Cyclacel's innovative and diverse oncology targeted pipeline highlighted in six presentations at AACR Annual Meeting

- Several presentations focus on CYC065 second-generation Cyclin-Dependent Kinase inhibitor with activity against drug-resistant cancers -

BERKELEY HEIGHTS, NJ – April 20, 2010 – Cyclacel Pharmaceuticals, Inc. (NASDAQ: CYCC, NASDAQ: CYCCP), 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 results for several of its pipeline compounds during the American Association of Cancer Research (AACR) 101st Annual Meeting 2010 in Washington, DC.

“Among the six abstracts, we are pleased to have data presented for the first time with regard to CYC065, our second generation inhibitor of cyclin-dependent kinases (CDKs). CYC065 is an oral multikinase inhibitor with the same CDK targeted profile as our seliciclib clinical-stage drug. Data presented at AACR show that CYC065 has promising anti-tumor activity in models of breast cancer and hematological malignancies,” said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. “In addition, translational studies highlighted the unique mechanisms of action and new potential clinical applications for sapacitabine and seliciclib, both of which are currently in multiple Phase 2 clinical trials. We are also encouraged by preclinical data with our recently discovered, oral, small molecule, anti-mitotic inhibitors of polo-like kinase 1 (Plk1), suggesting that they are suitable for further development.”

CYC065 and Second Generation CDK Inhibitors

Abstract No. 22: “Cyclin E amplification, a novel mechanism of resistance to trastuzumab in HER2 amplified breast cancer”

In an oral presentation at AACR, investigators from Vall d'Hebron University Hospital (Barcelona, Spain) and Memorial Sloan-Kettering Cancer Center (New York, NY) reported that HER2 positive breast cancer cell lines refractory to the anti-proliferative effects of the therapeutic antibody trastuzumab (Herceptin®) were killed by CYC065. The investigators found that resistant cell lines were addicted to and overexpressed cyclin E, a component of the CDK/cyclin target of CYC065. Cyclin E overexpression has been observed in patients positive for HER2, a protein that is the target of trastuzumab. The discovery that cyclin E amplification decreases sensitivity of breast cancer cells to trastuzumab provides a rationale for exploring the efficacy of CDK2/cyclin E inhibitors, such as CYC065 and seliciclib, in this patient population.

“We have determined that breast cancer cells resistant to therapeutic agents targeting HER2 are highly sensitive to CDK inhibition by CYC065,” said José Baselga, M.D., Ph.D., chairman of the Medical Oncology Service and director of the Division of Medical Oncology, Hematology and Radiation Oncology at the Vall d'Hebron Institute of Oncology, and lead investigator of the study. “Amplification and overexpression of cyclin E is a mechanism by which breast cancer cells develop resistance to trastuzumab. Targeting such cells with siRNA against cyclin E reduces cell growth and restores sensitivity to trastuzumab. Engineered overexpression of cyclin E in parental breast cancer cells markedly reduces trastuzumab’s effectiveness. In contrast, Cyclin E overexpressing, trastuzumab-resistant cells are more sensitive to pharmacological inhibition by CDK inhibitors, such as seliciclib or its more potent derivative, CYC065. CYC065 induces more apoptosis in cyclin E overexpressing than in parental breast cancer cells. CYC065 has promising in vivo activity in xenograft models of the resistant cells, which appears to be enhanced by the action of trastuzumab.”

Approximately 15 to 20 percent of breast cancers have an amplification of the HER2/neu gene or overexpression of its protein product, which is associated with increased disease recurrence and worse prognosis. Therapeutic agents targeting HER2 have been shown to improve survival. However, resistance to these agents is a major barrier to the effective treatment of breast cancer.

Cyclacel has developed CYC065 and other novel derivatives of seliciclib in collaboration with the Cancer Research UK Centre for Cancer Therapeutics at The Institute of Cancer Research (ICR), London, UK. CYC065 and related derivatives inhibit the same CDK/cyclin complexes, retaining the specificity and mechanism of action of seliciclib, but with increased anti-proliferative potency and improved pharmaceutical properties. Investigational new drug (IND) enabling studies for CYC065 are underway.

In 2001, the Nobel Prize in Physiology and Medicine was awarded for the discovery of cyclins and CDKs, key regulators of the cell cycle. By selectively modulating cell cycle regulation in cancer cells, inhibition of CDK/cyclin complexes represents a promising strategy for cancer therapy. Seliciclib (CYC202, R-roscovitine), a novel, first-in-class, orally available CDK inhibitor,

currently in Phase 2 clinical trials, selectively inhibits multiple CDK/cyclin targets, in particular CDK2/cyclin E, CDK2/cyclin A, CDK5, CDK7 and CDK9. Seliciclib also induces apoptosis in neutrophil granulocytes that mediate inflammation, indicating that CDK inhibitors may also hold promise in applications outside oncology, such as the treatment of chronic autoimmune and inflammatory diseases including arthritis or asthma.

