Curis Announces Positive Updated Data from Ongoing Phase 1/2 Study of CA-4948 Monotherapy in Patients with Relapsed or Refractory Acute Myeloid Leukemia and Myelodysplastic Syndromes

- Updated data show marrow blast reductions in 10 out of 12 evaluable patients with elevated blast counts at baseline -
- 5 objective responses observed, including 1 complete response (CR), 1 complete remission with incomplete hematologic recovery (CRi) and negative minimal residual disease, 1 partial response (PR), and 2 marrow CRs -
- 300mg BID, the dose currently used in ongoing Lymphoma and lower-risk MDS studies, confirmed as the recommended Phase 2 dose in AML and high-risk MDS -
- Management to host virtual KOL event today, Friday, June 11 at 8:00 a.m. ET -

LEXINGTON, Mass., June 11, 2021 /PRNewswire/ -- Curis, Inc. (NASDAQ: CRIS), a biotechnology company focused on the development of innovative therapeutics for the treatment of cancer, today announced updated data from its ongoing Phase 1/2 open-label, single arm, dose escalation and expansion trial of CA-4948, a novel, small molecule IRAK4 kinase inhibitor, in patients with acute myeloid leukemia (AML) or high-risk myelodysplastic syndromes (MDS) at the European Hematology Association 2021 Virtual Congress (EHA).

"As we have observed increasingly mature sets of data, we continue to be pleased by the steady progression of clinical activity demonstrated by CA-4948 monotherapy in this historically difficult-to-treat late-line population," said James Dentzer, President and Chief Executive Officer of Curis. "We believe these updated data further support the growing body of evidence that CA-4948's anti-cancer activity continues to deepen the longer patients remain on drug, which is enabled by its safety and durability profile to date. Further, after backfilling patient cohorts and evaluating additional data after the April 30, 2021 cut-off date for today's presentation, we have concluded 300mg BID is the optimal dose to take into Phase 2 studies."

Mr. Dentzer added, "We are especially pleased with the outcomes seen to date for patients with spliceosome or FLT3 mutations. All three patients with a spliceosome mutation achieved an objective response. The FLT3 patient also achieved an objective response and, after two cycles of CA-4948, the patient's FLT3 mutation was found to be completely eradicated. While these are early days, and we have a limited set of patient data, we are very encouraged about the potential CA-4948 may have to become a disease-modifying alternative for these late-line patients, where no approved therapies currently exist."

Mr. Dentzer continued, "In addition to the updated clinical data presented today, we are also excited by the preclinical combination synergy data announced, demonstrating that CA-4948 increases anti-cancer activity in AML cell lines resistant to clinically relevant concentrations of azacitidine and venetoclax, as well as synergistic antileukemic activity in combination with venetoclax and azacitidine. We look forward to initiating dosing in the Phase 1/2 combination study of CA-4948 plus azacitidine and CA-4948 plus venetoclax in patients with R/R AML and MDS later this year."

"As a clinician for patients with high-risk MDS or AML, I am acutely aware of the challenges of these diseases and the limitations of existing treatments. I continue to be very encouraged by the data coming out of this study," said Dr. Guillermo Garcia-Manero, Chief of the Section of Myelodysplastic Syndromes within the Department of Leukemia at The University of Texas MD Anderson Cancer Center and a lead investigator in the study. "This is a late-line population, in which patients have few options following repeated treatment failures and as a result, have deeply damaged and dysfunctional marrow, which severely limits their odds of hematologic recovery. Having an effective, non-myelosuppressive drug that does not further damage their already fragile marrow is of critical importance. The fact that some hematologic recovery has been observed and appears to continue while patients remain on therapy is an indication that CA-4948 may have the potential to provide, for the first time, a well-tolerated and clinically active treatment for this subset of heavily diseased patients."

The reported data are from Curis's ongoing open-label, single arm Phase 1/2 dose escalation 3+3 study of orally administered CA-4948 monotherapy in adult patients with AML or high-risk MDS. A total of 22 patients (11 with high-risk MDS, 11 with AML) were enrolled across dose cohorts of 200 mg BID, 300 mg BID, 400 mg BID, and 500 mg BID. The primary objective of the study is to determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) for CA-4948 based on safety and tolerability, dose-limiting toxicities (DLT), and any biologic activity, pharmacokinetic (PK), and pharmacodynamic (PD) findings from the trial population. Additional objectives include characterization of CA-4948's pharmacokinetic parameters and biomarker correlations.

