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Darmstadt, Germany

News Release

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Not intended for UK-based media

EMA's CHMP Issues Positive Opinion for Avelumab for the Treatment of Metastatic Merkel Cell Carcinoma

- **If approved, avelumab could be the first immunotherapy treatment indicated for this rare and aggressive skin cancer in the EU**
- **Decision by the EC is expected in the third quarter of 2017**

Darmstadt, Germany, and New York, US, July 21, 2017 – Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the U.S. and Canada, and Pfizer Inc. (NYSE: PFE) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended the approval of avelumab* (BAVENCIO®) as a monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (mMCC), a rare and aggressive skin cancer. The European Commission (EC) will now review the CHMP's recommendation, with a decision expected in the third quarter of 2017.

"We welcome the CHMP's recommendation, as there are currently no approved treatments in Europe for this type of skin cancer, which can be devastating for patients and their families," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "This is an important step towards making avelumab available to patients and we look forward to the European Commission's decision later this year."

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"Metastatic Merkel cell carcinoma is a devastating disease and patients in Europe currently have very few treatment options," said Chris Boshoff, M.D., PhD, Senior Vice President and Head of Immuno-Oncology, Early Development, Translational Oncology, Pfizer Global Product Development. "This milestone further demonstrates our commitment to tackle hard-to-treat cancers as we continue to explore the potential of avelumab in other tumors."

The CHMP positive opinion is based on data from JAVELIN Merkel 200, an international, multicenter, single-arm, open-label, Phase II study split into two parts:

- Part A included 88 patients with mMCC whose disease had progressed after at least one chemotherapy treatment, with 59% of patients reported to have had one prior anti-cancer therapy for mMCC and 41% had two or more prior therapies. Data submitted included a minimum of 18 months of follow-up.
- Part B, at the time of the data cut-off, included 39 patients with histologically confirmed mMCC who were treatment-naïve to systemic therapy in metastatic setting, 29 of whom had at least 13 weeks of follow-up. Enrolment in Part B of the study is ongoing and is planned to include 112 treatment-naïve patients.

The human anti-PD-L1 antibody, avelumab, previously received Orphan Drug Designation (ODD) from the EC for MCC. To qualify for ODD in the EU, a medicine must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating, and has a prevalence in the EU of not more than 5 in 10,000 people.

The US Food and Drug Administration (FDA) granted accelerated approval for avelumab in March 2017 for the treatment of mMCC in adults and pediatric patients 12 years and older; and in May 2017 for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy therapy, or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.[1] These indications were granted under accelerated approval based on tumor response rate and duration of response data/criteria. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

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The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and more than 6,000 patients evaluated across more than 15 different tumor types. In addition to mMCC, these cancers include breast, gastric/gastro-esophageal junction, head and neck, Hodgkin's lymphoma, melanoma, mesothelioma, non-small cell lung, ovarian, renal cell carcinoma and urothelial carcinoma.

* Avelumab is not approved for any indication in any market outside the US. BAVENCIO® is the proprietary name submitted to EMA for the investigational medicine avelumab.

About Metastatic Merkel Cell Carcinoma

Metastatic MCC is a rare and aggressive disease in which cancer cells form in the top layer of the skin, close to nerve endings.[2,3] MCC, which is also known as neuroendocrine carcinoma of the skin or trabecular cancer, often starts in those areas of skin that are most often exposed to the sun, including the head and neck, and arms.[2,4] Risk factors for MCC include sun exposure and infection with Merkel cell polyomavirus. Caucasian males older than 50 are at increased risk.[2,4] MCC is a highly immunogenic cancer, meaning that those with a weak immune system (i.e., solid organ transplant recipients, people with HIV/AIDS and people with other cancers, such as chronic lymphocytic leukemia) are also at a higher risk.[2,4] MCC is often misdiagnosed for other skin cancers and grows at an exponential rate on chronically sun-damaged skin.[4-6] Current treatment options for MCC in Europe include surgery, radiation and chemotherapy.[3] Treatment for metastatic or Stage IV MCC is generally palliative.[3]

About JAVELIN Merkel 200

The efficacy and safety of avelumab was demonstrated in the JAVELIN Merkel 200 trial, an international, multicenter, single-arm, open-label, Phase II study split into two parts:

- Part A was conducted in 88 patients with histologically confirmed mMCC whose disease had progressed on or after chemotherapy administered for distant metastatic disease, with life expectancy of more than 3 months. Overall, in Part A, 59% of patients were reported to have had one prior anti-cancer therapy for mMCC and 41% had two or more prior therapies. Data submitted included a minimum of 18 months follow-up. The major efficacy outcome

measures for Part A were confirmed best overall response (BOR) and duration of response (DOR), according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, as assessed by a blinded independent endpoint review committee (IERC); secondary efficacy outcome measures included duration of response (DOR), and progression-free survival (PFS).

- Part B, at the time of the data cut-off, included 39 patients with histologically confirmed mMCC who were treatment-naïve to systemic therapy in the metastatic setting, 29 of whom had at least 13 weeks of follow-up. Enrolment in Part B of the study is ongoing and is planned to include 112 treatment-naïve patients. The major efficacy outcome measure is durable response, defined as objective response (complete response [CR] or partial response [PR]) with a duration of at least 6 months; secondary outcome measures include BOR, DOR, progression-free survival (PFS) and overall survival (OS).

The trial excluded patients with active or a history of central nervous system (CNS) metastasis, active or a history of autoimmune disease, a history of other malignancies within the last 5 years, organ transplant, and conditions requiring therapeutic immune suppression or active infection with HIV, or hepatitis B or C. Patients received avelumab 10 mg/kg as an intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.

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

The US Food and Drug Administration (FDA) granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) mMCC in adults and pediatric patients 12 years and older and (ii) patients with locally advanced or metastatic 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 were 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 and INDICATIONS

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 re-initiation 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 anti-hyperglycemics 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 1738 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%).

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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 cancer (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%), gamma-glutamyltransferase increased (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.

Alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US
Immuno-oncology is a top priority for Merck KGaA, Darmstadt, Germany, and Pfizer Inc. The global strategic alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US, enables the companies to benefit from each other's strengths and capabilities and further explore the therapeutic potential of avelumab, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance will jointly develop and commercialize avelumab and advance Pfizer's PD-1 antibody. The alliance is focused on developing high-priority international clinical programs to investigate avelumab as a monotherapy, as well as in combination regimens, and is striving to find new ways to treat cancer.

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, operates as EMD Serono, MilliporeSigma and EMD Performance Materials in the United States and Canada.

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Pfizer Inc.: Working together for a healthier world®
At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of healthcare products. Our global portfolio includes medicines and vaccines, as well as many of the world's best-known consumer healthcare products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice
The information contained in this release is as of July 21, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about BAVENCIO (avelumab), including a potential indication in the EU as a monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (the "potential indication"), the Merck KGaA, Darmstadt, Germany-Pfizer Alliance involving anti-PD-L1 and anti-PD-1 therapies, and clinical development plans, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of BAVENCIO; the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable study results, including unfavorable new clinical data and additional analyses of existing clinical data; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether and when any other drug applications may be filed in any jurisdictions for potential indications for BAVENCIO, combination therapies or other product candidates; whether and when the European Commission may approve the pending marketing authorization application for the potential indication and whether and when regulatory authorities in any other jurisdictions where applications are pending or may be submitted for BAVENCIO, combination therapies or other product candidates may approve any such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of BAVENCIO, combination therapies or other product candidates; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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