Verastem Oncology Presents COPIKTRA™ (Duvelisib) Data at the European Hematology Association 2019 Annual Meeting

June 17, 2019

In CLL/SLL Patients in the DUO Study, Duvelisib Treatment Rapidly Increased Lymphocytes and Resulted in Shrinkage of Lymph Nodes, With 86% of Patients Achieving a Lymph Node Response

Dose Modifications Utilized in the DUO Study May Be Used to Manage Adverse Events for CLL/SLL Patients Receiving COPIKTRA

BOSTON--(BUSINESS WIRE)--Jun. 17, 2019-- Verastem, Inc. (Nasdaq:VSTM) (Verastem Oncology or the Company), a biopharmaceutical company focused on developing and commercializing medicines seeking to improve the survival and quality of life of cancer patients, today announced that two posters highlighting clinical data for COPIKTRA™ (duvelisib) in patients with relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) were presented at the European Hematology Association (EHA) 2019 Annual Meeting which took place June 13-16, 2019, in Amsterdam. One poster describes results from a post-hoc analysis evaluating the effect of COPIKTRA on lymphocytosis in patients with relapsed or refractory CLL/SLL from the Phase 3 DUO study, including patients with high-risk factors. The other poster describes dose modification data from patients with relapsed or refractory CLL/SLL in the DUO study.

COPIKTRA, a targeted oral inhibitor of phosphoinositide 3-kinase (PI3K), and the first approved dual inhibitor of PI3K-delta and PI3K-gamma, received approval as monotherapy from the U.S. Food and Drug Administration (FDA) in September 2018 for the treatment of patients with relapsed or refractory CLL/SLL after at least two prior therapies.

“Duvelisib is a potent oral dual inhibitor of PI3K-delta and -gamma with clinical activity in patients with CLL/SLL after at least two prior therapies,” said Hagop Youssoufian, MSc, M.D., Head of Medical Strategy at Verastem Oncology. “In a post-hoc analysis authored by Dr. Barrientos and colleagues, duvelisib induced rapid and transient lymphocytosis that was associated with a reduction in lymphadenopathy, including in high-risk patients. Notably, duvelisib also resulted in resolution of lymphocytosis at up to 21 weeks, and the majority of patients achieved a lymph node response and also achieved rapid shrinkage of their lymph nodes.”

Patterns of Duvelisib-Induced Lymphocytosis in Patients with Relapsed/Refractory CLL/SLL, Including Those with High-Risk Factors

In this study, researchers aimed to characterize the clinical profile and kinetics associated with duvelisib-related lymphocytosis. Lymphocytosis is an increase in the number of lymphocytes (white blood cells) in the blood and is a recognized biological marker of treatment with B-cell receptor pathway inhibitors. Similar to ibrutinib and idelalisib, duvelisib treatment induces lymphocytosis in patients with CLL. This post hoc analysis defined response in patients (n=158) with relapsed or refractory CLL/SLL, including high-risk subgroups, which were characterized by unmutated IGHV (n=110), 17p deletion/TP53 mutation (n=48), 11q deletion (n=38), and bulky disease (n=74).

Of 158 patients treated with duvelisib, 78% experienced lymphocytosis. Median time to onset of lymphocytosis was one week across all patients, including patients in the high-risk subgroups. Median time to resolution of lymphocytosis was 14 weeks, with a 50% reduction from baseline at 21 weeks. Similar results were observed regardless of high-risk status. Rapid shrinkage of lymph nodes was noted, with 86% of patients achieving lymph node response. Among patients who achieved a response with duvelisib at first or second assessment, 78% and 86%, respectively, experienced lymphocytosis; median time to resolution of lymphocytosis in these patients was 12 and 18 weeks, respectively. Prolonged lymphocytosis (for >12 months) occurred in 12 patients (8%). The overall response rate in patients with prolonged lymphocytosis was 83%. Of note, the median PFS was similar among patients with and without prolonged lymphocytosis; 22.1 months (95% CI, 12.9-27.6), compared to 24 months (95% CI, 20.5-NE), respectively. Overall, there were low rates of tumor lysis syndrome (1 patient; 0.6%). These results showed that duvelisib monotherapy induced rapid and transient lymphocytosis temporally associated with a reduction in lymphadenopathy in patients with relapsed or refractory CLL/SLL.

Effect of Dose Modification on Response to COPIKTRA in Patients with Relapsed or Refractory CLL/SLL in the Phase 3 DUO Study

The randomized, multicenter, open-label, Phase 3 DUO study, compared COPIKTRA versus ofatumumab in 319 adult patients with CLL (n=312) or SLL (n=7) after at least one prior therapy. The study randomized patients with a 1:1 ratio to receive either COPIKTRA 25mg twice daily until disease progression or unacceptable toxicity, or ofatumumab, an approved standard of care treatment for use in CLL/SLL, for 7 cycles. This analysis examined dose modification patterns and their impact on response to COPIKTRA. Dose interruptions or dose reductions to 15mg, 10mg or 5mg twice daily were permitted per study protocol to manage treatment-emergent adverse events (TEAEs). Responses were assessed per an Independent Review Committee.

