News Release

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ASCO Abstract #
Bintrafusp alfa (bifunctional fusion protein): TPS9114; **Tepotinib (MET kinase inhibitor):** 9005; **Discovery:** 2567; **ERBITUX® (cetuximab):** 3580; **BAVENCIO® (avelumab):** 9569; 101; 4552; 4072

Not intended for UK-based media

Merck KGaA, Darmstadt, Germany Data at ASCO 2019 Showcase Multiple Innovative Molecules with Potential to Impact Unmet Needs in Cancer Care

- **New biomarker analyses for BAVENCIO®* (avelumab) in combination with axitinib in first-line renal cell carcinoma (RCC)**
- **Data presented across several modalities and mechanisms showcase the scientific innovation and diversity of the company's pipeline, which includes bintrafusp alfa‡ (M7824) and tepotinib†**

Darmstadt, Germany, May 15, 2019 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that data across several modalities and mechanisms targeting difficult-to-treat cancers will be presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting, May 31–June 4, Chicago, IL, US. New data will be presented for BAVENCIO®* (avelumab) and ERBITUX® (cetuximab), including rational combinations with chemotherapy, radiation therapy and other targeted agents to try to identify new ways to improve patient outcomes. This includes an oral presentation of data defining biomarkers that differentiate therapy-specific outcomes in patients with advanced renal cell carcinoma (RCC), and who have been treated first-line with BAVENCIO® (avelumab) in combination with axitinib. Abstracts also showcase the scientific innovation and diversity of Merck KGaA, Darmstadt, Germany's pipeline, with results from a number

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of high-priority clinical development programs, including tepotinib[†], bintrafusp alfa[‡] (M7824) and the company's comprehensive DNA Damage Response (DDR) portfolio.

"At this year's ASCO meeting we continue to demonstrate the breadth and depth of our oncology and immuno-oncology portfolio. We will present examples of the latest precision medicine and biomarker research and some of the most exciting mechanisms being investigated today, including tepotinib and our first-in-class bifunctional fusion protein immunotherapy, bintrafusp alfa," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "Merck KGaA, Darmstadt, Germany's oncology pipeline has significant promise in the near term through our late-stage priority programs, and our early pipeline includes several potentially groundbreaking modalities. We look forward to sharing the latest science with the global oncology community."

For BAVENCIO® (avelumab), Merck KGaA, Darmstadt, Germany, will share data from five studies across tumor types including Merkel cell carcinoma, RCC, hepatocellular carcinoma and urothelial carcinoma. This includes an oral presentation of biomarker analyses of baseline tumor samples from the Phase III JAVELIN Renal 101 trial in previously untreated patients with advanced RCC. The trial indicated that PD-L1 expression (≥1% immune cells) was associated with the longest progression-free survival (PFS) in the avelumab plus axitinib arm and the shortest PFS in the sunitinib arm (HR, 0.63; 95% CI, 0.49, 0.81). An analysis of relevant gene expression signatures (GES) indicated that in the avelumab plus axitinib arm, PFS was enhanced in immune GES–positive patients vs those in the negative group (HR, 0.63; 95% CI, 0.46, 0.86; 2-sided p=0.004), and vs those in an independent dataset (JAVELIN Renal 100; Choueiri, *Lancet Oncol*, 2018) (HR, 0.46; 95% CI, 0.20, 1.05; 2-sided p=0.064). The combination demonstrated a safety and tolerability profile consistent with the known safety profiles of each drug alone. The most common adverse reactions (≥20%) were diarrhea, fatigue, hypertension, musculoskeletal pain, nausea, mucositis, palmar-plantar erythrodysesthesia, dysphonia, decreased appetite, hypothyroidism, rash, hepatotoxicity, cough, dyspnea, abdominal pain, and headache. Serious adverse reactions occurred in 35% of patients receiving BAVENCIO® (avelumab) in combination with axitinib. The incidence of major adverse cardiovascular events

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(MACE) was higher with BAVENCIO® (avelumab) in combination with axitinib vs sunitinib.

ERBITUX® (cetuximab) data from a retrospective analysis of overall survival (OS) by subsequent therapy in patients with RAS wild-type metastatic colorectal cancer from the Phase III EPIC study will be presented, to evaluate the effect of post-study therapies (with ERBITUX®, without ERBITUX®, or no subsequent therapy) on OS.

A number of the molecules to be featured were discovered in-house at Merck KGaA, Darmstadt, Germany. This includes tepotinib, an oral MET inhibitor designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, and bintrafusp alfa, a bifunctional fusion protein designed to simultaneously target two immuno-suppressive pathways. Merck KGaA, Darmstadt, Germany's partnership with GSK to jointly develop and commercialize bintrafusp alfa, announced in February 2019, is part of the company's strategic approach to oncology R&D. Together, Merck KGaA, Darmstadt, Germany, and GSK aim to rapidly and efficiently progress this molecule, which represents a potential step change in the treatment of cancer.

