Cyclacel Pharmaceuticals Reports Fadraciclib Phase 1 Data Suggesting Efficacy Against Tumors With CDKN2A, CDKN2B and MTAP Deletions

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- Patient Pharmacodynamic Data Show Decrease in CDKN2A, CDKN2B, and PRMT5 Protein Levels -

- A Squamous Non-Small Cell Lung Cancer Patient with CDKN2B Deletion Achieved Marked Tumor Shrinkage after One Cycle -

- Retrospective Analysis Identified CDKN2A, CDKN2B and/or MTAP Deletions in Four Patients Previously Dosed with Fadra Achieving Responses or Stable Disease -

- Forthcoming Phase 2 Study to Further Evaluate Fadra Efficacy -

BERKELEY HEIGHTS, N.J., Dec. 18, 2023 (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 today interim results from its Phase 1, dose escalation 065-101 study of fadraciclib ("fadra") in patients with advanced solid tumors and lymphoma.

"As we approach the end of the year we are excited to report that fadra continues to demonstrate anticancer activity as a single agent based on interim data reviewed to date from our 065-101 study," said Spiro Rombotis, President and Chief Executive Officer. "The data suggest tumor sensitivity in patients with one or more of three abnormalities, CDKN2A, CDKN2B and/or MTAP deletion subject to confirmation in further studies. We believe there is great unmet medical need and industry interest in the cancer patient populations identified by these abnormalities, which are closely located on chromosome 9 and are often co-deleted. The Phase 2 part of 065-101 is designed to evaluate fadra safety and efficacy in cohorts defined by histology and/or next generation sequencing (NGS). In addition, our plogosertib dose escalation study is progressing well. Based on interim data reviewed to date, good tolerability and anticancer activity of plogosertib as a single agent have been observed in multiple patients with various solid tumors."

"We are excited to see shrinkage of 22% in the sum of all target lesions after one cycle of fadra monotherapy in a squamous non-small cell lung cancer (NSCLC) patient with CDKN2B deletion refractory to standard of care chemotherapy and immunotherapy," said Mark Kirschbaum, M.D., Chief Medical Officer. "After retrospectively analyzing a subset of previously treated Phase 1 patients who experienced clinical benefit with fadra, we found four patients with CDKN2A, CDKN2B and/or MTAP deletions. These included an endometrial cancer patient who achieved CR and over three years of treatment in a previous study of fadra monotherapy and was found to have all three abnormalities. Further, pharmacodynamic data from patient biospecimens at dose levels 5 and 6A suggest that CDKN2A, CDKN2B, and PRMT5 protein levels are transiently decreased over the 4 to 8 hour half-life of the fadra dose, which we believe makes the tumor sensitive to CDK2 inhibition by fadra. Although these hypothesis-generating data are limited and cannot be generalized, we believe that patients with these types of tumors should be evaluated in the ongoing and subsequent studies."

065-101 Study of Oral Fadraciclib
In the ongoing 065-101 study of oral fadra, a CDK2/9 inhibitor, a total of 29 patients have been treated as monotherapy. The study is enrolling unselected, all comer patients with advanced solid tumors and lymphoma. Six patients have been treated on dose level 6A (125mg twice daily for 5 days per week, 4 out of 4 weeks). The sixth patient on dose level 6A with pancreatic cancer and CDKN2A deletion enrolled on the study experienced dose-limiting toxicity (DLT) of hyperglycemia. The patient, who has a diabetic profile history and was on metformin treatment, remains on study as blood glucose level was managed. A previous patient on dose level 6A with a pre-diabetic profile had DLT of hyperglycemia which also resolved rapidly.

The previous dose level 5 (100mg twice daily for 5 days per week, 4 out of 4 weeks) on this schedule accrued six patients with no DLT and per protocol is safe for continued development.

Dose level 6B (150mg once daily for 7 days per week, 4 out of 4 weeks) continues accrual with two patients treated, which are ongoing at three and five cycles of treatment.

To date single agent activity, including CR, PR and SD, has been observed in patients with advanced endometrial, squamous NSCLC lung cancer and T-cell lymphoma. Encouraging signals of activity were observed in patients with advanced cervical, hepatocellular, ovarian and pancreatic cancers.

The Company believes that fadra's inhibition of CDK2 and CDK9 may be superior to inhibiting either CDK2 or CDK9 alone. Fadra tablets can be given orally with repeat dosing which has led to transient suppression of anti-apoptosis proteins with generally good tolerability and no Grade 3 or higher hematological toxicity in the first cycle.

The Phase 2 part of the 065-101 study is designed to further evaluate fadra safety and efficacy in up to 8 cohorts defined by histology and/or NGS. The study is powered to demonstrate response in the molecular subtype suggested by the Phase 1 data and others that may be sensitive.

CDKN2A, CDKN2B, MTAP deletions
CDKN2A gene deletions occur in over 40% of several solid tumors, including glioma, head and neck, pancreatic, esophageal, lung (incl. squamous), bladder, melanoma, and others. CDKN2B deletions occur in over 30% of several solid tumors, including bladder, glioma, pancreatic, esophageal, lung (incl. squamous), head and neck, melanoma, and others. MTAP deletions occur in over 25% of several solid tumors, including glioma, mesothelioma, pancreatic, bladder, esophageal and others.[1] MTAP deletion confers dependency on the PRMT5 enzyme in cancer cells which was identified as a synthetic lethal target for MTAP deleted cancers.

140-101 Phase 1 Study of Oral Plogosertib
In the 140-101 study of oral plogosertib, PLK1 inhibitor, as monotherapy, patients are being recruited at dose level 5. The anticancer activity observed at low levels of continuous exposure may be due to plogosertib's novel epigenetic mechanism.

To date, 15 patients have been recruited at five dose escalation levels. Encouraging signals of activity were observed in five patients with advanced biliary, ovarian, NSCLC and other cancers. The Company expects to announce details of plogosertib's differentiated, epigenetic mechanism and biomarkers which may identify patients with sensitive tumors, after preclinical studies at collaborating laboratories are completed.

About Cyclacel Pharmaceuticals, Inc.
Cyclacel is a clinical-stage, biopharmaceutical company developing innovative cancer medicines based on cell cycle, transcriptional regulation, epigenetics and mitosis biology. The transcriptional regulation program is evaluating fadraciclib, a CDK2/9 inhibitor, and the epigenetic/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 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, without limitation: interim results of a clinical trial are not necessarily indicative of final results and one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data and as more patient data becomes available, including the risk that unconfirmed responses may not ultimately result in confirmed responses to treatment after follow-up evaluations; 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; potential delays in the commencement, enrollment and completion of clinical trials; 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, as amended, 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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[1] www.cbioportal.org.