Kronos Bio Presents Preclinical Data on Oral CDK9 Inhibitor KB-0742, Providing Additional Evidence of Potential Efficacy in MYC-Amplified and Transcriptionally Addicted Tumors at AACR

April 8, 2022

Preclinical data featured in three posters show potential of KB-0742 in triple-negative breast, lung and ovarian cancers, as well as lymphoma and rare, soft-tissue cancers, including sarcoma and chordoma

Company will also present data demonstrating the potential of its new liquid biopsy assay platform to help evaluate patient response to KB-0742 in the ongoing Phase 1/2 study

Kronos Bio continues to enroll patients in Phase 1/2 clinical trial, with additional data anticipated in Q4 2022

SAN MATEO, Calif. and CAMBRIDGE, Mass., April 08, 2022 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON), a company dedicated to transforming the lives of those affected by cancer and other serious diseases, today shared preclinical data on its internally discovered, highly selective, oral cyclin dependent kinase 9 (CDK9) inhibitor, KB-0742, adding to evidence that the compound has the potential to treat certain MYC-amplified and transcriptionally addicted solid tumors.

The data will be presented in three posters at the American Association for Cancer Research (AACR) Annual Meeting 2022, which begins today in New Orleans. The company will also present findings on a liquid biopsy assay platform that it has developed to potentially assess patient responses in the next stage of the ongoing Phase 1/2 clinical trial of KB-0742.

“These data provide growing evidence to support our approach to the clinical development of KB-0742 and represent important progress as we continue to advance the compound,” said Jorge DiMartino, M.D., Ph.D., chief medical officer and executive vice president, Clinical Development. “As we look ahead to the Phase 2 stage of the study, these data further demonstrate that KB-0742 has promise as a treatment for patients with MYC-amplified and transcriptionally addicted tumors.”

Kronos Bio began enrolling patients in the Phase 1/2 KB-0742 trial in February 2021 and presented initial positive findings from the study in November 2021. The company anticipates presenting additional data from the Phase 1 stage of the study, including the recommended Phase 2 dose, in the fourth quarter of 2022.

The data at AACR assess KB-0742 in multiple preclinical translational model systems and will be used to help the company prioritize specific tumor types for the expansion stage of the Phase 1/2 clinical study.

In the first poster, researchers evaluated 11 tumor types using immortalized cell lines, including patient-derived cell line (PDC), patient-derived organoid (PDO) and patient-derived xenograft (PDX) models. Of the 11 cancer types, triple-negative breast cancer, ovarian cancer and lymphoma showed good responses to KB-0742. Tumor regressions were observed in the three models of ovarian cancer. For triple-negative breast cancer and ovarian cancer, immortalized cell lines and patient-derived cell lines indicated lower half maximal inhibitory concentration (IC50) values with increased MYC amplification or expression, and in vivo assessments using PDX models showed good correlation of tumor growth inhibition and MYC amplification/expression. The data also showed antitumor activity of greater than 50% tumor growth inhibition in several xenograft models of lymphoma, including one double-hit model.

Based on the analysis, the researchers concluded that triple-negative breast and ovarian cancer showed the strongest correlation between sensitivity to KB-0742 and MYC expression.

In a second poster, KB-0742 was evaluated in certain tumors that rely on dysregulated activity of a particular transcription factor to drive their malignant phenotype. These include the fusion gene *EWS-FLI1* in Ewing sarcoma, *PAX3/7-FOXO1* fusions in rhabdomyosarcoma, and *brachyury (T)* in chordoma. The activity of KB-0742 was assessed in vivo using two PDX models of chordoma. In model CF466, a dose-dependent response was observed as evidenced by increased tumor growth inhibition activity and target engagement. Researchers then evaluated KB-0742 both as a single agent and in combination with afatinib (the standard-of-care EGFR inhibitor) in the CF539 model. KB-0742 as a single agent showed similar tumor growth inhibition activity as afatinib, and the combination showed an increased response.

These findings provide additional rationale for the use of KB-0742 as a potential treatment for chordoma, sarcoma and other transcriptionally addicted tumors.

In a third poster at AACR, the company evaluated KB-0742 in small-cell lung cancer. In a panel of six PDO small-cell lung cancer models with different treatment histories, KB-0742 was active in the models, regardless of treatment history. In a separate study of four treatment-naive PDO models, KB-0742 was active in three transcription factor-driven subtypes of small-cell lung cancer, and the response correlated significantly with *c-MYC* and *MYCL* expression. Lastly, researchers used four PDX models to evaluate KB-0742 activity in vivo. The tumor growth inhibition rate ranged from 54% to 92%, with tumor regressions observed in two of the four models, and one model showed greater tumor growth inhibition with KB-0742 when compared with standard of care.

Together, these data support the evaluation of KB-0742 as a potential treatment for small-cell lung cancer.

The company also presented data on its cell-free DNA (cfDNA) liquid biopsy assay, which is designed to allow for real-time assessment of the tumor mutational landscape. The assay has the potential to serve as an accelerated and cost-effective approach to monitor response to KB-0742 in the ongoing Phase 1/2 trial by tracking changes in tumor cell burden over time.

Presentation information

Poster Title: CDK9 inhibition via KB-0742 is a potential strategy to treat transcriptionally addicted cancers
Abstract Number: 2564
Date and Time: Tuesday, April 12, 2022, 9 a.m. – 12:30 p.m.

Poster Title: CDK9 inhibitor KB-0742 is active in preclinical models of small-cell lung cancer
Abstract Number: 2565
Date and Time: Tuesday, April 12, 2022, 9 a.m. – 12:30 p.m.

Poster Title: KB-0742 is active in preclinical MYC high models of triple-negative breast cancer, ovarian, and diffuse large B-cell lymphoma
Abstract Number: 2639
Date and Time: Tuesday, April 12, 2022, 9 a.m. – 12:30 p.m.

Poster Title: Development of a liquid biopsy assay to longitudinally monitor changes in mutations' allelic frequency in response to KB-0742
Abstract Number: 535
Date and Time: Sunday, April 10, 2022, 1:30 p.m. – 5 p.m.

All times are in Central Time.

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. KB-0742 was generated and optimized from a compound that was identified using the company's proprietary small molecule microarray (SMM) screening platform.

About Kronos Bio, Inc.

Kronos Bio is an integrated discovery through late-stage clinical development biopharmaceutical company, focused on developing therapies that target the dysregulated transcription that causes cancer and other serious diseases. Kronos Bio's lead investigational compound is entospletinib, an orally administered, selective inhibitor targeting spleen tyrosine kinase (SYK) in clinical development for the frontline treatment of NPM1-mutated acute myeloid leukemia (AML) in combination with intensive chemotherapy. The company is also developing KB-0742, an orally administered inhibitor of cyclin dependent kinase 9 (CDK9), in Phase 1/2 clinical development for the treatment of MYC-amplified or overexpressing solid tumors.

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. The press release, in some cases, uses terms such as "will," "expect," "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 promise of KB-0742 as a treatment for patients with MYC-amplified and transcriptionally addicted tumors, the potential of a new liquid biopsy assay platform to help evaluate patient response to KB-0742, the anticipated timing for announcing the recommended Phase 2 dose in Kronos Bio's ongoing Phase 1/2 clinical trial of KB-0742 as well as additional data from the Phase 1 stage of the 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: 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; 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, 2021, which was filed with the SEC on February 24, 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, 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.

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