

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

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Second Biologics License Application accepted by the FDA for avelumab Prognosis for urothelial carcinoma is currently poor, particularly when the disease has metastasized

EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the US and Canada, and Pfizer Inc. today announced that the US Food and Drug Administration (FDA) has accepted for Priority Review EMD Serono's Biologics License Application (BLA) for avelumab\* as a treatment for patients with locally advanced or metastatic urothelial carcinoma (mUC) with disease progression on or after platinum-based therapy. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of August 27, 2017, for avelumab in this indication.

"Taken together with last year's filing for metastatic Merkel cell carcinoma, this BLA acceptance confirms our rapid and continued progress in the clinical development of avelumab," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "We continue to evaluate avelumab in cancers that have limited or suboptimal treatment choices, such as metastatic or locally advanced urothelial carcinoma, to hopefully be able to provide patients with new treatment options for fighting their disease."

Despite advances in the treatment of UC, the prognosis for patients remains poor, particularly when the disease has metastasized. Bladder cancer makes up approximately 90% of urothelial cancers and is the sixth most common cancer in the US.[1],[2] "

Advanced urothelial carcinoma remains a difficult-to-treat tumor, which is why we are developing a comprehensive clinical development program that involves Phase I and III trials designed to address this challenge," 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're continuing to accelerate our urothelial carcinoma development program and look forward to continuing our dialogue with the FDA."

Avelumab is an investigational, fully human anti-PD-L1 antibody. The FDA's Priority Review status reduces the review time from 10 months to a goal of six months from the day of filing acceptance and is given to drugs that may offer major advances in treatment or may provide a treatment where no adequate therapy exists. In November 2016, the FDA accepted, and granted Priority Review status to, the BLA for avelumab for the treatment of patients with metastatic Merkel cell carcinoma.

The international clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs, including nine Phase III trials, and more than 4,000 patients evaluated across more than 15 tumor types. In December 2015, Merck KGaA, Darmstadt, Germany, and Pfizer announced the initiation of a Phase III study (JAVELIN Bladder 100) of avelumab in the first-line setting as a maintenance treatment in patients with locally advanced or metastatic UC. This trial is currently enrolling patients.

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

## References

1.National Comprehensive Cancer Network. NCCN Guidelines Version 1.2017 Updates. Bladder Cancer. Available from: [https://www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf). Last Accessed: February 2017.

2.Siegel RL, et al. Cancer Statistics, 2017. CA Cancer J Clin 2017;67:7-30. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28055103>. Last Accessed: February 2017.

3.American Cancer Society. Key Statistics for Bladder Cancer. Available from: <https://www.cancer.org/cancer/bladder-cancer/about/key-statistics.html>. Last Accessed: February 2017.

## About Metastatic Urothelial Carcinoma

Urothelial Carcinoma includes several tumors originating from the cells lining the bladder, renal pelvis and urethra. While cancers outside of the bladder are relatively uncommon, accounting for an estimated 10% of cases, bladder cancer represents 90% of urothelial cancers and is the ninth most common cancer globally.[1],[3] Worldwide, approximately 400,000 new cases of bladder cancer are diagnosed and 150,000 deaths are attributed to this disease each year.[3] The incidence and mortality of bladder cancer have remained unchanged over the past 25 years.[3]

## About Avelumab

Avelumab is a fully human antibody specific for a protein found on tumor cells called PD-L1, or programmed death ligand-1. 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. Common adverse reactions include fatigue, musculoskeletal pain, diarrhea, nausea peripheral edema, decreased appetite, and rash. Immune-mediated adverse reactions have also been reported.

## 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 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>

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 <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.

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 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 February 28, 2017. 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 urothelial 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 and regulatory submission 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 for the Potential Indication, the BLA and EU marketing authorization application for avelumab for the treatment of metastatic Merkel cell carcinoma or any such other 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>.