Verastem Presents Data at the 2014 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics

November 21, 2014

Results from the Phase 1 Dose Escalation Study of VS-6063 in Japanese Patients and New Preclinical Results Support Continued Clinical Development of VS-6063 and VS-5584 in Mesothelioma and Other Cancers

BOSTON--(BUSINESS WIRE)--Nov. 21, 2014-- Verastem, Inc. (NASDAQ:VSTM), focused on discovering and developing drugs to treat cancer by the targeted killing of cancer stem cells, today announced four poster presentations at the 26th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics taking place November 18 - 21, 2014, in Barcelona, Spain.

"We are pleased that the safety and pharmacokinetic profile observed in our Phase 1 study of VS-6063 in Japanese patients was consistent with that seen in the US Phase 1 study, permitting the inclusion of Japanese sites in COMMAND, the registration-directed study of VS-6063 in patients with mesothelioma following frontline chemotherapy. Also, we noted that the one patient in the Phase 1 study with relapsed mesothelioma appeared to receive clinical benefit with disease stabilization of almost 6 months," said Dr. Joanna Horobin, Verastem Chief Medical Officer. "Relapsed mesothelioma is highly aggressive with reported median progression free survival of six weeks in controlled clinical trials. The encouraging data reported here from the combination of VS-6063 and VS-5584 in pre-clinical models of mesothelioma offers a novel therapeutic approach in this setting. We look forward to initiating a new clinical study evaluating the combination of these two agents in patients with relapsed mesothelioma in the first quarter of 2015."

Verastem is presenting data at the EORC-NCI-AACR conference in support of its programs targeting cancer stem cells (CSCs) through inhibition of the focal adhesion kinase (FAK; VS-6063) and PI3K/mTOR (VS-5584) signaling pathways. Research on the FAK and PI3K/mTOR signaling pathways has revealed critical roles for each in CSC survival and disease progression. CSCs represent a subpopulation of cancer cells that have tumor-initiating capability, are particularly resistant to chemotherapy and can mediate tumor recurrence both locally and at metastatic sites.

"The preclinical posters presented at EORTC this year continue to expand our understanding of the activity of VS-6063 and VS-5584 along with their underlying biological mechanisms," said Dr. Jonathan Pachter, Verastem Head of Research. "In these presentations we provide evidence that VS-6063 and VS-5584 are potent inhibitors of cancer stem cells and have the potential to be used as single agents, alongside widely-used, standard-of-care treatments, or in combination with each other."

A summary of the data presented by Verastem at the conference is below:

Title: A first-in-Asian phase I dose escalation study to evaluate the safety and pharmacokinetics of VS-6063 (defactinib), a focal adhesion kinase inhibitor in subjects with non-hematologic malignancies
Abstract #: 296
Poster Board #: 076
Date: Thursday, November 20, 2014
Time: 9:00am GMT
Location: Exhibition Hall
Summary: Results were presented from a first-in-Asia, Phase 1 trial evaluating the safety and pharmacokinetics of single agent VS-6063 (defactinib) in Japanese patients with advanced solid tumors, including one patient with mesothelioma.

The Japanese Phase 1 is an open-label, dose-escalation study that enrolled nine subjects who received single-agent VS-6063 (200, 400 or 600mg; n=3 in each dose cohort) BID. The study results demonstrated that VS-6063 was well tolerated at all dose levels. There were no serious adverse events or evidence of dose-limiting toxicity. Pharmacokinetic results from the recommended Phase 2 dose of 400mg BID were consistent with previously reported data in non-Japanese subjects. These safety and pharmacokinetic results supported the entry of Japanese subjects at the RP2D into the ongoing multinational trial (COMMAND) of VS-6063 in malignant pleural mesothelioma (MPM) patients.

A copy of the poster presentation is available at http://bit.ly/R3M6wc.

Title: FAK inhibitor VS-6063 (defactinib) targets mesothelioma cancer stem cells which are enriched by standard of care chemotherapy
Abstract #: 302
Poster Board #: 082
Date: Thursday, November 20, 2014
Time: 9:00am GMT
Location: Exhibition Hall
Summary: MPM is an aggressive tumor in the lining of the lung often resulting from prior exposure to asbestos. Median overall survival with standard of care chemotherapy is only 12 months from diagnosis. 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, FAK inhibitor, VS-6063, markedly reduced the proportion of CSCs *in vitro*, *in vivo* and in tumors of VS-6063-treated mesothelioma patients. VS-6063 treatment also delayed tumor regrowth following cisplatin plus pemetrexed treatment *in vivo*. These data provide the rationale for the current clinical testing of VS-6063 in Verastem's registration-directed COMMAND trial, evaluating VS-6063 following treatment with pemetrexed plus platinum

to potentially prolong response to front line chemotherapy in patients with mesothelioma.

A copy of the poster presentation is available at http://bit.ly/R3M6wc.

