherapy (LENVIMA plus KEYTRUDA-based regimen), for the first-line treatment of patients with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastroesophageal adenocarcinoma.

At an interim analysis, the LENVIMA plus KEYTRUDA-based regimen demonstrated a statistically significant improvement in progression-free survival (PFS), one of the study's dual primary endpoints, and objective response rate (ORR), a key secondary endpoint, compared to standard of care chemotherapy. The study continued, and at the final analysis, it did not meet its other primary endpoint of overall survival (OS). The safety profile of the LENVIMA plus KEYTRUDA-based regimen was consistent with that observed in previously reported studies evaluating the combination. A full evaluation of the data from this study is ongoing, and Eisai and Merck & Co., Inc., Rahway, NJ, USA will present these results at an upcoming medical meeting.

"Locally advanced unresectable or metastatic gastroesophageal adenocarcinoma remains a challenging disease to treat and a leading cause of cancer death worldwide," said Dr. Gregory Lubiniecki, Vice President, Global Clinical Development, MSD Research Laboratories. "These study results add to our understanding of this combination and will inform our future research as we strive to improve outcomes for more patients with cancer."

“Gastric and gastroesophageal cancers continue to present challenges due to their heterogeneity and generally poor prognoses,” said Dr. Corina Dutcus, Senior Vice President, Oncology Global Clinical Development Lead at Eisai Inc. “While the LEAP-015 trial did not show a statistically significant increase in overall survival, we were pleased to observe an improvement in progression-free survival and objective response rate for patients treated with LENVIMA plus KEYTRUDA in combination with chemotherapy. These results contribute to the scientific community’s collective understanding of these complex diseases and add to the body of knowledge in oncology research. We are deeply grateful to the patients, caregivers and investigators who participated in this study.”

LENVIMA plus KEYTRUDA is approved in the U.S., the EU, Japan and other countries for the treatment of advanced renal cell carcinoma (RCC) and certain types of advanced endometrial carcinoma. Lenvatinib is marketed as KISPLYX® for advanced RCC in the EU. Eisai and Merck & Co., Inc., Rahway, NJ, USA are studying the LENVIMA plus KEYTRUDA combination through the LEAP (**LE**nvatinib **A**nd **P**embrolizumab) clinical program in hepatocellular carcinoma and esophageal cancer across multiple clinical trials.

Results from the LEAP-015 trial do not affect the current approved indications for KEYTRUDA plus LENVIMA or other ongoing trials from the LEAP clinical program.

About LEAP-015

LEAP-015 is a randomized, open-label, Phase 3 trial (ClinicalTrials.gov, NCT04662710) evaluating LENVIMA plus KEYTRUDA in combination with chemotherapy versus chemotherapy alone for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-negative gastroesophageal adenocarcinoma. There are two parts of the study: a safety run-in (Part 1) and the main study (Part 2). In Part 2, the primary endpoints are OS and PFS as assessed by blinded independent central review (BICR) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) in patients whose tumors express PD-L1 (Combined Positive Score [CPS] ≥1) and in all patients. Secondary endpoints are ORR and duration of response (DOR) as assessed by BICR per RECIST v1.1 in both patients whose tumors express PD-L1 (CPS ≥1) as well as in all patients, and safety. In Part 2, up to 880 patients were randomized 1:1 to receive:

- LENVIMA plus KEYTRUDA plus chemotherapy:
    - Induction Phase: approximately 12 weeks

        - Oral LENVIMA 8 mg every day (QD) plus KEYTRUDA 400 mg intravenously (IV) every six weeks (Q6W) x 2 cycles plus chemotherapy (CAPOX or mFOLFOX6)
            - CAPOX: oral capecitabine 1000 mg/m^2 twice daily (BID) for 14 days plus oxaliplatin 130 mg/m^2 IV, every 3 weeks (Q3W) x 4 cycles

                or
            - mFOLFOX6: bolus IV 5-fluorouracil (5-FU) 400 mg/m^2, plus 5-FU 2400 mg/m^2 continuous IV plus leucovorin 400 mg/m^2 IV or levoleucovorin 200 mg/m^2 IV plus oxaliplatin 85 mg/m^2 IV, every 2 weeks (Q2W) x 6 cycles
    - Consolidation Phase:
        - Oral LENVIMA 20 mg QD, plus KEYTRUDA 400 mg IV Q6W, for less than or equal to 16 doses ; or
- Chemotherapy (either CAPOX regimen or mFOLFOX6 regimen, dosed as above; maximum cycles per local standards).

