June 4, 2012

Cyclacel Presents Phase 1 Data of Sequential Sapacitabine and Seliciclib in Advanced Solid Tumors at ASCO Annual Meeting

Partial Responses Observed in Patients With Heavily Pretreated Breast, Ovarian and Pancreatic Cancers Carrying BRCA Mutations

BERKELEY HEIGHTS, N.J., June 4, 2012 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC) (Nasdaq:CYCCP) (Cyclacel or the Company), today announced new 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 CDK inhibitor, as an orally-administered sequential treatment regimen in heavily-pretreated patients with advanced solid tumors. Data were presented as a poster during the 2012 American Society of Clinical Oncology (ASCO) Annual Meeting being held June 1-5, 2012, in Chicago, Illinois.

"We are encouraged by the anti-tumor activity against advanced solid tumors with the sequential administration of sapacitabine and seliciclib," said Geoffrey Shapiro, M.D., Director, Early Drug Development Center, Dana-Farber Cancer Institute and Associate Professor, Department of Medicine, Harvard Medical School. "The partial responses in BRCA-mutation carrier patients with breast, pancreatic and ovarian cancers may be directly related to the mechanism of action of the oral investigational agents, sapacitabine and seliciclib, and their ability to interfere with DNA repair of cancer cells. The data warrant further investigation of the sequential administration of sapacitabine and seliciclib in advanced solid tumor patients that are BRCA-mutation carriers. BRCA status could be a potential biomarker for identifying responders across multiple solid tumor types."

Results

To date 34 heavily-pretreated patients with advanced solid tumors have been treated with escalating doses. At ASCO, the maximum tolerated dose (MTD) for sequential administration of sapacitabine and seliciclib was reported as sapacitabine 50 mg twice daily followed by seliciclib 1200 mg twice daily. Pharmacodynamic effects of sapacitabine and seliciclib were observed in skin biopsies showing a 2.3-fold increase in H2AX staining post-sapacitabine (n=16; p=0.007) and a further 0.58-fold increase post-seliciclib (n=12; p=0.069).

Among 19 patients treated at the MTD, 3 partial responses (PR) occurred in patients with breast, ovarian and pancreatic cancer and 1 stable disease in a patient with ovarian cancer. Thirteen out of the 19 patients are BRCA-mutation carriers, of which 7 were poly ADP-ribose polymerase (PARP)-inhibitor naive and 6 had prior PARP inhibitor treatment. All four responding patients were PARP inhibitor naive BRCA-mutation carriers. Stable disease was achieved in 6 additional patients treated with the other dosing schedules. The number of treatment cycles administered ranges from 2 to over 15 cycles. The breast cancer patient who achieved PR remains on study with over 15 cycles and both ovarian cancer patients remain on study with over 2 and 12 cycles respectively.

Study Design

In the open label Phase 1, single-arm dose escalation study of sapacitabine, an orally-available nucleoside analogue, and seliciclib, an orally-available CDK inhibitor, were administered sequentially in patients with incurable advanced solid tumors unresponsive to conventional treatment or for which no effective therapy exists. Sapacitabine was dosed twice daily for 7 days (Day 1-7) and seliciclib twice daily for 3 days (Day 8-11). One treatment cycle is three weeks. At least 3 patients were enrolled at each escalating dose level. The first tumor imaging study is conducted after 2 cycles of treatment and every 3 cycles thereafter. The primary objective of the study is to determine the MTD and recommended Phase 2 dosing schedule of the sapacitabine and seliciclib administered sequentially. The secondary objective was to evaluate the antitumor activity of sequential treatment and to explore the pharmacodynamic effect of this treatment in skin and peripheral blood mononuclear cells.

The abstract can be accessed through the ASCO website, www.asco.org:

"Phase I study of sequential sapacitabine and seliciclib in patients with advanced solid tumors"

Date/Time: Monday June 4, 2012, 8:00 AM Central

Location: S Hall A2 (Poster Board 14C)

About sapacitabine

Sapacitabine (CYC682), an orally-available nucleoside analogue, is in the SEAMLESS, registration-directed, Phase 3 trial in elderly patients with newly diagnosed acute myeloid leukemia (AML), Phase 2 trials in patients with hematological malignancies, including myelodysplastic syndromes (MDS), cutaneous T-cell lymphoma (CTCL), chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL), and non-small cell lung cancer (NSCLC), a Phase 1 trial in combination with seliciclib in patients with advanced solid tumors and an investigator-led, Phase 2/3 study comparing sapacitabine to low dose cytarabine as front-line treatment of elderly patients with AML or high risk MDS unfit for intensive chemotherapy. 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 DNA repair (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, CTCL and NSCLC and over 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, 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 response rate, low 4-week and 8-week mortality in elderly patients with AML aged 70 years or older receiving sapacitabine alternating with decitabine. 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 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

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 HRR defects in these and other tumors, including NSCLC[1] and AML[2]. Although BRCA 1/2 mutations are found in approximately 20% of high grade serous ovarian cancers,[3] around 50% are reported to be HRR-defective due to these and other modifications of HRR components. [4]

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.[4] Low protein expression of BRCA1 or BRCA2 was reported in 57% of NSCLC lung cancer samples.[1] Depletion or inhibition of HRR components (including ATM, BRCA1, BRCA2, Rad 51 and XRCC3) greatly sensitize tumor cell lines to sapacitabine-induced cell death, [5] outlining the potential clinical utility of sapacitabine in patients with HRD tumors.

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 oral capsules is in the SEAMLESS Phase 3 trial being conducted under an SPA with the FDA as front-line treatment of acute myeloid leukemia (AML) in the elderly, Phase 2 studies for AML, myelodysplastic syndromes (MDS), solid tumors including lung cancer, chronic lymphocytic leukemia and an investigator-led, Phase 2/3 study comparing sapacitabine to low dose cytarabine as front-line treatment of elderly patients with AML or high risk MDS unfit for intensive chemotherapy. Cyclacel's pipeline includes seliciclib oral capsules 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.

[1] Lee et al. Clin Cancer Res 2007, 13, 832. Paul et al. J. Pathol. 2011, 224: 564.

[2] Scardocci et al. Brit. J. Cancer 2006, 96: 1108.

[3] The Cancer Genome Atlas Research Network. Nature 2011, 474: 609.

[4] Mukhopadhyay et al. Clin. Cancer Res. 2010, 16: 2344.

[5] Liu, X., et al, Blood, 2010, 116, 1737; Frame, S., et al, Proc. 101st AACR, 2010, Abs. 3502.

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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