Verastem to Present Data Supporting FAK/PYK2 Inhibition at the 2016 American Academy of Cancer Research Annual Meeting

March 16, 2016

BOSTON--(BUSINESS WIRE)--Mar. 16, 2016-- Verastem, Inc. (NASDAQ:VSTM), focused on discovering and developing drugs to treat cancer, today announced the presentation of scientific data at the 2016 American Association of Cancer Research (AACR) Annual Meeting being held April 16-20, 2016 in New Orleans, LA.

“The data that will be presented at the upcoming 2016 AACR Annual Meeting continue to build on the premise that focal adhesion kinase (FAK), and the related proline-rich tyrosine kinase 2 (PYK2), inhibition enhances the efficacy of standard of care treatments such as platinum, and notably, immune checkpoint inhibitors,” said Dr. Jonathan Pachter, Verastem Head of Research. “Key immune-related observations include VS-6063 and VS-4718 dose-dependently stimulating proliferation of CD8+ cytotoxic T cells. This is in distinct contrast to other protein kinase inhibitors which impair the proliferation of CD8+ cytotoxic T cells. These data further extend the rationale for Verastem’s ongoing clinical trials testing FAK inhibitors in combination with the immune checkpoint inhibitors, pembrolizumab or avelumab.”

Details for the AACR presentations are as follows:

Poster Presentations

Title: FAK/PYK2 Inhibition Enhances Immune Checkpoint Inhibitor Efficacy
Session: Immunology: Immune Modulating Agents 1
Abstract No.: 568
Date and time: Sunday Apr 17, 2016 1:00 - 5:00 PM
Location: Convention Center, Halls G-J, Poster Section 26
Summary: Durable responses have been observed with single-agent immune checkpoint inhibitors, but combinations of immunotherapy agents with compounds that modulate the tumor microenvironment have the potential to overcome the mechanisms that tumor cells develop, which assist them in evading the immune attack. In addition to targeting cancer stem cells, Verastem’s dual FAK/PYK2 inhibitors, VS-6063 and VS-4718, have been shown to beneficially modulate the tumor microenvironment in squamous cell carcinoma models. In these study results, researchers at Verastem reported the findings from combinations of VS-6063 and VS-4718 with multiple immunotherapies.

The combination of VS-4718 with an anti-PD-1 monoclonal antibody (mAb) showed improved efficacy over anti-PD-1 mAb alone and extended survival *in vivo*. Analysis of the tumors at Day 12 of treatment revealed a significant increase in the CD8+ T cells/Treg ratios in tumors in the VS-4718 + anti-PD-1 combination group, providing a mechanistic understanding for the enhanced efficacy of this combination.

The combination of VS-4718 with anti-4-1BB was also tested in the same *in vivo* model. Consistent with what was observed with the anti-PD-1 combination, VS-4718 also enhanced the efficacy of the anti-4-1BB mAb. In *in vitro* T cell proliferation assays, VS-6063 and VS-4718 dose-dependently stimulated proliferation of CD8+ cytotoxic T cells isolated from healthy donors. In addition, both VS-4718 and VS-6063 decreased CD8+ T cell exhaustion markers, and increased T cell-mediated tumor cell killing in vitro. These data support the thesis that Verastem’s FAK/PYK2 inhibitors, VS-6063 and VS-4718, beneficially modulate the tumor microenvironment, and in combination with immune checkpoint inhibitors, may increase the breadth of responsive tumor types, increase the number of responders, and confer more durable anti-tumor responses.

Title: FAK Inhibition Re-sensitizes Platinum-resistant Serous Ovarian Cancer
Session: Novel targets: Experimental and Molecular Therapeutics
Abstract No.: 3811
Date and time: Tuesday Apr 19, 2016 1:00 - 5:00 PM
Location: Convention Center, Halls G-J, Poster Section 17
Summary: Ovarian cancer stem cell (CSC) resistance to chemotherapy treatment can give rise to tumor recurrence, which occurs in a high percentage of patients and is directly related to poor overall survival. FAK, an intracellular tyrosine kinase, has been linked to CSC survival in many cancers. In this study, researchers tested Verastem’s FAK inhibitor VS-4718 in certain ovarian cancer models.

In vitro results demonstrated that elevated FAK was present in platinum (CP)-resistant ovarian cancer cells and FAK tyrosine phosphorylation was increased after CP treatment of CP-sensitive ovarian cancer cells. VS-4718 selectively blocked CP-resistant ovarian carcinoma methylcellulose colony growth via cell cycle inhibition, but not apoptosis. *In vivo*, oral VS-4718 reduced CP-resistant orthotopic tumor burden with a simultaneous decrease in tumor-associated aldehyde dehydrogenase (ALDH) activity, a marker of ovarian CSCs. VS-4718 also reduced the expression of several other CSC-related biomarkers. These results suggest that FAK signaling facilitates ovarian carcinoma CSC phenotypes and support the testing of FAK inhibitors in combination with CP to prevent recurrent and chemo-resistant ovarian cancer.

A copy of the poster presentations will be available at http://bit.ly/R3M6wc following the respective presentation times of each poster.

About Focal Adhesion Kinase

Focal Adhesion Kinase (FAK) is a non-receptor tyrosine kinase encoded by the PTK-2 gene that is involved in cellular adhesion and, in cancer, metastatic capability. VS-6063 (defactinib) and VS-4718 are orally available compounds that are potent inhibitors of FAK. VS-6063 and VS-4718 utilize a multi-faceted approach to treat cancer by reducing cancer stem cells, enhancing anti-tumor immunity, and modulating the local tumor microenvironment. VS-6063 and VS-4718 are currently being studied in multiple clinical trials for their ability to improve patient outcome.

About Verastem, Inc.

Verastem, Inc. (NASDAQ:VSTM) is a biopharmaceutical company focused on discovering and developing drugs to improve outcomes for patients with cancer. Our product candidates utilize a multi-faceted approach to treat cancer by reducing cancer stem cells, enhancing anti-tumor immunity, and modulating the local tumor microenvironment. Our most advanced clinical product candidates are the Focal Adhesion Kinase inhibitors, VS-6063 and VS-4718, and the dual PI3K/mTOR inhibitor, VS-5584. For more information, please visit www.verastem.com.

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 Verastem's product candidates, VS-6063 and VS-4718, and Verastem's FAK and diagnostics programs generally, the utility of FAK inhibitors for the treatment of cancer including in combination with other cancer treatments, the timeline for clinical development and regulatory approval of our product candidates, the structure of our planned or pending clinical trials, 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 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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