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February 15, 2018

Merck KGaA, Darmstadt, Germany, and Pfizer Provide Update on Phase III JAVELIN Lung 200 Trial of Avelumab Monotherapy in Previously Treated Patients with Advanced Non-Small Cell Lung Cancer

Darmstadt, Germany, and New York, US, February 15, 2018 – Merck KGaA, Darmstadt, Germany, and Pfizer Inc. (NYSE: PFE) today announced results from the Phase III JAVELIN Lung 200 trial comparing avelumab* to docetaxel in patients with unresectable, recurrent or metastatic non-small cell lung cancer (NSCLC) whose disease progressed after treatment with a platinum-containing doublet therapy. While the trial did not meet its prespecified endpoint of improving overall survival (OS) in patients with programmed death ligand-1-positive (PD-L1+) (1% or higher) tumors (HR: 0.90 [96% CI: 0.72–1.12], p-value 0.1627, one-sided), the proportion of patients in the chemotherapy arm crossing over to immune checkpoint inhibitors outside the study was higher than previously reported in post-platinum immunotherapy clinical trials, and this may have confounded this trial outcome (percentage of patients receiving subsequent checkpoint inhibitor therapy: docetaxel arm 26.4%; avelumab arm 5.7%).

However, improvements in OS versus the control arm were observed in the moderate-to-high PD-L1+ expression (50% or greater, which represented approximately 40% of the study population) and high PD-L1+ expression population (PD-L1+ expression 80% or greater, which represented approximately 30% of the study population) (HR: 0.67 [95% CI: 0.51–0.89], p-value 0.0052, two-sided; and HR 0.59 [95% CI: 0.42–0.83], p-value 0.0022, two-sided, respectively**). The safety profile for avelumab in this trial was consistent with that observed in the overall JAVELIN clinical development program; no new safety signals were identified.

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“Avelumab performed in line with expectations in the trial from both an efficacy and safety perspective,” said primary investigator Fabrice Barlesi, M.D., Ph.D., Head of Multidisciplinary Oncology and Therapeutic Innovations Department at Aix-Marseille University and the Assistance Publique Hôpitaux de Marseille, France. “With immune checkpoint inhibitors approved for patients with previously treated, advanced non-small cell lung cancer, higher percentages of immunotherapy-naïve patients are receiving subsequent checkpoint inhibitors in their progressive treatments. This was observed in the JAVELIN Lung 200 control arm and may have confounded the primary outcome of the study.”

“Avelumab’s overall clinical activity in this study supports its profile with expected efficacy across several endpoints and subgroups,” said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany, which operates as EMD Serono in the US and Canada. “However, the chemotherapy group displayed improved overall survival compared with previous PDx trials, most likely due to the impact of crossover to other checkpoint inhibitors.”

“We are committed to understanding the data in the context of the subpopulations and the impact of access to other immune checkpoint inhibitors,” 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 will continue to progress the broad avelumab program, exploring various indications.”

Detailed results from the JAVELIN Lung 200 trial will be submitted for presentation at an upcoming medical congress, and the companies aim to share the data with regulatory agencies.

In 2017, avelumab first received accelerated approval[†] by the US Food and Drug Administration (FDA) for metastatic Merkel cell carcinoma (mMCC) and for previously treated patients with locally advanced or metastatic urothelial carcinoma (mUC), followed by the European Commission (EC) approval for mMCC later that year.

The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and over 7,000 patients evaluated across more than 15 different tumor types. In addition to NSCLC, these cancers include breast, gastric/gastro-esophageal junction, head and

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neck, Hodgkin's lymphoma, melanoma, mesothelioma, Merkel cell carcinoma, ovarian, renal cell carcinoma and urothelial carcinoma.

In December 2017, the FDA granted Breakthrough Therapy Designation for avelumab as a combination therapy for treatment-naïve patients with advanced renal cell carcinoma.

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

**When the primary endpoint is not met, statistical significance cannot be formally claimed with the predefined statistical significance level (i.e., 0.05 two-sided). In this circumstance, the Type I error is not strictly controlled and the p-value should be interpreted cautiously.

About JAVELIN Lung 200

JAVELIN Lung 200 is a Phase III, randomized, open-label, multicenter trial investigating avelumab versus docetaxel in patients with locally advanced unresectable, metastatic or recurrent NSCLC whose disease has progressed after a platinum-containing doublet chemotherapy. The trial included 792 patients from approximately 260 sites in North America, South America, Asia, Africa, Australia and Europe. The primary objective was to demonstrate superior OS compared with docetaxel in patients with PD-L1+ unresectable, recurrent or metastatic NSCLC whose disease progressed after treatment with a platinum-containing doublet therapy.

About JAVELIN Lung Program

In addition to JAVELIN Lung 200, avelumab's lung cancer clinical development program includes several other ongoing clinical trials investigating avelumab alone and in combination. JAVELIN Lung 100 is a Phase III randomized open-label, multicenter trial to assess the safety and efficacy of avelumab, compared with platinum-based doublet chemotherapy, in patients with metastatic NSCLC who have not previously received any systemic treatment for their NSCLC. JAVELIN Lung 101 is a Phase Ib/II multicenter, international, dose-finding trial designed to evaluate the safety and efficacy of avelumab in combination with either Pfizer's crizotinib or lorlatinib in patients with advanced or metastatic NSCLC. JAVELIN Medley is a Phase Ib/II randomized open-label, multicenter dose-finding trial of avelumab in combination with other immune modulators in patients with selected locally advanced or metastatic solid tumors, including NSCLC.

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About Non-Small Cell Lung Cancer

Globally, lung cancer is the most common cause of cancer-related deaths in men and the second most common in women,¹ responsible for more deaths than colon, breast and prostate cancer combined.² NSCLC is the most common type of lung cancer, accounting for 80 to 85% of all lung cancers.³ The five-year survival rate for people diagnosed with lung cancer that has spread (metastasized) to other areas of the body is 1%.⁴

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.⁵⁻⁷ Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.⁷⁻⁹ 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.

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

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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 \geq 3) hyperglycemia, and resume treatment when metabolic control is achieved.

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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 1,738 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.

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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, $\geq 20\%$) 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, $\geq 20\%$) 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, $\geq 20\%$) 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, $\geq 3\%$) 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 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, 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 2016, Merck KGaA, Darmstadt, Germany, generated sales of € 15.0 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" name and brand except in the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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.

www.emdserono.com

About Pfizer: 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 February 15, 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, 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

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regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed in any jurisdictions for 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.

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, 2016, 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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