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

Eisai Co., Ltd.
Investor Relations:
+81-(0) 3-3817-5122

Merck & Co., Inc., Rahway, NJ, USA
Media Relations
Julie Cunningham: +1-(617) 519-6264
John Infanti: +1-(609) 500-4714

Merck & Co., Inc., Rahway, NJ, USA
Investor Relations
Peter Dannenbaum: +1-(732) 594-1579
Damini Chokshi: +1-(732) 594-1577

Eisai and Merck & Co., Inc., Rahway, NJ, USA Provide Update on Phase 3 LEAP-001 Trial Evaluating LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) as First-Line Treatment for Patients with Advanced or Recurrent Endometrial Carcinoma

TOKYO and RAHWAY, NJ, Dec. 9, 2023 – 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 that the Phase 3 LEAP-001 trial evaluating LENVIMA®, the orally available multiple receptor tyrosine kinase inhibitor discovered by Eisai, plus KEYTRUDA®, the anti-PD-1 therapy from Merck & Co., Inc., Rahway, NJ, USA, did not meet its dual primary endpoints of overall survival (OS) and progression-free survival (PFS) for the first-line treatment of patients with advanced or recurrent endometrial carcinoma whose disease is mismatch repair proficient (pMMR)/not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) /MSI-H.

At the final analysis, KEYTRUDA plus LENVIMA did not improve OS or PFS sufficiently to meet the study's prespecified statistical criteria in the first-line treatment of certain patients with advanced or recurrent endometrial carcinoma versus a standard of care, platinum-based chemotherapy doublet (carboplatin plus paclitaxel). The safety profile of LENVIMA plus KEYTRUDA was consistent with that observed in previously reported studies evaluating the combination. A full evaluation of the data from this study is ongoing. The companies will work with investigators to share the results with the scientific community.

"We remain confident in the proven benefit of KEYTRUDA plus LENVIMA for the treatment of appropriate patients with certain types of previously-treated advanced endometrial carcinoma based on results from the KEYNOTE-775/Study 309 trial and will continue to research the KEYTRUDA plus LENVIMA combination in patients with other types of difficult-to-treat cancers," said Dr. Gregory Lubiniecki, Vice President, Global Clinical Development, Merck & Co., Inc., Rahway, NJ, USA Research Laboratories. "We are disappointed that the LEAP-001 trial did not

reach its primary endpoints, as we had hoped to bring another potential treatment option to patients when first diagnosed with certain types of advanced or recurrent endometrial carcinoma."

"Results from the LEAP-001 trial underscore the challenges of treating patients with advanced or recurrent endometrial carcinoma in the first-line setting," said Dr. Corina Dutcus, Senior Vice President, Oncology Global Clinical Development Lead at Eisai Inc. "We remain optimistic about clinical development program for LENVIMA plus KEYTRUDA and are proud that the combination has become a standard of care option for patients with certain types of advanced or recurrent endometrial carcinoma whose disease has progressed following prior systemic therapy, and will continue our efforts to contribute to these patients. We are grateful to the patients, their loved ones, and the investigators whose participation is what makes scientific advancement possible."

LENVIMA plus KEYTRUDA is approved in the U.S., the EU, Japan and other countries for the treatment of certain types of advanced endometrial carcinoma following prior systemic therapy in any setting and advanced renal cell carcinoma (RCC). 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 various tumor types, including but not limited to hepatocellular carcinoma, RCC, head and neck cancer, gastric cancer and esophageal cancer, across multiple clinical trials.

Results from the LEAP-001 trial do not affect the current approved indications for the KEYTRUDA plus LENVIMA combination or other ongoing trials from the LEAP clinical program.

