News Release

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ASCO Abstract #
Avelumab: 9507, 9537, 9090, 9008, 8563, 3057, 4544, e21531, e13603, e18932, e21623, e21620, e21544; **tepotinib (c-Met kinase inhibitor):** 9082, 9016; **M6620 (ATR inhibitor):** 2549, e21048; **M3814 (DNA-PK):** 2518 **M7824 (TGF-ß trap/anti-PD-L1):** 3007, 9017, 2566; **M2698 (dual p70S6k/Akt inhibitor):** 2584

Merck KGaA, Darmstadt, Germany data at ASCO 2018 to showcase progress and further optionality of oncology pipeline

- **Two-year safety and efficacy data in mMCC for avelumab from pivotal JAVELIN Merkel 200 trial**
- **Early clinical activity in advanced NSCLC and HPV-associated cancers for investigational bifunctional immunotherapy, M7824**
- **Encouraging interim analysis of Phase II data in NSCLC sub-population for investigational c-Met inhibitor, tepotinib**
- **Record number of abstracts accepted across oncology, immuno-oncology and DNA Damage Response (DDR)**

Darmstadt, Germany, May 16, 2018 – 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 new data from a number of high priority clinical development programs across its oncology portfolio to be presented at this year's American Society of Clinical Oncology Annual Meeting (ASCO), June 1-5, 2018, Chicago IL. Abstracts representing seven therapeutic agents and eight tumor types will highlight the company's position as a key emerging player in oncology.

"This year's data at ASCO demonstrate the potential of our pipeline to really deliver transformative advancements in cancer care," said Luciano Rossetti, Executive Vice

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President, Head of Global Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "With our strong commitment and focus on the areas we believe in most, Merck KGaA, Darmstadt, Germany's oncology and immuno-oncology pipeline is demonstrating significant potential in the near term with our later-stage priority programs and, in parallel, our early pipeline includes truly innovative programs that could make a real difference for patients."

New data for avelumab (BAVENCIO®), which is being jointly developed and commercialized with Pfizer, include an oral presentation on two-year results from the pivotal JAVELIN Merkel 200 trial. These long-term results include data on avelumab's duration of response and represent the first study to report long-term survival data for an immunotherapy in metastatic Merkel cell carcinoma (mMCC).

The company will also present further evidence for M7824, an investigational TGF-ß trap/anti-PD-L1 bi-functional immunotherapy fusion protein, from expansion cohorts of the ongoing M7824 Phase I clinical trial (NCT02517398) program. TGF-β, a cytokine released by cells (including tumor cells), suppresses anti-tumor immune responses through a vast number of mechanisms leading to uninhibited tumor growth and metastasis. These data include results in patients with human papillomavirus (HPV)-associated cancers (presented in collaboration with the National Cancer Institute) and data in patients with advanced non-small cell lung cancer (NSCLC). In second-line (2L) NSCLC, signs of clinical activity were seen across PD-L1 expression levels. At the recommended phase II dose, a confirmed overall response rate (ORR) of 40.7% (11/27) was observed in PD-L1+ patients (≥1%), and in patients with high PD-L1 expression (80%; Ab clone 73-10 [>80% = >50% with 22C3]), the ORR was 71.4% (5/7). These data signal the potential of M7824 and provide evidence that combining a transforming growth factor-β (TGF-β) trap with the anti-PD-L1 mechanism in one molecule may generate anti-tumor activity in these patient groups with significant medical need. Treatment with M7824 was well tolerated in both studies and safety data were consistent with that observed in the overall Phase I clinical program. No new safety signals were identified.

For tepotinib**, an investigational small molecule inhibitor of the c-Met receptor tyrosine kinase, new data to be presented include promising initial results from an ongoing Phase II VISION study providing further indication for the potential of

tepotinib in patients living with advanced NSCLC harboring *MET* exon 14 skipping mutations. Alterations of the c-Met signaling pathway are found in various cancer types and correlate with aggressive tumor behavior and poor clinical prognosis. Based on investigator assessment of data from 15 patients in the study, 60% (9/15) had a confirmed partial response (PR) and 20% (3/15) had stable disease (SD.) In addition, independent assessment of 13 patients demonstrated treatment with tepotinib led to a confirmed PR in 46.2% (6/13) and SD in 7.7% (1/13) of patients. In this study, the safety data are consistent with that observed in previous studies and confirm that treatment with tepotinib is well tolerated; no new safety signals were identified.

