Merck KGaA
Darmstadt, Germany

News Release

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Merck KGaA, Darmstadt, Germany, Highlights Commitment to Improving Cancer Outcomes at ASCO 2023

Not intended for UK-based media

Darmstadt, Germany, May 25, 2023 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that 43 abstracts covering several modalities and mechanisms will be presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting, June 2-6, Chicago, Ill., US. New data for the medicines BAVENCIO® (avelumab) and TEPMETKO® (tepotinib) and pipeline assets including the first-in-class investigational IAP (inhibitor of apoptosis protein) inhibitor xevinapant demonstrate the Company's efforts to pioneer novel medicines intended to improve the lives of people living with cancer.

"The research we will present at ASCO 2023 demonstrates that we are not only maximizing the impact of our standard-of-care treatments but also advancing development programs focused on synergistic approaches targeting key cancer pathways and mechanisms," said Victoria Zazulina, M.D., Head of Development Unit, Oncology, for the Healthcare business of Merck KGaA, Darmstadt, Germany.

Key presentations include:

- **BAVENCIO (Abstracts: 4515, 4516) clinical data reinforce its role as a standard of care in first-line maintenance for advanced urothelial carcinoma (UC):** Poster discussions, including long-term safety analyses and an analysis of quality-adjusted survival from the Phase III JAVELIN Bladder 100 study, confirm the acceptable long-term benefit-risk profile as well as the net benefit estimate of BAVENCIO first-line (1L) maintenance and further support its use as a standard of care for advanced UC. As part of the

JAVELIN Bladder regimen, BAVENCIO first-line maintenance has demonstrated the longest survival benefit seen to date in a global, randomized Phase III trial in advanced UC.

- **Xevinapant (Abstracts: TPS6101, 6027) preclinical data supporting dosing rationale for this investigational IAP inhibitor as well as a trial-in-progress poster outlining design of the recently initiated Phase III XRay Vision® study in locally advanced squamous cell carcinoma of the head and neck (LA SCCHN):** Preclinical data demonstrate the benefit of extended xevinapant treatment beyond the completion of xevinapant plus radiotherapy (RT) and support the rationale for administration of six cycles of xevinapant in the ongoing Phase III studies, while also indicating that restoring sensitivity to apoptosis may address some unmet treatment needs in LA SCCHN. The trial design of the ongoing randomized Phase III XRay Vision study also will be featured. This study is assessing xevinapant plus RT in patients with resected, high-risk LA SCCHN who are not eligible for cisplatin.

- **TEPMETKO (Abstracts: 9021, 9060, 9070, 9074) data continue to demonstrate durable efficacy for first-line treatment of *MET*ex14 advanced non-small cell lung cancer (NSCLC):** Long-term outcomes from the VISION study, the largest study of a MET inhibitor in patients with *MET*ex14-skipping advanced NSCLC (N=313), demonstrate the robust and durable clinical activity of TEPMETKO, particularly in the first-line setting, detected by liquid and/or tissue biopsy: with median follow-up of 32.6 months, in 164 first-line patients, overall response rate was 57.3% (95% CI: 49.4, 65.0) and median duration of response was 46.4 months (13.8, not estimable). A manageable safety profile further supports its use in clinical practice. Additional presentations for TEPMETKO include analyses from the INSIGHT 2 study in *EGFR*m *MET*amp NSCLC for patients treated with TEPMETKO plus osimertinib.

Additional company-sponsored activity at ASCO:

- CME Live Symposium & Webcast, "After More Than a Decade: Can We Now Enhance Treatment of Patients With LA SCCHN?" with course director Kevin

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Harrington, PhD, FRCR, FRCP, The Institute of Cancer Research, The Royal Marsden Hospital, London, UK, on June 3, 7:00-8:00 PM CDT, Hilton Chicago (720 South Michigan Ave.), room Continental A.

In addition to the data being presented at ASCO 2023, Merck KGaA, Darmstadt, Germany, will launch a new educational initiative for oncology professionals on the unmet medical need in LA SCCHN, cancer's resistance to apoptosis, and the role of apoptosis proteins. More information on the initiative can be found at www.TheWallinSCCHN.com.

