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News Release

September 25, 2015

Merck KGaA, Darmstadt, Germany, and Pfizer Announce FDA Orphan Drug Designation for Investigational Immunotherapy Avelumab in Merkel Cell Carcinoma

- **FDA orphan drug designation for avelumab an important regulatory milestone**
- **Alliance between Merck KGaA, Darmstadt, Germany, and Pfizer and continues to dedicate significant resources to accelerate clinical program for high-priority investigational anti-PD–L1**

Darmstadt, Germany, and New York, US, September 25, 2015 – Merck KGaA, Darmstadt, Germany, and Pfizer today announced that the US Food and Drug Administration (FDA) has granted orphan drug designation for the investigational cancer immunotherapy avelumab* for the treatment of Merkel cell carcinoma (MCC), a rare and aggressive type of skin cancer.^{1,2} Each year, there are approximately 1,500 new cases of MCC diagnosed in the US.³

Avelumab (also referred to as MSB0010718C) is an investigational fully human monoclonal IgG1 antibody against programmed death-ligand 1 (anti-PD–L1). 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 who have progressed after at least one prior chemotherapy regimen.



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“We continue to dedicate significant resources to accelerate our clinical trial program, with a goal of helping patients who are fighting rare and difficult-to-treat diseases, such as Merkel cell carcinoma,” said Dr. Luciano Rossetti, Head of Global Research & Development at the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. “It is encouraging to be included in the FDA’s orphan drug program as we eagerly await the results of our Phase II trial of avelumab in this deadly skin cancer.”

“This is a rare and lethal type of skin cancer, especially when it has progressed despite prior chemotherapy,” said Dr. Mace Rothenberg, Senior Vice President of Clinical Development and Medical Affairs and Chief Medical Officer for Pfizer Oncology. “There is a strong scientific rationale that by harnessing the body’s immune system, we may be able to control the disease and provide hope to patients fighting Merkel cell carcinoma.”

JAVELIN Merkel 200 is a multicenter, single-arm, open-label study evaluating patients with metastatic MCC who have previously received at least one line of chemotherapy. The primary endpoint is objective response rate, and secondary endpoints include duration of response, progression-free survival, overall survival and safety. The study, which exceeded its expected enrollment of 84 patients with 88 patients enrolled, is being conducted in sites across Asia Pacific, Australia, Europe and North America.

The JAVELIN clinical trial program also includes a Phase III study in Stage IIIb/IV or recurrent non-small cell lung cancer (NSCLC) designed to assess the efficacy and safety of avelumab compared with docetaxel in patients who have experienced disease progression after receiving a prior platinum-containing doublet therapy (JAVELIN Lung 200); a Phase Ib, open-label, multicenter, multiple-dose trial designed to estimate the maximum tolerated dose and select the recommended Phase II dose of avelumab in combination with axitinib** in patients with previously untreated advanced renal cell carcinoma (RCC, JAVELIN Renal 100); an international Phase I open-label, multiple ascending dose trial to investigate the safety, tolerability, pharmacokinetics, biological and clinical activity in patients with metastatic or locally advanced solid tumors (JAVELIN Solid Tumor); and a Phase I trial to investigate the tolerability, safety, pharmacokinetics,



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biological, and clinical activity of avelumab in Japanese patients with metastatic or locally advanced solid tumors (JAVELIN Solid Tumor Japan) with an expansion part in Asian patients with gastric cancer.

The clinical development program for avelumab now includes more than 1,000 patients treated across more than 15 tumor types, including NSCLC, breast cancer, gastric cancer, ovarian cancer, urothelial cancer (e.g. bladder), esophageal cancer, SCCHN, RCC, MCC, melanoma and mesothelioma.

About the FDA Orphan Drug Designation

FDA orphan drug designation is granted to drugs intended to treat rare diseases or disorders that affect fewer than 200,000 people in the US, or those that affect more than 200,000 people, but are unlikely to recover the costs of developing and marketing the drug. Orphan drug designation by the FDA qualifies the sponsor for incentives provided for in the Orphan Drug Act, which can include protocol assistance for clinical trials, prescription drug user fee waivers, tax incentives and seven years of market exclusivity upon approval. The granting of an orphan drug designation 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. The orphan drug designation for avelumab applies only to MCC.

*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.

**Axitinib is not approved for first-line treatment of advanced RCC.

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. 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):751–761.



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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.

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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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 www.pfizer.com.



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Merck KGaA, Darmstadt, Germany

Merck KGaA of Darmstadt, Germany, is a leading company for innovative and top-quality high-tech products in healthcare, life science and performance materials. The company has six businesses – Biopharmaceuticals, Consumer Health, Allergopharma, Biosimilars, Life Science and Performance Materials – and generated sales of € 11.3 billion in 2014. Around 39,000 employees work in 66 countries to improve the quality of life for patients, to foster the success of customers and to help meet global challenges. Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company – since 1668, the company has stood for innovation, business success and responsible entrepreneurship. Holding an approximately 70% interest, the founding family remains the majority owner of the company to this day. Merck KGaA, Darmstadt, Germany holds the global rights to the Merck name and brand. The only exceptions are Canada and the United States, where the company operates as EMD Serono, EMD Millipore and EMD Performance Materials.

Pfizer Disclosure Notice

The information contained in this release is as of September 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 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 and www.pfizer.com.