Kronos Bio Announces FDA Clearance of Investigational New Drug Application for Lanraplenib (LANRA) for Treatment of Patients with Acute Myeloid Leukemia (AML)

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Company intends to develop LANRA as a once-daily chronic treatment for genetically-defined AML patients

Two Phase 1/2 clinical trials of LANRA are planned, with first trial to initiate in Q4 2021

SAN MATEO, Calif. and CAMBRIDGE, Mass., July 27, 2021 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON), a company dedicated to transforming the lives of those affected by cancer, today announced the U.S. Food and Drug Administration (FDA) has cleared its Investigational New Drug Application (IND) for lanraplenib (LANRA), allowing the company to proceed with a Phase 1/2 clinical trial of LANRA in patients with relapsed or refractory FLT3-mutated acute myeloid leukemia (AML) in combination with gilteritinib. Kronos Bio expects to initiate the trial in the fourth quarter of this year. The company is developing LANRA as a next-generation spleen tyrosine kinase (SYK) inhibitor, with improved pharmacokinetic (PK) and pharmacologic properties compared with entospletinib (ENTO), the company's lead program. ENTO will be evaluated in combination with standard chemotherapy in a planned Phase 3 clinical trial in patients newly diagnosed with NPM1-mutated AML.

"This LANRA IND caps off an outstanding year for our SYK portfolio, which we acquired just over a year ago. Since that time, we have nearly completed the integration of the ENTO and LANRA programs with our systems, built out the requisite clinical, translational, regulatory and manufacturing infrastructure for LANRA and ENTO and had successful interactions with the FDA, both for the ENTO Phase 3 clinical trial, as well as for LANRA in relapsed/refractory FLT3-mututated AML patients. The stage is now set to demonstrate the value of SYK inhibition for patients with this life-threatening disease," said Jorge DiMartino, M.D., Ph.D., chief medical officer and executive vice president, clinical development of Kronos Bio. "Based on the existing clinical data and differentiated pharmacologic properties of ENTO and LANRA, we have designed a complementary development strategy that seeks to maximize the impact of both investigational medicines. ENTO is entering a registrational Phase 3 clinical trial that may support its accelerated approval to treat newly diagnosed NPM1-mutated AML patients in combination with chemotherapy for a defined duration of treatment. LANRA's differentiated pharmacologic properties support its evaluation as a component of more extended combination dosing regimens with gilteritinib or venetoclax/azacitidine, which are dosed to progression. We believe this precision oncology approach will allow us to systematically address patients with genetic mutations present in more than two-thirds of the AML patient population."

This is the first IND for LANRA in an oncology indication. Previously, LANRA demonstrated an acceptable safety profile in clinical trials of more than 250 healthy volunteers and patients with autoimmune diseases. In preclinical studies, LANRA showed anti-leukemic activity equivalent to ENTO in NPM1-mutated and FLT3-mutated AML patient blood and bone marrow samples. The PK profile of LANRA enables once-daily dosing in the fed or fasted state and is compatible with proton pump inhibitors, suggesting that it may be more suitable than ENTO for chronic treatment paradigms.

The first of the two planned Phase 1/2 clinical trials of LANRA will include a dose-escalation and an expansion cohort study design. The first stage will evaluate initial safety, PK and anti-leukemic activity of escalating once-daily doses of LANRA in combination with the standard approved dose of gilteritinib. This stage also will assess FLT3 measurable residual disease negativity (if any) in patients who achieve a complete response (CR) and explore the predictive value of a number of biomarkers that may correlate with clinical outcomes. Initial data from this first stage of the trial are anticipated to be available in the second half of 2022. Once a recommended dose is established, an expansion cohort of approximately 30 patients is planned to further evaluate the safety of LANRA and assess its anti-leukemic activity as measured by composite CR rate and duration of response. These data are anticipated in the second half of 2023.

In the first half of 2022, Kronos Bio plans to initiate a second Phase 1/2 clinical trial, also involving a dose-escalation and expansion cohort study design of LANRA in combination with venetoclax/azacitidine in patients newly diagnosed with NPM1-mutated and/or FLT3-mutated AML who are older than age 75 or not eligible for intensive induction chemotherapy. Kronos Bio anticipates initial data from this trial in the first half of 2023 and proof-of-concept data from an escalation cohort in late 2023 or early 2024.

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 lead to death as a result of bone marrow failure. 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 die from the disease each year.[1]

About Lanraplenib (LANRA)
Kronos Bio is developing LANRA, a next-generation selective inhibitor targeting spleen tyrosine kinase (SYK), for the treatment of patients with orelapsed/refractory FLT3-mutated acute myeloid leukemia (AML) and patients newly diagnosed with NPM1-mutated and/or FLT3-mutated AML wh are older than 75 years old or are not eligible for intensive induction chemotherapy. LANRA has been investigated in more than 250 healthy volunteers and patients with autoimmune diseases. In preclinical studies, LANRA was shown to have anti-leukemic activity against NPM1-mutated and FLT3-mutated AML samples. The first Phase 1/2 clinical trial for LANRA in AML is scheduled to begin in Q4 2021, with a second Phase 1/2 clinical trial for LANRA in AML scheduled to begin in the first half of 2022.

About Entospletinib (ENTO)
Kronos Bio is developing ENTO for the treatment of patients who are newly diagnosed with NPM1-mutated acute myeloid leukemia (AML) and eligible for intensive induction chemotherapy. ENTO 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] ENTO 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 and FLT3 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 is developing its portfolio of spleen tyrosine kinase (SYK) inhibitors, comprised of entospletinib (ENTO) and lanraplenib (LANRA), for the treatment of NPM1-mutated and FLT3-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-dependent 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,” “proceed,” “plan,” “seek,” “may,” “believe,” “potential,” “anticipated” and similar words 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: Kronos Bio’s plans to conduct a registrational Phase 3 trial of ENTO in frontline fit NPM1-mutated AML, and the timing thereof, and the trial potentially supporting accelerated approval; Kronos Bio’s plans to conduct a Phase 1/2 trial of LANRA in relapsed/refractory FLT3-mutated AML in combination with gilteritinib, and the design and timing thereof; Kronos Bio’s plans to conduct a Phase 1/2 trial of LANRA in frontline unfit NPM1-mutated and/or FLT3-mutated AML in combination with venetoclax/azacitidine, and the design and timing thereof; the timing of data from our planned Phase 1/2 trials of LANRA; LANRA’s suitability for chronic treatment paradigms; the ability of our development strategy to maximize the impact of ENTO and LANRA; our belief that we can potentially systematically address patients with genetic mutations through our precision oncology approach; 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 current and planned clinical trials of ENTO, LANRA and KB-0742 on the timelines expected, if at all, 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; 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 March 31, 2021, filed with the SEC on May 11, 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.

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