Cyclacel Reports Preliminary Data From Its Phase 1/2 Clinical Trial of Oral Fadraciclib in Patients With Solid Tumors and Lymphoma at ENA 2022

October 26, 2022

Daily dosing of fadraciclib was well tolerated; single agent activity observed across multiple tumor types including 2 PRs in T-cell lymphoma patients

BERKELEY HEIGHTS, N.J., Oct. 26, 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, reported today preliminary dose escalation data from its ongoing 065-101 Phase 1/2 clinical study of oral fadraciclib, a cyclin dependent kinase (CDK) 2/9 inhibitor, for the treatment of patients with advanced solid tumors and lymphoma. Of the 18 patients evaluable for response, two out of three T cell lymphoma patients treated achieved partial response and 11 out of 15 patients with various solid tumors achieved stable disease. No dose-limiting toxicities have been observed thus far. Data were presented during a poster presentation at the 34th EORTC-NCI-AACR (ENA) Symposium on Molecular Targets and Cancer Therapeutics, which is being held on October 26-28, in Barcelona, Spain.

“The findings reported in today’s poster presentation show that oral fadraciclib dosed daily as a single-agent is relatively well tolerated and active in a challenging Phase 1 population," said Mark Kirschbaum, M.D., Senior Vice President and Chief Medical Officer of Cyclacel. "We are encouraged by the antitumor activity observed up to dose level 5 and are now recruiting patients at the sixth dose level of 150mg administered twice daily four out of four weeks. We believe fadraciclib can be safely dosed at these levels that are predicted in target engagement studies to inhibit CDK2 and CDK9. We plan to optimize the dosing schedule and maximize target coverage. Once we determine the recommended Phase 2 dose (RP2D) we can advance into Phase 2 proof of concept stage.”

“We are excited by the progress of oral fadraciclib in the 065-101 study. We believe that the combination of daily dosing and dual targeting of both CDK2 and CDK9 at efficacious doses without dose limiting toxicities could potentially result in a competitive product profile for oral fadraciclib,” said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. “In our second program with oral CYC140, a differentiated PLK1 inhibitor, we have likewise observed early signs of anticancer activity as a single agent in a Phase 1/2 study in patients with solid tumors and lymphomas. We look forward to reviewing fadraciclib and CYC140 preclinical and clinical data at our upcoming Research & Development Day on Monday, October 31.”

Summary of findings:

- As of September 30, 2022, 18 evaluable patients were treated with oral fadraciclib as a single agent. Patients were heavily pretreated with various tumor types, including breast, cholangiocarcinoma, gynecological, head & neck, hepatocellular carcinoma, T-cell lymphoma, pancreatic and prostate cancers.
- Fadraciclib was well tolerated while escalating from dose levels 1 to 5 (up to and including 100mg BID, Monday-Friday, on week 1-4 in 28-day cycles).
- No treatment-related Serious Adverse Events (SAEs), or SUSAR, or Dose-Limiting Toxicities (DLTs) were reported.
- Initial anticancer activity was as follows:
  - Two partial responses (PRs) have been observed in T-cell lymphoma patients, one with CTCL and one with angioimmunoblastic PTCL.
  - Four patients (with cervical, endometrial, HCC, and ovarian cancers) achieved target lesion reductions.
  - A patient with pancreatic cancer achieved stable disease for 5 cycles.
- Plasma concentration of fadraciclib is dose proportional, crossing the target engagement threshold level for CDK2 and CDK9 with increasing duration at dose levels 4 and 5 after repeated oral administration.
- Enrollment continues at dose level 6 (150mg BID, Monday-Friday, on week 1-4 in 28-day cycles).

The ongoing trial is an open-label, multicenter, Phase 1/2 study in adult subjects with advanced solid tumors and lymphoma. Phase 1 explores both schedule and escalating doses of oral fadraciclib as a single-agent in 28-day cycles with a primary objective of identifying maximum tolerated dose (MTD) and/or recommended Phase 2 dose (RP2D). Once RP2D is established, Phase 2 will enroll patients in seven specific tumor-type groups and a basket cohort, utilizing a Simon two-stage optimal design to evaluate clinical activity. The primary objective of Phase 2 is to achieve proof of concept and determine preliminary efficacy by overall response rate. Safety, pharmacokinetics (PK) and efficacy will be investigated for all subjects. Exploratory objectives are to investigate clinical pharmacodynamics (PD) and pharmacogenomics (PGx) of fadraciclib.

Title:	A Phase 1/2, Open-label, Multi-center Study to Investigate the Safety, Pharmacokinetics, and Efficacy of Fadraciclib

	(CYC065), an Oral CDK2/9 Inhibitor, in Subjects with Advanced Solid Tumors and Lymphoma
Abstract No:	50
Date/Time:	Wednesday, October 26, 2022, 12:00 – 20:00 CEST
Location:	Exhibition Hall
Session Topic:	Molecular Targeted Agents 1
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The poster can be accessed via the Company's website at www.cyclacel.com

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. Fadraciclib is being tested in a Phase 1/2 trial for the treatment of advanced solid tumors and lymphoma (065-101; NCT#04983810) and a Phase 1/2 trial for the treatment of hematological malignancies (065-102; NCT#05168904).

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, subsequently achieved CR and continues on treatment with fadraciclib for over three years. 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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