News Release

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Not intended for UK-based media

Merck KGaA, Darmstadt, Germany, to Showcase Advances in the Science of Cancer With New Data Presented at ASCO 2024

- **First-in-human data for potential first-in-class anti-CEACAM5 ADC with topoisomerase 1 inhibitor payload, M9140, in treatment of metastatic colorectal cancer to be featured in oral presentation**
- **Phase I data for tuvusertib, lead asset from the company's unique portfolio of DDR inhibitors, including an oral presentation on the combination with a PARP inhibitor, support further clinical development**
- **New analyses contribute to totality of evidence supporting BAVENCIO first-line maintenance as a standard-of-care in advanced bladder cancer**

Darmstadt, Germany, May 23, 2024 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced new research from the company's diverse oncology portfolio will be presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting, May 31 to June 4, Chicago. Data from company- and investigator-sponsored studies include 31 accepted abstracts across more than 10 tumor types, including seven oral presentations, highlighting the company's innovative oncology pipeline encompassing potential first-in-class approaches designed to hit cancer at its core.

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"Our research at the 2024 ASCO Annual Meeting showcases the advancement of our novel pipeline designed to exploit the major vulnerabilities of cancer, with new data from our lead investigational antibody-drug conjugate and our DNA damage response portfolio," said Victoria Zazulina, M.D., Head of Development Unit, Oncology, for the Healthcare business of Merck KGaA, Darmstadt, Germany. "In addition, new analyses from pivotal studies and collaborations underline our determination to maximize the impact of our standard-of-care treatments as we seek to improve the lives of those living with cancer."

Highlights of the company's data include:

First-in-human data for the antibody-drug conjugate (ADC) M9140 (Abstract 3000). This Phase I trial is investigating the safety, tolerability, pharmacokinetics (PK), and preliminary clinical activity of M9140, the company's investigational ADC against carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5) with a novel exatecan payload, in heavily pretreated patients with metastatic colorectal cancer. Data from 40 patients treated across seven dose levels in Part 1A of the study showed encouraging clinical activity and a manageable and predictable safety profile in this population. The randomized dose-expansion part of the study is ongoing.

New findings for tuvusertib, the lead oral ATRi asset from the company's portfolio of DNA damage response (DDR) inhibitors (Abstracts 3018, 2612, 2614). Data from the DDRiver™ Clinical Trials program highlight the potential of the investigational oral ataxia telangiectasia and RAD3-related inhibitor (ATRi) tuvusertib in various combinations across solid tumors.

- Part B1 of the Phase I DDRiver Solid Tumors 301 study assessed safety as well as PK, pharmacodynamics, and preliminary efficacy of different dosing regimens of tuvusertib in combination with the poly-ADP ribose polymerase (PARP) inhibitor niraparib in patients with locally advanced or metastatic unresectable solid tumors refractory to standard treatment. Data show a manageable safety profile and preliminary efficacy in patients with advanced solid tumors, confirming suitability of this combination for further evaluation.
- Presentations from the Phase Ib DDRiver Solid Tumors 320 study showcase further data on the combination of tuvusertib with the company's ataxia

telangiectasia-mutated (ATM) inhibitor lartesertib, building on the safety and efficacy data presented at the AACR Annual Meeting in April 2024, and for the first time, with the company's immune checkpoint inhibitor BAVENCIO® (avelumab). The findings further support that both DDRi assets are well-positioned for combination development building on in-house expertise.

Post-hoc independent read confirmation of Phase II efficacy data for xevinapant (Abstract e18039). A previously published Phase II study of the investigational oral IAP (inhibitor of apoptosis protein) inhibitor xevinapant plus chemoradiotherapy (CRT) versus placebo plus CRT in patients with unresected locally advanced squamous cell carcinoma of the head and neck (LA SCCHN) showed improved efficacy outcomes. This post-hoc analysis showed consistent outcomes when comparing the review of selected efficacy endpoints by blinded independent review committee (BIRC) with previously reported outcomes by investigator review. Xevinapant plus CRT demonstrated a 62% reduction in the risk of disease progression (by BIRC) or death compared with placebo plus CRT, with prolonged duration of response and increased complete response rates.

