Verastem Announces Clinical Data from the Pivotal Phase 3 DUO™ Study: Duvelisib Significantly Improves Progression Free Survival in Relapsed or Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma

December 10, 2017

The DUO Study Achieves Primary Endpoint, Demonstrating Statistically Significant Improvement in PFS for Duvelisib Versus Ofatumumab (HR=0.52, p<0.0001)

Oral Duvelisib Monotherapy Also Achieves Significantly Higher ORR Compared to Ofatumumab (p<0.0001)

Duvelisib Continues to Demonstrate a Consistent and Manageable Safety Profile

BOSTON--(BUSINESS WIRE)--Dec. 10, 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 the results from the Phase 3 DUO study evaluating the efficacy and safety of duvelisib in patients with relapsed or refractory chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) 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 CLL/SLL and follicular lymphoma (FL). In addition, duvelisib is being studied in other hematologic malignancies including peripheral T cell lymphoma (PTCL).

“In the Phase 3 DUO study, oral duvelisib monotherapy achieved a statistically significant improvement in Progression-Free Survival (PFS) versus the approved standard of care treatment ofatumumab, along with a well characterized and manageable safety profile, in patients with previously treated CLL/SLL,” said Ian Flinn, MD, PhD, Director of the Blood Cancer Research Program at Sarah Cannon Research Institute and lead investigator of the DUO study. “Similar PFS advantages were also observed across all analyzed patient subgroups, including patients with 17p deletion, a genotype that historically correlates with poorer clinical outcomes. Duvelisib also achieved a statistically significant improvement in Overall Response Rate (ORR) and significantly reduced lymph node burden in the vast majority of patients. These data are encouraging for patients with CLL/SLL who progress or relapse following initial treatment.”

“CLL/SLL mostly affects elderly patients and many are unable or unwilling to be hospitalized or come into the clinic for frequent IV infusions. The CLL/SLL treatment landscape therefore is moving away from chemotherapies and toward more targeted, preferably oral regimens,” said Diep Le, MD, PhD, Chief Medical Officer of Verastem. “While patients are living longer many will be intolerant to, or relapse following, their initial therapy emphasizing the need for new options. 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 and may offer an appealing alternative for patients who have progressed or relapsed. We remain on track 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).”

DUO Efficacy Results

The DUO study met its primary endpoint with oral duvelisib monotherapy achieving a statistically significant improvement in median PFS (mPFS) compared to ofatumumab in patients with relapsed or refractory CLL/ SLL per a blinded Independent Review Committee (IRC) using iwCLL or revised IWG Response Criteria (modified iwCLL/IWG; 13.3 months vs 9.9 months, respectively; HR=0.52; p<0.0001), representing a 48% reduction in the risk of progression or death. Similar efficacy of duvelisib was observed regardless of whether patients had 17p deletion (del[17p]). The primary outcome of mPFS via IRC review in the del[17p] subpopulation significantly favored duvelisib over ofatumumab (12.7 months vs 9.0 months, respectively; HR=0.41; p=0.0011), representing a 59% reduction in the risk of progression or death. Per investigator assessment, duvelisib demonstrated a mPFS of 17.6 months, compared to 9.7 months for ofatumumab (HR=0.40, p<0.0001). Duvelisib maintained a PFS advantage in all patient subgroups analyzed as a subset of pre-specified sensitivity analyses.

The secondary efficacy outcome of ORR via IRC assessment according to modified iwCLL/IWG, significantly favored duvelisib over ofatumumab (73.8% vs 45.3%, respectively; p<0.0001), and reduced lymph node burden >50% in most patients vs ofatumumab (85% vs 16%). In the del[17p] subpopulation of patients, ORR was also significantly higher for duvelisib compared to ofatumumab, 70.0% versus 43.0%, respectively (p=0.0182). The Overall Survival (OS) in the ITT population was similar for those randomized to duvelisib and to ofatumumab during the study (HR=0.99; p=0.4807), demonstrating no detrimental effect on OS and was likely due to other available therapies following progression. Patients who progressed in the DUO study were given option to enroll in a crossover study to receive the opposite treatment. In the optional crossover study, 89 patients who were previously treated with ofatumumab in DUO and experienced disease progression were subsequently treated with duvelisib monotherapy. As in the parent DUO study, duvelisib demonstrated robust clinical activity in this crossover study with an ORR of 73%, a median duration of response of 12.7 months and a mPFS of 15 months by investigator assessments.

