



Cyclacel Provides Update on Clinical Progress With Sapacitabine in Solid Tumors Including Activity in BRCA Mutation-Positive Patients

- Partial responses and stable disease observed in patients with lung cancer and also in patients with breast, pancreatic and ovarian cancer carrying BRCA mutations -
- Sapacitabine unique among nucleoside analogues because of its oral dosing and broad therapeutic window of activity in both solid tumors and hematological malignancies -

BERKELEY HEIGHTS, N.J., Dec. 7, 2011 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC) (Nasdaq:CYCCP) (Cyclacel or the Company) announced today interim topline data from ongoing clinical studies with sapacitabine in heavily pretreated patients with advanced solid tumors, including Phase 2 single-agent data in non-small cell lung cancer (NSCLC) and Phase 1 data in combination with Cyclacel's seliciclib in breast, ovarian, pancreatic and other cancers. Partial responses (PR) and stable disease were observed in both studies. In the Phase 1 trial responding patients were found to be carriers of BRCA mutations.

"We are encouraged by the anti-tumor activity against solid tumors by single agent sapacitabine and its combination with seliciclib," said Judy H. Chiao, M.D., Vice President, Clinical Development and Regulatory Affairs of Cyclacel. "The responses in BRCA-mutation positive patients with breast, pancreatic and ovarian cancers may be directly related to sapacitabine's enhanced activity against cancer cells that are deficient in the homologous recombination DNA repair (HRR) pathway. Accordingly, BRCA status could be a potential biomarker for identifying responders across multiple solid tumor types. The interim data warrant further investigation of sapacitabine's utility in solid tumors, as we continue to progress our SEAMLESS Phase 3 pivotal trial of sapacitabine in patients with front-line acute myeloid leukemia (AML)," continued Dr. Chiao.

Phase 1 study of oral sapacitabine and oral seliciclib in patients with advanced cancers

In the ongoing Phase 1, single-arm study of sapacitabine, a nucleoside analogue, and seliciclib, a CDK inhibitor, as an orally-administered combination regimen in patients with advanced solid tumors, 27 patients have been treated to date. The primary objective of the study is to determine the recommended Phase 2 dosing schedule of the sapacitabine and seliciclib combination, which has been achieved. Among 11 patients treated at the recommended Phase 2 doses, 2 patients with advanced pancreatic cancer and breast cancer, respectively, achieved PR and 1 patient with advanced ovarian cancer achieved stable disease. All 3 responders were reported by the investigator to be carriers of BRCA mutations. The number of treatment cycles administered ranges from 7 to 9 cycles. The breast and ovarian cancer patients remain on study.

Phase 2 study of oral sapacitabine in patients with NSCLC who have had at least one prior chemotherapy

In the ongoing lead-in, dose escalation portion of a multicenter, Phase 2 study of sapacitabine as a single agent in patients with NSCLC who have had at least one prior chemotherapy, 48 patients were treated with two dosing schedules, either twice daily or once a day.

In the twice daily schedule 15 patients were treated with escalating doses. The recommended Phase 2 dose was reached at 75 mg twice daily for 5 days per week for 2 weeks every 3 weeks. Among 12 patients treated at this recommended Phase 2 dose, 4 achieved stable disease. All 4 responders had at least 2 prior therapies and have been discontinued from the study. Responders received an average of 7 treatment cycles.

In the once daily schedule 33 patients were treated with escalating doses. Maximum tolerated dose has not been reached at the upper limit of the dosing range as per protocol. Patients are currently being entered into the 200 mg once daily dosing level for 5 days per week for 2 weeks every 3 weeks. Among 25 patients treated with daily doses ranging from 100 mg to 175 mg, 2 patients achieved PR and 10 stable disease. The two PR responders had 3 or 4 prior therapies, respectively, and one remains on study. Among the 10 stable disease responders, 9 had at least 2 prior therapies and 2 remain on study. Responders received an average of 10 treatment cycles.

"Advanced non-small cell lung cancer patients are living longer and living better as a result of the availability of effective sequential therapies. Novel therapies are needed to build on our recent therapeutic advances," said Philip D. Bonomi, M.D., the Alice Pirie Wirtz Professor of Medical Oncology at Rush University Medical Center, Chicago and chair of the study. "Sapacitabine appears to be well tolerated and has activity against NSCLC. Future clinical development should focus on identifying a biomarker for patient selection and comparison to available therapies commonly used in this patient population,"

continued Dr. Bonomi.

About sapacitabine

Sapacitabine (CYC682), an orally-available nucleoside analogue, is currently being evaluated in a registration-directed, Phase 3 trial in front-line elderly acute myeloid leukemia (AML), Phase 2 trials in patients with hematological malignancies, including myelodysplastic syndromes (MDS), chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL), and solid tumors and in a Phase 1 trial in combination with seliciclib. Sapacitabine acts through a novel DNA single-strand breaking mechanism, leading to production of DNA double strand breaks (DSBs) and/or checkpoint activation. Unrepaired DSBs cause cell death. Repair of sapacitabine-induced DSBs is dependent on the HRR pathway. Both sapacitabine and CNDAC, its major metabolite, have demonstrated potent anti-tumor activity in preclinical studies.

