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

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-Next-Generation CDK2/9 Inhibitor Fadraciclib to Be Evaluated Across Multiple Solid Tumor and Lymphoma Types in Streamlined Registration-Directed Study-

BERKELEY HEIGHTS, N.J., July 13, 2021 (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 multi-cohort Phase 1/2 study of oral fadraciclib in patients with advanced solid tumors.

"Advancing oral fadraciclib, our lead candidate, into this Phase 1/2 trial, represents a key clinical milestone and corporate objective for our team," said Spiro Rombotis, Cyclacel's President and Chief Executive Officer. "This is the first of four streamlined Phase 1/2 studies we plan to open over the coming months as we expand our clinical programs to evaluate the potential of fadraciclib and CYC140, our oral PLK1 inhibitor, first in solid tumors and lymphomas and then in leukemias. We look forward to providing periodic updates on our clinical progress and data from these open-label studies."

"We are pleased to have dosed the first patient in this study and are delighted by the enthusiasm and strong interest from current and prospective investigators," said Mark Kirschbaum M.D., Senior Vice President & Chief Medical Officer of Cyclacel. "The study has initially opened at City of Hope and MD Anderson Cancer Center with more sites to join later on. We are building an excellent network of participating institutions both in terms of clinical and scientific expertise. In previous studies with single agent, intravenous fadraciclib we have observed durable suppression of MCL1 and other mechanistically-related proteins, including cyclin E and MYC, at tolerated doses. In addition, a patient with MCL1 amplified, advanced endometrial cancer experienced deep PR and 100% shrinkage of her target tumor lesions on single agent fadraciclib treatment. We are excited to begin mid-stage development of fadraciclib with the objective of registration-enabling outcomes and offering a new treatment option for patients with advanced solid tumors or lymphomas."

"Based upon prior clinical activity shown to date, further exploration of this novel CDK2/9 inhibitor is warranted across a number of solid tumor histologies," said Miguel Villalona-Calero, M.D., co-leader of the Developmental Cancer Therapeutics Program and Professor, Department of Medical Oncology & Therapeutics Research at the City of Hope, a world-renowned, independent research and treatment center for cancer, diabetes and other life-threatening diseases. "We look forward to enrolling patients in this trial and evaluating the potential treatment benefit of this experimental therapy both as a single agent and in combinations."

The Phase 1/2 registration-directed trial (CYC065-101) uses a streamlined design and will first determine the recommended Phase 2 dose (RP2D) for single-agent, oral fadraciclib. Once RP2D has been established, the trial will immediately enter into proof-of-concept, cohort stage, using a Simon 2-stage design, where single agent fadraciclib will be administered to patients in up to eight cohorts defined by histology thought to be sensitive to the drug's mechanism of action and informed by the clinical activity of fadraciclib in previous studies. The cohorts will include patients with breast cancer (selected for metastatic, hormone receptor positive, HER-2 negative, post-CDK4/6 inhibitor; HER-2 refractory; or triple negative), colorectal (including KRAS mutant), endometrial, hepatocellular and ovarian cancers, as well as certain lymphomas. An additional basket cohort will enroll patients with biomarkers relevant to the drug's mechanism, including MCL1, MYC and cyclin E, regardless of histology. The protocol allows for expansion of a cohort based on response which may allow acceleration of the clinical development and registration plan for fadraciclib.

About Cyclin-Dependent Kinases and Fadraciclib

Cyclin-dependent kinases (CDKs) are critical for cell cycle control and transcriptional regulation. Dysregulated CDKs have been linked to the cancer hallmarks of uncontrolled proliferation and increased cancer cell survival. Fadraciclib, a next generation CDK inhibitor, is a highly selective, potent, orally and intravenously available, inhibitor of CDK2 and CDK9. CDK2 drives cell cycle transitions and CDK9 regulates transcription of genes through phosphorylation of the carboxy-terminal domain (CTD) of RNA polymerase II (RNAP II). By inhibiting CDK2 and CDK9 fadraciclib causes apoptotic death of cancer cells at sub-micromolar concentrations.

Preclinical data suggest that fadraciclib may benefit patients with certain cyclin E-addicted or MYC-amplified solid tumors, including certain forms of breast cancer, neuroblastoma, ovarian cancer, uterine serous carcinoma and adult and pediatric hematological malignancies, such as ALL, AML, B-cell lymphoma, CLL, and multiple myeloma. Similarly to FDA-approved CDK4/6 inhibitors, fadraciclib may be useful in combination with other anticancer drugs, including HER2 inhibitors, such as trastuzumab, or BCL2 inhibitors, such as venetoclax.

In a prior Phase 1 open-label trial (CYC065-01), patients with high copy CCNE (cyclin E), MYC or MCL1 showed sensitivity to intravenously-administered, single-agent fadraciclib. A heavily pretreated patient with MCL1 amplified endometrial cancer achieved a radiographically confirmed partial response (PR) after a month and a half on fadraciclib. This patient continues on therapy for almost two years and reduction in her target tumor lesions has reached 100%. An additional patient with cyclin E amplified ovarian cancer achieved stable disease with 29% shrinkage in her target tumor lesions.

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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