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**Eisai and Merck & Co., Inc., Rahway, NJ, USA Provide
Update on Phase 3 LEAP-010 Trial Evaluating
LENVIMA® (lenvatinib) Plus KEYTRUDA® (pembrolizumab) in
Patients With Certain Types of Recurrent or
Metastatic Head and Neck Squamous Cell Carcinoma**

TOKYO and RAHWAY, N.J., August 25, 2023 – Eisai (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) and Merck & Co., Inc., Rahway, NJ, USA (known as MSD outside of the United States and Canada) today provided an update on the Phase 3 LEAP-010 trial evaluating LENVIMA®, the orally available multiple receptor tyrosine kinase inhibitor (TKI) discovered by Eisai, plus KEYTRUDA®, the anti-PD-1 therapy from Merck & Co., Inc., Rahway, NJ, USA, as a first-line treatment for patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) whose tumors express PD-L1. The primary endpoints of the study were overall survival (OS), progression-free survival (PFS), and objective response rate (ORR).

Two planned interim analyses were conducted by an independent Data Monitoring Committee (DMC) over an 11-month period. In the first analysis, LENVIMA plus KEYTRUDA showed a statistically significant improvement in PFS and ORR versus placebo plus KEYTRUDA. At the second analysis, LENVIMA plus KEYTRUDA did not demonstrate an improvement in OS compared to placebo plus KEYTRUDA, and the likelihood of reaching the protocol-specified threshold for statistical significance for OS was evaluated by Merck and Eisai and deemed to be low. Accordingly, the study will be closed, and the companies are informing investigators of this decision. The safety profile of KEYTRUDA plus LENVIMA was consistent with previously reported data on the combination. A full evaluation of the data from this study, including pre-planned subgroup analyses, is ongoing. The companies will work with investigators to share the results with the scientific community.

“With the LEAP-010 trial, we aimed to explore whether this combination could improve upon options already available with KEYTRUDA-based regimens for appropriate patients with metastatic or with unresectable, recurrent HNSCC,” said Dr. Gregory Lubiniecki, Vice President, Global Clinical Development, Merck Research Laboratories. “Although the progression-free survival results from this study were encouraging, unfortunately the combination did not result in an overall survival benefit for patients. We will apply lessons from this trial to help continue advancing research of this combination.”

“While we were initially encouraged to see that LENVIMA plus KEYTRUDA met two of its three primary endpoints at an earlier interim analysis, unfortunately the combination did not meet the threshold for the third primary endpoint of overall survival.” said Corina Dutcus, M.D., Senior Vice President, Global Clinical Development, Oncology at Eisai Inc. “Our clinical program is designed to help accelerate our efforts to tackle difficult-to-treat, advanced cancers, and while the outcome may not always be what we anticipate, we know that this is part of clinical development, and we remain committed to scientific exploration in pursuit of improving care for patients.”

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 (LEnvatinib And Pembrolizumab) clinical program in various tumor types, including but not limited to endometrial carcinoma, hepatocellular carcinoma, non-small cell lung cancer, RCC, head and neck cancer, gastric cancer and esophageal cancer across multiple clinical trials. KEYTRUDA is currently approved as monotherapy and in combination regimens for appropriate patients with metastatic or with unresectable, recurrent HNSCC in the U.S., Europe, China, Japan and other countries around the world.

Results from the LEAP-010 trial do not affect the current approved indications for LENVIMA plus KEYTRUDA or other ongoing trials from the LEAP clinical program, including the ongoing LEAP-009 trial, evaluating LENVIMA in combination with KEYTRUDA versus chemotherapy in people living with recurrent or metastatic HNSCC who progressed after platinum therapy and immunotherapy.

About LEAP-010

LEAP-010 is a randomized, placebo-controlled, double-blinded, Phase 3 trial (ClinicalTrials.gov, [NCT04199104](https://clinicaltrials.gov/ct2/show/study/NCT04199104)) evaluating LENVIMA plus KEYTRUDA versus KEYTRUDA

monotherapy as a first-line treatment for patients with recurrent or metastatic HNSCC whose tumors express PD-L1. The trial's three primary endpoints are OS, PFS and ORR. PFS and ORR were assessed by blinded independent central review (BICR) per Response Evaluation Criteria in Solid Tumors Version (RECIST) v1.1 modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ. The study enrolled an estimated 511 patients who were randomized 1:1 to receive:

- LENVIMA (20 mg orally once daily) plus KEYTRUDA (200 mg intravenously [IV] on Day 1 of each three-week cycle); or
- Placebo (orally once daily) plus KEYTRUDA (200 mg IV on Day 1 of each three-week cycle).

In both arms, 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 head and neck cancer

Head and neck cancer describes a number of different tumors that develop in or around the throat, larynx, nose, sinuses and mouth.¹ Most head and neck cancers are squamous cell carcinomas that begin in the flat, squamous cells that make up the thin surface layer of the structures in the head and neck.¹ Two substances that greatly increase the risk of developing head and neck cancer are tobacco and alcohol.¹ Worldwide, it is estimated there were more than 930,000 new cases of head and neck cancer diagnosed and over 465,000 deaths from the disease in 2020.² In the U.S., it is estimated there will be more than 66,000 new cases of head and neck cancer diagnosed and more than 15,000 deaths from the disease in 2023.³

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

(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 mismatch repair proficient (pMMR), as determined by an FDA-approved test, or not microsatellite instability-high (MSI-H), 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, 100 mg

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 of 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 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](#)) and LinkedIn (for [U.S.](#) and [EMEA](#)).

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 Cancer Net. Website, "introduction." Head and Neck Cancer.

<https://www.cancer.net/cancer-types/head-and-neck-cancer/introduction> .

² International Agency for Research on Cancer, World Health Organization. Cancer Today, 2020.

[Cancer Today \(iarc.fr\)](http://www.iarc.fr) .

³ Cancer Net. Website, "statistics." Head and Neck Cancer.

<https://www.cancer.net/cancer-types/head-and-neck-cancer/statistics> .

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