DUO Safety Results

Duvelisib monotherapy demonstrated a manageable safety profile, with results from this study consistent with the well-characterized safety profile of duvelisib monotherapy in patients with advanced hematologic malignancies in previous studies. For duvelisib-treated patients, the median time on treatment was 50.3 weeks (range, 0.9 - 160.0) compared to 23.1 weeks (range, 0.1 - 26.1) for ofatumumab. The most common Grade ≥3 treatment-emergent hematologic adverse events (occurring in >10% of patients) were neutropenia (30%) and anemia (13%). The most common Grade ≥3 non-hematologic treatment-emergent adverse events (occurring in >10% of patients) were diarrhea (15%), pneumonia (14%) and colitis (12%). The rate of severe opportunistic infections was 6%, including 2 patients (1%) with Pneumocystis jirovecii pneumonia (PJP), neither of whom was on

prophylaxis for PJP at the time of the event. 35% of patients discontinued duvelisib treatment due to an adverse event; ~40% of patients treated with duvelisib remained on treatment for over 18 months, with a median total follow-up of nearly 2 years. Adverse Events of Interest infrequently led to discontinuation of duvelisib treatment (e.g., diarrhea (5.1%), colitis (5.1%), pneumonitis (1.9%), neutropenia (1.3%), pneumonia (1.3%), transaminase elevations (0.6%), and rash (0.6%). Duvelisib treatment-related AEs leading to death (n=4) include general physical health deterioration (n=1); pneumonia staphylococcal (n=2) and sepsis (n=1)).

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

Regulatory Plan

Verastem plans to submit a NDA to the U.S. FDA 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 FL. The Company expects to submit the duvelisib NDA during the first quarter of 2018. Along with the clinical data from the DUO study, the duvelisib NDA submission will also contain the results from the Phase 2 DYNAMO™ study in patients with indolent non-Hodgkin's lymphoma that are double-refractory to both rituximab and chemotherapy or radioimmunotherapy.

About the Phase 3 DUO Study Design

In the Phase 3 DUO study, 319 patients were randomized 1:1 to receive either duvelisib 25mg orally twice daily or ofatumumab monotherapy, an approved standard of care treatment for use in CLL/SLL, per its label with an initial infusion of 300 mg followed by 7 weekly infusions and 4 monthly infusions of 2,000 mg. In addition to the primary endpoint of PFS per IRC in the ITT population, additional analyses to evaluate the outcome in several patient subgroups, including those with 17p deletion CLL/SLL, a known poor prognostic subgroup, were also conducted. PFS and other efficacy endpoints were analyzed using response determinations per the IRC using modified iwCLL/IWG criteria.

Verastem to Host R&D Event and Webcast at ASH 2017

On Sunday, December 10, 2017, Verastem will host a Research and Development event, which will feature a slide presentation and moderated panel discussion with recognized experts in the treatment of hematologic malignancies, including CLL/SLL, in a live Q&A session. Confirmed key opinion leader speakers include:

- Ian Flinn, MD, PhD, Sarah Cannon Research Institute
- Steven Horwitz, MD, Memorial Sloan Kettering Cancer Center
- Lori Kunkel, MD, Verastem Clinical and Scientific Advisory Board; former CMO, Pharmacyclics

In addition, Steve Bloom, Verastem's Chief Strategy Officer, will also participate, and Robert Forrester, Verastem's President and Chief Executive Officer will moderate.

The event will take place during the ASH 2017 annual meeting and interested parties can access a live webcast of the event beginning Sunday, December 10, 2017 at 8:15 p.m. ET on the "Presentations" page of the company's website at http://phx.corporate-ir.net/phoenix.zhtml?c=250749&p=irol-calendar. A replay of the webcast will be archived on the company's website for 90 days following the event.

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 full data from the DUO study will not be consistent with the previously presented results of the study; 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 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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