Verastem Oncology Presents New Preclinical Duvelisib Data at the 5th International Conference on New Concepts in Lymphoid Malignancies

October 3, 2019

Duvelisib's Dual Inhibition of PI3K-Delta and PI3K-Gamma Inhibits Migration and Proliferation of Mantle Cell Lymphoma Cells More Effectively Than PI3K-Delta Alone in Preclinical Models

BOSTON--(BUSINESS WIRE)--Oct. 3, 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 a poster highlighting new preclinical duvelisib (COPIKTRA™) data that will be presented at the 5th International Conference on New Concepts in Lymphoid Malignancies, which is hosted by the European School of Haematology (ESH), and is taking place October 3-5, 2019, in Estoril, Portugal. The poster features preclinical research that compared duvelisib with idelalisib in preclinical models of mantle cell lymphoma (MCL). COPIKTRA is not approved for use in MCL, diffuse large B-cell lymphoma (DLBCL), or marginal zone lymphoma (MZL).

"These data highlight MCL as a B-cell malignancy which expresses both PI3K-delta and PI3K-gamma in the malignant B cells, in addition to the role of PI3K-gamma which has already been established in cells of the supportive tumor microenvironment," said Jonathan Pachter, PhD, Chief Scientific Officer of Verastem Oncology. "Accordingly, the data show superior anti-cancer activity of the dual PI3K-delta/gamma inhibitor duvelisib compared to the PI3K-delta inhibitor idelalisib in these preclinical MCL models. At Verastem Oncology, we are working to expand into additional lymphoid malignancy indications and these data provide additional support for the future study of duvelisib through clinical trials in patients with MCL."

Duvelisib in Preclinical Models of MCL

MCL is a rare, aggressive B-cell non-Hodgkin lymphoma (NHL) that is incurable. The purpose of this research was to gain a functional understanding of the distinctive features associated with the malignant cells in MCL, with the goal of identifying potential new treatment strategies. PI3K-delta is known to be equally expressed in all B-cell malignancies and this research revealed that primary MCL cells show elevated expression of PI3K-gamma relative to primary cells from other B-cell malignancies, including chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and marginal zone lymphoma (MZL). These preliminary data suggest that high levels of PI3K-gamma in MCL cells correlate with poorer disease outcomes.

The researchers then examined the effects of inhibition of specific PI3K isoforms, including PI3K-alpha, PI3K-delta (idelalisib), PI3K-gamma, and dual PI3K-delta/gamma (duvelisib), on the migration and proliferation of malignant lymphocytes from patients with MCL. These preclinical models showed that inhibition of both PI3K-delta and gamma reduced the proliferation of MCL cells whereas inhibition of PI3K-delta alone had no effect. The functional role of PI3K-delta and gamma in MCL cells was further differentiated from that of PI3K-delta alone. PI3K-delta and gamma more effectively inhibited CCL21-induced migration of MCL cell lines and primary MCL cells than did PI3K-gamma inhibition alone. Inhibition of PI3K-delta or PI3K-alpha did not affect CCL21-induced migration of MCL cells. These data suggest that when PI3K-gamma is aberrantly expressed by MCL cells, these cells become reliant on this PI3K isoform for chemokine-induced migration and tissue residency. Thus, duvelisib may have potential in MCL therapy by restricting entry, retention, and proliferation of the malignant cells within the mantle zone.

Details for the ESH 2019 poster presentation are as follows:

Title: Aberrantly Expressed PI3Kγ Contributes to Cell Proliferation and Co-Operates with PI3δ to Mediate CCL21-Induced Migration in Mantle-Cell Lymphoma: Therapeutic Implications for Duvelisib
Lead author: Kathy Till, University of Liverpool
Date and time: Thursday, October 3, 2019, beginning at 7am through the end of the conference
Location: Poster Area

A PDF copy of this poster presentation will be available here after the meeting.

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% 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

- 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 accompanying 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 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 within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including 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 and the uncertainties inherent in research and development of COPIKTRA. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements.

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 June 30, 2019, as filed with the Securities and Exchange Commission (SEC) on August 1, 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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