Verastem Announces the Presentation of Phase 1 Duvelisib Combination Data in T-Cell Lymphomas at the ASH 2017 Annual Meeting

December 11, 2017

Duvelisib Demonstrates an Acceptable Safety Profile in Combination with Romidepsin or Bortezomib in Patients with Relapsed/Refractory TCL

Combination of Duvelisib and Romidepsin Achieves 60% Overall Response Rate Including a 27% Complete Response Rate in these patient populations

BOSTON--(BUSINESS WIRE)--Dec. 11, 2017-- Verastem, Inc. (NASDAQ: VSTM), focused on discovering and developing drugs to improve the survival and quality of life of cancer patients, today announced the presentation of new preclinical and Phase 1 clinical data from an investigator-sponsored study evaluating the safety and activity of oral duvelisib in combination with romidepsin (Istodax®) or bortezomib (Velcade®) in relapsed or refractory T-cell lymphomas (TCL) at the American Society of Hematology (ASH) 2017 Annual Meeting held December 9-12, 2017 in Atlanta. Duvelisib is a first-in-class oral dual inhibitor of phosphoinositide-3-kinase (PI3K)-delta and PI3K-gamma which is currently being developed for the treatment of relapsed or refractory Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL) and Follicular Lymphoma (FL). In addition, duvelisib is being studied in other hematologic malignancies including both peripheral and cutaneous T cell lymphoma (TCL).

“The data presented today at ASH demonstrate that oral duvelisib, combined with either romidepsin or bortezomib, has an acceptable safety profile in patients with relapsed or refractory TCL with response rates, while still preliminary, that appear promising when compared to those seen with currently approved therapies,” said Steven Horwitz, MD, Memorial Sloan Kettering Cancer Center (MSKCC), co-principal investigator of the Phase 1 study, and lead author of the oral presentation. “We were especially pleased to see that these response rates were even higher in patients with peripheral TCL (PTCL), a rare and aggressive type of non-Hodgkin lymphoma. These clinical results were further bolstered by important preclinical findings showing duvelisib’s cell killing activity *in vitro* and its ability to promote beneficial changes within the *in vivo* tumor microenvironment.”

“The preclinical and Phase 1 results reported today by the team at MSKCC are important because they provide further validation for our continued expansion of the duvelisib development program into T-cell malignancies including PTCL,” said Diep Le, MD, PhD, Chief Medical Officer of Verastem. “Overall, our data presentations at ASH this year continue to build upon the strong foundation of preclinical research and clinical investigation for Verastem’s product candidates, demonstrating their anti-cancer activity, either alone or in combination with other agents, across a wide variety of hematologic malignancies.”

Phase 1 Safety and Activity Results

This multicenter, Phase I trial is comprised of parallel arms evaluating oral duvelisib in combination with romidepsin (arm A) or bortezomib (arm B) in patients with relapsed/refractory TCL, including PTCL and cutaneous T-cell lymphoma (CTCL). Oral duvelisib was dosed at 25mg, 50mg, or 75mg twice-daily (BID) on days 1-28. Romidepsin 10mg/m^2 was dosed on Days 1, 8, and 15 (arm A) or bortezomib 1mg/m^2 on Days 1, 4, 8, and 11 (arm B), both cohorts on 28-day cycles.

In arm A, there were 15 patients evaluable for efficacy (PTCL, n=11; CTCL, n=4). Of these, nine responded (4 complete responses (CR) and 5 partial responses (PR) for an overall response rate (ORR) of 60%. Seven of the 11 patients with PTCL responded (4 CR and 3 PR) for an ORR of 64%. Among the 9 patients evaluable for safety (25mg, n=3; 50mg, n=3; 75mg, n=3), there were no dose limiting toxicities (DLT), therefore oral duvelisib 75mg BID in combination with romidepsin 10mg/m^2 IV was defined as the maximum tolerated dose (MTD). The most common Grade 1/2 adverse events were fatigue (n=9), nausea (n=8), altered taste (n=8) and diarrhea (n=6), rash (n=5), dysphagia (n=4) and anorexia (n=4). The most common Grade 3/4 adverse events were neutropenia (n=6), thrombocytopenia (n=1), lung infection (n=1), pleural effusion (n=1) and hyponatremia (n=1). There were two deaths (sepsis and diffuse alveolar hemorrhage following allogeneic stem cell transplant) that were both assessed as unrelated to study drug.

In arm B, there were 17 patients evaluable for efficacy (PTCL, n=10; CTCL, n=7). Of these, six responded (3 CRs and 3 PRs) for an ORR of 35%. Five of the 10 patients with PTCL responded (3 CRs and 2 PRs) for an ORR of 50%. Among the 14 patients evaluable for safety (25mg, n=6; 50mg, n=3; 75mg, n=5), there was one DLT (pneumonia) in the 25mg group. The MTD was determined to be oral duvelisib 25mg BID in combination with bortezomib 1mg/m^2 IV. The most common Grade 1/2 adverse events were diarrhea/colitis (n=11), nausea/vomiting (n=4), chills (n=4) and fatigue (n=4). The most common Grade 3/4 adverse events were ALT and AST elevation (n=6), rash (n=2) and neutropenia (n=2). There was a case of Stevens-Johnson syndrome resulting in death which was assessed by the investigator as possibly related to bortezomib, duvelisib, and trimethoprim-sulfamethoxazole, a medication that was initiated at the start of the study.

A copy of this oral presentation will be available here following the conclusion of the session.

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 Focal Adhesion Kinase

Focal Adhesion Kinase (FAK) is a non-receptor tyrosine kinase encoded by the PTK-2 gene that is involved in cellular adhesion and, in cancer, metastatic capability. Defactinib (VS-6063) and VS-4718 are orally available compounds that are potent inhibitors of FAK. Defactinib and VS-4718 utilize a multi-faceted approach to treat cancer by reducing cancer stem cells, enhancing anti-tumor immunity, and modulating the local tumor microenvironment. Defactinib is currently being studied in multiple clinical trials for patients with cancer.

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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Verastem, Inc.
Brian Sullivan, 781-292-4214
Senior Director, Corporate Development
bsullivan@verastem.com