Curis Reports Clinical Activity of CUDC-907 in Patients With DLBCL Harboring MYC Oncogene Alterations at the 2015 ASH Annual Meeting

Curis expects to initiate a randomized Phase 2 trial in patients with relapsed/refractory DLBCL with MYC alterations

LEXINGTON, Mass., Dec. 6, 2015 (GLOBE NEWSWIRE) -- Curis, Inc. (NASDAQCRIS), a biotechnology company focused on the development and commercialization of innovative drug candidates for the treatment of human cancers, today presented data from the completed dose escalation and ongoing expansion stages of the Phase 1 trial of CUDC-907, an oral dual inhibitor of histone deacetylase (HDAC) and phosphoinositide 3-kinase (PI3K) enzymes. These data were presented at the American Society of Hematology's (ASH) Annual Meeting in Orlando, FL. The data demonstrated that treatment with CUDC-907 resulted in complete (CRs) and partial responses (PRs) in heavily pretreated patients with relapsed/ refractory diffuse large B cell lymphoma (RR-DLBCL), including those harboring alterations of the *MYC* oncogene, a poor performing sub-group for which there are no approved targeted therapies.

In the ongoing Phase 1 trial of CUDC-907, 8 objective responses (3 CRs and 5 PRs) were reported in 18 response-evaluable patients out of a total of 25 patients with RR-DLBCL enrolled in the trial. These results include 1 CR among 2 response-evaluable patients out of a total of 3 patients treated with CUDC-907 in combination with the standard dose of rituximab. The remaining 16 evaluable patients were treated with CUDC-907 monotherapy. In a retrospective *post hoc* analysis, among the 8 patients who achieved objective responses, 5 had tumors with *MYC* oncogene alterations (defined as chromosome translocation involving *MYC* gene locus, gain in *MYC* gene copy number, or MYC protein over-expression in =40% tumor cells). Among the remaining 3 patients who achieved objective responses, 2 had MYC protein expression in less than 40% of tumor cells, and the third patient's MYC status is unknown.

In preclinical studies, CUDC-907 treatment of DLBCL cell lines was shown to result in complete suppression of MYC protein levels in a rapid and dose dependent manner. Additionally, anti-tumor activity was observed in multiple *in vivo* MYC-altered DLBCL models.

"Preliminary data for CUDC-907 in patients with multiply relapsed DLBCL appear encouraging, even in those with MYC-altered lymphoma, providing the rationale for further investigation in a Phase 2 trial," said Dr. Anas Younes, MD, Chief of the Lymphoma Service of the Memorial Sloan Kettering Cancer Center in New York City and the Principal Investigator of the Phase 1 trial. "There is a high unmet need for novel therapies for patients with RR-DLBCL, and particularly for the subset of patients with MYC-altered DLBCL due to their poor prognosis."

Based on promising clinical activity observed in patients with RR-DLBCL, particularly those with cancers harboring MYC alterations, Curis expects to initiate a Phase 2 trial to examine CUDC-907 in patients with MYC-altered DLBCL. In this trial, approximately 120 patients with relapsed/refractory disease will be randomly assigned to receive CUDC-907 as monotherapy or CUDC-907 with the standard dose of rituximab. Patients will remain on treatment until progression of disease, discontinuation for safety reasons, or other reasons for treatment discontinuation. The primary endpoint of the trial is objective response rate with secondary endpoints that include progression free survival, overall survival and duration of response. Positive results with CUDC-907 monotherapy will lead to an expansion of patient enrollment and discussion with the FDA regarding potential registration strategy in this patient population. The rituximab combination treatment arm of the Phase 2 trial is intended to inform the design of a confirmatory, randomized trial of CUDC-907 in combination with rituximab as compared to rituximab in combination with standard of care chemotherapy.

"We are pleased to report promising clinical activity of CUDC-907 in patients with DLBCL, particularly those with tumors that harbor MYC alterations," said Ali Fattaey, Ph.D., Curis' President and Chief Executive Officer. "These clinical results are consistent with our preclinical observations where CUDC-907 has a rapid and dramatic effect on MYC protein levels and provides significant anti-tumor activity in *in vivo* models. We are thankful to our patients for their participation in the Phase 1 clinical trial and, based on these data, we expect the start of a Phase 2 trial that will exclusively enroll patients with relapsed/ refractory DLBCL known to have MYC alterations based on pre-specified selection criteria."

The Phase 1 dose escalation and expansion trial was designed to determine the maximum tolerated dose (MTD), recommended Phase 2 dose and preliminary anti-cancer activity of oral CUDC-907 in patients with relapsed/refractory lymphoma or multiple myeloma (MM). At the time of data cut-off for the ASH presentation, a total of 72 patients had been enrolled in the trial, including 25 with RR-DLBCL. In the completed dose escalation phase, patients received CUDC-907 daily (QD, doses: 30 or 60 mg), or intermittently on twice weekly (BIW) or thrice weekly (TIW) schedules (doses: 60, 90, 120 or 150 mg) or on a 5 days on, 2 days off (5/2) schedule (dose: 60 mg). CUDC-907 dosed at 60 mg on the 5/2 schedule was determined to be the recommended Phase 2 dose (RP2D). The expansion phase of the trial is ongoing to assess the safety and tolerability of CUDC-907 at the RP2D of 60 mg 5/2 with or without the standard dose of rituximab.

The most common drug related adverse events (AEs) reported in the study have been low grade (Grade 1 and 2) diarrhea, fatigue and nausea. Dose limiting toxicities (DLTs) have consisted of diarrhea and hyperglycemia, and occurred on the QD, BIW and TIW schedules. No DLT occurred at the RP2D of 60 mg 5/2. Other drug-related Grade 3 or 4 AEs reported in 3 or more patients included thrombocytopenia and neutrophil decrease (hematologic AEs) as well as diarrhea, hyperglycemia and fatigue (non-hematologic AEs).