Over 350 patients have received sapacitabine in Phase 2 studies in AML, MDS, cutaneous T cell lymphoma (CTCL) and non-small cell lung cancer (NSCLC). Sapacitabine has been administered to approximately 170 patients in five Phase 1 studies with both hematological malignancies and solid tumors. In June 2009 at the Annual Meeting of the American Society of Hematology (ASH), Cyclacel reported data from a randomized Phase 2 study single agent study of sapacitabine including promising 1-year survival in elderly patients with AML aged 70 years or older. In June 2011 at the Annual Meeting of the American Society of Clinical Oncology (ASCO), Cyclacel reported data from a pilot Phase 1/2 study including promising 8-week mortality in elderly patients with AML aged 70 years or older receiving sapacitabine alternating with decitabine. The U.S. FDA and the European Medicines Agency have designated sapacitabine as an orphan drug for the treatment of both AML and MDS. Sapacitabine is part of Cyclacel's pipeline of small molecule drugs designed to target and stop uncontrolled cell division.

About seliciclib

Seliciclib is an orally-available CDK inhibitor molecule that selectively inhibits multiple enzyme targets, CDK2, CDK7 and CDK9, which are central to the process of cell division and cell cycle control. Seliciclib treatment has been reported to inhibit the two major DNA double-strand break (DSB) repair pathways, homologous recombination DNA repair (HRR) and non-homologous end joining (NHEJ), by reducing expression of components of each pathway (Federico, M., et al, Mol Cancer, 2010, 9, 208). Seliciclib has been evaluated to date in approximately 380 patients and is currently in randomized Phase 2 trials in patients with previously treated lung cancer and nasopharyngeal cancer.

About BRCA Genes and Mutations

BRCA1 and BRCA2, or breast cancer susceptibility genes, are tumor suppressor genes that help ensure the stability of DNA, the cell's genetic material, and help prevent uncontrolled cell growth. Genetic testing for BRCA-status is routinely available. BRCA mutation has been linked to predisposition to breast and ovarian cancer. According to the US National Cancer Institute, during her life time a woman has a 60% chance of developing breast cancer and 15-40% chance of developing ovarian cancer if she inherits a harmful BRCA mutation. These risks are 5 times and over 10 times more likely than for women without the mutation respectively. Risks are highest with a family history of multiple cases of breast cancer; cases of both breast and ovarian cancer; one or more family members with two primary cancers; Norwegian, Dutch, and Icelandic heritage; or Ashkenazi (Central and Eastern European) Jewish background.

Harmful BRCA1 mutations may additionally increase a woman's risk of developing triple-negative breast, cervical, uterine, pancreatic, and colon cancer. Harmful BRCA2 mutations may increase a woman's risk of pancreatic, stomach, gallbladder and bile duct cancer, and melanoma. Men with harmful BRCA1 mutations have an increased risk of male breast cancer and, possibly, of pancreatic, testicular, and early-onset prostate cancer. Harmful BRCA2 mutations may increase a man's risk of developing male breast, pancreatic, and prostate cancer.

About the homologous recombination DNA repair (HRR) pathway

DNA double strand breaks (DSBs) are considered the most lethal form of DNA damage. The two major DSB repair mechanisms are homologous recombination DNA repair (HRR) and the intrinsically error-prone non-homologous end joining (NHEJ). Loss of HRR function through mutation of HRR pathway components, such as BRCA1 and BRCA2, are associated with breast, ovarian, prostate and pancreatic cancers. The incidence of HRR deficiency (HRD or 'BRCAness') in many tumor types is reported to be significantly greater than that predicted by BRCA mutations alone. For example, gene mutation or altered protein levels of many HRR components (including BRCA1 and BRCA2) can contribute to HRR deficiency in up to 50% of epithelial ovarian cancers (Mukhopadhyay, A., et al, Clin Cancer Res, 2010, 16, 2344). Low protein expression of BRCA1 or BRCA2 was reported in 57% of NSCLC lung cancer samples (Lee, M., et al, Clin Cancer Res, 2007, 13, 832).

Depletion or inhibition of HRR components (including ATM, BRCA1, BRCA2, Rad 51 and XRCC3) greatly sensitize tumor cell lines to sapacitabine-induced cell death (Liu, X., et al, Blood, 2010, 116, 1737; Frame, S., et al, Proc. 101st AACR, 2010, Abs. 3502), outlining the potential clinical utility of sapacitabine in patients with HRD tumors.

About NSCLC

The American Cancer Society expects that in 2011 approximately 221,000 new cases of lung cancer will be diagnosed and nearly 157,000 deaths will result from the disease in the United States. Average five-year survival for patients with the most severe, advanced disease (Stage IIb/IV) 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.

Analyst & Institutional Investor Meeting

Cyclacel will host an Analyst and Institutional Investor meeting today, December 7, from 11:00 a.m. to 1:00 p.m. Eastern in New York City. During the meeting Cyclacel management will review the clinical development program for sapacitabine including the design of SEAMLESS, the Company's ongoing, registration-directed, Phase 3 trial being conducted under a Special Protocol Assessment (SPA) with the U.S. Food and Drug Administration (FDA). There will also be an expert overview of sapacitabine's mechanism of action and future approaches for clinical investigation, both as a single agent and in combinations, discussion of treatment alternatives for elderly patients with acute myeloid leukemia by expert hematologists and treatment alternatives for patients with non-small cell lung cancer (NSCLC) who progress on currently available therapies by a thoracic oncology expert.

The event will be webcast and may also be accessed by telephone. For the live and archived webcast, please visit the Corporate Presentations & Events page on the Cyclacel website at www.cyclacel.com. For accessing the event by telephone: US/Canada telecast: (877) 493-9121 / international telecast: (973) 582-2750. The telecast code is 32526199.

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 a Phase 3 trial being conducted under a SPA with the U.S. FDA for the front-line treatment of acute myeloid leukemia 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.

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 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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