Long-term efficacy and safety analyses from JAVELIN Bladder 100 (Abstracts 4566, 4567). New analyses of this Phase III study, which has previously shown in a post-hoc exploratory analysis a median overall survival of 29.7 months in patients who received BAVENCIO plus best supportive care (BSC) as measured from the start of first-line chemotherapy, confirm the benefit of BAVENCIO first-line maintenance in key subgroups of patients with advanced urothelial carcinoma that has not progressed on platinum-based chemotherapy, including those who have low tumor burden and in those with mixed histologic subtypes. These findings further support the use of the JAVELIN Bladder regimen as a standard of care in this setting and as an important first-line treatment regimen for patients with low tumor burden in particular, where pronounced efficacy with BAVENCIO (vs BSC alone) was observed.

Health-related quality-of-life data for TEPMETKO® (tepotinib) in NSCLC (Abstract 8575). This analysis reports health-related quality of life (HRQoL) outcomes from the Phase II VISION study of TEPMETKO in patients with metastatic non-small cell lung cancer (NSCLC) harboring *MET*ex14 skipping alterations with

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brain, liver, adrenal or bone metastases. These patients experienced stable HRQoL during treatment with TEPMETKO, with trends for improvement in cough, consistent with results for the overall population.

Additional company-sponsored activity at ASCO:

Medical Evening Lecture

What's new in LA SCCHN? An evasive enemy and an evolving landscape

Faculty: Kevin Harrington (chair), Institute of Cancer Research, UK; Ari Rosenberg, University of Chicago Medicine, USA; Jonathan Schoenfeld, Dana-Farber Cancer Institute, USA; Sue Yom, University of California, San Francisco, USA

June 2, 2024, 7:00PM-8:00PM CDT

W Chicago City Center hotel (172 West Adams Street), Great Room I

Select Merck KGaA, Darmstadt, Germany-related abstracts accepted for the ASCO 2024 Annual Meeting include (all times in CDT):

Title	Lead Author	Abstract	Session Information
M9140			
First-in-human trial of M9140, an anti-CEACAM5 antibody-drug conjugate (ADC) with exatecan payload, in patients with metastatic colorectal cancer.	Kopetz, S	3000	**Session Title:** Developmental Therapeutics—Molecularly Targeted Agents and Tumor Biology, HALL D1 **Date:** Saturday June 1, 2024 **Session Time:** 3:00-6:00PM **Presentation Time:** 3:00-3:06PM **Location:** Hall D1
DDRi			
A phase I study of highly potent oral ATR inhibitor tuvusertib plus oral PARP inhibitor niraparib in patients with solid tumors.	Yap, T	3018	**Session Title:** Developmental Therapeutics—Molecularly Targeted Agents and Tumor Biology **Date:** Monday June 3, 2024 **Session Time:** 8:00 -9:30AM **Presentation Time:** 9:00-9:12AM **Location:** S406
Pharmacodynamic and immunophenotyping analyses of ATR inhibitor tuvusertib + ATM inhibitor lartesertib in a phase Ib study in patients with advanced unresectable solid tumors.	Boni, V	2612	**Session Title:** Developmental Therapeutics—Immunotherapy **Date:** Saturday June 1, 2024 **Session Time:** 9:00AM-12:00PM **Location:** Hall A
Pharmacokinetic and pharmacodynamic findings from a phase 1b study of ATR inhibitor tuvusertib + anti-PD-L1 avelumab in patients with advanced unresectable solid tumors.	Tolcher, A	2614	**Session Title:** Developmental Therapeutics—Immunotherapy **Date:** Saturday June 1, 2024 **Session Time:** 9:00AM-12:00PM **Location:** Hall A
Xevinapant			
Phase 2 study of xevinapant + chemoradiotherapy (CRT) vs placebo + CRT in patients with unresected locally advanced squamous cell carcinoma of the head and neck: A post hoc activity analysis by blinded	Bourhis, J	e18039	Accepted for e-publication

