Personalized Medicine and Combination Potential of Cyclacel's Sapacitabine Highlighted at AACR

Translational Findings Highlight Novel Mechanism of Sapacitabine in BRCA-Defective Cancers

BERKELEY HEIGHTS, N.J., April 4, 2012 (GLOBE NEWSWIRE) -- 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 disorders, announced today the presentation of three studies reporting translational research findings for sapacitabine during the 103rd Annual Meeting of the American Association of Cancer Research (AACR) 2012 in Chicago, IL.

Sapacitabine:

Abstract No. 5666: "DNA repair defects enhance tumor cell sensitivity to sapacitabine"

Cyclacel researchers reported that treatment with sapacitabine's major active metabolite, CNDAC, of colon cancer, ovarian cancer and non-small cell lung cancer (NSCLC) cell lines after depletion or inactivation of BRCA1 or BRCA2 led to higher rates of cell death versus control. In addition, CNDAC synergized with either PARP inhibitors or cisplatin in both NSCLC and ovarian cancer cell lines. Previous clinical studies have demonstrated that tumors of patients with germline BRCA mutations can be highly sensitive to DNA-damaging agents, such as PARP inhibitors or cisplatin. CNDAC was also shown to act synergistically with seliciclib, Cyclacel's orally available, clinical-stage, CDK inhibitor, in a large panel of NSCLC, as well as colon and ovarian cancer cell lines. In this study, seliciclib was shown to reduce BRCA1 and BRCA2 expression in cell lines and the resulting inhibition of homologous recombination DNA repair (HRR) activity may contribute to the observed synergy of the agents by reducing the cell's capacity to repair CNDAC-induced double strand breaks (DSBs).

The findings further support the potential for sapacitabine to be used alone or in combinations to treat HRR defective tumors, such as ATM or BRCA defective tumors. An investigator-sponsored Phase 2 study of sapacitabine in chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) with deletion 11q22-23 is ongoing at The University of Texas M. D. Anderson Cancer Center (Houston, TX). A Phase 1, study of sapacitabine in combination with seliciclib in patients with advanced solid tumors, is ongoing at the Dana Farber Cancer Institute. As previously reported, among 11 patients in this study treated at the recommended Phase 2 doses, 3 with advanced breast, ovarian and pancreatic cancer responded. All 3 patients were reported by the investigator to be BRCA defective. Updated results from the latter study will be reported at the American Society of Clinical Oncology (ASCO) annual meeting.

Abstract No. 5667: "Mechanism-based combinations of agents impacting the homologous recombination and nucleotide excision repair pathways"

Investigators led by William Plunkett, Ph.D., Professor and Deputy Chair, Department of Experimental Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX have previously established that CNDAC-induced DNA single strand breaks (SSBs) can be repaired, albeit inefficiently, by transcription-coupled nucleotide excision repair (TC-NER), and that CNDAC-induced DSBs are dependent on the HRR pathway for repair. At AACR, Prof. Plunkett's group described the sensitization of HRR-defective model cell lines to CNDAC when combined with other DNA damaging agents whose effects are repaired by the NER or HRR pathways. Combinations of CNDAC with bendamustine, cisplatin, a cyclophosphamide analogue, or oxaliplatin, each showed at least additive effects in cells with HRR or NER defects. Combinations of CNDAC with cisplatin or oxaliplatin were reported not to be synergistic in HRR- proficient cell models, expanding the clinical rationale for these combinations.

Abstract No. 4668: "Patient AML cells and AML cell lines are highly sensitive to CNDAC, the active form of sapacitabine"

In a comparison of CNDAC, cytarabine and mitoxantrone activity in AML cell lines, as well as in bone marrow and peripheral blood cells from AML patients, Dr Kent W. Christopherson, Ph.D., Associate Professor, Rush Medical College (Chicago, IL) and colleagues concluded that low dose CNDAC and also mitoxantrone exhibited improved activity and induction of cell death in AML cell lines and patient samples compared with cytarabine.

About sapacitabine

Sapacitabine (CYC682), an orally-available nucleoside analogue, is currently being evaluated in SEAMLESS, a 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) and in a Phase 1 trial in combination 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 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. 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, 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 BRCA

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 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 the SEAMLESS Phase 3 trial being conducted under an SPA with the FDA for the front-line treatment of AML 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.

[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.

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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