Tepotinib is an important part of Merck KGaA, Darmstadt, Germany's strategic focus on precision medicines and these results reinforce the company's progress in delivering treatments to those patients more likely to benefit, in order to achieve the best possible outcomes. Both M7824 and tepotinib were discovered in-house at Merck KGaA, Darmstadt, Germany.

Further pipeline updates include Phase I dose escalation data for the investigational DNA-dependent protein kinase (DNA-PK) inhibitor M3814, Phase I triplet therapy with ATR-inhibitor, M6620 +veliparib+cisplatin in advanced solid tumors, and Phase I data for M2698, a potent and selective dual inhibitor of p70S6K and AKT1/3 in the PAM pathway (PI3K/AKT/mTOR pathway). The PAM pathway regulates cell survival and growth and this pathway often displays unusual activity in many human cancers.

Data for the legacy brand ERBITUX® continue to build on Merck KGaA, Darmstadt, Germany's heritage in oncology reinforcing its role as a standard of care in RAS wild-type metastatic colorectal cancer (mCRC), the standard of care in first-line recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN), and a standard of care 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 treatment of NSCLC, metastatic urothelial carcinoma (mUC), and mesothelioma, and has not been demonstrated to be safe and effective for these indications. There is no guarantee that avelumab will be approved for NSCLC, mUC, or mesothelioma by any health authority worldwide.

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

Tepotinib, M7824, M3814, M2698 and M6620 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

Accepted Merck KGaA, Darmstadt, Germany-supported key 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
Avelumab				
Oral Presentation				
Two-year efficacy and safety update from JAVELIN Merkel 200 part A: A registrational study of avelumab in metastatic Merkel cell carcinoma progressed on chemotherapy.	Paul Nghiem, MD, PhD	9507	Mon, Jun 04, 10:12 AM - 10:24 AM	Arie Crown Theater
Avelumab (anti–PD-L1) in combination with crizotinib or lorlatinib in patients with previously treated advanced NSCLC: Phase 1b results from JAVELIN Lung 101.	Alice Tsang Shaw, MD, PhD	9008	Fri, Jun 01, 4:30 PM - 4:42 PM	Hall D1
Poster Sessions				
Avelumab (anti–PD-L1) in patients with platinum-treated advanced NSCLC: 2.5-year follow-up from the JAVELIN Solid Tumor trial.	Arun Rajan, MD	9090	Sun, Jun 03, 8:00 AM - 11:30 AM	Hall A
Phase 1b study of avelumab in advanced previously treated mesothelioma: long-term follow-up from JAVELIN Solid Tumor.	Raffit Hassan, MD	8563	Sun, Jun 03, 8:00 AM - 11:30 AM	Hall A
Second-line avelumab treatment of patients (pts) with metastatic Merkel cell carcinoma (mMCC): Experience from a global expanded access program (EAP).	John WT Walker, MD, PhD	9537	Mon, Jun 04, 1:15 PM - 4:45 PM	Hall A
Association of efficacy and adverse events of special interest of avelumab in the JAVELIN solid tumor and JAVELIN Merkel 200 trials.	Karen Kelly, MD, FASCO	3057	Mon, Jun 04, 8:00 AM - 11:30 AM	Hall A

SPEAR-bladder (study informing treatment pathway decision in bladder cancer): First-through third-line time to treatment failure in the US.	Gurjyot K. Doshi, MD	4544	Sat, Jun 02, 8:00 AM - 11:30 AM	Hall A
Publications				
Avelumab in patients with previously treated metastatic melanoma: phase 1b results from the JAVELIN Solid Tumor trial	Keilholz U, Mehnert J, Bauer S, et al.	e21531		
Characteristics, treatment patterns and safety events From 4 cohorts of advanced or metastatic cancer patients based on healthcare claims data	Russo L, Esposito D, Lamy FX, et al.	e13603		
Healthcare resource use and expenditures among patients with Merkel cell carcinoma by level of comorbidity	Kearney M, Thokagevistk K, Boutmy E, et al.	e18932		
Projecting long-term survival for avelumab in patients with refractory Merkel cell carcinoma	Phatak H, Proskorovsky I, Lanitis T, et al.	e21623		
Predicting overall survival in patients (Pts) with treatment-naive metastatic Merkel cell carcinoma (mMCC) treated with avelumab	Bullement A, D'Angelo SP, Amin A, et al.	e21620		
A novel, open-access data commons for improved disease management in Merkel cell carcinoma patients	Murphy M, Sartor O, Bertagnolli M, et al.	e21544		

