



# FDA Accepts the Biologics License Application for Avelumab for the Treatment of Metastatic Merkel Cell Carcinoma for Priority Review

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If approved by the FDA, avelumab, an investigational immunotherapy, could be the first treatment indicated for patients with metastatic Merkel cell carcinoma (MCC). Avelumab has previously received FDA Breakthrough Therapy and Fast Track Designations for metastatic MCC, as well as FDA Orphan Drug Designation for MCC.

EMD Serono Inc., 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 accepted for Priority Review EMD Serono's Biologics License Application (BLA) for avelumab. This review relates to avelumab's proposed use in patients with metastatic Merkel cell carcinoma (MCC), based on tumor response results from the JAVELIN Merkel 200 trial. Avelumab is an investigational fully human anti-PD-L1 IgG1 monoclonal antibody and could be the first treatment indicated for metastatic MCC in the US, if approved.[\*] MCC is a rare and aggressive skin cancer, which impacts approximately 2,500 Americans a year.[1],[2]

"We are pleased the FDA has granted a Priority Review designation for avelumab," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany, which in the US and Canada operates as EMD Serono. "There are currently no approved treatment options for metastatic MCC, and we are committed to working with the FDA to potentially bring the first approved cancer immunotherapy to patients with this aggressive disease."

The avelumab metastatic MCC BLA submission is supported by data from JAVELIN Merkel 200, a multicenter, single-arm, open-label, Phase II study of 88 patients with metastatic MCC, whose disease had progressed after at least one chemotherapy treatment.[1] The JAVELIN Merkel 200 study represents the largest data set of any anti-PD-L1/PD-1 antibody reported in this patient population. These data were presented in June 2016 at the Annual Meeting of the American Society of Clinical Oncology (ASCO) and published in the Lancet Oncology in October 2016.[1]

"Metastatic Merkel cell carcinoma is an aggressive disease, and patients face a very poor prognosis, with less than 20 percent surviving beyond five years," said Chris Boshoff, M.D., Ph.D., Senior Vice President and Head of Immuno-oncology, Early Development and Translational Oncology, Pfizer Global Product Development. "We are encouraged by the results of our Phase II trial and believe avelumab may have potential to be an important treatment option for patients living with this hard-to-treat skin cancer."

The FDA's Priority Review status reduces the review time from 10 months to a goal of six months from the day of filing and is given to drugs that may offer major advances in treatment or may provide a treatment where no adequate therapy exists. The FDA previously granted avelumab Orphan Drug Designation for MCC, as well as Fast Track and Breakthrough Therapy Designations for the treatment of patients with metastatic MCC whose disease has progressed after at least one previous chemotherapy regimen. Breakthrough Therapy Designation is intended to expedite the development and review of treatments for serious or life-threatening disease where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies for one or more endpoints.[3] Additionally, the European Medicines Agency has validated for review Merck KGaA, Darmstadt, Germany's Marketing Authorization Application (MAA) for avelumab, for the proposed indication of metastatic MCC.

The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and more than 3,000 patients evaluated across more than 15 different tumor types. In addition to metastatic MCC, these cancers include breast, gastric/gastroesophageal junction, head and neck, Hodgkin's lymphoma, melanoma, mesothelioma, non-small cell lung, ovarian, renal cell carcinoma and urothelial (primarily bladder).

\*Avelumab is not approved for any indication in any market. This marks the first acceptance of an application by the US FDA to review the investigational product, avelumab.

## References

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## About Metastatic Merkel Cell Carcinoma (MCC)

Metastatic MCC is a rare and aggressive disease in which cancer cells form in the top layer of the skin, close to nerve endings.[1],[4] 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.[5] Risk factors for MCC include sun exposure and having a weak immune system (i.e., solid organ transplant recipients, people with HIV/AIDS and people with other cancers, such as chronic lymphocytic leukemia, are at higher risk). Caucasian males older than 50 are at increased risk.[5] MCC is often misdiagnosed for other skin cancers and grows at an exponential rate on chronically sun-damaged skin.[6]-[9] Current treatment options for MCC include surgery, radiation and chemotherapy.[10] Treatment for metastatic or Stage IV MCC is generally palliative.

## About Avelumab

Avelumab (also known as MSB0010718C) is an investigational, fully human anti-PD-L1 IgG1 monoclonal antibody. By inhibiting PD-L1 interactions, avelumab is thought to enable the activation of T-cells and the adaptive immune system. By retaining a native Fc-region, avelumab is thought to potentially engage the innate immune system and induce antibody-dependent cell-mediated cytotoxicity (ADCC). In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab. In the JAVELIN Merkel 200 trial, treatment-related adverse events (AEs) occurred in 62 (70%) of 88 patients including fatigue and infusion-related reactions. Five grade 3 treatment-related AEs were reported in four of 88 patients and include two patients with lymphopenia and three patients with isolated laboratory abnormalities (elevated blood creatine phosphokinase, blood cholesterol, and hepatic aminotransferase).[1] There were no grade 4 treatment-related AEs or deaths related to treatment.[1]

## About EMD Serono, Inc.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany in the US and Canada - a leading science and technology company - 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](http://www.emdserono.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 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 investigational anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance will jointly develop and commercialize avelumab and advance Pfizer's PD-1 antibody. The alliance is focused on developing high-priority international clinical programs to investigate avelumab as a monotherapy, as well as in combination regimens, and is striving to find new ways to treat cancer.

## About Merck KGaA, Darmstadt, Germany

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.

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 2015, Merck KGaA, Darmstadt, Germany, generated sales of € 12.85 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany operates as EMD Serono, MilliporeSigma and EMD Performance Materials in the United States and Canada.

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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 <http://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](https://www.facebook.com/Pfizer).

## Pfizer Disclosure Notice

The information contained in this release is as of November 29, 2016. 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 (MSB0010718C), including a potential indication for avelumab for the treatment of metastatic Merkel Cell carcinoma (the "Potential Indication"), Pfizer's and Merck KGaA, Darmstadt, Germany's immuno-oncology 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, the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates as well as the possibility of unfavorable study results; 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 other jurisdictions for the Potential Indication and whether and when drug applications may be filed in any jurisdictions for any other potential indications for avelumab, combination therapies or other product candidates; whether and when the BLA or MAA for the Potential Indication or any such applications 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 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, 2015, 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>.

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