Cancer Research Publication Highlights Importance of Merlin Loss and Cancer Stem Cells in Mesothelioma

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Research Demonstrates Cooperativity between Loss of Merlin and p16/ARF in Driving the Development of Highly Aggressive Disease In Vivo

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 24, 2014-- Verastem, Inc. (NASDAQ:VSTM), focused on discovering and developing drugs to treat cancer by the targeted killing of cancer stem cells, today announced that a publication in the journal *Cancer Research* supports the scientific rationale for the Company's ongoing development program of targeting cancer stem cells in mesothelioma. The paper, titled "Tumor Suppressor Alterations Cooperate to Drive Aggressive Mesotheliomas with Enriched Cancer Stem Cells via a p53–miR-34a–c-Met Axis," was co-authored by Verastem Head of Research Jonathan Pachter, Ph.D.

Malignant mesothelioma is a highly aggressive, asbestos-related cancer frequently marked by mutations in tumor suppressor genes Neurofibromatosis 2 (NF2) and p16/ARF. Inactivation of NF2 results in the absence of its protein product, merlin. Merlin loss is a critical driver of mesothelioma tumorigenesis and correlates with FAK inhibitor sensitivity in preclinical models. p16 and ARF are tumor suppressors, which bind to and regulate proteins involved in cell cycle progression and apoptosis. NF2 and p16/ARF are frequently co-inactivated in mesothelioma. The study results demonstrated *in vivo* that inactivation of NF2 and p16/ARF cooperate to drive the development of highly aggressive mesothelioma characterized by enhanced disease progression and an increase in cancer stem cells.

Verastem's lead compound is VS-6063, an orally available agent that targets cancer stem cells through potent inhibition of focal adhesion kinase (FAK), a critical signaling pathway in the development and survival of cancer stem cells. Cancer stem cells are an underlying cause of tumor resistance to chemotherapy, recurrence, and ultimate disease progression.

"These findings provide strong genetic evidence for the cooperativity between merlin and p16/ARF loss of function in driving the development of highly aggressive malignant mesothelioma marked by an enhanced presence of cancer stem cells that drive tumor progression," said Jonathan Pachter, Ph.D. "Collectively, these data further support the concept that cancer stem cells play a key role in the aggressiveness of merlin-low mesothelioma."

"The ongoing COMMAND trial is designed to evaluate the effect of VS-6063 in patients with mesothelioma," said Dr. Joanna Horobin, Verastem Chief Medical Officer. "This study contributes to our understanding of the driving factors in mesothelioma aggressiveness. Merlin-low mesothelioma cells and tumors appear to be particularly sensitive to FAK inhibition, so we have designed COMMAND to evaluate the effect of FAK inhibition on both the overall mesothelioma patient population and also in those whose tumors are merlin-low. Through this approach we believe that we can determine the potential of VS-6063 for the treatment of patients with this highly aggressive form of cancer."

Verastem is currently conducting multiple trials of two FAK inhibitors: VS-6063 and VS-4718. VS-6063 is in the registration-directed COMMAND study (www.COMMANDmeso.com) for patients with mesothelioma, a Phase 2 study in NSCLC, a Phase 1/1b combination study of VS-6063 and weekly paclitaxel for patients with ovarian cancer and a Phase 1 trial in Japanese patients. VS-4718 is in a Phase 1 study for patients with advanced cancers. The Company is also developing VS-5584, a PI3K/mTOR inhibitor which is currently being studied in a Phase 1 trial in patients with advanced solid tumors or lymphoma.

The Cancer Research abstract can be accessed at http://bit.ly/1bnjwiS.

About Malignant Pleural Mesothelioma

Malignant pleural mesothelioma is an aggressive form of cancer that occurs in the mesothelium, the thin layer of tissue that covers the lungs. Mesothelioma is associated with exposure to asbestos in most cases. According to the World Health Organization, a total of 59,000 deaths occur worldwide each year due to mesothelioma. Most mesotheliomas begin as one or more nodules that progressively grow to form a solid coating of tumor surrounding the lung leading to eventual suffocation and death. A high percentage of mesotheliomas contain cancer stem cells that are generally resistant to the currently available treatment options for advanced mesothelioma.

About VS-6063

VS-6063 is an orally available compound designed to target cancer stem cells through the potent inhibition of focal adhesion kinase (FAK). Cancer stem cells are an underlying cause of tumor resistance to chemotherapy, recurrence and ultimate disease progression. Research by Robert Weinberg, Ph.D., scientific cofounder and chair of Verastem's Scientific Advisory Board, and Verastem has demonstrated that the FAK pathway is critical for the growth and survival of cancer stem cells. VS-6063 is currently being studied in the registration-directed COMMAND trial in mesothelioma (www.COMMANDmeso.com), a Phase 1/1b study in combination with paclitaxel for patients with ovarian cancer, a Phase 1 study in Japan in patients with advanced solid tumors and a Phase 2 trial in patients with Kras-mutated non-small cell lung cancer. VS-6063 has been granted orphan drug designation in the U.S. and E.U. for use in mesothelioma.

About VS-4718

VS-4718 is an orally available compound designed to target cancer stem cells through the potent inhibition of focal adhesion kinase (FAK). VS-4718 is currently being studied in a Phase 1 dose escalation study in patients with advanced cancers.

About Verastem, Inc.

Verastem, Inc. (NASDAQ: VSTM) is discovering and developing drugs to treat cancer by the targeted killing of cancer stem cells. Cancer stem cells

are an underlying cause of tumor recurrence and metastasis. Verastem is developing small molecule inhibitors of signaling pathways that are critical to cancer stem cell survival and proliferation: FAK, PI3K/mTOR and Wnt. For more information, please visit www.verastem.com.

Forward-looking statements:

This press release includes forward-looking statements about the Company's strategy, future plans and prospects, including statements regarding the development of the Company's compounds, including VS-6063, VS-4718, VS-6062 and the Company's FAK inhibition program, the timeline for clinical development and regulatory approval of the Company's compounds, the expected timing for the reporting of data from ongoing trials, and the structure of the Company's planned or pending clinical trials, and potential indications 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 the Company's compounds and preliminary 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 the Company will be unable to successfully complete the clinical development of its compounds, including VS-6063 and VS-4718, that the development of the Company's compounds will take longer or cost more than planned, and that the Company's compounds will not receive regulatory approval or become commercially successful products. Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2012 and in any subsequent SEC filings. The forward-looking statements contained in this presentation reflect the Company's current views with respect to future events, and the Company does not undertake and specifically disclaims any obligation to update any forward-looking statements.

Source: Verastem, Inc.

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