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Cyclacel Reports Updated Data From Its DNA Damage Response Program on Seliciclib and Sapacitabine Combination in Patients With Solid Tumors at ASCO

Combination Showed 35.6% Disease Control Rate and Durable Responses including CR and PR in Heavily-Pretreated Patients with BRCA Mutations

BERKELEY HEIGHTS, N.J., June 06, 2016 (GLOBE NEWSWIRE) -- Cyclacel Pharmaceuticals, Inc. (NASDAQ:CYCC) (NASDAQ:CYCCP) (Cyclacel or the Company), reported today updated Phase 1 data from its DNA damage response program evaluating a combination regimen of two Cyclacel product candidates, seliciclib, a cyclin dependent kinase (CDK) inhibitor, and sapacitabine, a nucleoside analogue. The regimen was orally-administered as sequential (Part 1) or concomitant (Part 2) treatment to 67 heavily-pretreated patients with advanced solid tumors. Antitumor activity was demonstrated in a subgroup of 45 patients with breast, ovarian and pancreatic cancers who tested positive for BRCA mutations (44 germline and 1 sporadic) with a 35.6% disease control rate (1 CR, 5 PR and 10 SD). Treatment durations in responders ranged between 16 and over 240 weeks. No CR or PR was observed in BRCA negative patients. Data were presented at an oral presentation at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

"We are encouraged by the durable responses and stable disease seen with the seliciclib and sapacitabine combination in patients with BRCA mutations, in particular because most were heavily pretreated and many are able to remain on study for extended periods," said Sara M. Tolaney, M.D., M.P.H., Associate Director, Clinical Research, Breast Oncology, Dana-Farber Cancer Institute, Boston. "Our findings from Parts 1 and 2 of the study have shown that the orally-administered regimen is well tolerated with manageable toxicities. Based on the results, we believe that further clinical evaluation of this combination regimen is warranted. A Part 3 extension of the study is currently enrolling advanced breast cancer patients with BRCA mutations."

"The findings reported in Dr. Tolaney's presentation show that the combination treatment of seliciclib and sapacitabine is active and tolerable," said Judy Chiao, M.D., Vice President, Clinical Development and Regulatory Affairs of Cyclacel. "This clinical observation may be directly related to the drugs interference with the capacity of BRCA-mutated cancer cells to repair and survive sapacitabine-induced breaks in their DNA. If these preliminary findings are confirmed by further data, this regimen may provide an important treatment option for patients with BRCA-mutated cancers."

"The ASCO data build on earlier data from our DNA damage response program highlighted by the American Association for Cancer Research (AACR) Annual Meeting Program Committee in a 2013 press conference," said Spiro Rombotis, President and Chief Executive Officer of Cyclacel. "The updated data support and extend clinical evidence of efficacy with different schedules of the combination in this patient population. We are encouraged with the durability of responses and stable disease, with ongoing responding patients achieving treatment durations exceeding 1 and 4.5 years respectively. We look forward to reporting data from the ongoing Part 3 extension in BRCA positive patients with breast cancer and increasing our understanding of the potential benefits of this differentiated treatment strategy in a targeted patient population with significant unmet medical need."

Results

The trial is a dose escalation study conducted in patients with advanced and incurable solid tumors. The orally-administered regimen consists of sapacitabine administered twice daily for 7 days sequentially followed by seliciclib twice daily for 3 days over a 21 day cycle (Part 1, n=38); and sapacitabine dosed each morning followed by seliciclib each evening, each once daily for 5 days per week for 2 weeks of a 28 day cycle (Part 2, n=29). The primary objective of the trial is to determine the maximum tolerated dose with a secondary objective of antitumor activity of the combination. Sixty-seven patients have been treated in Parts 1 and 2 of the study, of which 44 were found to carry BRCA mutations and one a sporadic BRCA mutation.

