Cyclacel's CYC065 CDK Inhibitor Demonstrates Synergy With Venetoclax By Dual Targeting Of Chronic Lymphocytic Leukemia

April 17, 2018

Suppression of both BCl-2 and Mcl-1 anti-apoptotic proteins is a novel strategy in CLL

BERKELEY HEIGHTS, N.J., April 17, 2018 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (NASDAQ:CYCC) (NASDAQ:CYCCP) ("Cyclacel" or the "Company"), a biopharmaceutical company developing oral therapies that target various phases of cell cycle control for the treatment of cancer and other serious disorders, today announced the presentation by investigators led by William Plunkett, PhD, Professor and Deputy Chair, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, Texas, of preclinical data demonstrating strong synergy between Cyclacel's CDK2/9 inhibitor, CYC065, and the Bcl-2 inhibitor, venetoclax (ABT-199, AbbVie) in chronic lymphocytic leukemia (CLL) samples obtained from patients. The data were presented at the American Association for Cancer Research (AACR) Annual Meeting being held April 14-18, 2018 in Chicago, Illinois.

"The MD Anderson data show that the combination of CYC065 and venetoclax is strongly synergistic in primary CLL cells from patients, including those with 17p deletions. In addition, the combination was active in two CLL samples which were resistant to either agent alone. These findings support the hypothesis that dual targeting of the Mcl-1- and Bcl-2-dependent mechanisms could induce synergistic cell death by apoptosis," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "Last weekend during the same AACR conference, we reported that CYC065 durably suppresses Mcl-1, a member of the Bcl-2 family of survival proteins, in patients with advanced solid tumors[1]. Taken together the data highlight an exciting opportunity to rationally disrupt the pathways promoting the survival of CLL cells. Cyclacel plans to start soon a clinical study to evaluate CYC065 in combination with venetoclax in patients with relapsed/refractory CLL."

Details of the poster presentation are as follows:

Title:	Strategic combination of the cyclin-dependent kinase inhibitor CYC065 with venetoclax to target anti-apoptotic proteins in chronic lymphocytic leukemia
Presenter/Authors:	Rong Chen, Yuling Chen, Sheelagh Frame, David Blake, William G. Wierda, Daniella Zheleva and William Plunkett.
Category:	Experimental and Molecular Therapeutics
Session:	PO.ET07.03 - Receptor Targeting and the Tumor Microenvironment
Abstract #:	3905/ 5
Location:	McCormick Place South, Exhibit Hall A, Poster Section 38
Date and Time:	Tuesday, April 17, 2018, 8:00 AM - 12:00 PM

About CYC065

CYC065, a second generation CDK2/9 inhibitor, is being evaluated in a first-in-human, Phase 1 trial in patients with advanced solid tumors. It is mechanistically similar but has higher dose potency, *in vitro* and *in vivo*, and improved properties compared to seliciclib, a first generation CDK inhibitor. Similarly to FDA approved CDK4/6 inhibitors, CYC065 may be most useful in combination with other anticancer drugs, including Bcl-2 inhibitors, such as venetoclax, or HER2 inhibitors, such as trastuzumab. CYC065 durably suppresses Mcl-1, a member of the Bcl-2 family of survival proteins, in Phase 1 patients with advanced solid tumors. Preclinical data show that CYC065 may benefit patients with adult and pediatric hematological malignancies, including acute myeloid leukemias (AML), acute lymphocytic leukemias (ALL), and in particular those with MLL rearrangements, chronic lymphocytic leukemias (CLL), B-cell lymphomas, multiple myelomas, and certain solid tumors, including breast and uterine cancers, and neuroblastomas.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel Pharmaceuticals is a clinical-stage biopharmaceutical company using cell cycle, transcriptional regulation and DNA damage response biology to develop innovative, targeted medicines for cancer and other proliferative diseases. Cyclacel's transcriptional regulation program is evaluating CYC065, a CDK inhibitor, in patients with advanced cancers. The DNA damage response program is evaluating a sequential regimen of sapacitabine and seliciclib, a CDK inhibitor, in patients with BRCA positive, advanced solid cancers. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a pipeline of novel drug candidates. For additional information, please visit www.cyclacel.com.

Forward-looking Statements

This news release contains certain forward-looking statements that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. Such forward-looking statements include statements regarding, among other things, the efficacy, safety and intended utilization of Cyclacel's product candidates, the conduct and results of future clinical trials, plans regarding regulatory filings, future research and clinical trials and plans regarding partnering activities. Factors that may cause actual results to differ materially include the risk that product candidates that appeared promising in early research and clinical trials do not demonstrate safety and/or efficacy in larger-scale or later clinical trials, trials may have difficulty enrolling, Cyclacel may not obtain approval to market

its product candidates, the risks associated with reliance on outside financing to meet capital requirements, and the risks associated with reliance on collaborative partners for further clinical trials, development and commercialization of product candidates. You are urged to consider statements that include the words "may," "will," "would," "could," "should," "believes," "estimates," "projects," "potential," "expects," "plans," "anticipates," "intends," "continues," "forecast," "designed," "goal," or the negative of those words or other comparable words to be uncertain and forward-looking. For a further list and description of the risks and uncertainties the Company faces, please refer to our most recent Annual Report on Form 10-K and other periodic and other filings we file with the Securities and Exchange Commission and are available at www.sec.gov. Such forward-looking statements are current only as of the date they are made, and we assume no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Contacts

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[1]*Phase I safety, pharmacokinetic and pharmacodynamic study of CYC065, a cyclin dependent kinase inhibitor, in patients with advanced cancers (NCT02552953)**;** AACR 2018 Sunday, April 15, 2018, 3:35 PM (Abstract CT037).*

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