# Cyclacel Pharmaceuticals Reports New Clinical Data from Ongoing, Phase 2 Study of Oral Fadraciclib at the 2024 EORTC-NCI-AACR Symposium

October 23, 2024

**- Interim data for fadraciclib monotherapy in patients with advanced solid tumors preselected for CDKN2A and/or CDKN2B abnormalities -**

BERKELEY HEIGHTS, N.J., Oct. 23, 2024 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (NASDAQ: CYCC, NASDAQ: CYCCP; "Cyclacel" or the "Company"), a biopharmaceutical company developing innovative cancer medicines, today announced that initial safety and efficacy data from twelve patients with advanced solid tumors enrolled in the Phase 2 part of the 065-101 clinical study of fadraciclib, or “fadra”, as a single agent was presented as a poster at the 2024 EORTC-NCI-AACR 36$^{th}$ Symposium on Molecular Targets and Cancer Therapeutics (“Triple Meeting”), in Barcelona, Spain (October 23-25, 2024). The patients were enrolled in the biomarker-enriched, Cohort 8 of the proof of concept study and were preselected for CDKN2A and/or CDKN2B abnormalities.

“We are encouraged by the interim data of cohorts 6 and 8 in our Phase 2 study of fadra,” said Spiro Rombotis, President and Chief Executive Officer. “Although the data in Cohort 8 is immature with ongoing patients still to have a first scan and being followed up, we continue to see good tolerability and signals of efficacy in patients with CDKN2A/B abnormalities that have had their first scan and follow-up evaluation. We are grateful to our investigators, the patients and their families for their support of this important study.”

**Interim Phase 2 Data**

Fadraciclib was well tolerated in Cohort 8. Most common drug-related adverse events included diarrhea, nausea, vomiting and were similar to those seen at this dose in Phase 1. There were no Grade 3 or higher treatment-emergent adverse events in the Phase 2 study this far, consistent with the Phase 1 data. The majority of patients (12/14) had ECOG performance status of 1 and median number of prior therapies was 3.

In Cohort 8, four patients had pancreatic cancer, and one each cholangiocarcinoma, duodenal, melanoma, cervical, laryngeal, ovarian, squamous cell cancer with unknown primary (CUP) and thymus cancer. Out of six patients evaluable for efficacy, two achieved stable disease: a melanoma patient whose treatment duration was 125 days and a squamous cell CUP patient who achieved 11% tumor shrinkage in the sum of all lesions on first scan with treatment duration of over 85 days (ongoing). Two additional patients with ovarian and laryngeal cancer are ongoing but have not had their first scan yet.

The most common molecular characteristics of Cohort 8 patients were loss of function or deletion of CDKN2A and/or CDKN2B tumor suppressor genes. Other pharmacogenomic observations included CDKN2A/B, KRAS and/or TP53 mutations.

**Study Design**

Two Phase 2 dose expansion cohorts in the 065-101 study were initiated. Cohort 8 prospectively enrolled 12 patients with known CDKNA/B genetic alterations between April and September 2024. The rationale was to further evaluate observations of clinical activity in Phase 1 patients with known CDNK2A or CDKN2B genetic alterations. Cohort 6 is enrolling patients with T-cell Lymphoma with two patients treated so far. The rationale was to further evaluate observations of partial response (PR) in 2/3 Phase 1 patients with T-cell lymphoma. Certain T-Cell lymphomas are known to harbor CDNK2A genetic alterations. All patients were treated with oral fadraciclib 100mg BID, M-F, week 1-4 in 28-day cycles which was the Recommended Phase 2 dose (RP2D).

The primary objectives of the 065-101 study in the Dose Escalation stage are to determine maximum tolerated dose (MTD) and/or RP2D and in the Phase 2, Proof of Concept stage to evaluate preliminary efficacy of fadraciclib as measured by overall response rate (ORR). The secondary objectives in Dose Escalation are to assess safety and tolerability, pharmacokinetics, and ORR, while in Phase 2, Proof of Concept, to assess safety and tolerability, evaluate disease control rate (DCR), duration of response (DOR), progression free survival (PFS), and overall survival (OS). The study is utilizing a Simon two-stage optimal design to evaluate clinical activity. Exploratory objectives include investigation of clinical pharmacodynamics (PD) and pharmacogenomics (PGx).

Further information from the poster is available at: Link to poster

**About Fadraciclib**

Fadraciclib is a highly selective CDK2 ($IC_{50}$=5 nM) and CDK9 ($IC_{50}$=26 nM) inhibitor causing anaphase mitotic catastrophe and apoptotic death of cancer cells at sub-micromolar concentrations. Retrospective review of the dose escalation portion of Phase 1 studies suggested clinical activity in patients with known CDNK2A or CDKN2B genetic alterations. In a Phase 1 study of intravenous fadraciclib monotherapy (065-01) a heavily pretreated endometrial cancer patient with CDNK2A, CDKN2B and PRMT5 loss achieved confirmed complete response (CR).

In the Phase 1 oral fadraciclib monotherapy study (065-101), 7/38 treated patients were found to have known CDKN2A/B genetic alterations, of which 6 were evaluable for efficacy. A PTCL patient with CDKN2A P114L mutation reported a partial response (PR). A squamous cell NSCLC patient with CDKN2B loss reported stable disease (SD) and 22% reduction in tumor volume in the sum of all target lesions. A metastatic, testicular Leydig germ cell cancer patient with CDKN2A, CDKN2B and MTAP loss reported 12% reduction in tumor volume in the sum of all target lesions. The overall

response rate (ORR) was 17% (1/6) and the disease control rate (DCR) was 100% (6/6).

**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 plogosertib, 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, among other things, statements related to the efficacy and safety profile of fadraciclib in an incomplete clinical trial, Cyclacel's future plans and prospects, Cyclacel's anticipated cash runway and the planned timing of data results and continued development of fadraciclib. Factors that may cause actual results to differ materially include market and other conditions, 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 risks associated with reliance on collaborative partners for further clinical trials, development and commercialization of product candidates and Cyclacel's ability to regain and maintain compliance with Nasdaq's continued listing requirements, although no assurance to that effect can be given. 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.

**Contact**

Company: Paul McBarron, (908) 517-7330, IR@cyclacel.com