Cyclacel Pharmaceuticals Announces First Patient Treated in a Phase 1/2 Study of Sapacitabine and Venetoclax in Relapsed or Refractory AML or MDS Patients

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BERKELEY HEIGHTS, N.J., July 22, 2019 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC, Nasdaq:CYCCP) ("Cyclacel" or the "Company"), a biopharmaceutical company developing innovative medicines based on cancer biology, announced treatment of the first patient in a Phase 1/2 study evaluating the safety and effectiveness of oral sapacitabine, a nucleoside analogue, in combination with oral venetoclax, a BCL2 inhibitor, in patients with relapsed or refractory AML or MDS.

“Sapacitabine is an oral nucleoside analogue that is active in AML and MDS that is relapsed or refractory to prior therapy such as cytarabine or hypomethylating agents. Combining sapacitabine with venetoclax may offer an effective, oral treatment regimen for patients who have failed front-line therapy,” said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. “We are excited to follow up on the hypothesis generating results from our SEAMLESS study with a novel, orally-administered combination of sapacitabine and venetoclax given concomitantly. This study is the fourth protocol to open as part of our strategic alliance with The University of Texas MD Anderson Cancer Center with the objective of evaluating three Cyclacel drug candidates in patients with hematological malignancies.”

The Phase 1/2 study (NCT01211457) is intended to enroll up to 40 patients with relapsed or refractory AML or MDS with the objective of determining the safety and efficacy of the combination. Secondary objectives include duration of response, CR, CRp, PR, or major HI, transfusion requirements, number of hospitalized days and overall survival.

Preclinical Data on Combinations of Sapacitabine and BCL2 Inhibitors in AML
Oral sapacitabine is metabolized to CNDAC which causes single stranded breaks in the DNA of growing cells, resulting in double stranded breaks and cancer cell death when DNA is not repaired. The combination effect of CNDAC and the BCL2 inhibitor ABT-737 was studied *in vitro* in AML cellular models. A synergistic increase in induction of apoptosis of cancer cells was observed when MV4-11 AML cells were treated simultaneously with CNDAC and the BCL2 inhibitor. Treatment with cytarabine and BCL2 inhibitors resulted in similar synergy (Frame S et al., 14th European Hematology Association Congress, 2009).

About Venetoclax in AML
The FDA granted accelerated approval of oral venetoclax tablets (ABT-199) in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed AML in adults who are aged 75 years or older or have comorbidities that preclude use of intensive induction chemotherapy (Venetoclax Prescribing Information PDF). The approval is based on two non-randomized, open-label clinical studies (NCT02203773 and NCT02287233) in which complete remission rates of 54%, 37%, and 21% were observed for decitabine, azacitidine or low-dose cytarabine combinations with venetoclax, respectively. Azacitidine, cytarabine and decitabine are nucleoside analogues administered by intravenous or subcutaneous injection. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

About Sapacitabine Clinical Studies in AML/MDS
Sapacitabine is active in relapsed or refractory AML or MDS. In a Phase 1 dose escalation trial of single agent sapacitabine 11 patients with relapsed or refractory AML or MDS responded (4 CR, 2 CRp, 5 CRi). In a Phase 2 single agent study of 63 patients with MDS who had progressed or relapsed after decitabine or azacitidine 9 patients responded (2 CR, 2 CRp, 5 major HI).

Sapacitabine as a single agent is active in previously untreated AML. In a randomized Phase 2 study of sapacitabine of 105 patients aged 70 years or older with untreated or first relapse AML, 28 out of 86 previously untreated patients responded (9 CR, 1 CRp, 3 CRi, 2 PR and 13 HI). In a Pilot/Lead-in study of sapacitabine alternating with decitabine 46 newly diagnosed AML patients aged 70 or older were administered the same regimen as the experimental arm in SEAMLESS. Nineteen patients responded (10 CR, 4 PR and 5 HI).

The randomized, open-label, Phase 3 SEAMLESS study enrolled 482 patients, aged 70 or older, with newly diagnosed AML who were not candidates for or refused intensive therapy. Patients were stratified by peripheral baseline white blood cell count (WBC), antecedent hematologic disease (AHD) and bone marrow blasts and randomized 1:1 to receive either intravenous decitabine administered in alternating cycles with oral sapacitabine or intravenous decitabine alone. The primary endpoint of demonstrating statistically significant improvement in overall survival (OS) was not met. A higher CR rate, a secondary endpoint, was observed on the decitabine-sapacitabine arm (17% versus 11%). Other endpoints and safety were similar between the arms. Stratified subgroup analyses showed that in a large subgroup of patients (n=319) with low WBC a trend towards improved OS (HR=0.84 [0.66, 1.06], nominal p=0.14) and a significantly higher CR rate (21% versus 9%, nominal p=0.0017) were observed favoring decitabine-sapacitabine. The opposite effect was observed in the high WBC subgroup.

About Cyclacel Pharmaceuticals, Inc.
Cyclacel Pharmaceuticals is a clinical-stage biopharmaceutical company using cell cycle, transcriptional regulation and DNA damage response biology to develop innovative medicines based on cancer biology. Cyclacel's transcriptional regulation program is evaluating CYC065, a CDK 2/9 inhibitor, in relapsed, refractory CLL and AML patients. The recommended phase 2 dose of CYC065 has been determined in advanced solid tumors and an oral formulation is ready for evaluation. The DNA damage response program is evaluating a sequential regimen of sapacitabine and seliciclib, a CDK inhibitor, in patients with BRCA positive, advanced solid cancers. The anti-mitotic program is evaluating CYC140, a PLK1 inhibitor in AML patients. 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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