April 2, 2017

Cyclacel's Second-Generation CDK2/9 Inhibitor, CYC065, Elicits Marked Antineoplastic Effects in Lung Cancer by Engaging Anti-Metastatic Pathways

- Preclinical Data Presented at the AACR 2017 Meeting -

BERKELEY HEIGHTS, N.J., April 02, 2017 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (NASDAQ:CYCC) (NASDAQ:CYCCP) ("Cyclacel" or the "Company"), today announced the presentation by independent investigators of preclinical data demonstrating therapeutic potential of CYC065, the Company's second-generation, cyclin-dependent kinase (CDK) 2/9 inhibitor, as a targeted anti-cancer agent. The data show that CYC065 substantially inhibited growth, triggered apoptosis, and induced anaphase catastrophe in murine and human lung cancer cells with known high metastatic potential. This was in marked contrast to effects in immortalized pulmonary epithelial murine and human cells. CYC065 markedly inhibited migration and invasion of lung cancer cells and affected distinctive pathways involved in DNA damage response, apoptosis, cell cycle regulation and cell migration. The data were presented at the American Association for Cancer Research (AACR) Annual Meeting 2017, April 1 - 5, 2017, in Washington, D.C.

"This study adds to the growing evidence of the value of CDK inhibition as an approach to treating cancer," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "CYC065 is in a Phase 1, first-in-human trial to evaluate safety, tolerability and pharmacokinetics in patients with solid tumors. The trial is at an expanded sixth dose escalation level with the objective of determining maximum tolerated dose and recommended dosing for Phase 2. Evidence of target engagement with prolonged Mcl-1 suppression in peripheral blood cells has been observed in patient samples from the study. We believe that CYC065 is one of the first medicines to demonstrate this in a human trial and look forward to pursuing this lead as part of our transcription regulation program."

In the preclinical study, a group of researchers led by Professor Ethan Dmitrovsky, M.D., including Masanori Kawakami M.D., Ph.D., from The University of Texas MD Anderson Cancer Center, Houston, Texas, explored whether CYC065's antineoplastic effects engaged anti-metastatic pathways. *In vitro* migration and invasion assays showed that CYC065 markedly inhibited migration and invasion of lung cancer cell lines, including KRAS mutant line. Reverse Phase Protein Arrays (RPPA) interrogated nearly 300 growth-regulatory proteins in murine and human lung cancer.

CYC065 treatment resulted in up-regulation of proteins involved in DNA damage and apoptosis, and down-regulation of ones involved in mTOR- and integrin pathways. Ingenuity pathway analysis (IPA) revealed up-regulation of pathways that engaged ATM signaling, G2/M DNA damage checkpoint regulation, or apoptosis signaling, down-regulation of pathways involved in mTOR signaling, cell cycle regulation, or integrin—mediated cell migration.

Data presented at AACR show CYC065's potential to cause anaphase catastrophe and to inhibit migration and invasion of lung cancer cells including the one with mutant KRAS. Anaphase catastrophe is a novel mechanism of action which offers an innovative approach to combat aneuploid cancer cells containing abnormal numbers of chromosomes. The data highlight CYC065's potential to target key molecular features of cancers.

The study concluded that CYC065 elicits marked antineoplastic effects in lung cancers despite presence of KRAS mutations through anaphase catastrophe and also inhibited migration and invasion of lung cancer cells.

Abstract:	128
Title:	The next generation CDK2/9 inhibitor CYC065 elicits marked antineoplastic effects in lung cancer by engaging anti-metastatic pathways
Date/time:	Sunday, April 2, 2017 1:00 — 5:00 p.m. ET
Location:	Section 5, Poster Board 24
Session Title:	Novel Agents
Authors:	Masanori Kawakami[1], Jason Roszik[2,3], Lin Zheng[1], Jonathan Kurie[1], Lisa Maria Mustachio[1], Xi Liu[1], Ethan Dmitrovsky[1] *1. Department of Thoracic/Head and Neck Medical Oncology, 2. Genomic Medicine, 3.Cancer Biology; The University of Texas MD Anderson Cancer Center, Houston, Texas.*

The abstract can be accessed through the AACR website, www.aacr.org.

About CYC065

Cyclacel's second generation CDK2/9 inhibitor, CYC065, is being evaluated in an ongoing, first-in-human, Phase 1 trial in patients with advanced solid tumors. In addition to determining safety and recommended dosing for Phase 2, the study aims to investigate CYC065's effects on the Mcl-1 biomarker, which is implicated in the evolution of resistance in cancer. Evidence of target engagement with prolonged Mcl-1 suppression in peripheral blood cells was observed in patient samples from the study, as well as decreases in kinase substrate phosphorylation and increases in PARP cleavage, consistently with the Company's preclinical data. CYC065 is mechanistically similar but has much higher dose potency, in vitro and in vivo, and improved metabolic stability than seliciclib, Cyclacel's first generation CDK inhibitor. Similar to palbociclib, the first CDK inhibitor approved by FDA in 2015, CYC065 may be most useful as a therapy for patients with both liquid and solid tumors in combination with other anticancer agents, including Bcl-2 antagonists, such as venetoclax, or HER2 inhibitors, such as trastuzumab.

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 is analyzing stratified and exploratory subgroups from a Phase 3 study of sapacitabine in elderly patients with AML. 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.

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