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# Cyclacel Receives $1.9 Million Translational Medicine Grant Award From the UK Biomedical Catalyst to Advance Its CYC065 Targeted Drug for Leukemias

BERKELEY HEIGHTS, N.J. and DUNDEE, United Kingdom, Nov. 5, 2012 (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 diseases, announced today the award of a grant of approximately £1.2 ($1.9) million from the UK Government's Biomedical Catalyst to complete IND-directed preclinical development of CYC065, its novel, orally available, second generation, cyclin-dependent kinase (CDK) inhibitor.

"For over a decade Cyclacel has been a leader in the study of cell cycle biology and the identification of novel anticancer drugs that exploit mechanisms of cell cycle control" said Spiro Rombotis, Cyclacel's President & Chief Executive Officer. "The Biomedical Catalyst award recognizes the scientific excellence of our Company's researchers. The grant will allow us to explore CYC065's promising anticancer activity in a translational biology program targeting specific leukemia and other cancer disease pathways with the ultimate goal of filing for regulatory approval to begin clinical trials. If successful, the program will provide the basis for stratified clinical development of CYC065 or treating patients with cancers that match the genetic mechanism targeted by the drug. CYC065 is part of Cyclacel's deep pipeline of novel medicines designed to target and stop uncontrolled cell division, led by sapacitabine, an orally-available nucleoside analogue currently in a pivotal Phase 3 trial in elderly patients with acute myeloid leukemia (AML)."

The project aims to complete IND-directed preclinical development of CYC065 and following regulatory clearance enable first-in-humans Phase 1 clinical studies. A key component of the project is a translational biology effort which may lead to validating one or more patient stratification biomarkers. Such biomarkers will be used to inform clinical development of CYC065 and direct its administration to patient groups most likely to benefit from the drug's mechanism.

There is a strong preclinical rationale for the use of CYC065 as a stratified medicine, or matching the treatment with tumor genetics and other disease features selected on the basis of clinical biomarkers, for orphan diseases with a high unmet medical need, including certain adult, infant and pediatric leukemias. In particular, CYC065 has been shown to target key components of leukemogenic and survival pathways in acute leukemias, including the MCL1 anti-apoptotic protein, and also transcription, driven by the rearranged MLL or mixed lineage leukemia gene.

**About CYC065**

CYC065 is a novel, orally available, cell cycle kinase inhibitor currently in IND-directed preclinical development. CYC065 targets similar CDK/cyclin complexes to those targeted by seliciclib, Cyclacel's first generation CDK inhibitor currently in Phase 2 studies. CYC065 retains the high CDK specificity of seliciclib, but with substantially higher anti-proliferative potency and improved pharmaceutical properties. CYC065 is a second generation aminopurine which selectively inhibits CDK2, CDK5 and CDK9. Strong preclinical anti-cancer efficacy data for CYC065 in multiple myeloma, chronic lymphocytic leukemia (CLL) and mixed lineage leukemia (MLL) have been presented at the 2010 Annual Meetings of the American Society of Hematology (ASH) [1] and the American Association of Cancer Research (AACR). [2] [3] At the 2010 AACR CYC065 was also reported to be active in solid tumor models, including trastuzumab-resistant, cyclin E overexpressing breast cancer. These findings were subsequently published by Scaltriti, et al ("Cyclin E amplification/overexpression is a mechanism of trastuzumab resistance in $HER2^+$ breast cancer patients", PNAS, 2011:108:3761-3766). In addition CYC065 was shown to have preclinical efficacy in proliferative kidney disease models (Cyclacel data on file). Cyclacel discovered CYC065 in collaboration with the Cancer Research UK Centre for Cancer Therapeutics at The Institute of Cancer Research.

**About CDKs and Cyclins**

The discovery of CDKs, cyclins and their mechanisms of action were the subject of the 2001 Nobel Prize for Medicine and Physiology. Cyclin-dependent kinases (CDKs) are a group of signaling molecules that play a direct role in the regulation and progression of the cell cycle, a biological mechanism which in healthy humans regulates uncontrolled cell division. In people with cancer, cell cycle control mechanisms malfunction resulting in proliferation and disease progression. CDK activity is dependent on association with their regulatory subunits called cyclins. Production and destruction of cyclins are tightly regulated in coordination with cell cycle progression. Targeting CDK/cyclin complexes is an attractive strategy for the design of novel anticancer drugs.

**About MLL Leukemias**

MLL or mixed lineage leukemia is an aggressive cancer of the blood associated with chromosomal rearrangements of the MLL gene. MLL is predominantly a children's disease with poor prognosis despite treatment. Five year survival is less than 50%. MLL leukemia occurs in 5% of adult acute myeloid leukemia or AML, 15-20% of pediatric AML, 10% of therapy-related AML, and 22% of acute lymphoblastic leukemia or ALL of which 50% occurs in infants aged less than 1. There are no approved therapies for MLL leukemia. The MLL gene encodes a histone methyltransferase enzyme that is thought to regulate how genes transcribe DNA. MLL was first reported to span the breakpoint in 11q23 chromosomal translocations associated with human leukemias in 1991. [4]

**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 oral capsules is in the SEAMLESS Phase 3 trial being conducted under an SPA with the FDA as front-line treatment of acute myeloid leukemia (AML) in the elderly, Phase 2 studies for AML, myelodysplastic syndromes (MDS), chronic lymphocytic leukemia (CLL) and solid tumors including breast, lung, ovarian and pancreatic cancer. Cyclacel's pipeline includes seliciclib oral capsules, a CDK inhibitor, in Phase 2 for lung and nasopharyngeal cancer and in Phase 1 in combination with sapacitabine; and CYC065, a second generation CDK inhibitor, in IND-directed development. 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 additional information.

**About The Biomedical Catalyst**

The Biomedical Catalyst, announced by UK Prime Minister David Cameron in December 2011, is a programme of public funding designed to deliver growth to the UK life sciences sector. Delivered jointly by the Medical Research Council and the Technology Strategy Board, the Biomedical Catalyst provides responsive and effective support for the best life science opportunities arising in the UK. The programme is open to UK academics and small and medium enterprises (SMEs) and seeks to support those opportunities which demonstrate the highest scientific and commercial potential, irrespective of medical area. For further information please visit: http://www.innovateuk.org/content/competition/biomedical-catalyst.ashx

The Technology Strategy Board is the UK government's innovation agency. Its goal is to accelerate economic growth by stimulating and supporting business-led innovation. Sponsored by the Department for Business, Innovation and Skills (BIS), the Technology Strategy Board brings together business, research and the public sector, supporting and accelerating the development of innovative products and services to meet market needs, tackle major societal challenges and help build the future economy. For more information please visit www.innovateuk.org.

**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.



[1] Pozzi S et al. CYC065, a potent derivative of seliciclib, is active in multiple myeloma in preclinical studies. 52nd Annual Meeting of American Society of Hematology, 2010, Abstract 2999

[2] Chen R et al. A novel derivative of the CDK inhibitor roscovitine that induces apoptosis in CLL and overcomes stromal cell-mediated protection. Proceedings of the 101st Annual Meeting of the American Association for Cancer Research; 2010, Abstract 4431.

[3] Frame S et al. Therapeutic potential of CDK inhibitors in MLL leukemias. Proceedings of the 101st Annual Meeting of the American Association for Cancer Research; 2010, Abstract 3886.

[4] Ziemin-vd Poel, et al, Proc Natl Acad Sci U S A. 1991 December 1; 88 (23): 10735—10739.

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