

News Release

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Key ESMO Abstracts #

BAVENCIO® (avelumab): 1451; 3152; 4174; 4256; 4823; 5113, **ERBITUX® (cetuximab):** 1212, 2589, 4455, **Tepotinib (MET kinase inhibitor):** 3930; 5373; 5455, **M6620 (ATR inhibitor):** 1547, **Combinations:** 4062; 4934.

Not intended for UK-based media

New Data at ESMO 2019 for Merck KGaA, Darmstadt, Germany, Highlight Focused Clinical Development and Commitment to Patient Care

- **New subgroup analyses for first-line treatment of advanced renal cell carcinoma with BAVENCIO®* (avelumab) in combination with axitinib**
- **Three-year overall survival data for patients treated first-line with ERBITUX® (cetuximab) plus FOLFOX-4 in metastatic colorectal cancer**
- **Data across several therapeutic agents showcase progress of early- to late-stage pipeline, including tepotinib[†], and novel combinations**

Darmstadt, Germany, September 23, 2019 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, which operates its biopharmaceutical business as EMD Serono in the US and Canada, today announced that new data representing several key therapeutic agents from its diverse oncology pipeline will be presented at the 2019 European Society for Medical Oncology (ESMO) Congress, September 27–October 1, in Barcelona, Spain.

Spanning multiple tumor types, data being presented include new evidence supporting approved treatments BAVENCIO®* (avelumab) and ERBITUX®



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(cetuximab), and new research from Merck KGaA, Darmstadt, Germany's, early pipeline, including novel combinations and the investigational targeted therapy tepotinib[†], recently granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA) in patients with metastatic non-small cell lung cancer (NSCLC) harboring *MET* exon 14 skipping alterations who progressed following platinum-based cancer therapy. In March 2018, tepotinib's potential was also recognized by the Japanese Ministry of Health, Labour and Welfare (MHLW), which granted SAKIGAKE 'fast-track' designation for tepotinib in advanced NSCLC harboring *MET* exon 14 skipping alterations.

"Our presence at ESMO underscores our commitment to research and development in highly focused areas within immuno-oncology, precision medicine and DNA damage response," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "We believe that by applying cutting-edge science in our clinical programs we are getting closer to making a difference in patient outcomes."

New data for BAVENCIO[®] will include two poster discussions from the Phase III JAVELIN Renal 101 study evaluating efficacy of first-line treatment with avelumab in combination with axitinib compared with sunitinib in two clinically relevant subgroups of patients with advanced renal cell carcinoma (RCC): those with sarcomatoid histology and those who did not undergo upfront cytoreductive nephrectomy. Results from JAVELIN Renal 101 supported the recent US FDA approval and the positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) for BAVENCIO[®] plus axitinib for first-line treatment of adult patients with advanced RCC.

ERBITUX[®] data further reinforce the impact of primary tumor location on three-year overall survival among patients from China with *RAS* wild-type metastatic colorectal cancer (mCRC) treated with first-line FOLFOX-4 with or without cetuximab from the Phase III TAILOR trial. Additionally, a pooled analysis of patient-level data explores the effect on overall survival of cetuximab in combination with chemotherapy dosed once every two weeks, compared with once-weekly dosing, for first-line treatment in patients with *RAS* wild-type mCRC. These two sets of results underscore the

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clinical benefit of cetuximab and add to the growing body of evidence supporting its role in combination with chemotherapy in first-line *RAS* wild-type mCRC.

New research will be presented from across the company's earlier pipeline, including a pooled analysis of safety data across Phase I and II studies in advanced solid tumors for the investigational oral MET inhibitor tepotinib.

A number of investigator-sponsored studies (ISS) and collaborative research studies (CRS) exploring Merck KGaA, Darmstadt, Germany's pipeline will also be presented at this year's congress, including a late-breaking oral presentation on results from a randomized Phase II study of M6620[‡], an investigational ataxia telangiectasia and rad3-related (ATR) kinase inhibitor from the company's comprehensive DNA Damage Response (DDR) portfolio, in combination with gemcitabine compared with gemcitabine alone in platinum-resistant high-grade serous ovarian cancer. The study is sponsored by the National Cancer Institute (NCI) under its Cooperative Research and Development Agreement with Merck KGaA, Darmstadt, Germany for M6620, and these results are the first-ever randomized data to be presented for an ATR inhibitor.

