Curis Doses First Patient in Phase 1 Study of CA-4948 in Combination with Ibrutinib in Patients with Relapsed or Refractory Hematologic Malignancies

- Amends existing protocol of ongoing Phase 1 study in R/R NHL -
- Initial data expected in the fourth quarter of 2021 -

LEXINGTON, Mass., Feb. 9, 2021 /PRNewswire/ -- Curis, Inc. (NASDAQ: CRIS), a biotechnology company focused on the development of innovative therapeutics for the treatment of cancer, today announced that the first patient has been dosed in its Phase 1 trial evaluating CA-4948, a novel, small molecule IRAK4 kinase inhibitor, in combination with ibrutinib, a BTK inhibitor, in patients with relapsed or refractory (R/R) hematologic malignancies.

"In dosing the first patient in this Phase 1 study evaluating CA-4948 and ibrutinib, we are taking a highly anticipated step forward in bringing a potent oral therapeutic regimen to patients with relapsed or refractory hematologic malignancies," said James Dentzer, President and Chief Executive Officer of Curis. "BTK inhibitors are an approved category of therapies for patients with various lymphatic cancers yet they only target one of the two main pathways activating NF-κB in B-cell malignancies. CA-4948 targets the other main NF-κB-activating pathway by shutting down signaling through the Myddosome. We have shown highly encouraging increased tumor-reducing activity when combining both covalent and non-covalent BTK inhibitors with CA-4948 in preclinical models."

Mr. Dentzer continued, "We observed single-agent activity in the non-Hodgkin's lymphoma (NHL) monotherapy study, with the majority of patients treated at 300mg twice daily experiencing at least some reduction in tumor volume. We coordinated with our trial partners to amend the protocol of our existing study to include combination therapy starting at a previously demonstrated therapeutic dose. This will allow us to leverage the clinical sites and staff currently active in our monotherapy study and should save significant time and resources as we advance through the clinic."

"Given the profile CA-4948 has demonstrated in existing studies, it is a promising candidate for combination with a proven BTK inhibitor such as ibrutinib," said Dr. Erel Joffe, M.D., Assistant Attending with the Lymphoma Service at Memorial Sloan Ketting Cancer Center and a lead investigator on the study. "We believe there may be important synergies given that IRAK4 controls the critical TLR pathway that is parallel and complementary to the BTK pathway and that both of these pathways are primary and independent oncogenic activators of NF-κB in lymphoma and leukemia. Effective dual targeting of both independent pathways that drive excessive B-cell proliferation via NF-κB could potentially provide significantly improved outcomes over either treatment in a monotherapy setting."

About the CA-4948+ibrutinib Phase 1 Combination Study

The Phase 1 trial is a two-part, multicenter, open-label, dose escalation and expansion study designed to evaluate the safety, pharmacokinetics, pharmacodynamics, clinical activity, and biomarker correlations of CA-4948 and ibrutinib patients with relapsed or refractory hematologic malignancies. Part 1 of the study is a dose escalation using a 3+3 design. Approximately 18 patients will be enrolled in Part 1 and will receive a starting dose of 200mg CA-4948 BID with subsequent escalation to 300mg BID, both of which have been observed to be safe and effective in the NHL monotherapy study, combined with ibrutinib doses appropriate for their respective NHL subtype. The primary endpoints of Part 1 will be safety and tolerability, maximum tolerated dose, and the recommended Phase 2 dose. Secondary objectives will be pharmacokinetics and preliminary efficacy. Exploratory objectives will include biomarker correlations, such as MYD88-L265P mutations and IRAK4 pathway and NFκB inhibition.

Part 2 of the study will enroll patients across an expansion basket of four cohorts: marginal zone lymphoma (MZL), ABC-DLBCL, primary central nervous system lymphoma (PCNSL), and NHL with adaptive ibrutinib resistance. An interim futility analysis will be conducted after approximately 15-20 patients are enrolled in each cohort. Primary endpoints of Part 2 will be complete response or objective response rate and duration of response compared to historical controls. Secondary objectives will be safety and tolerability, progression-free survival, and population PK sampling for CA-4948. Exploratory objectives will include response correlation with biomarkers including MYD88-L265P or other genetic mutations, gene expressions, cell of origin, IRAK4 signaling, and resistance.

About Curis, Inc.

