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First Patient Dosed in IST of CDK Inhibitor Seliciclib in Cushing's Disease, a Serious Endocrine Disorder

- Unique Dual Action Through Inhibition of Cyclin E and ACTH Production in Pituitary Tumors -

BERKELEY HEIGHTS, N.J., July 2, 2015 (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 that the first patient has been dosed in an investigator sponsored trial (IST) of the Company's oral cyclin dependent kinase (CDK) inhibitor seliciclib in Cushing's disease (CD)[1]. Clinicians at Cedars-Sinai, Los Angeles, were awarded a grant from The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to evaluate seliciclib, a CDK2/9 inhibitor currently in clinical development to treat certain cancers, as a potential therapy for CD.

"Cushing's disease is a serious debilitating endocrine disorder with limited treatment options for patients," said Shlomo Melmed, M.D., Director of the Burns and Allen Research Institute, Principal Investigator and Dean of the Medical Faculty at Cedars-Sinai, Los Angeles. "We believe that seliciclib is unique among clinical stage CDK inhibitors in its potential effectiveness to treat this disease. Its mechanism of action has a dual effect as it impacts tumor growth by decreasing the levels and activity of cyclin E, as well as inhibiting ACTH production. If our trial with seliciclib proves successful, it could lead to dramatically improved treatment outcomes for patients with Cushing's disease."

CD is an endocrine disorder caused by adrenocorticotropin (ACTH)-producing pituitary tumors, often leading to obesity, diabetes, hypertension, osteoporosis and increased risk of death if inadequately controlled. Cell cycle dysregulation is a common feature of pituitary tumors, including upregulation of cyclin E, specifically seen in tumors of the corticotroph lineage, such as in CD. Dr. Melmed and Dr. Ning-Ai Liu have previously published preclinical proof-of-concept data showing that seliciclib is uniquely effective amongst CDK inhibitors in resolving the disease, with dual effects on pituitary growth and ACTH production[2].

The trial is a Phase 2 proof-of-concept, open-label, single arm study to assess the safety and efficacy of seliciclib in CD. Sixteen patients with *de novo*, persistent or recurrent CD will receive seliciclib for 4 weeks prior to standard-of-care treatment. The primary objective is to establish the efficacy of seliciclib on normalizing urinary free cortisol levels in patients with CD.

About Cushing's disease

CD is a rare endocrine, orphan disorder with estimated US prevalence of approximately 20,000. It is the most common cause of endogenous hypercortisolism, which predisposes patients to central obesity, diabetes, hypertension, osteoporosis and substantially increases their risk of infection, thrombosis and psychiatric disorders. If inadequately controlled, CD is fatal with mortality rate four-fold-higher than that of age- and sex-matched controls and median survival of 4.6 years. The leading cause of death in CD is cardiovascular disease. CD remains an unmet medical need despite available therapies.

About seliciclib and its mechanism of action in Cushing's disease

Seliciclib, an orally-available CDK2/9 inhibitor, has been evaluated to date in approximately 450 patients and is currently being explored in combination with Cyclacel's orally-available sapacitabine in patients with solid tumors.

Seliciclib has been shown in preclinical models to be uniquely effective amongst other CDK inhibitors. Seliciclib was subsequently shown, in mouse corticotroph tumor cells *in vitro,* to cause cell cycle arrest, accompanied by decreases in cyclin E levels, increased p27Kip1, p57Kip2 and p21Cip1 expression, and reduced Thr821 phosphorylation of the retinoblastoma (Rb) protein. Rb is reportedly a site phosphorylated by CDK2. In addition, ACTH concentrations in cell supernatant were also decreased by seliciclib, suggesting a dual impact of the compound on corticotroph tumorigenesis. *In vivo*, oral administration of seliciclib led to a 50% reduction in tumor weight, and consistent with *in vitro* observations, reduced plasma ACTH levels, serum cortisol levels and tumor PCNA staining.

1. ClinicalTrials.gov (NCT02160730).

2. Liu, N-A., Jiang, H., Ben-Shlomo, A., Wawrowsky, K. Fan, X-M., Lin, S. and Melmed, S. (2011) Targeting zebrafish and

murine pituitary corticotroph tumours with a cyclin-dependent kinase (CDK) inhibitor. PNAS doi: 10.1073/pnas.1018091108

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 gBRCA positive tumors, and CYC065, a novel CDK2/9 inhibitor, with 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 the Company's most recent Annual Report on Form 10-K and other periodic and other filings Cyclacel files 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 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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