**The combination of BAVENCIO® and axitinib is approved for the first-line treatment of advanced RCC only in the United States and Argentina. There is no guarantee that avelumab in combination with axitinib will be approved for RCC by any other health authority worldwide.*

†Tepotinib is the recommended International Nonproprietary Name (INN) for the MET kinase inhibitor (MSC2156119J). Tepotinib is currently under clinical investigation and not approved for any use anywhere in the world.

‡M6620 is currently under clinical investigation and not approved for any use anywhere in the world.

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Notes to Editors

Key Merck KGaA, Darmstadt, Germany, ISS and CRS scheduled for presentation are listed below.

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
BAVENCIO® (avelumab)				
Poster Discussions				
Efficacy and biomarker analysis of the sarcomatoid subgroup from the phase 3 JAVELIN Renal 101 trial of first-line avelumab plus axitinib (A + Ax) vs sunitinib (S) for advanced renal cell carcinoma (aRCC)	TK. Choueiri	4823	Sunday, September 29, 2019, 3:00–4:15 PM (3:15 PM lecture time)	Hall 2 – Pamplona Auditorium Poster Board No. 910PD
Primary renal tumour shrinkage in patients (pts) who did not undergo cytoreductive nephrectomy (CN): subgroup analysis from the phase 3 JAVELIN Renal 101 trial of first-line avelumab plus axitinib (A + Ax) vs sunitinib (S) for advanced renal cell carcinoma (aRCC)	L. Albiges	4174	Sunday, September 29, 2019, 3:00–3:15 PM (3:15 PM lecture time)	Hall 2 – Pamplona Auditorium Poster Board No. 908PD
Poster Sessions				
Long-term avelumab treatment in patients with advanced non-small cell lung cancer (NSCLC): post-hoc analysis from JAVELIN Solid Tumor	B. Hrinchenko	4256	Saturday, September 28, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 1493P
Assessing the impact of subsequent immunotherapy treatment on overall survival: a post-hoc analysis of the phase 3 JAVELIN Lung 200 study, 2L avelumab vs docetaxel in patients with platinum-treated NSCLC	F. Barlesi	5113	Saturday, September 28, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 1492P
Randomized phase 3 trial of avelumab + axitinib vs sunitinib as first-line treatment for advanced renal cell carcinoma: JAVELIN Renal 101 Japanese subgroup analysis	M. Uemura	1451	Monday, September 30, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 956P

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Health-related quality of life in patients with metastatic Merkel cell carcinoma receiving second-line or later avelumab treatment: 36-month follow-up data	SP. D'Angelo	3152	Monday, September 30, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 1320P
ERBITUX® (cetuximab)				
Poster Session				
Impact of primary tumor side on 3-year survival outcomes of first-line (1L) FOLFOX-4 ± cetuximab in patients with RAS wild-type (wt) metastatic colorectal cancer (mCRC) in the phase 3 TAILOR trial	S. Qin	4455	Sunday, September 29, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 591P
The cost of adverse event management in patients with RAS wild-type metastatic colorectal cancer treated with first-line cetuximab and panitumumab: an Italian healthcare payer perspective	K. Patterson	1212	Sunday, September 29, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 596P
Non-inferiority on overall survival of every- 2-weeks vs weekly schedule of cetuximab for the first-line treatment of RAS wild-type metastatic colorectal cancer	S. Kasper	2589	Sunday, September 29, 2019, 12:00 – 1:00 PM	Hall 4 – Poster Area Poster Board No. 584P
Tepotinib				
Poster Session				
Safety Profile of Tepotinib in Patients with Advanced Solid Tumors: Pooled Analysis of Phase I and II Data	T. Decaens	3930	Saturday, September 28, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 479P
Drug-drug interaction profile of tepotinib with CYP3A and P-gp substrates	J. Heuer	5373	Saturday, September 28, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 480P
Bioavailability of tepotinib: impact of omeprazole and food	J. Heuer	5455	Saturday, September 28, 2019, 12:00-1:00 PM	Hall 4 – Poster Area Poster Board No. 481P
Combinations				
M6620 Oral Session				
Randomized Phase 2 Study of ATR inhibitor M6620 in Combination with Gemcitabine versus Gemcitabine alone in Platinum Resistant High Grade Serous Ovarian Cancer (HGSOC) (NCT02595892)	PA. Konstantinopoulos	1547 LBA60	Friday, September 27, 2019, 4:45–5:00 PM	Hall 2 – Pamplona Auditorium
Poster Session				

