



## News Release

### Your Contacts

#### **Merck KGaA, Darmstadt, Germany**

Contact +1 781 427 4351  
noelle.piscitelli@emdserono.com  
Investor Relations +49 6151 72 3321  
investor.relations@emdgroup.com

#### **Pfizer Inc., New York, USA**

Media Jessica Smith +1 212 733 6213  
Investor Relations Ryan Crowe +1 212 733 8160

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### **Not intended for UK-based media**

## **Exploratory Analysis Reports Efficacy and Safety of BAVENCIO® (avelumab) Over Three Years in Previously Treated Metastatic Merkel Cell Carcinoma**

- **32% of patients were alive at three years; median duration of response was 40.5 months<sup>1</sup>**
- **Data represent the longest prospective follow-up for an immune checkpoint inhibitor in patients with mMCC,<sup>1</sup> a rare and aggressive type of skin cancer<sup>2</sup>**

Darmstadt, Germany and New York, NY, October 22, 2019 – Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the US and Canada, and Pfizer Inc. (NYSE: PFE) today announced three-year results from Part A of the pivotal Phase II JAVELIN Merkel 200 trial regarding long-term overall survival and durable responses in patients with previously treated metastatic Merkel cell carcinoma (mMCC) who received avelumab (BAVENCIO®).<sup>1</sup> In this exploratory analysis, the overall survival (OS) rate at three years was 32%; the median duration of response (DOR) was 40.5 months; and the objective response rate (ORR) was 33.0%, which was unchanged from the one-year analysis.<sup>1</sup> These data will be presented at the First International Symposium on Merkel Cell Carcinoma in Tampa, Florida on October 21-22, 2019.

“Historically, chemotherapy has been the only treatment for advanced Merkel cell carcinoma, with responses lasting for less than one year. In this updated analysis of the JAVELIN Merkel 200 trial, up to one-third of patients with this disease who received avelumab were alive at three years,” said Sandra P. D’Angelo, M.D., study global principal investigator, medical oncologist at Memorial Sloan Kettering Cancer Center. “The durability of clinical response and survival outcomes from avelumab treatment in this setting with three years of follow-up underscore the benefits of this medicine in the treatment of patients with metastatic Merkel cell carcinoma.”

Results from the Phase II, open-label, single-arm, multicenter JAVELIN Merkel 200 study supported the U.S. Food and Drug Administration (FDA) accelerated approval of BAVENCIO for mMCC in 2017. The analysis presented today shows that with a minimum follow-up of 36 months and a median follow-up of 40.8 months (range: 36.4–49.7), the ORR was 33.0% (95% CI: 23.3%, 43.8%) and median DOR was 40.5 months (95% CI: 18.0, NE). Among the 11.4% (10/88) of patients with complete responses (CR), half (n=5) had an ongoing response at the data cutoff. Progression-free survival (PFS) rates were 26% (95% CI: 17%, 36%) at two years and 21% (95% CI: 12%, 32%) at three years. Median OS was 12.6 months (95% CI: 7.5, 17.1), and OS rates were 36% (95% CI: 26%, 46%) at two years and 32% (95% CI: 23%, 42%) at three years.<sup>1</sup> An analysis of OS compared to historical control data was not part of this analysis.

No unanticipated adverse events (AEs) or late infusion-related reactions occurred with long-term treatment. Treatment-related AEs of any grade occurred in 77.3% of patients (grade  $\geq 3$  in 11.4%); 21.6% had an immune-related AE of any grade (grade  $\geq 3$  in 4.5%).<sup>1</sup>

### **About JAVELIN Merkel 200**

JAVELIN Merkel 200 is a Phase II, open-label, single-arm, multicenter study. Part A included 88 patients with Stage IV mMCC whose disease had progressed on or after chemotherapy administered for distant metastatic disease. The primary endpoint in Part A was best overall response (BOR) by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as assessed by a blinded independent central review committee (IRC);

secondary endpoints included IRC-assessed DOR and PFS by RECIST 1.1; OS; and safety and tolerability. Part B included 116 patients with mMCC who were treatment-naïve to systemic therapy in the metastatic setting. For Part B, the major efficacy outcome measure was durable response, defined as objective response (complete response or partial response) with a duration of at least six months; secondary outcome measures included BOR, DOR, PFS and OS. Patients received BAVENCIO 10 mg/kg as an intravenous infusion over 60 minutes every two weeks until disease progression or unacceptable toxicity.<sup>1</sup>

### **About 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.<sup>2,3</sup> 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, neck and arms.<sup>4,5</sup> Risk factors for MCC include sun exposure and infection with Merkel cell polyomavirus.<sup>6</sup> Caucasian males older than 50 are at increased risk.<sup>7</sup> MCC is often misdiagnosed as other skin cancers and grows at an exponential rate on chronically sun-damaged skin.<sup>5,8</sup>

### **About BAVENCIO® (avelumab)**

BAVENCIO is a human anti-programmed death ligand-1 (PD-L1) antibody. BAVENCIO 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, BAVENCIO has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.<sup>9-11</sup> BAVENCIO has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.<sup>11-13</sup> In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

### **BAVENCIO Approved Indications**

In the US, the FDA granted accelerated approval for 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.

Avelumab is currently approved for patients with MCC in more than 50 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

BAVENCIO® (avelumab) in combination with axitinib is indicated in the US for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

**BAVENCIO Important Safety Information from the US FDA-Approved Label**

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% 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 **hepatotoxicity and 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 occurred with BAVENCIO as a single agent in 0.9% of patients, including two (0.1%) patients with Grade 5, and 11 (0.6%) with Grade 3.

