

News Release

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ASCO Abstract #

BAVENCIO® (avelumab): LBA1, 5061; **Bintrafusp alfa (bifunctional fusion protein):** 9558; **Tepotinib (MET kinase inhibitor):** 9556, 9575.

Not intended for UK-based media

Data from Merck KGaA, Darmstadt, Germany, at ASCO 2020 to Showcase Significant Clinical Advances in Cancer Care

- **Late-breaking presentation of Phase III JAVELIN Bladder 100 data for BAVENCIO® showing overall survival benefit in first-line maintenance treatment of advanced urothelial carcinoma**
- **Primary efficacy and biomarker analyses from ongoing VISION study for first-in-class tepotinib[†] in NSCLC with *MET*_{ex14} skipping alterations**
- **Two-year follow-up for novel bifunctional fusion protein targeting TGF-β/PD-L1, bintrafusp alfa[‡], in second-line treatment of NSCLC**
- **Data from investigational and approved agents showcase scientific innovation of company's biology-driven portfolio across 11 tumor types with high unmet need**

Darmstadt, Germany, April 30, 2020 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced 25 abstracts will be presented at the 2020 American Society of Clinical Oncology (ASCO) Annual Meeting. These abstracts represent several innovative modalities and mechanisms that have the potential to advance treatment across a range of difficult-to-treat cancers. The meeting will be held virtually from May 29-31.

“We anticipate our late-breaking data for BAVENCIO® as first-line maintenance therapy for urothelial carcinoma will be some of the most exciting data to be shared



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at this year's ASCO meeting," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "In addition, studies from our ongoing clinical trials in advanced lung cancer from two of our in-house developed mechanisms—our oral MET inhibitor, tepotinib, and our first-in-class bifunctional fusion protein immunotherapy targeting TGF- β /PD-L1, bintrafusp alfa—reinforce the impact these investigational medicines may have in one of the leading causes of cancer mortality."

The first presentation of detailed results from the Phase III JAVELIN Bladder 100 study (Abstract #LBA1), which show an overall survival benefit for BAVENCIO[®] (avelumab) versus best supportive care in the first-line maintenance treatment of advanced urothelial carcinoma (UC)*, will take place during the plenary session on Sunday, May 31. BAVENCIO is co-developed and co-commercialized with Pfizer Inc.

Additional study findings will be presented for BAVENCIO in combination with INLYTA[®] (axitinib) for advanced renal cell carcinoma (RCC) and for the Company's first biology-driven leader, ERBITUX[®] (cetuximab), which continues to demonstrate its legacy as the backbone of treatment of squamous cell carcinoma of the head and neck (SCCHN) and its value across the continuum of care in metastatic colorectal cancer (mCRC).

Data to be presented at ASCO for Merck KGaA, Darmstadt, Germany's biology-driven portfolio, which focuses on three discovery platforms, in oncogenic pathways, immuno-oncology and DNA damage response inhibition (DDRi), continue to demonstrate transformative potential to address current unmet needs in a number of hard-to-treat tumor types through innovative treatment approaches and novel combinations. These include potential first-in-class/best-in-class early- and late-stage pipeline compounds and investigational uses of approved medicines across a number of cancers including non-small cell lung cancer (NSCLC), UC, RCC, Merkel cell carcinoma, SCCHN and mCRC.

**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.*

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[†]*Tepotinib is the International Nonproprietary Name (INN) for the MET kinase inhibitor MSC2156119J. 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.*

Notes to Editors

Key Merck KGaA, Darmstadt, Germany-supported abstracts slated for presentation are listed below. In addition, a number of investigator-sponsored studies have been accepted (not listed).

Title	Lead Author	Abstract #	Presentation Date / Time (All times EDT)
BAVENCIO (avelumab)			
Oral Session			
Maintenance avelumab + best supportive care (Ave + BSC) vs BSC alone after platinum-based first-line (1L) chemotherapy (CTx) in advanced urothelial carcinoma (aUC): results from the JAVELIN Bladder 100 phase 3 trial	T Powles	LBA1	Accepted for Plenary Session, Sunday, May 31 at 1 p.m. Abstract available online at the ASCO Meeting Library from Thursday, May 28 at 5 p.m.
Poster Presentation			
Association of neutrophil to lymphocyte ratio (NLR) with efficacy from JAVELIN Renal 101	MA Bilen	5061	ASCO Meeting Library, Wednesday, May 13 at 5 p.m.
Tepotinib			
Poster Presentation			
Tepotinib in patients (pts) with NSCLC with MET exon 14 (<i>METex14</i>) skipping: health-related quality of life (HRQoL) (VISION PRO)	PK Paik	9575	ASCO Meeting Library, Wednesday, May 13 at 5 p.m.
Primary efficacy and biomarker analyses from the VISION study of tepotinib in patients (pts) with NSCLC with <i>METex14</i> skipping	X Le	9556	ASCO Meeting Library, Wednesday, May 13 at 5 p.m.
Bintrafusp Alfa			
Poster Presentation			
Two-year follow-up of bintrafusp alfa, a bifunctional fusion protein targeting TGF- β and PD-L1, for second-line (2L) treatment of non-small cell lung cancer (NSCLC)	L Paz-Ares	9558	ASCO Meeting Library, Wednesday, May 13 at 5 p.m.
DDRi			
Poster Presentation			
A multicenter Phase Ib/II study of DNA-PK inhibitor peposertib (formerly M3814) in combination with capecitabine and radiotherapy in patients with locally advanced rectal cancer	P Romesser	TPS4117	ASCO Meeting Library, Wednesday, May 13 at 5 p.m.

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,

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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

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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

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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*

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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.

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The most common adverse reactions (all grades, $\geq 20\%$) 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, $\geq 20\%$) 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, $\geq 20\%$) 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, $\geq 3\%$) 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, $\geq 20\%$) 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%).

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Selected laboratory abnormalities (all grades, $\geq 20\%$) 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 ERBITUX® (cetuximab)

ERBITUX® is an IgG1 monoclonal antibody targeting the epidermal growth factor receptor (EGFR). As a monoclonal antibody, the mode of action of ERBITUX® is distinct from standard non-selective chemotherapy treatments in that it specifically targets and binds to the EGFR. This binding inhibits the activation of the receptor and the subsequent signal-transduction pathway, which results in reducing both the invasion of normal tissues by tumor cells and the spread of tumors to new sites. It is also believed to inhibit the ability of tumor cells to repair the damage caused by chemotherapy and radiotherapy and to inhibit the formation of new blood vessels inside tumors, which appears to lead to an overall suppression of tumor growth. Based on *in vitro* evidence, ERBITUX® also targets cytotoxic immune effector cells towards EGFR-expressing tumor cells (antibody-dependent cell-mediated cytotoxicity [ADCC]).

ERBITUX® has already obtained market authorization in over 100 countries worldwide for the treatment of RAS wild-type metastatic colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck. Merck KGaA, Darmstadt, Germany licensed the right to market ERBITUX®, a registered trademark of ImClone LLC, outside the U.S. and Canada from ImClone LLC, a wholly owned subsidiary of Eli Lilly and Company, in 1998.

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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 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.