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independent review committee evaluation.			
Xevinapant with radiation and concurrent carboplatin and paclitaxel in patients ineligible for cisplatin with locoregionally advanced squamous cell carcinoma of the head and neck (The EXtRaCT study)	Mir, NA	TPS6126	**Session Title**: Head and Neck Cancer **Date:** Sunday June 2, 2024 **Session Time:** 9:00AM-12:00PM **Location:** Hall A
BAVENCIO (avelumab)			
Avelumab first-line maintenance for advanced urothelial carcinoma: Long-term outcomes from JAVELIN Bladder 100 in patients with low tumor burden.	Bellmunt, J	4566	**Session Title:** Genitourinary Cancer—Kidney and Bladder **Date:** Sunday June 2, 2024 **Session Time:** 9:00AM-12:00PM **Location:** Hall A
Avelumab first-line maintenance for advanced urothelial carcinoma: Long-term outcomes from the JAVELIN Bladder 100 trial in patients with histological subtypes.	Loriot, Y	4567	**Session Title:** Genitourinary Cancer—Kidney and Bladder **Date:** Sunday June 2, 2024 **Session Time:** 9:00AM-12:00PM **Location:** Hall A
Avelumab + axitinib vs sunitinib in patients with advanced renal cell carcinoma: Final overall survival (OS) analysis from the JAVELIN Renal 101 phase 3 trial.	Motzer, R	4508	**Session Title:** Genitourinary Cancer—Kidney and Bladder **Date:** Monday June 3, 2024 **Session Time:** 8:00-11:00AM **Presentation Time:** 10:12-10:24AM **Location:** Hall B1
TEPMETKO (tepotinib)			
Health-related quality of life with tepotinib in patients with MET exon 14 (METex14) skipping non-small cell lung cancer with brain, liver, adrenal, or bone metastases in the phase II VISION trial.	Reinmuth, N	8575	**Session Title:** Lung Cancer—Non-Small Cell Metastatic **Date:** Monday June 3, 2024 **Session Time:** 1:30 -4:30PM **Location:** Hall A

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 M9140

M9140 is an investigational anti-CEACAM5 antibody-drug conjugate (ADC). Leveraging the company's novel linker-payload technology, M9140 is the first CEACAM5 ADC with an exatecan payload, a potent topoisomerase inhibitor (TOP1i), which has been rationally designed for stability in circulation and superior cancer cell killing activity. Beyond the direct effect on the target cell, M9140 has been shown in preclinical research to induce tumor cell death through a bystander effect permeating the cell membrane to neighboring cells, inducing apoptosis (cell death).

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This bystander effect within the tumor microenvironment may enhance efficacy, particularly in tumors with heterogenous CEACAM5 expression. M9140 is currently being investigated in advanced solid tumors in a first-in-human, Phase I dose-escalation clinical trial (NCT05464030).

About Tuvusertib

Tuvusertib (M1774), is the lead asset in the company's portfolio of DNA damage response inhibitors. Tuvusertib is an investigational, potentially best-in-class small-molecule oral inhibitor of the ataxia telangiectasia and Rad3-related (ATR) kinase, which serves as a major regulator of the replication stress response. Early clinical data for tuvusertib have shown potency, selectivity, and the potential to achieve high therapeutic doses without rate-limiting side effects. The company's DDRiver™ Clinical Trial Program is exploring the potential of tuvusertib as a backbone therapy in a variety of combinations with other DDR inhibitors, immune checkpoint inhibitors, or cytotoxic agents, touching on multiple clinical hypotheses across several types of cancer.

About Xevinapant

Xevinapant (formerly known as Debio 1143) is an investigational first-in-class potent oral small-molecule IAP (inhibitor of apoptosis protein) inhibitor developed for the treatment of LA SCCHN, with a proposed dual mechanism of action: xevinapant releases the brakes on apoptosis and increases anti-tumor immunity, re-initiating the programmed cell death of tumor cells. Via this dual mechanism, xevinapant is thought to enhance the effects of chemo- and radiotherapy. Xevinapant has demonstrated improved efficacy outcomes in combination with chemoradiotherapy (CRT), including 18-month locoregional control, three-year progression-free survival and five-year survival, compared with placebo plus CRT in a Phase II study in patients with unresected LA SCCHN. Xevinapant is being studied in two Phase III studies: TrilynX™, in patients with unresected LA SCCHN, and XRay Vision™, in patients with resected LA SCCHN who are at a high risk of recurrence and who are deemed cisplatin-ineligible. In March 2021, Merck KGaA, Darmstadt, Germany, gained exclusive rights from Debiopharm to develop and commercialize xevinapant worldwide. Xevinapant is not approved for any use anywhere in the world.

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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.

