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**Eisai and Merck & Co., Inc., Rahway, NJ, USA Provide Update on
Two Phase 3 Trials Evaluating LENVIMA® (lenvatinib) Plus KEYTRUDA®
(pembrolizumab) in Patients With Certain Types of
Metastatic Non-Small Cell Lung Cancer**

TOKYO and RAHWAY, N.J., Sept. 22, 2023 – Eisai (Headquarters: Tokyo, CEO: Haruo Naito) and Merck & Co., Inc., Rahway, NJ, USA (known as MSD outside of the United States and Canada) today provided updates on two Phase 3 trials, LEAP-006 and LEAP-008, evaluating LENVIMA, the orally available multiple receptor tyrosine kinase inhibitor discovered by Eisai, plus KEYTRUDA, the anti-PD-1 therapy from Merck & Co., Inc., Rahway, NJ, USA in patients with certain types of metastatic non-small cell lung cancer.

LEAP-006: The Phase 3 LEAP-006 trial evaluating LENVIMA plus KEYTRUDA in combination with pemetrexed (Alimta®) and platinum-containing chemotherapy versus KEYTRUDA with pemetrexed and platinum-containing chemotherapy, a current standard of care option in this disease setting, as a first-line treatment for adult patients with metastatic, nonsquamous non-small cell lung cancer (NSCLC) who have confirmation that *epidermal growth factor receptor (EGFR)*-, *anaplastic lymphoma kinase (ALK)*- or *c-ros oncogene 1 (ROS1)*- directed therapies are not indicated, did not meet its dual primary endpoints of overall survival (OS) and progression-free survival (PFS). At the study's final analysis, there was not an improvement in OS for patients treated with KEYTRUDA plus LENVIMA with chemotherapy compared to KEYTRUDA with chemotherapy. Earlier interim analyses did not demonstrate a statistically significant improvement in PFS or objective response rate (ORR), a key secondary endpoint.

LEAP-008: The Phase 3 LEAP-008 trial evaluating LENVIMA plus KEYTRUDA versus docetaxel, a current second line standard of care option, as a treatment for patients with metastatic NSCLC who progressed on or after platinum-containing chemotherapy and one prior anti-PD-1/L1 immunotherapy, and have confirmation that *EGFR*-, *ALK*- or *ROS1*-directed therapies are not

indicated, did not meet its dual primary endpoints of OS and PFS. At the final analysis of the study, there was not an improvement in OS for patients who received KEYTRUDA plus LENVIMA compared to docetaxel. Earlier interim analyses did not demonstrate a statistically significant improvement in PFS or ORR, a key secondary endpoint.

In both the LEAP-006 and LEAP-008 trials, the safety profiles of the LENVIMA plus KEYTRUDA-based treatment regimens were consistent with that observed in previously reported studies evaluating the combination. A full evaluation of the data from these studies is ongoing. The companies will work with investigators to share the results with the scientific community.

“As a leader in lung cancer research, we continue to try to advance science for our patients by building upon the standard we set several years ago with KEYTRUDA,” said Dr. Gregory Lubiniecki, Vice President, Global Clinical Development, Merck Research Laboratories. “While these results are not what we hoped for, we are proud of the foundational role that KEYTRUDA has established in the treatment of certain types of lung cancer, and we are committed to continuing to research how we can further improve responses to our medicines for patients with difficult-to-treat forms of the disease.”

“Despite great progress in recent years, unmet needs still remain in the treatment of patients with metastatic non-small cell lung cancer, particularly for those without targetable biomarkers,” said Dr. Corina Dutcus, Senior Vice President, Global Clinical Development, Oncology at Eisai Inc. “KEYTRUDA plus LENVIMA has demonstrated survival benefit in advanced renal cell carcinoma and advanced endometrial carcinoma, and while we are disappointed that the final analyses of these non-small cell lung cancer studies did not show the same benefit, we remain committed to applying learnings from these studies and furthering research in oncology for people with unmet needs. We thank all the patients, their families and the investigators involved.”

LENVIMA plus KEYTRUDA is approved in the U.S., the EU, Japan and other countries for the treatment of advanced renal cell carcinoma (RCC) and certain types of advanced endometrial carcinoma. Lenvatinib is marketed as KISPLYX® for advanced RCC in the EU. Eisai and Merck & Co., Inc., Rahway, NJ, USA are studying the LENVIMA plus KEYTRUDA combination through the LEAP (**L**Envatinib **A**nd **P**embrolizumab) clinical program in various tumor types, including but not limited to endometrial carcinoma, hepatocellular carcinoma, RCC, head and neck cancer, gastric cancer and esophageal cancer across multiple clinical trials.

