Kronos Bio Announces Pipeline Update and p300 KAT Inhibitor Development Candidate

December 18, 2023

Phase 1b portion of phase 1b/2 lanraplenib study in patients with relapsed/refractory FLT3-mutated acute myeloid leukemia completed; review of data does not support continuing to phase 2

New development candidate KB-9558 inhibits the KAT domain of p300 and thereby modulates IRF4, a key driver of multiple myeloma; IND-enabling studies underway for expected completion in Q4 2024

Kronos Bio's first development candidate, KB-0742, cleared 80 mg dose in dose escalation portion of the phase 1/2 trial; trial progresses in solid tumor expansion cohorts

Expected cash runway maintained into 2026

SAN MATEO, Calif. and CAMBRIDGE, Mass., Dec. 18, 2023 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON), a company dedicated to transforming the lives of those affected by cancer, today announced an update on its pipeline. After a review of data from the phase 1b portion of its phase 1b/2 trial of lanraplenib in combination with gilteritinib in FLT3-mutated relapsed/refractory acute myeloid leukemia (AML), the Company has decided not to proceed to phase 2. The Company is open to further development of lanraplenib, a SYK inhibitor, with a partner.

Kronos Bio also announced the designation of a new development candidate, KB-9558, which targets the lysine acetyltransferase (KAT) domain of p300, a critical node of the IRF4 transcription regulatory network (TRN). IRF4 is a key driver in multiple myeloma. KB-9558 is the second molecule to emerge from Kronos Bio's proprietary product engine and is currently in IND-enabling studies, which are expected to be completed in the fourth quarter of 2024.

Kronos Bio's first internally discovered molecule, KB-0742, an inhibitor of CDK9, has demonstrated on-mechanism, single agent anti-tumor activity and a manageable safety profile in pre-treated patients with transcriptionally addicted solid tumors. KB-0742 recently cleared the 80 mg dose in the dose escalation portion of the ongoing phase 1/2 trial. Patients currently in the two expansion cohorts will now be able to receive the 80 mg dose. The Company expects to provide data from the expansion phase of the trial in mid-2024.

"Kronos Bio was founded with a clear vision: to tackle the challenge of deregulated transcription, a hallmark of cancer," said Norbert Bischofberger, Ph.D., president and chief executive officer of Kronos Bio. "To best meet this challenge, we pursued a multi-pronged strategy using our proprietary product engine to map TRNs, find their key modulators, and identify novel drug candidates targeting those modulators. Simultaneously, we used our TRN mapping capabilities to identify existing clinical assets that we could acquire to accelerate our development efforts, such as lanraplenib. While we're disappointed not to bring lanraplenib forward, it's exciting to see our discovery efforts lead to the designation of a second internally discovered development candidate."

"KB-9558 modulates IRF4, a critical transcription factor that drives multiple myeloma," Dr. Bischofberger continued. "Existing therapies for this disease, including CAR-T and bispecific antibody therapies, are not curative, and there is substantial need for new therapies. Preclinical data indicate that treatment of multiple myeloma cells with KB-9558 leads to a rapid and potent down-regulation of IRF4, and we believe our product candidate has the potential to be an innovative treatment for patients with this incurable disease."

Dr. Bischofberger continued, "There is a strong biological rationale for targeting SYK in AML and while we observed target engagement and were able to escalate lanraplenib dosing up to 90 mg, we didn't see sufficient response in this patient population to justify continued investment. Based on these observations and other data, we believe there could be utility for lanraplenib in other indications, which we are open to pursuing with a partner. We are grateful to the patients and their families as well as the investigators and study teams for their participation in the study."

New development candidate, KB-9558

Kronos Bio's new development candidate, KB-9558, targets the KAT domain of p300, a critical node of the IRF4 TRN, which is a core oncogenic transcription program that drives multiple myeloma. IND-enabling studies for this molecule are underway and expected to complete in the fourth quarter of 2024.

