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## **Cyclacel's CDK Inhibitor CYC065 Causes Anaphase Catastrophe, a Novel Cancer-Specific Mechanism of Action, in Research Published in JNCI**

### **CYC065 found effective against lung cancer cell lines including those with KRAS mutations**

BERKELEY HEIGHTS, N.J., March 07, 2017 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC) (Nasdaq:CYCCP) ("Cyclacel" or the "Company"), today announced the publication of a peer-reviewed journal article featuring the company's cyclin dependent kinase 2/9 (CDK2/9) inhibitors. In an article published in the *Journal of National Cancer Institute* (JNCI), preclinical data demonstrated that both Cyclacel's CYC065, a second-generation, clinical stage, CDK2/9 inhibitor, and CCT68127, a pre-clinical stage CDK2/9 inhibitor, demonstrated prominent antitumor activity against lung cancer through anaphase catastrophe, a novel, cancer specific mechanism of action.

The *Journal of National Cancer Institute* article entitled, "Next-Generation CDK2/9 Inhibitors and Anaphase Catastrophe in Lung Cancer," demonstrates that CYC065 and CCT68127 cause multipolar anaphase and apoptosis in lung cancer cells with supernumerary centrosomes, known as anaphase catastrophe. This novel mechanism of action offers an innovative approach to combat aneuploid cancer cells which contain abnormal numbers of chromosomes. Aneuploidy is a hallmark for cancer development and occurs in virtually every cancer, but is particularly found in lung cancer. Approximately 90 percent of cancer cells in solid tumors and blood cancer are aneuploid.

The article further reported that inhibition of CDK2 was the key mechanism of action and, as a consequence, lung cancer cells underwent apoptosis or cell suicide by induction of a novel mechanism called anaphase catastrophe. Similarly to a previous report on seliciclib (Cyclacel's first generation CDK inhibitor), lung cancer cells with mutant KRAS were particularly sensitive to CYC065 and CCT68127. Combination of CCT68127 with the MEK inhibitor, trametinib, was synergistic. An efficacy study in syngeneic cancer models of lung cancer with mutant KRAS demonstrated tumor growth inhibitory effect and a significant decrease of circulating tumor cells.

#### **Citation:**

Kawakami M, Lisa, Mustachio M, Rodriguez-Canales J, Mino B, Roszik J, Tong P, Wang J, J. Lee J, Myung JH, Heymach JV, Johnson FM, Hong S, Zheng L, Hu S, Villalobos PA, Behrens C, Wistuba I, Freemantle S, Liu X, Dmitrovsky E. Next-Generation CDK2/9 Inhibitors and Anaphase Catastrophe in Lung Cancer. *J Natl Cancer Inst* (2017) 109(6): djw297.

#### **About CYC065**

Cyclacel's second generation CDK2/9 inhibitor, CYC065, is being evaluated in an ongoing, first-in-human, Phase 1 trial in patients with advanced solid tumors. In addition to determining safety and recommended dosing for Phase 2, the study aims to investigate CYC065's effects on the Mcl-1 biomarker, which is implicated in the evolution of resistance in cancer. Evidence of target engagement with prolonged Mcl-1 suppression in peripheral blood cells was observed in patient samples from the study, as well as decreases in kinase substrate phosphorylation and increases in PARP cleavage, which were consistent with the Company's preclinical data. CYC065 is mechanistically similar but has much higher dose potency, *in vitro* and *in vivo*, and improved metabolic stability than seliciclib, Cyclacel's first generation CDK inhibitor. Similar to palbociclib, the first CDK inhibitor approved by FDA in 2015, CYC065 may be most useful as a therapy for patients with both liquid and solid tumors in combination with other anticancer agents, including Bcl-2 antagonists, such as venetoclax, or HER2 inhibitors, such as trastuzumab.

#### **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 DNA damage response program is evaluating a sequential regimen of sapacitabine and seliciclib, a CDK inhibitor, in patients with BRCA positive, advanced solid cancers. The transcriptional regulation program is evaluating CYC065, a CDK inhibitor, in patients with advanced cancers. Cyclacel is analyzing stratified and exploratory subgroups from a Phase 3 study of sapacitabine in elderly patients with AML. 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](http://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](http://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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### Contacts

#### Company:

Paul McBarron, (908) 517-7330, [pmcbarron@cyclacel.com](mailto:pmcbarron@cyclacel.com)

#### Investor Relations:

Russo Partners LLC, Alexander Fudukidis, (646) 942-5632, [alex.fudukidis@russopartnersllc.com](mailto:alex.fudukidis@russopartnersllc.com)