Verastem Oncology Presents Data on Two Lead Drug Candidates at ASCO 2018 Annual Meeting

June 4, 2018

Duvelisib demonstrates robust clinical activity with 73% ORR and a median of 15 month PFS in the DUO crossover study of patients who became relapsed/refractory to ofatumumab in DUO™

Duvelisib's dual inhibition of PI3K-delta and PI3K-gamma results in beneficial changes in both the cancer cells and the supportive tumor microenvironment

Phase I results show defactinib in combination with pembrolizumab and gemcitabine is well tolerated and shows early signs of clinical activity in pancreatic cancer including confirmed partial response and long-term stable disease

BOSTON--(BUSINESS WIRE)--Jun. 4, 2018-- Verastem, Inc. (NASDAQ:VSTM) (Verastem Oncology or the Company), a biopharmaceutical company focused on developing and commercializing medicines to improve the survival and quality of life of cancer patients, today announced the presentation of five posters highlighting data for its two lead drug candidates, duvelisib and defactinib, at the 54th Annual Meeting of the American Society of Clinical Oncology (ASCO) being held June 1-5, 2018 in Chicago.

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 April, the U.S. Food and Drug Administration (FDA) accepted with Priority Review Verastem Oncology's New Drug Application for duvelisib, which has an FDA target action date of October 5, 2018. Defactinib is an oral small molecule inhibitor of focal adhesion kinase (FAK) and is currently being evaluated in combination with immunotherapeutic agents for the treatment of various cancers including pancreatic, ovarian and non-small cell lung cancer, and mesothelioma.

"The DUO crossover extension data reported at ASCO this year build upon the previously reported positive Phase 3 DUO study results and further support duvelisib's potential as an oral treatment option for patients with relapsed or refractory CLL/SLL," said Diep Le, MD, PhD, Chief Medical Officer of Verastem Oncology. "Post-crossover, oral duvelisib monotherapy demonstrated robust clinical activity with a 73% overall response rate (ORR) and a 15-month median PFS in the 89 patients that had previously received ofatumumab on DUO and subsequently progressed . Duvelisib monotherapy also demonstrated a manageable safety profile, with results from this study consistent with the well-characterized safety profile of duvelisib monotherapy in previous studies. It is encouraging to see such a robust response to duvelisib monotherapy, similar to response observed in the parent DUO study, in patients that had failed an additional line of therapy and needed a new treatment option."

Jonathan Pachter, PhD, Chief Scientific Officer of Verastem Oncology, commented, "The presented research by Drs. Casulo and Weaver continues to provide important evidence that the dual PI3K-delta/PI3K-gamma inhibitory activity of duvelisib results in beneficial anti-tumor effects on both the cancer cells and their supportive tumor microenvironment (TME) which has the potential to enhance clinical efficacy and improve outcomes for patients battling CLL/SLL and FL."

Dr. Le added, "Dr. Andrea Wang-Gillam presented initial results from an ongoing Phase 1 study evaluating our lead FAK inhibitor defactinib in combination with pembrolizumab and gemcitabine in patients with advanced pancreatic cancer. The triplet appears to be well tolerated, the recommended Phase 2 dose has been established, and the expansion phase of the study is ongoing. In addition, promising signs of clinical activity have been observed with 3 pancreatic cancer patients treated beyond 250 days, including a confirmed partial response and the other 2 patients with stable disease. All 3 of these patients have also shown meaningful reductions (57-96%) in the pancreatic cancer marker CA19-9. Analysis of paired biopsies have also shown that this treatment induced desirable biomarker changes including increased proliferating CD8+ T cells and reduced immunosuppressive Tregs and macrophages. Treatment of pancreatic cancer represents a very important unmet need for patients, and these initial results are certainly encouraging."

Details for the ASCO 2018 presentations are as follows:

Duvelisib

Title: The efficacy of duvelisib monotherapy following disease progression on ofatumumab monotherapy in patients with relapsed/refractory CLL or SLL in the DUO crossover extension study
Lead author: Dr. Bryone Kuss, Flinders Medical Centre
Abstract #: 7533
Summary: In the previously reported Phase 3 DUO™ study oral duvelisib monotherapy achieved a statistically significant improvement in median progression-free survival (mPFS) compared to ofatumumab in patients with relapsed or refractory CLL/ SLL (13.3 months versus 9.9 months, respectively; HR=0.52; p<0.0001), along with a manageable safety profile (Flinn, ASH 2017). The results reported here are from the open-label, DUO crossover extension study where patients with confirmed progressive disease (PD) following treatment with ofatumumab in DUO were given the option to receive treatment with duvelisib. Duvelisib 25mg BID was administered until PD, intolerance, death, or study withdrawal and responses were determined by investigators using modified IWCLL/IWG criteria.

