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News Release

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Merck KGaA, Darmstadt, Germany, and Pfizer Provide Update on Avelumab in Platinum-Resistant/Refractory Ovarian Cancer

Darmstadt, Germany, and New York, US, November 19, 2018 – Merck KGaA, Darmstadt, Germany, and Pfizer Inc. (NYSE: PFE) today announced that the Phase III JAVELIN Ovarian 200 trial evaluating avelumab* alone or in combination with pegylated liposomal doxorubicin (PLD), a type of chemotherapy, compared with PLD did not meet the prespecified primary endpoints of overall survival (OS) or progression-free survival (PFS) in patients with platinum-resistant or -refractory ovarian cancer. Signals were observed in the combination arm relative to PLD, and further analyses of the trial are warranted (HR for the primary PFS endpoint for avelumab + PLD vs PLD alone: 0.78 [repeated confidence interval (RCI): 0.587, 1.244; one-sided p-value: 0.0301]; HR for the primary OS endpoint for avelumab + PLD vs PLD alone: 0.89 [RCI: 0.744, 1.241; one-sided p-value: 0.2082]; HR for the primary PFS endpoint for avelumab alone vs PLD alone: 1.68 [RCI: 1.320, 2.601; one-sided p-value: >0.99]; HR for the primary OS endpoint for avelumab alone vs PLD alone: 1.14 [RCI: 0.948, 1.580; one-sided p-value: 0.8253]; objective response, a secondary endpoint: 13.3% [95% CI 8.8, 19.0] for avelumab + PLD; 3.7% [95% CI 1.5, 7.5] for avelumab alone; and 4.2% [95% CI 1.8, 8.1] for PLD alone). No new safety signals were observed for avelumab alone or in combination, and the safety profile for avelumab in this trial was consistent with that observed in the overall JAVELIN clinical development program. The data are currently being analyzed, and detailed results will be shared with the scientific community.

“JAVELIN Ovarian 200 enrolled a high proportion of patients with aggressive, refractory disease that had no response to prior platinum-based chemotherapy, a population known to have

disease that is challenging to treat; as such, this group of patients is typically not included in Phase III ovarian cancer trials," 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 initiated the JAVELIN Ovarian 200 trial as the first Phase III study of a checkpoint inhibitor in the platinum-resistant or -refractory setting recognizing these patients have the most pressing need for new treatment options. The results speak to the significant challenges these women face."

"Although OS and PFS did not reach statistical significance, study results indicate potential clinical activity of the combination of avelumab and chemotherapy which will be analyzed further," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany, which in the US and Canada operates as EMD Serono. "We thank the patients, their families and the investigators who participated in the JAVELIN Ovarian 200 trial, and wish to underscore that the alliance remains committed to driving advances in ovarian cancer, a commitment that includes two ongoing Phase III trials in previously untreated patients testing avelumab in combination with chemotherapy and, separately, one in combination with chemotherapy followed by maintenance treatment of avelumab in combination with a PARP inhibitor."

"Effective management of platinum-resistant or -refractory ovarian cancer remains the biggest unmet medical need facing women with recurrent ovarian cancer today. The current treatment options have only limited and short-lived efficacy for the majority of women, as evidenced by an average life expectancy that does not exceed one year for this group," said Eric Pujade-Lauraine, M.D., Ph.D., head of the Women Cancers and Clinical Research Department at Hôpitaux Universitaires Paris Centre, site Hôtel-Dieu. "As a researcher and clinician, I know how important it is to continue to improve the outlook for women with advanced ovarian cancer and look forward to the results of more trials exploring the role of avelumab in delaying recurrence in platinum-sensitive patients and earlier lines of therapy."

Four out of five patients with ovarian cancer are diagnosed at advanced stages. The disease often has no symptoms early on, when it is much more treatable.[1] Approximately 70% of patients with ovarian cancer who receive standard-of-care, frontline, platinum-based chemotherapy will relapse in the first three years.[2] At first relapse, approximately 20% to 25% of ovarian cancer patients have platinum-resistant or -refractory disease, and eventually almost all patients will become platinum-resistant.[3-6]

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JAVELIN Ovarian 200 is a Phase III, multicenter, randomized study investigating the efficacy and safety of avelumab alone or in combination with PLD versus PLD alone in 566 women with ovarian cancer that is resistant or refractory to platinum chemotherapy. The primary objectives were to demonstrate superior OS or PFS for one or both avelumab-based treatment regimens compared with PLD.

In addition to JAVELIN Ovarian 200, the avelumab ovarian cancer clinical development program includes several ongoing clinical trials investigating avelumab in combination with other therapies. JAVELIN Ovarian 100 is an open-label, international, multicenter, randomized Phase III study of avelumab in combination with and/or as follow-on (maintenance) treatment to platinum-based chemotherapy in previously untreated patients with locally advanced or metastatic (Stage III or Stage IV) epithelial ovarian cancer. JAVELIN Ovarian 100 is the first Phase III study to evaluate the addition of an immunotherapy to the standard of care in frontline treatment for this aggressive disease. JAVELIN Ovarian PARP 100 is a randomized, open-label, multicenter Phase III study of avelumab plus chemotherapy followed by maintenance therapy of avelumab in combination with a PARP inhibitor or chemotherapy followed by maintenance therapy with a PARP inhibitor, in patients with previously untreated advanced ovarian cancer. Avelumab is also undergoing investigation in combination with other therapies for gynecologic cancers.

