Cyclacel announces topline results from APPRAISE Phase 2b study of seliciclib

Berkeley Heights, NJ, December 21, 2010 – 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 diseases, announced today topline results from APPRAISE, the Company's Phase 2b, randomized discontinuation, double-blinded, placebo-controlled, study of oral seliciclib capsules as a third or more line treatment in patients with non-small cell lung cancer (NSCLC). Topline results, after unblinding the treatment assignment among randomized patients, showed that there was no difference between the seliciclib and placebo arms in terms of progression free survival, or PFS, (48 versus 53 days respectively) but an increase in median overall survival was observed favoring the seliciclib arm over the placebo arm (388 versus 218 days respectively).

"We were encouraged to discover an increase in overall survival favoring the seliciclib arm despite observing no difference in PFS and allowing patients whose cancer had progressed on placebo to cross-over to the seliciclib arm," said Dr. Judy Chiao, Vice President of Clinical Development and Regulatory Affairs of Cyclacel. "We plan to collect and analyze available biopsy samples from APPRAISE patients to assess whether there is a biological basis for these results."

APPRAISE Phase 2b Topline Results

A total of 187 patients from 21 centers in the United States were entered in the study after having progressed on at least two prior therapeutic regimens for their NSCLC. Of these, 53 (28%) were randomized, 27 on seliciclib and 26 on placebo. Forty-five out of 53 randomized patients (85%) received 3 or more prior therapies and 45 out of 53 randomized patients (85%) previously received at least one EGFR inhibitor drug (22 on seliciclib and 23 on placebo). Fourteen patients were crossed-over to the seliciclib arm after their cancer progressed while they were receiving placebo. Study data demonstrated seliciclib to be safe at the administered dose. There was no difference between the seliciclib and placebo arms in terms of PFS of 48 days on the seliciclib arm versus 53 days on the placebo arm. However an increase in median overall survival was observed of 388 days on the seliciclib arm versus 218 days on the placebo arm.

Biopsy Analysis

Cyclacel plans to collect and analyze available biopsy samples from APPRAISE patients who granted informed consent. The purpose of the biopsy analysis is to examine whether there is a biological basis for the difference in overall survival. Recent publications of preclinical data found seliciclib 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 family oncogenes, such as KRAS and NRAS, often have activating mutations, which make lung cancer cells highly resistant to approved drugs, including those targeting epidermal growth factor receptors (EGFR). Investigating a correlation between clinical outcomes and Ras mutation status, as well as other biomarkers, may provide a rationale to select lung cancer patients for targeted treatment with seliciclib or other CDK inhibitors based on their biomarker profile.

APPRAISE Study Design

The trial's primary efficacy endpoint is progression free survival. Secondary endpoints include overall survival, response rate, response duration, safety and tolerability. The study employed a randomized discontinuation design. All patients received seliciclib for at least three treatment cycles. Patients who achieved stable disease after three cycles were randomized to continue on seliciclib or receive placebo with best supportive care. Patients in the placebo group whose disease progressed were given the option to cross-over and receive seliciclib treatment again. As a trial with a cross-over feature, APPRAISE is not suitable for a potential registration submission. At study inception it was estimated that 80 randomized patients, or approximately 50% of the sample size, would be required to detect a doubling in PFS to 4 months for the seliciclib arm versus 2 months for placebo, benchmarked on previously reported time to progression for the placebo arm in the erlotinib registration study as a 2nd or 3rd line NSCLC treatment. The statistical power of APPRAISE was 80% with a two-tailed alpha of 0.05.

IDRC Interim Analysis

Cyclacel stopped enrolment in APPRAISE after an independent data review committee (IDRC) completed a per protocol first interim analysis including data from 173 patients, of whom 45, or 26%, were randomized. The IDRC stated that there were no safety concerns that would warrant stopping the study and that over 75% of the patients received seliciclib as a 4th or 5th line treatment. The IDRC also stated that the study would probably not demonstrate an improvement in PFS as there was no trend favoring the seliciclib arm. However, as a definitive conclusion could not be reached on the drug's impact on survival because

of immature data and a low number of events or patient deaths, the IDRC recommended that the study be continued.

Study Termination

After analyzing the IDRC's conclusions, the observed randomization rate and weighing the financial implications of increasing the sample size to approximately double the originally budgeted number of patients in order to achieve the prespecified level of statistical significance, Cyclacel decided to stop enrolling new patients and continue with already enrolled patients in APPRAISE until the last patient completed follow-up.

About Non-Small Cell Lung Cancer

The American Cancer Society expects that in 2010 about 222,520 new cases of lung cancer will be diagnosed and more than 157,300 deaths will result from the disease in the United States. Average five-year survival for patients with the most severe stage (IIb/IV) of the disease is estimated at 5% or less. NSCLC accounts for about 85% to 90% of lung cancers. There are 3 subtypes of NSCLC based on the size, shape, and chemical composition of cancer cells: squamous cell (25%-30%), adenocarcinoma (40%) and large cell or undifferentiated (10%-15%) lung cancer.

Lung cancer is a major public health issue and a disease with a staggering burden on the health care system. It is by far the leading cause of cancer death in the United States among both men and women. More people die of lung cancer than of colon, breast, and prostate cancers combined. Lung cancer mainly occurs in older people and about two-thirds of patients diagnosed with lung cancer are aged 65 or older. The average age at the time of diagnosis is about 71.

About seliciclib

Seliciclib is an orally-available molecule that selectively inhibits multiple 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 evaluated to date in approximately 380 patients and is currently being evaluated in randomized Phase 2 trials in patients with previously treated lung cancer and nasopharyngeal cancer.

About CDKs and Cyclins

Cyclin-dependent kinases (CDKs) are a group of signaling molecules that play a direct role in the regulation and progression of the cell cycle. CDK activity is dependent on the availability of their regulatory subunits called cyclins. Production and destruction of cyclins are tightly regulated in coordination with cell cycle progression. Targeting CDK/cyclin macromolecular complexes is an attractive strategy for the design of novel anticancer drugs.

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. For example Cyclacel's seliciclib (CYC202, R-roscovitine), a novel, first-in-class, orally available CDK inhibitor, currently in Phase 2 clinical trials, selectively targets multiple CDK/cyclin complexes, 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, such as arthritis or asthma.

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. Three product candidates are in clinical development. Sapacitabine (CYC682), a cell cycle modulating nucleoside analog, will be entering Phase 3 development for the treatment of acute myeloid leukemia in the elderly under a Special Protocol Assessment agreement with the U.S. Food and Drug Administration, and is in Phase 2 studies for 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.

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