Verastem Presents Encouraging Scientific Data on the Preferential Targeting of Cancer Stem Cells at the 2015 American Association of Cancer Research Annual Meeting

April 22, 2015

BOSTON--(BUSINESS WIRE)--Apr. 22, 2015-- Verastem, Inc. (NASDAQ:VSTM), focused on discovering and developing drugs to treat cancer by the targeted killing of cancer stem cells, today announced the presentation of scientific data at the 2015 American Association of Cancer Research (AACR) Annual Meeting being held April 18-22, 2015 at the Pennsylvania Convention Center in Philadelphia, PA.

"The scientific research presented by both Verastem and our collaborators this year at AACR continues to highlight the activity of our compounds in multiple cancer models, including mesothelioma, breast cancer, small cell lung cancer and hematological malignancies," said Dr. Jonathan Pachter, Verastem Head of Research. "The data presented provide continued evidence that VS-6063, VS-4718 and VS-5584 effectively target cancer stem cells, reduce tumor initiating capability and prolong the anti-tumor response to standard of care chemotherapy in preclinical models of multiple tumor types. The results from these studies support both ongoing and planned clinical trials. We believe these agents have the potential to be used alongside standard-of-care treatments, to address both the cancer stem cells and the bulk tumor cells, as a strategy to potentially generate more durable responses for patients with cancer."

Verastem, and its collaborators, are presenting these scientific data in support of Verastem's programs targeting cancer stem cells through inhibition of the focal adhesion kinase (FAK; VS-6063 and VS-4718) and PI3K/mTOR (VS-5584) signaling pathways. Research on the FAK and PI3K/mTOR signaling pathways has revealed critical roles for each in cancer stem cell survival and disease progression. Cancer stem cells have tumor-initiating capability, are particularly resistant to chemotherapy and can mediate tumor recurrence both locally and at metastatic sites.

Details for the data presentations at AACR are as follows:

Oral Presentation

Title: FAK inhibitors VS-6063 and VS-4718 target cancer stem cells: Implications for TNBC sequential and combination therapies
Date and time: Sunday, April 19, 2015, 3:20 pm – 3:35 pm ET
Location: Room 115
Abstract number: 974
Session: Session Title: Cancer Stem Cells 1; Session Category: Tumor Biology; Session Type: Minisymposium
Summary: Neoadjuvant chemotherapy has been shown to lead to an increase in markers of cancer stem cells (CSCs) in primary breast cancer. The presence of the ALDH cancer stem cell marker in residual cancer tissue in lymph nodes at surgery after neoadjuvant chemotherapy has been associated with a significantly worse prognosis following primary treatment. It is also evident that stem-like features of tumor cells are present in metastatic breast cancer indicating that targeting of CSCs may be valuable in metastatic disease. Verastem's CSC inhibitors, VS-6063 and VS-4718, diminished CSCs *in vitro*, *ex vivo* and in xenograft models in contrast to paclitaxel or cisplatin treatment which enriched CSCs. Consistent with the notion that CSCs are responsible for cancer relapse after chemotherapy, VS-6063 and VS-4718 substantially delayed tumor growth following cessation of paclitaxel or cisplatin treatment in models of triple negative breast cancer. Additionally, both VS-6063 and VS-4718 inhibited metastatic outgrowth and/or induced regression of metastases after primary tumor resection, whereas metastases progressed in all animals in the control group. These results support the clinical investigation of the CSC-targeting agents VS-6063 and VS-4718 in certain breast cancer settings to potentially delay time to relapse and improve the treatment outcome.

A copy of the oral presentation is available at http://bit.ly/12otlcV

Poster Presentations

Title: FAK and PI3K/mTOR inhibitors target cancer stem cells: Implications for SCLC treatment strategies
Date and time: Monday, April 20, 2015, 8:00 am – 12:00 pm ET
Location: Section 19; Poster Board 24
Abstract Number: 1525
Session: Session Title: Solid Tumor Stem Cells; Session Category: Tumor Biology
Summary: In most patients with small cell lung cancer (SCLC), tumors initially respond to first line chemotherapy, but subsequently experience rapid recurrence. In previously reported research, preclinical models of other cancers demonstrated that CSC populations are increased following chemotherapy, and that inhibitors of FAK and PI3K/mTOR have been shown to preferentially target CSCs. FAK and PI3K/mTOR inhibitors may be particularly valuable in a SCLC setting, where CSCs may be strong mediators of recurrence. In this study, the antitumor activity of FAK and PI3K/mTOR inhibitors (VS-4718 and VS-5584, respectively) were investigated in SCLC xenograft models *in vivo*.

