



# Two-Year Update of Pivotal JAVELIN Merkel 200 Trial Shows Continued Durable Responses with BAVENCIO® (avelumab)

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Two-year follow-up data on meaningful durable responses, overall survival (OS) and progression-free survival (PFS) to be presented in patients with metastatic Merkel cell carcinoma (mMCC), a rare and aggressive type of skin cancer

Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the US and Canada, and Pfizer Inc. (NYSE: PFE) today announced that updated efficacy and safety data from the pivotal JAVELIN Merkel 200 trial of BAVENCIO® (avelumab) in patients with metastatic Merkel cell carcinoma (mMCC), will be presented as an oral abstract session at the 54th American Society of Clinical Oncology (ASCO) Annual Meeting on Monday, June 4 from 10:12-10:24 a.m. CDT in Chicago, IL. At this two year follow-up update of the pivotal study, BAVENCIO continues to demonstrate clinically meaningful durable responses and stable rates of progression-free survival (PFS) and overall survival (OS) from previous analyses in patients who responded to this treatment. Clinical activity was observed across all patient subgroups, irrespective of PD-L1 expression in tumor tissue or Merkel cell polyomavirus status. The safety profile for BAVENCIO in this trial has not changed with longer follow-up and remains consistent with that observed in the overall JAVELIN clinical development program.

"These efficacy and safety results build upon the data that supported our FDA approval," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany. "Alongside our other data at ASCO, this two-year analysis is a significant advance in our understanding of the utility of BAVENCIO in MCC patients."

In JAVELIN Merkel 200 - an open-label, single-arm Phase II study - patients with histologically confirmed mMCC whose disease had progressed on or after chemotherapy administered for distant metastatic disease received BAVENCIO 10 mg/kg intravenously every two weeks until disease progression or unacceptable toxicity. Eighty-eight patients were followed for a median of 29.2 months (range 24.8-38.1 months). The confirmed overall response rate (ORR) of 33% (95% confidence interval [CI] 23.3-43.8; complete response in 11.4%) remained unchanged from previous analyses reported at both one year and 18 months. Responses remained ongoing in 19 of 29 patients who responded to treatment, including 12 patients whose duration of response exceeded two years. Durable responses led to stable rates of PFS (29% at 12 months, 29% at 18 months and 26% at 24 months). Median OS was 12.6 months (95% CI 7.5-17.1) and the two-year OS rate was 36% (50% at 12 months and 39% at 18 months). With a minimum follow-up of two years, no new safety signals were identified for BAVENCIO and was consistent with prior reports. Sixty-seven patients (76.1%) had a treatment-related adverse event (TRAE), 10 patients (11.4%) had a Grade 3 or less TRAE and 20 patients (22.7%) had an immune-related adverse event. No treatment-related deaths occurred.

"These results represent a key milestone for patients with mMCC, as chemotherapy has historically been the only treatment option for this devastating disease," said Chris Boshoff, M.D., Ph.D., Senior Vice President and Head of Immuno-Oncology, Early Development and Translational Oncology, Pfizer Global Product Development. "These data, alongside the additional real-world data which are also being presented at ASCO, strengthen our confidence in BAVENCIO as a treatment option for this rare and aggressive skin cancer."

In addition to these updated JAVELIN Merkel 200 data, results from a global expanded access program for BAVENCIO as a second-line treatment for patients with mMCC will be presented. These data will be presented during a poster session on Monday, June 4 from 1:15-4:45 p.m. CDT.

The alliance's JAVELIN clinical development program involves at least 30 clinical programs, including seven Phase III trials, and nearly 8,300 patients across more than 15 tumor types.

BAVENCIO® (avelumab) was first approved in the US in 2017 by the US Food and Drug Administration (FDA) for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC). In addition to the FDA accelerated approval in mMCC, avelumab is also approved in the US under accelerated approval 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. 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.

### **About JAVELIN Merkel 200**

JAVELIN Merkel 200 is an international, multicenter, open-label, single-arm Phase II study of BAVENCIO conducted in 88 patients with metastatic MCC. Patients in this study were generally elderly (median age was 72.5 years, range 33-88 years) and pre-treated, with at least one line of chemotherapy (one [59.1%], two [29.5%] or three or more [11.4%] previous treatments). Patients received BAVENCIO 10 mg/kg intravenously once every two weeks. The protocol-defined analysis set for efficacy and safety consisted of all patients who received at least one dose of study treatment. The cut-off date for the planned primary analysis was six months after start of study treatment of the last patient. The primary endpoint of the study was confirmed best overall response according to RECIST v1.1 and assessed by an independent review committee. Secondary endpoints were duration of response, PFS, OS, response status by RECIST at six and 12 months, safety and tolerability, pharmacokinetics, and immunogenicity of BAVENCIO.

### **About Avelumab**

Avelumab is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.[2]-[4] Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.[4]-[6] In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

### **Approved Indications in the US**

The FDA granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with

platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

### **Important Safety Information from the US FDA Approval 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% (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 reinitiation 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  $\geq 3$ ) 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 1,738 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,  $\geq 20\%$ ) 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%).

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

## **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. 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 avelumab, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance is jointly developing and commercializing avelumab and advancing 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 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. Almost 53,000 employees work to further develop technologies that improve and enhance life - from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries. Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany holds the global rights to the "Merck" name and brand except in the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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.

<http://www.emdserono.com>

### **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 <http://www.pfizer.com>. In addition, to learn more, please visit us at <http://www.pfizer.com> and follow us on Twitter at @Pfizer and @Pfizer\_News, LinkedIn YouTube 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 June 4, 2018. 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 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 avelumab; 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 regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed in any jurisdictions for potential indications for avelumab, combination therapies or other product candidates; whether and when regulatory authorities in any jurisdictions where applications are pending or may be submitted for avelumab, 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 avelumab, 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 <http://www.sec.gov> and <http://www.pfizer.com>.

## References

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