Nurix Announces Initial NX-1607 Phase 1 Data Presented at the 37th Annual Meeting of the Society for Immunotherapy of Cancer (SITC) Demonstrating Targeted CBL-B Inhibition in Patients with Advanced Malignancies

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Biomarker results are a positive demonstration of target engagement for this first-in-class CBL-B inhibitor

Biomarker levels achieved with NX-1607 treatment correspond to levels associated with potent anti-tumor activity in disease models

SAN FRANCISCO, Nov. 10, 2022 (GLOBE NEWSWIRE) -- Nurix Therapeutics, Inc. (Nasdaq: NRIX), a clinical-stage biopharmaceutical company developing targeted protein modulation drugs designed to treat patients with hematologic malignancies and solid tumors, presented initial biomarker data demonstrating successful target engagement of CBL-B in its ongoing Phase 1 clinical trial with oral dosing of NX-1607. These data are being presented at the 37th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), which is being held November 8 – 12th in Boston.

“We are particularly encouraged by these initial biomarker data from the Phase 1 trial of NX-1607 measured in patients with advanced malignancies, which demonstrate remarkable concordance with levels observed in preclinical studies that are associated with potent anti-tumor activity,” said Robert J. Brown, M.D., Nurix’s executive vice president of clinical development. “The proximal biomarker of CBL-B inhibition in activated T cells can be measured in whole blood and demonstrate dose-dependence in our clinical studies enabling us to assess target engagement in the clinic and guide our selection of an appropriate dose for further expansion of the trial.”

Arthur T. Sands, M.D., Ph.D., president and chief executive officer of Nurix, added, "Our multiple presentations at SITC illustrate the progress we have made in the development of our first-in-class CBL-B inhibitors. Of particular importance is the work we have done to identify, validate, and clinically implement assays of a key proximal biomarker of CBL-B inhibition which has enabled the first-in-human testing of NX-1607 and its novel mechanism of action. We look forward to providing additional clinical updates for NX-1607 in 2023.”

Summary of data presented at the SITC Annual Meeting:
NX-1607 Program

Title: Initial clinical characterization of novel proximal biomarkers for NX-1607, a first-in-class oral CBL-B inhibitor, in patients with advanced malignancies
Nurix has identified and characterized novel proximal biomarkers including phosphorylated hematopoietic lineage cell-specific protein 1 (pHS1) whose levels increase when CBL-B is inhibited and can be measured in *ex vivo* stimulated whole blood in animals and humans indicating the ability of these cells to become activated in the presence of an antigen signal such as those found in the tumor microenvironment. pHS1 is an important downstream signal of T cell activation. Preliminary pharmacokinetics and pharmacodynamic measurement of pHS1 were used to characterize the activity of NX-1607 in a first-in-human clinical trial (NCT05107674). These data demonstrate dose-responsive target engagement as measured by increases in biomarker levels in stimulated human whole blood with NX-1607 treatment reaching levels associated with anti-tumor activity in animal models at dose level 1 (5 mg) and increasing at higher doses. Preliminary PK data suggest NX-1607 has dose-proportional exposures and a mean half-life of 6 to 8 hours at doses ranging from 5 mg to 50 mg.

Title: NX-1607, a small molecule inhibitor of the CBL-B E3 ubiquitin ligase, promotes T and NK cell activation and enhances NK-mediated ADCC in a mouse lymphoma tumor model
These studies demonstrate that in addition to enhancing T-cell activation, NX-1607 renders T cells resistant to Treg and TGF-β-mediated suppression. In addition, the data demonstrate that NX-1607 treatment augments NK cell activity both in vitro, in an antibody-dependent cellular cytotoxicity (ADCC) assay using human NK cells, and in vivo, in a xenograft mouse tumor model. In a murine xenograft model of non-Hodgkin’s lymphoma (NHL), the combination of NX-1607 and rituximab (anti-CD20 Mab) significantly enhanced tumor growth inhibition and tumor rejections when compared to single agents' activity. Importantly, the survival benefit provided by the combination of NX-1607 plus rituximab was abrogated by depletion of NK cells.

