Verastem Initiates Phase 2 Trial of Defactinib in Lung Cancer

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Study Focuses on Patients with KRAS-mutated Non-Small Cell Lung Cancer

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 26, 2013-- Verastem, Inc. (NASDAQ: VSTM), focused on discovering and developing drugs to treat cancer by the targeted killing of cancer stem cells, today announced the initiation of a Phase 2 trial of defactinib (VS-6063), a potent inhibitor of focal adhesion kinase (FAK), in KRAS-mutated non-small cell lung cancer (NSCLC).

“We currently do not have any effective targeted treatment options for patients with KRAS-mutated non-small cell lung cancer (NSCLC) which represents about 30% of the NSCLC population,” said Dr. David Gerber, Associate Professor of Internal Medicine, Lung Cancer Specialist at the University of Texas Southwestern Medical Center and Study Chairman of the defactinib clinical trial. “Research by Dr. Scaglioni here at UTSW has demonstrated that inhibition of Focal Adhesion Kinase in KRAS-mutated NSCLC with a secondary mutation in either p16 or p53, extends survival in xenograft models of this disease.”

Dr. Scaglioni’s group at UTSW published a paper in 2013 in Cancer Discovery titled “RHOA-FAK is a Required Signaling Axis for the Maintenance of KRAS-Driven Lung Adenocarcinoma” that describes the critical role of FAK signaling in NSCLC that has both a KRAS-mutation and accompanying secondary mutation in the p16/ARF/INK4a locus (p16) or p53. As reported in the paper, genetic silencing or deletion of FAK replicated the effects of treatment with Verastem’s first generation small molecule inhibitor of FAK, VS-6062, in both in vitro and xenograft models of the disease.

"The reported rates vary, but we believe approximately 10-15% of NSCLC tumors have both the KRAS mutation and an accompanying secondary mutation in p16 or p53 leading to silencing of those tumor suppressor genes, which appears to be a prerequisite for the activity of FAK inhibitors in KRAS-mutated NSCLC models,” said Dr. Joanna Horobin, Verastem Chief Medical Officer. “Patients with KRAS mutated tumors derive limited benefit from chemotherapy. This study is designed to elucidate the role of the secondary mutation in response to FAK inhibitor treatment and hopefully make a meaningful impact on the clinical response to therapy in a subset of patients with difficult to treat NSCLC.”

The Phase 2 study is designed to assess the effect of defactinib on Progression Free Survival (PFS), Overall Response Rate (ORR) and Overall Survival (OS). There will be 4 study arms, including patients with a KRAS-mutation, or a KRAS-mutation with accompanying secondary mutations in p16, p53 or both p16 and p53. The trial is being conducted at 8-10 sites in the US and is expected to enroll up to 44 patients (11 per arm) in the first stage of the Simon two-stage trial design. A Simon two-stage trial design incorporates a single, pre-planned interim analysis to determine which enrollment arms are exhibiting a favorable response to treatment and allows for enrollment of an additional 12 patients with the same tumor mutation profile per arm.

“With the initiation of this study we now have a total of five clinical studies underway,” said Robert Forrester, Verastem President and Chief Executive Officer. “In addition to the NSCLC trial, we recently initiated the registration-directed COMMAND study in mesothelioma, a Phase 1 trial of defactinib in Japan and continue enrollment in the Phase 1b combination study of defactinib and paclitaxel for patients with ovarian cancer. In parallel to the development of defactinib, we have an ongoing Phase 1 study of VS-4718 in advanced solid tumors. We will continue to execute on our development plans and remain committed to bringing novel therapies targeting cancer stem cells to patients with few to no adequate treatment options.”

The paper “RHOA-FAK is a Required Signaling Axis for the Maintenance of KRAS-Driven Lung Adenocarcinoma” by Konstantinidou et. al., Cancer Discovery 2013, can be accessed at http://bit.ly/1bd1Zta

About Defactinib

Defactinib (VS-6063) is an oral 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. Defactinib is currently being studied in the registration-directed COMMAND trial in mesothelioma, a Phase 1/1b study in ovarian cancer, a Phase 1 study in Japan and a Phase 2 trial in KRAS-mutated Non-Small Cell Lung Cancer. Defactinib has been granted orphan drug designation in the U.S. and E.U. 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, 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, or defactinib, and the Company’s FAK and diagnostic programs generally, the timeline for clinical development and regulatory approval of the Company’s compounds, the expected timing for the reporting of data from ongoing trials, the structure of the Company’s planned or pending clinical trials and estimates of the Company’s ability to fund operations. 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 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 defactinib, 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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