Verastem Announces Publication of Scientific Data for VS-5584 in Cancer Research

January 16, 2015

BOSTON--(BUSINESS WIRE)--Jan. 16, 2015-- 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 paper, titled “PI3K/mTOR dual inhibitor VS-5584 preferentially targets cancer stem cells,” has been published in *Cancer Research*, a peer-reviewed journal of the American Association for Cancer Research (AACR).

The paper discusses results from preclinical research evaluating VS-5584, a highly potent, selective small molecule inhibitor of mTORC1/2 and Class I PI3K kinases, which preferentially targets cancer stem cells (CSCs) *in vitro* and *in vivo*. 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.

“In this study, we show clear evidence that the biological inhibition of PI3K alpha, beta and mTOR together, in contrast to inhibition of any one member of the pathway alone, is necessary for the killing of cancer stem cells across different carcinoma types, including breast, ovarian and small cell lung cancer,” said Jonathan Pachter, Ph.D., Verastem Head of Research and co-author of the paper. “VS-5584 demonstrates a profile that has broad inhibition of the Class I PI3K isoforms and mTOR kinase but, importantly, retains selectivity for these targets with no significant activity against over 400 other protein and lipid kinases. Of particular interest were results from two small cell lung cancer models demonstrating that VS-5584 may substantially extend antitumor response and delay tumor regrowth as a maintenance treatment after de-bulking tumors with a cytotoxic agent. These data continue to expand our understanding of the underlying mechanisms of VS-5584 and support the scientific rationale for Verastem’s ongoing clinical development of this compound in solid tumors.”

The study results demonstrated that VS-5584 is up to 30-fold more potent in inhibiting the proliferation and survival of CSCs compared to non-CSCs in solid tumor cell populations. VS-5584 preferentially diminished CSC levels in multiple mouse xenograft models of human cancer. Similarly, VS-5584 treatment *ex vivo* preferentially reduced CSCs in surgically resected breast and ovarian patient tumors. In contrast, chemotherapeutics such as paclitaxel, cisplatin and etoposide effectively targeted bulk tumor cells, but enriched CSCs. Mechanistic investigations revealed that knock down of PI3Kα, PI3Kβ or mTOR alone was insufficient to decrease CSCs, while knock down of PI3Kα, PI3Kβ and mTOR together effectively reduced CSCs mimicking the effect of VS-5584. Consistent with CSC ablation, VS-5584 delayed tumor regrowth following chemotherapy in xenograft models of small cell lung cancer. These data help to elucidate the mechanism of VS-5584 targeting CSCs and provide a strong rationale for the clinical development of VS-5584 in combination with chemotherapeutic agents targeting bulk tumor cells to achieve more durable clinical responses in cancer patients.

The full publication can be accessed online at http://bit.ly/1ER8DEB

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 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 activity of the Company’s product candidate VS-5584 and the Company’s PI3K/mTOR program generally and the proposed clinical development of VS-5584. 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 VS-5584 and preliminary or interim data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials with VS-5584, 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 VS-5584, and that VS-5584 will not receive regulatory approval or become a commercially successful product. 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.

Source: Verastem, Inc.

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