*Avelumab is under clinical investigation for treatment of ovarian cancer and has not been demonstrated to be safe and effective for this indication. There is no guarantee that avelumab will be approved for ovarian cancer by any health authority worldwide.

About the JAVELIN Clinical Trial Program

The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and more than 9,000 patients evaluated across more than 15 different tumor types. In addition to ovarian cancer, these tumor types include breast, gastric/gastro-esophageal junction and head and neck cancers, melanoma, mesothelioma, Merkel cell carcinoma, non-small cell lung cancer, renal cell carcinoma and urothelial carcinoma.

About Ovarian Cancer

Every year, more than 295,000 women are diagnosed with ovarian cancer worldwide.[7] The disease is generally advanced when it is diagnosed, as it often has few to no symptoms at the

early stages. This makes it difficult to detect until the disease has progressed. Symptoms can be vague or non-specific, making it easy to confuse with less serious non-cancerous conditions. The five-year survival rate ranges from approximately 30% to 50%, but for those with metastatic disease, it drops to less than 20%.[7,8]

About Avelumab

Avelumab 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.[9-11] Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) *in vitro*.[11-13] In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Approved Indications

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 35 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 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.

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation. Manage hypothyroidism with hormone replacement therapy and hyperthyroidism with medical management. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) thyroid disorders. Thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroiditis, were reported in 6% (98/1738) of patients, including three (0.2%) with Grade 3.

Type 1 diabetes mellitus including diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Withhold BAVENCIO and

administer antihyperglycemics or insulin in patients with severe or life-threatening (Grade ≥ 3) hyperglycemia, and resume treatment when metabolic control is achieved. Type 1 diabetes mellitus without an alternative etiology occurred in 0.1% (2/1738) of patients, including two cases of Grade 3 hyperglycemia.

BAVENCIO can cause **immune-mediated nephritis and renal dysfunction**. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater nephritis. Withhold BAVENCIO for moderate (Grade 2) or severe (Grade 3) nephritis until resolution to Grade 1 or lower. Permanently discontinue BAVENCIO for life-threatening (Grade 4) nephritis. Immune-mediated nephritis occurred in 0.1% (1/1738) of patients.

BAVENCIO can result in **other severe and fatal immune-mediated adverse reactions** involving any organ system during treatment or after treatment discontinuation. For suspected immune-mediated adverse reactions, evaluate to confirm or rule out an immune-mediated adverse reaction and to exclude other causes. Depending on the severity of the adverse reaction, withhold or permanently discontinue BAVENCIO, administer high-dose corticosteroids, and initiate hormone replacement therapy, if appropriate. Resume BAVENCIO when the immune-mediated adverse reaction remains at Grade 1 or lower following a corticosteroid taper. Permanently discontinue BAVENCIO for any severe (Grade 3) immune-mediated adverse reaction that recurs and for any life-threatening (Grade 4) immune-mediated adverse reaction. The following clinically significant immune-mediated adverse reactions occurred in less than 1% of 1738 patients treated with BAVENCIO: myocarditis with fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe (Grade 3) or life-threatening (Grade 4) **infusion-related reactions**. Patients should be premedicated with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent doses based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for mild (Grade 1) or moderate (Grade 2) infusion-related reactions. Permanently discontinue BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Infusion-related

reactions occurred in 25% (439/1738) of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

BAVENCIO can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing potential to use effective contraception during treatment with BAVENCIO and for at least 1 month after the last dose of BAVENCIO. It is not known whether BAVENCIO is excreted in human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

The most common adverse reactions (all grades, ≥ 20%) in patients with **metastatic Merkel cell carcinoma (MCC)** were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reaction (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

Selected treatment-emergent laboratory abnormalities (all grades, ≥ 20%) in patients with **metastatic MCC** were lymphopenia (49%), anemia (35%), increased aspartate aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

The most common adverse reactions (all grades, ≥ 20%) in patients with **locally advanced or metastatic urothelial carcinoma (UC)** were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%), and urinary tract infection (21%).

Selected laboratory abnormalities (Grades 3-4, ≥ 3%) in patients with **locally advanced or metastatic UC** were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

Please see full US Prescribing Information and Medication Guide available at http://www.BAVENCIO.com.

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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. The global strategic alliance between Merck KGaA, Darmstadt, Germany, and Pfizer enables the companies to benefit from each other's strengths and capabilities and further explore the therapeutic potential of avelumab, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance is jointly developing and commercializing avelumab and advancing 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 combination regimens, and is striving to find new ways to treat cancer.

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About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, the vibrant science and technology company, operates across healthcare, life science and performance materials. Around 53,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases, to enabling the intelligence of devices – the company is everywhere. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the company's business sectors operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 1666, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

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 health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care 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, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice
The information contained in this release is as of November 19, 2018. 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, including clinical trials evaluating avelumab for the treatment of ovarian cancer, the alliance between Merck KGaA, Darmstadt, Germany, and Pfizer 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, uncertainties regarding the commercial success of avelumab; 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, including unfavorable new clinical data and additional analyses of existing clinical data; 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 regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed for avelumab in any jurisdictions or for any potential indications for avelumab, combination therapies or other product candidates; whether and when regulatory authorities in any jurisdictions where applications are pending or may be submitted for avelumab, combination therapies or other product candidates may approve any such applications, 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.

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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, 2017, 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 www.sec.gov and www.pfizer.com.

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