

FOR IMMEDIATE RELEASE

Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A. Announce U.S. FDA Grants Breakthrough Therapy Designation for LENVIMA® in Combination with KEYTRUDA® as Therapy for Previously Treated Patients with Advanced and/or Metastatic non-MSI-H/pMMR Endometrial Carcinoma

TOKYO & KENILWORTH, N.J., July 31, 2018 – Eisai Co., Ltd. and Merck & Co., Inc. Kenilworth, N.J., U.S.A. (NYSE:MRK), known as MSD outside the United States and Canada, announced today that the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy designation for LENVIMA® (generic name: lenvatinib mesylate), the orally available kinase inhibitor discovered by Eisai, in combination with Merck & Co., Inc., Kenilworth, N.J., U.S.A.'s anti-PD-1 therapy KEYTRUDA® (generic name: pembrolizumab) for the potential treatment of patients with advanced and/or metastatic non-microsatellite instability high (MSI-H)/proficient mismatch repair (pMMR) endometrial carcinoma (EC) who have progressed following at least one prior systemic therapy.

The LENVIMA/KEYTRUDA combination therapy is being jointly developed by Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A. as part of the strategic collaboration announced in March 2018. This is the third Breakthrough Therapy designation for LENVIMA and the second Breakthrough Therapy designation for LENVIMA in combination with KEYTRUDA following the Breakthrough Therapy designation for the combination for advanced and/or metastatic renal cell carcinoma announced in January 2018.

The Breakthrough Therapy designation is an FDA program intended to expedite development and review of medicines for serious or life-threatening conditions. In order to qualify for this designation, preliminary clinical evidence must demonstrate that the drug may provide substantial improvement over currently available therapy on at least one clinically significant endpoint. The benefits of this Breakthrough Therapy designation include more intensive guidance on an efficient clinical development program, access to senior FDA managers and experienced FDA staff to help accelerate review time, as well as eligibility for rolling review and potentially priority review.

This Breakthrough Therapy designation was based on interim results of the EC cohort in Study 111/KEYNOTE-146, which were presented in June 2018 at the 54th American Society of Clinical Oncology (ASCO) Annual Meeting.^{1,2} Study 111/KEYNOTE-146 is a multi-center, open-label, single-arm Phase 1b/2 basket trial evaluating the efficacy and safety of LENVIMA in combination with KEYTRUDA in patients with selected solid tumors.

“This second Breakthrough Therapy designation for the LENVIMA/KEYTRUDA combination represents another step forward in our collaboration with Eisai and supports the continued evaluation of this combination in more than 11 types of cancer,” said Dr. Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories. “We will continue to work closely with Eisai to build on the robust data for the LENVIMA/KEYTRUDA combination in advanced endometrial carcinoma in an effort to offer a new option for these patients and potentially help address a critical unmet need.”

“We designed Study 111 to learn as much as we could about the LENVIMA/KEYTRUDA combination as efficiently as possible, driven by a sense of urgency to bring forward a potential new treatment option for patients in need,” said Dr. Takashi Owa, Vice President and Chief Medicine Creation Officer, Oncology Business Group, Eisai. “We are encouraged by the continued activity seen in patients with endometrial carcinoma, and the latest Breakthrough Therapy designation for LENVIMA and KEYTRUDA has strengthened our commitment, as part of our *human health care* mission, to expedite the path to ultimately benefitting patients living with endometrial carcinoma as quickly as possible.”

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

About Study 111/KEYNOTE-146

Study 111/KEYNOTE-146 is a multicenter, open-label, single-arm Phase 1b/2 basket trial evaluating the combination of LENVIMA (20 mg/day) with KEYTRUDA (200 mg intravenously every three weeks) in patients with selected solid tumors (renal cell carcinoma, EC, non-small cell lung cancer, urothelial cancer, squamous cell head and neck cancer, and melanoma). Patients were not preselected based on MSI or PD-L1 tumor biomarker status. The primary endpoint of the Phase 1b study was to determine the maximum tolerated dose of LENVIMA and KEYTRUDA in combination. The primary endpoint of the Phase 2 portion is investigator-assessed objective response rate (ORR) at week 24 based on immune-related RECIST (irRECIST). The secondary efficacy endpoints included ORR, progression-free survival and duration of response for patients with complete or partial responses. Fifty-three patients with previously treated, metastatic EC were evaluated in the EC cohort. Currently, the Phase 2 part is ongoing as an EC cohort expansion. This study is being conducted under an existing strategic collaboration between the two companies.