"While there have been great strides in the treatment of multiple myeloma, there remains a significant unmet need for novel therapies," said Nikhil C. Munshi, M.D., director of basic and correlative science at the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute. "Patients typically cycle through existing options and become refractory to available treatments. Our research with Kronos Bio has shown that targeting p300's enzymatic activity has emerged as a promising way to inhibit IRF4, an important multiple myeloma driver gene, especially in the treatment refractory context. We look forward to continuing to work with the Kronos Bio team to bring KB-9558 to patients."

"We believe that KB-9558 is positively differentiated from compounds targeting other p300 domains," said Christopher Dinsmore, Ph.D., chief scientific officer of Kronos Bio. "In addition to its mechanistic attributes, we believe KB-9558's pharmacological properties make it well-suited to target multiple myeloma, either as a single agent or in combination."

Lanraplenib program update

Kronos Bio will not proceed with the phase 2 portion of its phase 1b/2 trial of lanraplenib in combination with gilteritinib in patients with relapsed/refractory FLT3-mutated acute myeloid leukemia. This decision was based on a review of the data from 24 patients across the four dose cohorts (20 – 90 mg lanraplenib in combination with 120 mg gilteritinib). While there were blast reductions in some patients, no complete response (CR) or CR with partial hematologic recovery (CRh) was observed, with a number of patients discontinuing early in treatment.

“We completed the phase 1b dose escalation portion of our phase 1b/2 trial this year, where we administered lanraplenib at doses up to 90 mg in combination with the approved dose of gilteritinib, without encountering dose limiting toxicities. Patients in our study were older, more heavily pre-treated, and frailer than the relapsed/refractory patients in earlier studies. Many patients experienced non-drug related infectious disease complications leading to discontinuation during the first two months of treatment without achieving the count recovery needed to achieve a CR or CRh,” said Jorge DiMartino, M.D., Ph.D., chief medical officer and executive vice president of clinical development at Kronos Bio. “Given the changes in the treatment landscape for relapsed/refractory FLT3-mutated AML, it would be challenging to demonstrate the clinical benefit of adding lanraplenib to gilteritinib in this population.”

About Kronos Bio, Inc.

Kronos Bio is a biopharmaceutical company that is advancing an investigational CDK9 inhibitor compound, KB-0742, in clinical trials as a treatment for MYC-amplified solid tumors and other transcriptionally addicted solid tumors as well as a preclinical development candidate targeting the KAT domain of p300 for multiple myeloma. The Company’s scientific focus is on developing medicines that target the deregulated 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 https://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 “anticipate,” “believe,” “could,” “expect,” “on track,” “plan,” “potential,” “promising,” “will,” 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 expected timing for completing IND-enabling studies for KB-9558; Kronos Bio’s belief that KB-9558 is well-suited to target multiple myeloma; the potential to bring KB-9558 to the clinic; the expected timing for additional clinical data from the KB-0742 trial; future dosing in the expansion cohorts of the KB-0742 trial; the potential utility of lanraplenib in other indications and the potential pursuit of any such indications with a partner; the potential of Kronos Bio’s product candidates, including any potential implied from early clinical data; Kronos Bio’s expected cash runway; 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: changes in the macroeconomic environment or competitive landscape that impact Kronos Bio’s business; whether Kronos Bio will be able to progress its preclinical studies and clinical trials on the timelines anticipated, including due to risks inherent in the development of novel therapeutics; risks related to Kronos Bio’s limited experience as a company in conducting clinical trials; the risk that results of preclinical studies and early clinical trials (including preliminary results) are not necessarily predictive of future results; 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, filed with the SEC on November 13, 2023. 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.

Media Contact:
Sarah Connors
Vice President of Corporate Affairs, Kronos Bio
857-290-7305
sconnors@kronosbio.com

Investor Contact:
Margaux Bennett
Executive Director, Business Development and Investor Relations, Kronos Bio
650-781-5026
mbennett@kronosbio.com