Title: PI3K/mTOR inhibitor VS-5584 targets cancer stem cells and prevents tumor regrowth after chemotherapy in preclinical models of small cell lung cancer
Abstract #: 439
Poster Board #: 011
Date: Friday, November 21, 2014
Time: 9:00am GMT
Location: Exhibition Hall
Summary: Small cell lung cancer (SCLC) is a highly aggressive malignancy with a 5-year overall survival rate of only 5-10%. Most patients with SCLC initially respond to chemotherapy but subsequently experience aggressive tumor recurrence, which may be attributed to the presence of CSCs.

The study results presented here demonstrated that VS-5584 inhibits proliferation and induces apoptosis in SCLC cell lines *in vitro* and exhibited antitumor activity in SCLC xenograft models *in vivo*. In addition, VS-5584 also exhibited synergistic activity with standard-of-care agents, cisplatin and etoposide, in SCLC models. VS-5584 is currently being evaluated in a Phase 1 clinical trial in patients with solid tumors, and the preferential targeting of CSCs by VS-5584 in these preclinical models of SCLC provides the rationale for clinical development of VS-5584 either as a single agent or in combination with chemotherapeutic agents to potentially extend time to relapse and improve outcome for patients with small cell lung cancer.

A copy of the poster presentation is available at http://bit.ly/R3M6wc.

Title: The cancer stem cell inhibitors VS-6063 (defactinib) and VS-5584 exhibit synergistic anticancer activity in preclinical models of mesothelioma
Abstract #: 446
Poster Board #: 018
Date: Friday, November 21, 2014
Time: 9:00am GMT
Location: Exhibition Hall
Summary: MPM is an aggressive cancer of the lining of the lung in which CSCs may drive resistance to current chemotherapy. There is only one treatment regimen approved for use, pemetrexed plus a platinum agent, which is used as front-line therapy and results in median overall survival of only 12 months. Unfortunately, there are no approved second line options for patients with actively progressing disease after front-line therapy where the median progression free survival reported in controlled clinical trials is just six weeks.

In an effort to expand the mesothelioma patient population that may potentially benefit from drugs targeting CSCs, Verastem conducted this preclinical study to identify agents that show synergistic anticancer activity with VS-6063. An in vitro combination screen was carried out evaluating VS-6063 in combination with 20 anticancer agents including both cytotoxic drugs and targeted agents. Several anticancer agents, including Verastem's dual PI3K/mTOR inhibitor VS-5584, showed synergistic activity with VS-6063.

The study results demonstrated synergistic activity of VS-6063 and VS-5584 in mesothelioma models *in vitro* and *in vivo*. VS-6063 and VS-5584, alone and in combination, reduced the proportion of mesothelioma CSCs. In addition, single agent treatment with VS-6063 or VS-5584 reduced the viability of mesothelioma cells cultured in 3D matrigel, and the combination of VS-6063 and VS-5584 displayed synergistic reduction in cell viability based on multiple combination analysis models. When tested *in vivo* for reduction of mesothelioma tumor growth, VS-6063 and VS-5584 were each active as single agents. In combination, VS-5584 further enhanced the antitumor efficacy of VS-6063 in this model. The combination of VS-6063 and VS-5584 represents a novel therapeutic approach and these data support the clinical evaluation of the combination of VS-6063 and VS-5584 in patients with relapsed mesothelioma following front-line therapy.

A copy of the poster presentation is available at http://bit.ly/R3M6wc.

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, and a trial in patients with KRas-mutated non-small cell lung cancer. VS-6063 has been granted orphan drug designation in the U.S. and EU for use in mesothelioma.

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 Phase 1 dose escalation trial of VS-5584 in patients with advanced solid tumors.

About COMMAND

COMMAND is a registration-directed, double-blind, placebo-controlled trial of VS-6063 in patients with malignant pleural mesothelioma. The primary endpoints of COMMAND are progression free survival (PFS) and overall survival (OS). VS-6063 targets cancer stem cells which are an underlying cause of tumor progression and recurrence. The design of COMMAND allows the opportunity to enrich for patients with tumors low in the biomarker, merlin. Preclinical and early clinical research has demonstrated that low merlin levels may be predictive of increased effectiveness of FAK inhibitors such as VS-6063. The COMMAND study stratifies patients to evaluate the effect of VS-6063 in both the overall patient population and the subgroup of patients whose tumors are low in merlin.

COMMAND is expected to enroll approximately 350-400 patients at clinical sites in 12 countries, including the US, UK, Japan, Australia, Canada, South Africa, New Zealand and countries in mainland Europe. Eligible patients who had a partial response or stable disease following standard first-line therapy with platinum/pemetrexed will be stratified to merlin low or high and then randomized to receive either placebo or 400 mg of VS-6063. For more information visit www.COMMANDmeso.com.

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 and activity of the Company's product candidates, including VS-6063, or defactinib, and VS-5584, and the Company's FAK and PI3K/mTOR programs generally, the timeline for clinical development and regulatory approval of the Company's compounds, including the proposed commencement of the VS-6063/VS-5584 combination study, 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 the Company will be unable to successfully complete the clinical development of its product candidates, including VS-6063 and VS-5584, 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, 2013 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.

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