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Darmstadt, Germany

News Release

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ESMO 2017 abstract #
Erbitux®: 576P, 593P, 1068P, 1579P; **avelumab:** 1227P, 913P, 1377TiP, 882P, 856P; **M6620** (ATR inhibitor): 242PD; **M2698** (dual p70S6K/Akt inhibitor): 370PD, 393P; **tepotinib** (c-Met kinase inhibitor)**:** 701P

Merck KGaA, Darmstadt, Germany: Driving Innovation in Cancer Care at ESMO 2017 With New Data in Hard-to-Treat Cancers

- **Data to showcase Merck KGaA, Darmstadt, Germany's strong and diverse pipeline ranging from immuno-oncology to DNA damage response**
- **Avelumab data validate potential in hard-to-treat cancers and highlight progress of the JAVELIN clinical development program**
- **First stand-alone data in mTNBC for ATR inhibitor (M6620) from Merck KGaA, Darmstadt, Germany's comprehensive portfolio in DNA damage response**

Darmstadt, Germany, August 31, 2017 – Merck KGaA, Darmstadt, Germany**,** a leading science and technology company, today announced it will present data for a number of tumor types across its rapidly evolving pipeline. A total of 23 abstracts, representing five therapeutic agents, will highlight the company's expanding scientific expertise at this year's European Society for Medical Oncology congress (ESMO 2017; September 8–12, Madrid, Spain).

Data to be presented include continued reinforcement of the role of established brand Erbitux® (cetuximab) as a standard of care therapy, with quality of life (QoL) data in colorectal cancer (CRC) and real-world data in both CRC and squamous cell carcinoma of the head and neck (SCCHN); updated efficacy and safety data for avelumab in metastatic Merkel cell carcinoma (mMCC) and urothelial carcinoma (UC) among other cancers; and new data and updates from Merck KGaA,

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Darmstadt, Germany's rapidly evolving pipeline, including first stand-alone data in metastatic triple negative breast cancer (mTNBC) from potential first-in-class ataxia telangiectasia and Rad3-related protein (ATR) inhibitor M6620* (also known as VX-970).

"The Merck KGaA, Darmstadt, Germany Oncology Franchise has had a momentous year, particularly with the positive regulatory milestones achieved for avelumab. The story continues to evolve at ESMO 2017 from our legacy with Erbitux to our diverse and robust pipeline which has potential novel molecules that could become new standards of care," said Luciano Rossetti, Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "The data reinforce Merck KGaA, Darmstadt, Germany's commitment to pursuing approaches that will bring important benefits to patients and transform the way cancer is treated."

Merck KGaA, Darmstadt, Germany's innovative approach and strategic collaborations in oncology are exemplified through the ongoing partnership with Pfizer, and the significant progress of avelumab. Granted two accelerated approvals** by the U.S. Food and Drug Administration (FDA) this year, more recently the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending the approval of avelumab as monotherapy for the treatment of adult patients with mMCC. ESMO 2017 includes new data for avelumab in the treatment of mMCC, a rare and aggressive skin cancer, and 12-month follow-up data in pre-treated patients with locally advanced or metastatic UC. The progress of the broader JAVELIN clinical development program will also be highlighted, with updated data in hard-to-treat tumors such as metastatic adrenocortical carcinoma (mACC).

The addition of the recently acquired Vertex DNA damage response (DDR) portfolio to its own in-house DDR platform has positioned Merck KGaA, Darmstadt, Germany as one of the key players in the DDR field. The company's broad DDR portfolio includes inhibitors for enzymes of major DDR pathways, such as ATR, DNA-PK and ATM. At ESMO 2017, first stand-alone data will be presented for ATR inhibitor M6620

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in metastatic triple-negative breast cancer (mTNBC). M6620 is currently being investigated in several ongoing Phase I trials across a variety of tumor types.

Other pipeline updates will include data on the potential first-in-class dual p70S6K/Atk inhibitor M2698*; and tepotinib***, a highly selective c-Met kinase inhibitor, in patients with advanced hepatocellular carcinoma (HCC).

Product related information contained herein is subject to local product approval and can therefore vary from country to country. For information relevant to your country, please check in with local regulatory authorities.

*M6620, M2698 and tepotinib 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.

***Tepotinib is the proposed International Non-proprietary Name (INN) for the c-Met kinase inhibitor (also known as MSC2156119J).

Notes to editors

Accepted Merck KGaA, Darmstadt, Germany-supported key abstracts at ESMO 2017 are listed below. In addition, a number of abstracts with data from investigator-sponsored studies have been accepted, including abstracts related to Erbitux (not listed).

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
Avelumab				
Poster sessions				
JAVELIN Lung 100: updated design of a phase 3 trial of avelumab vs platinum doublet chemotherapy as first-line (1L) treatment for metastatic or recurrent PD-L1+ non-small-cell lung cancer (NSCLC)	Reck M.	1377TiP	September 9 13:15 – 14:15	Hall 8
JAVELIN MERKEL 200: Avelumab treatment in chemotherapy-naïve patients with metastatic Merkel cell carcinoma (mMCC).	D'Angelo S.P.	1227P	September 10 13:15-14:15	Hall 8
Avelumab in patients with metastatic adrenocortical carcinoma (mACC): results from	Le Tourneau C.	913P	September 10 13:15-14:15	Hall 8

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the JAVELIN Solid Tumor trial				
Potential impact of avelumab+axitinib (A+Ax) on tumor size (TS) compared with historical data of sunitinib (S) as evaluated by a modeling and simulation (MS) approach	Zheng J.	882P	September 10 13:15-14:15	Hall 8
Avelumab treatment of metastatic urothelial carcinoma (mUC) in the phase 1b JAVELIN Solid Tumor study: updated analysis with ≥6 months of follow-up in all patients	Apolo A.B.	856P	September 10 13:15-14:15	Hall 8

