Nurix Therapeutics Presents Positive Clinical Data from Its Novel Bruton's Tyrosine Kinase (BTK) Degrader Programs, NX-5948 and NX-2127, at the 65th American Society of Hematology (ASH) Annual Meeting

December 11, 2023

Positive preliminary efficacy data with a favorable safety profile support plans to develop NX-5948 broadly in chronic lymphocytic leukemia (CLL)

Rapid durable complete responses in a heavily pretreated relapsed/refractory patient population support continued development of NX-2127 in non-Hodgkin lymphoma (NHL)

Nurix will webcast a Key Opinion Leader (KOL) event at 8:30 p.m. PT today to review data presented at the ASH meeting from its BTK degrader portfolio

SAN FRANCISCO, Dec. 11, 2023 (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, today presented positive clinical data from its orally available degraders of BTK, NX-5948 and NX-2127, which are being evaluated in separate Phase 1a/1b clinical trials in patients with relapsed or refractory (r/r) B-cell malignancies, including CLL, mantle cell lymphoma (MCL), diffuse large B-cell lymphoma (DLBCL), marginal zone lymphoma (MZL), follicular lymphoma (FL), primary CNS lymphoma (PCNS), and Waldenström's macroglobulinemia (WM). These data were presented in two posters at the 65th American Society of Hematology (ASH) Annual Meeting and Exposition, which is being held in San Diego, California.

"Targeting BTK is an established treatment paradigm for patients with CLL and other B-cell malignancies. BTK degraders represent a novel next generation therapy for these patients," said Alexey Danilov, M.D., Ph.D. Professor and Co-Director, Toni Stephenson Lymphoma Center, City of Hope National Medical Center and an investigator on both studies. "CLL patients whose disease progresses on or after treatment with BTK inhibitors, most often due to the development of resistance, have no effective treatment options. The oral availability of BTK degraders, their ability to target BTK mutations, and their acceptable tolerability highlight the potential for these agents in the refractory CLL treatment landscape and potentially in earlier lines of therapy."

"The emerging efficacy and safety finding from our differentiated BTK degraders, NX-5948 and NX-2127, highlight the potential of degraders to become the next dominant class of agents in the valuable BTK-targeted therapy market," said Arthur T. Sands, M.D., Ph.D., president and chief executive officer of Nurix. "This first clinical disclosure for NX-5948 supports our strategy to broadly develop NX-5948 in CLL and other non-Hodgkin lymphoma conditions."

Nurix reported data from the dose escalation stage of its Phase 1a/1b clinical trial evaluating daily oral dosing of BTK degrader NX-5948 in patients with r/r B-cell malignancies. These data were from 26 patients enrolled in cohorts 1-5 (50-450 mg) who had received a median of four prior therapies (range 2-10, including BTKi, BCL2i, bispecific antibody or CAR-T therapy) and included patients with acquired mutations associated with drug resistance. Dose-dependent pharmacokinetics (PK) were observed, resulting in rapid, robust, and sustained BTK degradation in all patients treated once daily with oral NX-5948. In the CLL population that received doses ranging from 50 to 200 mg, six of seven patients demonstrated clinical benefit with three partial responses (PR) that were all ongoing as of the October 17, 2023 data cut, including one over nine months and three showing stable disease (SD), with treatment ongoing in two patients. In NHL patients (n= 19) who were treated with doses from 50 to 450 mg, durable responses were seen across indications, with almost half the patients continuing to receive treatment as of the cut-off date. NX-5948 was well-tolerated across all doses tested (50-450 mg) with no dose limiting toxicities (DLTs) or treatment-related serious adverse events (SAEs) and no treatment emergent adverse events (TEAEs) that resulted in drug discontinuation. Importantly, there were no incidences of atrial fibrillation or hypertension. Dose escalation continues across all indications and the study is actively enrolling patients in the United States, the United Kingdom, and the Netherlands. Additional data with higher dose levels and longer treatment duration are expected in 2024.

