



December 16, 2014

## **Cyclacel Announces Enrollment of 486 Patients, DSMB Recommendations and That the Seamless Phase 3 Trial of Sapacitabine in AML Will Continue to Final Analysis**

***- DSMB determined that the planned futility boundary has been crossed; but saw no reason for patients to discontinue from study -***

***- Conference Call Scheduled December 16, 2014 at 9:00 a.m. EST -***

BERKELEY HEIGHTS, N.J., Dec. 16, 2014 (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 enrollment of 486 patients, continuation to final analysis and recommendations of the independent Data and Safety Monitoring Board (DSMB) of the Company's Phase 3 SEAMLESS study of oral sapacitabine capsules in acute myeloid leukemia (AML). All patients will continue to be followed up until mature data become available for final analysis. The DSMB conducted its planned interim analysis for futility after 247 events and the final safety review of 470 randomized patients. The DSMB found no safety concerns. However, the planned futility boundary has been crossed and the DSMB determined that based on available interim data, it would be unlikely for the study to reach statistically significant improvement in survival. The DSMB saw no reasons why patients should discontinue treatment on their assigned arm and recommended that recruited patients stay on treatment.

"At this stage all patients should stay on study," said Hagop Kantarjian, M.D., Chairman & Professor, Department of Leukemia, The University of Texas MD Anderson Cancer Center and chair of the SEAMLESS study. "It is essential that we have complete follow-up of all patients to ensure that the mature survival data does not miss any potential survival benefit in the overall patient population or subgroup of patients."

Judy H. Chiao, M.D., Vice President, Clinical Development and Regulatory Affairs for Cyclacel said, "We were surprised and disappointed to learn of the outcome of the interim analysis for futility suggesting that it is unlikely that the experimental arm of sapacitabine alternating with decitabine will be superior to the decitabine control arm in the final analysis. We agree with the DSMB's recommendation to keep all patients on treatment and complete the study, as the DSMB advised that response rates were similar between the arms and there was no evidence of adverse outcomes for patients on the experimental arm. We thank the DSMB for their work and especially the patients and clinical investigators in the U.S. and Europe for their support of our efforts during the last three years to enroll SEAMLESS, one of the largest studies in this population."

The interim analysis for futility is primarily driven by the deaths within the first 6 months of patients entering into the trial. Of 247 deaths in SEAMLESS, 173 (70%) have occurred in the first 6 months. This means that the survival curves beyond 6 months are poorly estimated at this time. Furthermore, follow up of European patients is significantly shorter than that of US patients due to the fact that the study opened for European accrual in April 2014. It is important to have complete follow up of all patients to ensure that a potential treatment effect beyond 6 months is not missed.

The Company remains blinded and in accordance with the DSMB's recommendations, will follow-up patients as per the study protocol until the prespecified 424 events have been observed. This is estimated to occur between the second half of 2015 and the first half of 2016. The Company has adequate financial resources to reach beyond the later time point in this estimate. Depending on the results from the final data, the Company may meet with regulatory authorities in Europe and the U.S. to discuss registration submissions for sapacitabine in this indication. The Company wishes to draw investors' attention to the precedent of decitabine's European approval in AML in a similar population based on a Phase 3 study which did not reach statistical significance comparing intravenous decitabine with intravenous chemotherapy.

"Absence of early benefit in this Phase 3 study does not preclude emergence of a late benefit with longer follow up. As the well-being of patients is a paramount concern and the DSMB recommends that patients remain on study, we are encouraged that patients on the sapacitabine regimen are not disadvantaged to those on the control arm," said Spiro Rombotis, President & Chief Executive Officer of Cyclacel. "We have sufficient capital resources to follow up patients, reach the final analysis of SEAMLESS and continue existing programs through 2016. The feasibility assessment for our Phase 2b randomized trial of sapacitabine in myelodysplastic syndromes (MDS) is in progress. Obviously, we will review and consider any impact of the SEAMLESS interim analysis on our plans for the MDS study. Our emerging cyclin dependent kinase (CDK) inhibitor program continues to progress as planned. This includes the Phase 1 study of our oral regimen of seliciclib in combination with sapacitabine in Homologous Recombination (HR) repair-deficient solid tumors and CYC065, our novel CDK 2/9 inhibitor, with potential utility in both hematological malignancies and solid tumors."

The SEAMLESS study is a Phase 3, randomized, registration-directed study of oral sapacitabine capsules in elderly (70 years or older) patients with AML who are unfit for or have refused intensive chemotherapy from approximately 110 U.S. and European sites. SEAMLESS has enrolled 486 patients and is one of the largest studies in this population. The primary endpoint is overall survival. SEAMLESS is comparing a regimen of oral sapacitabine alternating with intravenous decitabine versus a control of intravenous decitabine. SEAMLESS is being conducted under a Special Protocol Assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA). Sapacitabine has orphan drug designation in the U.S. and Europe for both AML and myelodysplastic syndromes.

#### **Conference call and Webcast Information:**

Cyclacel will conduct a conference call on December 16, 2014 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:

Conference call information:

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 54535033

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 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 being conducted under an SPA with the FDA as front-line treatment for acute myeloid leukemia (AML) in the elderly, and other studies for myelodysplastic syndromes (MDS) and chronic lymphocytic leukemia (CLL). 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 CDK 2/9 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](http://www.cyclacel.com) for additional information.

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