FOR UK TRADE, MEDICAL AND CONSUMER MEDIA

THE NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE ISSUES POSITIVE APPRAISAL CONSULTATION DOCUMENT (ACD) FOR EISAI'S KISPLYX® (LENVATINIB) IN COMBINATION WITH MSD'S KEYTRUDA® (PEMBROLIZUMAB) FOR FIRST-LINE TREATMENT OF INTERMEDIATE AND POOR RISK ADVANCED RENAL CELL CARCINOMA

- *Following publication of the positive appraisal consultation document (ACD), lenvatinib plus pembrolizumab is now available to eligible people living in England*
- *There are approximately 13,300 new kidney cancer cases in the UK every year*[1]
- *In the UK, there has been an almost 88% increase in the incidence rate of kidney cancer since the early 1990s and approximately 9 in 10 of these cases are renal cell carcinomas*[1, 2]
- *Approximately one third (36%) of people in the UK who are diagnosed with kidney cancer were diagnosed at an advanced or metastatic stage of the disease (stage 3 or 4)*[3] *when prognosis is significantly worse* [4]

HATFIELD, HERTFORDSHIRE & LONDON, UK, 18 August, 2022 – The National Institute for Health and Care Excellence (NICE) has published an appraisal consultation document (ACD) recommending the use of lenvatinib, the oral multiple receptor tyrosine kinase inhibitor discovered by Eisai, plus pembrolizumab, MSD's anti-PD-1 therapy, as a therapeutic option for untreated intermediate or poor risk advanced renal cell carcinoma (RCC) in adults, only if nivolumab with ipilimumab would otherwise be offered.[5] This follows the Scottish Medicines Consortium's positive recommendation of the combination for advanced RCC in June 2022.[6] This combination will receive interim funding in England via the Cancer Drugs Fund until publication of the technology appraisal guidance, which is expected early 2023.

Lenvatinib is indicated for the treatment of adults with advanced renal cell carcinoma in combination with pembrolizumab, as first-line treatment.[7] RCC is the most common type of kidney cancer, accounting for approximately 9 in 10 kidney cancer cases in the UK.[2] Between 2013 and 2017, approximately one third (36%) of people in the UK diagnosed with kidney cancer, and followed up with until 2018, were diagnosed at an advanced or metastatic stage of the disease (stage 3 or 4).[3] It has the highest mortality rate of the genitourinary cancers, as more than a third of

patients with RCC will die from the disease[8], therefore, providing more treatment options for people with advanced RCC remains a priority.

“We are happy to have supported Eisai’s clinical trial programme, to help develop this alternative first-line combination therapy and are delighted to see NICE deliver a positive ACD, now making this treatment available to patients across England,” said Professor Thomas Powles, Director of Barts Cancer Centre at St. Bartholomew's Hospital. “With more treatment options available to patients in more countries, we can provide personalised care plans that align more closely to their needs.”

“We are delighted that NICE is recommending this alternative first-line combination treatment option for patients living with advanced kidney cancer across England. We know through our annual Kidney Cancer UK patient survey that 42% of patients in the UK are diagnosed at an advanced stage when survival rates are typically lower. Having this combination option available through the Cancer Drugs Fund is great news which will be welcomed.” said Nick Turkentine, Chief Operating Officer, Kidney Cancer UK.

The decision by NICE is based on data from the Phase 3 trial: CLEAR (Study 307) / KEYNOTE-581, which demonstrated statistically significant improvements versus sunitinib in progression-free survival and overall survival among adults with advanced RCC.[9] The trial’s primary endpoint was progression-free survival and secondary endpoints were overall survival and objective response as assessed by an independent review committee.[9] Progression-free survival (PFS) was longer with lenvatinib plus pembrolizumab than with sunitinib, with a median PFS of 23.9 months versus 9.2 months for sunitinib (HR=0.39 [95% CI, 0.32-0.49]; p<0.001). Overall survival was also longer with lenvatinib plus pembrolizumab than with sunitinib, with 79.2% of patients in the lenvatinib and pembrolizumab group versus 70.4% of patients in the sunitinib group alive at 24 months (HR=0.66 [95% CI, 0.49-0.88]; p=0.005).[9] The most common adverse events (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%).[9]

