Cyclacel Announces Dosing of First Patient in Phase 1/2 Study of Oral Cyc140 in Patients With Advanced Solid Tumors and Lymphomas

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- CYC140, a Potent and Selective PLK1 Inhibitor to Be Evaluated as a Single Agent Across Multiple Solid Tumor and Lymphoma Types in Streamlined, Registration-Directed Study -

BERKELEY HEIGHTS, N.J., April 19, 2022 (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 dosing of the first patient in the Company's streamlined, multi-cohort Phase 1/2 study of oral CYC140 in patients with advanced solid tumors and lymphomas.

"With the start of this trial, Cyclacel is now enrolling patients across three registration-directed studies to evaluate safety and efficacy of our two lead drug candidates, fadraciclib and CYC140, for the treatment of various solid tumors, lymphomas and leukemias," said Spiro Rombotis, Cyclacel's President and Chief Executive Officer. "As with the fadraciclib studies, the Phase 1 stage of this trial will determine an optimal dosing regimen of oral CYC140 and provide insights with respect to safety, tolerability and clinical activity. The Phase 2 stage will enroll up to seven cohorts by histology and also a basket cohort. We expect initial data from this trial during the first half of 2023. We also look forward to reporting initial data from the fadraciclib clinical study in advanced solid tumors during the first half of 2022."

"Overexpression of PLK1 is known to be important in many types of cancer," said Mark Kirschbaum M.D., Senior Vice President and Chief Medical Officer. "We have optimized the properties of CYC140 to fit its apoptosis-driven mechanism, including a short half-life and differentiated structural and biological properties, compared to other PLK1 inhibitors in development. In preclinical studies CYC140 has demonstrated promising activity in multiple solid tumors and leukemias. The study has initially opened at City of Hope and MD Anderson Cancer Center with more sites to join later on. In addition to patients with certain PLK1 over-expressing tumors, the study will enroll patients with MYC amplified and KRAS-mutated cancers in which PLK1 inhibition may be effective. If successful, CYC140 may provide new treatment options for patients with advanced solid tumors or lymphomas."

"As a key regulator of cell mitosis, PLK1 plays an integral role in prolonged survival of many cancer cells, including p53(-) and KRAS mutant genotypes," said Miguel Villalona-Calero, M.D., co-leader of the Development Cancer Therapeutics Program and Professor, Department of Medical Oncology & Therapeutics Research at City of Hope, one of the largest cancer research and treatment organizations in the United States. "The totality of preclinical evidence suggests that CYC140 has significant potency and single-agent activity. This novel agent warrants clinical investigation across multiple solid tumors and lymphomas."

The Phase 1/2 registration-directed trial, designated CYC140-101, uses a streamlined design and will first determine in a dose escalation stage the recommended Phase 2 dose (RP2D) for single-agent CYC140. Once RP2D has been established, the trial will immediately enter into proof-of-concept, cohort stage, using a Simon 2-stage design. In this stage CYC140 will be administered to patients in up to 7 mechanistically-relevant cohorts including patients with bladder, breast, colorectal (including KRAS mutant), hepatocellular and biliary tract, and lung cancers (both small cell and non-small cell), as well as lymphomas. An additional basket cohort will enroll patients with biomarkers relevant to the drug's mechanism, including MYC amplified tumors. The protocol allows for expansion of individual cohorts based on response which may allow acceleration of the clinical development and registration plan for CYC140.

About Polo-like kinase 1 (PLK1) and CYC140

Polo-like kinase 1 (PLK1) is a serine/threonine kinase that plays a central role in cell division or mitosis. PLK1 is an important regulator of the DNA damage cell cycle checkpoint, mitotic entry and exit, spindle formation and cytokinesis, or cell separation into daughter cells. Cancer cells in general, and in particular KRAS mutated and p53(-) cells, are very sensitive to PLK1 depletion. In contrast normal cells with intact cell cycle checkpoints are less sensitive. Pharmacological inhibition of PLK1 in cancer cells blocks proliferation by prolonged mitotic arrest and induces onset of apoptotic death of such cells.

CYC140 is a novel, small molecule, selective and potent PLK1 inhibitor. It has demonstrated impressive efficacy in human tumor xenografts at nontoxic doses. Cyclacel's translational biology program supports the development of CYC140 in solid tumors and leukemias. CYC140 was designed with improved pharmaceutical properties over earlier clinical-stage PLK inhibitors. Recent data suggest that PLK1 inhibition may be effective in KRAS-mutated metastatic colorectal cancer. PLK1 overexpression correlates with poor patient prognosis in several tumors, including esophageal, gastric, leukemia, lung, ovarian, and squamous cell cancers, as well as MYC-amplified cancers.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel is a clinical-stage, biopharmaceutical company developing innovative cancer medicines based on cell cycle, transcriptional regulation and mitosis biology. The transcriptional regulation program is evaluating fadraciclib, a CDK2/9 inhibitor, and the anti-mitotic program CYC140, a PLK1 inhibitor, in patients with both solid tumors and hematological malignancies. Cyclacel's strategy is to build a diversified biopharmaceutical business based on a pipeline of novel drug candidates addressing oncology and hematology indications. 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, the potential effects of the COVID-19 pandemic, 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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