In the preclinical models studied, the standard-of-care agents, cisplatin and etoposide, enriched the proportion of CSCs. In direct contrast, both VS-5584 and VS-4718 reduced SCLC CSCs *in vivo* when combined with chemotherapy. VS-5584 and VS-4718 also delayed tumor regrowth after treatment with these cytotoxic agents in SCLC xenograft models of switch maintenance therapy. The preferential targeting of CSCs in preclinical SCLC models provides an important rationale for clinical development of VS-5584 and VS-4718 in combination with chemotherapy to potentially lengthen the time to relapse and improve the treatment outcome for patients with SCLC.

A copy of the poster presentation is available at http://bit.ly/12otlcV

Title: FAK inhibitor VS-6063 (defactinib) targets mesothelioma cancer stem cells, which are enriched by standard of care chemotherapy
Date and time: Tuesday, April 21, 2015, 1:00 pm – 5:00 pm ET

Location: Section 21; Poster Board 23
Abstract Number: 4236
Session: Session Title: Therapeutics Targeting Cancer Stem Cells; Session Category: Tumor Biology
Summary: Malignant pleural mesothelioma (MPM) is an aggressive tumor in the lining of the lung and median overall survival with standard of care chemotherapy is only 12 months. This poor prognosis may be attributable at least in part to CSCs which are resistant to chemotherapy and can mediate cancer recurrence and progression. FAK has been shown to play an essential role in the survival, self-renewal and tumor-initiating capability of CSCs.

In the preclinical models and patient biopsies studied, two standard-of-care agents, pemetrexed and platinum, enrich the proportion of CSCs. In direct contrast, the FAK inhibitor, VS-6063, markedly reduced CSCs in models of mesothelioma. In addition, in tumors that are low in the biomarker merlin, marked bulk tumor reduction was observed. In a switch maintenance model, VS-6063 treatment also delayed tumor regrowth following cisplatin plus pemetrexed treatment *in vivo*. These data provide strong rationale for the current clinical testing of VS-6063 in Verastem's registration-directed COMMAND trial, evaluating VS-6063 in a maintenance setting to potentially prolong response to front line chemotherapy in patients with mesothelioma.

A copy of the poster presentation is available at http://bit.ly/12otlcV

Title: Targeting Focal Adhesion Kinase is a novel approach to therapy of high-risk, Ikaros-mutant acute B-cell lymphoblastic leukemia
Date and time: Tuesday, April 21, 2015, 1:00 pm – 5:00 pm ET
Location: Section 20; Poster Board 17
Abstract Number: 4202
Session: Session Title: Mouse Models of Human Cancer 3; Session Category: Tumor Biology

This research includes work on VS-4718 and was presented by collaborators. A copy of the poster presentation is available at http://bit.ly/12otlcV

About VS-6063
VS-6063 (defactinib) 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 FAK activity 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 "Window of Opportunity" study in patients with mesothelioma prior to surgery, a Phase 1/1b study in combination with paclitaxel in patients with ovarian cancer, a trial in patients with Kras-mutated non-small cell lung cancer and a trial evaluating the combination of VS-6063 and VS-5584 in patients with relapsed mesothelioma. VS-6063 has been granted orphan drug designation in the U.S. and EU 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 VS-5584
VS-5584 is an orally available compound that has demonstrated potent and highly selective activity against class 1 PI3K enzymes and dual inhibitory actions against mTORC1 and mTORC2. In preclinical studies, VS-5584 has been shown to reduce the percentage of cancer stem cells and induce tumor regression in chemotherapy-resistant models. Verastem is currently conducting a dose escalation trial of VS-5584 in patients with advanced solid tumors as a single agent and a combination trial of VS-5584 and VS-6063 in patients with relapsed mesothelioma. VS-5584 has been granted orphan drug designation in the U.S. and EU for use in mesothelioma.

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 and PI3K/mTOR. 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 and activity of the Company's product candidates, VS-6063, VS-4718 and VS-5584, and the Company's FAK and PI3K/mTOR, potential plans for clinical development of the Company's product candidates, and the structure of the Company's planned or pending clinical trials. 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 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 our product candidates will cause unexpected safety events, that the Company will be unable to successfully initiate or complete the clinical development of its product candidates, that the development of the Company's product candidates will take longer or cost more than planned, and that the Company'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 the Company's Annual Report on Form 10-K for the year ended December 31, 2014 and in any subsequent SEC filings. The forward-looking statements contained in this press release 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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