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

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

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

Merck & Co., Inc., Rahway, NJ, USA
Investor Relations
Peter Dannenbaum: +1-(732) 594-1579
Steven Graziano: +1-(732) 594-1583

LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) Demonstrates Durable 5-Year Survival Benefit Versus Chemotherapy for Patients With Advanced Endometrial Carcinoma Following One Prior Platinum-Based Regimen

At five years, LENVIMA plus KEYTRUDA showed a 16.7% overall survival (OS) rate for these patients with mismatch repair proficient (pMMR) advanced endometrial carcinoma versus 7.3% for chemotherapy alone in the pivotal Phase 3 Study 309/KEYNOTE-775 trial

Five-year OS results in the pMMR subgroup were consistent with the all-comers study population, which demonstrated an OS rate of 19.9% for LENVIMA plus KEYTRUDA versus 7.7% for chemotherapy

TOKYO and RAHWAY, NJ, Oct. 20, 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 long-term follow-up data continued to show durable benefit of 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, compared to chemotherapy for patients with advanced endometrial carcinoma following at least one prior platinum-based regimen in any setting. The findings, based on five years of follow-up from the Phase 3 Study 309/KEYNOTE-775 trial evaluating LENVIMA plus KEYTRUDA versus chemotherapy (treatment of physician's choice of doxorubicin or paclitaxel), for these patients with advanced endometrial carcinoma were presented during a poster session at the European Society for Medical Oncology (ESMO) Congress 2025 in Berlin, Germany (Presentation #1119P).

In the trial, a total of 827 patients (697 whose cancer was mismatch repair proficient [pMMR] and 130 whose cancer was mismatch repair deficient [dMMR]) were randomized to receive LENVIMA plus KEYTRUDA (n=411) or chemotherapy (n=416). The trial's primary endpoints, overall survival (OS) and progression-free survival (PFS), were evaluated in patients

with pMMR disease and in the intent-to-treat population (also known as the all-comers population), which included all randomized patients (both pMMR and dMMR).

In the pMMR subgroup, after a median follow-up of 68.8 months (range, 60.8-79.0 months for KEYTRUDA plus LENVIMA; range, 60.9-80.0 for chemotherapy), the five-year OS rate was 16.7% for LENVIMA plus KEYTRUDA versus 7.3% for chemotherapy alone. Median OS was 18.0 months (95% CI, 14.9-20.5) for LENVIMA plus KEYTRUDA versus 12.2 months (95% CI, 11.0-14.1) for chemotherapy alone (HR 0.70; 95% CI, 0.60-0.83). Five-year OS results in the pMMR subgroup were consistent with the all-comers population, which demonstrated an OS rate of 19.9% for LENVIMA plus KEYTRUDA versus 7.7% for chemotherapy; median OS was 18.7 months (95% CI, 15.6-21.3) for LENVIMA plus KEYTRUDA versus 11.9 months (95% CI, 10.6-13.3) for chemotherapy (HR 0.66; 95% CI, 0.57-0.77).

Treatment-related adverse events (TRAEs) occurred in 97.3% of patients receiving LENVIMA plus KEYTRUDA versus 93.8% of patients receiving chemotherapy and led to the discontinuation of LENVIMA and/or KEYTRUDA in 40.1% of patients (16.0% discontinued both drugs) versus the discontinuation of chemotherapy in 8.0% of patients. The most common adverse events (≥ 20%) in the LENVIMA plus KEYTRUDA group were hypertension (61.8%), hypothyroidism (55.7%), diarrhea (43.3%), nausea (40.1%), decreased appetite (37.9%), fatigue (28.8%), proteinuria (27.6%), vomiting (24.4%), arthralgia (23.9%), decreased weight (22.7%) and palmar-plantar erythrodysesthesia syndrome (20.7%).

The long-term OS data were consistent with the primary analysis presented at the Society of Gynecologic Oncology (SGO) 2021 Annual Meeting[1] and published in the *New England Journal of Medicine*.[2] In the primary analysis, the median OS was 17.4 months (95% CI, 14.2-19.9) for LENVIMA plus KEYTRUDA versus 12.0 months (95% CI, 10.8-13.3) for chemotherapy in the pMMR subgroup, and 18.3 months (95% CI, 15.2-20.5) versus 11.4 months (95% CI, 10.5-12.9) in the all-comers population. In the five-year analysis, there were no new safety signals and the safety profile of LENVIMA plus KEYTRUDA was consistent with previously reported data on the combination.

