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

Merck & Co., Inc., Kenilworth, N.J., U.S.A.
Media Relations
Melissa Moody: +1-(215) 407-3536
Nikki Sullivan: +1-(718) 644-0730

Eisai Co., Ltd.
Investor Relations:
+81-(0)70-8688-9685

Merck & Co., Inc., Kenilworth, N.J., U.S.A.
Investor Relations
Peter Dannenbaum: +1- (908) 740-1037
Raychel Kruper: +1-(908) 740-2107

European Commission Approves LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) for Patients With Certain Types of Endometrial Carcinoma

First Combination of Tyrosine Kinase Inhibitor with Immunotherapy Approved in Europe for Adult Patients With Advanced or Recurrent Endometrial Carcinoma With 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

Approval Based on Study 309/KEYNOTE-775 Results Demonstrating Statistically Significant Improvements in Overall Survival and Progression-Free Survival Compared With Chemotherapy

TOKYO and KENILWORTH, N.J., November 29, 2021 – Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") and Merck & Co., Inc., Kenilworth, N.J., U.S.A. (known as MSD outside the United States and Canada) today announced that the European Commission has approved the combination of LENVIMA, the orally available multiple receptor tyrosine kinase inhibitor discovered by Eisai, plus KEYTRUDA, the anti-PD-1 therapy from Merck & Co., Inc., Kenilworth, N.J., U.S.A., for 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. This marks the first combination of tyrosine kinase inhibitor with immunotherapy approved in Europe for these patients with advanced or recurrent endometrial carcinoma.

The approval is based on results from the pivotal Phase 3 Study 309/KEYNOTE-775 trial, in which 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.

"This approval is welcome news for patients in Europe, and is based on the first Phase 3 study evaluating an immunotherapy and tyrosine kinase inhibitor combination that showed superior overall survival for patients with advanced or recurrent endometrial cancer compared to chemotherapy," said Dr. Gregory Lubiniecki, Vice President, Clinical Research, Merck & Co., Inc., Kenilworth, N.J., U.S.A. Research Laboratories. "Regardless of mismatch repair status, patients whose endometrial cancer progresses or returns after prior platinum-containing systemic therapies now have a combination treatment option in KEYTRUDA plus LENVIMA that demonstrated a 38% reduction in risk of death compared to chemotherapy alone."

"Until recently, women in Europe with advanced or recurrent endometrial cancer have faced a difficult prognosis and had few treatment options," said Corina Dutcus, M.D., Vice President, Clinical Research, Oncology Business Group at Eisai Inc. "The approval of LENVIMA plus KEYTRUDA in this setting reflects the progress that we have made in our collaboration with Merck & Co., Inc., Kenilworth, N.J., U.S.A. in developing solutions for those diagnosed with difficult-to-treat cancers. We thank the patients, families and healthcare providers who made this milestone possible."

In the Study 309 trial, the most common adverse reactions of these patients (≥20%) for LENVIMA plus KEYTRUDA* were hypertension (63%), diarrhoea (57%), hypothyroidism (56%), nausea (51%), decreased appetite (47%), vomiting (39%), fatigue (38%), decreased weight (35%), arthralgia (33%), proteinuria (29%), constipation (27%), headache (27%), urinary tract infection (27%), dysphonia (25%), abdominal pain (23%), asthenia (23%), palmar-plantar erythrodysaesthesia syndrome (23%), stomatitis (23%), anaemia (22%), and hypomagnesaemia (20%).

This approval allows marketing of LENVIMA plus KEYTRUDA in all 27 EU member states plus Iceland, Liechtenstein, Norway and Northern Ireland. LENVIMA plus KEYTRUDA is now approved by the European Commission for two different types of cancer: for 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 and for the first-line treatment of adult patients with advanced renal cell carcinoma.

*According to the information listed in the SmPC (Summary of Product Characteristics)

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. 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 BP (>150/90 mmHg), significant cardiovascular impairment or event within previous 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 RECIST v1.1. Secondary efficacy outcome measures included ORR as assessed by BICR.

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. A total of 121/411 (29%) of patients treated with LENVIMA plus KEYTRUDA received continued study therapy beyond RECIST-defined disease progression. The median duration of the post-progression therapy was 2.8 months. Assessment of tumor status was performed every eight weeks.

About Endometrial Cancer[1,2,3,4,5]

Endometrial cancer 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. Worldwide, it was estimated there were more than 417,000 new cases and more than 97,000 deaths from uterine body cancers in 2020 (these estimates include both endometrial cancers and uterine sarcomas; more than 90% of uterine body cancers occur in the endometrium, so the actual numbers for endometrial cancer cases and deaths are slightly lower than these estimates). 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. 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. The five-year relative survival rate for metastatic endometrial cancer (stage IV) is estimated to be approximately 17%.

About LENVIMA® (lenvatinib) Capsules

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 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 is approved in combination with KEYTRUDA (generic name: pembrolizumab) 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.

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., Kenilworth, N.J., U.S.A. 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., Kenilworth, N.J., U.S.A. 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.

Eisai's Focus on Cancer

Eisai focuses on the development of anticancer drugs, targeting the tumor microenvironment (with experience and knowledge from existing in-house discovered

compounds) and the driver gene mutation and aberrant splicing (leveraging RNA Splicing Platform) as areas (*Ricchi*) where real patient needs are still unmet, and where Eisai can aim to become a frontrunner in oncology. Eisai aspires to discover innovative new drugs with new targets and mechanisms of action from these *Ricchi*, with the aim of contributing to the cure of cancers.

About Eisai

Eisai is a leading global research and development-based pharmaceutical company headquartered in Japan, with approximately 10,000 employees worldwide. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. We strive to realize our *hhc* philosophy by delivering innovative products in therapeutic areas with high unmet medical needs, including Oncology and Neurology. In the spirit of *hhc*, we take that commitment even further by applying our scientific expertise, clinical capabilities and patient insights to discover and develop innovative solutions that help address society's toughest unmet needs, including neglected tropical diseases and the Sustainable Development Goals.

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 Twitter (U.S. and global) and LinkedIn (for U.S. and EMEA).

Merck & Co., Inc., Kenilworth, N.J., U.S.A.'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., Kenilworth, N.J., U.S.A., 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., Kenilworth, N.J., U.S.A. 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., Kenilworth, N.J., U.S.A.

For over 130 years, Merck & Co., Inc., Kenilworth, N.J., U.S.A., 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., Kenilworth, N.J., U.S.A. 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., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., 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 products that the products 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 2020 Annual Report on Form 10-K and the company's other filings with

the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

[1] American Cancer Society, "Causes, Risks, Prevention." Endometrial Cancer. https://www.cancer.org/content/dam/CRC/PDF/Public/8610.00.pdf .
[2] 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 .
[3] 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 .
[4] American Cancer Society, "About and Key Statistics." Endometrial Cancer. https://www.cancer.org/content/dam/CRC/PDF/Public/8609.00.pdf .
[5] American Cancer Society, "Detection, Diagnosis, Staging." Endometrial Cancer. https://www.cancer.org/content/dam/CRC/PDF/Public/8610.00.pdf .

# # #