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# WELIREG® (belzutifan) Plus LENVIMA® (lenvatinib) Reduced the Risk of Disease Progression or Death by 30% Compared to Cabozantinib in Certain Previously Treated Patients With Advanced Renal Cell Carcinoma (RCC)

## This is the first positive Phase 3 trial of a multi-targeted tyrosine kinase inhibitor in combination with a HIF-2 alpha inhibitor, the first for patients with RCC whose disease progressed on or after treatment with anti-PD-1/L1 therapy, and the first to improve PFS compared to a modern tyrosine kinase inhibitor

## Based on these data, the U.S. FDA accepts for review two supplemental New Drug Applications for WELIREG plus LENVIMA in certain previously treated patients with advanced RCC

RAHWAY, N.J., and Tokyo, March 2, 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 the first presentation of results from the Phase 3 LITESPARK-011 trial evaluating the dual oral regimen of WELIREG® (belzutifan), Merck & Co., Inc., Rahway, NJ, USA's first-in-class oral hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor, plus LENVIMA® (lenvatinib), an orally available multiple receptor tyrosine kinase inhibitor (TKI) discovered by Eisai, for the treatment of patients with advanced renal cell carcinoma (RCC) whose disease progressed on or after treatment with anti-programmed death receptor-1 (PD-1)/ programmed death-ligand 1 (PD-L1) therapy. These data are being presented as a late-breaking oral abstract at the 2026 American Society of Clinical Oncology (ASCO) Genitourinary (GU) Cancers Symposium (abstract #LBA417) and are included in the official ASCO GU Press Program.

At a pre-specified interim analysis with a median follow-up of 29.0 months (range, 19.3-49.2), WELIREG plus LENVIMA demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of progression-free survival (PFS), reducing the risk of disease progression or death by 30% (HR=0.70 [95% CI, 0.59-0.84]; p=0.00007) compared to cabozantinib. For WELIREG plus LENVIMA, the median PFS was 14.8 months (95% CI, 11.2-16.6) versus 10.7 months (95% CI, 9.2-11.1) for cabozantinib. A trend toward improvement in overall survival (OS), the trial's other primary endpoint, was also observed for WELIREG plus LENVIMA (HR=0.85 [95% CI, 0.68-1.05]; p=0.06075). The median OS was 34.9 months (95% CI, 27.5-NR) for WELIREG plus LENVIMA versus 27.6 months (95% CI, 24.0-31.4) for cabozantinib. The trial is continuing, and OS will be evaluated at a subsequent analysis per the clinical trial protocol.

Based on data from the LITESPARK-011 trial, the U.S. Food and Drug Administration (FDA) has accepted two supplemental New Drug Applications (sNDA) for review seeking approval for WELIREG plus LENVIMA for the treatment of adult patients with advanced RCC with a clear cell component following a

PD-1 or PD-L1 inhibitor. The FDA set a Prescription Drug User Fee Act (PDUFA), or target action date, of October 4, 2026, for both the WELIREG and LENVIMA sNDAs. Merck & Co., Inc., Rahway, NJ, USA and Eisai will also discuss these data with regulatory authorities worldwide to support potential submissions outside the United States.

“Choosing the right treatment for patients with advanced renal cell carcinoma after immunotherapy has been an ongoing challenge, and treatment options in this setting had not previously been evaluated against a current standard of care tyrosine kinase inhibitor in a Phase 3 trial,” said Dr. Robert Motzer, Principal Investigator and Genitourinary Medical Oncologist, Memorial Sloan Kettering Cancer Center. “The LITESPARK-011 study demonstrated a 30% reduction in the risk of disease progression or death with belzutifan plus lenvatinib compared to cabozantinib, and 52.6% of patients experienced a response to treatment. These findings mark a critical step forward for these patients.”

“The LITESPARK-011 trial highlights the potential of this first-of-its-kind combination regimen to deliver a meaningful benefit for patients with advanced renal cell carcinoma whose disease progresses after PD-1/L1 therapy,” said Dr. M. Catherine Pietanza, Vice President, Global Clinical Development, MSD Research Laboratories. “These WELIREG plus LENVIMA data demonstrate important progress for patients with advanced renal cell carcinoma and reinforce our commitment to improving the lives of patients through innovative treatment strategies.”

“The LITESPARK-011 results reinforce LENVIMA's established role in renal cell carcinoma and highlight the potential of this novel combination to address an area of significant unmet need,” said Dr. Corina Dutcus, Senior Vice President, Oncology Global Clinical Development Lead at Eisai. “The acceptance of this regulatory filing is an important milestone, and we remain committed to working toward approval to bring this option to patients as soon as possible. We are grateful to the patients, their families, and the investigators, whose dedication made this research possible.”

**Additional findings**

Data for objective response rate (ORR) and duration of response (DOR), two key secondary endpoints, were also reported. At the first interim analysis with a median follow-up of 19.6 months (range, 9.9-39.8), WELIREG plus LENVIMA met ORR, demonstrating a statistically significant improvement compared to cabozantinib. A confirmed ORR of 52.6% (95% CI, 47.3-57.7) was observed for WELIREG plus LENVIMA versus 39.6% (95% CI, 34.6-44.8) for cabozantinib. At the second interim analysis with a median follow-up of 29.0 months, the median DOR was 23.0 months (95% CI, 2.0-44.3+) for WELIREG plus LENVIMA versus 12.3 months (95% CI, 1.8+-35.9+) for cabozantinib.

WELIREG plus LENVIMA was administered to 370 patients and cabozantinib was administered to 371 patients. Grade ≥3 treatment-related adverse events (TRAEs) occurred in 71.6% of patients receiving WELIREG plus LENVIMA versus 65.8% of patients receiving cabozantinib. Adverse events led to treatment discontinuation in 11.1% of patients receiving WELIREG plus LENVIMA and in 11.3% of patients receiving cabozantinib, respectively. Serious adverse events were observed in 51.6% of patients receiving WELIREG plus LENVIMA versus 43.9% of patients receiving cabozantinib, and AEs led to death in 5.4% of patients (two were treatment-related: thrombotic microangiopathy [n=1] and pneumonitis [n=1]) versus 3.2% (one was treatment-related: hemoptysis [n=1]) of patients, respectively.

LITESPARK-011 is part of a comprehensive late-stage clinical development program for WELIREG comprised of several Phase 2 and Phase 3 trials in pheochromocytoma and paraganglioma, von Hippel-Lindau disease-associated neoplasms and RCC. The Phase 3 LITESPARK-012 trial is evaluating the

addition of WELIREG to KEYTRUDA® (pembrolizumab), Merck & Co., Inc., Rahway, NJ, USA's anti-PD-1 therapy, 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. 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.

Dr. Motzer has provided consulting and advisory services for Merck & Co., Inc., Rahway, NJ, USA and Eisai.

**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 Response Evaluation Criteria in Solid Tumors version 1.1 (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, DOR per RECIST v1.1 as assessed by BICR, and safety. The trial enrolled 747 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 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 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 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 WELIREG® (belzutifan) 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 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 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 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, 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).

[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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