Select Merck KGaA, Darmstadt, Germany-related abstracts accepted for presentation at ASCO 2023 include (all times in CDT):

Title	Lead Author	Abstract	Session Information
BAVENCIO (avelumab)			
Advanced Urothelial Carcinoma			
Long-term safety of avelumab first-line (1L) maintenance for advanced urothelial carcinoma (aUC) in the JAVELIN Bladder 100 trial	Bellmunt J	4516	Genitourinary Cancer: Kidney and Bladder Saturday, June 3, 2023 8:00AM-11:00AM Poster Discussion Time: 3:00PM-4:30PM
Estimated net benefit of avelumab (AVE) + best supportive care (BSC) vs BSC alone for patients (pts) with advanced urothelial carcinoma (aUC) using a quality-adjusted time without cancer symptoms or toxicity (Q-TWiST) analysis	Powles T	4515	Genitourinary Cancer: Kidney and Bladder Saturday, June 3, 2023 8:00AM-11:00AM Poster Discussion Time: 3:00PM-4:30PM
Real-world response (rwR) rates and clinical outcomes of patients treated with first-line (1L) platinum-based chemotherapy (PBC) for advanced urothelial cancer (aUC)	Moon HH	4567	Genitourinary Cancer—Kidney and Bladder Saturday, June 3, 2023 8:00 AM-11:00 AM
Metastatic Merkel Cell Carcinoma			
Avelumab as second-line or later (2L+) treatment in patients (pts) with metastatic Merkel cell carcinoma (mMCC): analysis of real-world outcomes in France using the CARADERM registry and the French national healthcare database	Blom A	9537	Melanoma/Skin Cancers Saturday, June 3, 2023 1:15PM-4:15PM
Metastatic Colorectal Cancer			
Modified FOLFOXIRI plus cetuximab and avelumab as initial therapy in RAS wild-type unresectable metastatic colorectal cancer: results of the phase II AVETRIC trial by GONO	Conca V	3575	Gastrointestinal Cancer: Colorectal and Anal Monday, June 5, 2023 8:00AM-11:00AM
Xevinapant			

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Phase 3 study of xevinapant plus radiotherapy (RT) for high-risk, cisplatin-ineligible patients with resected, locally advanced squamous cell carcinoma of the head and neck (LA SCCHN)	Ferris RL	TPS6101	Head and Neck Cancer Monday, June 5, 2023 1:15PM-4:15PM
Effect of extended treatment with IAP inhibitor xevinapant post radiotherapy (RT) on efficacy and the tumor microenvironment (TME) in preclinical models	Yeung TL	6027	Head and Neck Cancer Monday, June 5, 2023 1:15PM-4:15PM
TEPMETKO (tepotinib)			
Long-term outcomes of tepotinib in patients with MET exon 14 skipping NSCLC from the VISION study	Paik P	9060	Lung Cancer: Non-Small Cell Metastatic Sunday, June 4, 2023 8:00AM-11:00AM
Tepotinib + osimertinib for EGFR mutant (EGFRm) NSCLC with MET amplification (METamp) after first-line (1L) osimertinib	Tan D	9021	Lung Cancer: Non-Small Cell Metastatic Sunday, June 4, 2023 8:00AM-11:00AM Poster Discussion Time: 4:30PM-6:00PM
Detection of MET amplification (METamp) in patients with EGFR mutant (m) NSCLC after first-line (1L) osimertinib	Yu H	9074	Lung Cancer: Non-Small Cell Metastatic Sunday, June 4, 2023 8:00AM-11:00AM
Patients with EGFR-mutant (m) MET-altered NSCLC receiving tepotinib with an EGFR tyrosine kinase inhibitor (TKI): a case series	Le X	9070	Lung Cancer: Non-Small Cell Metastatic Sunday, June 4, 2023 8:00 AM-11:00 AM

Advancing the Future of Cancer Care

At Merck KGaA, Darmstadt, Germany, we strive every day to improve the futures of people living with cancer. Our research explores the full potential of promising mechanisms in cancer research, focused on synergistic approaches designed to hit cancer at its core. We are determined to maximize the impact of our standard-of-care treatments and to continue pioneering novel medicines. Our vision is to create a world where more cancer patients will become cancer survivors. Learn more at www.emdseronooncology.com.

About BAVENCIO® (avelumab)

BAVENCIO is a human anti-programmed death ligand-1 (PD-L1) antibody. BAVENCIO has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, BAVENCIO has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models. The Merck KGaA, Darmstadt,

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Germany-Pfizer strategic alliance regarding BAVENCIO was mutually terminated, with an effective date of June 30, 2023, with Merck KGaA, Darmstadt, Germany regaining exclusive worldwide rights for BAVENCIO.

