Kronos Bio Announces Positive End-of-Phase 2 Meeting with FDA for Entospletinib in Newly Diagnosed NPM1-mutated Acute Myeloid Leukemia (AML)

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Registrational Phase 3 trial will assess measurable residual disease (MRD) negative complete response (CR) as the primary endpoint to support potential accelerated approval

First time MRD could serve as the basis for regulatory approval in AML

Trial to begin in mid-2021, with MRD negative CR data expected in second half of 2023

SAN MATEO, Calif. and CAMBRIDGE, Mass., March 04, 2021 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON) today announced, following receipt of minutes from its End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA), that the company will proceed with its plan to assess measurable residual disease (MRD) negative complete response (CR) as the primary endpoint in a registrational Phase 3 trial to support potential accelerated approval of entospletinib in patients newly diagnosed with NPM1-mutated acute myeloid leukemia (AML). The company plans to initiate the Phase 3 trial in mid-2021, with MRD negative CR data expected in the second half of 2023.

“Even with current therapies, about half of patients with newly diagnosed NPM1-mutated AML will die from the disease within five years. Given this urgent need, we are pleased with the outcome of the FDA meeting and look forward to initiating our Phase 3 trial to establish the benefit of entospletinib, in combination with chemotherapy, as a frontline treatment for NPM1-mutated AML,” said Norbert Bischofberger, Ph.D., president and CEO of Kronos Bio. “As the first AML trial to use MRD negative CR as a primary endpoint, our trial is breaking new ground that may help deliver effective, targeted therapies more expeditiously to patients living with this devastating disease.”

MRD is a term that describes small numbers of leukemic cells that are still detectable during or after treatment, even when a patient has achieved CR by standard criteria. Remaining leukemia cells in the body can become active and start to multiply, resulting in a relapse of the disease, which is fatal for the majority of patients. Achieving MRD negativity, which is associated with longer remissions and improved survival, means that a treatment has reduced the number of leukemic cells to below the limit of detection by the most sensitive analytical methods.

“MRD has been used as a surrogate endpoint for approvals in other forms of leukemia but not for AML, in part due to the requirement for a unique marker that can be used to track rare residual leukemia cells. In the case of NPM1-mutated AML, the mutated gene itself provides that unique marker,” said John Byrd, M.D., D. Warren Brown Chair of Leukemia Research and Distinguished University Professor at The Ohio State University Comprehensive Cancer Center and chief medical officer of the Leukemia & Lymphoma Society’s Beat AML Master Trial. “The association between MRD negativity and improved survival in patients with NPM1-mutated AML is well established in the literature. Based on this body of evidence, AML experts around the world recommend monitoring MRD in patients with NPM1 mutation to guide treatment decisions. The best opportunity to achieve long-lasting remission and extend survival is to achieve MRD negativity with the first attempt at treatment.”

Kronos Bio’s global, randomized, double-blind, placebo-controlled Phase 3 trial is designed to assess the efficacy and safety of entospletinib in approximately 180 adults who have been newly diagnosed with NPM1-mutated AML. Patients will be randomized to receive entospletinib or placebo, in combination with standard induction and consolidation chemotherapy, for a minimum of two cycles. The primary endpoint of the trial will be MRD negative CR as measured by next-generation sequencing, which affords a high degree of sensitivity to detect MRD. Event-free survival (EFS) will be a key secondary endpoint, and mature EFS data will be used to support potential full approval.

About Acute Myeloid Leukemia (AML)
Acute myeloid leukemia (AML) primarily affects adults and is one of the most difficult-to-treat blood cancers. AML starts in the bone marrow and can quickly move to the blood and other parts of the body including the lymph nodes, spleen and central nervous system. Approximately 20,000 Americans are diagnosed with AML each year,[1] with the NPM1 genetic mutation found in approximately 30% of cases.[2] Relapse in AML is common,[3] and despite available treatments, nearly 11,000 Americans will die from the disease each year.[1]

About Entospletinib
Kronos Bio is developing entospletinib for the frontline treatment of NPM1-mutated acute myeloid leukemia (AML). Entospletinib is a selective inhibitor targeting spleen tyrosine kinase (SYK), a critical node in a dysregulated transcription regulatory network within AML defined by persistent high expression of the transcription factors HOXA9 and MEIS1 (HOX/MEIS).[4] Multiple AML driver mutations, including NPM1 and MLL gene rearrangements, have been associated with elevation of HOX/MEIS.[5,6] Entospletinib has been investigated in more than 700 patients with a variety of hematologic malignancies, including AML, with clinical results observed in AML patients with NPM1 mutations and MLL rearrangements that support further development of the therapy.[6,7]

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.

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

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, implied and express statements regarding intentions, beliefs or current expectations concerning, among other things: our expectations about timing and execution of anticipated milestones, including planned trial initiation; the availability of clinical data from such trials; the timing of data readout; and the timing of anticipated regulatory filings. These forward-looking statements may be accompanied by words such as “will,” “potential,” “could,” "expects," “expected,” "planned," “plans,” “look forward,” "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Any forward-looking statements in this press release are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: the impact of COVID-19 on regions in which we have operations or do business, as well as on the timing and anticipated results of our clinical trials, strategy and future operations; the delay of any current or planned clinical trials or the development of our drug candidates, including but not limited to entospletinib; the risk that the results of our clinical trials may not be predictive of future results in connection with future clinical trials; our ability to successfully demonstrate the safety and efficacy of drug candidates; the timing and outcome of our planned interactions with regulatory authorities; and obtaining, maintaining and protecting our intellectual property. These and other risks and uncertainties are described in greater detail in Kronos Bio’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, 2020, filed with the SEC on November 18, 2020. 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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