Verastem Oncology Presents COPIKTRA™ (Duvelisib) Data in Peripheral T-Cell Lymphoma at the 2019 International Conference on Malignant Lymphoma

June 21, 2019 at 7:00 AM EDT

Steven Horwitz, MD, Gives Oral Presentation Highlighting Phase 1 Duvelisib Data in Patients with Relapsed or Refractory PTCL

Data from Two Phase 1 Studies Show Response Rates of 44-57%, Including Complete Response Rates of 15-22%

BOSTON--(BUSINESS WIRE)--Jun. 21, 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 an oral presentation highlighting supportive Phase 1 clinical data for duvelisib (COPIKTRA™) in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL) at the 2019 International Conference on Malignant Lymphoma (ICML) being held June 18-22, 2019, in Lugano, Switzerland. Verastem Oncology is currently investigating the safety and efficacy of duvelisib monotherapy in the Phase 2 clinical trial PRIMO in patients with histologically confirmed relapsed or refractory PTCL.

“Patients with relapsed or refractory PTCL who were treated with duvelisib demonstrated preliminary, but compelling clinical activity,” said Steven Horwitz, MD, Memorial Sloan Kettering Cancer Center, co-principal investigator of the Phase 1 and 2 studies, and lead author of the oral presentation. “Although the patient numbers are small in these two Phase 1 studies, we see a positive trend in response rates. The goal of the ongoing Phase 2 PRIMO study is to provide guidance on a duvelisib monotherapy dosing regimen in patients with relapsed or refractory PTCL and to further characterize its efficacy and tolerability in this population.”

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

Summary of Phase 1 Experience with Duvelisib in PTCL and Rationale for Phase 2

Relapsed or refractory PTCL is associated with a poor prognosis, with most therapies inducing responses in less than 30% of patients and median progression-free survival (PFS) less than 6 months. In this presentation, researchers summarized the safety and activity of duvelisib in patients with relapsed or refractory PTCL from two Phase 1 studies. In the first Phase 1 study, patients (n=13) received duvelisib until disease progression or intolerance as part of a dose-escalation phase. In the other Phase 1 study, patients (n=16) received duvelisib monotherapy 25mg or 75mg twice daily for one month as a lead-in to a combination regimen with romidepsin or bortezomib.

Across both studies, a total of 29 patients received duvelisib at 25mg or 75mg twice daily. Among patients who received duvelisib 75mg dosed twice daily as monotherapy or lead-in monotherapy before romidepsin, the ORR was 54% and 44%, respectively, with complete response (CR) rates of 15% to 22%, respectively. Notably, the overall response rate was 57% among patients receiving duvelisib 25mg twice daily as lead-in monotherapy before bortezomib. The responses reported here of patients receiving duvelisib as a lead-in monotherapy experienced these responses at the end of cycle 1. In the phase 1 dose-escalation study, median progression-free survival was 8.3 months and median overall survival was 16.2 months. In this same study, response to duvelisib typically occurred by the first assessment (cycle 2) and was observed across a spectrum of PTCL subtypes. The preliminary safety profile of duvelisib in patients with relapsed or refractory PTCL was considered reasonable and consistent with prior studies.

A PDF copy of this oral presentation is available on www.lymphcon.ch.

Details for the ICML 2019 oral presentation are as follows:

Title: Duvelisib, an oral dual PI3K-δ,γ inhibitor, efficacy and safety in patients with relapsed or refractory (RR) peripheral T-cell lymphoma: rationale for the phase 2 PRIMO trial
Lead author: Steven Horwitz, Memorial Sloan Kettering Cancer Center
Abstract #: 033
Session: Focus On: Results from Single-Agent Trials
Location: Auditorium (USI Università)

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.

Important Safety Information

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

See full prescribing information for complete boxed warning

- 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 (18/442; 4%), infections occurred in 31% of patients receiving COPIKTRA 25 mg BID (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 (range: 1 day to 32 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. For grade 3 or higher infection, withhold COPIKTRA until infection has resolved. Resume COPIKTRA at the same or reduced dose.