About gastric cancer

Gastric (stomach) cancer tends to develop slowly over many years and rarely causes early symptoms, resulting in most cases going undetected until an advanced stage.[1,2] More than 70% of patients with gastric cancer develop advanced-stage disease.[3] Most gastric cancers are adenocarcinomas (about 90% to 95%), which develop from cells in the innermost lining of the stomach (known as the mucosa).[1] Gastric cancer is the fifth most diagnosed cancer and the fifth leading cause of cancer death worldwide, with approximately 969,000 patients diagnosed and 660,000 deaths from the disease globally in 2022.[4] In Japan, it is estimated there were approximately 126,000 patients diagnosed with gastric cancer and almost 44,000 deaths from the disease in 2022.[5] In the U.S., it is estimated there will be approximately 27,000 patients diagnosed with gastric cancer and almost 11,000 deaths from the disease in 2024.[6] The five-year relative survival rate for patients diagnosed with gastric cancer at a distant stage is 7% in the U.S.[7]

About esophageal cancer

Esophageal cancer is the 11th most commonly diagnosed cancer and the seventh leading cause of death from cancer worldwide.[4] It is estimated there were 511,000 new cases of esophageal cancer diagnosed and about 445,000 deaths resulting from the disease worldwide in 2022.[4] In Japan, it is estimated there were approximately 20,000 patients diagnosed with esophageal cancer and almost 12,000 deaths from the disease in 2022.[5] In the U.S., it is estimated there will be approximately 22,000 patients diagnosed with esophageal cancer and

almost 16,000 deaths from the disease in 2024.[8] The five-year relative survival rate for patients diagnosed with advanced esophageal cancer is 6% in the US.[9] Cancers that start in gland cells (cells that make mucus) are called adenocarcinomas and are often found in the lower third of the esophagus (lower thoracic esophagus).[10] Adenocarcinoma is the most common form of esophageal cancer in the U.S. and its incidence is rapidly increasing in other parts of the world.[11,12]

About LENVIMA® (lenvatinib) Capsules

LENVIMA, discovered and developed by Eisai, is an orally available multiple receptor tyrosine 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. LENVIMA has been approved for the indications below.

Thyroid cancer

- Indication as monotherapy

(Approved mainly in Japan, the United States, Europe, China and Asia)

Japan: Unresectable thyroid cancer

The United States: The treatment of patients with locally recurrent or metastatic, progressive, radioiodine-refractory differentiated thyroid cancer (DTC)

Europe: The treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI)

Hepatocellular carcinoma

- Indication as monotherapy

(Approved mainly in Japan, the United States, Europe, China and Asia)

Japan: Unresectable hepatocellular carcinoma

The United States: The first-line treatment of patients with unresectable hepatocellular carcinoma (HCC)

Europe: The treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have received no prior systemic therapy

Thymic carcinoma

- Indication as monotherapy (Approved in Japan)

Japan: Unresectable thymic carcinoma

Renal cell carcinoma (In Europe, the agent was launched under the brand name Kisplyx®)

- Indication in combination with everolimus

(Approved mainly in the United States, Europe and Asia)

The United States: The treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy

Europe: The treatment of adult patients with advanced renal cell carcinoma following one prior vascular endothelial growth factor (VEGF) targeted therapy

- Indication in combination with KEYTRUDA (generic name: pembrolizumab)

(Approved mainly in Japan, the United States, Europe and Asia)

Japan: Radically unresectable or metastatic renal cell carcinoma

The United States: The first-line treatment of adult patients with advanced renal cell carcinoma

Europe: The first-line treatment of adult patients with advanced renal cell carcinoma

Endometrial carcinoma

- Indication in combination with KEYTRUDA

(Approved mainly in Japan, the United States, Europe and Asia)

Japan: Unresectable, advanced or recurrent endometrial carcinoma that progressed after cancer chemotherapy

The United States: The treatment of patients with advanced endometrial carcinoma (EC) 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

Europe: The treatment of adult patients with advanced or recurrent endometrial carcinoma (EC) who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and are not candidates for curative surgery

About KEYTRUDA® (pembrolizumab) Injection, 100mg

KEYTRUDA is an anti-programmed death receptor-1 (PD-1) therapy that works by increasing the ability of the body’s immune system to help detect and fight tumor cells. KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumor cells and healthy cells.

