Verastem Announces Dosing of First Patient in Combination Trial of Defactinib and Avelumab in Patients with Ovarian Cancer

January 26, 2017

Phase 1/2 Study Expected to Enroll Approximately 100 Patients at up to 15 sites in the U.S.

BOSTON--(BUSINESS WIRE)--Jan. 26, 2017-- Verastem, Inc., (NASDAQ:VSTM) today announced dosing of the first patient in a new clinical trial evaluating avelumab*, an investigational fully human anti-PD-L1 IgG1 monoclonal antibody, in combination with Verastem's defactinib**, an investigational focal adhesion kinase (FAK) inhibitor, in patients with advanced ovarian cancer. The Phase 1/2 clinical trial is being conducted in collaboration with the alliance between Merck KGaA, Darmstadt, Germany, which in the US and Canada operates as EMD Serono, and Pfizer, and is expected to enroll approximately 100 patients at up to 15 sites across the U.S.

Robert Forrester, President and Chief Exececutive Officer of Verastem, stated, "Initiation of this clinical trial evaluating the combination of avelumab and defactinib represents an important milestone for Verastem, and together with our collaborators at Merck KGaA, Darmstadt, Germany, and Pfizer, we are eager to evaluate the potential of this combination to provide ovarian cancer patients with a new treatment option."

The Phase 1/2 multicenter, open-label, dose-escalation and dose expansion study is designed to assess the safety, pharmacokinetics, pharmacodynamics, and initial observations of clinical activity of the avelumab/defactinib combination in patients with recurrent or refractory stage III-IV ovarian cancer. Additional primary objectives of the study include identification of the recommended Phase 2 dose (RP2D), and assessment of the best overall response according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

"Our goal, through this collaboration, is to increase our understanding of FAK inhibition, and further demonstrate the alliance's commitment to exploring a diverse range of novel combinations with avelumab," said Chris Boshoff, M.D., Ph.D., Senior Vice President and Head of Immuno-oncology, Early Development and Translational Oncology, Pfizer Global Product Development.

"Patients with late-stage ovarian cancer are in dire need of effective new treatments. We are eager to review the results of this important study as we continue to investigate the potential of avelumab to address the unmet needs for this hard-to-treat cancer," said Dr. Alise Reicin, Head of Global Clinical Development at Merck KGaA, Darmstadt, Germany's biopharma business.

FAK is a protein which is often overproduced in tumors, enabling cancer cells to evade attack by the immune system. As reported in *Cell*, and *Nature Medicine,* pre-clinical research shows that FAK inhibition can modulate the balance of immune cells in the tumor, increasing the presence of cytotoxic T cells in the tumor and decreasing the presence of immunosuppressive T regulatory cells.[1,2]

*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.

**VS-6063 (defactinib) is under clinical investigation and has not be 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.

More About the Phase 1/2 Study

The study is comprised of 2 sequential parts: Part A (Dose Escalation) and Part B (Expansion). In Part A (Dose Escalation), approximately 18 subjects will receive avelumab IV treatment in 28-day cycles (10 mg/kg over approximately 1 hour on Days 1 and 15) and oral defactinib twice-daily (BID) continuously starting on Day 1 of Cycle 1. Subject enrollment will proceed according to a standard 3+3 design. In the absence of dose-limiting toxicity, each subject will receive the study drug regimen for a minimum of 28 days (Cycle 1) and may continue to receive additional cycles of study treatment until disease progression has been documented or unacceptable toxicity or other treatment discontinuation criteria have been met. All subjects in a cohort must have completed at least 1 cycle of dosing before dose escalation involving new subjects entered into the next dose cohort can occur. Based on the safety and PK data obtained in the dose escalation portion of the study, the RP2D of the combination will be determined.

In Part B (Expansion), approximately 80 subjects will be enrolled and will receive avelumab IV treatment in 28-day cycles (10 mg/kg over approximately 1 hour on Days 1 and 15) and oral defactinib at the RP2D dose continuously starting on Day 1 of Cycle 1.