Serious, including fatal, Pneumocystis jirovecii pneumonia (PJP) occurred in 1% of patients taking COPIKTRA. Provide prophylaxis for PJP during treatment with COPIKTRA and following completion of treatment with COPIKTRA until the absolute CD4+ T cell count is greater than 200 cells/μL. Withhold COPIKTRA in patients with suspected PJP of any grade, and permanently discontinue if PJP is confirmed.

Cytomegalovirus (CMV) reactivation/infection occurred in 1% of patients taking COPIKTRA. Consider prophylactic antivirals during COPIKTRA treatment to prevent CMV infection including CMV reactivation. For clinical CMV infection or viremia, withhold COPIKTRA until infection or viremia resolves. If COPIKTRA is resumed, administer the same or reduced dose and monitor patients for CMV reactivation by PCR or antigen test at least monthly.

Diarrhea or Colitis: Serious, including fatal (1/442; <1%), diarrhea or colitis occurred in 18% of patients receiving COPIKTRA 25 mg BID (N=442). Median time to onset of any grade diarrhea or colitis was 4 months (range: 1 day to 33 months), with 75% of cases occurring by 8 months. The median event duration was 0.5 months (range: 1 day to 29 months; 75th percentile: 1 month).

Advise patients to report any new or worsening diarrhea. For patients presenting with mild or moderate diarrhea (Grade 1-2) (i.e., up to 6 stools per day over baseline) or asymptomatic (Grade 1) colitis, initiate supportive care with antidiarrheal agents, continue COPIKTRA at the current dose, and monitor the patient at least weekly until the event resolves. If the diarrhea is unresponsive to antidiarrheal therapy, withhold COPIKTRA and initiate supportive therapy with enteric acting steroids (e.g., budesonide). Monitor the patient at least weekly. Upon resolution of the diarrhea, consider restarting COPIKTRA at a reduced dose.

For patients presenting with abdominal pain, stool with mucus or blood, change in bowel habits, peritoneal signs, or with severe diarrhea (Grade 3) (i.e., > 6 stools per day over baseline), withhold COPIKTRA and initiate supportive therapy with enteric acting steroids (e.g., budesonide) or systemic steroids. A diagnostic work-up to determine etiology, including colonoscopy, should be performed. Monitor at least weekly. Upon resolution of the diarrhea or colitis, restart COPIKTRA at a reduced dose. For recurrent Grade 3 diarrhea or recurrent colitis of any grade, discontinue COPIKTRA. Discontinue COPIKTRA for life-threatening diarrhea or colitis.

Cutaneous Reactions: Serious, including fatal (2/442; <1%), cutaneous reactions occurred in 5% of patients receiving COPIKTRA 25 mg BID (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 (range: 1 day to 29 months, 75th percentile: 6 months) with a median event duration of 1 month (range: 1 day to 37 months, 75th percentile: 2 months).

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. Review all concomitant medications and discontinue any medications potentially contributing to the event. For patients presenting with mild or moderate (Grade 1-2) cutaneous reactions, continue COPIKTRA at the current dose, initiate supportive care with emollients, antihistamines (for pruritus), or topical steroids, and monitor the patient closely. Withhold COPIKTRA for severe (Grade 3) cutaneous reaction until resolution. Initiate supportive care with steroids (topical or systemic) or antihistamines (for pruritus). Monitor at least weekly until resolved. Upon resolution of the event, restart COPIKTRA at a reduced dose. Discontinue COPIKTRA if severe cutaneous reaction does not improve, worsens, or recurs. For life-threatening cutaneous reactions, discontinue COPIKTRA. In patients with SJS, TEN, or DRESS of any grade, discontinue COPIKTRA.

Pneumonitis: Serious, including fatal (1/442; <1%), pneumonitis without an apparent infectious cause occurred in 5% of patients receiving COPIKTRA 25 mg BID (N=442). Median time to onset of any grade pneumonitis was 4 months (range: 9 days to 27 months), with 75% of cases occurring within 9 months. The median event duration was 1 month, with 75% of cases resolving by 2 months.

