News Release

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Not intended for UK-based media

Breakthrough Innovation in Cancer Care From Merck KGaA, Darmstadt, Germany, Pipeline to Be Presented at ASCO 2020

- **Results from two studies of BAVENCIO® to be featured in ASCO press briefing**
- **Primary efficacy, biomarker and HRQoL analyses for tepotinib†, the first MET inhibitor to have received a regulatory approval for NSCLC with *MET* gene alterations**
- **Two-year follow-up for first-in-class bifunctional immunotherapy bintrafusp alfa‡ targeting TGF-β/PD-L1, in second-line NSCLC**

Darmstadt, Germany, May 13, 2020 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced data for its innovative investigational agents and investigational uses of marketed medicines to be presented at the American Society of Clinical Oncology (ASCO) ASCO20 Virtual Scientific Program, to be held virtually from May 29-31.

This year ASCO will be highlighting—during its embargoed presscast on Tuesday, May 26 and at the plenary session on Sunday, May 31—the Phase III JAVELIN Bladder 100 study (Abstract# LBA1) of BAVENCIO® (avelumab) in the first-line maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC)*. Additional data will be presented for early- to late-stage molecules discovered and developed in-house that demonstrate the Company's commitment and relentless drive to discover, develop and deliver innovative treatment options in its hope to turn cancer patients into cancer survivors. Research from several investigator-sponsored and collaborative research studies also will be shared. This

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includes a late-breaking oral presentation of results of the investigator-sponsored, multicenter Phase II TROPHIMMUN study of avelumab for the treatment of chemotherapy-resistant gestational trophoblastic tumors (Cohort A), which also will be featured in the ASCO press program (Abstract# LBA6008).

"Despite the many advances in cancer treatment, we have an urgency to continue to discover and develop innovative treatment options that will have a major impact on the lives of people living with cancer," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "Taking on this challenge, we've applied our deep knowledge of cancer biology to highly focused areas to develop the first-in-class oral MET inhibitor tepotinib, which received the first approval anywhere in the world for the treatment of NSCLC with *MET* gene alterations, and our first-in-class bifunctional fusion protein immunotherapy, bintrafusp alfa, both of which have promising outcomes featured at this year's ASCO meeting."

For tepotinib[†], approved in Japan for the treatment of patients with unresectable, advanced or recurrent non-small cell lung cancer (NSCLC) with *MET* exon 14 (*MET*ex14) skipping alterations and the first oral MET inhibitor indicated for the treatment of advanced NSCLC harboring *MET* gene alterations to receive a regulatory approval, data will be presented from the primary analysis of the VISION study with promising activity in patients with advanced *EGFR/ALK* wild-type, *MET*ex14 skipping NSCLC who were prospectively enrolled using liquid biopsy or tissue biopsy. Results (Abstract #9556) include ≥6-month follow-up data for the primary endpoint of objective response rate (ORR) as determined by independent review committee. Secondary endpoints include ORR as assessed by investigators, duration of response, disease control rate, progression-free survival, molecular responses, and safety data. Additionally, patient-reported outcomes (PROs) of health-related quality of life (HRQoL) for the VISION study will be presented at the meeting (Abstract# 9575). These outcomes are the first time HRQoL have been reported for patients with *MET*ex14 skipping NSCLC.

For bintrafusp alfa, a novel bifunctional fusion protein targeting TGF-β and PD-L1, two-year follow-up data from a global Phase I study in second-line NSCLC will be

presented (Abstract# 9558). These data continue to show manageable safety with durable responses and encouraging long-term survival, especially in patients with high PD-L1 expression (≥80%). The overall safety profile has remained consistent since the interim analysis, with no new safety signals or deaths and one additional treatment-related discontinuation (blood alkaline phosphatase increased). Studies in the bintrafusp alfa lung cancer program include:

- INTR@PID LUNG 037: Adaptive Phase III, randomized, open-label controlled study of bintrafusp alfa compared with pembrolizumab as a first-line treatment in patients with PD-L1 expressing advanced NSCLC;
- INTR@PID LUNG 005: Phase II study of bintrafusp alfa with concurrent chemoradiation therapy (cCRT) in unresectable Stage III NSCLC; and
- INTR@PID LUNG 024: Phase Ib/II, open-label study of bintrafusp alfa in combination with chemotherapy in participants with Stage IV NSCLC regardless of PD-L1 expression status.

The Company's broad portfolio of investigational DNA damage response (DDR) inhibitors represents multiple development paths, including combinations with other agents and modalities. A trial-in-progress poster (Abstract #TPS4117) will review a multicenter Phase Ib/II study evaluating the safety, tolerability, pharmacokinetics and efficacy of the DNA-PK inhibitor peposertib (formerly M3814) in combination with capecitabine and radiotherapy as neoadjuvant treatment in patients with locally advanced rectal cancer.

**BAVENCIO is under clinical investigation for the first-line maintenance treatment of advanced UC. There is no guarantee that BAVENCIO will be approved for first-line maintenance treatment of advanced UC by any health authority worldwide.*

†Tepotinib is currently under clinical investigation in NSCLC and not yet approved in any markets outside of Japan.

‡Bintrafusp alfa is currently under clinical investigation and not approved for any use anywhere in the world.

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.[10-12] In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

BAVENCIO Approved Indications

BAVENCIO® (avelumab) 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 (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) 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. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Avelumab is currently approved for patients with MCC in 50 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

BAVENCIO Important Safety Information from the US FDA-Approved Label

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 moderate (Grade 2) and permanently discontinue for severe (Grade 3), life-threatening (Grade 4), or recurrent moderate (Grade 2) pneumonitis. Pneumonitis occurred in 1.2% of patients, including one (0.1%) patient with Grade 5, one (0.1%) with Grade 4, and five (0.3%) with Grade 3.