BAVENCIO Approved Indications

BAVENCIO® (avelumab) is indicated in the US for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy. BAVENCIO is also indicated for the treatment of patients with locally advanced or metastatic UC who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

BAVENCIO in combination with INLYTA (axitinib) is indicated in the US for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

In the US, the FDA granted accelerated approval for BAVENCIO for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC). This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

BAVENCIO is currently approved for at least one indication for patients in more than 50 countries.

BAVENCIO Important Safety Information from the US FDA-Approved Label

BAVENCIO can cause **severe and fatal immune-mediated adverse reactions** in any organ system or tissue and at any time after starting treatment with a PD-1/PD-L1 blocking antibody, including after discontinuation of treatment.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In

cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

No dose reduction for BAVENCIO is recommended. For immune-mediated adverse reactions, withhold or permanently discontinue BAVENCIO depending on severity. In general, withhold BAVENCIO for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue BAVENCIO for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids. In general, if BAVENCIO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic corticosteroids (eg, endocrinopathies and dermatologic reactions) are discussed in subsequent sections.

BAVENCIO can cause **immune-mediated pneumonitis**, including fatal cases. Monitor patients for signs and symptoms of pneumonitis and evaluate suspected cases with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold BAVENCIO for Grade 2 and permanently discontinue for Grade 3 or Grade 4 pneumonitis. Immune-mediated pneumonitis occurred in 1.2% (21/1738) of patients, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (0.3%) and Grade 2 (0.6%) adverse reactions. Systemic corticosteroids were required in all (21/21) patients with pneumonitis.

BAVENCIO can cause **immune-mediated colitis**. The primary component of immune-mediated colitis consisted of diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider

repeating infectious workup to exclude alternative etiologies. Withhold BAVENCIO for Grade 2 or Grade 3, and permanently discontinue for Grade 4 colitis. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including Grade 3 (0.4%) and Grade 2 (0.7%) adverse reactions. Systemic corticosteroids were required in all (26/26) patients with colitis.

BAVENCIO can cause **hepatotoxicity and immune-mediated hepatitis**. Withhold or permanently discontinue BAVENCIO based on tumor involvement of the liver and severity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin elevation. Immune-mediated hepatitis occurred with BAVENCIO as a single agent in 0.9% (16/1738) of patients, including fatal (0.1%), Grade 3 (0.6%), and Grade 2 (0.1%) adverse reactions. Systemic corticosteroids were required in all (16/16) patients with hepatitis.

> ***BAVENCIO in combination with INLYTA*** can cause **hepatotoxicity** with higher than expected frequencies of Grade 3 and 4 ALT and AST elevation compared to BAVENCIO alone. Consider more frequent monitoring of liver enzymes as compared to when the drugs are used as monotherapy. Withhold or permanently discontinue both BAVENCIO and INLYTA based on severity of AST, ALT, or total bilirubin elevation, and consider administering corticosteroids as needed. Consider rechallenge with BAVENCIO or INLYTA, or sequential rechallenge with both BAVENCIO and INLYTA, after recovery. In patients treated with BAVENCIO in combination with INLYTA in the advanced RCC trials, increased ALT and increased AST were reported in 9% (Grade 3) and 7% (Grade 4) of patients. Immune-mediated hepatitis was reported in 7% of patients including 4.9% with Grade 3 or 4 immune-mediated hepatitis. Thirty-four patients were treated with corticosteroids and one patient was treated with a non-steroidal immunosuppressant.

BAVENCIO can cause primary or secondary **immune-mediated adrenal insufficiency**. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement, as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated adrenal insufficiency occurred in 0.5% (8/1738) of patients, including Grade 3 (0.1%) and

Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in all (8/8) patients with adrenal insufficiency.

BAVENCIO can cause **immune-mediated hypophysitis**. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement, as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated pituitary disorders occurred in 0.1% (1/1738) of patients, which was a Grade 2 (0.1%) adverse reaction.

BAVENCIO can cause **immune-mediated thyroid disorders**. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism, as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Thyroiditis occurred in 0.2% (4/1738) of patients, including Grade 2 (0.1%) adverse reactions. Hyperthyroidism occurred in 0.4% (7/1738) of patients, including Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in 29% (2/7) of patients with hyperthyroidism. Hypothyroidism occurred in 5% (90/1738) of patients, including Grade 3 (0.2%) and Grade 2 (3.7%) adverse reactions. Systemic corticosteroids were required in 7% (6/90) of patients with hypothyroidism.

