Kronos Bio Highlights Data at AACR Ovarian Cancer Research Symposium that Supports Clinical Evaluation of Istisociclib in Advanced Ovarian Cancer

September 23, 2024

– New data show istisociclib (KB-0742) triggered cell death in preclinical ovarian cancer models of platinum and PARP-inhibitor (PARPi) resistance –

– New PK/PD results demonstrate that istisociclib given at 80mg on a 4 days on/3 days off schedule resulted in sustained downregulation of CDK9-dependent genes in peripheral blood mononuclear cells (PBMCs) –

SAN MATEO, Calif. and CAMBRIDGE, Mass., Sept. 23, 2024 (GLOBE NEWSWIRE) -- Kronos Bio, Inc. (Nasdaq: KRON), a company dedicated to developing small molecule therapeutics that address cancers and other diseases driven by deregulated transcription, today highlighted new preclinical data from a study of istisociclib (KB-0742). The poster presentation took place over the weekend at the American Association for Cancer Research (AACR) 15th Biennial Ovarian Cancer Research Symposium.

Kronos Bio is currently evaluating istisociclib, a CDK9 inhibitor, in an expansion cohort of a Phase 1/2 clinical trial to explore single agent activity in platinum-resistant high-grade serous ovarian cancer (HGSOC).

"We've demonstrated preclinical evidence that istisociclib induced DNA damage and subsequent cell death, which further supports our clinical program focused on platinum-resistant high-grade serous ovarian cancer," said Luis A. Carvajal, Ph.D., Director of Translational Development at Kronos Bio, the lead author on the poster. "Importantly, platinum or PARPi insensitive cell lines showed greater sensitivity to istisociclib in cell viability assays. Moreover, ovarian cancer cells with PARPi resistance were sensitized to PARP inhibition in the presence of istisociclib."

Dr. Carvajal added, "Based on new PK data from our ongoing clinical trial, we conclude that plasma levels were consistent with efficacious exposures observed in preclinical models of ovarian cancer, and we are excited to be enrolling patients into an expansion cohort of patients with platinum-resistant high-grade serous ovarian cancer."

From the presentation, "Preclinical and clinical data support clinical expansion of istisociclib (KB-0742), an oral CDK9 inhibitor, into platinum-resistant ovarian cancer," a summary of results is outlined below.

- *In vitro* data demonstrate that istisociclib induced apoptosis/cell death
- Istisociclib resulted in the accumulation of γH2AX, a sensitive molecular marker of DNA damage
- Istisociclib disrupted homologous recombination (HR) DNA damage repair by downregulating BRCA1 and RAD51 creating a "BRCAness" phenotype in platinum and PARP resistant HR-proficient ovarian cancer cells

From the dose escalation portion of the Company's ongoing Phase 1/2 trial of istisociclib in relapsed or refractory transcriptionally addicted advanced solid tumors, new pharmacokinetic/pharmacodynamic (PK/PD) results were presented. From the dose and schedule optimization portion of the trial evaluating 60mg and 80mg of istisociclib administered once daily on a 4 days on/3 days off schedule:

- Clinical exposures resulted in a long half-life of approximately 24 hours, and increased and prolonged weekly exposures consistent with efficacious levels observed in preclinical models
- Concurrent with increased and prolonged istisociclib exposure, deeper and more sustained downregulation of CDK9-dependent genes was observed in peripheral blood mononuclear cells (PBMCs)

The poster from the presentation is available under the Science & Pipeline section of the Kronos Bio website.

About Kronos Bio
Kronos Bio, Inc. (Nasdaq: KRON) is a clinical-stage company dedicated to developing small molecule therapeutics that address deregulated transcription, a hallmark of cancer and other diseases. Our proprietary discovery engine decodes complex transcription factor regulatory networks to identify druggable cofactors. We screen for and optimize small molecules that target these cofactors in a tumor-specific context. These efforts have yielded a preclinical pipeline along with two internally developed drug candidates. Istisociclib (KB-0742) targets CDK9 to address MYC deregulation in solid tumors and KB-9558 targets p300 to address IRF4 dependence in multiple myeloma.

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.

Contact Information: Investors: Margaux Bennett Vice President, Corporate Development and Investor Relations, Kronos Bio 650-781-5026 mbennett@kronosbio.com Media: Kelli Perkins kelli@redhousecomms.com