Additional information on the clinical trial can be found at: http://bit.ly/2g6bnXA

About Ovarian Cancer

Globally, ovarian cancer is the seventh most common cancer in women.[3] Annually, nearly 239,000 cases are diagnosed worldwide.[4] Ovarian cancer may be difficult to diagnose, as symptoms may appear only in the later stages, when the disease has spread beyond the ovaries.[4] Outcomes for women with ovarian cancer are generally poor due to most patients presenting with advanced disease.[5] The 5-year prevalence of women globally living with ovarian cancer is 22.6 per 100,000.[4] Current treatment options for epithelial ovarian cancer may include surgery, radiotherapy, chemotherapy and targeted therapies.[6] 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.[7] Platinum-refractory ovarian cancer is defined as ovarian cancer that progresses during treatment with a platinum-based chemotherapy regimen.[7] There is still a clear unmet need in ovarian cancer in relation to general disease awareness,[4] improving initial investigations in primary and secondary care and novel therapies with demonstrable efficacy.[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 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.

About Defactinib

Defactinib (VS-6063) is an investigational inhibitor of Focal Adhesion Kinase (FAK), a non-receptor tyrosine kinase encoded by the PTK-2 gene that mediates oncogenic signaling in response to cellular adhesion and growth factors.[9] Based on the multi-faceted roles of FAK, defactinib is used to treat cancer through modulation of the tumor microenvironment, enhancement of anti-tumor immunity, and reduction of cancer stem cells.[1,2] Defactinib is currently being evaluated in three separate clinical collaborations in combination with immunotherapeutic agents for the treatment of several different cancer types including pancreatic, ovarian, non-small cell lung cancer, and mesothelioma. These studies are combination clinical trials with pembrolizumab and avelumab from Merck & Co. and Pfizer/Merck KGaA, Darmstadt, Germany, respectively.[11,12,13] Information about these and additional clinical trials evaluating the safety and efficacy of defactinib can be found on www.clinicaltrials.gov.

About Verastem, Inc.

Verastem, Inc. (NASDAQ:VSTM) is a biopharmaceutical company focused on discovering and developing drugs to improve outcomes for patients with cancer. Verastem is currently developing duvelisib, a dual inhibitor of phosphoinositide-3-kinase (PI3K)-delta and PI3K-gamma, which has successfully met its primary endpoint in a Phase 2 study and is currently being evaluated in a Phase 3 clinical trial in patients with chronic lymphocytic leukemia (CLL). Other clinical product candidates include focal adhesion kinase (FAK) inhibitors defactinib and VS-4718, and dual PI3K/mTOR inhibitor VS-5584. Defactinib is currently being evaluated in three separate clinical collaborations in combination with immunotherapeutic agents for the treatment of several different cancer types, including pancreatic, ovarian and non-small cell lung cancer, and mesothelioma. Verastem's product candidates seek to treat cancer by modulating the local tumor microenvironment, enhancing anti-tumor immunity and reducing cancer stem cells. For more information, please visit www.verastem.com.

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 combination regimens, and is striving to find new ways to treat cancer.

Verastem forward-looking statements notice

This press release includes forward-looking statements about Verastem's strategy, future plans and prospects, including statements regarding the development and activity of VS-6063 (defactinib), Verastem's FAK and diagnostics programs generally, the structure of our planned and pending clinical trials and the timeline for clinical development, our rights to develop or commercialize our product candidates and our ability to finance contemplated development activities and fund operations for a specified period. The words "anticipate," "appear," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks that the preclinical testing of Verastem's product candidates and preliminary or interim data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials, that data may not be available when we expect it to be, that enrollment of clinical trials may take longer than expected, that our product candidates will cause unexpected safety events, that Verastem will be unable to successfully initiate or complete the clinical development of its product candidates, that the development of Verastem's product candidates will take longer or cost more than planned, and that Verastem's product candidates will not receive regulatory approval or become commercially successful products. Other risks and uncertainties include those identified under the heading "Risk Factors" in Verastem's Annual Report on Form 10-K for the year ended December 31, 2015 as filed on March 3, 2016, Verastem's quarterly report on Form 10-Q filed on November 7, 2016 and in any subsequent SEC filings. The forward-looking statements contained in this press release reflect Verastem's current views with respect to future events, and Verastem does not undertake and specifically disclaims any obligation to update any forward-looking statements.

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