BAVENCIO can cause **immune-mediated type I diabetes mellitus**, which can present with diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated type I diabetes mellitus occurred in 0.1% (2/1738) of patients, including Grade 3 (0.1%) adverse reactions.

BAVENCIO can cause **immune-mediated nephritis with renal dysfunction**. Withhold BAVENCIO for Grade 2 or Grade 3, and permanently discontinue for Grade 4 increased blood creatinine. Immune-mediated nephritis with renal dysfunction

occurred in 0.1% (1/1738) of patients, which was a Grade 2 (0.1%) adverse reaction. Systemic corticosteroids were required in this patient.

BAVENCIO can cause **immune-mediated dermatologic adverse reactions**, including rash or dermatitis. Exfoliative dermatitis including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold BAVENCIO for suspected and permanently discontinue for confirmed SJS, TEN, or DRESS. Immune-mediated dermatologic adverse reactions occurred in 5% (90/1738) of patients, including Grade 3 (0.1%) and Grade 2 (2.0%) adverse reactions. Systemic corticosteroids were required in 29% (26/90) of patients with dermatologic adverse reactions.

BAVENCIO can result in other **immune-mediated adverse reactions**. Other clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in patients who received BAVENCIO or were reported with the use of other PD-1/PD-L1 blocking antibodies. For myocarditis, permanently discontinue BAVENCIO for Grade 2, Grade 3, or Grade 4. For neurological toxicities, withhold BAVENCIO for Grade 2 and permanently discontinue for Grade 3 or Grade 4.

BAVENCIO can cause **severe or life-threatening infusion-related reactions**. Premedicate patients with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent infusions based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 infusion-related reactions. Permanently discontinue BAVENCIO for Grade 3 or Grade 4 infusion-related reactions. Infusion-related reactions occurred in 25% of patients, including three (0.2%) Grade 4 and nine (0.5%) Grade 3 infusion-related reactions. Eleven (92%) of the 12 patients with Grade ≥3 reactions were treated with intravenous corticosteroids.

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Fatal and other serious **complications of allogeneic hematopoietic stem cell transplantation (HSCT)** can occur in patients who receive HSCT before or after being treated with a PD-1/PD-L1 blocking antibody. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

BAVENCIO **in combination with INLYTA** can cause **major adverse cardiovascular events (MACE)** including severe and fatal events. Consider baseline and periodic evaluations of left ventricular ejection fraction. Monitor for signs and symptoms of cardiovascular events. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Permanently discontinue BAVENCIO and INLYTA for Grade 3-4 cardiovascular events. MACE occurred in 7% of patients with advanced RCC treated with BAVENCIO in combination with INLYTA compared to 3.4% treated with sunitinib in a randomized trial. These events included death due to cardiac events (1.4%), Grade 3-4 myocardial infarction (2.8%), and Grade 3-4 congestive heart failure (1.8%).

BAVENCIO can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing potential to use effective contraception during treatment with BAVENCIO and for at least 1 month after the last dose of BAVENCIO. It is not known whether BAVENCIO is excreted in human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

The most common adverse reactions (all grades, ≥20%) in patients with **metastatic Merkel cell carcinoma (MCC)** were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reaction (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

Selected treatment-emergent laboratory abnormalities (all grades, ≥20%) in patients with **metastatic MCC** were lymphopenia (49%), anemia (35%), increased aspartate aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

A **fatal adverse reaction** (sepsis) occurred in one (0.3%) patient with **locally advanced or metastatic urothelial carcinoma (UC)** receiving BAVENCIO + best supportive care (BSC) as first-line maintenance treatment. In patients with previously treated locally advanced or metastatic UC, fourteen patients (6%) who were treated with BAVENCIO experienced either pneumonitis, respiratory failure, sepsis/urosepsis, cerebrovascular accident, or gastrointestinal adverse events, which led to death.

The most common adverse reactions (all grades, ≥20%) in patients with **locally advanced or metastatic UC** receiving BAVENCIO + BSC (vs BSC alone) as first-line maintenance treatment were fatigue (35% vs 13%), musculoskeletal pain (24% vs 15%), urinary tract infection (20% vs 11%), and rash (20% vs 2.3%). In patients with previously treated locally advanced or metastatic UC receiving BAVENCIO, the most common adverse reactions (all grades, ≥20%) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

Selected laboratory abnormalities (all grades, ≥20%) in patients with **locally advanced or metastatic UC** receiving BAVENCIO + BSC (vs BSC alone) as first-line maintenance treatment were blood triglycerides increased (34% vs 28%), alkaline phosphatase increased (30% vs 20%), blood sodium decreased (28% vs 20%), lipase increased (25% vs 16%), aspartate aminotransferase (AST) increased (24% vs 12%), blood potassium increased (24% vs 16%), alanine aminotransferase (ALT) increased (24% vs 12%), blood cholesterol increased (22% vs 16%), serum amylase increased (21% vs 12%), hemoglobin decreased (28% vs 18%), and white blood cell decreased (20% vs 10%).

