Kronos Bio Presents Preclinical Data for Oral CDK9 Inhibitor KB-0742 Demonstrating Sustained Inhibition of Tumor Growth in Multiple Cancers at AACR Annual Meeting 2021

April 10, 2021

San Mateo, Calif. and Cambridge, Mass., April 10, 2021 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON), a company dedicated to transforming the lives of those affected by cancer, today presented preclinical data for KB-0742, a highly selective, orally bioavailable cyclin dependent kinase 9 (CDK9) inhibitor being developed to treat MYC-amplified solid tumors. The data showed that CDK9 inhibition on an intermittent dosing schedule with KB-0742 resulted in sustained inhibition of tumor growth in multiple types of solid tumors. The data also suggested that genomic amplification of MYC, a well-characterized transcription factor and a long-recognized driver of cancer, is a key factor of sensitivity to CDK9 inhibition. These findings were presented in a poster session today at the virtual American Association for Cancer Research (AACR) Annual Meeting 2021.

“These preclinical data support our approach to leveraging CDK9 inhibition to treat cancers that express high levels of MYC. Furthermore, the anti-tumor activity seen with intermittent dosing of KB-0742 in multiple cancer cell lines suggests that constant inhibition may not be needed in order to achieve desired target coverage,” said Jorge DiMartino, M.D., Ph.D., chief medical officer and executive vice president, clinical development. “Having recently initiated our clinical development program for KB-0742, we are eager to determine if these preclinical results translate to the clinic. If this proves to be the case, we believe KB-0742 has the potential to be an important advance in the treatment of MYC-amplified solid tumors.”

Kronos Bio researchers, in collaboration with colleagues from Baylor College of Medicine, the University of Washington and the Broad Institute, conducted several experiments to better define molecular sensitivity to transcriptional inhibition by profiling the sensitivity of various tumor types to KB-0742. They found that MYC genomic amplification emerged as a key driver of CDK9 inhibitor sensitivity, especially in non-small cell lung cancer. Additionally, MYC amplification and over-expression in tumor cells and patient-derived xenografts conferred sensitivity to CDK9 inhibition. In these CDK9-sensitive models, suppression of oncogenic transcription for more than eight hours was followed by cell death (apoptosis). Importantly, CDK9 inhibitor sensitivity was observed for both treatment-naïve and heavily pretreated patient samples, and CDK9 inhibition on an intermittent dosing schedule achieved sustained target coverage, as evidenced by both direct readouts of CDK9 activity and corresponding transcriptional response, ultimately inhibiting tumor growth in multiple solid tumor types.

The poster is now available on the AACR Annual Meeting website and in the Publications section of the Kronos Bio website. Details of the presentation are as follows:

- Title: CDK9 inhibition is selective for transcriptionally addicted tumors harboring MYC genomic amplifications
- Abstract Number: 1141
- Session Category: Experimental and Molecular Therapeutics
- Session Title: Epigenetic Targets

In February, Kronos Bio initiated a Phase 1/2 clinical trial for KB-0742 in patients with advanced solid tumors or non-Hodgkin lymphoma. The company expects to report initial safety, pharmacokinetic and pharmacodynamic data from the dose-escalation stage of the study in the fourth quarter of this year. Initial data from the study’s expansion cohorts are expected in 2022.

About KB-0742

KB-0742 is a highly selective, orally bioavailable inhibitor of cyclin dependent kinase 9 (CDK9) in development for the treatment of MYC-amplified solid tumors. CDK9 is a global regulator of transcription and plays an essential role in both the expression and function of MYC, a well-characterized transcription factor and a long-recognized driver of cancer that is amplified in approximately 30% of solid tumors, including those affecting the lungs, ovaries, esophagus, breast, stomach, pancreas and liver.1 KB-0742 was generated and optimized from a compound that was identified using the company’s proprietary small molecule microarray (SMM) screening platform.

About the Small Molecule Microarray (SMM) Screening Platform

Kronos Bio leverages its SMM screening platform to conduct high-throughput screens against traditionally undruggable target proteins, in particular transcription factors. The SMM platform directly addresses the historical challenges of targeting transcription factors by screening in conditions that preserve their associated context-dependent structures and multi-protein complexes. Using the company’s library of approximately 240,000 compounds in microarray format on slides, Kronos Bio screens for small molecule binders of the target transcription factor in context-relevant tumor nuclear lysates. Hits derived from SMM screening have the potential to act through a variety of mechanisms against various members of a transcription factor’s complex and, as such, hits are characterized for their ability to selectively modulate an oncogenic transcription factor’s activity as important criteria for further lead selection and optimization.

About Kronos Bio, Inc.

Kronos Bio is a clinical-stage biopharmaceutical company dedicated to discovering and developing therapies that seek to transform the lives of those affected by cancer. The company focuses on targeting dysregulated transcription factors and the regulatory networks within cells that drive cancerous growth. Kronos Bio’s lead investigational therapy is entospletinib, a selective inhibitor targeting spleen tyrosine kinase (SYK) in development for the frontline treatment of NPM1-mutated acute myeloid leukemia (AML). The company is also developing KB-0742, an oral inhibitor of cyclin dependent kinase 9 (CDK9), for the treatment of MYC-amplified solid tumors.
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. The press release, in some cases, uses terms such as “expected,” “leverage,” “suggest,” “achieve,” “determine,” “translate,” “believe,” “potential” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding Kronos Bio’s intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, the potential of KB-0742 to be an important advance in the treatment of MYC-amplified solid tumors; the design of the KB-0742 Phase 1/2 clinical trial, including to establish clinical proof of concept to enable potential further development; the timing of any results, including PK/PD data, from the KB-0742 Phase 1/2 clinical trial; 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 Kronos Bio will be able to complete the Phase 1/2 clinical trial of KB-0742, including due to risks associated with the COVID-19 pandemic and risks inherent in the clinical development of novel therapeutics; risks related to Kronos Bio’s lack of experience as a company in conducting clinical trials; the risk that results of preclinical studies and early clinical trials are not necessarily predictive of future results; the risk that due to the relatively small number of patients that Kronos Bio plans to dose in the planned Phase 1/2 KB-0742 clinical trial, the results from such trial, once completed, may be less reliable than results achieved in larger clinical trials, which may hinder Kronos Bio’s efforts to further develop and obtain regulatory approval for KB-0742; and risks associated with the sufficiency of Kronos Bio’s cash resources and need for additional capital. These and other risks are described in greater detail in Kronos Bio’s filings with the Securities and Exchange Commission (SEC), including under the heading “Risk Factors” in its Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 23, 2021. 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, Kronos Bio 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.

References