Kronos Bio Announces First Patient Dosed in AGILITY Phase 3 Clinical Trial of Entospletinib in Patients With Newly Diagnosed NPM1-mutated Acute Myeloid Leukemia

December 6, 2021

Data in the second half of 2023 could potentially lead to accelerated approval
If approved, entospletinib would be the first treatment for newly diagnosed patients with the NPM1 mutation who are fit for intensive induction

SAN MATEO, Calif. and CAMBRIDGE, Mass., Dec. 06, 2021 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON), a company dedicated to transforming the lives of those affected by cancer, today announced that the first patient has been dosed in the registrational Phase 3 AGILITY clinical trial of entospletinib, a selective inhibitor targeting spleen tyrosine kinase (SYK), in combination with standard of care anthracycline and cytarabine (7+3) chemotherapy. This trial is the first in acute myeloid leukemia (AML) to use measurable residual disease (MRD) as the primary endpoint and has the potential to support accelerated approval of entospletinib by the U.S. Food and Drug Administration (FDA) as a treatment for patients newly diagnosed with NPM1-mutated AML who are fit for intensive induction.

“With the initiation of this trial, we are taking an important step forward for patients with AML, a form of blood cancer that has been difficult to treat historically,” said Norbert Bischofberger, Ph.D., president and chief executive officer of Kronos Bio. “Even with current therapies, about half of people newly diagnosed with NPM1-mutated AML will die from the disease within five years. The use of the novel endpoint of MRD provides a pathway to potentially bring entospletinib to patients more quickly.”

Entospletinib is Kronos Bio’s lead product candidate, and the company expects to share data from the trial in the second half of 2023. The randomized, double-blind, placebo-controlled trial is designed to assess the efficacy and safety of entospletinib in combination with intensive induction and consolidation chemotherapy in approximately 180 adults who have been newly diagnosed with NPM1-mutated AML. This trial will test the hypothesis, based on robust preclinical and Phase 2 clinical data, that NPM1 mutation leads to dependency on SYK signaling. The NPM1 mutation is present in about 30% of all adult patients with AML.

“We are pleased to be participating in this trial, with the goal of improving outcomes for patients with AML,” said Karamjeet S. Sandhu, M.D., assistant professor in the Department of Hematology and Hematopoietic Cell Transplantation at City of Hope, a world-renowned research and treatment organization near Los Angeles that was the first to dose a patient in the trial. “Patients with NPM1-mutated AML are in need of better treatment options, and we are excited that we are the first center to begin treating a patient in this trial.”

The primary endpoint of the trial is MRD negative complete response (CR), as measured by molecular detection of mutant NPM1 alleles in bone marrow, which affords a high degree of sensitivity to detect MRD. Numerous clinical studies have shown that patients with NPM1 mutations who achieve MRD negative CR after induction chemotherapy survive longer than patients who achieve CR but have detectable MRD. If successful, this would be the first time MRD is used as the basis for seeking accelerated approval in AML.

The decision to proceed with this trial design was made after an End-of-Phase 2 discussion with the FDA. In the trial, patients will be randomized 1:1 to receive either entospletinib or placebo in combination with standard induction and consolidation chemotherapy. Remission and MRD status will be assessed after the first two cycles of chemotherapy and patients may receive up to a total of five cycles. Event-free survival (EFS) is a key secondary endpoint, and mature EFS data will potentially be used to support full approval.

Kronos Bio acquired entospletinib and another SYK inhibitor, lanraplenib, from Gilead Sciences in July 2020. As previously announced, under the agreement with Gilead, the initiation of the Phase 3 trial triggers a $29 million milestone payment from Kronos Bio to Gilead. The payment will be recorded in the fourth quarter.

Lanraplenib is being developed for the treatment of patients with relapsed/refractory FLT3-mutated AML and patients newly diagnosed with NPM1-mutated and/or FLT3-mutated AML who are older than 75 years old or are not eligible for intensive induction chemotherapy.

About Acute Myeloid Leukemia
Acute myeloid leukemia (AML) primarily affects adults and is one of the most difficult-to-treat blood cancers. AML starts in the bone marrow, impairing its ability to produce mature red blood cells, white blood cells and platelets. Without treatment, patients die within weeks to months from progressive bone marrow failure leading to infections, bleeding and heart failure. Approximately 20,000 people are diagnosed with AML in the United States each year, with the NPM1 genetic mutation found in approximately 30% of cases. Relapse in AML is common, and despite available treatments, nearly 11,000 people die from the disease each year in the United States.

About Measurable Residual Disease
Measurable residual 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 complete response by standard criteria. Remaining leukemic cells in the body can become active and start to multiply, resulting in a relapse of the disease, which is fatal for most 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 can be detected using fluorescently labeled antibodies that recognize specific proteins on the surface of the leukemic cells (multi-parameter flow cytometry (MFC)) or by molecular methods such as DNA sequencing or polymerase chain reaction (PCR). Molecular methods are viewed as more sensitive and reliable than MFC, but require a unique mutation or DNA sequence that is only found in the leukemic cells. NPM1 mutations provide that unique sequence in patients with NPM1-mutated AML.

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). Multiple AML driver mutations, including NPM1 and MLL gene rearrangements, have been associated with elevation of HOX/MEIS. Entospletinib has been investigated in more than 700 patients with a variety of hematologic malignancies, including AML, with clinical results observed in patients with AML who have NPM1 mutations and MLL rearrangements that support further development of the therapy.

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
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 "believe," "potential," "could," "expects," "will," "seek," "further" 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 timing for expected data from the Phase 3 clinical trial of entospletinib, potential approval and potential accelerated approval of entospletinib, the design of the Phase 3 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 3 clinical trial of entospletinib on the timeframe expected, or at all, including due to risks associated with the COVID-19 pandemic and risks inherent in the clinical development of novel therapeutics; to date there have not been any regulatory approvals on the basis of MRD status in AML; 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 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, 2021, filed with the SEC on November 9, 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.

Company Contact:
Marni Kottle
Kronos Bio
650-900-3450
mkottle@kronosbio.com

Investors:
Claudia Styslinger
Argot Partners
212-600-1902
kronosbio@argotpartners.com

Media:
Sheryl Seapy
Real Chemistry
949-903-4750
sseapy@realchemistry.com