Fatal adverse reactions occurred in 1.8% of patients with **advanced renal cell carcinoma (RCC)** receiving BAVENCIO in combination with INLYTA. These included sudden cardiac death (1.2%), stroke (0.2%), myocarditis (0.2%), and necrotizing pancreatitis (0.2%).

The **most common adverse reactions** (all grades, ≥20%) in patients with **advanced RCC** receiving BAVENCIO in combination with INLYTA (vs sunitinib) were

diarrhea (62% vs 48%), fatigue (53% vs 54%), hypertension (50% vs 36%), musculoskeletal pain (40% vs 33%), nausea (34% vs 39%), mucositis (34% vs 35%), palmar-plantar erythrodysesthesia (33% vs 34%), dysphonia (31% vs 3.2%), decreased appetite (26% vs 29%), hypothyroidism (25% vs 14%), rash (25% vs 16%), hepatotoxicity (24% vs 18%), cough (23% vs 19%), dyspnea (23% vs 16%), abdominal pain (22% vs 19%), and headache (21% vs 16%).

Selected laboratory abnormalities (all grades, ≥20%) worsening from baseline in patients with **advanced RCC** receiving BAVENCIO in combination with INLYTA (vs sunitinib) were blood triglycerides increased (71% vs 48%), blood creatinine increased (62% vs 68%), blood cholesterol increased (57% vs 22%), alanine aminotransferase increased (ALT) (50% vs 46%), aspartate aminotransferase increased (AST) (47% vs 57%), blood sodium decreased (38% vs 37%), lipase increased (37% vs 25%), blood potassium increased (35% vs 28%), platelet count decreased (27% vs 80%), blood bilirubin increased (21% vs 23%), and hemoglobin decreased (21% vs 65%).

Please see full US Prescribing Information and Medication Guide available at http://www.BAVENCIO.com.

About TEPMETKO® (tepotinib)

TEPMETKO is a once-daily oral MET inhibitor that inhibits the oncogenic MET receptor signaling caused by *MET* (gene) alterations. Discovered and developed in-house at Merck KGaA, Darmstadt, Germany, TEPMETKO has a highly selective mechanism of action, with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations.

TEPMETKO was the first oral MET inhibitor to receive a regulatory approval anywhere in the world for the treatment of advanced NSCLC harboring *MET* gene alterations, with its approval in Japan in March 2020. In February 2021, the US Food and Drug Administration granted accelerated approval to TEPMETKO, making it the first and only once-daily oral MET inhibitor approved for patients in the US with metastatic NSCLC with *MET*ex14-skipping alterations. In February 2022, the European Commission (EC) approved once-daily oral TEPMETKO as monotherapy for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC)

harboring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (*MET*ex14) skipping, who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.

TEPMETKO is available in a number of countries. To meet an urgent clinical need, TEPMETKO is also available in a pilot zone of China in line with the government policy to drive early access for innovative medicines approved outside of China.

Merck KGaA, Darmstadt, Germany is also investigating the potential role of tepotinib in treating patients with NSCLC and acquired resistance due to *MET* amplification in the Phase II INSIGHT 2 study of tepotinib in combination with osimertinib in *MET* amplified, advanced or metastatic NSCLC harboring activating EGFR mutations that has progressed following first-line treatment with osimertinib.

TEPMETKO Approved Indication in the US

TEPMETKO is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal epithelial transition (MET) exon 14 skipping alterations. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Important Safety Information from the US FDA-Approved Label

TEPMETKO can cause **interstitial lung disease (ILD)/pneumonitis**, which can be fatal. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold TEPMETKO in patients with suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified. ILD/pneumonitis occurred in 2.2% of patients treated with TEPMETKO, with one patient experiencing a Grade 3 or higher event; this event resulted in death.