Key findings from an oral presentation today at EHA presented by Dr. Garcia-Manero from an April 30, 2021 cutoff in 17 evaluable patients (9 MDS and 8 AML), include:

Bone marrow blast reductions observed at all tested doses in 10 of 12 patients who were evaluable for bone marrow response (elevated blast count at baseline and at least one malignancy assessment following first cycle).
5 objective responses observed included:

- 1 patient experiencing a full hematologic recovery CR
- 1 patient with CRi with negative minimal residual disease
- 1 patient with partial response
- 2 patients with marrow CRs

3 patients had SF3B1 or U2AF1 spliceosome mutation and all 3 achieved marrow CR or better.
All patients with objective responses also saw signs of hematologic recovery.
Genomic analyses from multiple patients show disease modification by CA-4948:

- DNA sequencing demonstrates disease modification with the reduction of cancer-associated variant allele frequency after CA-4948 treatment
- RNA sequencing demonstrates disease modification with the reduction of long/short ratio of IRAK4 after CA-4948 treatment

No significant myeloid suppressive adverse events were observed.

Key findings from additional information included in today's management's KOL presentation:

An AML patient with spliceosome mutation SF3B1 who has experienced a durable objective response has been on study for over 8 months. In December 2020, this patient was reported as having a Marrow CR and has since improved to a CRi with negative minimal residual disease.
An AML patient with a FLT3 mutation, whose disease had relapsed after prior treatment with decitabine and venetoclax and was refractory to subsequent treatment with gilteritinib, experienced a partial response (90% decrease in marrow blast count, from 60% to 6%) as well as elimination of detectable FLT3 mutation based on genomic analysis post-treatment with CA-4948.
An AML patient with 4 prior lines of chemotherapy treatment showed reduction of IRAK4-L expression following CA-4948 treatment as well as a full recovery of hematologic parameters and has been on study for over 7 months.

Key findings in determining 300mg BID to be the Recommended Phase 2 Dose include:

Safety: No DLTs observed
PK/PD: PK exposure correlates with 98% target inhibition
Efficacy: 12 evaluable patients in the study had elevated blasts at baseline;
4 of these patients were dosed at 300mg BID;
All 4 patients achieved blast reductions, including CRi and negative MRD
Including additional patients enrolled after the April 30, 2021 cut-off at doses higher than the Recommended Phase 2 Dose, a total of 4 DLTs were observed:

- 400mg: 13% of patients experienced DLT (2 Grade 3 rhabdomyolysis)
- 500mg: 66% of patients experienced DLT (1 Grade 3 rhabdomyolysis and 1 Grade 3 syncope)

All three rhabdomyolysis cases were quickly detected by elevated CPK and resolved after dosing interruption; no cases involved renal dysfunction.

Key findings from a poster presentation today at EHA of preclinical data in AML cell lines:

Combination with CA-4948 increased the antitumor effect of azacitidine
Combination with CA-4948 increased the antitumor effect of venetoclax
Combination with CA-4948 increased the antitumor effect of venetoclax + azacitidine
We believe synergistic activity observed in leukemia cells provides a rationale for clinical testing of CA-4948 + azacitidine, CA-4948 + venetoclax, and the triplet combination of all three agents together in patients with AML.

Webcast Event Information

Curis management will host a virtual KOL event today, June 11, 2021 at 8:00 am ET to discuss these results with Dr. Guillermo Garcia-Manero. To access the webcast, please visit the Events & Presentations section of the Curis website at www.curis.com.

About CA-4948

CA-4948 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, CA-4948. CA-4948 is currently undergoing testing in a Phase 1/2 trial in patients with non-Hodgkin's lymphoma both as a monotherapy and in combination the with BTK inhibitor ibrutinib. Curis is also evaluating CA-4948 in a Phase 1/2 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' website at www.curis.com.

Cautionary Note Regarding 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 with respect to the potency, anti-cancer activity, durability and tolerability of CA-4948, future studies with respect to CA-4948, the potential advantages and benefits of CA-4948 and small molecule checkpoint antagonists, and the Company's plans to advance its development 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, 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 their respective portions of the research, development and commercialization costs, or that the parties will successfully discover, develop or commercialize drug candidates under the collaborations. 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 caption "Risk Factors" in Curis's most recent Form 10-K and Form 10-Q and the factors that are discussed in other filings that Curis 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'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.

For further information: Investor Relations, Stephanie Ascher, Stern Investor Relations, Inc., (212) 362-1200, stephanie.ascher@sternir.com

---