Cyclacel’s seliciclib found effective against lung cancer cell Lines including K-RAS mutations

- Seliciclib kills lung cancer cells addicted to CDK2/cyclin E; Phase 2 study in lung cancer ongoing -

BERKELEY HEIGHTS, NJ - January 7, 2010 - Cyclacel Pharmaceuticals, Inc. (NASDAQ: CYCC, NASDAQ: CYCCP) today announced the publication of two peer-reviewed journal articles featuring the company's seliciclib (CYC202 or R-roscovitine) drug candidate, an orally available inhibitor of multiple cyclin-dependent kinases (CDKs). CDKs have been extensively investigated as therapeutic targets in light of their frequent deregulation in lung carcinogenesis. In an article published in *Clinical Cancer Research*, seliciclib was found to be effective in killing lung cancer cells through a novel apoptotic mechanism or induction of cancer cell suicide. Nearly all lung cancer cell lines against which seliciclib was most effective had Ras-activating mutations. Ras is a family of mutations which make lung cancer cells highly resistant to approved drugs such as those targeting epidermal growth factor receptors (EGFR).

"Drugs that target EGFR, such as cetuximab (Erbitux®), erlotinib (Tarceva®) and gefitinib (Iressa®), are active against non-small cell lung cancer (NSCLC). However Ras family mutations, such as K-RAS and N-RAS, in NSCLC patients are associated with increased resistance to treatment. Approximately 15%-30% of patients with NSCLC harbor Ras mutations and have a poor prognosis," said Professor David Glover, Ph.D., Cyclacel's Chief Scientist. "The data published in *Clinical Cancer Research* show a high correlation between Ras mutations and sensitivity to seliciclib. Investigating a correlation between clinical outcomes and Ras mutation status in patients from completed seliciclib trials may provide a rationale to select patients for treatment with seliciclib or other CDK inhibitors based on mutational profile. We look forward to unblinding data from our completed Phase 2, randomized, double-blinded APPRAISE trial in patients with pretreated NSCLC during 2010. If seliciclib is found to be effective in patients with Ras-mutant NSCLC, it could address an area of high unmet medical need."

Among 52 cell lines of NSCLC origin tested, 2 (4%) were relatively insensitive to seliciclib, 21 (40%) displayed modest sensitivity and 29 (56%) showed marked sensitivity. Of the 13 lung cancer cell lines which had the highest sensitivity to seliciclib, 12 (92%) had Ras-activating mutations, including K-RAS and N-RAS. However of the 15 lung cancer cell lines which were least sensitive to seliciclib, none had Ras-activating mutations.

The *Clinical Cancer Research* article entitled, "Targeting the Cyclin E-Cdk-2 Complex Represses Lung Cancer Growth by Triggering Anaphase Catastrophe" reported that inhibition of CDK2 by seliciclib suppressed lung cancer growth both *in vitro* and *in vivo* of lung cancer cells addicted to CDK2/cyclin E. As a consequence, lung cancer cells underwent apoptosis or cell suicide by induction of a novel mechanism called anaphase catastrophe, as illustrated in the journal's front cover.

Combining seliciclib with microtubule-targeting agents, such as paclitaxel or docetaxel, was found to be an attractive clinical regimen to consider in patients with lung cancer. The authors also reported studying second-generation CDK inhibitors from Cyclacel with greater potency to seliciclib in terms of inhibiting the growth of lung cancer cells. *Citation*: Galimberti F., et. al., *Clinical Cancer Research*, 2010 16:1:109-120.

Seliciclib is currently being evaluated in the APPRAISE trial, a Phase 2b randomized, double-blinded, placebo-controlled trial studying the efficacy and safety of single-agent seliciclib as a third, fourth or fifth line treatment in patients with NSCLC. The trial is using a randomized discontinuation design. The primary endpoint is progression free survival (PFS).

A second peer-reviewed article is entitled "R-roscovitine (seliciclib) affects CLL cells more strongly than combinations of fludarabine or cladribine with cyclophosphamide: Inhibition of CDK7 sensitizes leukemic cells to caspase-dependent apoptosis". While CDK inhibitors are known to have clinical activity against B-cell Chronic Lymphocytic Leukemia (B-CLL) cells, this publication directly compares the activity of seliciclib with commonly used therapeutic options, such as the combination of fludarabine and cyclophosphamide. In these *ex vivo* studies, seliciclib was compared to ﬂudarabine and cladribine given in combination with cyclophosphamide. Seliciclib was found to be the most effective at inducing apoptosis or programmed cell death in malignant B-CLL cells while resulting in significantly less apoptosis induction in "normal" peripheral blood mononuclear cells, suggesting the largest therapeutic window among the treatments studied. *Citation*: Rogalinska M., et. al., *Journal of Cell Biochemistry*, 2010 Jan 1, 109:1:217-235.

About seliciclib

Seliciclib is an orally available molecule that selectively inhibits multiple CDK enzyme targets, CDK2/E, CDK2/A, CDK7 and CDK9, that are central to the process of cell division and cell cycle control. Seliciclib has been administered to approximately

420 patients in Phase 1 and Phase 2 trials. It is currently being evaluated in the APPRAISE trial, a Phase 2b randomized, placebo-controlled, double-blinded study as a treatment in patients with non-small cell lung cancer (NSCLC) who failed at least two prior therapies and in a randomized Phase 2 study as a single agent in patients with nasopharyngeal cancer.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel is a biopharmaceutical company dedicated to the discovery, development and commercialization of novel, mechanism-targeted drugs to treat human cancers and other serious disorders. Three orally-available Cyclacel drugs are in clinical development. Sapacitabine (CYC682), a cell cycle modulating nucleoside analog, is in Phase 2 studies for the treatment of acute myeloid leukemia in the elderly, myelodysplastic syndromes and lung cancer. The Company plans to submit a Special Protocol Assessment (SPA) request for a pivotal study with sapacitabine during the first quarter of 2010. Seliciclib (CYC202 or R-roscovitine), a 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. CYC116, an Aurora kinase and VEGFR2 inhibitor, is in a Phase 1 trial in patients with solid tumors. 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.

Risk factors

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, the risk that Cyclacel will not obtain approval to market its products, 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. These factors and others are more fully discussed under "Risk Factors" in the Annual Report on Form 10-K for the year ended December 31, 2008, as supplemented by the interim quarterly reports, filed with the SEC.

Contacts for Cyclacel Pharmaceuticals, Inc.

Investors/Media:
Corey Sohmer, (908) 517-7330
csohmer@cyclacel.com