Abstract No. 3886: "Therapeutic potential of CDK inhibitors in MLL leukemias"

Chromosomal rearrangements involving the human mixed-lineage leukemia (MLL) gene are associated with the development of de novo acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) as well as in therapy-related AML. In a study reported at AACR, Cyclacel investigators studied the effect of CYC065, a second generation CDK inhibitor, on AML cell lines with and without MLL rearrangements. MLL-rearranged cells required 24 to 72 hours exposure to cytarabine for maximal response. In contrast AML cells, with or without MLL rearrangements, were exquisitely sensitive to short CYC065 treatments (5 to 8 hours) which completely inhibited proliferation. Rapid induction of p53 and downregulation of Mcl-1, Meis1 and Hoxa1 followed by apoptosis were observed. The high sensitivity of AML cell lines with MLL rearrangements was also confirmed *in vivo*. A highly potent and durable effect was observed in an AML mouse xenograft model after oral administration of CYC065 resulting in 97% tumor growth inhibition. The data suggest that both AML and MLL-rearranged leukemias are very sensitive to CYC065 and justify further exploration of its therapeutic potential in these indications.

Abstract No. 4431: "A novel derivative of the CDK inhibitor roscovitine that induces apoptosis in CLL and overcomes stromal cell-mediated protection"

Chronic lymphocytic leukemia (CLL) is characterized by the accumulation of malignant, apoptosis-resistant B-cells. In a study reported at AACR, investigators led by William K. Plunkett, Jr., Ph.D., Professor and Chief, Section of Molecular and Cellular Oncology, Department of Experimental Therapeutics at The University of Texas M. D. Anderson Cancer Center (Houston, TX) studied the effect of CYC065 in CLL. Similarly to seliciclib, CYC065 induced apoptosis in CLL cell lines *in vitro* by reducing CDK9-dependent transcription resulting in a rapid loss of short lived mRNAs or anti-apoptotic proteins such as Mcl-1. Loss of Mcl-1 was associated with induction of cancer cell death by apoptosis. CYC065 demonstrated approximately 30 times greater potency than seliciclib, its parent compound. The data suggests that CYC065 is also a promising candidate for clinical development in CLL.

Sapacitabine:

Abstract No. 3502: "Understanding the pathways involved in the repair of CNDAC induced DNA damage"

CNDAC is the main active metabolite of sapacitabine, Cyclacel's orally available nucleoside analogue, currently in Phase 2 trials in hematological and solid cancer. Unlike other nucleoside analogues, CNDAC causes the formation of double-stranded (ds) DNA breaks that activate the dsDNA damage checkpoint and cause arrest in the G2/M phase of the cell cycle. CNDAC-induced dsDNA damage is repaired by the homologous recombination (HR) DNA repair pathway. The work described in the poster discusses different methods of targeting the HR pathway to enhance CNDAC's potency against cancer cells.

Breast cancer susceptibility proteins BRCA1 and BRCA2 are tumor suppressors that ensure the stability of the cell's DNA and prevent uncontrolled cell growth in normal cells. BRCA gene mutations are common in breast and ovarian cancer. The BRCA1 and 2 proteins are involved in the HR DNA repair pathway. Recently published clinical data have validated that BRCA mutations can sensitize tumors to DNA damaging agents such as PARP inhibitors or cisplatin.

Investigators from Cyclacel reported that inactivation of BRCA1 or 2 by siRNA leads to a significant increase in the cancer cell cytotoxicity of CNDAC. In an isogenic cell line pair differing only in BRCA2 status, the BRCA2 deficient cell line was 50 times more sensitive to CNDAC than the parental cancer cell line with normal BRCA2 function. Importantly there was no difference in the sensitivity of both cell lines to gemcitabine, demonstrating that sapacitabine and gemcitabine work by different mechanisms. In the BRCA2 deficient cell line, CNDAC was more potent than gemcitabine. This data indicates that evaluation of sapacitabine in patients with either triple negative breast cancer or ovarian cancer would be advisable as patients with either of these tumors have a high proportion of BRCA mutations.

