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FDA Grants BAVENCIO® (avelumab) Approval for a Common Type of Advanced Bladder Cancer

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Second approval for BAVENCIO in less than two months Advanced urothelial carcinoma is an aggressive disease with a high rate of recurrence

EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the US and Canada, and Pfizer Inc. (NYSE: PFE) today announced that the US Food and Drug Administration (FDA) has approved BAVENCIO® (avelumab) Injection for the treatment of 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. BAVENCIO was previously granted accelerated approval from the FDA for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC). These indications are approved under accelerated approval based on tumor response and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.[1]

"This approval for BAVENCIO in patients with locally advanced or metastatic urothelial carcinoma exemplifies our unwavering commitment to finding new treatments for the most challenging cancers," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "Coming just a few weeks after the approval for metastatic Merkel cell carcinoma, we continue to demonstrate our ability to accelerate access to innovative medicines for patients in need."

"This approval builds on the ongoing clinical development program for BAVENCIO in urothelial carcinoma and reinforces our commitment to providing new medicines to patients with difficult-to-treat cancers," said Liz Barrett, Global President, Pfizer Oncology. "By drawing on the strength of the alliance, as well as Pfizer's deep experience in genitourinary cancers, we believe BAVENCIO will be an important treatment option, and we hope it will help to improve outcomes for these patients."

Bladder cancer makes up approximately 90% of urothelial carcinomas and is the sixth most common cancer in the US.[2,3] When the disease has metastasized, the five-year survival rate is approximately 5%.[4] Despite advances in the treatment of locally advanced or metastatic urothelial carcinoma, the prognosis for patients remains poor and more treatment options are needed.[2]

"Once urothelial carcinoma progresses after treatment with chemotherapy, the five-year survival rate is alarmingly low," said Dr. Andrea Apolo, National Cancer Institute, Bethesda, MD, US. "Until recently, there had been limited innovation in urothelial carcinoma, and this approval gives us another treatment to help battle this aggressive disease."

The efficacy and safety of BAVENCIO was demonstrated in the urothelial carcinoma cohorts (N=242) of the JAVELIN Solid Tumor trial, a Phase I, open-label, single-arm, multicenter study of BAVENCIO in the treatment of various solid tumors. The urothelial carcinoma cohorts enrolled patients with locally advanced or metastatic urothelial carcinoma with disease progression on or after platinum-containing chemotherapy or who had disease progression within 12 months of treatment with a platinum-containing neoadjuvant or adjuvant chemotherapy regimen. These data will be presented at an upcoming medical congress.

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. The most common adverse reactions (reported in at least 20% of patients) in patients with locally advanced or metastatic urothelial carcinoma were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%) and urinary tract infection (21%).1 For more information, please see Important Safety Information for BAVENCIO below.

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.[1] BAVENCIO has also been shown to induce antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.[1]

The alliance is committed to providing industry-leading patient access and reimbursement support through its CoverOne™ program. This program provides a spectrum of patient access and reimbursement support services intended to help patients receive appropriate access to BAVENCIO in the United States. CoverOne may be reached by phone at 844-8COVER1 (844-826-8371) or online at www.CoverOne.com.

About Urothelial Carcinoma Cohorts in JAVELIN Solid Tumor Trial The efficacy and safety of BAVENCIO was demonstrated in the urothelial carcinoma cohorts of the JAVELIN Solid Tumor trial, a Phase I, open-label, single-arm, multicenter study that included 242 patients with locally advanced or metastatic urothelial carcinoma with disease progression on or after platinum- containing chemotherapy or who had disease progression within 12 months of treatment with a platinum-containing neoadjuvant or adjuvant chemotherapy regimen who were treated with BAVENCIO.

Patients with active or a history of central nervous system metastasis; other malignancies within the last five years; an organ transplant; conditions requiring therapeutic immune suppression; or active infection with HIV, hepatitis B or C were excluded. Patients with autoimmune disease, other than type 1 diabetes, vitiligo, psoriasis, or thyroid disease that did not require immunosuppressive treatment, were excluded. Patients were included regardless of their PD-L1 status. Patients received BAVENCIO at a dose of 10 mg/kg intravenously over 60 minutes every two weeks until disease progression or unacceptable toxicity. Tumor response assessments were performed every six weeks, as assessed by an Independent Endpoint Review Committee (IERC) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Efficacy outcome measures included confirmed overall response rate, (ORR) and duration of response (DOR). Efficacy measures were evaluated in patients who were followed for a minimum of both 13 weeks and 6 months at the time of data cut-off.

Out of the total 226 patients evaluable for efficacy, 44% had non-bladder urothelial carcinoma, including 23% of patients with upper tract disease; 83% of patients had visceral metastases; 34% of patients had liver metastases. Nine patients (4%) had disease progression following prior platinum-containing neoadjuvant or adjuvant therapy only. Forty-seven percent of patients only received prior cisplatin-based regimens, 32% received only prior carboplatin-based regimens, and 20% received both cisplatin and carboplatin-based regimens.

The international clinical development program for avelumab, known as JAVELIN, involves more than 30 clinical programs, including nine Phase III trials, and more than 5,200 patients across more than 15 tumor types.

In December 2015, Merck KGaA, Darmstadt, Germany and Pfizer announced the initiation of a Phase III multicenter, multinational, randomized, open-label, parallel-arm study (JAVELIN Bladder 100) of BAVENCIO plus best supportive care versus best supportive care alone as a maintenance treatment in patients with locally advanced or metastatic urothelial carcinoma whose disease did not progress after completion of first-line platinum-containing chemotherapy. This trial is currently enrolling patients.

For more information about JAVELIN trials, please visit www.clinicaltrials.gov.

For full prescribing information and medication guide for BAVENCIO, please see www.BAVENCIO.com.

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%).

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%).

INDICATIONS

BAVENCIO is indicated for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC).

BAVENCIO is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) 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 and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Please see full Prescribing Information and Medication Guide.

Avelumab has not yet been approved for any indication in any market outside of the US. As announced on October 31, 2016, the European Medicines Agency (EMA) has validated for review Merck KGaA, Darmstadt, Germany's Marketing Authorization Application for avelumab, for the proposed indication of metastatic Merkel cell carcinoma.

About BAVENCIO® (avelumab) BAVENCIO is a human programmed death ligand-1 (PD-L1) blocking antibody indicated in the US for the treatment of patients with locally advanced or metastatic urothelial carcinoma 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, as well as for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma.[1] These indications are approved under accelerated approval based on tumor response and duration of response. Continued approval for these indications is contingent upon verification and description of clinical benefit in confirmatory trials.

BAVENCIO is not approved for any indication in any market outside the US.

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 EMD Serono, Inc. EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany – a leading science and technology company – in the US and Canada focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-

leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,200 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Merck KGaA, Darmstadt, Germany All Merck KGaA, Darmstadt, Germany Press Releases are distributed by e-mail at the same time they become available on the Merck KGaA, Darmstadt, Germany Website. Please go to www.emdgroup.com/subscribe to register online, change your selection or discontinue this service.

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.

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 health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care 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, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @PfizerNews, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice

The information contained in this release is as of May 9, 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), the alliance between Merck KGaA, Darmstadt, Germany and Pfizer 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 drug applications may be filed in any other jurisdictions for the Indication or in any jurisdictions for any other potential indications for BAVENCIO, combination therapies or other product candidates; whether and when any such applications (including the pending application for BAVENCIO for metastatic Merkel cell carcinoma in the EU) may be approved by regulatory authorities, 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.

References

1. BAVENCIO Prescribing Information. Rockland, MA: EMD Serono Inc.; 2017.

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