*BAVENCIO in combination with axitinib* can cause **hepatotoxicity** with higher than expected frequencies of Grade 3 and 4 alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevation. Consider more frequent monitoring of liver enzymes as compared to when the drugs are used as monotherapy. Withhold BAVENCIO and axitinib for moderate (Grade 2) hepatotoxicity and permanently discontinue the combination for severe or life-threatening (Grade 3 or 4) hepatotoxicity. Administer corticosteroids as needed. In patients treated with BAVENCIO in combination with axitinib, Grades 3 and 4 increased ALT and AST occurred in 9% and 7% of patients, respectively, and immune-mediated hepatitis occurred in 7% of patients, including 4.9% with Grade 3 or 4.

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 until resolution. Permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% 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% 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% 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  $\geq 3$ ) hyperglycemia, and resume treatment when metabolic control is achieved. Type 1 diabetes mellitus without an alternative etiology occurred in 0.1% 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% 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 as a single agent or in 489 patients who received *BAVENCIO in combination with axitinib*: myocarditis including fatal cases, pancreatitis including fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis,

erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe or life-threatening **infusion-related reactions**. Premedicate patients with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent infusions 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% of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

*BAVENCIO in combination with axitinib* can cause **major adverse cardiovascular events (MACE)** including severe and fatal events. Consider baseline and periodic evaluations of left ventricular ejection fraction. Monitor for signs and symptoms of cardiovascular events. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue BAVENCIO and axitinib for Grade 3-4 cardiovascular events. MACE occurred in 7% of patients with advanced RCC treated with BAVENCIO in combination with axitinib compared to 3.4% treated with sunitinib. These events included death due to cardiac events (1.4%), Grade 3-4 myocardial infarction (2.8%), and Grade 3-4 congestive heart failure (1.8%).

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,  $\geq 20\%$ ) 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,  $\geq 20\%$ ) 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,  $\geq 20\%$ ) 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,  $\geq 3\%$ ) in patients with locally advanced or metastatic UC were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

Fatal adverse reactions occurred in 1.8% of patients with advanced renal cell carcinoma (RCC) receiving BAVENCIO in combination with axitinib. These included sudden cardiac death (1.2%), stroke (0.2%), myocarditis (0.2%), and necrotizing pancreatitis (0.2%).

The most common adverse reactions (all grades,  $\geq 20\%$ ) in patients with advanced RCC receiving BAVENCIO in combination with axitinib (vs sunitinib) were diarrhea (62% vs 48%), fatigue (53% vs 54%), hypertension (50% vs 36%), musculoskeletal pain (40% vs 33%), nausea (34% vs 39%), mucositis (34% vs 35%), palmar-plantar erythrodysesthesia (33% vs 34%), dysphonia (31% vs 3.2%), decreased appetite (26% vs 29%), hypothyroidism (25% vs 14%), rash (25% vs 16%), hepatotoxicity

(24% vs 18%), cough (23% vs 19%), dyspnea (23% vs 16%), abdominal pain (22% vs 19%), and headache (21% vs 16%).

Selected laboratory abnormalities (all grades,  $\geq 20\%$ ) worsening from baseline in patients with advanced RCC receiving BAVENCIO in combination with axitinib (vs sunitinib) were blood triglycerides increased (71% vs 48%), blood creatinine increased (62% vs 68%), blood cholesterol increased (57% vs 22%), alanine aminotransferase increased (ALT) (50% vs 46%), aspartate aminotransferase increased (AST) (47% vs 57%), blood sodium decreased (38% vs 37%), lipase increased (37% vs 25%), blood potassium increased (35% vs 28%), platelet count decreased (27% vs 80%), blood bilirubin increased (21% vs 23%), and hemoglobin decreased (21% vs 65%).

Please see full [US Prescribing Information](#) and [Medication Guide](#) available at <http://www.BAVENCIO.com>.

#### **About Merck KGaA, Darmstadt, Germany-Pfizer Alliance**

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

All Merck KGaA, Darmstadt, Germany, press releases are distributed by e-mail at the same time they become available on the EMD Group Website. In case you are a resident of the USA or Canada please go to [www.emdgroup.com/subscribe](http://www.emdgroup.com/subscribe) to register again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

#### **About Merck KGaA, Darmstadt, Germany**

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 56,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2018, Merck KGaA, Darmstadt, Germany, generated sales of € 14.8 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

#### **Pfizer Inc.: Breakthroughs that change patients' lives**



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, including innovative medicines and vaccines. 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](http://www.pfizer.com). In addition, to learn more, please visit us on [www.pfizer.com](http://www.pfizer.com) and follow us on Twitter at [@Pfizer](https://twitter.com/Pfizer) and [@Pfizer\\_News](https://twitter.com/Pfizer_News), [LinkedIn](https://www.linkedin.com/company/pfizer), [YouTube](https://www.youtube.com/Pfizer) and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

#### **Pfizer Disclosure Notice**

The information contained in this release is as of October 22, 2019. 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 BAVENCIO 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 endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed for BAVENCIO in any jurisdictions for potential indications for BAVENCIO or combination therapies or other product candidates; whether and when regulatory authorities in any jurisdictions where applications are pending or may be submitted for BAVENCIO or combination therapies or other product candidates may approve any such applications, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy, and, if approved, whether they will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of BAVENCIO or 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, 2018, 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](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

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