A randomized, international, two-arm Phase 3 study in recurrent EC is underway (Study 309/KEYNOTE-775; NCT03517449; please visit clinicaltrials.gov for more information).

About Endometrial Carcinoma

Endometrial cancer begins in the inner lining of the uterus (endometrium), and nearly all cancers of the uterus are endometrial carcinomas.³ In 2018, it is estimated there will be approximately 63,230 new cases of uterine cancer, and there will be approximately 11,350 deaths from uterine cancer (with the figures for endometrial cancer being slightly lower than this combined estimate).⁴ Stages of endometrial cancer range from stage 1 through 4.⁵ The five-year survival rate for women diagnosed with stage 1A endometrial cancer is 88% and drops to 15% for those diagnosed with stage 4B.⁶

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., through an affiliate, entered into a strategic collaboration for the worldwide co-development and co-commercialization of LENVIMA. Under the agreement, the companies will develop and commercialize LENVIMA jointly, both as monotherapy and in combination with Merck & Co., Inc. Kenilworth N.J., U.S.A.'s anti-PD-1 therapy KEYTRUDA. In addition to ongoing clinical studies of the combination, the companies will jointly initiate new clinical studies evaluating the combination to support 11 potential indications in six types of cancer (bladder cancer, endometrial cancer, head and neck cancer, hepatocellular carcinoma, melanoma and non-small cell lung cancer), as well as a basket trial targeting six additional cancer types. The combination of LENVIMA and KEYTRUDA is investigational. The efficacy and safety of this combination has not been established. The LENVIMA/KEYTRUDA combination is not approved in any cancer types today.

About LENVIMA® (lenvatinib mesylate)

LENVIMA, discovered and developed in-house by Eisai, is an orally administered receptor tyrosine kinase (RTK) inhibitor with a novel binding mode that selectively inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors (VEGFR1, VEGFR2 and VEGFR3) and fibroblast growth factor (FGF) receptors (FGFR1, FGFR2, FGFR3 and FGFR4) in addition to other proangiogenic and oncogenic pathway-related RTKs (including the platelet-derived growth factor (PDGF) receptor PDGFR α ; KIT; and RET) involved in tumor proliferation.

Currently, Eisai has obtained approval for LENVIMA as a treatment for refractory thyroid cancer in over 50 countries, including the United States, Japan, and in Europe. Additionally, Eisai has obtained approval for the agent in combination with everolimus as a treatment for renal cell carcinoma (second-line) in over 40

countries, including the United States and in Europe. In Europe, the agent was launched under the brand name Kisplyx® for renal cell carcinoma.

Furthermore, LENVIMA is approved in Japan for use in the treatment of unresectable hepatocellular carcinoma. Eisai has submitted applications for an indication covering hepatocellular carcinoma in the United States and Europe (July 2017), China (October 2017) as well as Taiwan (December 2017).

About KEYTRUDA® (pembrolizumab)

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.

About Eisai Co., Ltd.

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. 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. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products in various therapeutic areas with high unmet medical needs, including Oncology and Neurology.

As a global pharmaceutical company, our mission extends to patients around the world through our investment and participation in partnership-based initiatives to improve access to medicines in developing and emerging countries.

For more information about Eisai Co., Ltd., please visit <https://www.eisai.com>.

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

For more than a century, Merck & Co., Inc., Kenilworth, N.J., U.S.A., a leading global biopharmaceutical company 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. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. 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

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 2017 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 Makker V, et al. Lenvatinib + pembrolizumab in patients with advanced endometrial cancer: Update results. ASCO Meeting Abstract, 2018; #5596

² Makker V, et al. Biomarker results and preclinical rationale for combination lenvatinib and pembrolizumab in advanced endometrial carcinoma. ASCO Meeting Abstract, 2018; #5597

³ American Cancer Society. What Is Endometrial Cancer. <https://www.cancer.org/cancer/endometrial-cancer/about/what-is-endometrial-cancer.html>.

⁴ American Cancer Society. Key Statistics for Endometrial Cancer. <https://www.cancer.org/cancer/endometrial-cancer/about/key-statistics.html>.

⁵ American Cancer Society. Endometrial Cancer Stages. <https://www.cancer.org/cancer/endometrial-cancer/detection-diagnosis-staging/staging.html>.

⁶ American Cancer Society. Endometrial Cancer Survival Rates, by Stage. <https://www.cancer.org/cancer/endometrial-cancer/detection-diagnosis-staging/survival-rates.html>.