Depletion of CHK1 kinase, a regulator of the G2/M damage induced checkpoint, was also shown to increase the sensitivity of cancer cells to CNDAC. This finding was supported by demonstrating that CNDAC is synergistic in combination with CHK1 inhibitors. The strongest synergy was observed between CNDAC and the CHK inhibitor PF477736, with the combination producing a very significant increase in cell death compared to either single agent alone. As a number of CHK inhibitors are now in Phase 1 clinical trials, this combination also represents an attractive opportunity for clinical evaluation.

Anti-mitotic Therapies:

Anti-mitotic drugs that target tubulin, such as vinca alkaloids and taxanes, are widely used for the treatment of cancer, but have limitations related to the role of tubulin in the cytoskeleton of normal cells. Cyclacel has discovered and is developing new

compounds that inhibit targets with specific functions in mitosis, such as Aurora kinases and polo-like kinases (PLKs), which show promising anti-tumor activity in preclinical models. These targets are only expressed in dividing cells and specific drugs are designed to avoid damaging non-dividing cells, thereby enabling an improved therapeutic index compared to existing anti-mitotic drugs that target tubulin.

Abstract No. 633: "Tumor cell resistance mechanisms to aurora kinase inhibitors"

CYC116, an Aurora kinase inhibitor discovered and developed by Cyclacel, is currently in a Phase 1 clinical trial in patients with advanced solid tumors. While CYC116 has demonstrated significant anti-proliferative activity in preclinical studies, induction of acquired resistance to this Aurora kinase inhibitor has not been established.

In a study presented at AACR, researchers identified the molecular basis of acquired tumor resistance to CYC116 *in vitro*. The group led by Marian Hajduch, M.D., Ph.D., Associate Professor of Oncology and Head of Laboratory of Experimental Medicine, at Palacky University and University Hospital (Olomouc, Czech Republic) has developed resistant clones of colon carcinoma cell lines to study mechanisms of CYC116-induced resistance. Data were presented on characterization of the derived clones in relation to their resistance toward CYC116, cross resistance to other Aurora kinase inhibitors and chemotherapeutic agents, cell cycle profile, biomarker modulation, important drug transporters, and expression profiles of Aurora kinases. Data show that all CYC116 resistant clones became stably tetraploid and displayed high cross-resistance to other Aurora kinase inhibitors. No over expression of Aurora kinases or up regulation of P-glycoprotein (PgP) drug transporter was observed. Some drug resistant clones over-expressed multidrug resistance-associated protein 1 (MRP1). These studies help understand potential acquired resistance mechanisms and design combination treatment regimens to overcome such resistance.

Abstract No. 4435: "Discovery, biological characterization and oral antitumor activity of polo-like kinase 1 (Plk1) selective small molecule inhibitors"

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. The inhibition of Plk1 by small molecules or siRNA has been shown to interfere with several stages of mitosis. Therefore, targeting Plk1 offers an opportunity to treat cancer with a targeted anti-mitotic approach that will inhibit several important regulatory events in tumor cells.

Cyclacel employed high throughput screening, *in silico* screening and *de novo* ligand design approaches to discover multiple Plk1 inhibitor series. In a study presented at AACR Cyclacel scientists showed preclinical data for a set of potent and highly selective Plk1 inhibitors with broad anti-proliferative activity across a range of tumor cell lines, independent of tumor cell origin or oncogenic Ras or p53 tumor suppressor status. The poster illustrated use of intracellular biomarkers ensuring on-target activity during lead optimization to deliver preclinical candidate compounds that are highly active in xenograft models of human cancers. Significant anti-tumor efficacy was observed, including tumor regression and tumor free cures after repeated oral dosing. The data reported underline the suitability of these compounds for further development as orally available Plk1 inhibitors for the treatment of human cancers.

Further details of all presentations referenced in this press release can be accessed through the AACR website, www.aacr.org. In relevant presentations CYC065 is denoted as Compound 5.

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 disorders. Three product candidates 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.

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, 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. 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 current filings that have been filed 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.

The Institute of Cancer Research (ICR)
The ICR is Europe's leading cancer research centre and has been ranked the UK's top academic research center. Working closely with its partner, The Royal Marsden NHS Foundation Trust, the two organisations together form the largest comprehensive cancer centre in Europe ensuring patients immediately benefit from new research. Over its 100-year history, the ICR's achievements include identifying the potential link between smoking and lung cancer which was subsequently confirmed, discovering that DNA damage is the basic cause of cancer and isolating more cancer-related genes than any other organisation in the world. Several important anti-cancer drugs used worldwide were synthesized at the ICR. ICR has discovered an average of two preclinical candidates each year over the past five years. For more information please visit www.icr.ac.uk.

Cancer Research UK
For further information about Cancer Research UK's work or to find out how to support the charity, please visit www.cancerresearchuk.org.uk.

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