Title	Lead Author	Abstract #	Presentation Date / Time (CDT)	Location
M7824 (TGF β-trap/anti-PD-L1)				
Oral Presentation				
Safety and activity of M7824, a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients with HPV associated cancers.	Julius Strauss, MD	3007	Sat, Jun 02, 5:12 PM - 5:24 PM	Hall B1
Poster Discussion				
Results from a second-line (2L) NSCLC cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1.	Luis G. Paz-Ares, MD, PhD	9017	Sun, Jun 03, 11:30 AM - 12: 45 PM	Arie Crown Theatre
Poster Session				
Selection of the recommended phase 2 dose (RP2D) for M7824	Yulia Vugmeyster, PhD	2566	Mon, Jun 04, 8:00 AM - 11:30 AM	Hall A

(MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1.				

Title	Lead Author	Abstract #	Presentation Date / Time (CDT)	Location
Tepotinib				
Poster Discussion				
Tepotinib in patients with advanced non-small cell lung cancer (NSCLC) harboring *MET* exon 14-skipping mutations: Phase II trial.	Enriqueta Felip, MD	9016	Sun, Jun 03, 11:30 AM - 12:45 PM	Arie Crown Theater
Poster Session				
Can duration of response be used as a surrogate endpoint for overall survival in advanced non-small cell lung cancer?	Boris M Pfeiffer	9082	Sun, Jun 03, 8:00 AM - 11:30 AM	Hall A

Title	Lead Author	Abstract #	Presentation Date / Time (CDT)	Location
M2698				
Poster Session				
Precision oncology: Results of a phase I study of M2698, a p70S6K/AKT targeted agent in patients with advanced cancer and tumor PI3K/AKT/mTOR (PAM) pathway abnormalities.	Apostolia Maria Tsimberidou, MD, PhD	2584	Mon, Jun 04, 8:00 AM - 11:30 AM	Hall A

Title	Lead Author	Abstract #	Presentation Date / Time (CDT)	Location
M3814				
Poster Discussion				
A phase Ia/Ib trial of the DNA-PK inhibitor M3814 in combination with radiotherapy (RT) in patients (pts) with advanced solid tumors: Dose-escalation results.	Baukelien Van Triest, MD, PhD	2518	Mon, Jun 04, 3:00 PM - 4:15 PM	S406

Title	Lead Author	Abstract #	Presentation Date / Time (CDT)	Location
M6620				
Poster Discussion				
Phase I trial of the triplet M6620 (formerly VX970) + veliparib + cisplatin in patients with advanced solid tumors.	Geraldine Helen O'Sullivan Coyne, MD, PhD	2549	Mon, Jun 04, 8:00 AM - 11:30 AM	Hall A
Publication				

Safety and tolerability of intravenous M6620 (VX-970) administered with gemcitabine in subjects with advanced non-small cell lung cancer (NSCLC)	Plummer R, Cook N, Arkenau H-T, et al.	e21048	Mon, Jun 04, 8:00 AM - 11:30 AM	Hall A

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. Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via 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.

Approved Indications in the US

The 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

The warnings and precautions for 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 BAVENCIO for mMCC and patients with locally advanced or mUC 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).

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.

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 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 M2698
M2698 is an investigational small-molecule which is thought to inhibit p70S6K and Akt. Both targets are part of the PI3K/AKT/mTOR (PAM)pathway, which is often dysregulated in solid tumors.

About tepotinib
Tepotinib (MSC2156119J) 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 it is thought to correlate with aggressive tumor behavior and poor clinical prognosis.

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 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.