Merck & Co., Inc., Rahway, NJ, USA has the industry's largest immuno-oncology clinical research program. There are currently more than 1,600 trials studying KEYTRUDA across a wide variety of cancers and treatment settings. The KEYTRUDA clinical program seeks to understand the role of KEYTRUDA across cancers and the factors that may predict a patient's likelihood of benefitting from treatment with KEYTRUDA, including exploring several different biomarkers.

About the Eisai and Merck & Co., Inc., Rahway, NJ, USA Strategic Collaboration

In March 2018, Eisai and Merck & Co., Inc., Rahway, NJ, USA, known as MSD outside of 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 jointly develop, manufacture and commercialize LENVIMA, both as monotherapy and in combination with KEYTRUDA, the anti-PD-1 therapy from Merck & Co., Inc., Rahway, NJ, USA. Eisai and Merck & Co., Inc., Rahway, NJ, USA are studying the LENVIMA plus KEYTRUDA combination through the LEAP (LEnvatinib And Pembrolizumab) clinical program in hepatocellular carcinoma and esophageal cancer across multiple clinical trials.

Eisai's Focus on Cancer

Eisai acknowledges "Oncology" as one of its key strategic areas, and will continue to focus on the discovery and development of anti-cancer drugs within drug discovery domains including "microenvironment", "protein integrity and homeostasis", and "cell lineage and cell differentiation" under the Deep Human Biology Learning (DHBL) drug discovery and development organization. Eisai aspires to discover innovative new drugs with new targets and mechanisms of action from these domains, with the aim of contributing to the cure of cancers.

About Eisai

Eisai's Corporate Concept is "to give first thought to patients and people in the daily living domain, and to increase the benefits that health care provides." Under this Concept [also known as our *human health care* (*hhc*) Concept], we aim to effectively achieve social good in the form of relieving anxiety over health and reducing health disparities. With a global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to create and deliver innovative products to target diseases with high unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.

In addition, our continued commitment to the elimination of neglected tropical diseases (NTDs), which is a target (3.3) of the United Nations Sustainable Development Goals (SDGs), is demonstrated by our work on various activities together with global partners.

For more information about Eisai, please visit www.eisai.com (for global headquarters: Eisai. Co., Ltd.), us.eisai.com (for U.S. headquarters: Eisai, Inc.) or www.eisai.eu (for Europe, Middle East, Africa, Russia, Australia and New Zealand headquarters: Eisai Europe Ltd.), and connect with us on X (U.S. and global), LinkedIn (for global, U.S. and EMEA) and Facebook (global).

Merck & Co., Inc., Rahway, NJ, USA's Focus on Cancer

Every day, we follow the science as we work to discover innovations that can help patients, no matter what stage of cancer they have. As a leading oncology company, we are pursuing research where scientific opportunity and medical need converge, underpinned by our diverse pipeline of more than 25 novel mechanisms. With one of the largest clinical development programs across more than 30 tumor types, we strive to advance breakthrough science that will shape the future of oncology. By addressing barriers to clinical trial participation, screening and treatment, we work with urgency to reduce disparities and help ensure patients have access to high-quality cancer care. Our unwavering commitment is what will bring us closer to our goal of bringing life to more patients with cancer. For more information, visit https://www.merck.com/research/oncology.

About Merck & Co., Inc., Rahway, NJ, USA

At Merck & Co., Inc., Rahway, NJ, USA, known as MSD outside of the United States and Canada, we are unified around our purpose: We use the power of leading-edge science to save and improve lives around the world. For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals. We foster a diverse and inclusive global workforce and operate responsibly every day to enable a safe, sustainable and healthy future for all people and communities. For more information, visit www.merck.com and connect with us on X (formerly Twitter), Facebook, Instagram, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Rahway, NJ, USA

This news release of Merck & Co., Inc., Rahway, NJ, USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs

and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's Annual Report on Form 10-K for the year ended December 31, 2023 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

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