Cyclacel Presents Phase 1 Clinical Data Showing Safety, Anti-Tumor Activity and Good Oral Bioavailability of Fadraciclib in Patients With Advanced Solid Tumors at the EORTC-NCI-AACR Symposium 2020

October 26, 2020

A patient with MCL1 amplified endometrial cancer achieved partial response (PR) with 92% target tumor shrinkage on single-agent fadraciclib

BERKELEY HEIGHTS, N.J., Oct. 26, 2020 (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 clinical data demonstrating safety, anti-tumor activity and good oral bioavailability of Cyclacel's CDK2/9 inhibitor fadraciclib in patients with advanced solid tumors. The data were presented at an oral presentation at the Plenary Session of the 32nd EORTC-NCI-AACR (ENA) Symposium 2020 held virtually on October 24-25, 2020.

"In addition to good oral bioavailability, we are pleased to report a durable PR with continuing shrinkage of target lesions reaching 92% in a patient with MCL1 amplified endometrial cancer. Four other patients achieved stable disease," said Spiro Rombotis, Chief Executive Officer of Cyclacel. “The data support clinical development of fadraciclib in our planned Phase 1b/2a study in advanced endometrial and ovarian cancer and CDK4/6 inhibitor resistant breast cancer. Along with safety and efficacy the study will evaluate cyclin E, MCL1 and/or MYC biomarkers which are relevant to fadraciclib’s mechanism of action. In addition to our studies in solid tumors we are encouraged by evidence of antileukemic activity in our studies of fadraciclib in hematological malignancies. We are looking forward to reporting updated data from ongoing studies of fadraciclib and CYC140, our selective PLK1 inhibitor.”

Presentation Highlights: Phase 1 Safety, Pharmacokinetic and Pharmacodynamic Study of Fadraciclib (CYC065), a Cyclin-Dependent Kinase Inhibitor, in Patients with Advanced Cancers

Twenty-four heavily pretreated patients with various advanced solid tumors, including ovarian, endometrial/uterine, breast, and fallopian cancer, were enrolled in part 2 with intravenous (i.v.) administration and five patients in part 3 with oral administration of this ongoing Phase 1, open label, dose escalation study.

Primary Objective:

- Determine MTD and recommended phase 2 dose (RP2D)

Secondary Objectives:

- Evaluate pharmacokinetics
- Assess pharmacodynamic markers

Design:

- Administration schedule of flat dosing schedule of single-agent fadraciclib (CYC065) given either by 1-hour infusion or orally on days 1, 2, 8 and 9 every 3 weeks

Safety:

- The trial advanced through four dose levels (DL) with a range of 90mg to 213mg, administered as a 1-hour intravenous infusion on days 1, 2, 8 and 9 and two DL with a range of 75mg to 150mg as an orally administered formulation on days 1, 2, 8 and 9; both in 3-week cycles.
- Eleven patients were treated at DL4 (213 mg). Dose limiting toxicity at DL4 was reversible neutropenia. The 160mg dose level is being expanded to define RP2D.
- No major or unexpected toxicities were observed.

Efficacy (n=24, i.v. formulation only):

- One confirmed partial response and two stable disease (SD) out of 11 patients on 213mg i.v. formulation:
  - PR after a month and a half on fadraciclib: MCL1-amplified endometrial cancer; failed seven lines of prior therapy; continuing treatment for more than 16 months with 92% reduction in target tumor lesions.
  - SD: Cyclin E amplified ovarian cancer with 29% tumor shrinkage after four months.
  - SD: Fallopian tube adenocarcinoma (undetermined protein level).

Pharmacokinetics (PK):

- Increases in fadraciclib exposure with increasing dosing levels.
- High oral bioavailability and comparable PK profile after oral or 1 hour-infusion administration.

The presentation was part of the 32nd EORTC-NCI-AACR (ENA) Symposium 2020 and is available on the "Presentation and Events" section of the Cyclacel website at https://investor.cyclacel.com/events-and-presentations/events.

Presentation Details:

Title: Phase 1 safety, pharmacokinetic and pharmacodynamic study of fadraciclib (CYC065), a cyclin dependent kinase inhibitor, in patients with advanced cancers (NCT02552953)
Session Title: Late Breaking and Best Proffered Papers
Session Date and Time: Saturday 24 October 15:05 CET
Presentation Number: ORAL-002

About Cyclin-Dependent Kinases and Fadraciclib

Cyclin-dependent kinases (CDKs) are critical for cell cycle regulation and transcriptional elongation. Dysregulated CDKs have been linked to the cancer hallmarks of uncontrolled proliferation and increased survival. Fadraciclib is a potent orally and intravenously available inhibitor of CDK2 and CDK9.

Fadraciclib is in an ongoing Phase 1, first-in-human study in patients with advanced solid tumors. In part 1 of the study, target engagement and durable suppression of the MCL1 biomarker were observed after a single dose of fadraciclib by 4-hour infusion. Tumor shrinkage and stable disease were observed in five patients with cyclin E, MCL1 or MYC amplified advanced cancers treated at the RP2D. In the ongoing part 2 of the study evaluating a more intensive dosing regimen, 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 more than a year and reduction in her target tumor lesions has reached 92%. An additional patient with cyclin E amplified ovarian cancer achieved stable disease with 29% tumor shrinkage. Part 3 is investigating an oral dose formulation.

Fadraciclib is also being evaluated in Phase 1 combination studies with venetoclax in relapsed or refractory CLL and in relapsed or refractory AML or MDS. Similarly to FDA-approved CDK4/6 inhibitors, fadraciclib may be most useful in combination with other anticancer drugs, including BCL2 inhibitors, such as venetoclax, or HER2 inhibitors, such as trastuzumab. Preclinical data suggest that fadraciclib may benefit patients with adult and pediatric hematological malignancies such as CLL, AML, ALL, B-cell lymphomas, multiple myeloma and certain cyclin E-addicted or MYC-amplified solid tumors, including certain forms of breast cancer, neuroblastoma, ovarian cancer and uterine serous carcinoma.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel Pharmaceuticals is a clinical-stage biopharmaceutical company developing innovative cancer medicines based on cell cycle, transcriptional regulation, and DNA damage response biology. The transcriptional regulation program is evaluating fadraciclib as a single-agent in solid tumors and in combination with venetoclax in patients with relapsed or refractory AML/MDS and CLL. The anti-mitotic program is evaluating CYC140, a PLK1 inhibitor, in advanced leukemias/MDS patients. The DNA damage response program is evaluating an oral combination of sapacitabine and venetoclax in patients with relapsed or refractory AML/MDS. An investigator-sponsored trial (IST) is evaluating an oral combination of sapacitabine and olaparib in patients with BRCA mutant breast cancer. Cyclacel's strategy is to build a diversified biopharmaceutical business focused on 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 Cyclacel files with the Securities and Exchange Commission which are available at www.sec.gov. Such forward-looking statements are current only as of the date they are made, and Cyclacel assumes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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