# Cyclacel's Novel Polo-Like Kinase 1 (Plk1) Inhibitors Highlighted at AACR

## Presentation Demonstrates Preclinical Activity of Plk1 Targeted Agent in Esophageal Cancer Cells

BERKELEY HEIGHTS, N.J., April 2, 2012 (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, announced today the presentation of translational research findings and characterization of selective Polo-Like Kinase 1 (Plk1) and Aurora A kinase inhibitors discovered by Cyclacel during the 103rd Annual Meeting of the American Association of Cancer Research (AACR) 2012 in Chicago, IL.

"Plk1 is a promising therapeutic target for cancer, with several Plk1 inhibitors demonstrating encouraging results in Phase 1 or 2 clinical trials," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "In the presentation at AACR, we report on the development of a potent and selective Plk1 inhibitor in addition to proposing a predictive biomarker-driven, clinical development strategy using p53 protein status. This discovery leverages the efforts of Cyclacel's pioneering founders in the areas of p53 and mitotic kinases, such as Polo, to develop oral therapies that target the various phases of cell cycle control for the treatment of cancer and other serious diseases."

**Polo-like kinase 1 (Plk1) Inhibitors:**

*Abstract No. 2814: "Potent and selective small molecule inhibitors of polo-like kinase 1: Biological characterization"*

Cyclacel scientists and academic collaborators reported the biological characterization of Compound 4, a potent and selective, preclinical-stage, Plk1 inhibitor, selected for further development from Cyclacel's novel Plk1 inhibitor series. In a panel of esophageal cancer cell lines, sensitivity to Compound 4 correlated with p53 status. Esophageal cell lines lacking functional p53 showed the greatest sensitivity to Compound 4. Short drug exposure times demonstrated differential sensitivity between cancerous esophageal cells versus control, outlining the potential broad therapeutic index for Compound 4 in treating esophageal cancers, and in particular those with non-functional p53. Status of p53 could be used as a predictive biomarker in clinical trials to identify responders.

In addition to the presentation by Cyclacel scientists, the Company's collaborators presented new data regarding one of Cyclacel's Aurora kinase A inhibitors:

**Aurora Kinase A Inhibitors:**

*Abstract No. 1924: "The aurora kinase inhibitor CYC3 synergizes with low concentrations of paclitaxel in pancreatic cancer cells in vitro"*

Cyclacel collaborators led by Duncan Jodrell, Ph.D., Professor of Cancer Therapeutics, Department of Oncology, University of Cambridge (Cambridge, UK) tested the activity of CYC3, a novel Cyclacel Aurora Kinase A specific inhibitor, in pancreatic cancer cell lines. The Cambridge team reported that CYC3 suppresses pancreatic cancer cell growth, inducing mitotic arrest and apoptosis. CYC3 was also shown to act synergistically against pancreatic cancer cell lines in combination with paclitaxel at a 10-fold lower dose resulting in comparable anti-proliferative activity to standard paclitaxel dosing. As myelosuppression is associated with paclitaxel administration, the CYC3/low-dose paclitaxel combination was compared with high-dose paclitaxel in an *in vitro* granulocyte and macrophage assay in which the CYC3/low-dose paclitaxel combination displayed less myelotoxicity. The combination merits further investigation and has the potential for improved therapeutic index *in vivo*.

**About Esophageal Cancer**

Esophageal cancer is a leading cause of cancer death and represents a high unmet medical need. The American Cancer Society's 2012 estimates for esophageal cancer in the United States are about 17,460 new esophageal cancer cases diagnosed (13,950 in men and 3,510 in women) and about 15,070 deaths from esophageal cancer (12,040 in men and 3,030 in women). The disease is 3 to 4 times more common among men than women. The lifetime risk of esophageal cancer in the United States is about 1 in 125 in men and about 1 in 400 in women. Five-year survival of patients with esophageal cancer ranges from 3% for distant disease to 37% for localized disease. Approximately 50—80% of esophageal tumors have been found to have mutations in the p53 tumor suppressor gene which are thought to be a major cause of resistance to

chemotherapy and radiotherapy.

**About Plk1 (Polo-Like Kinase 1)**

Polo-like kinases are enzymes that were first discovered in the fruit fly model of human cancer by Prof. David Glover, Cyclacel's Chief Scientist. Professor Glover is a world authority on Aurora kinases, Polo kinases and related mechanisms controlling cell division. 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.[1] Plk1 may have a role in oncogenesis through its regulation of tumor suppressors such as p53 and BRCA2. The inhibition of Plk1 by small molecules or siRNA has been shown to interfere with several stages of mitosis. Therefore Cyclacel's Plk1 inhibitors may represent an opportunity to treat cancer with a targeted anti-mitotic approach that will inhibit several important regulatory events in tumor cells.

**About Aurora Kinase**

Aurora kinases are enzymes that were first discovered in the fruit fly model of human cancer by Prof. David Glover, Cyclacel's Chief Scientist. Professor Glover is a world authority on Aurora kinases, Polo kinases and related mechanisms controlling cell division. He studied extensively and described in detail the role played by such enzymes in regulating the late stage of the cell cycle known as mitosis. Cyclacel scientists under the direction of Professor Glover have identified several hundred genes regulating mitosis and amassed a substantial intellectual property estate on drug targets and novel molecules. Overexpression of Aurora kinase A is reported to induce resistance to taxanes[2] and has been observed in various tumor types including pancreatic cancer.[3]

**About Cyclacel Pharmaceuticals, Inc.**

Cyclacel is a biopharmaceutical company developing oral therapies that target the various phases of cell cycle control for the treatment of cancer and other serious diseases. Sapacitabine (CYC682), an orally-available, cell cycle modulating, nucleoside analogue, is in the SEAMLESS Phase 3 trial being conducted under an SPA with the FDA for the front-line treatment of AML in the elderly and Phase 2 studies for myelodysplastic syndromes, lung cancer and chronic lymphocytic leukemia. Seliciclib (CYC202 or R-roscovitine), an orally-available, CDK (cyclin dependent kinase) inhibitor, is in Phase 2 studies for the treatment of lung cancer and nasopharyngeal cancer and in a Phase 1 trial in combination with sapacitabine. Cyclacel's ALIGN Pharmaceuticals subsidiary markets directly in the U.S. Xclair® Cream for radiation dermatitis, Numoisyn® Liquid and Numoisyn® Lozenges for xerostomia. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a portfolio of commercial products and a development pipeline of novel drug candidates. Please visit www.cyclacel.com for additional information.

[1] Kanaji et al, Oncology 2006:70:126. Weichert et al, Cancer Sci. 2006:97:271. Yamada et al, Oncogene 2004:23: 5901

[2] Anand et al. Cancer Cell 2003, 3: 51

[3] Li et al. Clin. Cancer Res. 2003, 9: 991

**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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