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Eisai and Merck & Co., Inc., Kenilworth, N.J., U.S.A. Receive Positive EU CHMP Opinions for LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) in Two Different Types of Cancer

Positive Opinion Granted for Advanced Renal Cell Carcinoma Based on Significant Progression-Free Survival (PFS), Overall Survival (OS) and Objective Response Rate (ORR) Benefit Compared to Sunitinib in CLEAR/KEYNOTE-581 Trial

Positive Opinion Granted for Advanced Endometrial Carcinoma Based on Significant OS and PFS Benefit Compared to Chemotherapy in Study 309/KEYNOTE-775 Trial

TOKYO and KENILWORTH, N.J., Oct. 18, 2021 – Eisai (Headquarters: Tokyo, CEO: Haruo Naito) and Merck & Co., Inc., Kenilworth, N.J., U.S.A. (known as MSD outside the United States and Canada) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency has adopted positive opinions recommending approval of the combination of LENVIMA® (marketed as Kisplyx® in the European Union [EU] for the treatment of advanced renal cell carcinoma [RCC]), 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 two different indications. One positive opinion is for the first-line treatment of adult patients with advanced RCC, and the other is for 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 or radiation. Decisions on the CHMP's recommendations will be given by the European Commission for marketing authorization in the EU, and are expected in the fourth quarter of 2021. If approved, this would be the first combination of an anti-PD-1 therapy with a tyrosine kinase inhibitor approved for the treatment of two different types of cancer in the EU.

The positive CHMP opinions are based on data from two pivotal Phase 3 trials: CLEAR (Study 307)/KEYNOTE-581 evaluating the combination in adult patients with advanced RCC and Study 309/KEYNOTE-775 evaluating the combination in certain patients with advanced EC.

In CLEAR/KEYNOTE-581, LENVIMA plus KEYTRUDA demonstrated statistically significant improvements versus sunitinib in the efficacy outcome measures of overall survival (OS), reducing the risk of death by 34% (HR=0.66 [95% CI, 0.49-0.88]; p=0.0049) versus sunitinib, and progression-free survival (PFS), reducing the risk of disease progression or death by 61% (HR=0.39 [95% CI, 0.32-0.49]; p<0.0001) with a median PFS of 23.9 months versus 9.2 months for sunitinib. Additionally, the confirmed objective response rate was 71% (95% CI: 66-76) (n=252) for patients who received LENVIMA plus KEYTRUDA versus 36% with sunitinib (95% CI: 31-41) (n=129).

In Study 309/KEYNOTE-775, LENVIMA plus KEYTRUDA demonstrated statistically significant improvements in the study's dual efficacy outcome measures of OS, reducing the risk of death by 38% (HR=0.62 [95% CI, 0.51-0.75]; p<0.0001) with a median OS of 18.3 months versus 11.4 months for chemotherapy (investigator's choice of doxorubicin or paclitaxel), and PFS, reducing the risk of disease progression or death by 44% (HR=0.56 [95% CI, 0.47-0.66]; p<0.0001), with a median PFS of 7.2 months versus 3.8 months for chemotherapy (investigator's choice of doxorubicin or paclitaxel).

"KEYTRUDA plus LENVIMA demonstrated a survival benefit for advanced renal cell carcinoma in the first-line setting and represents an important potential new treatment option for these patients. Additionally, KEYTRUDA plus LENVIMA is the first anti-PD-1 and tyrosine kinase inhibitor combination to demonstrate a survival benefit in advanced endometrial carcinoma patients, and the benefit was shown regardless of mismatch repair status," said Dr. Gregory Lubiniecki, Vice President, Clinical Research, Merck & Co., Inc., Kenilworth, N.J., U.S.A. Research Laboratories. "We are pleased that the CHMP has recognized the important role of the combination therapy in these difficult-to-treat cancers."

"We appreciate the positive opinions rendered by the EU CHMP recommending approval of LENVIMA plus KEYTRUDA in advanced renal cell carcinoma and advanced endometrial carcinoma, underscoring the potential significance of the outcomes observed in the CLEAR/KEYNOTE-581 and Study 309/KEYNOTE-775 trials" said Dr. Takashi Owa, President, Oncology Business Group at Eisai. "We are grateful to the patients who participated in these studies, their families and clinicians. Their commitment made these meaningful milestones possible"

In CLEAR/KEYNOTE-581, the most common adverse reactions (≥30%) for LENVIMA plus KEYTRUDA* were diarrhoea (61.8%), hypertension (51.5%) fatigue (47.1%), hypothyroidism (45.1%), decreased appetite (42.1%), nausea (39.6%), stomatitis (36.6%), proteinuria (33.0%), dysphonia (32.8%), and arthralgia (32.4%).

In Study 309/KEYNOTE-775, 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%).

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

About Renal Cell Carcinoma (RCC)[1,2,3,4,5,6]

Worldwide, it is estimated there were more than 431,000 new cases of kidney cancer diagnosed and more than 179,000 deaths from the disease in 2020. In Japan, there were more than 25,000 new cases and 8,000 deaths in 2020. In the U.S. alone, it is estimated there will be approximately 76,000 new cases of kidney cancer diagnosed and almost 14,000 deaths from the disease in 2021. In Europe, it is estimated there were more than 138,000 new cases of kidney cancer diagnosed and more than 54,000 deaths from the disease in 2020. Renal cell carcinoma is by far the most common type of kidney cancer; about nine out of 10 kidney cancer diagnoses are RCC. RCC is about twice as common in men as in women. Most cases of RCC are discovered incidentally during imaging tests for other abdominal diseases. Approximately 30% of patients with RCC will have metastatic disease at diagnosis. Survival is highly dependent on the stage at diagnosis, and the five-year survival rate is 13% for patients diagnosed with metastatic disease.

About Endometrial Cancer[2,7,8,9]

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 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); available as 10mg and 4mg capsules

LENVIMA, discovered and developed by Eisai, is a 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, the combination of lenvatinib with an anti-PD-1 monoclonal antibody decreased tumor-associated macrophages, increased activated cytotoxic T cells, and demonstrated greater antitumor activity 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 has been 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. LENVIMA has been approved in combination with KEYTRUDA (generic name: pembrolizumab) 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.

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 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 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).

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