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Combination Potential of Cyclacel's Sapacitabine and Seliciclib Reported at AACR

Sequential Treatment Showed Antitumor Activity in Patients With Incurable BRCA-Deficient Cancers

BERKELEY HEIGHTS, N.J., April 9, 2013 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC) (Nasdaq:CYCCP) ("Cyclacel" or the "Company") today announced updated data from an open label, single arm, Phase 1 escalation trial of the Company's two product candidates, sapacitabine, a nucleoside analogue, and seliciclib, a cyclin-dependent kinase (CDK) inhibitor, as an orally-administered sequential treatment regimen in heavily-pretreated patients with advanced solid tumors. Data were presented as an oral presentation during the 104th Annual Meeting of the American Association of Cancer Research (AACR) 2013 in Washington, D.C.

"We are encouraged by the responses seen with the sequential administration of sapacitabine and seliciclib in patients who carry a BRCA mutation," said Geoffrey Shapiro, M.D., Director, Early Drug Development Center, Dana-Farber Cancer Institute and Associate Professor, Department of Medicine, Harvard Medical School. "Our findings have shown that some patients who carried a BRCA mutation achieved durable partial responses and prolonged stable disease by this treatment regimen."

"The promising findings of Dr. Shapiro's work on the Phase 1 study show that sequential treatment with sapacitabine and seliciclib is tolerable and active," said Judy Chiao, M.D., Vice President Clinical Development and Regulatory Affairs of Cyclacel. "This clinical observation may be directly related to the drugs' mechanism of action acting on the ability of cancer cells to undergo DNA repair through the homologous recombination or HR pathway. If these preliminary findings are confirmed by further work, these drugs may provide an important treatment alternative for patients with BRCA-deficient cancers."

Based on these emerging results, the investigators continue to enroll an enriched population of patients who carried a BRCA mutation in the trial, in whom the combination has been most efficacious. Additional schedules of the combination therapy are under evaluation. BRCA mutation carrier status and homologous recombination defect (HRD) status may be potential biomarkers for response to this combination across multiple tumor types.

Results

To date, 38 patients with incurable solid tumors and adequate organ function have been enrolled in the Phase 1 study, 16 of them found to be BRCA mutation carriers. Sapacitabine was administered twice daily for seven days followed by seliciclib twice daily for three days. Four patients with BRCA-deficient pancreatic, breast or ovarian cancers had confirmed partial responses to the drug combination. Based on available follow-up to date, three patients are experiencing durable partial responses, with the longest lasting more than 78 weeks. Researchers observed stable disease of 12 weeks or more in eight additional patients, including two patients with ovarian and breast cancers who carried BRCA mutations and whose stable disease lasted 64 weeks and 21 weeks, respectively. The maximum tolerated doses were 50 mg sapacitabine twice daily and 1,200 mg seliciclib twice daily. Dose-limiting toxicities included reversible transaminase elevations and neutropenia. Adverse events were mild to moderate in intensity. Results of skin biopsies after treatment showed a 2.3-fold increase in DNA damage induced by sapacitabine, as measured by gamma-H2AX immunohistochemistry. Additional DNA damage occurred after treatment with seliciclib with a 0.58-fold further increase in gamma-H2AX staining.

About sapacitabine

Sapacitabine (CYC682), an orally-available nucleoside analogue, is being studied in SEAMLESS, an ongoing, Phase 3, registration-directed trial in elderly patients aged 70 years or older with newly diagnosed AML who are not candidates for or have refused induction chemotherapy. Sapacitabine is in Phase 2 trials in patients with hematological malignancies, including AML, myelodysplastic syndromes (MDS), cutaneous T-cell lymphoma (CTCL), chronic lymphocytic leukemia, small lymphocytic lymphoma, and also non-small cell lung cancer (NSCLC), and a Phase 1 trial with seliciclib in patients with advanced solid tumors. 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 homologous recombination (HR) DNA repair pathway. Both sapacitabine and CNDAC, its major metabolite, have demonstrated potent anti-tumor activity in preclinical studies.

Over 650 patients have received sapacitabine in clinical studies in patients with AML, MDS, CTCL, NSCLC, hematological malignancies and solid tumors. At the 2012 American Society of Hematology (ASH) Annual Meeting, data from the pilot study and lead-in phase of SEAMLESS showed promising response rate, overall survival and low 30-day and 60-day mortality in

elderly patients with AML aged 70 years or older receiving sapacitabine alternating with decitabine. Data, presented at The Eighth Annual Hematologic Malignancies 2012 Conference, from an ongoing, multicenter, Phase 2 randomized trial of single-agent oral sapacitabine capsules in older patients with intermediate-2 or high-risk myelodysplastic syndromes (MDS) after treatment failure of front-line hypomethylating agents, such as azacitidine and/or decitabine, showed sapacitabine nearly doubled expected median survival of elderly patients with MDS after front-line therapy failure. Results from a randomized Phase 2, single-agent study of sapacitabine, including promising 1-year survival in elderly patients with AML aged 70 years or older, were published in *The Lancet Oncology* in November 2012. In a Phase 1 study, sapacitabine, in combination with Cyclacel's seliciclib, showed antitumor activity in cancer patients found to be carriers of BRCA mutations. The 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 (HR) and non-homologous end joining (NHEJ), by reducing expression of components of each pathway. 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

Breast cancer susceptibility proteins BRCA1 and BRCA2 are tumor suppressors that ensure DNA stability and prevent uncontrolled cell growth in normal cells. BRCA gene mutations are common in breast and ovarian cancer, but other defects including suppression of BRCA1/2 expression by promoter hypermethylation can produce HR defects in these and other tumors, including NSCLC and AML. Although BRCA1/2 mutations are found in approximately 20% of high grade serous ovarian cancers, around 50% are reported to be HR-defective due to these and other modifications of HR components.

Genetic testing for BRCA status is routinely available and reimbursed by payors. 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 respectively than for women without the mutation. 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, or 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, colon, pancreatic and uterine cancer. Harmful BRCA2 mutations may increase a woman's risk of bile duct, gallbladder, stomach, pancreatic cancer and melanoma. Men with harmful BRCA1 mutations have an increased risk of male breast cancer and possibly pancreatic, early-onset prostate, and testicular cancer. Harmful BRCA2 mutations may increase a man's risk of developing male breast, pancreatic and prostate cancer.

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, Cyclacel's most advanced product candidate, is the subject of SEAMLESS, a Phase 3 trial being conducted under an SPA with the FDA as front-line treatment for acute myeloid leukemia (AML) in the elderly, and other studies for myelodysplastic syndromes (MDS), chronic lymphocytic leukemia (CLL) and solid tumors including breast, lung, ovarian and pancreatic cancer. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on 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 product candidates, 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 other filings we file 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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