Title	Lead author	Abstract #	Presentation date/time (CEST)	Location
M6620 (VX-970)				
Poster session				
Initial results of a phase 1 dose expansion cohort of M6620 (VX-970), a first-in-class ATR inhibitor, in combination with cisplatin (Cis) in patients (pts) with metastatic triple-negative breast cancer (mTNBC) (NCT02157792)	Telli M.L.	242PD	September 10 09:15 - 10:45	Sevilla auditorium

Title	Lead author	Abstract #	Presentation date/time (CEST)	Location
M2698				
Poster session				
Phase I dose escalation study of M2698, a p70S6K/AKT inhibitor, in patients with advanced cancer	Tsimberidou A.M.	370PD	September 9 16:30-18:00	Alicante auditorium
Pharmacodynamic (PD) biomarkers for the p70S6K/Akt inhibitor, M2698: translation from animal to human and its relevance for dosing rationale	Xiong W.	393P	September 11 13:15-14:15	Hall 8

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Title	Lead author	Abstract #	Presentation date/time (CEST)	Location
Erbitux®:				
Poster session				
Biomarker testing practices in the SECURE (proSpective obsErvational clinical practiCe stUdy in the first-line management of metastatic colorectal cancer [mCRC] with eRbitux in combination with chemothErapy) study	Aravantinos G.	576P	September 9 13:15-14:15	Hall 8
Quality of life (QoL) analyses in patients with RAS wild-type (wt) metastatic colorectal cancer (mCRC) treated with first-line FOLFOX-4 ± cetuximab in the phase 3 TAILOR trial	Liu T.	593P	September 9 13:15-14:15	Hall 8
ENCORE: a phase 4 observational study of cetuximab and platinum-based therapy (PBT) for the first-line treatment of patients with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN)	Le Tourneau C.	1068P	September 10 13:15-14:15	Hall 8
A survey of patient acceptance of skin toxicities from cetuximab-based therapy	Tischer B.	1579P	September 10 13:15-14:15	Hall 8

Title	Lead author	Abstract #	Presentation date/time (CEST)	Location
Tepotinib				
Poster session				
Final data from a phase Ib trial of tepotinib in Asian patients with advanced hepatocellular carcinoma (HCC)	Qin S.	701P	September 9 13:15-14:15	Hall 8

Title	Lead author	Abstract #	Presentation date/time (CEST)	Location
Anti-PD-L1/TGF-ß pathways				
Poster session				
Analysis of programmed death-ligand 1 (PD-L1) expression, transforming growth factor (TGF)-β gene expression	Zhang Y.	1645P	September 11 13:15-14:15	Hall 8

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signatures (GES) and tumor-infiltrating immune cells (IC) in hepatocellular carcinoma (HCC): rationale for targeting PD-L1- and TGF-β				

About avelumab
Avelumab is a human antibody specific for a protein called PD-L1, or programmed death ligand-1. Avelumab is designed to potentially engage both the adaptive and innate immune systems. By binding to PD-L1, avelumab is thought to prevent tumor cells from using PD-L1 for protection against white blood cells, such as T-cells, exposing them to anti-tumor responses. Avelumab has been shown to induce antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro. In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

****Indications in the US**
The U.S. Food and Drug Administration (FDA) granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) metastatic Merkel cell carcinoma (mMCC) in adults and pediatric patients 12 years and older and (ii) patients with locally advanced or metastatic urothelial carcinoma (UC) who have disease progression during or following platinum-containing chemotherapy, or who 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 not approved for any indication in any market outside the U.S.

Important Safety Information
The warnings and precautions for avelumab (BAVENCIO®) include immune-mediated adverse reactions (such as pneumonitis, hepatitis, colitis, endocrinopathies, nephritis and renal dysfunction and other adverse reactions), infusion-related reactions and embryo-fetal toxicity.

Common adverse reactions (reported in at least 20% of patients) in patients treated with avelumab for mMCC and patients with locally advanced or metastatic UC include fatigue, musculoskeletal pain, diarrhea, nausea, infusion-related reaction, peripheral edema, decreased appetite/hypophagia, urinary tract infection and rash.

About Erbitux® (cetuximab)
Erbitux® is a highly active 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. Erbitux also targets cytotoxic immune effector cells towards EGFR expressing tumor cells (antibody dependent cell-mediated cytotoxicity, ADCC).

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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 90 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.

About M6620
Also known as VX-970, M6620 is an investigational small-molecule inhibitor of ataxia telangiectasia and Rad3-related protein (ATR). ATR is a key sensor for DNA damage, activating the DNA damage checkpoint and leading to cell cycle arrest. It is thought that inhibition of ATR can enhance the efficacy of DNA-damaging agents, and could potentially also be efficacious as monotherapy against tumors with high levels of replication stress induced by overexpression of oncogenes. M6620 complements our strong DDR portfolio and is currently being investigated in Phase I and II trials.

About M2698
A potential first-in-class, investigational small-molecule that is designed to inhibit both p70S6K and Akt. Both targets are part of the phosphoinositide 3-kinase (PI3K) pathway, which is often dysregulated in solid tumors.

About tepotinib
Tepotinib is an investigational small-molecule inhibitor of the c-Met receptor tyrosine kinase. Alterations of the c-Met signaling pathway are found in various cancer types and correlate with aggressive tumor behavior and poor clinical prognosis. Tepotinib is being investigated in two Phase II studies in non-small cell lung cancer and hepatocellular carcinoma.

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About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 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 2016, Merck KGaA, Darmstadt, Germany, generated sales of € 15.0 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 except in the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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