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EISAI AND MERCK RECEIVE SIMULTANEOUS POSITIVE CHMP OPINIONS FOR LENVIMA® (LENVATINIB) PLUS KEYTRUDA® (PEMBROLIZUMAB) IN ADVANCED ENDOMETRIAL CARCINOMA AND KISPLYX® (LENVATINIB) PLUS KEYTRUDA® (PEMBROLIZUMAB) IN ADVANCED RENAL CELL CARCINOMA

- *Recommendation set to pave the way for combination therapy to expand treatment options and address unmet need for patients with advanced endometrial carcinoma (EC) (irrespective of sub-type), following prior systemic treatment with a platinum-containing regimen*
- *Combination therapy also recommended for first-line use in advanced renal cell carcinoma (RCC)*

HATFIELD, HERTFORDSHIRE, UK, 15 October 2021 – Eisai and Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency has adopted positive opinions recommending approval of the combination of lenvatinib, the oral multiple receptor tyrosine kinase inhibitor discovered by Eisai, plus pembrolizumab, Merck's anti-PD-1 therapy, for two different indications in advanced EC and advanced RCC.

The positive opinion for advanced or recurrent EC is for the treatment of adult patients who have disease progression on, or following, prior treatment with a platinum-containing therapy in any setting and are not candidates for curative surgery or radiation. People with advanced or recurrent EC typically have a poor prognosis, largely due to a lack of diverse treatment options in the metastatic setting.[1,2]

"The CHMP's recommendation is welcome news for clinicians, particularly for those of us caring for patients with advanced endometrial cancer where there has been very little treatment innovation in the last four decades," said Professor Nicoletta Colombo, Associate Professor of Obstetrics and Gynaecology at the University of Milan-Bicocca and European Institute of Oncology. "Up until now there had been no standard, recommended treatment for those patients who are unable to undergo surgery and have progressed on chemotherapy-based regimes. If approved, this will significantly expand our ability to support these patients and improve the prognosis of these patients with high unmet needs."

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For RCC, the positive opinion is for the first-line treatment of adult patients with advanced disease. The European Commission's decision on both CHMP recommendations for marketing authorisation in the European Union is expected by the end of 2021.

"Up to a third of patients with renal cell carcinoma will be diagnosed with late-stage disease – when prognosis is often worse – highlighting the need for new treatment options for these patients in Europe," said Professor Viktor Gruenwald, Interdisciplinary Genitourinary Oncology, University Hospital Essen, Germany. "The introduction of this particular combination in the first-line setting will further expand the ever-growing armory of tools that clinicians have to manage metastatic disease and extend the overall survival of patients."

"The treatment of advanced renal cell carcinoma and endometrial cancer remains highly challenging for clinicians, and this is magnified by the lack of treatment options currently available to patients," said Miguel Marcão, Vice President, Eisai EMEA Oncology Business Group.

"We are pleased that the CHMP has recognised the important role of the lenvatinib plus pembrolizumab combination in treating these advanced cancers as we take a critical step forward in our journey of delivering new options to patients in Europe and across the world," added Dr. Gregory Lubiniecki, Vice President, Clinical Research, Merck Research Laboratories.

The positive CHMP opinion for EC is based on data from the pivotal Phase 3 trial: KEYNOTE-775 / Study 309 which evaluated the combination in patients with advanced EC. In the trial, lenvatinib plus pembrolizumab demonstrated statistically significant improvements in the study's co-primary endpoints of OS, reducing the risk of death by 32% (HR=0.68 [95% CI, 0.56-0.84]; p=0.0001), and PFS, reducing the risk of disease progression or death by 40% (HR=0.60 [95% CI, 0.50-0.72]; p<0.0001), versus chemotherapy (investigator's choice of doxorubicin or paclitaxel).[3] The most common adverse reactions of these patients (all grades ≥20%) for lenvatinib plus pembrolizumab were hypertension (64%), hypothyroidism (57%), diarrhoea (54%), nausea (50%), decreased appetite (45%), vomiting (37%), decreased weight (34%), fatigue (33%), arthralgia (31%), proteinuria (29%), anemia (26%), constipation (26%), urinary tract infection (26%), headache (25%) and asthenia (24%).[3]