Among the 158 COPIKTRA-treated patients in the DUO study, the median duration of exposure was 11.6 months, versus 5.3 months for patients treated with ofatumumab. The most common cause of dose interruption was diarrhea (23%), followed by neutropenia (12%) and pneumonia or colitis (11% each). Among responders (n=118), median time to first response on COPIKTRA was 1.9 months and the estimated median duration of response was 11.1 months. Median time to first dose interruption was 3.9 months and median duration of dose interruption was 15 days (range 1 to 133 days). Response to COPIKTRA was improved or maintained in most patients evaluated for response who had at least one dose interruption for >1 week (84%) or >2 weeks (82%) followed by at least 3 weeks on COPIKTRA. In a landmark analysis, median PFS was similar in patients with dose interruptions and those without dose interruptions for >1 week (17.8 versus 16.3 months) or >2 weeks (17.8 versus 16.3 months) within the first 3 months. The median time to dose reduction after a complete response or partial response was 5.6 months (n=25) and median duration was 3.4 months. Median time to onset across adverse events of special interest (AESIs) after starting COPIKTRA ranged from 2.2 to 4.3 months. Median time to resolution was within 4 weeks across AESIs. Proportions of patients experiencing AESIs were stable or decreased over time after 3-6 months: 0-3 months, 64%; >3-6 months, 63%; >6-9 months, 47%; >9-12 months, 52%, and seldom led to discontinuation of COPIKTRA (≤10%). These findings support the thesis that dose interruptions or dose reductions may be useful in managing TEAEs with COPIKTRA and that dose interruptions of >1-2

weeks or more did not appear to significantly impact response to COPIKTRA or PFS.

PDF copies of these poster presentations are available here.

Details for the EHA 2019 poster presentations are as follows:

Title: Effect of dose modifications on response to duvelisib in patients with relapsed/refractory (R/R) CLL/SLL in the DUO trial
Lead author: Paolo Ghia, Università Vita-Salute San Raffaele
Session: 6. Chronic lymphocytic leukemia and related disorders - Clinical
Abstract #: PS1157

Title: Patterns of duvelisib-induced lymphocytosis in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic leukemia including those with high-risk factors treated in the DUO trial
Lead author: Jacqueline Barrientos, Zucker School of Medicine at Hofstra/Northwell
Session: 6. Chronic lymphocytic leukemia and related disorders - Clinical
Abstract #: PS1160

Important Safety Information

WARNING: FATAL AND SERIOUS TOXICITIES: INFECTIONS, DIARRHEA OR COLITIS, CUTANEOUS REACTIONS, and PNEUMONITIS

•Fatal and/or serious infections occurred in 31% of COPIKTRA-treated patients. Monitor for signs and symptoms of infection. Withhold COPIKTRA if infection is suspected.

•Fatal and/or serious diarrhea or colitis occurred in 18% of COPIKTRA-treated patients. Monitor for the development of severe diarrhea or colitis. Withhold COPIKTRA.

•Fatal and/or serious cutaneous reactions occurred in 5% of COPIKTRA-treated patients. Withhold COPIKTRA.

•Fatal and/or serious pneumonitis occurred in 5% of COPIKTRA-treated patients. Monitor for pulmonary symptoms and interstitial infiltrates. Withhold COPIKTRA.

WARNINGS AND PRECAUTIONS

Infections: Serious, including fatal (4%), infections occurred in 31% of patients receiving COPIKTRA (N=442). The most common serious infections were pneumonia, sepsis, and lower respiratory infections. Median time to onset of any grade infection was 3 months, with 75% of cases occurring within 6 months. Treat infections prior to initiation of COPIKTRA. Advise patients to report new or worsening signs and symptoms of infection. Cases of Pneumocystis jirovecii pneumonia (PJP) (1%) and cytomegalovirus (CMV) reactivation/infection (1%) occurred in patients taking COPIKTRA. Provide prophylaxis for PJP during treatment and following completion of treatment until the absolute CD4+ T cell count is greater than 200 cells/µL. Consider prophylactic antivirals during COPIKTRA treatment to prevent CMV infection including CMV reactivation.

Diarrhea or Colitis: Serious, including fatal (<1%), diarrhea or colitis occurred in 18% of patients receiving COPIKTRA (N=442). Median time to onset of any grade diarrhea or colitis was 4 months, with 75% of cases occurring by 8 months. The median event duration was 0.5 months. Advise patients to report any new or worsening diarrhea.

