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Merck & Co., Inc., Rahway, NJ, USA and Eisai Announce WELIREG® (belzutifan) Plus LENVIMA® (lenvatinib) Met Primary Endpoint of Progression-Free Survival (PFS) in Certain Previously Treated Patients With Advanced Renal Cell Carcinoma

First treatment regimen to demonstrate a statistically significant improvement in PFS for patients whose disease progressed following anti-PD-1/L1 therapy, compared with cabozantinib in Phase 3 study

LITESPARK-011 marks the first positive Phase 3 study of a HIF-2 alpha inhibitor in combination with a multi-targeted VEGF tyrosine kinase inhibitor

RAHWAY, NJ and TOKYO, October 28, 2025 – 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 that the Phase 3 LITESPARK-011 trial evaluating the dual oral regimen of WELIREG® (belzutifan), the first-in-class oral hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor from Merck & Co., Inc., Rahway, NJ, USA (known as MSD outside of the United States and Canada), plus LENVIMA® (lenvatinib), an orally available multiple receptor tyrosine kinase inhibitor (TKI) discovered by Eisai, met one of its primary endpoints of progression-free survival (PFS) for the treatment of patients with advanced renal cell carcinoma (RCC) whose disease progressed on or after treatment with anti-PD-1/L1 therapy.

At a pre-specified interim analysis, WELIREG plus LENVIMA demonstrated a statistically significant and clinically meaningful improvement in PFS compared to cabozantinib in these patients. The combination also showed a statistically significant improvement in the trial's key secondary endpoint of objective response rate (ORR) compared to cabozantinib. A trend toward improvement in overall survival (OS), the study's other primary endpoint, was observed; however, this result did not reach statistical significance at the time of this interim analysis. OS will be tested at a subsequent analysis per the clinical protocol.

The safety profiles of WELIREG and LENVIMA in this trial were consistent with those observed in previously reported studies for the individual therapies; no new safety signals were observed.

Merck & Co., Inc., Rahway, NJ, USA and Eisai will discuss these data with regulatory authorities worldwide and will present them at an upcoming medical meeting.

“Despite recent treatment advances, many patients with advanced RCC may still experience disease progression following treatment with a PD-1/L1 inhibitor,” said Dr. M. Catherine Pietanza, Vice President, Global Clinical Development, MSD Research Laboratories. “These positive results from LITESPARK-011 show the potential of this novel combination to reduce the risk of disease progression or death for patients who are in need of innovative options on or after treatment with immunotherapy.”

“We are encouraged by the data observed in the LITESPARK-011 trial, which bolster our belief in the role of LENVIMA in various combinations as a treatment option for patients impacted by advanced RCC,” said Dr. Corina Dutcus, Senior Vice President, Oncology Global Clinical Development Lead at Eisai. “These results further demonstrate Eisai’s commitment to people living with advanced RCC and invigorate our mission to address the unmet needs of patients with difficult-to-treat cancers. We look forward to sharing these investigational findings with regulatory authorities worldwide, with the goal of bringing this treatment option to patients as soon as possible. We extend our heartfelt gratitude to the patients, caregivers and investigators for their participation in this study and for helping us move this important research forward.”

LITESPARK-011 is part of a comprehensive late-stage clinical development program for WELIREG comprised of several Phase 2 and Phase 3 trials in RCC, pheochromocytoma and paraganglioma, and von Hippel-Lindau disease-associated neoplasms. The Phase 3 LITESPARK-012 trial is evaluating the addition of WELIREG to KEYTRUDA® (pembrolizumab) plus LENVIMA in the first-line advanced RCC disease setting.

WELIREG is approved in the U.S., European Union (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.

KEYTRUDA plus LENVIMA is approved in the U.S., the EU, Japan and other countries for the treatment of advanced RCC and certain types of advanced endometrial carcinoma. 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.

About LITESPARK-011

LITESPARK-011 is a randomized, open-label Phase 3 trial (ClinicalTrials.gov, NCT04586231) evaluating WELIREG in combination with LENVIMA compared to cabozantinib for the treatment of patients with advanced clear cell RCC that has progressed on or after anti-PD-1/L1 therapy. The dual primary endpoints are PFS per RECIST v1.1 as assessed by blinded independent central review (BICR) and OS. Key secondary endpoints include ORR per RECIST v1.1 as assessed by BICR, duration of response (DOR) per RECIST v1.1 as assessed by BICR, and safety. The trial enrolled an estimated 708 patients who were randomized to receive WELIREG (120 mg orally once daily) plus LENVIMA (20 mg orally once daily) or cabozantinib (60 mg orally once daily).

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.[1] In 2022, there were about 435,000 new cases of kidney cancer diagnoses and approximately 156,000 deaths from the disease worldwide.[2] RCC is about twice as common in men as in women.[1] Most cases of RCC are discovered incidentally during imaging tests for other abdominal diseases. Approximately 30% of patients with kidney cancer are diagnosed at an advanced stage.[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 (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 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 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", "protein integrity and homeostasis", and "cell lineage and cell differentiation" 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 X (U.S. and global), LinkedIn (for global, 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 25 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, 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 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, 2024 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

[1] American Cancer Society, "What Is Kidney Cancer?" https://www.cancer.org/cancer/types/kidney-cancer/about/what-is-kidney-cancer.html

[2] International Agency for Research on Cancer, World Health Organization. "Kidney fact sheet" Cancer Today, GLOBOCAN 2022. https://gco.iarc.who.int/media/globocan/factsheets/cancers/29-kidney-fact-sheet.pdf

[3] E. Esterberg et al. Real-World Treatment Patterns and Clinical Outcomes Among Patients With Advanced Renal Cell Carcinoma. *Clinical Genitourinary Cancer* April 2024, Vol. 22, No. 2, 115–125. https://www.sciencedirect.com/science/article/pii/S1558767323002203

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