Study Published in Nature Medicine Highlights Potential Role of FAK Inhibition in Pancreatic Cancer

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- FAK Inhibition Renders Previously Unresponsive Pancreatic Tumors Responsive to Chemo- and Immunotherapy –

- Preclinical Results Support Ongoing Phase 1 Clinical Trial in Patients with Pancreatic Cancer –

BOSTON--(BUSINESS WIRE)--Jul. 5, 2016-- Verastem, Inc. (NASDAQ:VSTM), focused on discovering and developing drugs to treat cancer, today announced the publication of preclinical research in the journal *Nature Medicine* by the Company's researchers and scientific collaborators. The research, which was led by David G. DeNardo, PhD, Assistant Professor of Medicine, Division of Oncology, Department of Immunology, Washington University School of Medicine in St. Louis, and co-author of the paper, demonstrated that focal adhesion kinase (FAK) inhibition decreases fibrosis and immunosuppressive cell populations in pancreatic ductal adenocarcinoma (PDAC), rendering previously unresponsive tumors sensitive to chemo- and immunotherapy.

"The application of immunotherapy holds great promise to improve outcomes for patients with pancreatic cancer, as it has for melanoma and lung cancer patients," said Dr. DeNardo. "To date, however, attempts at immunotherapy in PDAC have achieved limited clinical benefit when deployed as single agents. This is likely due in part to the presence of a uniquely immunosuppressive tumor microenvironment which is dominant in most human cases of PDAC. Major drivers of this pro-tumorigenic microenvironment include a highly fibrotic stroma and extensive infiltration by immunosuppressive cell populations. Thus, agents that can potentially overcome excessive fibrosis while altering immune suppression would be particularly attractive targets for PDAC."

The paper, titled "Targeting Focal Adhesion Kinase Renders Pancreatic Cancers Responsive to Checkpoint Immunotherapy," (Jiang, et al., advanced online publication, July 4, 2016 (doi:10.1038/nm.4123) describes the therapeutic targeting of FAK in *in vivo* murine PDAC models. Prior research has demonstrated that hyperactivated FAK activity is a significant regulator of the fibrotic and immunosuppressive tumor microenvironment (TME) in PDAC tumor cells.

In this study, researchers show that FAK signaling is a key driver of fibrosis, immunosuppression and PDAC progression. It was then demonstrated that single-agent treatment with Verastem's FAK inhibitor VS-4718 significantly limited tumor progression, resulting in a doubling of survival in an *in vivo* model of human PDAC. This slowing of tumor progression was associated with dramatically reduced tumor fibrosis, and a reduced number of tumor-infiltrating immunosuppressive cells. Given these findings, it was then hypothesized that the resulting effects of FAK inhibition on the TME may render PDAC tumors more sensitive to immunotherapy. Study results then demonstrated that FAK inhibition rendered previously unresponsive *in vivo* models responsive to T cell therapy and anti-PD1 antagonists. These data strongly support the ongoing clinical evaluation of FAK inhibitors in combination with checkpoint immunotherapy in patients with pancreatic cancer.

"FAK signaling has been shown to be important in several carcinomas, including pancreatic tumors, but its compelling role in creating an immunosuppressive tumor microenvironment is just emerging," said Jonathan Pachter, PhD, Chief Scientific Officer of Verastem, and co-author of the paper. "Another study, recently published in *Cell,* found that FAK inhibition can modulate certain immune cell populations, namely CD8+ T cells and Tregs, enabling an immune response that destroys tumors. Similarly, in the current study, we found that FAK inhibition alters tumor cell production of pro-inflammatory and immunosuppressive cytokines and reduces the tumor's ability to avoid immune surveillance. Together these findings provide important support and rationale for the ongoing Phase 1 dose-escalation clinical study evaluating Verastem's FAK inhibitor VS-6063 in combination with pembrolizumab and gemcitabine in patients with pancreatic cancer."

In early 2016, Verastem launched a new clinical development program focused on advancing its FAK inhibitors in combination with immuno-oncology agents and other current and emerging standard of care treatments. The Company's lead FAK inhibitor, VS-6063 is currently being evaluated in a Phase 1 dose-escalation study at the Washington University in Saint Louis in combination with Merck & Co.'s PD-1 inhibitor pembrolizumab and gemcitabine in patients with pancreatic cancer. VS-6063 is also the subject of an additional clinical collaboration between Merck KGaA, Pfizer and Verastem where it will be evaluated in a Phase 1/1b study in combination with avelumab, an investigational fully human anti-PD-L1 IgG1 monoclonal antibody, in patients with advanced ovarian cancer. This collaboration trial is expected to begin during the second half of 2016.

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 patients with cancer.

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 programs generally, the utility of FAK

inhibitors for the treatment of cancers, the structure of our planned and pending clinical trials and the timeline for clinical development. 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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Source: Verastem, Inc.

Verastem, Inc.
Brian Sullivan, 781-292-4214
bsullivan@verastem.com