Cyclacel Announces Presentation of Phase 1 Data of Sapacitabine Regimen in Patients With BRCA Mutant Breast Cancer at AACR 2019

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-- Clinical benefit in PARP inhibitor-naïve patients supports ongoing Phase 1b/2 IST study of sapacitabine and olaparib combination in BRCA mutant breast cancer --

BERKELEY HEIGHTS, N.J., April 01, 2019 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC) (Nasdaq:CYCCP) (Cyclacel or the Company), a biopharmaceutical company developing innovative medicines based on cancer cell biology, announced Phase 1 clinical data from the company's DNA damage response program with an oral, sequential regimen of sapacitabine and seliciclib as a treatment in patients with BRCA mutant metastatic breast cancer. Data from the study was presented today at the 2019 American Association for Cancer Research (AACR) Annual Meeting and demonstrated that the regimen was safe and led to a clinical benefit rate of 30%. All eight PARP inhibitor naïve patients, half of the patients previously treated with platinum agents and one on previous PARP inhibitor responded. Progression on previous platinum or PARP inhibitors was associated with lack of benefit. Both sapacitabine and PARP inhibitors are more effective in cancer cells with BRCA mutations or other homologous recombination repair deficiencies. Based on these data, the investigators are enrolling a Phase 1b/2 study of sapacitabine in combination with a PARP inhibitor in PARP inhibitor-naïve patients with BRCA mutant breast cancer.

“We are encouraged by the durable responses and stable disease in PARP inhibitor-naïve patients with BRCA mutant metastatic breast cancer,” said Sara M. Tolaney, MD, MPH, Senior Physician, Director, Clinical Trials, Breast Oncology, Dana-Farber Cancer Institute, Boston and Principal Investigator of the study. “We are very excited about the ongoing evaluation of the combination of sapacitabine and the PARP inhibitor olaparib in PARP inhibitor-naïve patients with metastatic BRCA mutant breast cancer.”

Study Details

The study evaluated an oral, sequential regimen of sapacitabine, a nucleoside analog prodrug, and seliciclib, a 1st generation CDK2/9 inhibitor, in patients with metastatic breast cancer harboring BRCA1/2 mutations. Patients received seven days of sapacitabine followed by three days of seliciclib. Of 20 patients treated, six progressed on prior platinum therapy and seven on prior PARP inhibitor.

- Two patients achieved confirmed PR and four SD of at least 6 months duration for an overall clinical benefit rate of 30%. Of the two patients achieving PR, one progressed previously on platinum treatment and one had received no prior platinum or PARP inhibitor.
- Responses (PR or SD regardless of duration) occurred in 12 patients: 8/8 without prior progression on platinum or a PARP inhibitor (1 PR, 7 SDs), 3/6 patients who progressed on platinum (1 PR, 2 SDs), and 1/7 patients who progressed on a PARP inhibitor (1 SD).
- The most frequent grade 3 adverse events were neutropenia (15%), AST/ALT elevation (20%), and rash (10%). The only grade 4 adverse events were neutropenia in 2 patients.
- Progression on previous platinum agents or PARP inhibitors was associated with lack of benefit, putatively associated in some cases with BRCA reversion alterations.

The poster abstract at the 2019 AACR titled “Expansion cohort of Phase I study of oral sapacitabine and oral seliciclib in patients with metastatic breast cancer and *BRCA1/2* mutations” is available at (https://www.abstractsonline.com/pp8/#!/6812/presentation/9865).

Both sapacitabine and PARP inhibitors are more effective in cancer cells with BRCA mutations or other homologous recombination repair deficiencies and combine synergistically in preclinical models. As a result of these findings, a concomitant administration regimen of sapacitabine and olaparib PARP inhibitor is now being evaluated in an investigator-sponsored trial in approximately 64 patients with PARP inhibitor-naïve, metastatic HER2-negative breast cancer with germline BRCA1/2 mutation (https://clinicaltrials.gov/ct2/show/NCT03641755).

CYC065 AACR Poster Details

Preclinical data for Cyclacel’s CYC065 CDK2/9 inhibitor will also be presented at the 2019 AACR in a poster titled “Next generation CDK2/9 inhibitor CYC065 triggers anaphase catastrophe in diverse aneuploid cancers and markedly inhibits growth and metastasis.” Researchers from MD Anderson Cancer Center and Frederick National Laboratory for Cancer Research report that CDK2 inhibition preferentially targets aneuploid cancer cells and that CYC065 induces cell death in diverse cancer cell lines and animal models, irrespective of KRAS mutation status. This CYC065 activity is demonstrated to be a consequence of CDK2/9 inhibition, resulting in anaphase catastrophe, Mcl-1 down-regulation and suppression of proteins that regulate metastasis (https://www.abstractsonline.com/pp8/#!/6812/presentation/5901).

About sapacitabine

Sapacitabine (CYC682), an orally-available nucleoside analogue, acts through a novel DNA single-strand breaking (SSB) 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 repair (HRR) pathway. Both sapacitabine and its major metabolite, CNDAC, have demonstrated potent anti-tumor activity in preclinical studies. Sapacitabine has been studied in the SEAMLESS Phase 3 study in elderly patients with AML who were

unfit or refused intensive induction chemotherapy, Phase 2 studies in patients with myelodysplastic syndromes (MDS), cutaneous T cell lymphoma (CTCL) and non-small cell lung cancer (NSCLC), Phase 1/2 studies in sequential administration with seliciclib and concomitant administration with olaparib in patients with BRCA mutant cancers.

About CYC065

CYC065 is a highly-selective, 2nd generation inhibitor of cyclin dependent kinases (CDK) 2 and 9. CYC065 is in an ongoing Phase 1, first-in-human study in patients with advanced solid tumors. In this study target engagement and durable suppression of the Mcl-1 biomarker were observed after a single dose of CYC065 at the recommended phase 2 dose. CYC065 is also being evaluated in a Phase 1 study in combination with venetoclax in patients with relapsed/refractory CLL. Preclinical data suggest that CYC065 may benefit patients with adult and pediatric hematological malignancies such as CLL, AML, ALL, B-cell lymphomas, multiple myeloma and certain cyclin E-addicted or MYC-amplified solid tumors, including HER2+ breast cancer, uterine serous carcinoma and neuroblastoma.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel Pharmaceuticals is a clinical-stage biopharmaceutical company using its expertise in cell cycle, transcriptional regulation and DNA damage response biology in cancer cells to develop innovative medicines. The transcriptional regulation program is evaluating CYC065, a CDK inhibitor, in patients with advanced solid cancers and in combination with venetoclax in patients with advanced hematological malignancies, including CLL and AML. The DNA damage response program is evaluating a sequential regimen of sapacitabine and seliciclib, a CDK inhibitor, in BRCA positive patients with advanced solid cancers and a concomitant regimen of sapacitabine and olaparib, a PARP inhibitor, in BRCA positive patients with breast cancer. CYC140, a PLK inhibitor, is in a Phase 1 first-in-human study in patients with advanced leukemias. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a pipeline of novel drug candidates. For additional information, please visit www.cyclacel.com.

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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