News Release

Your Contact
Brenda Mulligan +1 978 821 5345
Investor relations +49 6151 72 3321

ESMO Abstract #
Avelumab: LBA6_PR, 659P, 1290P, 1291P, 1282P, 877P; **M7824 (TGF β-trap/anti-PD-L1):** 1048O, 1463P, 1931P, 757P, 643P, 642P, 661P; **tepotinib (MET kinase inhibitor):** 1377O, 621PD, 698P; **M6620:** 1437P; **M3814:** 1845P; **M7583:** 1014PD; **abituzumab:** 487P

October 9, 2018

Not intended for distribution in the U.K.

Merck KGaA, Darmstadt, Germany Data at ESMO 2018 Congress Highlight Multiple Therapeutics with Potential to Transform Cancer Care

- **First presentation of Phase III data for avelumab (plus axitinib) in previously untreated, advanced kidney cancer**
- **New and updated data for bifunctional immunotherapy M7824**
- **Results from Phase II trials for tepotinib, including in EGFR TKI-resistant NSCLC**
- **Additional pipeline data feature abstracts for a further four innovative agents across multiple tumor types with a significant patient need**

Darmstadt, Germany, October 9, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced that new data from a variety of high-priority clinical development programs will be presented at the ESMO 2018 Congress (European Society for Medical Oncology Annual Meeting), October 19–23, 2018, Munich, Germany.

In the year that Merck KGaA, Darmstadt, Germany celebrates its 350-year anniversary, abstracts at the congress represent a company record with eight

Frankfurter Strasse 250
64293 Darmstadt · Germany
Hotline +49 6151 72-5000
www.emdgroup.com

Head Media Relations -62445
Spokesperson: -9591 / -7144 / -6328
Fax +49 6151 72 3138
media.relations@emdgroup.com

therapeutic agents across 14 tumor types, reinforcing Merck KGaA, Darmstadt, Germany's position at the forefront of clinical development in oncology.

"Our data at this year's European Society for Medical Oncology Congress expand our understanding of avelumab in renal cell carcinoma and other tumors, and demonstrate the headway we are making with our pipeline, including bifunctional immunotherapy M7824 and tepotinib," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "We look forward to many more years of real and significant progress towards our vision of transforming the management and treatment of cancer."

Data from the Phase III study JAVELIN Renal 101, evaluating avelumab* in combination with axitinib, compared with sunitinib as initial therapy for patients with advanced renal cell carcinoma (RCC), will be presented for the first time during the Presidential Symposium at ESMO on Sunday, October 21, 2018 at 5:20 PM – 5:35 PM CEST. Avelumab is being jointly developed and commercialized with Pfizer. The results represent the first positive Phase III immunotherapy trial in combination with a tyrosine kinase inhibitor (TKI) in any tumor type, supporting Merck KGaA, Darmstadt, Germany's interest in the potential use of avelumab in combination with currently approved therapies and novel agents. These results will be submitted for publication in a peer-reviewed journal. Other updates include new avelumab data in Merkel cell carcinoma (MCC) and advanced gastric or gastroesophageal junction (GEJ) cancer.

New data for M7824 will be presented from expansion cohorts of two ongoing Phase I clinical trials, including the first tumor-specific data for squamous cell carcinoma of the head and neck (SCCHN), biliary tract cancer, esophageal squamous cell carcinoma and esophageal adenocarcinoma. In addition, updated data for M7824 in patients with gastric cancer and non-small cell lung cancer (NSCLC) will be shared. M7824, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational bifunctional immunotherapy designed to combine a transforming growth factor β (TGF-β) trap by 'fusing' it with the anti-programmed death ligand-1 (PD-L1) mechanism. To date more than 650 patients with various types of solid tumors have been treated across the program with M7824 and the safety profile is consistent with that observed with other PD-1/PD-L1 inhibitors and previously

described skin lesions (keratoacanthomas, SCC, hyperkeratosis) associated with TGF-β-inhibiting therapies.

Data for tepotinib** include results from three Phase II trials in epidermal growth factor receptor (EGFR) TKI-resistant NSCLC and advanced hepatocellular carcinoma, providing further evidence of this precision medicine's potential clinical activity in a range of tumors. Tepotinib, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational, oral MET inhibitor that is designed to selectively inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations or MET protein overexpression.

Additional pipeline abstracts feature updated data from Merck KGaA, Darmstadt, Germany's comprehensive DNA damage response (DDR) portfolio. These include results from a Phase I trial investigating M6620 (formerly VX-970) in combination with gemcitabine in patients with advanced NSCLC, and combined data from two Phase I trials of DNA-dependent protein kinase inhibitor, M3814. Results will also be shared from a Phase I/II trial of M7583, a Bruton's TKI, in patients with B-cell malignancies, as well as a retrospective analysis of the Phase I/II Poseidon study investigating abituzumab in patients with metastatic colorectal cancer (mCRC).

