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# Merck & Co., Inc., Rahway, NJ, USA and Eisai Provide Update on Phase 3 LITESPARK-012 Trial Evaluating First-Line Combination Treatments for Certain Patients With Advanced Renal Cell Carcinoma (RCC)

RAHWAY, N.J. and Tokyo, April 21, 2026 – Merck & Co., Inc., Rahway, NJ, USA (known as MSD outside of the United States and Canada), and Eisai (Headquarters: Tokyo, CEO: Haruo Naito) today announced results from the Phase 3 LITESPARK-012 trial evaluating combination treatments for the first-line treatment of patients with advanced clear cell renal cell carcinoma (RCC). The trial evaluated the triplet therapy of KEYTRUDA® (pembrolizumab), Merck & Co., Inc., Rahway, NJ, USA's anti-PD-1 therapy, plus LENVIMA® (lenvatinib), the orally available multiple receptor tyrosine kinase inhibitor (TKI) discovered by Eisai, plus WELIREG® (belzutifan), Merck & Co., Inc., Rahway, NJ, USA's first-in-class hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor. The study also evaluated MK-1308A, the coformulation of KEYTRUDA and quavonlimab, Merck & Co., Inc., Rahway, NJ, USA's investigational anti-CTLA-4 antibody, plus LENVIMA. Both combination regimens were compared to KEYTRUDA plus LENVIMA for these patients.

At a pre-specified interim analysis, the combination regimens did not meet the dual primary endpoints of progression-free survival (PFS) and overall survival (OS) for the first-line treatment of patients with RCC compared to KEYTRUDA plus LENVIMA. The safety profiles of the combination regimens were consistent with those observed in previously reported studies evaluating the individual medicines and the KEYTRUDA plus LENVIMA combination. A full evaluation of the data from this study is ongoing, and Merck & Co., Inc., Rahway, NJ, USA and Eisai will work with investigators to share the results with the scientific community.

"With the LITESPARK-012 trial, we explored whether combining therapies with established activity could improve upon well-established standards set by KEYTRUDA-based regimens, reflecting our commitment to continuously explore ways to improve outcomes for the kidney cancer community," said Dr. M. Catherine Pietanza, Vice President, Global Clinical Development, MSD Research Laboratories. "While these regimens did not demonstrate the results we hoped, the data deepen our understanding of advanced renal cell carcinoma and will help shape the next generation of treatment approaches."

"While we are disappointed that LITESPARK-012 did not meet its primary endpoints, the findings reinforce the central role of KEYTRUDA plus LENVIMA in the first-line treatment of patients with advanced renal cell carcinoma," said Dr. Corina Dutcus, Senior Vice President, Oncology Global Clinical Development Lead at Eisai Inc. "Findings from trials such as this play an important role in shaping health care providers'

perspectives as the treatment paradigm for advanced renal cell carcinoma continues to evolve. We are committed to advancing the care of people living with this disease and we are grateful to the patients, caregivers and investigators whose participation and dedication made this research possible."

Results from the LITESPARK-012 trial do not affect other ongoing trials from the LITESPARK clinical program, including those conducted jointly with Eisai. As previously announced, the U.S. Food and Drug Administration (FDA) has accepted two supplemental New Drug Applications (sNDA) for review based on Phase 3 LITESPARK-011 trial evaluating WELIREG in combination with LENVIMA for certain previously treated patients with advanced RCC and has set a Prescription Drug User Fee Act (PDUFA), or target action, date of Oct 4, 2026.

KEYTRUDA is currently approved as adjuvant monotherapy and in combination regimens for appropriate patients with RCC in the U.S., European Union (EU), Japan and other countries around the world.

KEYTRUDA plus LENVIMA is approved in the U.S., the EU, Japan and other countries for the first-line treatment of adult patients with advanced RCC. Lenvatinib is approved as KISPLYX for advanced RCC in the EU.

LENVIMA in combination with everolimus is approved in the U.S., EU and other regions for the treatment of adult patients with advanced RCC following one prior anti-angiogenic therapy.

WELIREG is approved in the U.S., EU, Japan and other countries for the treatment of adult patients with advanced clear cell RCC following a PD-1/PD-L1 inhibitor and 1-2 VEGF-TKIs based on results from the Phase 3 LITESPARK-005 trial.

**About LITESPARK-012**

LITESPARK-012 is a randomized, open-label Phase 3 trial (ClinicalTrials.gov, NCT04736706) evaluating either the triplet therapy of KEYTRUDA plus LENVIMA plus WELIREG or MK-1308A plus LENVIMA compared to KEYTRUDA plus LENVIMA for the first-line treatment of patients with advanced clear cell RCC. The primary endpoints are PFS, as assessed by blinded independent central review (BICR) according to Response Evaluation Criteria in Solid Tumors version 1.1 (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 are objective response rate and duration of response as assessed by BICR according to RECIST v1.1, as well as safety. The study enrolled 1,688 patients who were randomized to receive:

- KEYTRUDA (400 mg intravenously [IV] every six weeks [Q6W]) plus LENVIMA (20 mg orally once daily [QD]) plus WELIREG (120 mg orally QD);
- MK-1308A (coformulation of pembrolizumab [400 mg] and quavonlimab [25 mg] IV Q6W) plus LENVIMA (20 mg orally QD);
- KEYTRUDA (400 mg IV Q6W) plus LENVIMA (20 mg orally QD).

All study drugs were continued until protocol-specified discontinuation criteria. KEYTRUDA and MK-1308A were administered for up to two years (approximately 18 cycles). WELIREG and LENVIMA may have been administered in combination or as a single agent until progressive disease or discontinuation.

