April 4, 2017

Cyclacel Presents Identification of Sensitive Target Indications and Synergistic Drug Combinations for Novel PLK1 Inhibitor CYC140

- Preclinical Data Presented at the AACR 2017 Meeting -

BERKELEY HEIGHTS, N.J., April 04, 2017 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (NASDAQ:CYCC) (NASDAQ:CYCCP) (Cyclacel or the Company), today announced the presentation of preclinical data outlining the potential therapeutic utility of CYC140, a polo-like kinase (PLK) 1 inhibitor, for the treatment of esophageal cancer and acute leukemia. The findings were presented during the American Academy of Cancer Research (AACR) Annual Meeting, April 1-5, in Washington, D.C.

"We believe these findings further validate the potential utility of CYC140 and its selection as a clinical candidate," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "CYC140 is a potent and selective inhibitor of PLK1, an oncogenic regulator of cell division. These preclinical data suggest that CYC140 can be targeted against esophageal cancer and acute leukemia. In addition, the data demonstrate the potential for CYC140 to be used in synergistic combinations with other targeted agents, including EGFR inhibitors and PI3K pathway inhibitors, to enhance cancer cell death or growth suppression. CYC140 was discovered and developed in-house, drawing on our strong scientific experience in cell cycle biology. Based on these results and the conclusion of IND-directed development we plan to make an Investigational New Drug submission for CYC140."

Esophageal cancer and acute leukemia were identified as highly sensitive cancer indications from a panel of 300 cancer cell lines and non-malignant comparators following short exposure to CYC140. CYC140 demonstrated good selectivity over non-malignant cell lines. Potent, dose-dependent antitumor activity of CYC140 was demonstrated in preclinical xenograft models of esophageal cancer and acute leukemia with tumor growth delay, tumor regression and cures observed.

In esophageal cancer cell lines CYC140 combined synergistically with EGFR inhibitors or PI3K pathway inhibitors and can also be combined with approved cytotoxics such as cisplatin. Consistent with PLK1 inhibition, CYC140 reduced phosphorylation of nucleophosmin, a PLK1 substrate, and caused accumulation of mitotic cells *in vitro* and *in vivo*.

The study concluded that CYC140 is a selective PLK1 inhibitor which preferentially induces growth inhibition and cell death in malignant versus non-malignant cells. Identification of several pharmacodynamic markers and demonstration of activity in a majority of malignant cell lines derived from acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) and esophageal cancer support prospective clinical development of CYC140, alone and in potential combination with targeted agents.

Abstract:	4178
Title:	The novel PLK1 inhibitor, CYC140: Identification of pharmacodynamic markers, sensitive target indications and potential combinations
Date/Time:	Tues. April 4, 2017: 1 p.m. - 5 p.m. EDT
Location:	Section 7, Poster Board 1
Session Title:	Targeting Protein Kinases and DNA
Authors:	Sylvie Moureau, Craig MacKay, Chiara Saladino, Elizabeth Pohler, Karin Kroboth, Jonathan Hollick, Daniella Zheleva, Sheelagh Frame, David Blake. Cyclacel Ltd, Dundee, United Kingdom

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

About PLK inhibition

Polo kinases were discovered by Professor David Glover, Cyclacel's Chief Scientist. They are a family of enzymes that regulate cell cycle progression through mitosis or cell division. PLKs are part of the biological machinery that regulate spindle formation and activation of CDK/cyclin complexes during mitosis. Activity of the mitotic kinase PLK1 is strongly associated with cancer progression. Several studies have shown correlations between elevated PLK1 expression, histological grade and poor prognosis in several types of cancer. PLK1 may have a role in oncogenesis through its regulation of tumor suppressors, such as p53 and BRCA2. Inhibition of PLK1 by small molecules or siRNA has been shown to interfere with several stages of mitosis. PLK1 inhibition offers an opportunity to treat cancer with a targeted anti-mitotic approach.

About CYC140

Cyclacel employed high throughput screening, *in silico* screening and *de novo* ligand design approaches to discover multiple PLK1 inhibitor series. The lead series includes potent and highly selective PLK1 inhibitors with broad anti-proliferative activity across a range of tumor cell lines, which are highly active in xenograft models of human cancers when dosed orally. CYC140 was selected as a clinical candidate following optimization for drug-like properties, cellular activity and pharmacokinetic profile. CYC140 has recently completed IND-enabling studies.

A grant of approximately $3.7 million from the U.K. Government's Biomedical Catalyst has supported IND-directed development of CYC140.

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 which 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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