Data to be presented at the congress for Erbitux® will add to the growing body of real-world evidence supporting the therapy's role as a standard of care in RAS wild-type mCRC and first-line recurrent or metastatic SCCHN (R/M SCCHN), and for patients with locally advanced SCCHN (LA SCCHN) who may not be able to tolerate cisplatin-based regimens in full.

*Avelumab is under clinical investigation for the treatment of RCC, MCC, CRC, gastric and GEJ cancer, and has not been demonstrated to be safe and effective for these indications. There is no guarantee that avelumab will be approved for RCC, CRC, gastric or GEJ cancer by any 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.

Tepotinib, M7824, M3814, M7583, M6620 and abituzumab are under clinical investigation and have not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication by any health authority worldwide.

Notes to Editors

Key abstracts supported by Merck KGaA, Darmstadt, Germany, 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 (CEST)	Location
Avelumab				
Late-Breaking Abstracts				
JAVELIN Renal 101: a randomized, phase 3 study of avelumab + axitinib vs sunitinib as first-line treatment of advanced renal cell carcinoma (aRCC)	R Motzer	LBA6_PR	Sun, Oct 21, 4:30 – 6:10 PM (5:20 – 5:35 PM lecture time)	Hall A2 – Room 18
Poster Sessions				
Avelumab (anti–PD-L1) in Japanese patients with advanced gastric or gastroesophageal junction cancer (GC/GEJC): updated results from the phase 1b JAVELIN Solid Tumor JPN trial	T Doi	659P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Avelumab in European patients (pts) with metastatic Merkel cell carcinoma (mMCC): experience from an ad hoc expanded access program (EAP)	P Nathan	1290P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Cost-effectiveness (CE) of avelumab vs standard care (SC) for the treatment of patients (pts) with metastatic Merkel cell carcinoma (mMCC)	M Bharmal	1291P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Responder analysis based on patient-reported outcomes (PROs) and clinical endpoints (CEPs) in patients (pts) with metastatic Merkel cell carcinoma (mMCC) treated with avelumab	SP D'Angelo	1282P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
First-line (1L) or second-line (2L) avelumab monotherapy in patients (pts) with advanced renal cell carcinoma (aRCC) enrolled in the phase 1b JAVELIN Solid Tumor trial	UN Vaishampayan	877P	Mon, Oct 22, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M7824 (TGF β-trap/anti-PD-L1)				
Proffered Paper Session				
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients (pts) with advanced SCCHN: results from a phase 1 cohort	BC Cho	1048O	Mon, Oct 22, 2:45 – 4:15 PM (3:00 PM lecture time)	ICM, Room 14B
Poster Sessions				
Updated results of M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1, in second-line (2L) NSCLC	L Paz-Ares	1463P	Sat, Oct 20, 12:30 – 1:30 PM	Hall A3 – Poster Area Networking Hub
Assessment of PD1/ PD-L1 colocalization in hepatocellular carcinoma (HCC) using brightfield double labeling and quantitative digital image analysis	T Mrowiec	1931P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in Asian patients with pretreated biliary tract cancer: preliminary results from a phase 1 trial	C Yoo	757P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients with post-platinum esophageal adenocarcinoma (EAC): preliminary results from a phase 1 cohort	B Tan	643P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Phase 1 study results from an esophageal squamous cell carcinoma (ESCC) cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting transforming growth factor β (TGF-β) and PD-L1	CC Lin	642P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Updated results from a phase 1 trial of M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients with pretreated recurrent or refractory gastric cancer	YJ Bang	661P	Sun, Oct 21, 12:45 – 1.45 PM	Hall A3 – Poster Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
Tepotinib				
Proffered Paper Session				
Phase 2 study of tepotinib + gefitinib (TEP+GEF) in MET-positive (MET+)/epidermal growth factor receptor (EGFR)-mutant (MT) non-small lung cancer (NSCLC)	YL Wu	1377O	Fri, Oct 19, 4:00 – 5:30 PM (4:51 PM lecture time)	Hall A2, Room 18
Poster Discussion				
Phase 2 trial of tepotinib vs sorafenib in Asian patients (pts) with advanced hepatocellular carcinoma (HCC)	BY Ryoo	621PD	Fri, Oct 19, 3:45 – 5:30 PM (4:25 PM lecture time)	Hall B3, Room 21
Poster Session				
Phase 2 efficacy and safety data for the MET inhibitor tepotinib in patients (pts) with sorafenib-treated advanced hepatocellular carcinoma (HCC)	T Decaens	698P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M6620				
Poster Session				
Phase I dose expansion data for M6620 (formerly VX-970), a first-in-class ATR inhibitor, combined with gemcitabine (Gem) in patients (pts) with advanced non-small cell lung cancer (NSCLC)	R Plummer	1437P	Sat, Oct 20, 12:30 – 1:30 PM	Hall A3 – Poster Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M3814				
Poster Session				
Safety, clinical activity and pharmacological biomarker evaluation of the DNA-dependent protein kinase (DNAPK) inhibitor M3814: results from two phase I trials	M Mau-Sørensen	1845P	Sat, Oct 20, 12:30 – 1:30 PM	Hall A3 – Poster Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M7583				
Poster Session				
Phase I/II, first in human trial with M7583, a Bruton's tyrosine kinase inhibitor (BTKi), in patients with B cell malignancies	W Jurczak	1014PD	Sun, Oct 21, 4:30 – 5:45 PM	Hall B3 – Room 21

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
Abituzumab				
Poster session				
Patient selection for targeting integrin with abituzumab in patients with metastatic colorectal cancer (mCRC). A retrospective analysis of the randomized phase I/II Poseidon study	R Laeufle	487P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

About Avelumab
Avelumab is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab 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, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.[1-3] Avelumab 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 avelumab.