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Phase 1b, open-label, dose-escalation study of M9241 (NHS-IL12) plus avelumab in patients (pts) with advanced solid tumors	J. Strauss	4062	Monday, September 30, 2019, 12:00–1:00 PM	Hall 4 – Poster Area Poster Board No. 1264P
Avelumab-cetuximab-radiotherapy versus standards of care in locally advanced squamous cell carcinoma of head and neck: safety phase of randomized trial GORTEC 2017-01 (REACH)	Y. Tao	4934	Saturday, September 28, 2019, 8:45–9:45 AM (9:05 AM lecture time)	Hall 5 – Bilbao Auditorium Poster Board No. 1118PD

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.¹⁻³ BAVENCIO® has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.³⁻⁵ In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO®.

The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and about 10,000 patients evaluated across more than 15 different tumor types. These tumor types include RCC, gastric/gastro-esophageal junction cancer, head and neck cancer, Merkel cell carcinoma, non-small cell lung cancer, and urothelial carcinoma.

BAVENCIO Approved Indications in the US

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

In the US, the FDA granted accelerated approval for BAVENCIO for the treatment of (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 more than 45 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

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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 INLYTA 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 INLYTA 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 INLYTA, 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. Immune-mediated hepatitis was reported in 7% of patients including 4.9% with Grade 3 or 4 immune-mediated hepatitis. Hepatotoxicity led to permanent discontinuation in 6.5% and immune-mediated hepatitis led to permanent discontinuation of either BAVENCIO or axitinib in 5.3% of patients.

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

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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 INLYTA*: 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 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

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hypertension, diabetes, or dyslipidemia. 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. 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.

Clinical chemistry and hematology laboratory values abnormalities have been reported with BAVENCIO and also BAVENCIO in combination with INLYTA including but not limited to grade 3-4 lymphopenia, anemia, elevated cholesterol and liver enzymes.

Please see full [US Prescribing Information](#) and [Medication Guide](#) available at <http://www.BAVENCIO.com>.

INLYTA Important Safety Information from the US FDA-Approved Label
Hypertension including **hypertensive crisis** has been observed with INLYTA. Blood pressure should be well controlled prior to initiating INLYTA. Monitor for hypertension and treat as needed. For persistent hypertension, despite use of antihypertensive medications, reduce the dose. Discontinue INLYTA if hypertension is severe and persistent despite use of antihypertensive therapy and dose reduction of INLYTA, and discontinuation should be considered if there is evidence of hypertensive crisis.

Arterial and venous thrombotic events have been observed with INLYTA and can be fatal. Use with caution in patients who are at increased risk or who have a history of these events.

Hemorrhagic events, including fatal events, have been reported with INLYTA. INLYTA has not been studied in patients with evidence of untreated brain metastasis or recent active gastrointestinal bleeding and should not be used in those patients. If any bleeding requires medical intervention, temporarily interrupt the INLYTA dose.

Cardiac failure has been observed with INLYTA and can be fatal. Monitor for signs or symptoms of cardiac failure throughout treatment with INLYTA. Management of cardiac failure may require permanent discontinuation of INLYTA.

