



Nurix Therapeutics Reports First Clinical Evidence of CNS Activity of NX-5948, a Brain-Penetrant, Orally Available, BTK Degradator in Development for B Cell Malignancies

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Presented new case studies demonstrating clinical responses in two patients with B cell malignancies, chronic lymphocytic leukemia (CLL) and primary central nervous system lymphoma (PCNSL), each with central nervous system (CNS) involvement

Data presented at the American Association for Cancer Research (AACR) 2024 Annual Meeting

Brain activity highlights potential for broader application of NX-5948 in autoimmune disorders with CNS involvement

SAN FRANCISCO, April 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 announced the presentation of the first findings of clinical responses in the brain for NX-5948, an orally available, selective degrader of Bruton's tyrosine kinase (BTK). The presentation included case studies for two patients, one with CLL with CNS involvement and the other with PCNSL, each demonstrating clinically meaningful responses. The presentation also provided evidence of measurable drug levels in the CNS of multiple patients in the ongoing Phase 1 trial who had CNS tumor involvement. These data were presented by Gwenn M. Hansen, Ph.D., chief scientific officer of Nurix, as part of the Major Symposium session *Molecular Glues, PROTACs, and Next-Gen Degradators: Discovery and Early Preclinical Advances* at the AACR 2024 Annual Meeting, which is being held from April 5-10, 2024, in San Diego, CA.

"These data are the first demonstration of clinical activity in the brain of a targeted protein degrader, opening the door for new therapeutic strategies to treat leukemias and lymphomas with CNS involvement," said Dr. Hansen. "The brain penetration of NX-5948 coupled with the clinical activity and safety profile presented to date, suggests a potential role in the treatment of B-cell lymphomas and chronic lymphocytic leukemia involving the CNS which are notoriously difficult to treat. It also suggests the potential to use NX-5948 as a therapeutic option for immune indications with CNS involvement such as multiple sclerosis."

Dr. Hansen's presentation included new data from the dose escalation stage of Nurix's Phase 1a/1b clinical trial evaluating daily oral dosing of BTK degrader NX-5948 in patients with relapsed or refractory B-cell malignancies. Data were presented demonstrating detection of NX-5948 in the cerebrospinal fluid (CSF) from all patients with available CSF samples. Case studies were presented for two of these patients.

In one case study, a CLL patient was enrolled with secondary CNS involvement whose disease progressed following three prior lines of treatment, including both a BCL2 inhibitor in combination with rituximab and a BTK inhibitor (acalabrutinib). This patient, who presented with malignant cells in the CSF at study entry and the high-risk cytogenetic marker Del17p, received NX-5948 at a once daily dose of 100 mg. By week 8, the patient had significant lymph node reduction and spleen reduction consistent with stable disease. By week 16, the patient had experienced continued reduction in lymph nodes and spleen size and improvements in hematologic measures consistent with a partial response. By week 24, the partial response was confirmed and the patient no longer had measurable tumor cells in the CSF. As of March 4th, the patient remains on treatment in cycle 10 of therapy (>36 weeks).

In the other case study, a patient was enrolled with primary central nervous system lymphoma (PCNSL) with the high-risk cytogenetic marker of MYC rearrangement and whose disease progressed after two prior lines of therapy, including high dose multi-drug chemotherapy with rituximab in the first-line setting, and ibrutinib in the second line, which yielded a best response of stable disease. The patient presented with three measurable lesions in the right temporal lobe and received NX-5948 at the 450 mg once daily dose. By week 8, the patient experienced complete regression of all three lesions and demonstrated a complete response (CR). A subsequent 16 week scan revealed that this patient's disease had progressed with the emergence of a new brain lesion.

"These clinical responses seen to date with NX-5948 in patients with significant brain disease support future exploration of NX-5948 both as a single agent and in combination with other therapies that are used for primary and secondary CNS lymphoma and leukemia," said Arthur T. Sands, M.D., Ph.D., president and chief executive officer of Nurix. "The CLL patient with CNS involvement showed an impressive durable response with NX-5948 as single agent therapy in this setting. The patient with PCNSL, and an aggressive NHL histology, showed a rapid, complete response, providing clear evidence of therapeutic effect in the brain that has the potential to be augmented through combination therapies to improve durability of response."

About Central Nervous System (CNS) Lymphoma

CNS involvement of B cell malignancies span various conditions including: Primary CNS lymphoma (PCNSL) comprising 4% of all primary CNS tumors and 4-6% of all extranodal lymphomas; secondary CNS lymphoma (SCNSL) which represents a risk of ~5% in patients with diffuse large B cell lymphoma (DLBCL); and CNS involvement in CLL which albeit rare, presents a poor prognosis in patients with clinically significant disease.

About NX-5948

NX-5948 is an investigational, orally bioavailable, brain penetrant, 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. Nurix has previously reported that NX-5948 is highly potent against a range of tumor cell lines that are resistant to current BTK inhibitor therapies, an important consideration in heavily pretreated CLL/SLL patient populations. Additional information on the ongoing clinical trial can be accessed at [clinicaltrials.gov \(NCT05131022\)](https://clinicaltrials.gov/NCT05131022).

About Nurix

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 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 plans and strategies with respect to NX-5948, including the future use of NX-5948 both as a single agent and in combination with other therapies, and the potential advantages and therapeutic benefits of NX-5948, including its potential role in the treatment B-cell lymphomas and CLL involving the CNS, its potential as a therapeutic option for immune indications with CNS involvement, and its potential when used in combination with other therapies. 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; (iv) whether Nurix will be able to fund its research and development activities and achieve its research and development goals; (v) the impact of economic and market conditions and global and regional events on Nurix's business, clinical trials, financial condition, liquidity and results of operations; (vi) whether Nurix will be able to protect intellectual property and (vii) other risks and uncertainties described under the heading "Risk Factors" in Nurix's Annual Report on Form 10-K for the fiscal year ended November 30, 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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