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

Merck & Co., Inc., Kenilworth, N.J., U.S.A.
Media Relations
Pamela Eisele: (267) 305-3558
Rebecca Newberry: (484) 678-2952

Eisai Co., Ltd.
Investor Relations:
+81-(0)3-3817-3016

Merck & Co., Inc., Kenilworth, N.J., U.S.A.
Investor Relations
Peter Dannenbaum: (908) 740-1037
Courtney Ronaldo: (908) 740-6132

LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) Combination Demonstrated Statistically Significant Improvement in Overall Survival, Progression-Free Survival and Objective Response Rate Versus Chemotherapy in Patients With Advanced Endometrial Cancer Following Prior Systemic Therapy in Phase 3 Study

First Overall Survival Analysis for LENVIMA Plus KEYTRUDA Combination in a Phase 3 Study in Advanced Endometrial Cancer

TOKYO and KENILWORTH, N.J., Dec.16, 2020 – 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 pivotal Phase 3 Study 309/KEYNOTE-775 trial evaluating the investigational use 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., met its dual primary endpoints of overall survival (OS) and progression-free survival (PFS) and its secondary efficacy endpoint of objective response rate (ORR) in patients with advanced endometrial cancer, following at least one prior platinum-based regimen. These positive results were observed in the mismatch repair proficient (pMMR) subgroup and the intention-to-treat (ITT) study population, which includes both patients with endometrial carcinoma that is pMMR as well as patients whose disease is microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR). Based on an analysis conducted by an independent Data Monitoring Committee, LENVIMA plus KEYTRUDA demonstrated a statistically significant and clinically meaningful improvement in OS, PFS and ORR versus chemotherapy (treatment of physician's choice [TPC] of doxorubicin or paclitaxel). The safety profile of the LENVIMA plus KEYTRUDA combination was consistent with previously reported studies. Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A. will discuss these data with regulatory authorities worldwide, with the intent to submit marketing authorization

applications based on these results, and plan to present these results at an upcoming medical meeting.

"Women with advanced endometrial cancer are faced with high mortality rates and limited treatment options following initial systemic therapy," said Dr. Gregory Lubiniecki, Associate Vice President, Oncology Clinical Research, Merck & Co., Inc., Kenilworth, N.J., U.S.A. Research Laboratories. "These are the first results from a Phase 3 trial of a combination regimen including immunotherapy in advanced endometrial carcinoma that have shown a statistically significant improvement in overall survival, progression-free survival and objective response rate versus chemotherapy. Merck & Co., Inc., Kenilworth, N.J., U.S.A. and Eisai are dedicated to continuing to research the KEYTRUDA plus LENVIMA combination and discover new approaches to address unmet needs for devastating diseases such as endometrial carcinoma."

"We are encouraged by the data observed in Study 309/KEYNOTE-775, which represent a possible step forward for patients impacted by advanced endometrial carcinoma and support the results seen in the advanced endometrial cancer cohort of Study 111/KEYNOTE-146." said Dr. Takashi Owa, Vice President, Chief Medicine Creation Officer and Chief Discovery Officer, Oncology Business Group at Eisai. "As more clinical data from the LEAP (LEnvatinib And Pembrolizumab) program are revealed, we cannot help but be energized by the trajectory of our collaboration with Merck & Co., Inc., Kenilworth, N.J., U.S.A. and the benefits we hope to provide to patients together. Most importantly, we are grateful for the trust that the patients and healthcare professionals who participated in this trial have shown us."

Study 309/KEYNOTE-775 is the confirmatory trial for Study 111/KEYNOTE-146, which supported the U.S. Food and Drug Administration's (FDA) 2019 accelerated approval of the LENVIMA plus KEYTRUDA combination for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation. This accelerated approval was based on tumor response rate and durability of response and was the first approval granted under Project Orbis, an initiative of the FDA Oncology Center of Excellence that provides a framework for concurrent submission and review of oncology drugs among its international partners. Under Project Orbis, Health Canada and Australia's Therapeutic Goods Administration (TGA) granted conditional and provisional approvals, respectively, for this indication.

Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A. are studying the LENVIMA plus KEYTRUDA combination through the LEAP (LEnvatinib And Pembrolizumab) clinical program in

13 different tumor types across 20 clinical trials, including a Phase 3 trial evaluating the combination in the first-line setting for patients with advanced endometrial carcinoma (LEAP-001).

.

About Study 309/KEYNOTE-775

Study 309/KEYNOTE-775 is a multicenter, randomized, open-label, Phase 3 trial (ClinicalTrials.gov, NCT03517449) evaluating LENVIMA in combination with KEYTRUDA in patients with advanced endometrial cancer following at least one prior platinum-based regimen. The dual primary endpoints are OS and PFS, as assessed by Blinded Independent Central Review (BICR) per Response Evaluation Criteria in Solid Tumors Version (RECIST) v1.1. Select secondary endpoints include objective response rate (ORR) by BICR per RECIST v1.1 and safety/tolerability. Of the 827 patients enrolled, 697 patients had tumors that were non-MSI-H or pMMR, and 130 patients had tumors that were MSI-H or dMMR. Patients were randomized 1:1 to receive:

- KEYTRUDA (200 mg intravenously [IV] every three weeks) for up to 35 cycles (approximately two years) in combination with LENVIMA (20 mg orally once daily); or
- Chemotherapy (Treatment of physician's choice [TPC] of either doxorubicin 60 mg/m^2 IV every three weeks for up to a maximum cumulative dose of 500 mg/m^2 or paclitaxel 80 mg/m^2 IV on a 28-day cycle [three weeks of receiving weekly paclitaxel and one week of not receiving paclitaxel])

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. In 2018, it was estimated there were more than 382,000 new cases and nearly 90,000 deaths from uterine body cancers worldwide (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 almost 16,000 new cases of uterine body cancer and nearly 2,500 deaths from the disease in 2018. In the U.S., it is estimated there will be almost 66,000 new cases of uterine body cancer and nearly 13,000 deaths from the disease in 2020. The five-year survival rate for advanced or metastatic endometrial cancer (stage IV) is estimated to be approximately 17%.

About LENVIMA® (lenvatinib) Capsules

LENVIMA, discovered and developed by Eisai, is a 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, lenvatinib 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 65 countries including Japan, the United States, in Europe and Asia, and for unresectable hepatocellular carcinoma in over 65 countries including Japan, the United States, in Europe, China and in Asia. Additionally, it is also approved in combination with everolimus as a treatment for renal cell carcinoma following prior antiangiogenic therapy in over 55 countries, including the United States, in Europe and Asia. In Europe, the agent was launched under the brand name Kisplyx® for renal cell carcinoma. In addition, it is approved in combination with KEYTRUDA as a treatment for advanced endometrial cancer that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), in patients who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation in countries including the United States, Australia and Canada. Continued approval for this indication is contingent upon verification and description of clinical benefit in the confirmatory trials.

About KEYTRUDA® (pembrolizumab) Injection, 100 mg

KEYTRUDA is an anti-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 1,300 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 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 KEYTRUDA plus LENVIMA 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 13 different tumor types (endometrial carcinoma, hepatocellular carcinoma, melanoma, non-small cell lung cancer, renal cell carcinoma, squamous cell carcinoma of the head and neck, urothelial cancer, biliary tract cancer, colorectal cancer, gastric cancer, glioblastoma, ovarian cancer and triple-negative breast cancer) across 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), us.eisai.com (for U.S.) or www.eisai.eu (for Europe, Middle East, Africa), and connect with us on Twitter (U.S. and global) and LinkedIn (for U.S.).

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 more than 125 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 2019 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]Henley et al. 2018: https://www.cdc.gov/mmwr/volumes/67/wr/mm6748a1.htm
[2]Cancer Research Institute website, accessed 10/29/2020: https://www.cancerresearch.org/immunotherapy/cancer-types/uterine-endometrial-cancer
[3]American Cancer Society, Facts & Figures 2020 pdf: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2020.html
[4]Cancer Registry and Statistics. Cancer Information Service, National Cancer Center, Japan (Vital Statistics of Japan): https://ganjoho.jp/reg_stat/statistics/dl/index.html
[5]American Cancer Society website, accessed 10/29/2020: https://www.cancer.org/cancer/endometrial-cancer/detection-diagnosis-staging/survival-rates.html

# # #