



## Nurix Therapeutics Presents New Positive Data from Phase 1a/1b Clinical Trial of NX-5948 in Chronic Lymphocytic Leukemia at the 66th American Society of Hematology Annual Meeting

December 9, 2024

*Durable responses are rapid and deepen on treatment as demonstrated by an initial 75.5% Objective Response Rate which increased to 84.2% in patients with at least two disease assessments*

*Treatment responses observed in heavily pre-treated population with mutations associated with poor prognosis and/or resistance to BTK inhibitors, including patients with CNS involvement*

*Favorable safety profile across all doses tested*

*Nurix will host a webcast to discuss the data presented at the ASH Annual Meeting and provide a corporate update today at 8:15 p.m. PT (11:15 p.m. ET)*

SAN FRANCISCO, Dec. 09, 2024 (GLOBE NEWSWIRE) -- Nurix Therapeutics, Inc. (Nasdaq: NRIX), a clinical stage biopharmaceutical company developing targeted protein modulation drugs designed to treat patients with cancer and inflammatory diseases, today presented new positive clinical data from patients with relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) treated in the Phase 1a/1b clinical trial of its Bruton's tyrosine kinase (BTK) degrader NX-5948. These data were presented by Nirav N. Shah, M.D., M.S.H.P., Associate Professor of Medicine, Division of Hematology and Oncology, at the Medical College of Wisconsin, and a clinical investigator on the trial, in an oral session at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition being held December 7-10, 2024, in San Diego, CA. In addition, Nurix and its collaborators presented new preclinical data for NX-5948 and its BTK and IKZF1/3 degrader NX-2127 in separate poster and oral presentations at the ASH Annual Meeting.

"We are excited to report our latest results based on enrollment of sixty relapsed/refractory CLL/SLL patients, almost double the number of patients in our previous mid-year 2024 update. With a greater number of patients and longer duration of treatment, we are highly encouraged to see a deepening of therapeutic responses over time while maintaining a favorable safety profile," said Paula G. O'Connor, M.D., chief medical officer of Nurix. "These positive results are particularly impressive given the inclusion of patients with a high incidence of baseline genetic mutations in BTK, PLCG2, and TP53, and challenging clinical factors, such as central nervous system involvement, which are associated with poor prognosis. We continue to enroll patients in the United States, the United Kingdom, and Europe in the Phase 1b portion of the trial and are on track to initiate pivotal trials of NX-5948 in 2025."

### **NX-5948 Phase 1a/1b clinical update**

As of the October 10, 2024 data cut, sixty (60) patients with relapsed or refractory CLL/SLL were enrolled. This cohort of CLL/SLL patients was a heavily pretreated population that had received a median of four prior lines of therapy (range = 1-12) including prior covalent BTK inhibitors (98.3%), prior BCL2 inhibitors (83.3%), and prior non-covalent BTK inhibitors (28.3%). At baseline, a large number of patients had mutations associated with BTK inhibitor resistance, including mutations in BTK (38.6%) and PLC2G (12.3%). Poor prognostic features were common, including TP53 mutations (40.4%), and five patients (8.3%) had central nervous system (CNS) involvement.

The data presented at the ASH Annual Meeting include safety findings for all patients in the NX-5948 Phase 1a/1b dose escalation and expansion cohorts (n=125), including those with CLL/SLL and those with non-Hodgkin's lymphoma (NHL). Patients were treated with NX-5948 at starting doses ranging from 50 mg to 600 mg once daily by oral administration, and intra-patient dose escalation was permitted per protocol. NX-5948 was well tolerated across all doses evaluated, and safety findings in the CLL/SLL cohort were consistent with the overall population as well as previous safety analyses. Among the CLL/SLL patients, the most common treatment emergent adverse events were purpura/contusion (36.7%, all grade 1 or 2), fatigue (26.7%, all grade 1 or 2), petechiae (26.7%, all grade 1 or 2), neutropenia (23.3%, 18.3% grade 3 or higher), and rash (23.3%, 1.7% grade 3 or higher). Importantly, across the entire population, there was only one case of grade 1 atrial fibrillation in a patient with pre-existing atrial fibrillation.

Among the efficacy evaluable patients with CLL/SLL (n=49), NX-5948 treatment resulted in a robust objective response rate (ORR) of 75.5% across all doses tested, with the majority of responses occurring at the first assessment (Week 8). With longer time on treatment, the ORR increased to 84.2% based on an exploratory efficacy analysis of patients who had at least two response assessments (Week 16). Responses were observed across all populations regardless of prior treatment, baseline mutations, high-risk molecular features, or CNS involvement. This includes patients with baseline BTK mutations associated with treatment resistance to both covalent and non-covalent BTK inhibitors. Robust BTK degradation was observed in all patients, including those with baseline BTK mutations.

