Verastem Presents Preclinical Data at ASCO-SITC Highlighting the Synergistic Effects of Duvelisib in Combination with Immune Checkpoint or Co-Stimulatory Antibodies in B Cell Lymphoma Model

January 26, 2018

Data Support Further Exploration of Duvelisib in Combination with Anti-PD-1/PD-L1 or Co-Stimulatory Antibodies in Patients with B Cell Malignancies

BOSTON--(BUSINESS WIRE)--Jan. 26, 2018-- Verastem, Inc. (NASDAQ:VSTM), focused on discovering and developing drugs to improve the survival and quality of life of cancer patients, today announced that a poster highlighting the synergistic effects of duvelisib in combination with immune checkpoint or co-stimulatory antibodies in preclinical models of B cell lymphoma was presented at ASCO-SITC Clinical Immuno-Oncology Symposium being held January 25-27, 2018 in San Francisco. Duvelisib is a first-in-class oral dual inhibitor of phosphoinositide 3-kinase (PI3K)-delta and PI3K-gamma that is currently being developed for the treatment of relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and follicular lymphoma (FL). In addition, duvelisib is being studied in other hematologic malignancies including peripheral T cell lymphoma (PTCL).

“In patients with relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma and follicular lymphoma, oral duvelisib monotherapy has demonstrated efficacy, along with a consistent and manageable safety profile. However, emerging data suggest that some aggressive lymphomas will likely require combination therapy to improve clinical outcomes,” said Jonathan Pachter, PhD, Chief Scientific Officer of Verastem. “Our research presented this year at ASCO-SITC indicates that the dual PI3K-delta/PI3K-gamma inhibitory activity of duvelisib enables duvelisib to reduce both T-regulatory (Treg) and myeloid immunosuppressive cells in a murine A20 B cell lymphoma model. As a result of these beneficial changes within the tumor microenvironment, we observed a striking enhancement by duvelisib of the anti-tumor efficacy of immune checkpoint or co-stimulatory antibodies in this preclinical B cell lymphoma model. These data support further exploration of duvelisib in combination with immunotherapeutic agents for the treatment of aggressive lymphomas.”

Oral duvelisib is the first PI3K inhibitor to show efficacy as an oral monotherapy in a randomized Phase 3 study in patients with relapsed or refractory CLL/SLL (the DUO™ study). In the Phase 2 DYNAMO study, duvelisib achieved meaningful clinical activity in patients diagnosed with follicular lymphoma (FL), small lymphocytic lymphoma (SLL), or marginal zone lymphoma (MZL) whose disease is refractory to rituximab and to a chemotherapy regimen or radioimmunotherapy. Verastem plans to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) during the first quarter of 2018 requesting full approval of duvelisib for the treatment of patients with relapsed or refractory CLL/SLL and accelerated approval for the treatment of patients with relapsed or refractory follicular lymphoma (FL).

Details for the poster presentation at ASCO-SITC 2018 are:

Title: Dual PI3K-δ,γ inhibitor duvelisib reduces immunosuppressive Tregs and myeloid cells enhancing efficacy of checkpoint and co-stimulatory antibodies in a B cell lymphoma model
Session: Developmental Therapeutics – Poster Session B
Abstract #: 33
Location: Golden Gate Hall – B2 Level – Poster Board D1
Date and time: Friday, January 26, 2018; 11:30am to 1:00pm PT and 5:30 to 6:30pm PT
Summary: Prior published research has shown that PI3K-delta inhibition reduces immunosuppressive Tregs and PI3K-gamma inhibition reduces immunosuppressive myeloid cells. As a result, it was hypothesized that duvelisib may augment the efficacy of immune checkpoint or co-stimulatory antibodies. For this study, Verastem researchers administered duvelisib alone, anti-PD-1 alone, anti-OX40 alone, duvelisib + anti-PD-1, duvelisib + anti-OX40, or vehicle control to mice bearing syngeneic A20 B cell lymphoma tumors.

Duvelisib alone, anti-PD-1 alone and anti-OX40 alone each induced tumor growth delay. When duvelisib and anti-PD-1 were combined, strong anti-tumor synergy was observed. When duvelisib and anti-OX40 were combined, tumor regression was observed which correlated with strong reduction of tumor Tregs, M2 macrophages and myeloid-derived suppressor cells. Immune memory was also assessed by injecting mice that had become tumor free with A20 cells following anti-OX40 alone or duvelisib + anti-OX40 with no further treatment. The mice that had received anti-OX40 alone grew new tumors upon A20 re-challenge, however, all mice that had received duvelisib + anti-OX40 did not grow tumors upon re-challenge and showed elevated memory T cells in blood and spleen. These findings indicate that treatment with duvelisib + anti-OX40 established immune memory. The dual inhibition of PI3K-δ and PI3K-γ appears to make duvelisib effective in reducing both lymphoid and myeloid immuno-suppressive populations, consistent with prior data suggesting that PI3K-δ inhibition reduces immunosuppressive Tregs, whereas PI3K-γ inhibition reduces immunosuppressive myeloid cells. We believe these results showing that dual PI3K-δ and PI3K-γ inhibition can enhance the anti-tumor efficacy of immune checkpoint and co-stimulatory antibodies which potentially support the clinical exploration of duvelisib in combination with these agents.

A copy of the poster presentation will be available **here** following the conclusion of the poster sessions.