Among the 89 evaluable patients (median three prior therapies (range 2-8), oral duvelisib monotherapy achieved a 73% overall response rate (ORR; 95% CI: 64, 82; 5% complete response with incomplete marrow recovery (CRis), 68% partial responses [PRs]) in the extension study. While on ofatumamab in the DUO study, these 89 patients had a 28% ORR (95% CI: 19, 37; 1% complete response (CR), 27% PRs). The mPFS for duvelisib in the extension study was 15 months (95% CI: 10, 17). While on ofatumamab in the DUO study, these 89 patients had a mPFS of 9 months (95% CI: 9, 11), per investigator's assessment. Notably, 83% of patients in the duvelisib arm post-crossover had >50% reductions in the size of their target nodal

lesions. These same 89 patients had 27% reductions in the size of their target nodal lesions in the DUO ofatumumab arm. Median exposure to duvelisib in the extension study was 32 weeks. The safety profile of duvelisib monotherapy was manageable and consistent with what was observed in the Phase 3 DUO study. The most common Grade ≥3 treatment-emergent adverse events were neutropenia (22%), diarrhea (17%), colitis (9%), pneumonia (9%), rash (5%) and pyrexia (4%). These data build upon the previously reported positive DUO results and further support oral duvelisib monotherapy as an effective oral treatment option for patients with relapsed or refractory CLL/SLL.

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

Title: The effect of duvelisib, a dual inhibitor of PI3K-δ,γ, on components of the tumor microenvironment in previously untreated follicular lymphoma
Lead author: Dr. Carla Casulo, University of Rochester, Wilmot Cancer Center
Abstract #: 7579
Summary: In previously reported data from the CONTEMPO trial, treatment-naive FL patients treated with duvelisib in combination with rituxumab had an ORR of 93% (36% CRR), and an ORR of 89% (41% CRR) was observed for patients treated with duvelisib in combination with obinutuzumab. In this study, blood samples from healthy volunteers and FL patients treated in the CONTEMPO study, both pre- and post-duvelisib treatment, were analyzed. *Ex vivo* and *in vitro* PI3K-γ assays and PI3K-δ assays, with PI3K-δ-selective (idelalisib, TGR-1202, IPI-3063) and PI3K-γ-selective (IPI-549) inhibitors were compared.

Duvelisib and idelalisib potently inhibited LPS-induced human monocytes via PI3K-δ, compared with the PI3K-γ selective IPI-549. For TGR-1202, the IC50 was below the recommended Phase 2 dose (RP2D) clinical exposure. Duvelisib and IPI-549 potently inhibited PI3K-γ dependent fMLP-stimulated human monocytes compared to idelalisib and TGR-1202. In FL patients treated with duvelisib, these PI3K-γ and PI3K-δ selective assays were inhibited 1-4 hours post treatment. Consistent with a PI3K-γ mechanism, both duvelisib and IPI-549 inhibited macrophage polarization to M2, reduced CXCL12-induced macrophage migration, and blocked CXCL12-induced T cell migration, which was not observed with PI3K-δ inhibitor IPI-3063. Collectively, these results support the thesis that duvelisib disrupts PI3K- δ,γ function in FL patients inhibiting the TME through cancer-supportive macrophages and T cells.

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

Title: The PRIMO study: A phase 2 study of duvelisib efficacy and safety in patients with relapsed or refractory peripheral t-cell lymphoma (PTCL)
Lead author: Dr. Steven Horwitz, Memorial Sloan Kettering Cancer Center
Abstract #: TPS7590
Summary: This poster describes the PRIMO study, a Phase 2 open-label clinical trial evaluating duvelisib monotherapy in adult patients with PTCL, one of the most aggressive forms of non-Hodgkin lymphoma (NHL). The study employs a dose optimization phase (DOP) and an Expansion Phase (EP). The primary objectives are to identify the optimal dose of duvelisib in PTCL and examine the efficacy, safety, and tolerability of duvelisib at the optimal dose. The study is expected to enroll up to 120 patients with histologically confirmed PTCL subtypes of PTCL-NOS, angioimmunoblastic TCL, anaplastic large cell lymphoma, and natural-killer TCL. Disease responses will be measured by PET-CT scanning as assessed by an independent review committee per IWG criteria. The primary endpoint is ORR (CR + PR) in all patients receiving the optimal dose for at least 1 cycle in either phase. Secondary endpoints include safety, duration of response, and PFS. This study is open for enrollment. Duvelisib has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for the treatment of patients with PTCL who have received at least one prior therapy.