“We are delighted that NICE is issuing a positive ACD for lenvatinib in combination with pembrolizumab as an alternative first-line treatment option in kidney cancer,” said Pam Ganju, Vice President, Oncology Alliance Management & Business Unit Director, Eisai UK & Ireland. “The joint

clinical development programme for these compounds has been specifically designed to address the unmet need in some of the most difficult-to-treat cancers, and the availability of this combination through NHS England is fantastic news for kidney cancer patients."

David Long, Executive Director Oncology, MSD UK said: "We are pleased to have worked with Eisai and the NHS to bring forward this alternative treatment option for kidney cancer patients. Despite kidney cancer being in the top ten most common cancers, there have been few new treatment options, and widespread variation in care, as seen in a report from Kidney Cancer UK last month. This makes today's approval especially meaningful as we hope that this new treatment option will continue to raise the profile of kidney cancer and lead to better outcomes for patients."

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Notes to editors

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.[10] Kidney cancer is of particular significance within Western Europe where it has one of the highest incidences in the world.[11,4] In the UK, on average over 13,300 people are diagnosed with kidney cancer and over 4,700 die from the disease each year.[12] RCC is by far the most common type of kidney cancer in the UK; accounting for approximately 9 in 10 kidney cancer cases in the UK.[2] Most cases of RCC are discovered incidentally during imaging tests for other abdominal diseases.[4] Approximately one third (36%) of people in the UK who are diagnosed with kidney cancer were diagnosed at an advanced or metastatic stage of the disease (stage 3 or 4)[3] when prognosis is significantly worse.[4] As many as 40% of patients will develop metastases after primary surgical treatment for localised RCC.[13] 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.[4]

About Kisplyx® (lenvatinib)

Lenvatinib is an oral receptor tyrosine kinase inhibitor which works by blocking the activity of tyrosine kinases which can be found in certain receptors in cancer cells. This helps to block the formation of new blood vessels and hence reduces cancer cell growth by cutting off the blood supply to the cancer cells.[14,7]

Lenvatinib is also indicated in Europe in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma, following one prior vascular endothelial growth factor (VEGF)-targeted therapy.[7]

Please see Summary of Product Characteristics for lenvatinib at https://www.medicines.org.uk/emc/product/7380/smpc and Patient Information Leaflet for lenvatinib at https://www.medicines.org.uk/emc/product/7380/pil.

About Keytruda® (pembrolizumab)

Pembrolizumab is an anti-programmed cell death receptor-1 (PD-1) therapy that works by increasing the ability of the body's immune system to help detect and fight tumour cells. Pembrolizumab is a humanised 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 tumour cells and healthy cells.[15]

Please see Summary of Product Characteristics for pembrolizumab at www.medicines.org.uk/emc/product/2498/smpc and Patient Information Leaflet for pembrolizumab at www.medicines.org.uk/emc/product/2498/pil.

About Eisai

At Eisai, everything we do is dedicated to giving our first thought to patients and their families through our *human health care (hhc)* philosophy.

Our collective passion and dedication to patient care is the driving force behind our efforts to discover, and develop, innovative medicines in areas where a high unmet medical need remains, including oncology. Eisai's oncology treatments strive to give patients with cancer as much meaningful time as possible. Together, we continue to drive the discovery, development and production of innovative oncology therapies that can make a difference and positively impact the lives of patients and their families.

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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 please visit www.eisai.eu.

About MSD

At MSD, known as Merck & Co., Inc., Rahway, NJ, USA in 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.msd-uk.com and connect with us @MSDintheUK on Twitter, LinkedIn, Instagram, YouTube and Facebook.

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. If underlying assumptions prove inaccurate or risks or uncertainties materialise, 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, 2021 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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