Curis Announces Gastroenterology Publication of Encouraging Preclinical Data of Emavusertib in Pancreatic Cancers

LEXINGTON, Mass., March 7, 2022 /PRNewswire/ -- Curis, Inc. (NASDAQ: CRIS), a biotechnology company focused on the development of innovative therapeutics for the treatment of cancer, today announced that a manuscript has been published in the peer-reviewed journal *Gastroenterology,* authored by Curis collaborators at Washington University School of Medicine in St. Louis, on the role of IRAK4 in pancreatic ductal adenocarcinoma (PDAC) and the preclinical efficacy of emavusertib (CA-4948), a novel, small molecule IRAK4 inhibitor, in combination with checkpoint immunotherapy.

"Through our emavusertib clinical trials, we have seen the potential of targeting IRAK4 in indications like non-Hodgkin's lymphoma, acute myeloid leukemia and myelodysplastic syndromes," said James Dentzer, President and Chief Executive Officer of Curis. "Given the early, but compelling preclinical data outlined in *Gastroenterology*, IRAK4 targeting may have a broader application in treating solid tumors such as pancreatic cancer. We are thrilled to continue to identify new opportunities to potentially expand the development of emavusertib into additional cancer types as we work towards our goal of delivering novel, innovative cancer therapeutics in areas with significant unmet patient need."

The manuscript titled "*IRAK4 signaling drives resistance to checkpoint immunotherapy in pancreatic ductal adenocarcinoma*" concluded that tumor IRAK4 drives T-cell exhaustion in PDAC and is a promising therapeutic target when combined with checkpoint immunotherapy. Specifically, the experiments demonstrated that IRAK4 controls the NF-kB pathway and production of multiple checkpoint ligands, suppressive chemokines/cytokines, as well as hyaluronan synthase 2, all of which suppress T cell immune function against cancer. The study demonstrated that in a genetic mouse model that develops highly aggressive pancreatic cancer, IRAK4 can be targeted to overcome the immunosuppressive tumor microenvironment and drive response to checkpoint immunotherapy and validate the study of CA-4948 as a means to improve immunotherapeutic response in pancreatic cancer. The study team further confirmed this finding by generating a genetic mouse model in which the *IRAK4* gene is deleted from the pancreatic cancer, providing firm evidence that IRAK4 is a promising therapeutic target in this deadly disease.

"Historically, the tumor microenvironment's strong defense mechanisms have made cancers such as PDAC nearly impossible to treat effectively. Checkpoint immunotherapies, which have had a groundbreaking impact on other areas of oncology, are largely ineffective in PDAC," said Dr. Kian-Huat Lim, MD, PhD, Associate Professor of Medicine at Washington University School of Medicine, and Director of the GI Oncology Program. "Given the role of IRAK4 in NF-kB activation, we sought to explore whether there could be a translational benefit to targeting IRAK4 in PDAC. The results of our preclinical study show the promising effects of targeting IRAK4 in combination with chemotherapy and checkpoint immunotherapy, highlighting the potential of emavusertib to deliver effective therapeutic options to pancreatic cancer patients, who continue to have very limited therapeutic options."

The manuscript is available online at https://www.gastrojournal.org/article/S0016-5085(22)00201-3/pdf.

About Emavusertib (CA-4948)

Emavusertib is an IRAK4 kinase inhibitor and IRAK4 plays an essential role in the toll-like receptor (TLR) and interleukin-1 receptor (IL-1R) signaling pathways, which are frequently dysregulated in patients with AML and MDS. Third parties have recently discovered that the long form of IRAK4 (IRAK4-L) is oncogenic and preferentially expressed in over half of patients with AML and MDS. The overexpression of IRAK4-L is believed to be driven by a variety of factors, including specific spliceosome mutations such as SF3B1 and U2AF1.

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, emavusertib (CA-4948). Emavusertib is currently undergoing testing in the Phase 1/2 TakeAim Lymphoma trial, in patients with non-Hodgkin's lymphoma both as a monotherapy and in combination with BTK inhibitor ibrutinib. Curis is also evaluating emavusertib in the Phase 1/2 TakeAim Leukemia trial in patients with acute myeloid leukemia and myelodysplastic syndromes, for which it has received Orphan Drug Designation from the U.S. Food and Drug Administration. 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 1 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's 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, any statements concerning product research, development, clinical trials and studies and commercialization plans, timelines, anticipated results or the therapeutic potential of drug candidates including any statements regarding the activity, safety and tolerability of emavusertib (CA-4948) and any preclinical findings including potential combinations and indications; and statements of assumptions underlying any of the foregoing. Forward-looking statements may contain the words "believes," "expects," "anticipates," "plans," "intends," "seeks," "estimates," "assumes," "predicts," "projects," "targets," "will," "may," "would," "could," "should," "continue," "potential," "focus," "strategy," "mission," 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, or the CRADA with NCI, 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 and its collaborators face the risk of 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 captions "Risk Factor Summary" and "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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