BAVENCIO can cause **hepatotoxicity and immune-mediated hepatitis**, including fatal cases. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater

hepatitis. Withhold BAVENCIO for moderate (Grade 2) immune-mediated hepatitis until resolution and permanently discontinue for severe (Grade 3) or life-threatening (Grade 4) immune-mediated hepatitis. Immune-mediated hepatitis occurred with BAVENCIO as a single agent in 0.9% of patients, including two (0.1%) patients with Grade 5, and 11 (0.6%) with Grade 3.

BAVENCIO in combination with axitinib can cause **hepatotoxicity** with higher than expected frequencies of Grade 3 and 4 alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevation. Consider more frequent monitoring of liver enzymes as compared to when the drugs are used as monotherapy. Withhold BAVENCIO and axitinib for moderate (Grade 2) hepatotoxicity and permanently discontinue the combination for severe or life-threatening (Grade 3 or 4) hepatotoxicity. Administer corticosteroids as needed. In patients treated with BAVENCIO in combination with axitinib, Grades 3 and 4 increased ALT and AST occurred in 9% and 7% of patients, respectively, and immune-mediated hepatitis occurred in 7% of patients, including 4.9% with Grade 3 or 4.

BAVENCIO can cause **immune-mediated colitis**. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold BAVENCIO until resolution for moderate or severe (Grade 2 or 3) colitis until resolution. Permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% of patients, including seven (0.4%) with Grade 3.

BAVENCIO can cause **immune-mediated endocrinopathies**, including adrenal insufficiency, thyroid disorders, and type 1 diabetes mellitus.

Monitor patients for signs and symptoms of **adrenal insufficiency** during and after treatment, and administer corticosteroids as appropriate. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency. Adrenal insufficiency was reported in 0.5% of patients, including one (0.1%) with Grade 3.

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation. Manage hypothyroidism with hormone replacement therapy and hyperthyroidism with medical management. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) thyroid disorders. Thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroiditis, were reported in 6% of patients, including three (0.2%) with Grade 3.

Type 1 diabetes mellitus including diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Withhold BAVENCIO and administer antihyperglycemics or insulin in patients with severe or life-threatening (Grade ≥3) hyperglycemia, and resume treatment when metabolic control is achieved. Type 1 diabetes mellitus without an alternative etiology occurred in 0.1% of patients, including two cases of Grade 3 hyperglycemia.

BAVENCIO can cause **immune-mediated nephritis and renal dysfunction**. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater nephritis. Withhold BAVENCIO for moderate (Grade 2) or severe (Grade 3) nephritis until resolution to Grade 1 or lower. Permanently discontinue BAVENCIO for life-threatening (Grade 4) nephritis. Immune-mediated nephritis occurred in 0.1% of patients.

BAVENCIO can result in **other severe and fatal immune-mediated adverse reactions** involving any organ system during treatment or after treatment discontinuation. For suspected immune-mediated adverse reactions, evaluate to confirm or rule out an immune-mediated adverse reaction and to exclude other causes. Depending on the severity of the adverse reaction, withhold or permanently discontinue BAVENCIO, administer high-dose corticosteroids, and initiate hormone replacement therapy, if appropriate. Resume BAVENCIO when the immune-mediated adverse reaction remains at Grade 1 or lower following a corticosteroid taper. Permanently discontinue BAVENCIO for any severe (Grade 3) immune-mediated adverse reaction that recurs and for any life-threatening (Grade 4) immune-mediated adverse reaction. The following clinically significant immune-

mediated adverse reactions occurred in less than 1% of 1738 patients treated with BAVENCIO as a single agent or in 489 patients who received *BAVENCIO in combination with axitinib*: myocarditis including fatal cases, pancreatitis including fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

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 mild (Grade 1) or moderate (Grade 2) infusion-related reactions. Permanently discontinue BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Infusion-related reactions occurred in 25% of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

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. 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. 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%).

The most common adverse reactions (all grades, ≥ 20%) in patients with locally advanced or metastatic urothelial carcinoma (UC) were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%), and urinary tract infection (21%).

Selected laboratory abnormalities (Grades 3-4, ≥ 3%) in patients with locally advanced or metastatic UC were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

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.

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About tepotinib
Tepotinib is an oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, including both *MET*ex14 skipping alterations and *MET* amplifications, or MET protein overexpression. Discovered in-house at Merck KGaA, Darmstadt, Germany, it has been designed to have a highly selective mechanism of action,[7] with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations. Tepotinib is currently under clinical investigation in NSCLC and not yet approved in any markets outside of Japan. Merck KGaA, Darmstadt, Germany is actively assessing the potential of investigating tepotinib in combination with novel therapies and in other tumor indications. Tepotinib is approved under the brand name TEPMETKO® in Japan for the treatment of unresectable, advanced or recurrent non-small cell lung cancer (NSCLC) with *MET* exon 14 (*MET*ex14) skipping alterations. The brand name TEPMETKO® is not approved for use outside of Japan.

About bintrafusp alfa
Bintrafusp alfa (M7824), discovered in-house at Merck KGaA, Darmstadt, Germany, 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.

INTR@PID is the global clinical trial program investigating the potential co-localized, dual inhibition of TGF-β and PD-L1 with bintrafusp alfa (M7824) in multiple tumor types. Current clinical trial information can be found on the INTR@PID website at www.intrapidclinicaltrials.com. To date, more than 850 patients with various types of solid tumors have been treated globally in the bintrafusp alfa INTR@PID clinical development program.

News Release

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 57,000 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 2019, Merck KGaA, Darmstadt, Germany, generated sales of € 16.2 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 EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 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.