“Endometrial carcinoma is difficult-to-treat in the recurrent or advanced stage, especially when tumors are mismatch repair proficient and therefore harder to target with immunotherapy alone,” said Dr. Vicky Makker, Principal Investigator and Gynecologic Medical Oncologist,

Memorial Sloan Kettering Cancer Center. “Five-year follow-up data from the Study 309/KEYNOTE-775 trial show sustained survival benefit in patients treated with pembrolizumab plus lenvatinib and underscore the role of this combination as an effective treatment option for patients with advanced endometrial carcinoma who need further treatment after receiving prior platinum-based therapy.”

“Recent advances have led to steady improvement in outcomes for patients with advanced endometrial carcinoma,” said Dr. Gregory Lubiniecki, Vice President, Global Clinical Development, MSD Research Laboratories. “These five-year data highlight the durable survival benefit of LENVIMA plus KEYTRUDA in patients with advanced endometrial carcinoma who have received prior platinum-based therapy and are the result of our ongoing commitment to delivering impactful treatment options for people affected by women’s cancers.”

"The five-year results from Study 309/KEYNOTE-775 represent the longest reported follow-up for a trial evaluating an immunotherapy plus tyrosine kinase inhibitor combination in advanced endometrial carcinoma," said Dr. Corina Dutcus, Senior Vice President, Oncology Global Clinical Development Lead at Eisai Inc. "These findings demonstrate the continued overall survival benefit observed with LENVIMA plus KEYTRUDA, further supporting the combination’s therapeutic value for patients facing this disease. We are deeply grateful to the patients, their families, and the dedicated investigators whose participation and commitment made this research possible."

Based on the primary analysis results in 2021 from the Phase 3 Study 309/KEYNOTE-775 trial, LENVIMA plus KEYTRUDA is approved in the U.S. for patients with advanced endometrial carcinoma that is pMMR or not microsatellite instability-high (MSI-H), as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation. LENVIMA plus KEYTRUDA is also approved in the European Union and Japan for certain patients with advanced or recurrent endometrial carcinoma regardless of mismatch repair status. Lenvatinib is approved as KISPLYX® for advanced renal cell carcinoma in the EU.

Dr. Makker has provided consulting and advisory services for Merck & Co., Inc., Rahway, NJ, USA and Eisai.

Study design and additional data from Study 309/KEYNOTE-775

Study 309/KEYNOTE-775 (ClinicalTrials.gov, NCT03517449) is a Phase 3, multicenter, open-label, randomized, active-controlled study evaluating LENVIMA plus KEYTRUDA for the treatment of 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. Participants may have received up to two platinum-containing therapies in total, as long as one was given in the neoadjuvant or adjuvant treatment setting. The study excluded patients with endometrial sarcoma, carcinosarcoma, pre-existing Grade ≥3 fistula, uncontrolled blood pressure (>150/90 mmHg), significant cardiovascular impairment or event within the last 12 months or patients who had active autoimmune disease or a medical condition that required immunosuppression. The primary efficacy outcome measures were OS and PFS as assessed by blinded independent central review (BICR) according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1). Secondary efficacy outcome measures included objective response rate (ORR) as assessed by BICR and safety. The study randomized 827 patients 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 35 cycles. Administration of LENVIMA plus KEYTRUDA was permitted beyond RECIST v1.1-defined disease progression if the treating investigator considered the patient to be deriving clinical benefit and the treatment was tolerated.

In the pMMR subgroup, LENVIMA plus KEYTRUDA demonstrated a five-year PFS rate of 6.3% versus 2.1% for chemotherapy alone. Median PFS was 6.7 months (95% CI, 5.6-7.4) for LENVIMA plus KEYTRUDA versus 3.8 months (95% CI, 3.6-5.0) for chemotherapy alone. At five years, ORR was 32.4% (95% CI, 27.5-37.6) for LENVIMA plus KEYTRUDA compared with 14.8% (95% CI, 11.3-19.0) for chemotherapy.