About LEAP-001

LEAP-001 is a randomized, open-label Phase 3 trial (ClinicalTrials.gov, NCT03884101) evaluating LENVIMA plus KEYTRUDA versus carboplatin plus paclitaxel for the first-line treatment of advanced or recurrent endometrial carcinoma. The dual primary endpoints are PFS, as assessed by blinded independent central review (BICR) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ, and OS. The secondary endpoints include objective response rate, as assessed by BICR per RECIST v1.1, quality of life measures, and safety. The study enrolled an estimated 842 patients who were randomized 1:1 to receive:

- LENVIMA (20 mg orally once daily) plus KEYTRUDA (200 mg intravenously [IV] on Day 1 of each three-week cycle); or

- Paclitaxel (175 mg/m^2 IV on Day 1 of each three-week cycle) plus carboplatin (IV infusion at a total dose of area-under-the-curve 6 [per Calvert's formula] given on Day 1 of each three-week cycle).

About Endometrial Carcinoma

Endometrial carcinoma begins in the inner lining of the uterus, which is known as the endometrium and is the most common type of cancer in the uterus.[1,2] Worldwide, 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 in 2020 (these estimates include both endometrial carcinomas and uterine sarcomas,[3] more than 90% of uterine body cancers occur in the endometrium, so the actual numbers for endometrial carcinoma cases and deaths may be slightly lower than these estimates).[4] In Japan, there were more than 17,000 new cases of uterine body cancer and more than 3,000 deaths from the disease in 2020.[5] In the U.S., it is estimated there will be approximately 66,000 new cases of uterine body cancer diagnosed and approximately 13,000 deaths from the disease in 2023.[6,7] In Europe, it is estimated there were more than 130,000 new cases of uterine body cancer and more than 29,000 deaths in 2020.[3] The five-year relative survival rate for metastatic endometrial carcinoma (stage IV) is estimated to be approximately 20%.[8]

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 in over 80 countries including Japan, the United States, China, and countries in Europe 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 in over 80 countries including Japan, the United States, China, and countries in Europe 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 in over 65 countries including the United States, and countries in 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 in over 45 countries including Japan, the United States, and countries in 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 [including conditional approval] in over 50 countries including Japan, the United States, and countries in 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 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 and are evaluating the combination in various tumor types 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", "proteostasis disruption", "cell lineage and cell differentiation", and "inflammation, hypoxia, oxidative stress and cell senescence" 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

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck & Co., Inc., Rahway, NJ, USA, the potential to bring new hope to people with cancer drives our purpose and supporting accessibility to our cancer medicines is our commitment. As part of our focus on cancer, Merck & Co., Inc., Rahway, NJ, USA is committed to exploring the potential of immuno-oncology with one of the largest development programs in the industry across more than 30 tumor types. We also continue to strengthen our portfolio through strategic acquisitions and are prioritizing the development of

several promising oncology candidates with the potential to improve the treatment of advanced cancers. For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

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

For over 130 years, Merck & Co., Inc., Rahway, NJ, USA, known as MSD outside of the United States and Canada, 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. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck & Co., Inc., Rahway, NJ, USA 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.merck.com and connect with us on 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 the global outbreak of novel coronavirus disease (COVID-19); 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, 2022 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

[1] Mayo clinic, "Endometrial Cancer?" https://www.mayoclinic.org/diseases-conditions/endometrial-cancer/symptoms-causes/syc-20352461#:~:text=Endometrial%20cancer%20begins%20in%20the%20layer%20of%20cells%20that%20form,less%20common%20than%20endometrial%20cancer.

[2] American Cancer Society, "What Is Endometrial Cancer?" https://www.cancer.org/cancer/endometrial-cancer/about/what-is-endometrial-cancer.html#:~:text=Endometrial%20cancer%20starts%20when%20cells,other%20parts%20of%20the%20body.

[3] 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

[4] American Cancer Society, "Key Statistics for Endometrial Cancer." https://www.cancer.org/cancer/endometrial-cancer/about/key-statistics.html

[5] 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

[6] American Cancer Society, "Cancer Facts & Figures 2023." https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf

[7] Cancer Net ®." Uterine Cancer" https://www.cancer.net/cancer-types/uterine-cancer/view-all#:~:text=The%20average%20age%20of%20diagnosis,when%20it%20occurs%20after%20menopause.

[8] American Cancer Society, "Survival Rates for Endometrial Cancer." https://www.cancer.org/cancer/endometrial-cancer/detection-diagnosis-staging/survival-rates.html

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