The positive CHMP opinion for the combination in adults with advanced RCC is based on the pivotal Phase 3 trial CLEAR (Study 307) / KEYNOTE-581. In the trial, lenvatinib plus pembrolizumab demonstrated statistically significant improvements versus sunitinib in the efficacy outcome measures of progression-free survival (PFS), reducing the risk of disease progression or death by 61% (HR=0.39 [95% CI, 0.32-0.49]; p<0.001) with a median PFS of 23.9 months versus 9.2 months for sunitinib and overall survival (OS), reducing the risk of death by 34% (HR=0.66 [95% CI, 0.49-0.88]; p=0.005) versus sunitinib.[4] The most common adverse reactions (all grades

≥25%) for lenvatinib plus pembrolizumab were diarrhoea (61%), hypertension (55%), hypothyroidism (47%), decreased appetite (40%), fatigue (40%), nausea (36%), stomatitis (35%), dysphonia (30%), weight loss (30%), proteinuria (30%), PPE syndrome (29%), arthralgia (28%), rash (27%), vomiting (26%) and constipation (25%).[4]

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Notes to editors

About endometrial carcinoma (EC)

EC begins in the inner lining of the uterus, which is known as the endometrium, and is the most common type of cancer of the uterus. Worldwide, it is estimated there were more than 417,000 new cases and more than 97,000 deaths from uterine body cancers in 2020 (these estimates include both EC and uterine sarcomas; more than 90% of uterine body cancers occur in the endometrium, so the actual numbers for EC cases and deaths are slightly lower than these estimates).[5] In Europe, it is estimated there were more than 130,000 new cases and more than 29,000 deaths in 2020.[5] The five-year relative survival rate for metastatic EC (stage IV) is estimated to be approximately 17%.[6]

About renal cell carcinoma (RCC)

Worldwide, it is estimated there were more than 431,000 new cases diagnosed and more than 179,000 deaths from the disease in 2020.[7] Kidney cancer is of particular significance within Europe where it has one of the highest incidences in the world.[8,10] In Europe, it is estimated there were more than 138,000 new cases diagnosed and more than 54,000 deaths from the disease in 2020.[7] RCC is by far the most common type of kidney cancer; about nine out of 10 kidney cancers are RCCs.[9] Most cases of RCC are discovered incidentally during imaging tests for other abdominal diseases.[10] Approximately 30% of patients with RCC will have metastatic disease at diagnosis, and as many as 40% of patients will develop metastases after primary surgical treatment for localised RCC.[11,12] Survival is highly dependent on the stage at diagnosis, and with a 5-year survival rate of 12% for metastatic disease, the prognosis for these patients is poor.[10]

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About Kisplyx® / Lenvima® (lenvatinib)

Lenvatinib is also indicated in Europe for the additional indications of:

- Monotherapy for the treatment of adult patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine.[13]
- Monotherapy for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma who have received no prior systemic therapy.[13]
- In combination with everolimus for the treatment of adult patients with advanced RCC following one prior vascular endothelial growth factor-targeted therapy.[14]

About Eisai EMEA

At Eisai, everything we do is dedicated to giving our first thought to patients and their families through our human health care (*hhc*) philosophy. We are the European hub of Tokyo-based Eisai Co. Ltd., forming part of a multinational team working across a global network of R&D facilities, manufacturing sites and marketing subsidiaries.

Our collective passion and dedication to patient care is the driving force behind our efforts to discover and develop innovative medicines in a variety of therapeutic areas in which a high unmet medical need remains, including oncology and neurology.

Our mission is clear; we strive to make a significant long-lasting contribution to society in an ethical, compliant and sustainable way by embodying our *hhc* philosophy in everything we do.

For more information about Eisai in the EMEA region please visit www.eisai.eu.

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