



Verastem Oncology Presents Phase 2 PRIMO Study Data Evaluating Duvelisib in Relapsed or Refractory Peripheral T-Cell Lymphoma at the American Society of Hematology 2019 Annual Meeting

December 7, 2019 at 9:00 AM EST

Duvelisib Achieves Overall Response Rate of 62% in Patients with Relapsed or Refractory PTCL with Manageable Safety Profile in Initial Phase of PRIMO Trial

Data Presented Support Potential of Duvelisib Across Indications, Lines of Therapy and in Combination

BOSTON--(BUSINESS WIRE)--Dec. 7, 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 the presentation of key abstracts highlighting COPIKTRA® (duvelisib) data at the American Society of Hematology 2019 Annual Meeting taking place December 7-10, 2019, in Orlando.

"Given the aggressive nature of peripheral T-cell lymphoma (PTCL) and the lack of effective therapeutic options for these patients, we are pleased to present data from the dose optimization phase of our PRIMO trial that demonstrated a 62% overall response rate (ORR), as assessed by independent central review, with a manageable safety profile consistent with previous clinical trials. The results of the trial also identified the optimal dosing regimen for future clinical study," said Brian Stuglik, Chief Executive Officer of Verastem Oncology. "The expansion phase of this registration-directed study is well underway. Upon completion, we plan to build upon our existing Fast Track Designation and Orphan Drug Designation and submit a regulatory package to the U.S. FDA with the goal of broadening the use of COPIKTRA to include treatment of PTCL."

Results from the Dose Optimization Portion of the Phase 2 PRIMO Study in Relapsed or Refractory PTCL

The PRIMO study is a multi-center, open-label, registration-directed Phase 2 study evaluating duvelisib in patients with relapsed or refractory PTCL that is expected to enroll approximately 120 patients. In the dose optimization portion of the study, patients were randomized to receive duvelisib 25mg twice daily with an option for dose escalation (cohort 1) or duvelisib 75mg twice daily continuously (cohort 2) until disease progression or unacceptable toxicity. The primary endpoint of the study was investigator-assessed overall response rate (ORR), and secondary endpoints included duration of response (DOR) and safety.

A total of 33 patients (cohort 1, n=20; cohort 2, n=13) were treated in the dose optimization phase. Investigator-assessed ORRs were 35% in cohort 1 and 54% in cohort 2, with complete response (CR) rates of 25% and 31% in cohort 1 and cohort 2, respectively. ORR, as assessed by blinded independent central review was 40% in cohort 1 and 62% in cohort 2. Thirteen of 20 patients in cohort 1 and all patients in cohort 2 were able to complete one cycle of therapy. Seven patients in cohort 1 discontinued therapy early due to disease progression and/or toxicity. Most responses were observed at the end of cycle 1 (cycle=28 days). At a median follow-up of 21.4 weeks, the majority of responders were still in response at the time of their last assessment. The most common (≥4 patients) Grade ≥3 adverse events (AEs) in all patients receiving duvelisib were neutropenia, thrombocytopenia, diarrhea, rash/maculopapular, lymphocytopenia, pneumonia and sepsis. Serious AEs occurring in ≥2 patients were colitis, diarrhea, abdominal pain, pyrexia, sepsis, pneumonia, hyponatremia, rash/maculopapular, dyspnea, and respiratory failure.

Based on these efficacy and safety data, the investigators have elected to investigate duvelisib starting at 75mg twice daily for two cycles, followed by 25mg twice daily, during the dose expansion portion of the study which is currently ongoing.

"In the dose optimization portion of the PRIMO study we observed encouraging results, including complete and durable responses at both dose levels," said Steven Horwitz, MD, Memorial Sloan Kettering Cancer Center, and principal investigator of Phase 2 PRIMO study. "We also identified a strategy for the expansion phase dosing regimen starting with 75mg twice daily for two cycles to achieve more a reliable initial tumor response, followed by 25mg twice daily to try to maintain longer-term disease control by mitigating the potential for later onset toxicity in these patients with relapsed or refractory disease."

Results from Phase 1 Study Investigating Duvelisib and Venetoclax in Patients with Relapsed or Refractory CLL/SLL

Another key presentation at the meeting highlights new data from an investigator-sponsored Phase 1 study exploring duvelisib in combination with venetoclax in relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Duvelisib plus venetoclax demonstrated promising clinical activity, a manageable tolerability profile, and a recommended Phase 2 dose (RP2D) of 400mg of venetoclax was determined for this regimen.

In the study, 12 patients were enrolled and received oral duvelisib and oral venetoclax. The primary endpoints of the study are dose limiting toxicities (DLTs), maximum tolerated dose (MTD) and identification of the RP2D. Secondary endpoints include pharmacokinetics and preliminary efficacy.

Among the 12 evaluable patients, 11 achieved a response for an ORR of 92%, including four (33%) CRs and seven (58%) partial responses. Four patients had undetectable minimum residual disease (uMRD) in the peripheral blood and bone marrow, including two patients with a CR. The most common Grade 1 and 2 AEs were fatigue (92%), hyperglycemia (83%), anemia (67%), and thrombocytopenia (67%). The most common Grade ≥3 AEs were neutropenia (84%), hypocalcemia (50%), and hypophosphatemia (25%). No DLTs were observed, and the RP2D of venetoclax was identified as 400mg once daily when given with standard dose duvelisib 25mg twice daily. This study is now in a Phase 2 portion in CLL/SLL and Richter's Syndrome and is currently accruing new patients.

