News Release

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Data from Merck KGaA, Darmstadt, Germany's Oncology Portfolio Highlight Significant Advances in Cancer Care at ASCO21

- **New analyses from pivotal BAVENCIO® study reinforce unique clinical benefits across different subgroups in the treatment of advanced urothelial carcinoma**
- **New data from VISION study of TEPMETKO® show association between liquid biopsy-identified biomarker and clinical response in *MET*ex14 skipping NSCLC, supporting liquid biopsy as a means for monitoring treatment response**
- **TEPMETKO® shows efficacy in *MET*ex14 skipping NSCLC patients with brain metastases consistent with overall treatment population**

Darmstadt, Germany, May 19, 2021 – Merck KGaA, Darmstadt, Germany, a leading science and technology company today announced 40 abstracts, including seven oral presentations and seven poster discussions, from Company- and investigator-sponsored studies (ISS) and external collaborations, representing the Company's innovative oncology portfolio will be presented at this year's American Society of Clinical Oncology (ASCO) Annual Meeting, June 4-8, 2021.

"Important new analyses from our pivotal studies in urothelial cancer and non-small cell lung cancer, which have led to recent regulatory approvals for BAVENCIO® (avelumab) and TEPMETKO® (tepotinib) in these tumor types, demonstrate how our research continues to drive forward new standards of care in certain cancers with

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high unmet medical need," said Danny Bar-Zohar, Global Head of Development for the Healthcare business of Merck KGaA, Darmstadt, Germany. "These analyses, along with additional data informing the understanding of new and emerging mechanisms under investigation, are the latest examples of our dedication to advancing the science of cancer treatment to make a meaningful difference for patients."

The Company's research programs, focused on synergistic approaches in immuno-oncology, oncogenic pathways, and DNA damage response (DDR), aim to tackle some of the most challenging tumor types, including urothelial cancer (UC), non-small cell lung cancer (NSCLC), renal cell carcinoma (RCC), colorectal cancer (CRC), and cervical cancer (CC).

Key Data Highlights at ASCO

BAVENCIO (avelumab)

Data across three approved indications for BAVENCIO (avelumab) provide further evidence of continued patient benefit:

- **Advanced urothelial cancer** (presentations: 4520, 4525, 4527). New analyses from the Phase III JAVELIN Bladder 100 study demonstrated consistent survival benefit of BAVENCIO (avelumab) as first-line maintenance treatment across key subgroups including those defined by the treatment-free interval from the end of chemotherapy to the start of maintenance, disease stage, site of metastasis, or genomic subtype. These data further reinforce the role of BAVENCIO for patients with advanced UC that have not progressed on 1L platinum-containing chemotherapy.

- **Advanced renal cell carcinoma (aRCC)** (presentations: 4514, 4574). Data from the extended follow-up of the Phase III JAVELIN Renal 101 study explored the effects of subsequent therapies on outcomes for patients with aRCC treated with BAVENCIO (avelumab) plus axitinib and confirmed the efficacy benefits of the combination across International Metastatic RCC Data Consortium (IMDC) risk groups including in the favorable risk group.

- **Metastatic Merkel cell carcinoma (mMCC)** (presentation: 9517). In previously treated patients with metastatic MCC (mMCC), treatment with BAVENCIO (avelumab) provided meaningful long-term overall survival (OS),

based on more than five years of follow-up in Part A of the Phase II JAVELIN Merkel 200 study with 48- and 60-month OS rates 30% (95% CI, 20%-40%) and 26% (95% CI, 17%-36%), respectively. These results further support the role of avelumab as a standard-of-care treatment for patients with mMCC.

TEPMETKO (tepotinib)

ASCO highlights for TEPMETKO (tepotinib) include new data from the Phase II VISION study:

- ***MET*ex14 NSCLC biomarker response detected in liquid biopsy (LBx) abstract** (oral presentation: 9012). In this analysis, reduction in variant allele frequency following tepotinib treatment was related to an improved treatment outcome. Further, this investigation provides evidence that liquid biopsy may provide a reliable means for monitoring response to treatment, understanding resistance mechanisms, and improving patient outcomes and quality of life.

