Cyclacel Announces Presentation of Phase 1 Clinical Data for CDK Inhibitor CYC065 at AACR 2018 Annual Meeting

April 16, 2018

Durable Mcl-1 suppression of at least 24 hours after a single dose of CYC065

BERKELEY HEIGHTS, N.J., April 16, 2018 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (NASDAQ:CYCC) (NASDAQ:CYCCP) ("Cyclacel" or the "Company"), a biopharmaceutical company developing oral therapies that target the various phases of cell cycle control for the treatment of cancer and other serious disorders, today announced results from a Phase 1 safety, pharmacokinetic and pharmacodynamic study of CYC065, the Company's novel cyclin dependent kinase, or CDK2/9 inhibitor, in patients with advanced cancers. Data were reported at an oral presentation on Sunday, April 15, at 3:35 PM CT at the American Association for Cancer Research (AACR) Annual Meeting held in Chicago, IL.

"Our findings show that CYC065 is effective in suppressing the cancer survival protein Mcl-1 in peripheral blood for at least 24 hours," said Geoffrey Shapiro, MD, PhD, Director, Early Drug Development Center, Dana-Faber Cancer Institute and Professor of Medicine, Harvard Medical School, Boston, MA. "The durable target inhibition achieved at the recommended Phase 2 dose provides a rationale to further evaluate this novel agent in Mcl-1, MYC or cyclin E amplified tumors."

"The clinical data support biomarker-driven clinical development of CYC065 in selected patient populations," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "In addition, the durable suppression of the Mcl-1 survival protein presents an exciting opportunity to combine CYC065 with other agents targeting the apoptosis pathway, such as venetoclax. We will soon be starting a clinical study testing CYC065 in combination with venetoclax in patients with relapsed/refractory chronic lymphocytic leukemia."

Details of the Phase 1 study

The objective of part 1 of the Phase 1 dose escalating, monotherapy, first-in-human study was to evaluate safety, pharmacokinetics (PK), pharmacodynamics (PD) and identify RP2D. Certain features of the trial are as follows:

- 26 heavily treated patients with various advanced solid tumors were enrolled;
- The trial advanced through seven DL cohorts with a range of 8 to 288 mg/m^2/day, administered as a 4-hour intravenous infusion once every 3 weeks;
- Dose limiting toxicity at DL7 was reversible neutropenia, febrile neutropenia and diarrhea;
- Thirteen patients were treated at DL6;
- PK parameters have demonstrated increases in CYC065 exposure with increasing dosing levels;
- A biologically effective dose was established from analysis of surrogate tissue, supporting a RP2D of 192 mg/m^2/day;
- Consistent Mcl-1 suppression over 24 hours after a single dose was observed in 11 out of 13 patients at DL6;
- Clinical response was reported in patients with Mcl-1 (ovarian cancer, parotid acinic cell carcinoma), MYC (uterine carcinosarcoma, ovarian cancer) and cyclin E (ovarian cancer) amplified tumors; and
- Stable disease was best response, longest response approximately one year.

Having successfully achieved the objectives of part 1 of the study, part 2 has been initiated to evaluate CYC065 in a more intensive schedule for 2 days per week for 2 weeks of a three week cycle. Part 2 will enroll patients with advanced cancers to evaluate efficacy in Mcl-1, MYC and cyclin E amplified cancers. The Company also plans to initiate a clinical study in patients with chronic lymphocytic leukemia in combination with venetoclax, a Bcl-2 inhibitor, where durable suppression of Mcl-1 may be beneficial.

Details of the oral presentation are as follows:

Title:	Phase I safety, pharmacokinetic and pharmacodynamic study of CYC065, a cyclin dependent kinase inhibitor, in patients with advanced cancers (NCT02552953)
Presenter/Authors:	K. T. Do, N. Chau, A. Wolanski, B. Beardslee, F. Hassinger, K. Bhushan, S. Pruitt-Thompson, A. Scotton, S. Frame, D. I. Zheleva, D. Blake, J. Chiao, G. I. Shapiro.
Category:	Phase I Adult Clinical Trials
Session:	CTMS01 - New Treatment Approaches for Breast and Ovarian Cancer
Abstract #:	CT037
Location:	Room N427 - McCormick Place North (Level 4)
Date and Time:	Sunday, April 15, 2018, 3:35 PM

About CYC065

CYC065, a second generation CDK2/9 inhibitor, is being evaluated in a first-in-human, Phase 1 trial in patients with advanced solid tumors. It is mechanistically similar but has higher dose potency, *in vitro* and *in vivo*, and improved properties compared to seliciclib, a first generation CDK inhibitor. Similarly to FDA approved CDK4/6 inhibitors, CYC065 may be most useful in combination with other anticancer drugs, including Bcl-2

inhibitors, such as venetoclax, or HER2 inhibitors, such as trastuzumab. Preclinical data show that CYC065 may benefit patients with adult and pediatric hematological malignancies, including acute myeloid leukemias (AML), acute lymphocytic leukemias (ALL), and in particular those with MLL rearrangements, chronic lymphocytic leukemias (CLL), B-cell lymphomas, multiple myelomas, and certain solid tumors, including breast and uterine cancers, and neuroblastomas.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel Pharmaceuticals is a clinical-stage biopharmaceutical company using cell cycle, transcriptional regulation and DNA damage response biology to develop innovative, targeted medicines for cancer and other proliferative diseases. Cyclacel's transcriptional regulation program is evaluating CYC065, a CDK inhibitor, in patients with advanced cancers. The DNA damage response program is evaluating a sequential regimen of sapacitabine and seliciclib, a CDK inhibitor, in patients with BRCA positive, advanced solid cancers. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in 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 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.

Contacts

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