Curis is a biotechnology company focused on the development of innovative therapeutics for the treatment of cancer. In 2015, Curis entered into a 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

immune checkpoints including the VISTA/PDL1 antagonist CA-170, and the TIM3/PDL1 antagonist CA-327, as well as the IRAK4 kinase inhibitor, CA-4948. CA-4948 is currently undergoing testing in a Phase 1 in patients with non-Hodgkin's lymphoma both as a monotherapy and in combination with BTK inhibitor ibrutinib. Curis is also evaluating CA-4948 in a Phase 1 trial in patients with acute myeloid leukemia and myelodysplastic syndromes. In addition, Curis is engaged in a collaboration with ImmuNext for development of CI-8993, a monoclonal anti-VISTA antibody, which is currently undergoing testing in a Phase 1a/1b trial in patients with solid tumors. Curis is also party to a collaboration with Genentech, a member of the Roche Group, under which Genentech and Roche are commercializing Erivedge® for the treatment of advanced basal cell carcinoma. For more information, visit Curis' website at www.curis.com.

Forward-Looking Statements:

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, including, without limitation, statements regarding any expectations of the potential for the Company's proprietary drug candidate CA-4948, including the potential developments and benefits of CA-4948 in combination with BTK inhibitors such as ibrutinib, statements with respect to the timing of the Company's studies, including enrollment and reporting of data, and the Company's ability to advance and broaden its clinical programs. Forward-looking statements may contain the words "believes," "expects," "anticipates," "plans," "intends," "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 may experience adverse results, delays and/or failures in its drug development programs and may not be able to successfully advance the development of its drug candidates in the time frames it projects, if at all. Curis's drug candidates may cause unexpected toxicities, fail to demonstrate sufficient safety and efficacy in clinical studies and/or may never achieve the requisite regulatory approvals needed for commercialization. Favorable results seen in preclinical studies and early clinical trials of Curis's drug candidates may not be replicated in later trials. There can be no guarantee that the collaboration agreements with Aurigene and ImmuNext will continue for their full terms, that Curis or its collaborators will each maintain the financial and other resources necessary to continue financing its portion of the research, development and commercialization costs, or that the parties will successfully discover, develop or commercialize drug candidates under the collaboration. Regulatory authorities may determine to delay or restrict Genentech's and/or Roche's ability to continue to develop or commercialize Erivedge in BCC. Erivedge may not demonstrate sufficient or any activity to merit its further development in disease indications other than BCC. Competing drugs may be developed that are superior to Erivedge. In connection with its agreement with Oberland Capital, Curis faces risks relating to the transfer and encumbrance of certain royalty and royalty-related payments on commercial sales of Erivedge, including the risk that, in the event of a default by Curis or its wholly-owned subsidiary, Curis could lose all retained rights to future royalty and royalty-related payments, Curis could be required to repurchase such future royalty and royalty-related payments at a price that is a multiple of the payments it has received, and its ability to enter into future arrangements may be inhibited, all of which could have a material adverse effect on its business, financial condition and stock price. Curis will require substantial additional capital to fund its business. If it is not able to obtain sufficient funding, it will be forced to delay, reduce in scope or eliminate some of its research and development programs, including related clinical trials and operating expenses, potentially delaying the time to market for, or preventing the marketing of, any of its product candidates, which could adversely affect its business prospects and its ability to continue operations, and would have a negative impact on its financial condition and its ability to pursue its business strategies. Curis faces substantial competition. Curis also faces risks relating to potential adverse decisions made by the FDA and other regulatory authorities, investigational review boards, and publication review bodies. Curis may not obtain or maintain necessary patent protection and could become involved in expensive and time-consuming patent litigation and interference proceedings. Unstable market and economic conditions, natural disasters, public health crises, political crises and other events outside of Curis's control could significantly disrupt its operations or the operations of third parties on which Curis depends, and could adversely impact Curis's operating results and its ability to raise capital. For example, the COVID-19 pandemic may result in closures of third-party facilities, impact enrollment in clinical trials or impact sales of Erivedge by Genentech and/or Roche. The extent to which the COVID-19 pandemic may impact Curis's business or operating results is uncertain. Other important factors that may cause or contribute to actual results being materially different from those indicated by forward-looking statements include the factors set forth under the caption "Risk Factors" in our most recent Form 10-K and Form 10-Q and the factors that are discussed in other filings that we periodically make with the Securities and Exchange Commission ("SEC"). In addition, any forward-looking statements represent the views of Curis only as of today and should not be relied upon as representing Curis's 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.

SOURCE Curis, Inc.

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