“Duvelisib plus venetoclax is a promising combination for further study, as we have found early signals of robust activity along with a manageable tolerability profile,” said Matthew S. Davids, MD, Associate Director, Center for Chronic Lymphocytic Leukemia at Dana-Farber Cancer Institute, and Principal Investigator for the trial. “We are now actively accruing patients in the Phase 2 portion of the study to evaluate the efficacy of this combination in patients with CLL/SLL, with a separate cohort exploring the activity of this regimen for patients with Richter’s Syndrome, a particularly hard to treat population.”

Other poster presentations at the meeting include: an analysis of cytogenetic and molecular markers associated with improved outcomes in the patients who had received 1 prior therapy in the Phase 3 DUO study and a description of the soon to be initiated TEMPO study investigating an intermittent dosing regimen of duvelisib in patients with indolent non-Hodgkin lymphoma.

The data from these studies continues to support the future potential expansion of duvelisib across multiple indications and lines of therapy.

Details for the ASH 2019 presentations are as follows:

Poster Presentations

Title: Dose Optimization of Duvelisib in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma from the Phase 2 PRIMO Trial: Selection of Regimen for the Dose-Expansion Phase

Lead author: Steven Horwitz, Memorial Sloan Kettering Cancer Center

Poster #: 1567

Session: 624. Hodgkin Lymphoma and T/NK Cell Lymphoma – Clinical Studies: Poster I

Date and Time: Saturday, December 7, 2019; 5:30-7:30PM ET

Location: Orange County Convention Center, Hall B

Title: A Phase I Study of Duvelisib and Venetoclax in Patients with Relapsed or Refractory CLL / SLL

Lead author: Jennifer Crombie, Dana-Farber Cancer Institute

Poster #: 1763

Session: 642. CLL: Therapy, excluding Transplantation: Poster I

Date and Time: Saturday, December 7, 2019; 5:30-7:30 PM ET

Location: Orange County Convention Center, Hall B

Title: The Dual PI3K- δ/γ Inhibitor Duvelisib in Combination with the Bcl-2 Inhibitor Venetoclax Shows Promising Responses in Richter Syndrome-PDX Models

Lead author: Andrea Iannello, University of Turin

Poster #: 2862

Session: 625. Lymphoma: Pre-Clinical—Chemotherapy and Biologic Agents: Poster II

Date and Time: Sunday, December 8, 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Title: Cytogenetic and Molecular Marker Associations to Outcomes with Duvelisib and Ofatumumab Treatment in Patients with Relapsed or Refractory CLL/SLL in the DUO Trial

Lead author: Jennifer Brown, Dana-Farber Cancer Institute

Poster #: 4312

Session: 642. CLL: Therapy, excluding Transplantation: Poster III

Date and Time: Monday, December 9, 2019; 6:00-8:00 PM ET

Location: Orange County Convention Center, Hall B

Publication Only Presentations

Title: *Trial in Progress (TIP):* A Phase 2, Randomized, Open-Label, 2-Arm Study Comparing 2 Intermittent Dosing Schedules of Duvelisib in Patients with Indolent Non-Hodgkin Lymphoma (iNHL) (TEMPO)

Lead author: Reem Karmali, Lurie Cancer Center, Northwestern University

Session: 623. Mantle cell, follicular, and other indolent B Cell Lymphoma – Clinical studies

PDF copies of these poster presentations will be available [here](#) after the meeting.

COPIKTRA is indicated in the US for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies and in relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies. Accelerated approval in FL was based on overall response rate and continued approval may be contingent upon confirmatory trials.

SELECT IMPORTANT SAFETY INFORMATION

This does not include all information needed to use COPIKTRA® (duvelisib) safely and effectively. [See full Prescribing 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% (4% fatal) 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% (<1% fatal) of COPIKTRA-treated patients. Monitor for the development of severe

diarrhea or colitis. Withhold COPIKTRA.

- Fatal and/or serious cutaneous reactions occurred in 5% (<1% fatal) of COPIKTRA-treated patients. Withhold COPIKTRA.
- Fatal and/or serious pneumonitis occurred in 5% (<1% fatal) of COPIKTRA-treated patients. Monitor for pulmonary symptoms and interstitial infiltrates. Withhold COPIKTRA.

WARNINGS AND PRECAUTIONS

- Hepatotoxicity: Monitor hepatic function.
- Neutropenia: Monitor blood counts.
- Embryo-Fetal toxicity: COPIKTRA can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) are diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain, and anemia.

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).

DRUG INTERACTIONS

- CYP3A inducers: Avoid co-administration with strong CYP3A inducers.
- CYP3A inhibitors: Monitor for COPIKTRA toxicities when co-administered with strong or moderate CYP3A inhibitors. Reduce COPIKTRA dose to 15 mg twice daily when co-administered with strong CYP3A4 inhibitors.
- CYP3A substrates: Monitor for signs of toxicities when co-administering COPIKTRA with sensitive CYP3A substrates.

USE IN SPECIFIC POPULATIONS

Lactation: Advise women not to breastfeed.

Please see full [Prescribing Information](#), including **Boxed Warning**.

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 Orphan Drug Designation, 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 includes 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, its commercialization of COPIKTRA, the potential commercial success of COPIKTRA, 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., Sanofi 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 September 30, 2019, as filed with the Securities and Exchange Commission (SEC) on October 30, 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.

Dr. Horwitz and Dr. Davids have been compensated for consulting services by Verastem Oncology and also receive research support from the company.

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