Cutaneous Reactions: Serious, including fatal (<1%), cutaneous reactions occurred in 5% of patients receiving COPIKTRA (N=442). Fatal cases included drug reaction with eosinophilia and systemic symptoms (DRESS) and toxic epidermal necrolysis (TEN). Median time to onset of any grade cutaneous reaction was 3 months with a median event duration of 1 month. Presenting features for the serious events were primarily described as pruritic, erythematous, or maculo-papular. Less common presenting features include exanthem, desquamation, erythroderma, skin exfoliation, keratinocyte necrosis, and papular rash. Advise patients to report new or worsening cutaneous reactions.

Pneumonitis: Serious, including fatal (<1%), pneumonitis without an apparent infectious cause occurred in 5% of patients receiving COPIKTRA (N=442). Median time to onset of any grade pneumonitis was 4 months with 75% of cases occurring within 9 months. The median event duration was 1 month with 75% of cases resolving by 2 months.

Hepatotoxicity: Grade 3 and 4 ALT and/or AST elevation developed in 8% and 2%, respectively, of patients receiving COPIKTRA (N=442). Two percent of patients had both an ALT or AST > 3 X ULN and total bilirubin > 2 X ULN. Median time to onset of any grade transaminase elevation was 2 months with a median event duration of 1 month. Monitor hepatic function during treatment with COPIKTRA.

Neutropenia: Grade 3 or 4 neutropenia occurred in 42% of patients receiving COPIKTRA (N=442), with Grade 4 neutropenia occurring in 24% of all patients. Median time to onset of grade ≥3 neutropenia was 2 months. Monitor neutrophil counts at least every 2 weeks for the first 2 months of COPIKTRA therapy, and at least weekly in patients with neutrophil counts < 1.0 Gi/L (Grade 3-4).

Embryo-Fetal Toxicity: COPIKTRA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus and conduct pregnancy testing before initiating COPIKTRA treatment. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose.

ADVERSE REACTIONS

B-cell Malignancies Summary

Fatal adverse reactions within 30 days of the last dose occurred in 8% (36/442) of patients treated with COPIKTRA 25 mg BID. Serious adverse reactions were reported in 289 patients (65%). The most frequent serious adverse reactions that occurred were infection (31%), diarrhea or colitis (18%), pneumonia (17%), rash (5%), and pneumonitis (5%). The most common adverse reactions (reported in ≥20% of patients) were diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain and anemia.

CLL/SLL

Fatal adverse reactions within 30 days of the last dose occurred in 12% (19/158) of patients treated with COPIKTRA and in 4% (7/155) of patients treated with ofatumumab. Serious adverse reactions were reported in 73% (115/158) of patients treated with COPIKTRA and most often involved infection (38%; 60/158) and diarrhea or colitis (23%; 36/158). The most common adverse reactions with COPIKTRA (≥20% of patients) were diarrhea or colitis, neutropenia, pyrexia, upper respiratory tract infection, pneumonia, rash, fatigue, nausea, anemia and cough.

For specific information on the management of the adverse reactions above, please review *Dose Modifications for Adverse Reactions* within the full Prescribing Information.

DRUG INTERACTIONS

CYP3A Inducers: Coadministration with a strong CYP3A inducer may reduce COPIKTRA efficacy. Avoid coadministration with strong CYP3A4 inducers.

CYP3A Inhibitors: Coadministration with a strong CYP3A inhibitor may increase the risk of COPIKTRA toxicities. Reduce COPIKTRA dose to 15 mg BID when coadministered with a strong CYP3A4 inhibitor.

CYP3A Substrates: Coadministration of COPIKTRA with sensitive CYP3A4 substrates may increase the risk of toxicities of these drugs. Consider reducing the dose of the sensitive CYP3A4 substrate and monitor for signs of toxicities of the coadministered sensitive CYP3A substrate.

To report Adverse Reactions, contact FDA at 1-800-FDA-1088 (1-800-332-1088) or www.fda.gov/medwatch and Verastem Oncology at 1-877-7RXVSTM (1-877-779-8786).

Please see accompanying full Prescribing Information, including Boxed Warning.

About Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are cancers that affect lymphocytes and are essentially the same disease, with the only difference being the location where the cancer primarily occurs. When most of the cancer cells are located in the bloodstream and the bone marrow, the disease is referred to as CLL, although the lymph nodes and spleen are often involved. When the cancer cells are located mostly in the lymph nodes, the disease is called SLL. The symptoms of CLL/SLL include a tender, swollen abdomen and feeling full even after eating only a small amount. Other symptoms can include fatigue, shortness of breath, anemia, bruising easily, night sweats, weight loss, and frequent infections. However, many patients with CLL/SLL will live for years without symptoms. There are approximately 200,000 patients in the US affected by CLL/SLL with nearly 20,000 new diagnoses this year alone. While there are therapies currently available, real-world data reveals that a significant number of patients either relapse following treatment, become refractory to current agents, or are unable to tolerate treatment, representing a significant medical need. The potential of additional oral agents, particularly as a monotherapy that can be used in the general community physician's armamentarium, may hold significant value in the treatment of patients with CLL/SLL.

About COPIKTRA™ (duvelisib)

COPIKTRA is an oral inhibitor of phosphoinositide 3-kinase (PI3K), and the first approved dual inhibitor of PI3K-delta and PI3K-gamma, two enzymes known to help support the growth and survival of malignant B-cells. PI3K signaling may lead to the proliferation of malignant B-cells and is thought to play a role in the formation and maintenance of the supportive tumor microenvironment.[1,2,3] COPIKTRA is indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) after at least two prior therapies and relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies. COPIKTRA is also being developed by Verastem Oncology for the treatment of peripheral T-cell lymphoma (PTCL), for which it has received Fast Track status, and is being investigated in combination with other agents through investigator-sponsored studies.[4] For more information on COPIKTRA, please visit www.COPIKTRA.com. Information about duvelisib clinical trials can be found on www.clinicaltrials.gov.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a commercial biopharmaceutical company committed to the development and commercialization of medicines to improve the lives of patients diagnosed with cancer. We are driven by the strength, tenacity and courage of those battling cancer – single-minded in our resolve to deliver new therapies that not only keep cancer at bay, but improve the lives of patients diagnosed with cancer. Because for us, it's personal.

Our first FDA approved product is now available for the treatment of patients with certain types of indolent non-Hodgkin's lymphoma (iNHL). Our pipeline comprises product candidates that seek to treat cancer by modulating the local tumor microenvironment. For more information, please visit www.verastem.com.

Forward looking statements notice

This press release and the commentary in the conference call to be held today each include forward-looking statements about Verastem Oncology's strategy, future plans and prospects, including statements regarding the development and activity of Verastem Oncology's lead product COPIKTRA, and Verastem Oncology's PI3K program generally, its commercialization of COPIKTRA, the potential commercial success of COPIKTRA, including financial guidance and patient population estimates, the anticipated adoption of COPIKTRA by patients and physicians, the structure of its planned and pending clinical trials and the timeline and indications for clinical development, regulatory submissions and commercialization activities. 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 and uncertainties, among other things, regarding: the commercial success of COPIKTRA in the United States; physician and patient adoption of COPIKTRA, including those related to the safety and efficacy of COPIKTRA; the uncertainties inherent in research and development of COPIKTRA, such as negative or unexpected results of clinical trials; whether and when any applications for COPIKTRA may be filed with regulatory authorities in any other jurisdictions; whether and when regulatory authorities in any other jurisdictions may approve any such other applications that may be filed for COPIKTRA, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted and, if approved, whether COPIKTRA will be commercially successful in such jurisdictions; our ability to obtain, maintain and enforce patent and other intellectual property protection for COPIKTRA and our other product candidates; the scope, timing, and outcome of any legal proceedings; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of COPIKTRA; the fact that regulatory authorities in the U.S. or other jurisdictions, if approved, could withdraw approval; whether preclinical testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that third-party payors (including government agencies) may not reimburse for COPIKTRA; 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 COPIKTRA or our other product candidates will cause unexpected safety events, experience manufacturing or supply interruptions or failures, or result in unmanageable safety profiles as compared to their levels of efficacy; that COPIKTRA will be ineffective at treating patients with lymphoid malignancies; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned; that we may not have sufficient cash to fund our contemplated operations; that we, CSPC Pharmaceutical Group, Yakult Honsha Co., Ltd. or Infinity Pharmaceuticals, Inc. will fail to fully perform under the duvelisib license agreements; that we may be unable to make additional draws under our debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates, including for duvelisib in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) or indolent non-Hodgkin lymphoma (iNHL) in other jurisdictions; and that our 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 Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2019, as filed with the Securities and Exchange Commission (SEC) on May 9, 2019, its Annual Report on Form 10-K for the year ended December 31, 2018 as filed with the SEC on March 12, 2019 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

[1] Winkler D.G., Faia K.L., DiNitto J.P. 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 K 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 M 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, NCT03372057.

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Source: Verastem, Inc.

Verastem Oncology:
John Doyle
Vice President, Investor Relations & Finance
+1 781-469-1546
jdoyle@verastem.com

Investors:
Joseph Rayne
Argot Partners
+1 617-340-6075
joseph@argotpartners.com