Gastrointestinal perforation and fistula, including death, have occurred with INLYTA. Use with caution in patients at risk for gastrointestinal perforation or fistula. Monitor for symptoms of gastrointestinal perforation or fistula periodically throughout treatment.

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Hypothyroidism requiring thyroid hormone replacement has been reported with INLYTA. Monitor thyroid function before initiation of, and periodically throughout, treatment.

No formal studies of the effect of INLYTA on **wound healing** have been conducted. Stop INLYTA at least 24 hours prior to scheduled surgery.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been observed with INLYTA. If signs or symptoms occur, permanently discontinue treatment.

Proteinuria has been observed with INLYTA. Monitor for proteinuria before initiation of, and periodically throughout, treatment with INLYTA. For moderate to severe proteinuria, reduce the dose or temporarily interrupt treatment.

Liver enzyme elevation has been observed during treatment with INLYTA. Monitor ALT, AST, and bilirubin before initiation of, and periodically throughout, treatment.

For patients with moderate **hepatic impairment**, the starting dose should be decreased. INLYTA has not been studied in patients with severe hepatic impairment.

INLYTA can cause **fetal harm**. Advise patients of the potential risk to the fetus and to use effective contraception during treatment.

Avoid strong **CYP3A4/5 inhibitors**. If unavoidable, reduce the dose. Grapefruit or grapefruit juice may also increase INLYTA plasma concentrations and should be avoided.

Avoid strong **CYP3A4/5 inducers** and, if possible, avoid moderate CYP3A4/5 inducers.

For more information and full Prescribing Information, visit www.INLYTA.com.

ADVERSE REACTIONS (BAVENCIO + INLYTA)

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, $\geq 20\%$) 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, $\geq 20\%$) 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

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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%).

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.

ERBITUX® Important Safety Information from the US FDA-Approved Label
The US Prescribing Information for ERBITUX® includes BOX WARNINGS for infusion reactions and cardiopulmonary arrest. Very commonly ($\geq 25\%$) reported side effects with ERBITUX® include cutaneous adverse reactions (including acne-like skin rash, pruritus, and nail changes), headache, diarrhea, infection and hypomagnesemia.

WARNING: INFUSION REACTIONS and CARDIOPULMONARY ARREST

Infusion Reactions: ERBITUX® can cause serious and fatal infusion reactions [see Warnings and Precautions (5.1), Adverse Reactions (6)]. Immediately interrupt and permanently discontinue ERBITUX® for serious infusion reactions [see Dosage and Administration (2.4)].

Cardiopulmonary Arrest: Cardiopulmonary arrest or sudden death occurred in patients with squamous cell carcinoma of the head and neck receiving ERBITUX® with radiation therapy or a cetuximab product with platinum-based therapy and fluorouracil. Carefully consider use of ERBITUX with radiation therapy, or platinum-based therapy with fluorouracil, in head and neck cancer patients with a history of coronary artery disease, congestive heart failure, or arrhythmias. Monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after ERBITUX® administration [see Warnings and Precautions (5.2, 5.6)].

Please see full [US Prescribing Information](http://www.accessdata.fda.gov) available at www.accessdata.fda.gov

About Tepotinib

Tepotinib, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, including both *MET* exon 14 skipping mutations and *MET* amplifications, or MET protein overexpression. It has been designed to have a highly selective mechanism of action, with the potential

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to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations.

Tepotinib is currently being investigated in NSCLC and Merck KGaA, Darmstadt, Germany is actively assessing the potential of investigating tepotinib in combination with novel therapies and other tumor indications.

References

1. Dolan DE and Gupta S. Cancer Control 2014;21:231-7.
2. Dahan R, et al. Cancer Cell 2015;28:285-95.
3. Boyerinas B, et al. Cancer Immunol Res 2015;3:1148-57.
4. Kohrt HE, et al. Immunotherapy 2012;4:511-27.
5. Hamilton G and Rath B. Expert Opin Biol Ther 2017;17:515-23.

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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 52,000 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 2018, Merck KGaA, Darmstadt, Germany, generated sales of € 14.8 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.