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News Release

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Not intended for UK-based media

European Commission Approves Bavencio (Avelumab) for Metastatic Merkel Cell Carcinoma

- **First approved immunotherapy for rare and aggressive skin cancer in the European Union, with initial launches planned in Germany and the UK**
- **Builds on Bavencio's previous accelerated approvals in the US and recent approval in Switzerland**
- **Approval based on data from Javelin Merkel 200 study including durable tumor response rate and duration of response**

Darmstadt, Germany, and New York, US, September 21, 2017 – Merck KGaA, Darmstadt, Germany and Pfizer Inc. (NYSE: PFE) today announced that the European Commission (EC) has granted marketing authorization for BAVENCIO® (avelumab) as a monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (mMCC), a rare and aggressive skin cancer.[1] BAVENCIO will have marketing authorization in the 28 countries of the European Union (EU) in addition to Norway, Liechtenstein and Iceland. BAVENCIO is expected to become commercially available to patients in Europe by prescription within the coming months, with initial launches in Germany and UK expected as early as October 2017.

"The EC's decision is significant for BAVENCIO and, more importantly, for European patients living with this very challenging skin cancer," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany, which operates as EMD Serono in the

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US and Canada. “Our alliance with Pfizer continues to demonstrate the power of working together, and we are grateful to everyone who has helped to bring the first and only approved immunotherapy for mMCC to European patients.”

“This European approval further establishes our continued momentum, building on the accelerated approvals BAVENCIO received in the US earlier this year,” said Liz Barrett, Global President, Pfizer Oncology. “Importantly, we are now one step closer to our goal of making BAVENCIO available to patients around the world.”

Approximately 2,500 Europeans are affected by MCC each year, with metastatic disease diagnosed in 5–12% of patients with MCC. Fewer than 20% of patients with metastatic MCC survive beyond 5 years. [2-6]

“Merkel cell carcinoma is a particularly aggressive form of skin cancer with very poor outcomes, especially for those with metastatic disease,” said Dirk Schadendorf, MD, Director of Dermatology, University Hospital Essen, Germany. “This approval is a meaningful development for patients and their families suffering from this devastating disease.”

The EC approval is based on data from JAVELIN Merkel 200, an international, multicenter, single-arm, open-label, Phase II study; with two parts:[1]

- Part A included 88 patients with mMCC whose disease had progressed after at least one chemotherapy treatment. The objective response rate was 33%, with 11% of patients experiencing a complete response and 22% of patients experiencing a partial response. At the time of analysis, tumor responses were durable, with 93% of responses lasting at least 6 months (n=25) and 71% of responses lasting at least 12 months (n=13). Duration of response (DOR) ranged from 2.8 to more than 24.9 months.
- 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. The objective response rate was 62%, with 14% of patients experiencing a complete response (CR) and 48% of patients experiencing a partial response (PR). Sixty-seven percent of patients experienced a progression-free survival (PFS) rate of 3 months.

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The safety of avelumab has been evaluated in 1,738 patients with solid tumours including metastatic MCC (N=88) receiving 10 mg/kg every 2 weeks of avelumab in clinical studies.[1]

- 1,738 patients with solid tumors received 10 mg/kg every 2 weeks. In this patient population, the most common adverse reactions were fatigue (32.4%), nausea (25.1%), diarrhea (18.9%), decreased appetite (18.4%), constipation (18.4%), infusion-related reactions (17.1%), weight decreased (16.6%), and vomiting (16.2%). The most common Grade ≥ 3 adverse reactions were anaemia (6.0%), dyspnoea (3.9%), and abdominal pain (3.0%). Serious adverse reactions were immune-related adverse reactions and infusion-related reaction.

The EC's decision follows the US Food and Drug Administration's (FDA) accelerated approval* for BAVENCIO earlier this year for the treatment of mMCC and patients with locally advanced or metastatic urothelial carcinoma (UC) who have disease progression during or following platinum-containing chemotherapy. BAVENCIO was also granted marketing authorization by Swissmedic on September 05, 2017, in Switzerland for the treatment of patients with mMCC, whose disease has progressed after at least one chemotherapy treatment.

The clinical development program for BAVENCIO, known as JAVELIN, involves at least 30 clinical programs and more than 6,300 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, emelanoma, mesothelioma, non-small cell lung, ovarian, renal cell carcinoma and urothelial carcinoma.

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.[7-8] 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.[8,10] Risk factors for MCC include sun exposure and infection with Merkel cell polyomavirus. Caucasian males older than 50 are at increased risk.[8,10] MCC is often misdiagnosed as other skin cancers and grows at an exponential rate on chronically

sun-damaged skin.[11-14] Current treatment options for MCC in Europe include surgery, radiation and chemotherapy.[15] Treatment for metastatic or Stage IV MCC is generally palliative.[16]

About JAVELIN Merkel 200

The efficacy and safety of BAVENCIO was demonstrated in the JAVELIN Merkel 200 trial, a Phase II, open-label, single-arm, multicenter study, split into two parts:[1]

- 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, and a minimum follow-up of 18 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. The major efficacy outcome measures for Part A were confirmed best overall response (BOR) and DOR, according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, as assessed by a blinded independent endpoint review committee (IERC).
- Part B, at the time of the data cut-off, included 39 patients with histologically confirmed mMCC who were treatment-naïve to systemic therapy, 29 of whom had at least 13 weeks of follow-up. Enrollment in Part B of the study is ongoing and is planned to include 112 treatment-naïve patients. For Part B, the major efficacy outcome measure is durable response, defined as objective response (CR or PR) with a duration of at least 6 months; secondary outcome measures include BOR, DOR, PFS and overall survival (OS).

The trial excluded patients with active or a history of central nervous system metastasis, prior treatment with anti-PD-1, anti-PD-L1, or anti-CTLA-4 antibodies, 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 BAVENCIO 10 mg/kg as an intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.

About BAVENCIO

BAVENCIO® (avelumab) is a human antibody specific for a protein called PD-L1, or programmed death ligand-1. BAVENCIO is designed to potentially engage both the adaptive and innate immune systems. By binding to PD-L1, BAVENCIO 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. BAVENCIO 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 BAVENCIO.

***Indications in the US**[16]

The US Food and Drug Administration (FDA) granted accelerated approval for BAVENCIO for the treatment of (i) 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 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

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.

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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 antihyperglycemics or insulin in patients with severe or life-threatening (Grade 3 equal to or greater) 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 one 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 one 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, greater than or equal to 20%) in patients with **metastatic Merkel cell carcinoma (MCC)** were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reactions (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

Selected treatment-emergent laboratory abnormalities (all grades, greater than or equal to 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 greater than or equal to 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, greater than or equal to 3%) inpatients with **locally advanced or metastatic UC** were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatatse (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

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

Alliance between Merck KGaA, Darmstadt, Germay, 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.

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

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 September 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 new indication in the EU as a monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma 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 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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