In the all-comers population, LENVIMA plus KEYTRUDA demonstrated a five-year PFS rate of 9.8% versus 3.2% for chemotherapy alone. Median PFS was 7.3 months (95% CI, 5.7-7.6) for LENVIMA plus KEYTRUDA versus 3.8 months (95% CI, 3.6-4.2) for chemotherapy alone.

At five years, ORR was 33.8% (95% CI, 29.3-38.6) for LENVIMA plus KEYTRUDA compared with 14.4% (95% CI, 11.2-18.2) for chemotherapy.

The long-term PFS data were also consistent with the primary analysis, in which the median PFS was 6.6 months (95% CI, 5.6-7.4) for KEYTRUDA plus LENVIMA versus 3.8 months (95% CI, 3.6-5.0) for chemotherapy in the pMMR subgroup, and 7.2 months (95% CI, 5.7-7.6) versus 3.8 months (95% CI, 3.6-4.2) in the all-comers population.

In the all-comers population, 44.8% of patients treated with LENVIMA plus KEYTRUDA and 51.2% of patients treated with chemotherapy used subsequent systemic anticancer therapy (compared with 28.0% and 48.1%, respectively, at the primary analysis). In the chemotherapy group, 10.1% of patients crossed over to receive LENVIMA plus KEYTRUDA. At the data cut-off (Feb. 26, 2025), 86 patients were alive after treatment with LENVIMA plus KEYTRUDA, compared to 53 patients treated with chemotherapy.

While the trial was not powered to compare LENVIMA plus KEYTRUDA with chemotherapy in the dMMR subgroup, a clinically meaningful improvement was observed across efficacy endpoints. The five-year OS rate was 36.5% for LENVIMA plus KEYTRUDA versus 9.8% for chemotherapy alone. Median OS was 31.9 months (95% CI, 15.6‑47.7) for LENVIMA plus KEYTRUDA versus 8.6 months (95% CI, 5.5‑13.4) for chemotherapy alone. LENVIMA plus KEYTRUDA demonstrated a five-year PFS rate of 26.4% versus 10.8% for chemotherapy. Median PFS was 14.8 months (95% CI, 5.6-31.9) for LENVIMA plus KEYTRUDA versus 3.7 months (95% CI, 3.1–4.4) for chemotherapy alone. The ORR at five years was 41.5% (95% CI, 29.4-54.4) for LENVIMA plus KEYTRUDA compared with 12.3% (95% CI, 5.5-22.8) for chemotherapy.

About endometrial carcinoma[3,4,5,6,7,8]

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. More than 90% of uterine body cancers occur in the endometrium. In Japan, there were more than 18,000 patients diagnosed with uterine body cancer and more than 3,000 patient deaths from the disease in 2022. In the U.S., it is estimated there will be approximately 69,000 patients diagnosed with uterine body cancer and approximately 14,000 patient deaths from the disease in 2025. In the European Union, it is estimated there were more than 69,000 patients diagnosed with uterine body cancer and more than 17,000 patient deaths in 2022. Globally, endometrial cancer is the sixth most common cancer in women and the 15th most common cancer overall. Following primary treatment, patients

face a risk of their cancer returning, often as distant metastasis, which is associated with poorer outcomes.

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

- Indication in combination with KEYTRUDA (generic name: pembrolizumab) and transarterial chemoembolization (Approved in China)

Thymic carcinoma

- Indication as monotherapy (Approved in Japan)

Japan: Unresectable thymic carcinoma

Renal cell carcinoma (In Europe other than the United Kingdom, 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

(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 that is pMMR or not microsatellite instability-high (MSI-H), as determined by an FDA-approved test, 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.

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, 2024 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

[1] Eisai Co., Ltd. Home page. "LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) Significantly Improved Progression-Free Survival and Overall Survival Versus Chemotherapy in Patients With Advanced Endometrial Cancer Following Prior Platinum-Based Chemotherapy in Phase 3 Study". News release. https://www.eisai.com/news/2021/news202116.html .

[2] Eisai Co., Ltd. Home page. "Results From Pivotal Phase 3 Study 309/KEYNOTE-775 Trial of LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) in Advanced Endometrial Carcinoma Published in the New England Journal of Medicine". News release. https://www.eisai.com/news/2022/news202207.html .

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[7] American Cancer Society, "About and Key Statistics." Surveilance, epidemiology, and End Result Program https://www.cancer.org/cancer/types/endometrial-cancer/about/key-statistics.html .

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