Verastem Oncology Announces Investigator Sponsored Study on Duvelisib in Combination with Venetoclax

September 6, 2018

Phase I/II Trial to Investigate Combination Therapy in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma to take place at Dana-Farber Cancer Institute

BOSTON--(BUSINESS WIRE)--Sep. 6, 2018-- Verastem, Inc. (Nasdaq:VSTM), operating as Verastem Oncology, a biopharmaceutical company focused on developing and commercializing medicines to improve the survival and quality of life of cancer patients, today announced dosing of the first patient in a multicenter Phase I/II clinical trial at the Dana-Farber/Harvard Cancer Center of duvelisib in combination with venetoclax in patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

“Duvelisib and venetoclax target different pathways fundamental to CLL biology and have distinct mechanisms of action. We have found that CLL cells from duvelisib-treated patients are primed for apoptosis in response to treatment with agents such as venetoclax. We now have the opportunity to explore whether this combination may be an effective therapy for the treatment of patients with CLL,” said Matthew Davids, MD, MMSc, Assistant Professor of Medicine, Harvard Medical School, and Associate Director, Center for Chronic Lymphocytic Leukemia, Dana-Farber Cancer Institute and the study’s principal investigator. “We are excited to conduct this trial, as these new, targeted agents in development have the potential to improve patients’ response through combination therapies.”

This trial will investigate venetoclax, an oral, potent, selective inhibitor of BCL-2 – a key mediator of the intrinsic pathway of apoptosis, the process of programmed cell death – given in combination with duvelisib. Preclinical data support this combination, as duvelisib has been shown to upregulate BCL-2 transcript and protein expression levels and enhance the ability of venetoclax to induce apoptosis in ex vivo human CLL cells. The trial will use BH3 profiling – a functional assay that determines the apoptotic threshold of a cell – which Davids and colleagues previously used to show that inhibition of phosphoinositide 3-kinase (PI3K) enhances the apoptotic threshold of CLL cells and sensitivity to BCL-2 inhibition.

The phase I primary objectives are to determine the maximum tolerated dose, as well as the recommended phase II dose of venetoclax for this combination regimen with duvelisib in patients with relapsed or refractory CLL/SLL. The phase II primary objective is to determine the rate of complete response (CR) of the combination, as defined by the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2008 criteria.

“As we continue to explore the potential of duvelisib, we are very encouraged by the strong scientific rationale and the preclinical data supporting the combination of duvelisib and venetoclax. We expect this trial will help enhance our understanding of the effects of this combination in the treatment of patients with CLL/SLL,” said Diep Le, MD, PhD, Chief Medical Officer of Verastem Oncology. “Our goal at Verastem Oncology is to bring innovative therapeutic options to patients living with cancers that are in need of additional treatment options. Given the significant unmet need that exists among patients living with CLL and SLL, we look forward to the insight generated from this trial that could inform potential future clinical development for duvelisib.”

More information about this trial is available at www.clinicaltrials.gov.

About Duvelisib

Duvelisib is a first-in-class investigational oral, 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 was 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/small lymphocytic lymphoma (CLL/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. Verastem Oncology’s 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) was accepted for filing by the U.S. Food and Drug Administration (FDA), granted Priority Review and assigned a target action date of October 5, 2018. Duvelisib is also being developed by Verastem Oncology 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 Oncology

Verastem, Inc. (Nasdaq:VSTM), operating as Verastem Oncology, is a biopharmaceutical company focused on developing and commercializing medicines to improve the survival and quality of life of cancer patients. Verastem Oncology 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 indolent Non-Hodgkin Lymphoma (iNHL) and a Phase 3 clinical trial in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Verastem Oncology’s 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) was accepted for filing by the U.S. Food and Drug Administration (FDA), granted Priority Review and assigned a target action date of October 5, 2018. In addition, Verastem Oncology 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 (NSCLC), and mesothelioma. Verastem Oncology’s product candidates seek to treat cancer by modulating the local tumor microenvironment and enhancing anti-tumor immunity. For more information, please visit www.verastem.com.

Forward-looking statements notice:

This press release includes forward-looking statements about Verastem Oncology's strategy, future plans and prospects, including statements regarding the development and activity of Verastem Oncology's investigational product candidates, including duvelisib and defactinib, and Verastem Oncology's PI3K and FAK programs generally, the structure of our planned and pending clinical trials, Verastem Oncology's financial guidance 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 approval of Verastem Oncology's New Drug Application for duvelisib will not occur on the expected timeframe or at all, including by the U.S. Food and Drug Administration's target action date; that a filing of a European Marketing Application may not be achieved in fiscal year 2019 or at all; that even if data from clinical trials is positive, regulatory authorities may require additional studies for approval or may approve for indications or patient populations that are not as broad as intended and the product may not prove to be safe and effective or may require labeling with use or distribution restrictions; that the preclinical testing of Verastem Oncology'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 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 Oncology will be unable to successfully initiate or complete the clinical development and eventual commercialization of its product candidates; that the development and commercialization of Verastem Oncology's product candidates will take longer or cost more than planned; that Verastem Oncology may not have sufficient cash to fund its contemplated operations; that Verastem Oncology or Infinity Pharmaceuticals, Inc. will fail to fully perform under the duvelisib license agreement; that Verastem Oncology 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 Oncology will not pursue or submit regulatory filings for its product candidates, including for duvelisib in patients with CLL/SLL or iNHL; and that Verastem Oncology'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 the Company's Annual Report on Form 10-K for the year ended December 31, 2017 as filed with the Securities and Exchange Commission (SEC) on March 13, 2018 and in any subsequent filings with the SEC. The forward-looking statements contained in this press release reflect Verastem Oncology's views as of the date hereof, and the Company does not assume and specifically disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

References

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[4] www.clinicaltrials.gov, NCT02004522

[5] www.clinicaltrials.gov, NCT01882803

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Verastem Oncology
Marianne M. Lambertson, +1 781-292-4273
Vice President, Corporate Communications
Investor Relations/Public Relations
mlambertson@verastem.com