Merck KGaA, Darmstadt, Germany, and Pfizer Announce Discontinuation of Phase III JAVELIN Ovarian PARP 100 Trial in Previously Untreated Advanced Ovarian Cancer

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Darmstadt, Germany and New York, US, March 19, 2019 – Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the US and Canada, and Pfizer Inc. (NYSE: PFE) today announced the discontinuation of the ongoing Phase III JAVELIN Ovarian PARP 100 study evaluating the efficacy and safety of avelumab in combination with chemotherapy followed by maintenance therapy of avelumab in combination with talazoparib,* a poly (ADP-ribose) polymerase (PARP) inhibitor, versus an active comparator in treatment-naïve patients with locally advanced or metastatic ovarian cancer (Stage III or Stage IV). The alliance has notified health authorities and trial investigators of the decision to discontinue the trial.

The decision was based on several emerging factors since the trial's initiation, including the previously announced interim results from JAVELIN Ovarian 100. The alliance determined that the degree of benefit observed with avelumab in frontline ovarian cancer in that study does not support continuation of the JAVELIN Ovarian PARP 100 trial in an unselected patient population and emphasizes the need to better understand the role of immunotherapy in ovarian cancer. Additional factors include the rapidly changing treatment landscape and the approval of a PARP inhibitor in the frontline maintenance setting. The decision to discontinue the JAVELIN Ovarian PARP 100 trial was not made for safety reasons.

The alliance between Merck KGaA, Darmstadt, Germany and Pfizer was the first to test an immunotherapy in this indication, given the significant unmet need in the treatment of ovarian cancer. Four out of five women with ovarian cancer are diagnosed with disease that has spread to the lymph nodes or to distant organs.1 Most women with advanced ovarian cancer ultimately die within five years due to refractory, resistant or recurrent disease.2,3

JAVELIN Ovarian PARP 100 (B9991030) is an open-label, international, multi-center, randomized study designed to evaluate the efficacy and safety of avelumab in combination with chemotherapy followed by maintenance therapy of avelumab in combination with talazoparib versus an active comparator in treatment-naïve patients with locally advanced or metastatic ovarian cancer (Stage III or Stage IV). The primary endpoint is progression-free survival (PFS) as determined based on blinded independent central review (BICR) assessment per RECIST v1.1.

The decision to discontinue the JAVELIN Ovarian PARP 100 trial does not impact the currently approved indications for avelumab or the remainder of the ongoing JAVELIN clinical development program. The program involves at least 30 clinical programs and more than 9,000 patients evaluated across more than 15 different tumor types, including breast, gastric/gastro-esophageal junction, and head and neck cancers, Merkel cell carcinoma, non-small cell lung cancer, and urothelial carcinoma.

*Avelumab and talazoparib are under clinical investigation for the treatment of advanced ovarian cancer and have not been demonstrated to be safe and effective for this use.

About Avelumab (BAVENCIO®)

Avelumab (BAVENCIO®) is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.4-6 Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.6-8 In November 2014, Merck and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Approved Indications in the US

In the US, the FDA granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial

carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Avelumab is currently approved for patients with MCC in more than 45 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

Important Safety Information from the BAVENCIO® US FDA-Approved Label

BAVENCIO can cause **immune-mediated pneumonitis**, including fatal cases. Monitor patients for signs and symptoms of pneumonitis, and evaluate suspected cases with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold BAVENCIO for moderate (Grade 2) and permanently discontinue for severe (Grade 3), life-threatening (Grade 4), or recurrent moderate (Grade 2) pneumonitis. Pneumonitis occurred in 1.2% (21/1738) of patients, including one (0.1%) patient with Grade 5, one (0.1%) with Grade 4, and five (0.3%) with Grade 3.

BAVENCIO can cause **immune-mediated hepatitis**, including fatal cases. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater hepatitis. Withhold BAVENCIO for moderate (Grade 2) immune-mediated hepatitis until resolution and permanently discontinue for severe (Grade 3) or life-threatening (Grade 4) immune-mediated hepatitis. Immune-mediated hepatitis was reported in 0.9% (16/1738) of patients, including two (0.1%) patients with Grade 5, and 11 (0.6%) with Grade 3.

BAVENCIO can cause **immune-mediated colitis**. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold BAVENCIO until resolution for moderate or severe (Grade 2 or 3) colitis, and permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including seven (0.4%) with Grade 3.

BAVENCIO can cause **immune-mediated endocrinopathies**, including adrenal insufficiency, thyroid disorders, and type 1 diabetes mellitus.

Monitor patients for signs and symptoms of **adrenal insufficiency** during and after treatment, and administer corticosteroids as appropriate. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency. Adrenal insufficiency was reported in 0.5% (8/1738) of patients, including one (0.1%) with Grade 3.