Results from the LEAP-006 and LEAP-008 trials do not affect the current approved indications for the LENVIMA and KEYTRUDA combination or other ongoing trials from the LEAP clinical program.

About LEAP-006

LEAP-006 is a randomized, placebo-controlled Phase 3 trial ([ClinicalTrials.gov, NCT03829319](https://clinicaltrials.gov/ct2/show/study/NCT03829319)) evaluating LENVIMA plus KEYTRUDA with pemetrexed and platinum-containing chemotherapy versus placebo plus KEYTRUDA with pemetrexed and platinum-containing chemotherapy for the first-line treatment of adult patients with metastatic, nonsquamous NSCLC who have confirmation that *EGFR*-, *ALK*- or *ROS1*-directed therapies are not indicated. The dual primary endpoints are PFS, as assessed by blinded independent central review (BICR) per Response Evaluation Criteria in Solid Tumors version 1.1 (RESIST v1.1) modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ, and OS. Secondary endpoints include ORR and duration of response (DOR), as assessed by BICR per RECIST v1.1, quality of life and safety. The study enrolled an estimated 748 patients who were randomized 1:1 to receive:

- LENVIMA (8 mg orally once daily) plus KEYTRUDA (200 mg intravenously [IV] on Day 1 of each three-week cycle [Q3W]) with pemetrexed 500 mg/m² IV Q3W and carboplatin Area Under Curve 5 mg/mL/min (AUC5) or cisplatin 75 mg/m² Q3W IV; or
- Placebo (oral capsule once daily) plus KEYTRUDA (200 mg IV Q3W) with pemetrexed 500 mg/m² IV Q3W and carboplatin AUC5 or cisplatin 75 mg/m² Q3W IV

All study drugs were continued until protocol-specified discontinuation criteria. KEYTRUDA was administered for up to 35 cycles (approximately two years). After completing two years of combination therapy, LENVIMA may have been administered as a single agent until protocol-specified discontinuation criteria were met. Carboplatin or cisplatin was administered for up to four cycles. The LEAP-006 study was conducted in collaboration with Eli Lilly and Company, the makers of Alimta® (pemetrexed).

About LEAP-008

LEAP-008 is a randomized, open-label Phase 3 trial ([ClinicalTrials.gov, NCT03976375](https://clinicaltrials.gov/ct2/show/study/NCT03976375)) evaluating LENVIMA plus KEYTRUDA versus docetaxel for the treatment of patients with metastatic NSCLC who progressed on or after platinum-containing chemotherapy and one prior anti-PD-1/-L1 therapy, and have confirmation that *EGFR*-, *ALK*- or *ROS1*-directed therapies are not indicated. The trial's dual primary endpoints are PFS, as assessed by BICR per RECIST v1.1) modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ,

and OS. Secondary endpoints include ORR and DOR as assessed by BICR per RECIST v1.1, quality of life and safety. The study enrolled an estimated 422 patients who were randomized 4:4:1 to receive:

- LENVIMA (20 mg orally once daily) plus KEYTRUDA (200 mg IV every three-weeks);
or
- Docetaxel (75 mg/m² IV every three-weeks); or
- LENVIMA (24 mg orally once daily).

KEYTRUDA was administered for up to 35 cycles (approximately two years) or until protocol-specified discontinuation criteria were met. After completing two years of combination therapy, LENVIMA may have been administered as a single agent until protocol-specified discontinuation criteria were met.

About lung cancer

Lung cancer is the leading cause of cancer death worldwide.¹ In 2020 alone, there were more than 2.2 million new cases and 1.8 million deaths from lung cancer globally.² Non-small cell lung cancer is the most common type of lung cancer in the U.S., accounting for about 81% of all cases.³ In the U.S., the overall five-year survival rate for patients diagnosed with lung cancer is 25%, which is a 21% improvement over the last five years.⁴ Improved survival rates are due, in part, to earlier detection and screening, reduction in smoking, advances in diagnostic and surgical procedures as well as the introduction of new therapies.³ Early detection and screening remain an important unmet need, as 44% of lung cancer cases are not found until they are advanced.⁴ Only 5.8% of people in the U.S. who are eligible were screened for lung cancer in 2021.⁴

About LENVIMA® (lenvatinib) Capsules

LENVIMA, discovered and developed by Eisai, is an orally available 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 (PDGFR α), 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. LENVIMA has been approved for the indications below.