Data from the Phase 1a dose escalation and Phase 1b dose expansion cohorts (CLL, MCL and DLBCL) of Nurix's clinical trial of NX-2127, an orally available degrader of both BTK and cereblon neosubstrates Ikaros (IKZF1) and Aiolos (IKZF3) were reported in a second poster presentation. The presentation included data from 54 patients with r/r B-cell malignancies treated once daily with NX-2127 at doses that ranged from 100 to 300 mg. The patient population had a median age of 72.5 years (range 50-92 years) and had received a median of four prior lines of therapy (range 2-11, including BTKi, BCL2i, IMiDs, bispecific antibodies, or CAR-T therapy). Among the patients with CLL, 36% had acquired BTK mutations associated with BTK inhibitor drug resistance prior to entry in the study. NX-2127 exhibited dose-dependent PK, leading to robust and sustained degradation of BTK and biologically-relevant degradation of Ikaros. Treatment with NX-2127 resulted in encouraging rapid and durable responses in this heavily pre-treated patient population with complete responses (CR) reported in two (MCL and DLBCL) of the 17 evaluable NHL patients. These responses were durable for over one year. Two PRs in other NHL patients (MZL and FL) were also reported. Among the 27 evaluable patients with CLL, 11 experienced a PR for an overall response rate (ORR) of 40.7%. This compares favorably to earlier results presented at ASH 2022 showing a preliminary 33% ORR.

NX-2127 had a manageable safety profile that was consistent with previous reports for BTK-targeted and immunomodulatory therapies. The most common grade ≥3 TEAEs were neutropenia, which showed evidence of dose response, hypertension and anemia. Atrial fibrillation was observed in six patients (11.1%, down from 17% reported previously), with three patients (5.6%) having grade ≥3 events. Twenty-one patients (38.9%) had serious TEAEs, of which eight (14.8%) had serious adverse events considered related to NX-2127 treatment. Two patients experienced DLTs (cognitive disturbance; neutropenia), and 13 patients developed TEAEs that resulted in discontinuation of NX-2127. As of the September 15, 2023 cutoff date,

treatment was ongoing in 13 patients.

Webcast details
The live webcast KOL event, which will begin at 8:30 p.m. PT (11:30 p.m. ET) on Monday, December 11, 2023, and the subsequent replay, will be available in the Investors section of the Nurix website under Events and Presentations.

About NX-5948
NX-5948 is an investigational, orally bioavailable, small molecule degrader of BTK. NX-5948 is currently being evaluated in a Phase 1 clinical trial in patients with relapsed or refractory B cell malignancies. Additional information on the ongoing clinical trial can be accessed at clinicaltrials.gov (NCT05131022).

About NX-2127
NX-2127 is a novel bifunctional molecule that degrades BTK and cereblon neosubstrates Ikaros (IKZF1) and Aiolos (IKZF3). NX-2127 is currently being evaluated in a Phase 1 clinical trial in patients with relapsed or refractory B cell malignancies. Additional information on the ongoing clinical trial can be accessed at www.clinicaltrials.gov (NCT04830137).

About Nurix Therapeutics, Inc.
Nurix Therapeutics is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative medicines 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 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, clinical stage 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 activation of multiple immune cell types including T cell and NK cells. Nurix is headquartered in San Francisco, California. For additional information visit http://www.nurixtx.com.

Forward-Looking Statements

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: Nurix's future plans, prospects and strategies; the therapeutic potential of BTK degraders; the market potential of degraders; the tolerability, safety profile, therapeutic potential and other advantages of NX-5948 and NX-2127; the planned timing and conduct of the clinical trials for NX-5948 and NX-2127; the planned timing for the provision of updates and findings from Nurix's clinical trials; 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 regarding the future of Nurix's business, its future plans and strategies, its preclinical and clinical results, future conditions and other factors Nurix believes are appropriate in the circumstances. 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-5948 and NX-2127 and receive results on its expected timelines, or, at all; (ii) the unexpected emergence of adverse events or other undesirable side effects during clinical development; (iii) whether Nurix will be able to successfully complete clinical development for NX-5948 and NX-2127; (iv) the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; (v) whether regulatory authorities will be satisfied with the results from Nurix's clinical studies; (vi) whether Nurix will be able to obtain regulatory approval of and ultimately commercialize its drug candidates; (vii) whether Nurix will be able to fund development activities and achieve development goals; (viii) the impact of macroeconomic conditions and global events on Nurix's clinical trials and operations; and (ix) 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, 2023, 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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