- ***MET*ex14 skipping NSCLC with brain metastases** (presentation: 9084). Data demonstrated efficacy in patients with mesenchymal epithelial transition (*MET)* exon *14 (MET*ex14) skipping NSCLC with brain metastases consistent with the overall treatment population, complemented by intracranial activity in an ad hoc retrospective analysis of brain lesions determined by CT/MRI. Brain metastases are reported in 20% to 40% of patients with *MET*ex14 skipping NSCLC and are associated with poor prognosis.

- **NSCLC with *MET* amplification (*MET*amp)** (presentation: 9021). Clinical activity observed in VISION Cohort B, the first study of a MET inhibitor in people with NSCLC with *MET*amp prospectively detected by liquid biopsy, showed the potential of tepotinib to target *MET*amp-driven disease, particularly in the treatment-naïve setting where there is high unmet need. *MET* amplification is a genetic alteration occurring in approximately 1% to 5% of patients with NSCLC and has no approved targeted therapies.

Tepotinib is also being investigated in two ongoing studies, which are currently recruiting patients: INSIGHT 2 (Presentation: TPS9136), assessing the combination of osimertinib and tepotinib in patients with epithelial growth factor receptor (EGFR)-mutant NSCLC that has developed resistance to first-line osimertinib

treatment due to *MET* amplification; and PERSPECTIVE (Presentation: TPS3616), evaluating tepotinib in combination with cetuximab in mCRC having acquired resistance to anti-EGFR antibody-targeted therapy due to *MET* amplification.

Bintrafusp alfa (M7824)

Data for bintrafusp alfa, an investigational bifunctional fusion protein, continue to shed light on the potential benefits of dual inhibition of the TGF-β and PD-L1 pathways:

- **Recurrent/metastatic cervical cancer** (oral presentation: 5509). A pooled analysis of data from the Phase I **INTR@PID Solid Tumor 001** study and a National Cancer Institute (NCI)-led Phase II study demonstrated that bintrafusp alfa monotherapy has a manageable safety profile and clinical activity in patients with platinum-pretreated, immune checkpoint inhibitor-naïve recurrent/metastatic cervical cancer.

- **HPV 16+ advanced malignancies** (oral presentation: 2501). Data from this NCI-led Phase II clinical study of patients with advanced HPV 16+ cancers provided early evidence of the clinical activity of a triple combination of bintrafusp alfa, NHS-IL12 and PDS0101, with a manageable safety profile.

Merck KGaA, Darmstadt, Germany is a science-led organization dedicated to delivering transformative medicines with the goal of making a meaningful difference in the lives of people affected by cancer. Our oncology research efforts aim to leverage our synergistic portfolio in oncogenic pathways, immuno-oncology, and DNA Damage Response (DDR) to tackle challenging tumor types in gastrointestinal, genitourinary, and thoracic cancers. Our curiosity drives our pursuit of treatments for even the most complex cancers, as we work to illuminate a path to scientific breakthroughs that transform patient outcomes. 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. In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

BAVENCIO 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, 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 patients in 50 countries for at least one use.

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 (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 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 an 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. TEPMETKO was approved in the United States in February 2021 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. Tepotinib is currently under clinical investigation and not yet approved in any markets outside of Japan and the United States.

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.

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.

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

About Bintrafusp Alfa
Bintrafusp alfa (M7824), discovered in-house at Merck KGaA, Darmstadt, Germany, and currently in clinical development through a strategic alliance with GSK, is a potential first-in-class investigational bifunctional fusion protein designed to simultaneously block two immunosuppressive pathways, TGF-β and PD-L1, within the tumor microenvironment. This bifunctional approach is thought to control tumor growth by potentially restoring and enhancing anti-tumor responses. In preclinical studies, bintrafusp alfa has demonstrated antitumor activity both as monotherapy and in combination with chemotherapy. Based on its mechanism of action, bintrafusp alfa offers a potential targeted approach to addressing the underlying pathophysiology of difficult-to-treat cancers.

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About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and electronics. Around 58,000 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 advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2020, Merck KGaA, Darmstadt, Germany, generated sales of € 17.5 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 EMD Serono in healthcare, MilliporeSigma in life science, and EMD 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.