About NX-1607
NX-1607 is an orally bioavailable inhibitor of Casitas B-lineage lymphoma proto-oncogene B (CBL-B) for immuno-oncology indications, including a range of solid tumor types. NX-1607 acts on T cells, NK cells, and dendritic cells to enhance anti-tumor immunity, and has demonstrated single-agent anti-tumor activity in multiple tumor models. Nurix is evaluating NX-1607 in an

ongoing, Phase 1 dose escalation and expansion trial in adults with a variety of oncology indications at multiple clinical sites. Additional information on the clinical trial can be accessed at www.clinicaltrials.gov (NCT05107674).

About Nurix Therapeutics, Inc.
Nurix Therapeutics is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of small molecule and cell therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer and other challenging diseases. Leveraging extensive expertise in E3 ligases together with its proprietary DNA-encoded libraries, Nurix has built DELigase, an integrated discovery platform to identify and advance novel drug candidates targeting E3 ligases, a broad class of enzymes that can modulate proteins within the cell. Nurix's drug discovery approach is to either harness or inhibit the natural function of E3 ligases within the ubiquitin proteasome system to selectively decrease or increase cellular protein levels. Nurix's wholly owned pipeline includes targeted protein degraders of Bruton's tyrosine kinase, a B-cell signaling protein, and inhibitors of Casitas B-lineage lymphoma proto-oncogene B, an E3 ligase that regulates T cell activation. Nurix is headquartered in San Francisco, California. For additional information visit http://www.nurixtx.com.

Forward Looking Statement
This press release contains statements that relate to future events and expectations and as such constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. When or if used in this press release, the words "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "outlook," "plan," "predict," "should," "will," and similar expressions and their variants, as they relate to Nurix, may identify forward-looking statements. All statements that reflect Nurix's expectations, assumptions or projections about the future, other than statements of historical fact, are forward-looking statements, including, without limitation, statements regarding the therapeutic potential and other advantages of NX-1607 and Nurix's other drug candidates; the planned timing and conduct of the clinical trials for NX-1607 and Nurix's other drug candidates; the planned timing for the provision of updates and findings from Nurix's clinical trials; the extent animal model data predicts human efficacy; and the extent to which Nurix's drug candidates and scientific approach may potentially address a broad range of diseases. Forward-looking statements reflect Nurix's current beliefs, expectations, and assumptions. Although Nurix believes the expectations and assumptions reflected in such forward-looking statements are reasonable, Nurix can give no assurance that they will prove to be correct. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and changes in circumstances that are difficult to predict, which could cause Nurix's actual activities and results to differ materially from those expressed in any forward-looking statement. Such risks and uncertainties include, but are not limited to: (i) whether Nurix will be able to successfully conduct Phase 1 clinical trials for NX-1607 and its other drug candidates and receive results on its expected timelines, or, at all; (ii) whether Nurix will be able to successfully complete clinical development for NX-1607 and its other drug candidates; (iii) the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; (iv) whether regulatory authorities will be satisfied with the results from Nurix's clinical studies; (v) whether Nurix will be able to obtain regulatory approval of and ultimately commercialize its drug candidates; (vi) whether Nurix will be able to fund development activities and achieve development goals; (vii) the impact of the COVID-19 pandemic on Nurix's clinical trials and operations; and (viii) other risks and uncertainties described under the heading "Risk Factors" in Nurix's Quarterly Report on Form 10-Q for the fiscal quarter ended August 31, 2022, and other SEC filings. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. The statements in this press release speak only as of the date of this press release, even if subsequently made available by Nurix on its website or otherwise. Nurix disclaims any intention or obligation to update publicly any forward-looking statements, whether in response to new information, future events, or otherwise, except as required by applicable law.

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