Kronos Bio Announces Selection of Recommended Phase 2 Dose for its Oral CDK9 Inhibitor, KB-0742, After Reaching Target Engagement Goal with Acceptable Safety Profile in Ongoing Phase 1/2 Clinical Trial

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Kronos Bio to move into Phase 2 stage of study, evaluating compound in patients with MYC-amplified and other transcriptionally addicted tumors

Data demonstrate achievement of target engagement goal, differentiated pharmacokinetic profile and long half-life

Detailed results from Phase 1 stage of study and initial data from Phase 2 expansion stage to be presented at medical conference in second half of 2023

SAN MATEO, Calif. and CAMBRIDGE, Mass., Dec. 07, 2022 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON), a company dedicated to transforming the lives of those affected by cancer, today announced that data from the ongoing dose-escalation stage of its Phase 1/2 clinical trial of KB-0742, the company's cyclin dependent kinase 9 (CDK9) inhibitor being developed to treat *MYC*-amplified and transcriptionally addicted solid tumors, support a recommended Phase 2 dose (RP2D) of 60 mg.

Results from the trial, including the Phase 1 stage and initial data from the Phase 2 expansion stage, will be presented at a medical conference in the second half of 2023.

An analysis of the trial results demonstrated that treatment with a 60 mg dose of KB-0742 led to a targeted reduction of approximately 50% in levels of phosphorylated Ser2 on RNA Polymerase II (pSer2), a direct substrate target of CDK9 in PBMCs. This level of target engagement is consistent with demonstrating anti-tumor activity based on preclinical models. The analysis further showed that KB-0742 continues to demonstrate a differentiated pharmacokinetic (PK) profile, with oral bioavailability and dose-proportional exposure across all four dose levels, and low to moderate variability between patients. A total of 26 patients have been enrolled and treated in the dose escalation phase of the study. Among those patients, PK data were collected and analyzed for 25 patients and KB-0742 continued to demonstrate a terminal half-life of 24 hours, with approximately 2.1 to 2.5-fold accumulation between Day 1 and Day 10. These results are consistent with findings from an initial analysis announced last year.

The long plasma half-life enables KB-0742 to achieve sustained pharmacologically active concentrations while avoiding potentially toxic peak (Cmax) concentrations. This PK profile, combined with the biochemical selectivity of KB-0742 for CDK9 over other CDK enzymes, is critical to supporting Kronos Bio's approach to defining a therapeutic window for CDK9 using a three-day-on/four-day-off treatment regimen.

In addition to achieving 50% or greater suppression of CDK9, the 60 mg dose appears to have an acceptable safety profile and the maximum tolerated dose has not yet been defined.

"These data represent important progress for our KB-0742 program, demonstrating that we were able to reach our target engagement goal, without broadly and unselectively suppressing transcription," said Norbert Bischofberger, Ph.D., president and chief executive officer of Kronos Bio. "CDK9 is a target that has been pursued for many years with limited success because of the difficulty of achieving a therapeutic window. We believe we have identified that window for KB-0742 and look forward to moving to the next stage of the study."

While the dose escalation stage of the trial will continue with the goal of reaching a maximum tolerated dose, Kronos Bio will immediately move into the second stage of the two-stage trial and begin assessing the anti-tumor activity of KB-0742 at the RP2D. Kronos Bio will enroll two cohorts of patients in this Phase 2 stage of the study. Cohort A will include patients with *MYC*-amplified tumors: triple negative breast cancer, non-small cell lung cancer and ovarian cancer. Cohort B will include patients with transcriptionally addicted cancers, including chordomas, sarcomas and small cell lung cancer.

"We are very pleased to have reached our RP2D and to begin evaluating KB-0742 in patients who we believe are most likely to benefit from treatment with the compound," said Jorge DiMartino, M.D., PhD., chief medical officer and executive vice president of Clinical Development for Kronos Bio. "We look forward to providing further updates on this program, as we now begin to evaluate the efficacy of KB-0742 in these patient populations."

The company expects to share detailed data from the Phase 1 dose escalation stage of the trial, as well as initial results from the Phase 2 expansion cohorts, at a medical conference in the second half of 2023.

About Kronos Bio, Inc.
Kronos Bio is a biopharmaceutical company that is advancing two investigational compounds in clinical trials for patients with cancer. The company is developing the CDK9 inhibitor, KB-0742, as a treatment for *MYC*-amplified solid tumors, and lanraplenib, a next-generation SYK inhibitor, for patients with relapsed/refractory FLT3-mutated acute myeloid leukemia. The company's scientific focus is on developing medicines that target the dysregulated transcription that is the hallmark of cancer and other serious diseases.

Kronos Bio is based in San Mateo, Calif., and has a research facility in Cambridge, Mass. For more information, visit www.kronosbio.com or follow the company on LinkedIn.

Forward-Looking Statements

Statements in this press release that are not statements of historical fact are forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. This press release, in some cases, uses terms such as "to be," "will," "expects," "anticipates" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: our plan to move

into the Phase 2 stage of the Phase 1/2 clinical trial of KB-0742 and the enrollment plans and trial design for such stage; our expectation to present data from such Phase 1/2 clinical trial at a future medical conference; the potential safety profile of KB-0742; and other statements that are not historical fact. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, including, without limitation: whether we will be able to initiate and complete ongoing enrollment for the Phase 2 stage of the Phase 1/2 clinical trial of KB-0742 on the timeline expected, or at all, including due to risks associated with the COVID-19 pandemic; risks inherent in the clinical development of novel therapeutics; risks related to our lack of experience as a company in conducting clinical trials; and risks associated with the sufficiency of our cash resources and need for additional capital. These and other risks and uncertainties are described in greater detail in the company's filings with the Securities and Exchange Commission ("SEC"), including under the heading "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, filed with the SEC on November 8, 2022. Any forward-looking statements that are made in this press release speak only as of the date of this press release and are based on management's assumptions and estimates as of such date. Except as required by law, the company assumes no obligation to update the forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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