Out of the 25 patients with RR-DLBCL included in the ASH presentation, 18 were evaluable for response assessment per protocol at the time of data cut-off. The best responses observed in patients with RR-DLBCL were CR (3 patients), PR (5 patients) stable disease or SD (4 patients) and progressive disease or PD (6 patients). A *post hoc* analysis of pathology reports and/or tumor samples collected showed that 5 of the 8 patients with objective responses had tumors with alterations in *MYC* oncogene. MYC

alterations in the tumor tissue were determined by established criteria used to identify either *MYC* gene aberrations (copy number gains or translocations) by fluorescent *in situ* hybridization (FISH) or MYC protein expression by immunohistochemistry (IHC).

About CUDC-907:

CUDC-907 is an oral, dual inhibitor of Class I and II HDAC, as well as Class I PI3K enzymes. Specifically, CUDC-907 is designed to inhibit HDACs 1, 2, 3, 6 and 10 and PI3K-alpha, delta and beta isoforms. CUDC-907 is currently undergoing investigation in a Phase 1 trial to assess its safety, pharmacokinetics and preliminary anti-cancer activity in patients with relapsed/refractory lymphomas and multiple myeloma. CUDC-907 is also being investigated in a separate Phase 1 trial in patients with advanced solid tumors including those with hormone receptor positive breast cancer or with NUT midline carcinoma. The development of CUDC-907 has been supported in part by The Leukemia & Lymphoma Society (LLS) under a funding agreement established in 2011 between Curis and LLS's Therapy Acceleration Program. For additional details of CUDC-907's Phase 1 studies, please refer to www.clinicaltrials.gov (study identifiers: NCT01742988 and NCT02307240).

About Curis, Inc.

Curis is a biotechnology company focused on the development and commercialization of innovative drug candidates for the treatment of human cancers, including its lead development candidate, CUDC-907, a dual HDAC and PI3K inhibitor that is being investigated in two clinical studies in patients with lymphomas and solid tumors. Curis is also engaged in a broad collaboration with Aurigene in the areas of immuno-oncology and precision oncology. As part of this collaboration, Curis has exclusive licenses to oral small molecule antagonists of the PD-1 pathway/ VISTA, including PD-L1/VISTA antagonist CA-170, as well as to molecules designed to inhibit IRAK4. Curis is also party to a collaboration with Genentech, a member of the Roche Group, under which Genentech and Roche are developing and commercializing Erivedge® for the treatment of advanced basal cell carcinoma.

Cautionary Note Regarding Forward-Looking Statements:

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including without limitation Curis' expectations regarding: its plans and timing for conducting ongoing and planned clinical studies with CUDC-907 in various indications, including its planned phase 2 clinical trial of CUDC-907 in patients with relapsed/ refractory DLBCL with MYC alterations and the potential benefits of CUDC-907, among others. Forward-looking statements used in this press release may contain the words "believes," "expects," "anticipates," "plans," "seeks," "estimates," "assumes," "will," "may," "could" or similar expressions. These forward-looking statements are not guarantees of future performance and involve risks, uncertainties, assumptions and other important factors that may cause actual results to be materially different from those indicated by such forward-looking statements. For example, Curis and its collaborators may experience adverse results, delays and/or failures in their drug development programs. Curis' drug candidates may cause unexpected toxicities and/or fail to demonstrate sufficient safety and efficacy in clinical trials and may never achieve the requisite regulatory approval needed for commercialization. There can be no guarantee that Curis' collaboration agreement with Aurigene will continue for its full term, that Curis or Aurigene will maintain the financial resources necessary to continue financing its portion of research, development and commercialization costs or that the parties will successfully discover, develop or commercialize drug candidates under the collaboration. Genentech and Roche may experience delays or failures in the manufacture and commercialization of Erivedge, regulatory authorities may determine to delay or restrict Genentech's and/or Roche's ability to continue to develop or commercialize Erivedge, and competing drugs may be developed that are superior to Erivedge, any of which could adversely affect the amount of royalty revenue that Curis receives from sales of Erivedge. Curis also faces risks relating to its wholly-owned subsidiary's Erivedge royalty-collateralized loan transaction, including the risk that it may not receive sufficient levels of royalty revenue from sales of Erivedge to satisfy the debt obligation or may otherwise lose its rights to royalties and royalty-related payments as a result of a foreclosure of the loan. Curis may not obtain or maintain necessary patent protection for its programs and could become involved in expensive and time consuming patent litigation and interference proceedings. Curis faces substantial competition from other companies developing cancer therapeutics. Curis will require substantial additional capital to fund its business and such capital may not be available on reasonable terms, or at all. Unstable market and economic conditions may adversely affect Curis' financial conditions and its ability to access capital to fund the growth of its business. Curis also faces other important risks relating to its business, operations, financial condition and future prospects that are discussed in its Quarterly Report on Form 10-Q for the quarter ended September 30, 2015 and other filings that it periodically makes with the Securities and Exchange Commission.

In addition, any forward-looking statements represent the views of Curis only as of today and should not be relied upon as representing Curis' views as of any subsequent date. Curis disclaims any intention or obligation to update any of the forward-looking statements after the date of this press release whether as a result of new information, future events or otherwise, except as may be required by law.

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https://investors.curis.com/Curis-Reports-Clinical-Activity-of-CUDC-907-in-Patients-With-DLBCL-Harboring-MYC-Oncogene-Alterations-at-the-2015-ASH-Annual-Meeting