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

Title: Duvelisib inhibition of chemokines in patients with CLL (DUO study) and iNHL (DYNAMO study)
Lead author: Dr. David Weaver, Verastem Oncology
Abstract #: 12048
Summary: PI3K-δ inhibition directly targets proliferation and survival of malignant leukemia and lymphoma cells, while PI3K-γ inhibition modulates the TME through key support cells, including tumor-associated macrophages, nurse-like stroma and T cells, and via soluble factors stimulating tumor growth, survival and migration. Serum samples from patients in the Phase 3 DUO study in relapsed/refractory CLL/SLL and the Phase 2 DYNAMO study in relapsed/refractory indolent NHL were collected at baseline and at C2D1 and used for correlative studies of 24 chemokines, cytokines and serum factors.

In serum samples from the DUO study, CCL1, CCL17, CXCL9, CXCL10, CXCL11, and IL-10 were reduced in patients treated with duvelisib (median 43.8%) but not in those treated with ofatumumab (p≤0.0009). Eight chemokines were reduced in both treatment arms, but the level of reduction was significantly greater for duvelisib-treated patients (median 64.6% for duvelisib versus 26.8% for ofatumumab [p≤0.001]). Many of the chemokines inhibited following duvelisib treatment are associated with the TME, including TNFα, IL-10, IL2Rα, IL12P40, CCL1, CCL17, CCL19, CXCL9, CXCL10, CXCL11, and CXCL13. In serum samples from the DYNAMO study, 13 corresponding chemokines were also inhibited (p≤0.008), including TME factors. Reductions occurred rapidly (by C2D1) in both studies. In DUO, there was a correlation between duration of response and reduction of the following chemokines: CCL17, CXCL11, IL-6, TRAIL, VEGF-D and TPO. These data support the hypothesis that treatment with duvelisib results in significant reduction of chemokines potentially derived from the tumor cells and TME and that further investigation of the effects of duvelisib on TME pharmacodynamic markers is warranted.

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

Defactinib

Title: Phase I study of defactinib combined with pembrolizumab and gemcitabine in patients with advanced cancer
Lead author: Dr. Andrea Wang-Gillam, Washington University in St. Louis
Abstract #: 2561
Summary: FAK is consistently hyperactivated in multiple tumor types including pancreatic ductal adenocarcinoma (PDAC). Previously reported preclinical research showed that FAK and PD-1 inhibitors elicit significant tumor regression, and a maximal response is achieved by combining FAK and PD-1 inhibitors with gemcitabine, suggesting the need for a cytotoxic agent to bolster antigen presentation. In this ongoing Phase 1, dose-escalation study, defactinib is being evaluated in combination with Merck's PD-1 inhibitor pembrolizumab and gemcitabine in patients with PDAC.

The dose escalation cohort has been completed with a total of 20 patients with refractory solid tumors. Of the 15 patients evaluable for treatment response, 1 (7%) achieved a confirmed PR and 8 (53%) achieved stable disease (SD). Of the 8 PDAC patients, 1 (13%) achieved a confirmed PR and

3 (38%) achieved SD. The median time on treatment was 132 days for all evaluable patients and 158 days for patients with PDAC. Paired biopsies from PDAC patients showed increased proliferating CD8+ T cells and decreased T regs in patients with controlled disease compared to patients with progressive disease. The combination regimen was well tolerated with no dose limiting toxicities, and therefore the RP2D dose was established as defactinib (400mg BID, Days 1-21), pembrolizumab (200mg, Day 1) and gemcitabine (1,000mg/m^2, Day 1 and 8). The common treatment-emergent adverse events were anorexia (50%), fatigue (40%), diarrhea (40%), fever (40%) and vomiting (35%), but nearly all were Grade 1/2. There was 1 case of Grade ≥3 diarrhea. An expansion cohort in patients with PDAC is currently ongoing.

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

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 Defactinib

Defactinib is an investigational inhibitor of focal adhesion kinase (FAK), a non-receptor tyrosine kinase that mediates oncogenic signaling in response to cellular adhesion and growth factors.[7] Based on the multi-faceted roles of FAK, defactinib is used to treat cancer through modulation of the tumor microenvironment and enhancement of anti-tumor immunity.[8,9] Defactinib 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. These studies are combination clinical trials with pembrolizumab and avelumab from Merck & Co. and Pfizer/Merck KGaA, respectively.[10,11,12] Information about these and additional clinical trials evaluating the safety and efficacy of defactinib can be found on www.clinicaltrials.gov.

About Verastem Oncology, Inc.

Verastem, (NASDAQ:VSTM), operating as Verastem Oncology, is a biopharmaceutical company focused on developing and commercializing drugs 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 2018 or at all; 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 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 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 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.

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