Withhold COPIKTRA in patients with new or progressive pulmonary signs and symptoms such as cough, dyspnea, hypoxia, interstitial infiltrates on a radiologic exam, or a decline by more than 5% in oxygen saturation, and evaluate for etiology. If the pneumonitis is infectious, patients may be restarted on COPIKTRA at the previous dose once the infection, pulmonary signs and symptoms resolve. For moderate non-infectious pneumonitis (Grade 2), treat with systemic corticosteroids and resume COPIKTRA at a reduced dose upon resolution. If non-infectious pneumonitis recurs or does not respond to steroid therapy, discontinue COPIKTRA. For severe or life-threatening non-infectious pneumonitis, discontinue COPIKTRA and treat with systemic steroids.

Hepatotoxicity: Grade 3 and 4 ALT and/or AST elevation developed in 8% and 2%, respectively, of patients receiving COPIKTRA 25 mg BID (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 (range: 3 days to 26 months), with a median event duration of 1 month (range: 1 day to 16 months).

Monitor hepatic function during treatment with COPIKTRA. For Grade 2 ALT/AST elevation (> 3 to 5 X ULN), maintain COPIKTRA dose and monitor at least weekly until return to < 3 X ULN. For Grade 3 ALT/AST elevation (> 5 to 20 X ULN), withhold COPIKTRA and monitor at least weekly until return to < 3 X ULN. Resume COPIKTRA at the same dose (first occurrence) or at a reduced dose for subsequent occurrences. For grade 4 ALT/AST elevation (> 20 X ULN), discontinue COPIKTRA.

Neutropenia: Grade 3 or 4 neutropenia occurred in 42% of patients receiving COPIKTRA 25 mg BID (N=442), with Grade 4 neutropenia occurring in 24% of all patients. Median time to onset of grade ≥3 neutropenia was 2 months (range: 3 days to 31 months), with 75% of cases occurring within 4 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). Withhold COPIKTRA in patients presenting with neutrophil counts < 0.5 Gi/L (Grade 4). Monitor until ANC is > 0.5 Gi/L, then resume COPIKTRA at same dose for the first occurrence or at a reduced dose for subsequent occurrences.

Embryo-Fetal Toxicity: Based on findings in animals and its mechanism of action, COPIKTRA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. 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%).

Adverse reactions resulted in treatment discontinuation in 156 patients (35%) most often due to diarrhea or colitis, infection, and rash. COPIKTRA was dose reduced in 104 patients (24%) due to adverse reactions, most often due to diarrhea or colitis and transaminase elevation. 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). COPIKTRA was discontinued in 57 patients (36%), most often due to diarrhea or colitis, infection, and rash. COPIKTRA was dose reduced in 46 patients (29%) due to adverse reactions, most often due to diarrhea or colitis and rash. The most common adverse reactions with COPIKTRA (reported in ≥20% of patients) were diarrhea or colitis, neutropenia, pyrexia, upper respiratory tract infection, pneumonia, rash, fatigue, nausea, anemia and cough.

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.

Please see the full Prescribing Information, including BOXED WARNING, and patient Medication Guide found on www.COPIKTRA.com.

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 Peripheral T-Cell Lymphoma

Peripheral T-cell lymphoma (PTCL) is a rare, aggressive type of non-Hodgkin lymphoma (NHL) that develops in mature white blood cells called "T cells" and "natural killer (NK) cells" [5] which circulate with the lymphatic system.[6] PTCL accounts for between 10-15% of all non-Hodgkin lymphomas (NHLs) and generally affects people aged 60 years and older.[1] Although there are many different subtypes of peripheral T-cell lymphoma, they often present in a similar way, with widespread, enlarged, painless lymph nodes in the neck, armpit or groin.[6] There is currently no established standard of

care for patients with relapsed or refractory disease.[5]

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

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[4] www.clinicaltrials.gov, NCT03372057.

[5] The Leukemia & Lymphoma Society. Peripheral T-Cell Lymphoma Facts. July 2014.

[6] Leukemia Foundation. http://www.leukaemia.org.au/blood-cancers/lymphomas/non-hodgkin-lymphoma-nhl/peripheral-t-cell-lymphoma

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Source: Verastem, Inc.

Investors:

John Doyle
Vice President, Investor Relations & Finance
+1 781-292-4279
jdoyle@verastem.com

Media:

Lisa Buffington
Corporate Communications
+1 781-292-4205
lbuffington@verastem.com