# New Study in CCR demonstrates potential for seliciclib in treating breast cancer resistant to hormone therapy

## - Seliciclib kills hormone receptor positive breast cancer cells resistant to letrozole -

**BERKELEY HEIGHTS, NJ – February 17, 2010** – Cyclacel Pharmaceuticals, Inc. (NASDAQ: CYCC, NASDAQ: CYCCP) today announced that a newly published study demonstrates that the company's seliciclib (CYC202 or R-roscovitine), an orally available inhibitor of multiple cyclin-dependent kinases (CDKs), reversed resistance to the aromatase inhibitor letrozole (Femara®) and killed hormone receptor positive breast cancer cells that had become insensitive to the effects of letrozole. The new study was published in the current edition of *Clinical Cancer Research*, a journal of the American Association for Cancer Research. Seliciclib is currently in Phase 2 clinical trials for non-small cell lung cancer and nasopharyngeal cancer.

“Resistance to aromatase inhibitors, such as letrozole, is a major challenge for the long-term management of hormone receptor positive breast cancer,” said Professor David Glover, Ph.D., Cyclacel’s Chief Scientist. “The data published in Clinical Cancer Research are encouraging as they show that seliciclib can kill resistant breast cancer cells by targeting a form of cyclin E that is a major cause of the resistance. This is further evidence that seliciclib's unique mechanism of action can be effective against certain cancer cells, such as breast and lung cancer, that fail to respond to standard cancer treatments.”

Approximately 3 out of 4 women suffering from breast cancer after menopause have cancers that express the hormonal receptors for estrogen and progesterone and are offered treatment with aromatase inhibitor drugs including letrozole. Letrozole treatment reduces the risk of early metastasis in women with estrogen receptor–positive breast cancer. Letrozole is believed to interact with a natural CDK inhibitor p27 which in turns regulates the activity of the CDK2/cyclin E complex. Over time, breast cancer cells develop resistance to letrozole and the therapy becomes ineffective.

Researchers from The University of Texas M.D. Anderson Cancer Center led by Khandan Keyomarsi, Ph.D., professor in the Department of Experimental Radiation Oncology, found that a key cause of resistance to letrozole is overexpression of the low molecular weight form of cyclin E, which also predicted for lower overall survival and higher chance of cancer recurrence after aromatase inhibitor treatment. However, after they treated letrozole-resistant breast cancer cells with seliciclib, a CDK2/cyclin E inhibitor, the resistant cancer cells were killed. The researchers concluded that their data support clinical investigation of CDK inhibitors such as seliciclib as targeted therapy in a specific patient population of postmenopausal women with hormone receptor–positive, low molecular weight cyclin E expressing breast cancer. Citation: Akli S., et. al., Clinical Cancer Research, 2010 16:4:1179–90.

### About seliciclib

Seliciclib is an orally available molecule that selectively inhibits multiple cyclin-dependent kinase or CDK 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 450 patients in Phase 1 and Phase 2 trials. It is currently being evaluated in the APPRAISE trial, a Phase 2b randomized, double-blinded, placebo-controlled 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.

The APPRAISE trial is assessing the efficacy and safety of single-agent seliciclib as a third, fourth or fifth line treatment in patients with NSCLC. The study is using a randomized discontinuation design with a primary endpoint of progression free survival.

### About CDK2/cyclin E

Cyclin E, a cell cycle protein, binds to its partner enzyme CDK2, a cyclin-dependent kinase, forming a complex. The CDK2/cyclin E complex plays a key role in regulating the progression of cells through the four stages of the cell cycle and the two cell cycle arrest checkpoints where cells are checked for damage to their DNA before they divide. Unlike normal cells, cancer cells modify cyclin E to a low molecular weight form which has been associated with genomic instability, uncontrolled proliferation and overtime the evolution of resistance to cancer treatments.

### About letrozole

Letrozole is an aromatase inhibitor indicated for the adjuvant treatment of postmenopausal women with hormone receptor

positive early breast cancer, the first-line treatment of postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer and the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy.

**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. 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.

**Contact for Cyclacel Pharmaceuticals, Inc.**

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