November 23, 2015

CYC065, Cyclacel's Novel CDK2/9 Inhibitor, Prolongs Survival in MYCN-Addicted Neuroblastoma Models

In Vitro and In Vivo Preclinical Data to be Presented at the Neuroblastoma UK Annual Meeting

BERKELEY HEIGHTS, N.J., Nov. 23, 2015 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (Nasdaq:CYCC) (Nasdaq:CYCCP) ("Cyclacel" or the "Company"), today announced the presentation of preclinical data demonstrating that CYC065, a highly-selective, second-generation cyclin dependent kinase (CDK) 2/9 inhibitor prolongs survival in *MYCN*-addicted neuroblastoma models. The *in vitro* and *in vivo* preclinical data will be presented at the 4th Neuroblastoma Symposium, November 26-27, 2015 in Newcastle Upon Tyne, United Kingdom.

"MYC activates a major genetic pathway in cancer that is very difficult to target directly," said Spiro Rombotis, Cyclacel's President and Chief Executive Officer. "CYC065 treatment of MYC-addicted neuroblastoma via CDK2/cyclin E inhibition offers a novel approach to target this critical cancer mechanism. Tumor regression or improved survival is seldom seen in animal models of cancers addicted to MYC proteins, such as *MYCN*. We are encouraged by the CYC065 data as they add to the growing evidence of the value of CDK inhibition as an innovative approach to treat cancer. Previous data demonstrated that CDK2/9 inhibitors target key molecular features of cancers with poor prognosis, such as cyclin E amplification/overexpression, MLL rearrangements and MYC-amplification/overexpression. We have recently initiated a first-in-human, Phase 1 trial of CYC065 in patients with advanced solid tumors."

The study evaluated the ability of two Cyclacel CDK2/9 inhibitors, CYC065 and CCT68127, to inhibit cell proliferation and induce apoptosis of neuroblastoma cells *in vitro* and *in vivo*. *In vivo* efficacy was evaluated in subcutaneous xenograft models of both *MYCN*-amplified and non-amplified neuroblastoma cells and the Th-*MYCN* genetically-engineered mouse model of neuroblastoma. The study showed that neuroblastoma cell lines with *MYCN* amplification and high *MYCN* expression levels were sensitive to both CDK2/9 inhibitors. CYC065 and CCT68127 depleted *MYCN* protein in a time- and dose-dependent manner, blocked neuroblastoma cell proliferation and induced apoptosis. Both CYC065 and CCT68127 resulted in significantly reduced tumor burdens and prolonged survival in *MYCN*-addicted neuroblastoma models *in vivo*.

Presentation details:

Presentation title: Orally available small molecule CDK inhibitors CYC065 and CCT68127 prolong survival in *MYCN*-addicted neuroblastoma models.

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Location: 4th Neuroblastoma Society Symposium 2015, 26 — 27 November, Newcastle, UK

About *MYCN*

The *MYCN* gene encodes a transcription factor that is expressed in fetal brain and neural crest and is critical for normal development of brain and nerve. *MYCN* is over-expressed in a number of different types of cancer, most notably neuroblastoma, but also including rhabdomyosarcoma, medulloblastoma, astrocytoma, Wilms' tumor, and small cell lung cancer. Amplification of the *MYCN* oncogene is the most common genomic alteration in aggressive neuroblastomas and is associated with poor clinical outcome. No drugs that directly target *MYCN* are available prompting the investigation of indirect approaches such as exploitation of a synthetic lethal relationship between *MYCN* amplification/overexpression and inhibition of CDK2.

About Neuroblastoma

According to the American Cancer Society, neuroblastoma is the most common cancer in infants less than one year old and it accounts for about six percent of all pediatric cancers or about 700 cases per year. The disease kills one in every seven children diagnosed with it. There are no approved treatments. The presented study demonstrated that CYC065 and CCT68127 target *MYCN*, and have potent *in vitro* and *in vivo* anti-tumor activities, suggesting therapeutic potential in neuroblastoma with amplification of *MYCN* oncogene.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel is a biopharmaceutical company developing oral therapies that target the various phases of cell cycle control for the treatment of cancer and other serious diseases. Sapacitabine, Cyclacel's most advanced product candidate, is the subject of SEAMLESS, a Phase 3 trial, which has completed enrollment and is being conducted under an SPA with the FDA

as front-line treatment for acute myeloid leukemia (AML) in the elderly, and other indications including myelodysplastic syndromes (MDS). Cyclacel's pipeline includes an oral regimen of seliciclib in combination with sapacitabine in a Phase 1 study of patients with Homologous Recombination (HR) repair-deficient breast, ovarian and pancreatic cancers, including BRCA positive tumors, and CYC065, a novel CDK2/9 inhibitor in a Phase 1 study of patients with solid tumors and potential utility in both hematological malignancies and solid tumors. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a development pipeline of novel drug candidates. Please visit www.cyclacel.com for more information.

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.

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