Thyroid cancer

- Indication as monotherapy

(Approved in over 80 countries including Japan, the United States, China, and countries in Europe and Asia)

Japan: Unresectable thyroid cancer

The United States: The treatment of patients with locally recurrent or metastatic, progressive, radioiodine-refractory differentiated thyroid cancer (DTC)

Europe: The treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI)

Hepatocellular carcinoma

- Indication as monotherapy

(Approved in over 80 countries including Japan, the United States, China, and countries in Europe and Asia)

Japan: Unresectable hepatocellular carcinoma

The United States: The first-line treatment of patients with unresectable hepatocellular carcinoma (HCC)

Europe: The treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have received no prior systemic therapy

Thymic carcinoma

- Indication as monotherapy (Approved in Japan)

Japan: Unresectable thymic carcinoma

Renal cell carcinoma (In Europe, the agent was launched under the brand name Kisplyx®)

- Indication in combination with everolimus

(Approved in over 65 countries including the United States, and countries in Europe and Asia)

The United States: The treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy

Europe: The treatment of adult patients with advanced renal cell carcinoma following one prior vascular endothelial growth factor (VEGF) targeted therapy

- Indication in combination with KEYTRUDA (generic name: pembrolizumab)

(Approved in over 45 countries including Japan, the United States, and countries in Europe and Asia)

Japan: Radically unresectable or metastatic renal cell carcinoma

The United States: The first-line treatment of adult patients with advanced renal cell carcinoma

Europe: The first-line treatment of adult patients with advanced renal cell carcinoma

Endometrial carcinoma

- Indication in combination with KEYTRUDA

(Approved [including conditional approval] in over 50 countries including Japan, the United States, and countries in Europe and Asia)

Japan: Unresectable, advanced or recurrent endometrial carcinoma that progressed after cancer chemotherapy

The United States: The treatment of patients with advanced endometrial carcinoma (EC) 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.

Europe: 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

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., Rahway, NJ, USA 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., Rahway, NJ, USA Strategic Collaboration

In March 2018, Eisai and Merck & Co., Inc., Rahway, NJ, USA, 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., Rahway, NJ, USA.

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 various tumor types across multiple clinical trials.

Eisai's Focus on Cancer

Eisai acknowledges "Oncology" as one of its key strategic areas, and will continue to focus on the discovery and development of anti-cancer drugs within drug discovery domains including "microenvironment", "proteostasis disruption", "cell lineage and cell differentiation", and "inflammation, hypoxia, oxidative stress and cell senescence" under the Deep Human Biology Learning (DHBL) drug discovery and development organization. Eisai aspires to discover innovative new drugs with new targets and mechanisms of action from these domains, with the aim of contributing to the cure of cancers.

About Eisai

Eisai's Corporate Concept is "to give first thought to patients and people in the daily living domain, and to increase the benefits that health care provides." Under this Concept [also known as our *human health care (hhc)* Concept], we aim to effectively achieve social good in the form of relieving anxiety over health and reducing health disparities. With a global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to create and deliver innovative products to target diseases with high unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology.

In addition, our continued commitment to the elimination of neglected tropical diseases (NTDs), which is a target (3.3) of the United Nations Sustainable Development Goals (SDGs), is demonstrated by our work on various activities together with global partners.

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](#)), LinkedIn (for [global](#), [U.S.](#) and [EMEA](#)) and Facebook ([global](#)).

Merck & Co., Inc., Rahway, NJ, USA'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., Rahway, NJ, USA, 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., Rahway, NJ, USA 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., Rahway, NJ, USA

For over 130 years, Merck & Co., Inc., Rahway, NJ, USA, 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., Rahway, NJ, USA 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., Rahway, NJ, USA

This news release of Merck & Co., Inc., Rahway, NJ, 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 candidates that the candidates 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 Annual Report on Form 10-K for the year ended December 31, 2022 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

¹ World Health Organization. "Lung cancer" Fact sheet.

<https://www.who.int/news-room/fact-sheets/detail/lung-cancer> .

² Hyuna S. et al. Global cancer statistics 2020. *CA Cancer J Clin.* 2021; 71: 209-249.

<https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21660> .

³ American Cancer Society. Cancer Facts & Figures

<https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf> .

⁴ American Lung Association. "Key findings." State of lung cancer.

<https://www.lung.org/research/state-of-lung-cancer/key-findings> .

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