Responses were durable with the median duration of response not reached. Thirteen patients had duration of response greater than six months, and five patients remain on treatment and in response beyond one year of treatment.

### **Additional preclinical data presentations**

Nurix and its collaborators presented new preclinical data for NX-5948 in an animal model of primary CNS lymphoma (PCNSL) and assessed the impact of NX-2127 on T cell function.

Preclinical data were presented demonstrating the positive effects of brain-penetrant NX-5948 treatment on survival in a patient-derived xenograft model of primary central nervous system lymphoma (PCNSL) in a poster titled: *BTK Degradation As a Novel Therapeutic Strategy in Relapsed CNS*

*Lymphoma: Proof of Concept Studies in Intracranial Patient-Derived, Rodent Models.* The data demonstrate that daily oral administration of NX-5948 drives potent degradation of BTK, inhibition of extracellular signal-regulated kinase (ERK) and prolonged survival in the setting of CNS lymphoma. In addition, transcriptional changes associated with enhanced tumor antigen presentation and reduced tumor progression were observed in NX-5948 treated animals. Notably, oral administration of ibrutinib resulted in similar level of ERK inhibition but did not lead to prolonged survival or the same pattern of transcriptional changes in the model, suggesting that BTK degradation by NX-5948 exhibits differential biology relative to BTK inhibition by ibrutinib, a result that may be associated with the elimination of BTK's scaffolding function by NX-5948.

In addition, preclinical results were presented demonstrating that although both NX-2127 and NX-5948 effectively degrade BTK in primary CLL cells while preserving T-cell activation and survival *in vitro*, NX-2127 demonstrates unique immunomodulatory activity. These data were the subject of an oral presentation titled: *NX-2127 and NX-5948, Two Clinical Stage Cereblon-Recruiting BTK Degraders, Facilitate T Cell Functionality in Chronic Lymphocytic Leukemia*. Specifically, the data demonstrate distinct immunomodulatory effects in NX-2127 treated CLL cells, including upregulation of CD38, an interferon (IFN)-response gene, bolstering the immune response, promotion of T cell differentiation towards a TH1 phenotype, enhancing anti-tumor immunity, reduction in Treg differentiation, which supports a shift toward a less immunosuppressive microenvironment and enhancement of immunological synapse formation, and T cell-mediated cytotoxicity. In addition, RNA sequencing revealed unique patterns of gene expression in NX-2127-treated CLL cells, distinguishing responders from non-responders and further demonstrating its distinctive T cell modulatory effects.

**About NX-5948:** NX-5948 is an investigational, orally bioavailable degrader of BTK that is currently being evaluated in a Phase 1a/b clinical trial in adults with relapsed or refractory B-cell malignancies. Additional information on the Phase 1a/b clinical trial can be accessed at [www.clinicaltrials.gov \(NCT05131022\)](http://www.clinicaltrials.gov/NCT05131022).

**About NX-2127:** NX-2127 is an investigational, orally bioavailable degrader of BTK and cereblon neosubstrates Ikaros (IKZF1) and Aiolos (IKZF3). NX-2127 is currently being evaluated in a Phase 1a/b clinical trial in adults with relapsed or refractory B-cell malignancies. Additional information on the ongoing clinical trial can be accessed at [www.clinicaltrials.gov \(NCT04830137\)](http://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 small molecules and antibody therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer, inflammatory conditions, 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 cells 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 plans to initiate pivotal trials of NX-5948 in 2025 and statements regarding the tolerability, safety profile, therapeutic potential and other advantages of NX-5948 and NX-2127. 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) the risks inherent in the drug development process, including the unexpected emergence of adverse events or other undesirable side effects during clinical development; (ii) uncertainties related to the timing and results of clinical trials; (iii) the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; (iv) whether Nurix will be able to successfully complete clinical development for, obtain regulatory approval of, and ultimately commercialize NX-5948 and NX-2127; (v) whether Nurix will be able to fund its research and development activities and achieve its research and development goals; (vi) the impact of economic and market conditions and global and regional events on Nurix's business and clinical trials; (vii) whether Nurix will be able to protect intellectual property and (viii) other risks and uncertainties described under the heading "Risk Factors" in Nurix's Quarterly Report on Form 10-Q for the fiscal period ended August 31, 2024, 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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