

# Merck KGaA, Darmstadt, Germany, and Pfizer Receive Positive Opinion for Orphan Drug Designation for Avelumab in Merkel Cell Carcinoma from EMA Committee for Orphan Medicinal Products

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EMA ODD is an important regulatory milestone for avelumab in metastatic Merkel cell carcinoma (MCC)

Merck KGaA, Darmstadt, Germany, and Pfizer today announced that the European Medicines Agency (EMA)'s Committee for Orphan Medicinal Products (COMP) has issued a positive opinion for Orphan Drug designation (ODD) for avelumab\*, an investigational fully human anti-PD-L1 IgG1 monoclonal antibody, pending an official decision by the European Commission (EC), expected in December. The COMP positive opinion is for the cancer immunotherapy avelumab, for the treatment of Merkel cell carcinoma (MCC), a rare and aggressive type of skin cancer.<sup>1,2</sup> Each year, there are approximately 2,500 new cases of MCC diagnosed in the European Union (EU).<sup>3</sup> There is currently no therapy approved specifically for the treatment of metastatic MCC.<sup>4</sup>

“While significant therapeutic advances have been made against other types of skin cancer, similar progress has not been made against Merkel cell carcinoma. There is a great need for effective therapies in this disease,” said Dr. Mace Rothenberg, Senior Vice President of Clinical Development and Medical Affairs and Chief Medical Officer for Pfizer Oncology. “Orphan Drug Designation is an important regulatory tool that can help facilitate development of a new treatment option for patients in Europe with this serious and rare condition.”

The COMP's positive opinion follows the US Food and Drug Administration's ODD for avelumab for the treatment of MCC that was received in September, Fast Track designation for avelumab for the treatment of metastatic MCC that was received in October, and Breakthrough Therapy Designation for avelumab for the treatment of metastatic MCC that was received in November. In order for a drug to be granted ODD by the EMA, it must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating; the prevalence of the condition in the EU must not be more than 5 in 10,000 or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development; and where no satisfactory treatment is currently available.

“We are delighted the EMA's Committee for Orphan Medicinal Products has considered that avelumab matches the Orphan Drug designation criteria for metastatic Merkel cell carcinoma in the EU,” said Dr. Luciano Rossetti, Head of Global Research & Development at Merck KGaA, Darmstadt, Germany's biopharma business. “We look forward to working closely with the EMA to make this potential treatment available to patients as soon as possible, and we eagerly await the results of our Phase II trial in this rare skin cancer.”

Merck KGaA, Darmstadt, Germany, and Pfizer are currently conducting a Phase II study (JAVELIN Merkel 200) to assess the safety and efficacy of avelumab in patients with metastatic MCC whose disease has progressed after at least one prior chemotherapy regimen. JAVELIN Merkel 200 is a multicenter, single-arm, open-label Phase II study with a primary objective of objective response rate.

The clinical development program for avelumab now includes more than 1,400 patients who have been treated across more than 15 tumor types, including breast cancer, gastric/gastro-esophageal junction cancers, head and neck cancer, MCC, mesothelioma, melanoma, non-small cell lung cancer, ovarian cancer, renal cell carcinoma and urothelial (e.g. bladder) cancer.

### **About the EMA Orphan Drug Designation**

An ODD by the EMA allows a pharmaceutical company to benefit from incentives from the EU to develop a medicine for a rare disease. Applications for ODD are examined by the COMP, which adopts an opinion that is forwarded to the EC. The EC then decides whether to grant an orphan designation for the medicine in question within 30 days of receipt of the COMP opinion.

Pharmaceutical companies that obtain ODD benefit from a number of incentives, including protocol assistance, a type of scientific advice specific for designated orphan medicines, and market exclusivity once the medicine is on the market. Fee reductions are also available, depending on the status of the sponsor and the type of service required.

\*Avelumab is the proposed International Nonproprietary Name for the anti-PD-L1 monoclonal antibody (MSB0010718C). Avelumab is under clinical investigation and has not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication by any health authority worldwide.

### **References**

1. Hughes MP et al. Merkel cell carcinoma: epidemiology, target, and therapy. *Curr Dermatol Rep* 2014;3:46–53.
2. Kaae J et al. Merkel cell carcinoma: incidence, mortality, and risk of other cancers. *J Natl Cancer Inst* 2010;102(11):793–801.
3. IMMOMECC (European Commission). Merkel cell carcinoma. Available at: <http://www.immomecc.eu/project/objectives/background/merkel-cell-carcinoma/> Last accessed November 2015
4. Miller NJ et al. Emerging and mechanism-based therapies for recurrent or metastatic Merkel cell carcinoma. *Curr Treat Options Oncol*; 2013 14(2): 249–6

### **About Merkel Cell Carcinoma (MCC)**

MCC is a rare and aggressive disease in which cancer cells form in the top layer of the skin, close to nerve endings. 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, arms, legs, and trunk. 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 over age 50 are at increased risk. MCC tends to metastasize at an early stage, spreading initially to nearby lymph nodes, and then potentially to more distant areas in the body, including other lymph nodes or areas of skin, lungs, brain, bones or other organs. Current treatment options for MCC include surgery, radiation and chemotherapy. 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 potentially enable the activation of T-cells and the adaptive immune system. By retaining a native Fc-region, avelumab is thought to 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.

## **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 companies will collaborate on up to 20 high-priority immuno-oncology clinical development programs, including combination trials, many of which are expected to commence in 2015.

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

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 40,000 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 2014, Merck KGaA, Darmstadt, Germany, generated sales of € 11.3 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 KGaA, Darmstadt, Germany, name and brand. The

only exceptions are the United States and Canada, where the company operates as EMD Serono, EMD Millipore and EMD Performance Materials.

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.

### **Pfizer Disclosure Notice**

The information contained in this release is as of November 25, 2015. 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 the treatment of metastatic MCC, 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 any jurisdictions for any potential indications for avelumab, combination therapies or other product candidates; whether and when 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, 2014, 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 SEC and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

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