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Cyclacel's Novel PLK1 Inhibitor, CYC140, Demonstrates Therapeutic Potential in Esophageal Cancer and Acute Leukemia

-Preclinical Data Presented at the 28th EORTC-NCI-AACR Symposium-

BERKELEY HEIGHTS, N.J., Dec. 01, 2016 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC) (Nasdaq:CYCCP) ("Cyclacel" or the "Company"), a biopharmaceutical company developing oral therapies that target the various phases of cell cycle control for the treatment of cancer and other serious disorders, today announced the presentation of preclinical data demonstrating the therapeutic potential of the Company's novel polo-like kinase (PLK) 1 inhibitor, CYC140, as a targeted anti-cancer agent. The data demonstrates that CYC140 is a selective PLK1 inhibitor which preferentially induces growth inhibition and cell death in malignant versus non-malignant cells. The data were presented at the 28th EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium in Munich, Germany.

"CYC140 is a selective and potent inhibitor of PLK1, an important cancer therapy target. We selected this promising targeted molecule as a clinical candidate after completing IND-enabling studies," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "Data presented at EORTC-NCI-AACR highlights CYC140's potential as an agent to treat a variety of cancer indications, including esophageal cancer and acute leukemia. We look forward to making an Investigational New Drug submission with the goal of initiating a first-in-human Phase 1 trial. In the meantime we continue to progress our later stage programs, including our Phase 3 SEAMLESS study with oral sapacitabine capsules, where we anticipate reporting top line results late in the fourth quarter of 2016 or in early 2017."

Treatment of proliferating cells with CYC140 resulted in reduced phosphorylation of the PLK1 substrate phospho-nucleophosmin, accumulation of cells in mitosis and increase in the proportion of mitotic cells with monopolar spindles, all features consistent with PLK1 inhibition. In a cell line panel derived from esophageal cancer and various non-malignant solid tissues, CYC140 was preferentially cytotoxic to malignant cells. Its differential cytotoxicity is further increased through pulse treatment. Malignant cells which are sensitive to CYC140 undergo complete growth inhibition and induction of cell death in response to treatment. In contrast, non-malignant cells are only temporarily arrested and normal cell cycle transit is restored.

Potent anti-tumor activity of CYC140 has been demonstrated in preclinical xenograft models of acute leukemia and solid tumors, including esophageal cancer, with tumor growth delay, tumor regression and cures being observed. 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 several potential combinations with targeted agents.

Abstract:	355
Title:	Therapeutic potential of novel PLK1 inhibitor, CYC140, in esophageal cancer and acute leukemia
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Session Title:	'Cytotoxics'
Authors:	S. Moureau, E. Pohler, K. Kroboth, C. Saladino, C. MacKay, J. Hollick, D. Zheleva, S. Frame, D. Blake, Cyclacel Ltd, Dundee, Scotland, UK

The abstract can be accessed through the *EORTC-NCI-AACR* website, http://www.ecco-org.eu/ENA2016.

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 control and DNA damage response biology to develop innovative, targeted medicines for cancer and other proliferative diseases. The SEAMLESS randomized Phase 3 trial of sapacitabine as front-line treatment for AML in the elderly under an SPA with FDA has completed enrollment and follow-up. Cyclacel's pipeline includes an oral combination of seliciclib (CDK inhibitor) and sapacitabine in Phase 1 in advanced solid tumors, including patients with BRCA mutations; sapacitabine in Phase 2 in MDS; and CYC065 (CDK inhibitor) in Phase 1 in solid tumors with potential utility based on preclinical data also in hematological malignancies. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a pipeline of novel drug candidates. Please visit www.cyclacel.com for more information.

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

Company: Paul McBarron, (908) 517-7330, pmcbarron@cyclacel.com
Investor Relations: Russo Partners LLC, Alexander Fudukidis, (646) 942-5632, alex.fudukidis@russopartnersllc.com