



Merck KGaA, Darmstadt, Germany and Pfizer Advance Clinical Development Program with Two Additional Phase III Trials of Avelumab

Tuesday, December 22, 2015 - 03:00am

Initiation of Phase III JAVELIN Ovarian 200 trial investigating avelumab as a treatment for platinum-resistant/refractory ovarian cancer
Initiation of Phase III JAVELIN Bladder 100 trial investigating avelumab as a maintenance treatment, in the first-line setting, for patients with urothelial cancer
Merck KGaA, Darmstadt, Germany-Pfizer Alliance achieves 2015 goal of initiating six pivotal trials with JAVELIN Ovarian 200 and JAVELIN Bladder 100 trials

Merck KGaA, Darmstadt, Germany and Pfizer today announced the opening of trial sites for an international Phase III study of avelumab*, an investigational fully human anti-PD-L1 IgG1 monoclonal antibody, in patients with platinum-resistant/refractory ovarian cancer. The JAVELIN Ovarian 200 trial is the first Phase III study of a PD-L1 inhibitor investigated as a treatment for platinum-resistant/refractory ovarian cancer. The alliance also announced that the US Food and Drug Administration has provided approval to move forward with a Phase III study of avelumab as a maintenance treatment, in the first-line setting, in patients with locally advanced or metastatic urothelial cancer. The first trial sites are expected to open shortly.

"There are limited treatment options for women with ovarian cancer, and the prognosis for women with platinum-resistant ovarian cancer is especially poor," said Chris Boshoff, Vice President and Head of Early Development, Translational and Immuno-Oncology at Pfizer Oncology. "We have observed encouraging signs of early clinical activity of avelumab in patients with platinum-resistant or platinum-refractory ovarian cancer, and we hope to build on these results next year through a planned Phase III study of

avelumab in combination with platinum therapy in patients with previously untreated ovarian cancer.”

This Phase III, randomized (1:1:1), open-label, parallel, multicenter, global study (JAVELIN Ovarian 200) is designed to evaluate the superiority of avelumab as a monotherapy or in combination with pegylated liposomal doxorubicin (PLD), compared with PLD alone, in treating patients with platinum-resistant/refractory ovarian cancer. The primary endpoint is overall survival (OS). Study investigators anticipate enrolling approximately 550 patients across more than 190 sites in Asia, Europe and North America.

Merck KGaA, Darmstadt, Germany, and Pfizer have also initiated a Phase III study (JAVELIN Bladder 100) investigating avelumab as a maintenance treatment, in the first-line setting, in patients with locally advanced or metastatic urothelial cancer. This is currently the only Phase III trial designed to evaluate an immunotherapy agent as a maintenance treatment, in the first-line setting, in patients with urothelial cancer.

“Locally advanced or metastatic urothelial cancer is another aggressive cancer, with the disease often progressing quickly following first-line treatment,” said Dr. Alise Reicin, Head of Global Clinical Development at Merck KGaA, Darmstadt, Germany’s biopharma business. “It’s an exciting time for the Merck KGaA, Darmstadt, Germany, and Pfizer Alliance as we continue to accelerate our clinical development program, and now into urothelial cancer. This disease has an exceptionally high unmet need and we believe there is potential for our anti-PD-L1 antibody to be part of future treatment strategies.”

This open-label, multicenter, randomized, global, Phase III study is designed to evaluate the safety and efficacy of avelumab plus best supportive care (BSC), compared with BSC alone, in patients with unresectable locally advanced or metastatic urothelial cancer whose disease did not progress on (or following) completion of first-line treatment with a platinum-containing chemotherapy. The primary endpoint of the study is OS, which will be assessed in two urothelial cancer patient populations: patients with PD-L1 positivity and all randomized patients.

JAVELIN Bladder 100 is expected to enroll 668 patients across more than 200 sites in 38 countries. PD-L1 expression status will be determined by retrospective analysis of mandatory tumor samples collected from patients enrolled in the trial. It is estimated that at least half of those patients randomized to treatment will be PD-L1-positive.