About the Tumor Microenvironment

The tumor microenvironment encompasses various cellular populations and extracellular matrices within the tumor or cancer niche that support cancer cell survival. This includes immunosuppressive cell populations such as regulatory T-cells, myeloid-derived suppressor cells, M2 TAMS, as well as tumor-associated fibroblasts and extracellular matrix proteins which can hamper the entry and therapeutic benefit of cytotoxic immune cells and anti-cancer drugs. In addition to targeting the proliferative and survival signaling of cancer cells, Verastem’s compounds duvelisib and defactinib target the tumor microenvironment as a mechanism of action to potentially improve a patient’s response to therapy.

About Duvelisib

Duvelisib is a first-in-class investigational, dual inhibitor of phosphoinositide 3-kinase (PI3K)-delta and PI3K-gamma, two enzymes known to help support the growth and survival of malignant B-cells and T-cells. PI3K signaling may lead to the proliferation of malignant B- and T-cells and is thought to play a role in the formation and maintenance of the supportive tumor microenvironment.[1,2,3] Duvelisib is currently being evaluated in late- and mid-stage extension trials, including DUO™, a randomized, Phase 3 monotherapy study in patients with relapsed or refractory chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL),[4] and DYNAMO™, a single-arm, Phase 2 monotherapy study in patients with refractory indolent non-Hodgkin lymphoma (iNHL).[5] Both DUO and DYNAMO achieved their primary endpoints and Verastem intends to submit a New Drug Application (NDA) requesting the full approval of duvelisib for the treatment of patients with relapsed or refractory CLL/SLL, and accelerated approval for the treatment of patients with relapsed or refractory follicular lymphoma (FL). Duvelisib is also being developed by Verastem for the treatment of peripheral T-cell lymphoma (PTCL), and is being investigated in combination with other agents through investigator-sponsored studies.[6] Information about duvelisib clinical trials can be found on www.clinicaltrials.gov.

About Verastem, Inc.

Verastem, Inc. (NASDAQ:VSTM) is a biopharmaceutical company focused on discovering and developing drugs to improve outcomes for patients with cancer. Verastem is currently developing duvelisib, a dual inhibitor of PI3K-delta and PI3K-gamma, which has successfully met its primary endpoint in a Phase 2 study in iNHL and a Phase 3 clinical trial in patients with CLL/SLL. In addition, Verastem is developing the FAK inhibitor defactinib, which is currently being evaluated in three separate clinical collaborations in combination with immunotherapeutic agents for the treatment of several different cancer types, including pancreatic cancer, ovarian cancer, non-small cell lung cancer, and mesothelioma. Verastem's product candidates seek to treat cancer by modulating the local tumor microenvironment, enhancing anti-tumor immunity, and reducing cancer stem cells. For more information, please visit www.verastem.com.

Verastem, Inc. forward-looking statements notice:

This press release includes forward-looking statements about Verastem's strategy, future plans and prospects, including statements regarding the development and activity of Verastem's investigational product candidates, including duvelisib and defactinib, and Verastem's PI3K and FAK programs generally, the structure of our planned and pending clinical trials and the timeline and indications for clinical development and regulatory submissions. The words "anticipate," "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 Verastem'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 the full data from the DUO study will not be consistent with the previously presented results of the study; that data may not be available when expected, including for the Phase 3 DUO™ study; that even if data from clinical trials is positive, regulatory authorities may require additional studies for approval and the product may not prove to be safe and effective; that the degree of market acceptance of product candidates, if approved, may be lower than expected; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that our product candidates will cause unexpected safety events or result in an unmanageable safety profile as compared to their level of efficacy; that duvelisib will be ineffective at treating patients with lymphoid malignancies; that Verastem will be unable to successfully initiate or complete the clinical development of its product candidates; that the development of Verastem's product candidates will take longer or cost more than planned; that Verastem may not have sufficient cash to fund its contemplated operations; that Verastem or Infinity Pharmaceuticals, Inc. (Infinity) will fail to fully perform under the duvelisib license agreement; that Verastem may be unable to make additional draws under its debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that Verastem will not pursue or submit regulatory filings for its product candidates, including for duvelisib in patients with CLL or iNHL; and that Verastem's product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients. Other risks and uncertainties include those identified under the heading "Risk Factors" in Verastem's Annual Report on Form 10-K for the year ended December 31, 2016 and in any subsequent filings with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Verastem's views as of the date of this release, and Verastem does not undertake and specifically disclaims any obligation to update any forward-looking statements.

References

[1] Winkler et al. PI3K-delta and PI3K-gamma inhibition by IPI-145 abrogates immune responses and suppresses activity in autoimmune and inflammatory disease models. Chem Biol 2013; 20:1-11.

[2] Reif et al. Cutting Edge: Differential roles for phosphoinositide 3 kinases, p110-gamma and p110-delta, in lymphocyte chemotaxis and homing. J Immunol 2004:173:2236-2240.

[3] Schmid et al. Receptor tyrosine kinases and TLR/IL1Rs unexpectedly activate myeloid cell PI3K, a single convergent point promoting tumor inflammation and progression. Cancer Cell 2011;19:715-727.

[4] www.clinicaltrials.gov, NCT02004522

[5] www.clinicaltrials.gov, NCT01882803

[6] www.clinicaltrials.gov, NCT02783625, NCT02158091

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