Verastem Publishes Scientific Data Highlighting Potential Role of FAK Inhibition in Pancreatic and Breast Cancer

July 25, 2017

Preclinical Data Supportive of Ongoing Clinical Collaboration Trials Evaluating FAK Inhibition in Combination with Chemotherapeutic and Immunotherapeutic Agents

BOSTON--(BUSINESS WIRE)--Jul. 25, 2017-- Verastem, Inc. (NASDAQ:VSTM), focused on discovering and developing drugs to improve the survival and quality of life of cancer patients, today announced scientific findings from studies evaluating focal adhesion kinase (FAK) inhibition in preclinical models of pancreatic and breast cancer with the publication of two papers in the peer-reviewed journals, *PLoS One* and *Oncotarget*. The two published articles continue to validate the underlying thesis for ongoing clinical collaborations evaluating Verastem's lead FAK inhibitor defactinib in combination with chemotherapeutic and leading immunotherapeutic agents in several difficult to treat types of cancer.

Jonathan Pachter, Ph.D., Chief Scientific Officer of Verastem, stated, "The data published in *PLoS One* illustrate the impact of combining a FAK inhibitor with standard chemotherapy, demonstrating inhibited tumor growth, along with limited metastatic dissemination in pancreatic ductal adenocarcinoma (PDAC), one of the deadliest types of cancer. Importantly, these data also provide additional rationale for the ongoing clinical studies evaluating defactinib in combination with Merck's pembrolizumab for the treatment of patients with pancreatic cancer. Our data in the *Oncotarget* paper further delineate the anti-tumor mechanisms of our FAK inhibitors, and demonstrate the benefit of adding a FAK inhibitor to overcome key restrictive features of the tumor microenvironment (TME) to enable longer survival and reduced metastatic outgrowth."

***PLoS ONE* Publication Highlights Potential Role of FAK Inhibition in Pancreatic Cancer**

In a paper titled "The Extracellular Matrix and Focal Adhesion Kinase Signaling Regulate Cancer Stem Cell Function in Pancreatic Ductal Adenocarcinoma," Verastem researchers, along with scientific collaborators led by William Matsui at Johns Hopkins University School of Medicine, describe findings demonstrating that FAK inhibition extended the anti-tumor response to gemcitabine and nab-paclitaxel (Gem-Pac) in preclinical models of PDAC. Prior research has demonstrated that the desmoplastic TME of PDAC plays a role in therapeutic resistance, and this study demonstrates that intra-tumoral fibrosis enhances tumor-initiating and self-renewal potential.

The researchers show that the TME in PDAC is dramatically altered by several ECM proteins, including type I collagen. Type I collagen increases PDAC tumor-initiating potential, self-renewal and the frequency of cancer stem cells (CSCs) through the activation of FAK. While FAK overexpression increased tumor initiation, it was demonstrated that FAK inhibition reduced PDAC growth *in vitro* and *in vivo*. In an *in vivo* murine PDAC model, FAK inhibitor-treated tumors grew significantly slower than tumors in vehicle-treated control animals. In addition, tumor regression was enhanced by the addition of a FAK inhibitor to Gem-Pac and tumor regrowth was also significantly delayed in animals treated with the combination of a FAK inhibitor with Gem-Pac, as compared to Gem-Pac alone.

***Oncotarget* Publication Describing the Preferential Targeting of Cancer Stem Cells by FAK Inhibition in Breast Cancer Models**

In a paper by Vihren Kolev et al., titled "Inhibition of FAK Kinase Activity Preferentially Targets Cancer Stem Cells," Verastem researchers demonstrated that FAK inhibition significantly reduced the proportion of CSCs in mice bearing xenograft models of triple-negative breast cancer (TNBC), as evidenced by a reduced tumor-initiating capability upon re-implantation. In contrast, the cytotoxic chemotherapeutic agents, paclitaxel and carboplatin, enriched the number of CSCs. Importantly, FAK inhibition weakened the chemotherapy-induced enrichment of CSCs *in vitro* and delayed tumor regrowth following cessation of chemotherapy. In addition, an active mutant form of β-catenin reversed the preferential targeting of CSCs by FAK inhibition, suggesting that this targeting is mediated, at least in part, through attenuating β-catenin activation. The preferential targeting of CSCs by FAK inhibitors provides a rationale for the clinical development of FAK inhibitors aimed to increase durable responses for cancer patients.

About the Tumor Microenvironment

The TME encompasses multiple tumor and non-tumor cell populations and an extracellular matrix that support cancer cell survival. This includes immunosuppressive regulatory T-cells, myeloid-derived suppressor cells, tumor-associated macrophages, cancer-associated fibroblasts, and extracellular matrix proteins that can hamper the entry and therapeutic benefit of cytotoxic T-cells and anti-cancer drugs. In addition to targeting the proliferative and survival signaling of cancer cells, Verastem's product candidates, including duvelisib and defactinib, also target the TME to potentially improve response to therapy.

About Focal Adhesion Kinase and 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.[1] 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.[2,3] 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, respectively.[4,5,6] 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 PI3K-delta and PI3K-gamma, which has successfully met its primary endpoint in a Phase 2 study in iNHL and is currently being evaluated in a Phase 3 clinical trial in patients with CLL. In addition, Verastem is developing the FAK inhibitor defactinib, which is currently being evaluated in three separate clinical collaborations in combination with immunotherapeutic agents for the treatment of several different cancer types, including pancreatic cancer, ovarian cancer, 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.

Verastem, Inc. forward-looking statements notice:

This press release includes forward-looking statements about Verastem's strategy, future plans and prospects, including statements regarding results of the Phase 2 DYNAMO® study, and Verastem's PI3K/mTOR and FAK programs generally, the structure of our planned and pending clinical trials and the timeline and indications for clinical development, including reporting top-line data, and regulatory submissions and, our rights to develop or commercialize our product candidates. 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 expected, including for the Phase 3 DUO study; that enrollment of clinical trials may take longer than expected; that our product candidates will cause unexpected safety events or result in an unmanageable safety profile as compared to their level of efficacy; that duvelisib will be ineffective at treating patients with lymphoid malignancies; 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; that Verastem may not have sufficient cash to fund its contemplated operations; that Verastem or Infinity will fail to fully perform under the license agreement; that the transition of the duvelisib program from Infinity will not be completed; that Verastem will not pursue or submit regulatory filings for its product candidates, including for duvelisib in patients with CLL or iNHL; and that Verastem's product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients. 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, the Company'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.

References

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[2] Jiang H et al. Targeting focal adhesion kinase renders pancreatic cancers responsive to checkpoint immunotherapy. Nat Med 2016: Aug 22(8) 851-60.

[3] Sulzmaier F.J. et al. FAK in cancer: mechanistic findings and clinical applications. Nature Rev Cancer. 2014 14: 598-610.

[4] www.clinicaltrials.gov, NCT02546531

[5] www.clinicaltrials.gov, NCT02943317

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Source: Verastem, Inc.

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