**About renal cell carcinoma**

Renal cell carcinoma is the most common type of kidney cancer, with about nine out of 10 kidney cancer diagnoses being RCC. In 2022, there were about 435,000 new cases of kidney cancer diagnosed and approximately 156,000 deaths from the disease worldwide. 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, and about 70% are a form called clear cell RCC, which tends to be more aggressive and faster spreading. Approximately 30% of patients with kidney cancer are diagnosed at an advanced stage.

**About Merck & Co., Inc., Rahway, NJ, USA's research in genitourinary cancers**

Merck & Co., Inc., Rahway, NJ, USA is advancing research aimed at helping transform the treatment landscape and broaden options for people with genitourinary (GU) cancers, including bladder, kidney and prostate cancers. Globally, GU cancers account for an estimated 2.6 million new cancer diagnoses each year, equaling over 1 in 8 of all cancer incidences. Through a robust clinical development program with more than 50 ongoing clinical trials evaluating more than 22,000 patients around the world, Merck & Co., Inc., Rahway, NJ, USA is investigating the potential of several portfolio medicines and pipeline assets, leveraging multiple novel combination strategies, across various stages of disease, to help address unmet needs in GU cancers.

**About KEYTRUDA® (pembrolizumab) injection for intravenous use, 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 2,800 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 LENVIMA® (lenvatinib); available as 10 mg and 4 mg 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 (PDGFRα), 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 mainly in Japan, the United States, Europe, China 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 mainly in Japan, the United States, Europe, China 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
- Indication in combination with KEYTRUDA (generic name: pembrolizumab) and transarterial chemoembolization (Approved in China)

*Thymic carcinoma*
- Indication as monotherapy (Approved in Japan)
Japan: Unresectable thymic carcinoma

*Renal cell carcinoma* (In Europe other than the United Kingdom, the agent was launched under the brand name Kisplyx®)
- Indication in combination with everolimus
(Approved mainly in the United States, 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 mainly in Japan, the United States, 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 mainly in Japan, the United States, 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 that is pMMR or not microsatellite instability-high (MSI-H), as determined by an FDA-approved test, 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 WELIREG® (belzutifan); available as 40 mg tablets, for oral use**

WELIREG, Merck & Co., Inc., Rahway, NJ, USA's first-in-class hypoxia-inducible factor 2 alpha (HIF-2α) inhibitor, is an orally administered small-molecule designed to reduce transcription and expression of HIF-2α target genes associated with cellular proliferation, angiogenesis and tumor growth. By inhibiting HIF-2α signaling, WELIREG aims to disrupt key pathways certain tumors may use to adapt to low-oxygen conditions, including those that help promote abnormal blood vessel formation and support tumor survival.

WELIREG has demonstrated antitumor activity in certain von Hippel-Lindau (VHL) disease-associated tumors, renal cell carcinoma and in pheochromocytoma or paraganglioma. As part of a broader clinical program, Merck & Co., Inc., Rahway, NJ, USA continues to research WELIREG monotherapy and combination approaches for people with genitourinary, breast and gynecologic cancers across a range of treatment settings to further define where HIF-2α inhibition may provide clinical benefit and to better understand which patients are most likely to respond.

**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 jointly develop, manufacture and commercialize LENVIMA, both as monotherapy and in combination with Merck & Co., Inc., Rahway, NJ, USA's anti-PD-1 therapy, KEYTRUDA, and HIF-2α inhibitor, WELIREG.

**Eisai's focus on cancer**

Eisai positions Oncology as one of its key strategic areas, and aims to contribute to the cure of cancers through the discovery of innovative new drugs with new targets and mechanisms of action under the Deep Human Biology Learning (DHBL) drug discovery and development organization.

By utilizing biomarker data obtained from our products to elucidate the mechanisms of the incidence and root causes of cancer, as well as drug resistance, and using Eisai Group's precision chemistry technology to turn undruggable intracellular therapeutic targets into druggable ones, we will create new backbone therapeutic drugs.

**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 X (U.S. and global), LinkedIn (for U.S. and EMEA) and Facebook (global).

**Merck & Co., Inc., Rahway, NJ, USA's Focus on Cancer**

Every day, we follow the science as we work to discover innovations that can help patients, no matter what stage of cancer they have. As a leading oncology company, we are pursuing research where scientific opportunity and medical need converge, underpinned by our diverse pipeline of more than 20 novel mechanisms. With one of the largest clinical development programs across more than 30 tumor types, we strive to advance breakthrough science that will shape the future of oncology. By addressing barriers to clinical trial participation, screening and treatment, we work with urgency to reduce disparities and help ensure patients have access to high-quality cancer care. Our unwavering commitment is what will bring us closer to our goal of bringing life to more patients with cancer. For more information, visit https://www.merck.com/research/oncology.

**About Merck & Co., Inc., Rahway, NJ, USA**

At Merck & Co., Inc., Rahway, NJ, USA, known as MSD outside of the United States and Canada, we are unified around our purpose: We use the power of leading-edge science to save and improve lives around the world. For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals. We foster a diverse and inclusive global workforce and operate responsibly every day to enable

a safe, sustainable and healthy future for all people and communities. For more information, visit www.merck.com and connect with us on X (formerly Twitter), Facebook, Instagram, YouTube and LinkedIn.

**Forward-Looking Statement of Merck & Co., Inc., Rahway, N.J., USA**

This news release of Merck & Co., Inc., Rahway, 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 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 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, 2025 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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