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European Commission Approves LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) as First-Line Treatment for Adult Patients With Advanced Renal Cell Carcinoma

Approval Based on Results From CLEAR/KEYNOTE-581 Trial Demonstrating LENVIMA Plus KEYTRUDA Significantly Reduced the Risk of Disease Progression or Death by 61%, With a Median Progression-Free Survival of Nearly Two Years Versus Nine Months for Sunitinib

TOKYO and KENILWORTH, N.J., November. 29, 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 European Commission has approved the combination of LENVIMA (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 the first-line treatment of adult patients with advanced RCC.

The approval for advanced RCC is based on results from the pivotal Phase 3 CLEAR (Study 307)/KEYNOTE-581 trial, in which LENVIMA plus KEYTRUDA demonstrated statistically significant improvements versus sunitinib in the efficacy outcome measures of 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, and overall survival (OS), reducing the risk of death by 34% (HR=0.66 [95% CI, 0.49-0.88]; p=0.0049) versus sunitinib. Median OS was not reached at the time of analysis in either study arm. The objective response rate (ORR) was 71% (95% CI: 66-76) for patients treated with LENVIMA plus KEYTRUDA (n=355) versus 36% (95% CI: 31-41) for patients treated with sunitinib (n=357; p<0.0001). Patients treated with LENVIMA plus KEYTRUDA achieved a complete response (CR) rate of 16% and partial response (PR) rate of 55% versus a CR rate of 4% and a PR rate of 32% for patients treated with sunitinib.

"A key focus of our collaboration with Eisai is to advance our clinical development program to evaluate the potential of KEYTRUDA plus LENVIMA to improve responses across different types of cancer, including renal cell carcinoma," said Dr. Gregory Lubiniecki, Vice President, Clinical Research, Merck & Co., Inc., Kenilworth, N.J., U.S.A. Research Laboratories. "Today's approval of KEYTRUDA plus LENVIMA brings a new treatment option to patients with advanced renal cell carcinoma in Europe, and further validates our efforts to research this promising combination of an immunotherapy and tyrosine kinase inhibitor for some of the most difficult-to-treat cancers."

"Renal cell carcinoma is the most common type of kidney cancer in both men and women, marking the significance of the European approval for the LENVIMA plus KEYTRUDA combination," said Corina Dutcus, M.D., Vice President, Clinical Research, Oncology Business Group at Eisai Inc. "We remain committed to continuing to explore this combination therapy with the goal of improving care for people living with cancer. The participation of many patients, families and healthcare providers made this approval possible, for which we are very grateful."

In the CLEAR/KEYNOTE-581 trial, 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%).

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 the first-line treatment of adult patients with advanced renal cell carcinoma and 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.

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

About CLEAR/KEYNOTE-581 Trial

The approval was based on data from the CLEAR(Study 307)/KEYNOTE-581 trial (ClinicalTrials.gov, NCT02811861), a Phase 3, multicenter, open-label, randomized trial conducted in 1,069 patients with advanced RCC with clear cell component including other histological features such as sarcomatoid and papillary in the first-line setting. Patients were enrolled regardless of PD-L1 tumor expression status. The study excluded patients with active autoimmune disease or a medical condition that required immunosuppression. Randomization was stratified by geographic region (North America and Western Europe vs. "Rest of the World")

and Memorial Sloan Kettering Cancer Center (MSKCC) prognostic groups (favorable vs. intermediate vs. poor). The primary efficacy outcome measure was PFS based on Blinded Independent Central Review (BICR) using RECIST 1.1, and PFS results were consistent across pre-specified subgroups, MSKCC prognostic groups and PD-L1 tumor expression status. Key secondary efficacy outcome measures were OS and ORR.

Patients were randomized 1:1:1 to receive LENVIMA (20 mg orally once daily) plus KEYTRUDA (200 mg intravenously every three weeks for up to 24 months), or LENVIMA (18 mg orally once daily) plus everolimus (5 mg orally once daily), or sunitinib (50 mg orally once daily for four weeks on treatment, followed by two weeks off treatment). Treatment continued until unacceptable toxicity or disease progression as determined by investigator and confirmed by BICR using RECIST 1.1. Administration of LENVIMA plus KEYTRUDA was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered by the investigator to be deriving clinical benefit. KEYTRUDA was continued for a maximum of 24 months; however, treatment with LENVIMA could be continued beyond 24 months. Assessment of tumor status was performed at baseline and then every eight weeks.

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 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. Renal cell carcinoma 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 LENVIMA® (lenvatinib); available as 10mg and 4mg 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 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 (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. 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).

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[6] Cancer. Net. "Statistics, 2021." Kidney cancer. https://www.cancer.net/cancer-types/kidney-cancer/statistics .

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