For tepotinib, promising updated results from the ongoing Phase II VISION study in 85 patients with non-small cell lung cancer (NSCLC) with *MET* exon 14 skipping mutations (identified by liquid biopsy [LBx] or tumor biopsy [TBx]) will be shared. Results show an overall response rate (ORR) of 51.4% for LBx patients (independent review committee [IRC]-assessed) or 63.9% (investigator-assessed). The ORR for TBx patients was 41.5% (IRC-assessed) or 58.5% (investigator-assessed). Median duration of response was 9.8 (IRC-assessed) or 17.1 months (investigator-assessed) for LBx patients and 12.4 (IRC-assessed) or 14.3 months (investigator-assessed) for TBx patients. Any grade treatment-related adverse events (TRAEs) reported by ≥10% of 69 patients evaluable for safety were peripheral edema (47.8%), diarrhea (18.8%), nausea (15.9%) and asthenia (10.1%). No Grade 4 or 5 TRAEs were observed. TRAEs led to permanent discontinuation in two (2.9%) patients (one interstitial lung disease, one diarrhea and nausea). These data continue to mature, and an updated data cut from the VISION study will be given as an oral presentation at the ASCO meeting on Monday, June 3.

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For bintrafusp alfa, a trial-in-progress poster will be shared on the open-label study of bintrafusp alfa vs pembrolizumab as a first-line treatment in patients with PD-L1-expressing advanced NSCLC.

Merck KGaA, Darmstadt, Germany takes a personalized approach to R&D, and precision medicine has long been a priority. Abstracts being presented at ASCO also include biomarker research programs that aim to help identify the patients most likely to benefit from specific treatments so they can achieve the best possible medical outcomes.

**The combination of BAVENCIO and axitinib is approved for the first-line treatment of advanced RCC only in the United States. 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.

[‡]Bintrafusp alfa is the proposed International Nonproprietary Name (INN) for the bifunctional immunotherapy M7824. 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 (CDT)	Location
BAVENCIO® (avelumab)				
Oral Session				
Biomarker analyses from JAVELIN Renal 101: avelumab + axitinib (A+Ax) vs sunitinib (S) in advanced renal cell carcinoma (aRCC)	T.K. Choueiri	101	Sat, Jun 1, 8:00 AM – 9:30 AM (8:12 AM – 8:24 AM lecture time)	Hall D1
Poster Sessions				
5-factor prognostic model for survival of patients with metastatic urothelial carcinoma receiving 3 different post-platinum PD-L1 inhibitors	G. Sonpavde	4552	Mon, Jun 3, 1:15 PM – 4:15 PM	Hall A

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First-line avelumab + axitinib in patients with advanced hepatocellular carcinoma: results from a phase 1b trial (VEGF Liver 100)	M. Kudo	4072	Mon, Jun 3, 8:00 AM – 11:00 AM	Hall A
Integrative molecular analysis of metastatic Merkel cell carcinoma to identify predictive biomarkers of response to avelumab	S. Georges	9569	Mon, Jun 3, 1:15 PM – 4:15 PM	Hall A
Bintrafusp Alfa				
Poster Session				
Randomized open-label study of M7824 vs pembrolizumab as first-line (1L) treatment in patients with PD-L1 expressing advanced non-small cell lung cancer (NSCLC)	L. Paz-Ares	TPS9114	Sun, Jun 2, 8:00 AM – 11:00 AM	Hall A
Discovery				
Poster Session				
Understanding contribution and independence of multiple biomarkers for predicting response to atezolizumab	P.K. Shah	2567	Sat, Jun 1, 8:00 AM – 11:00 AM	Hall A
ERBITUX® (cetuximab)				
Poster Session				
Retrospective Analysis of Overall Survival (OS) by Subsequent Therapy in Patients With RAS-Wild-type (wt) Metastatic Colorectal Cancer (mCRC) Receiving Cetuximab ± Irinotecan	A. Sobrero	3580	Mon, Jun 3, 8:00 AM – 11:00 AM	Hall A
Tepotinib				
Oral Session				
Phase II study of tepotinib in NSCLC patients with *MET*ex14 mutations	P.K. Paik	9005	Mon, Jun 3, 8:00 AM – 11:00 AM (9:24 AM – 9:36 AM lecture time)	Hall B1

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 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.

About Bintrafusp Alfa (M7824)

Bintrafusp alfa is an investigational bifunctional immunotherapy that is designed to combine a TGF-β trap with the anti-PD-L1 mechanism in one fusion protein. Bintrafusp alfa is designed to combine co-localized blocking of the two immuno-suppressive pathways – targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses. Bintrafusp alfa is currently in Phase I studies for solid tumors, as well as a randomized Phase II trial to investigate bintrafusp alfa compared with pembrolizumab as a first-line treatment in patients with PD-L1 expressing advanced NSCLC. The multicenter, randomized, open-label, controlled study is evaluating the safety and efficacy of bintrafusp alfa versus pembrolizumab as a monotherapy treatment.

To date, nearly 700 patients have been treated with bintrafusp alfa across more than 10 tumor types in Phase I studies. Encouraging data from the ongoing Phase I studies indicates bintrafusp alfa's potential safety and clinical anti-tumor activity across multiple types of difficult-to-treat cancers, including advanced NSCLC, human papillomavirus-associated cancers, biliary tract cancer and gastric cancer. In addition, in pre-clinical studies bintrafusp alfa demonstrated superior anti-tumor activity, compared with anti-PD-L1 alone or with anti-PD-L1 and TGF-β trap when co-administered. In total, eight high-priority immuno-oncology clinical development studies are ongoing or expected to commence in 2019, including studies in non-small cell lung and biliary tract cancers.

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.

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 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 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 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.

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%).

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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%).

About Erbitux® (cetuximab)

Erbitux® is a 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).

Very commonly reported side effects with Erbitux® include acne-like skin rash, mild to moderate infusion-related reactions and hypomagnesemia.

Erbitux® has already obtained market authorization in 114 countries world-wide for the treatment of RAS wild-type metastatic colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck (SCCHN). 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.

References

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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.