



February 23, 2017

## **Cyclacel Announces Top-Line Results From Pivotal Phase 3 SEAMLESS Study in Elderly Patients With Acute Myeloid Leukemia**

*- Study did not reach statistically significant improvement in the primary endpoint of overall survival -*

*- Improvement in secondary endpoint of complete remission rate for the experimental arm -*

*- Conference call scheduled today at 9:00 AM Eastern Time -*

BERKELEY HEIGHTS, N.J., Feb. 23, 2017 (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 reported top-line results from the pivotal Phase 3 SEAMLESS study in elderly patients aged 70 years or older with newly diagnosed acute myeloid leukemia (AML), who are not candidates for or have refused intensive induction chemotherapy.

The trial did not meet its primary endpoint of demonstrating statistically significant improvement in overall survival (OS) for the experimental arm versus an active control. An improved rate of complete remission (CR), a secondary endpoint, was observed in patients who had discontinued therapy at the time of analysis. Other endpoints and safety were similar between the arms. In the stratified subgroup of patients with low baseline peripheral white blood cell count, comprising approximately two-thirds of the study's population, an improvement in OS was observed for the experimental arm. The opposite was true for patients with high white blood cell count. Full results from the SEAMLESS study will be submitted for presentation at an upcoming medical conference.

"The results of the SEAMLESS Phase 3 study demonstrate that sapacitabine is active and safe in elderly AML patients," said Hagop Kantarjian M.D., Professor and Chair, Department of Leukemia, The University of Texas MD Anderson Cancer Center, and chair of the SEAMLESS study. "Although the experimental arm of alternating decitabine-sapacitabine did not reach statistically significant superiority in overall survival, it is remarkable that an improvement in complete remission rate was observed. Additional analysis of stratified and exploratory subgroups is warranted to identify patients who are most likely to benefit from treatment with the experimental arm."

"We are disappointed not to have reached the primary endpoint of SEAMLESS. Nevertheless, the improvement in CR rate and similar safety profile are encouraging. We plan to discuss the data with European and US regulatory authorities once subgroup analyses are completed over the next few months and will report our further plans as they develop. We are grateful to the clinical investigators, and especially the patients and their families, for their contributions to this large study," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "In parallel with data analysis and regulatory discussions, we will reevaluate our continued investment in sapacitabine in hematological malignancies. Our clinical development strategy in oncology will now concentrate on our two ongoing, clinical programs in DNA damage response and transcriptional regulation, which include our area of historical expertise in CDK inhibitors. These programs target biomarker-selected patients, such as those with BRCA mutations or resistance to existing cancer therapies. Our cash resources are projected to fund these activities and operations through the end of 2018."

### **Clinical Development Strategy**

For the past few years the Company has been progressing clinical investigation of two programs in parallel with the SEAMLESS study based on promising scientific and preclinical data. The DNA damage response program is evaluating an orally-administered, sequential regimen of sapacitabine and seliciclib, a CDK2/9 inhibitor, in patients with BRCA positive, advanced solid cancers. The transcriptional regulation program is evaluating CYC065, a CDK2/9 inhibitor, in patients with advanced cancers with emphasis on downregulation of the Mcl-1 biomarker.

### **DNA Damage Response Program**

Phase 1 data from this program in 67 patients with various advanced cancers were reported at an oral presentation during the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting. Antitumor activity with durable clinical responses was demonstrated in a subgroup of 45 patients with breast, ovarian and pancreatic cancers who tested positive for BRCA mutations. A cohort of breast cancer patients who carry BRCA mutations is being enrolled as an expansion of this study. A

further cohort is in preparation which will evaluate alternative dosing schedules and collect more data in BRCA positive patients with solid tumors other than breast cancer. The DNA Damage Response program is benefiting from the historical experience with sapacitabine in hematological malignancies, understanding of its mechanism of action and sizable patient safety database.

### **Transcriptional Regulation Program**

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. The study has reached the seventh dose escalation level without observations of serious toxicity. Evidence of target engagement of 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.

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.

### **Conference Call and Webcast Information:**

Cyclacel will hold a conference call on February 23, 2017 at 9:00 a.m. Eastern Time to discuss the Company's plans with regard to SEAMLESS. Conference call and webcast details are as follows:

US/Canada call: (877) 493-9121/ international call: (973) 582-2750

US/Canada archive: (800) 585-8367 / international archive: (404) 537-3406

Code for live and archived conference call is: 77162157

For the live and archived webcast, please visit the Corporate Presentations and Events page on the Cyclacel website at [www.cyclacel.com](http://www.cyclacel.com). The webcast will be archived for 90 days and the audio replay for 7 days.

### **About SEAMLESS**

The Phase 3, randomized trial compared an investigational arm of oral sapacitabine administered in alternating cycles with intravenous decitabine compared with an active control arm of intravenous decitabine administered alone. The trial was conducted at 110 US and EU sites and randomized 491 patients, over an approximately three year period. Stratification factors at randomization were antecedent hematologic disorders, baseline peripheral white blood cells and baseline bone marrow blasts. In December 2014, the study's monitoring committee determined after an interim analysis that the futility boundary was crossed. In accordance with the committee's recommendations, the Company continued to follow up enrolled patients to maturity.

### **About Sapacitabine**

Sapacitabine (CYC682), an orally-available nucleoside analogue, acts through a novel DNA single-strand breaking mechanism, leading to production of DNA double strand breaks (DSBs) and/or checkpoint activation. Unrepaired DSBs cause cell death. Repair of sapacitabine-induced DSBs is dependent on the homologous recombination repair (HRR) pathway. Both sapacitabine and its major metabolite, CNDAC, have demonstrated potent anti-tumor activity in preclinical studies.

In addition to the SEAMLESS Phase 3 study in elderly patients with AML who were unfit or refused intensive induction chemotherapy, other Phase 2 studies evaluated sapacitabine in patients with myelodysplastic syndromes (MDS), cutaneous T cell lymphoma (CTCL) and non-small cell lung cancer (NSCLC). The US FDA and the European Medicines Agency have designated sapacitabine as an orphan drug for the treatment of both AML and MDS. Sapacitabine is part of Cyclacel's pipeline of small molecule drugs designed to target and stop uncontrolled cell division.

### **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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