Best Responses

	PART 1		PART 2	
	BRCA carriers (n=16)	Others (n=22)	BRCA carriers (n= 28)	Others (n=1)
CR	1	-	-	-

PR	**3**	**-**	**2**	**-**
SD	**2**	**6**	**7**	**1***
ORR (CR/PR)	**25%**	**0%**	**7%**	**0%**
Disease Control (CR/PR/SD)	**6 (37.5%)**	**6 (27.3%)**	**9 (32.1%)**	**1 (100.0%)**

** One patient had a sporadic BRCA mutation. CR=complete response, PR=partial response, SD=stable disease.*

One CR and five PR were observed in BRCA mutation carriers with breast, ovarian and pancreatic cancers. Treatment durations for the 3 breast/ovarian cancer responders in Part 1 are 54, 93, over 240 weeks and the one breast cancer responder in Part 2 over 76 weeks respectively. Treatment durations for the two pancreatic cancer responders, one each in Parts 1 and 2, are 21 and 16 weeks respectively. Responders included patients who underwent prior treatment with PARP inhibitors and PARP naïve patients. SD was observed in 9 BRCA mutation carriers and 1 sporadic BRCA positive patient with treatment durations ranging from 16 to 88 weeks.

Overall in BRCA positive patients (Parts 1 and 2, n=45), disease control rate is 35.6% and overall response rate (ORR) is 11% (Part 1 ORR 25% and Part 2 7%). The difference in Part 1 and Part 2 ORRs may suggest that the seliciclib dose in the Part 2 schedule may be too low for enhancing the activity of sapacitabine.

Pharmacodynamic effects of the seliciclib and sapacitabine combination were observed in skin biopsies. Part 1 biopsies following treatment showed a 2.3-fold increase in DNA damage induced by sapacitabine, as measured by gamma-H2AX immunohistochemistry. Additional DNA damage occurred after treatment with seliciclib with a 0.58-fold further increase in gamma-H2AX staining.

In Part 1 recommended Phase 2 doses (RP2D) are: sapacitabine 50 mg b.i.d./seliciclib 800 mg b.i.d. Most frequent grade 3/4 adverse events were neutropenia (16%) and elevation in AST (16%). In Part 2 RP2D are: sapacitabine 250 mg q.d./seliciclib 200 mg q.d. Most frequent grade 3/4 adverse events were neutropenia (28%) and elevation in AST (10%). Dose limiting toxicities were reversible elevations in transaminase and bilirubin, neutropenia or febrile neutropenia and pneumonia.

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The abstract can be accessed through the ASCO website, http://www.asco.org/internal/meetings/2016-asco-annual-meeting.

About sapacitabine

Sapacitabine is an oral nucleoside analogue prodrug whose metabolite, CNDAC, generates single-strand DNA breaks (SSB), either leading to arrest of the cell cycle at G2 phase or development of double-strand DNA breaks (DSB). CNDAC-induced DSB repair is dependent on homologous recombination (HR). BRCA mutations in cancer cells are a cause of HR deficiency, making them susceptible to cell death induced by sapacitabine. Sapacitabine is the subject of SEAMLESS, a Phase 3 trial, which has completed enrollment and is being conducted under an SPA with the U.S. Food and Drug Administration (FDA) as front-line treatment for acute myeloid leukemia (AML) in the elderly. Sapacitabine has been evaluated to date in over 1000 patients including randomized Phase 2 and 3 trials in patients with hematological malignancies and previously treated solid tumors, including lung cancer.

About seliciclib

Seliciclib is an orally-available CDK inhibitor molecule that selectively inhibits enzyme targets, CDK2 and CDK9, which are central to the process of cell growth, survival and cell cycle control. Seliciclib treatment has been reported to inhibit the two

major DNA double-strand break (DSB) repair pathways, homologous recombination (HR) and non-homologous end joining (NHEJ), by reducing expression of components of each pathway. It may potentiate the activity of sapacitabine by compromising HR protein expression and activation or by potentiating apoptosis following sapacitabine-induced DNA damage. Seliciclib has been evaluated to date in approximately 450 patients including randomized Phase 2 trials in patients with previously treated lung cancer and nasopharyngeal cancer.

About Cyclacel Pharmaceuticals, Inc.

Cyclacel Pharmaceuticals is a clinical-stage biopharmaceutical company using cell cycle control and DNA damage response biology to develop innovative, targeted medicines for cancer and other proliferative diseases. The SEAMLESS randomized Phase 3 trial of sapacitabine as front-line treatment for AML in the elderly under an SPA with FDA has completed enrollment. Cyclacel's pipeline includes an oral combination of seliciclib (CDK2/9 inhibitor) and sapacitabine in Phase 1 in advanced solid tumors including patients with BRCA mutations; sapacitabine in Phase 2 in MDS; and CYC065 (CDK2/9 inhibitor) in Phase 1 in solid tumors and lymphomas with potential utility based on preclinical data in other hematological malignancies. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a 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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