

# Merck KGaA, Darmstadt, Germany, and Pfizer Receive FDA Breakthrough Therapy Designation for Avelumab in Metastatic Merkel Cell Carcinoma

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Breakthrough Therapy designation highlights the potential of avelumab\* as a new immunotherapy for patients with metastatic Merkel cell carcinoma (MCC) Metastatic MCC is a devastating disease and if approved, avelumab could potentially become the first immunotherapy to treat metastatic MCC

Merck KGaA, Darmstadt, Germany, and Pfizer today announced that the US Food and Drug Administration (FDA) has granted avelumab\*, an investigational fully human anti-PD-L1 IgG1 monoclonal antibody, Breakthrough Therapy designation for the treatment of patients with metastatic Merkel cell carcinoma (MCC) who have progressed after at least one previous chemotherapy regimen. Breakthrough Therapy designation is designed to accelerate the development and review of medicines that are intended to treat a serious condition, and preliminary clinical evidence indicates that the therapy may demonstrate a substantial improvement over current available therapies. MCC is a rare and aggressive type of skin cancer.<sup>1,2</sup> Each year, there are approximately 1,500 new cases of MCC diagnosed in the US.<sup>3</sup> There is currently no therapy approved specifically for the treatment of metastatic MCC.<sup>4</sup>

The Breakthrough Therapy designation is based on the preliminary evaluation of clinical data from the global Phase II study, JAVELIN Merkel 200, which is assessing the safety and efficacy of avelumab in patients with metastatic MCC whose disease has progressed after at least one prior chemotherapy regimen. Results from this Phase II study are planned for presentation at upcoming scientific congresses in 2016. The designation represents a significant milestone and has the potential to speed the development of avelumab for metastatic MCC patients.

JAVELIN Merkel 200 is a multicenter, single-arm, open-label Phase II study with a primary objective of overall response rate. Secondary endpoints include duration of response, progression-free survival, overall survival and safety. The study, which enrolled 88 patients, is being conducted in sites across Asia Pacific, Australia, Europe and North America.

“Metastatic Merkel cell carcinoma is a devastating disease with limited treatment options currently available for patients,” said Dr. Luciano Rossetti, Global Head of Research & Development of the biopharma business of Merck KGaA, Darmstadt, Germany. “With this Breakthrough Therapy designation, we are one step closer to our goal of making a significant difference to patients living with difficult-to-treat cancers, such as metastatic Merkel cell carcinoma, by researching and developing potential new treatment options.”

“In less than two months, the alliance between Merck KGaA, Darmstadt, Germany, and Pfizer has achieved its third regulatory milestone for avelumab, including Orphan Drug designation and Fast Track designation granted in September and October,” said Dr. Mace Rothenberg, Senior Vice President of Clinical Development and Medical Affairs and Chief Medical Officer for Pfizer Oncology. “We are very pleased with the progress of the JAVELIN clinical development program and we are looking forward to presenting additional data on the potential of this investigational compound in Merkel cell carcinoma and other tumor types in 2016.”

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 FDA Designations**

Breakthrough Therapy designation is designed to expedite the development and review of drugs which are intended to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s). The FDA also recently granted avelumab Fast Track and Orphan Drug designations for the treatment of metastatic MCC. The FDA’s granting of the Breakthrough Therapy, Fast Track and Orphan Drug designations for metastatic MCC does not alter the standard regulatory requirement to establish the safety and effectiveness of a drug through adequate and well-controlled studies to support approval.

\*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 Jan 22(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. Lemos BD et al. Pathologic nodal evaluation improves prognostic accuracy in Merkel cell carcinoma: analysis of 5823 cases as the basis of the first consensus staging system. *J Am Acad Dermatol* 2010 63(5): 751–61
4. Miller NJ et al. Emerging and mechanism-based therapies for recurrent or metastatic Merkel cell carcinoma. *Curr Treat Options Oncol* 2013 14(2): 249–63

### **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.

## **Pfizer Inc.; Working together for a healthier world®**

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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.

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### ***Pfizer Disclosure Notice***

*The information contained in this release is as of November 18, 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, including the risk that the final results of the Phase I study for avelumab and/or additional clinical trials may be different from (including less favorable than) the interim data results and may not support further clinical development; 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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