The clinical development program for avelumab now includes more than 1,500 patients who have been treated across more than 15 tumor types, including breast cancer, gastric/gastro-esophageal junction cancers, head and neck cancer, melanoma, Merkel cell

carcinoma, non-small cell lung cancer, ovarian cancer, renal cell carcinoma and urothelial (e.g. bladder) cancer. The alliance has initiated six pivotal trials, reaching its goal for 2015, with additional trials expected to initiate in 2016.

*Avelumab is the proposed International Non-proprietary 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.

References

1. Ferlay J, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>. Accessed December 2015.
2. World Cancer Research Fund International. Ovarian Cancer Statistics. Available from: <http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/ovarian-cancer-statistics>. Accessed November 2015.
3. NICE. Ovarian Cancer: Recognition and Initial Management. <https://www.nice.org.uk/guidance/cg122>. Accessed November 2015.
4. National Cancer Institute. Ovarian Epithelial, Fallopian Tube, and Primary Peritoneal Cancer Treatment (PDQ®). Available from: <http://www.cancer.gov/types/ovarian/patient/ovarian-epithelial-treatment-pdq>. Accessed November 2015.
5. Lederman JA, et al. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2013; 24 Suppl 6: vi24-32.
6. Ojavo LS, et al. Emerging immunotherapies in ovarian cancer. *Discov Med* 2015; 20: 97-109.
7. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer Version 2. 2015. Available at: <https://www.nccn.org/store/login/login.aspx?ReturnURL=http://www.nccn.org/professionals/p> Accessed December 2015.
8. Malats N, Real FX. Epidemiology of Bladder Cancer. *Hematol Oncol Clin North Am* 2015; 29(2): 177-89.

About Ovarian Cancer

Globally, ovarian cancer is the seventh most common cancer in women.¹ Annually, nearly 239,000 cases are diagnosed worldwide.² Ovarian cancer may be difficult to diagnose, as symptoms may appear only in the later stages, when the disease has spread beyond the ovaries.² Outcomes for women with ovarian cancer are generally poor due to most patients presenting with advanced disease.³ The 5-year prevalence of women globally living with ovarian cancer is 22.6 per 100,000.² Current treatment options for epithelial ovarian cancer may include surgery, radiotherapy, chemotherapy and targeted therapies.⁴ Women who are unable to undergo treatment with platinum-based chemotherapy, due to resistance or refractory disease, currently have very limited treatment options. Platinum-resistant ovarian cancer is defined as ovarian cancer that recurs within six months of completing primary chemotherapy with a platinum-based medication.⁵ Platinum-refractory ovarian cancer is defined as ovarian cancer that progresses during treatment with a platinum-based chemotherapy regimen.⁵ There is still a clear unmet need in ovarian cancer in relation to general disease awareness,² improving initial investigations in primary and secondary care and novel therapies with demonstrable efficacy.⁶

About Urothelial Cancer

Urothelial cancer includes several tumors originating from the urothelial cells lining the bladder, renal pelvis and urethra.⁷ Bladder cancer accounts for 90% of urothelial cancers,⁷ and is the ninth most common cancer globally. Approximately 400,000 new cases of bladder cancer are diagnosed and 150,000 deaths are attributed to this disease each year.⁸ The incidence and mortality of bladder cancer have remained unchanged over the past 25 years.⁸

About 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 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 alliance 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.

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 www.pfizer.com.

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 2014, Merck KGaA, Darmstadt, Germany, generated sales of € 11.3 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 KGaA, Darmstadt, Germany, name and brand. The only exceptions are the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and

EMD Performance Materials.

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 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.

Pfizer Disclosure Notice

The information contained in this release is as of December 22, 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 avelumab for the treatment of patients with platinum-resistant/refractory ovarian cancer and as a potential indication for the treatment of patients with locally advanced or metastatic urothelial cancer, 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; 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.

Merck KGaA, Darmstadt, Germany Media: Gangolf Schrimpf +49 6151 72 9591 or Investor Relations: +49 6151 72 3321 or Pfizer Inc., New York, USA Media: Sally Beatty +1 212-733-6566 or Investor Relations: Ryan Crowe +1 212-733-8160