Avelumab is currently being evaluated in the JAVELIN clinical development program, which involves at least 30 clinical programs, including seven Phase III trials, and more than 8,600 patients across more than 15 different tumor types. For a comprehensive list of all avelumab trials, please visit clinicaltrials.gov.

Approved Indications in the US
The US Food and Drug Administration (FDA) granted accelerated approval for avelumab (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.

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% (21/1738) 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 **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 was reported in 0.9% (16/1738) of patients, including two (0.1%) patients with Grade 5, and 11 (0.6%) with Grade 3.

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, and permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% (26/1738) 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% (8/1738) 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% (98/1738) 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% (2/1738) 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% (1/1738) 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 1,738 patients treated with BAVENCIO: myocarditis with fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe (Grade 3) or life-threatening (Grade 4) **infusion-related reactions**. Patients should be premedicated with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent doses 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% (439/1738) of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

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%).

Please see full US Prescribing Information and Medication Guide available at http://www.BAVENCIO.com.

About M7824
M7824 is an investigational bifunctional immunotherapy that is designed to bring together a TGF-β trap and 'fuse' it with the anti-PD-L1 mechanism. M7824 is designed to simultaneously block the two immunosuppressive pathways – targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is currently in Phase I studies for solid tumors.

About Tepotinib
Tepotinib (MSC2156119J) is an investigational, oral MET inhibitor that is thought to inhibit oncogenic MET receptor signaling caused by *MET* (gene) alterations, including both *MET* exon 14 skipping mutations and *MET* amplifications, or MET protein overexpression. It is a precision medicine and is designed to have a highly selective mechanism of action.

About M6620
M6620 (previously known as VX-970) is an investigational small-molecule thought to inhibit ataxia telangiectasia and Rad3-related protein (ATR). ATR is believed to be a key sensor for DNA damage, activating the DNA damage checkpoint and leading to cell cycle arrest. Inhibition of ATR could potentially enhance the efficacy of DNA-damaging agents, but is also being investigated as a monotherapy against tumors with high levels of replication stress induced by overexpression of oncogenes.

About M3814
M3814 is an investigational small-molecule which is thought to inhibit DNA-dependent protein kinase (DNA-PK). DNA-PK is a key enzyme for non-homologous end-joining (NHEJ), an important DNA double-strand break (DSB) repair pathway. Clinical studies investigating combinations of M3814 with other commonly used DNA-damaging agents such as radiotherapy and chemotherapy are underway.

About M7583
M7583 is an investigational therapy that is thought to be a highly selective covalent inhibitor of Bruton's tyrosine kinase (BTKi) designed to minimize off-target effects.

About Abituzumab
Abituzumab is an investigational pan-αv integrin inhibiting monoclonal antibody thought to show activity against αvβ1, 3, 5, 6 and 8 integrin heterodimers. Merck KGaA, Darmstadt, Germany entered into a development agreement with the SFJ Pharmaceuticals Group for abituzumab in metastatic colorectal cancer (mCRC). This collaboration will allow Merck KGaA, Darmstadt, Germany and SFJ to develop the

potential of abituzumab in a targeted way, focusing on a patient population that may benefit from the treatment the most.

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).

The most commonly reported side effect with Erbitux is an acne-like skin rash. In approximately 5% of patients, hypersensitivity reactions may occur during treatment with Erbitux; about half of these reactions are severe.

Erbitux has already obtained market authorization in over 100 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
1. Dolan DE, Gupta S. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. Cancer Control 2014;21:231–7.
2. Dahan R et al. FcγRs modulate the anti-tumor activity of antibodies targeting the PD-1/PD-L1 axis. Cancer Cell 2015;28:285–95.
3. Boyerinas B et al. Antibody-dependent cellular cytotoxicity activity of a novel anti-PD-L1 antibody avelumab (MSB0010718C) on human tumor cells. Cancer Immunol Res 2015;3:1148–57.
4. Kohrt HE et al. Combination strategies to enhance antitumor ADCC. Immunotherapy 2012;4:511–27.
5. Hamilton G, Rath B. Avelumab: combining immune checkpoint inhibition and antibody-dependent cytotoxicity. Expert Opin Biol Ther 2017;17:515–23.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Almost 53,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany, holds the global rights to the "Merck" name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.