TEPMETKO can cause **hepatotoxicity**, which can be fatal. Monitor liver function tests (including ALT, AST, and total bilirubin) prior to the start of TEPMETKO, every 2 weeks during the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop increased

transaminases or total bilirubin. Based on the severity of the adverse reaction, withhold, dose reduce, or permanently discontinue TEPMETKO. Increased alanine aminotransferase (ALT)/increased aspartate aminotransferase (AST) occurred in 13% of patients treated with TEPMETKO. Grade 3 or 4 increased ALT/AST occurred in 4.2% of patients. A fatal adverse reaction of hepatic failure occurred in one patient (0.2%). The median time-to-onset of Grade 3 or higher increased ALT/AST was 30 days (range 1 to 178).

TEPMETKO can cause **embryo-fetal toxicity**. Based on findings in animal studies and its mechanism of action, TEPMETKO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential or males with female partners of reproductive potential to use effective contraception during treatment with TEPMETKO and for one week after the final dose.

Avoid concomitant use of TEPMETKO with dual strong **CYP3A inhibitors** and **P-gp inhibitors** and strong **CYP3A inducers**. Avoid concomitant use of TEPMETKO with certain **P-gp substrates** where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, reduce the P-gp substrate dosage if recommended in its approved product labeling.

Fatal adverse reactions occurred in one patient (0.4%) due to pneumonitis, one patient (0.4%) due to hepatic failure, and one patient (0.4%) due to dyspnea from fluid overload.

Serious adverse reactions occurred in 45% of patients who received TEPMETKO. Serious adverse reactions in >2% of patients included pleural effusion (7%), pneumonia (5%), edema (3.9%), dyspnea (3.9%), general health deterioration (3.5%), pulmonary embolism (2%), and musculoskeletal pain (2%).

The most common adverse reactions (≥20%) in patients who received TEPMETKO were edema, fatigue, nausea, diarrhea, musculoskeletal pain, and dyspnea.

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Clinically relevant adverse reactions in <10% of patients who received TEPMETKO included ILD/pneumonitis, rash, fever, dizziness, pruritus, and headache.

Selected laboratory abnormalities (≥20%) from baseline in patients receiving TEPMETKO in descending order were: decreased albumin (76%), increased creatinine (55%), increased alkaline phosphatase (ALP) (50%), decreased lymphocytes (48%), increased alanine aminotransferase (ALT) (44%), increased aspartate aminotransferase (AST) (35%), decreased sodium (31%), decreased hemoglobin (27%), increased potassium (25%), increased gamma-glutamyltransferase (GGT) (24%), increased amylase (23%), and decreased leukocytes (23%).

The most common Grade 3 to 4 laboratory abnormalities (≥2%) in descending order were: decreased lymphocytes (11%), decreased albumin (9%), decreased sodium (8%), increased GGT (5%), increased amylase (4.6%), increased ALT (4.1%), increased AST (2.5%), and decreased hemoglobin (2%).

A clinically relevant laboratory abnormality in <20% of patients who received TEPMETKO was increased lipase in 18% of patients, including 3.7% Grades 3 to 4.

For more information about TEPMETKO, please see full Prescribing Information, and visit www.TEPMETKO.com.

About Xevinapant

Xevinapant (formerly known as Debio 1143) is an investigational first-in-class potent oral small-molecule IAP (inhibitor of apoptosis protein) inhibitor for the treatment of LA SCCHN. In preclinical studies, xevinapant restored sensitivity to apoptosis in cancer cells, thereby enhancing the effects of chemotherapy and radiotherapy. Xevinapant, the most clinically advanced IAP inhibitor, improved efficacy outcomes in combination with chemoradiotherapy (CRT), including three-year progression-free survival and five-year survival, compared with placebo plus CRT in a Phase II study in patients with unresected locally advanced squamous cell carcinoma of the head and neck (LA SCCHN). In March 2021, Merck KGaA, Darmstadt, Germany, gained exclusive rights from Debiopharm to develop and

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commercialize xevinapant worldwide. Xevinapant is not approved for any use anywhere in the world.

All Merck KGaA, Darmstadt, Germany, press releases are distributed by e-mail at the same time they become available on the EMD Group website. In case you are a resident of the USA or Canada, please go to www.emdgroup.com/subscribe to register for your online, change your selection or discontinue this service.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. More than 64,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From providing products and services that accelerate drug development and manufacturing as well as discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2022, Merck KGaA, Darmstadt, Germany, generated sales of € 22.2 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany, operate as MilliporeSigma in life science, EMD Serono in healthcare and EMD Electronics in electronics. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.