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

In the US, BAVENCIO is indicated for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC).

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 axitinib*** 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 axitinib based on severity of AST, ALT, or total bilirubin elevation, and consider administering corticosteroids as needed. Consider rechallenge with BAVENCIO or axitinib, or sequential rechallenge with both BAVENCIO and axitinib, after recovery. In patients treated with BAVENCIO in combination with axitinib 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 axitinib** 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 axitinib for Grade 3-4 cardiovascular events. MACE occurred in 7% of patients with advanced RCC treated with BAVENCIO in combination with axitinib 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 axitinib. 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 axitinib (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 axitinib (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 is the first oral MET inhibitor to have received a regulatory approval anywhere in the world for the treatment of advanced non-small cell lung cancer (NSCLC) harboring *MET* gene alterations, with its approval in Japan in March 2020. In February 2022, the European Commission (EC) approved once-daily oral TEPMETKO as monotherapy for the treatment of adult patients with advanced 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. In February

2024, the US Food and Drug Administration granted full approval for TEPMETKO. The conversion from accelerated approval, which the company received in February 2021, to full FDA approval is based on additional data from the ongoing Phase II VISION study, the largest trial of its kind. The updated label includes revised data for overall response rate and duration of response, as well as safety outcomes for more than 300 patients who were treated with TEPMETKO once-daily for metastatic NSCLC with *MET*ex14 skipping alterations.

TEPMETKO has been granted market authorization in a number of countries/regions and is marketed in 30+ countries (including 'named patient use' programs). Submissions and reviews of applications to medical authorities in other regions are ongoing.

TEPMETKO Approved Indications

TEPMETKO is indicated in the US for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (*MET*) exon 14 skipping alterations.

TEPMETKO Important Safety Information From the 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% 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 alanine aminotransferase [ALT], aspartate aminotransferase [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 ALT/increased AST occurred in 18% of patients treated with TEPMETKO. Grade 3 or 4 increased ALT/AST occurred in

4.7% 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 47 days (range 1 to 262).

TEPMETKO can cause **pancreatic toxicity** in the form of elevations in amylase and lipase levels. Increased amylase and/or lipase occurred in 13% of patients, with Grade 3 and 4 increases occurring in 5% and 1.2% of patients, respectively. Monitor amylase and lipase levels at baseline and regularly during treatment with TEPMETKO and temporarily withhold, dose reduce, or permanently discontinue based on severity of the adverse event.

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 last dose.

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 (0.3%) due to pneumonitis, one patient (0.3%) due to hepatic failure, one patient (0.3%) due to dyspnea from fluid overload, one patient (0.3%) due to pneumonia, one patient (0.3%) due to sepsis, and one patient (0.3%) from unknown cause.
Serious adverse reactions occurred in 51% of patients who received TEPMETKO. Serious adverse reactions in >2% of patients included pleural effusion (6%), pneumonia (6%), edema (5%), general health deterioration (3.8%), dyspnea (3.5%), musculoskeletal pain (2.9%), and pulmonary embolism (2.2%).

The most common adverse reactions (≥20%) in patients who received TEPMETKO were edema (81%), nausea (31%), fatigue (30%), musculoskeletal pain

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(30%), diarrhea (29%), dyspnea (24%), rash (21%), and decreased appetite (21%).

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

Selected laboratory abnormalities (≥20%) from baseline in patients receiving TEPMETKO in descending order were: decreased albumin (81%), increased creatinine (60%), decreased lymphocytes (57%), increased alkaline phosphatase (ALP) (52%), increased ALT (50%), increased AST (40%), decreased sodium (36%), decreased hemoglobin (31%), increased gamma-glutamyltransferase (GGT) (29%), increased potassium (26%), increased amylase (25%), decreased leukocytes (25%), decreased platelets (24%), and increased lipase (21%).

The most common Grade 3-4 laboratory abnormalities (≥2%) in descending order were: decreased lymphocytes (15%), decreased albumin (9%), decreased sodium (9%), increased GGT (6%), increased amylase (5%), increased lipase (5%), increased ALT (4.9%), increased AST (3.6%), and decreased hemoglobin (3.6%).
Please see the full US Prescribing Information for TEPMETKO.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. Around 63,000 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 2023, Merck KGaA, Darmstadt, Germany, generated sales of € 21 billion in 65 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.