Nurix Therapeutics Announces Initial Data from the First Phase 1a Dose Escalation Trial of NX-2127 in Patients with Relapsed or Refractory B Cell Malignancies

October 27, 2021

Robust BTK target degradation achieved in all patients treated to date

Greater than 90% degradation of BTK was achieved at the 200 mg dose of NX-2127

These data represent the first proof of mechanism of targeted protein degradation in patients with hematologic malignancies

Nurix to host a conference call today at 8:30 a.m. ET

SAN FRANCISCO, Oct. 27, 2021 (GLOBE NEWSWIRE) -- Nurix Therapeutics, Inc. (Nasdaq: NRIX), a biopharmaceutical company developing targeted protein modulation drugs, today announced initial data demonstrating clinically meaningful degradation of Bruton's tyrosine kinase (BTK) in patients with relapsed or refractory B cell malignancies, including in a chronic lymphocytic leukemia (CLL) patient with significant mutations in the BTK gene associated with resistance to standard of care BTK inhibitors. These results will be presented by Nurix's president and chief executive officer Arthur T. Sands, M.D., Ph.D., and Nurix's senior vice president of clinical development Robert J. Brown, M.D., at the 4 th Annual Targeted Protein Degradation (TPD) Summit at 11:45 a.m. ET today, October 27, 2021. The slides for this presentation will be made available in the investor section of the company's website.

"The initial data from our study are the first proof-of-mechanism of targeted protein degradation in patients with hematologic malignancies," said Arthur T. Sands, M.D., Ph.D., president and chief executive officer of Nurix. "The concept of degrading BTK as a new therapeutic strategy in hematologic cancer has taken an important step forward, and the NX-2127 program has hit an exciting milestone in its clinical development."

Initial PK and PD data from the first two completed cohorts of 100 mg and 200 mg, which included a total of six patients, showed BTK levels in peripheral blood significantly decreased in all patients in the trial starting on day 1 and remained suppressed throughout the dosing period. BTK degradation exceeded 80% at steady state in the first dose cohort and exceeded 90% in the second dose cohort. Such levels of BTK degradation have been associated with anti-tumor effects in preclinical animal models. For example, in a preclinical lymphoma model, BTK degradation of 80% in the peripheral blood was associated with 74% tumor growth inhibition, and BTK degradation of 90% was associated with 100% tumor growth inhibition.

The clinical data presented includes a notable case study with early evidence of clinical activity in the first patient enrolled (Cohort 1, n=1 at 100 mg dose). Patient 1 is a 78-year-old male diagnosed with CLL who had received 2 prior lines of therapy including most recently ibrutinib. Genetic analysis of CLL cells from this patient prior to initiation of NX-2127 revealed a BTK mutation in 68% of leukemic cells with multiple mutations at site C481 which has been associated with resistance to ibrutinib. Patient 1 remains on study now over 4 months, allowing for two disease assessments at prespecified periods which showed that the patient has thus far achieved a partial response with improved clinical parameters.

"Patients with relapsed and refractory B cell malignancies continue to require new drugs and new modalities to address their unmet medical need, and we believe that NX-2127 may offer a novel mechanism to block uncontrolled B cell signaling and tumor growth with the further potential to overcome acquired resistance to current treatments," said Robert J. Brown, M.D., senior vice president of clinical development. "The safety profile of NX-2127 to date is encouraging and we look forward to completing the dose escalation portion of the study and moving into the expansion phase in selected cancers in the first half of 2022."

The Phase 1a dose escalation portion of the Phase 1a/1b trial is ongoing with enrollment of patients with a variety of relapsed or refractory B cell malignancies. The trial is evaluating once daily oral NX-2127 starting at a dose of 100 mg. Pharmacokinetic (PK) and pharmacodynamic (PD) measurements are taken at multiple time points on day 1 and throughout the dosing period. NX-2127 dosed orally once daily was tolerated, and there were no dose limiting toxicities (DLTs) observed at the 100 mg and 200 mg dose levels, with the 300 mg dose now open for enrollment. NX-2127 appears to be well-tolerated at this early stage with a safety profile that is consistent with its known mechanisms of action. Five of six patients remain on NX-2127 for durations ranging from 4 to 19 weeks. One patient with Waldenstrom's macroglobulinemia discontinued treatment after two weeks due to progressive disease.

Conference Call Information

Nurix will host a live conference call and webcast on Wednesday, October 27, 2021 at 8:30 a.m. ET. To join the live conference call by telephone, please dial 1 (844) 348-6877 (U.S.) or +1 (253) 336-3591 (International). The conference ID number for the live call is 1837008.

To access the live webcast, please visit the Investors section of the Company's website and follow the link under Events & Presentations. A replay of the webcast will be available on the Company's website for approximately 30 days.

Presentation Details

- Conference: 4th Annual Targeted Protein Degradation Summit
- Session: Clinical Update on Degraders in the Clinic, Key Learnings & Future Directions
- Title: Turning Degraders into Drugs – NX-2127 & NX-5948
- Time: 11:45 a.m. ET
- Presenter: Arthur T. Sands, M.D., Ph.D., President and CEO

About NX-2127
Nurix's lead drug candidate from its protein degradation portfolio, NX-2127, is an orally bioavailable degrader of BTK with immunomodulatory drug (IMiD) activity for the treatment of relapsed or refractory B-cell malignancies. NX-2127 harnesses the normal cellular protein degradation mechanism, the E3 ligase-mediated ubiquitin-proteasome pathway, to catalyze degradation of BTK. BTK is an enzyme involved in B-cell development, differentiation and signaling that is critical for proliferation and survival of lymphoma and leukemia cells in many B-cell malignancies. Inhibitors of BTK, such as ibrutinib, are approved for treatment of B-cell cancers, however certain patients cannot tolerate them and in other patients, specific mutations can arise in the BTK protein that confer resistance to these agents, thereby reducing their efficacy. Degradation of BTK has the potential to overcome resistance in patients harboring such mutations in BTK. In addition, NX-2127 catalyzes degradation of transcription factors involved in regulating T-cell function, resulting in T-cell activation in a similar fashion to IMiDs that have demonstrated efficacy in some aggressive B-cell malignancies.

About the Phase 1, Dose Escalation Study of NX-2127
The multicenter Phase 1a/1b study is designed to evaluate safety, pharmacokinetics, pharmacodynamics and preliminary clinical activity of orally administered NX-2127 in adult patients with relapsed or refractory B-cell malignancies. The study will be conducted in two parts. The Phase 1a element is a dose-escalation study in which cohorts of patients will receive ascending oral doses of NX-2127 once daily to determine the maximum tolerated dose (MTD) and/or the optimal Phase 1b dose based on safety and tolerability. The second portion of the study, Phase 1b, is a dose expansion phase in which cohorts of patients with specific cancers will receive NX-2127 to further evaluate the safety, and clinical activity of the recommended dose. The study is expected to enroll eligible patients with the following cancers: chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) with or without BTK mutations, Waldenstrom's macroglobulinemia (WM), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), follicular lymphoma (FL), and diffuse large B-cell lymphoma (DLBCL), who have required and received prior systemic therapies. Additional information on the clinical trial can be accessed at ClinicalTrials.gov (NCT04830137).

About Nurix Therapeutics, Inc.
Nurix Therapeutics is a biopharmaceutical company focused on the discovery, development, and commercialization of small molecule therapies designed to modulate cellular protein levels as a novel treatment approach for cancer and other challenging diseases. Leveraging Nurix's 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 more information, please 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 our future financial or business performance, conditions, plans, prospects, trends or strategies and other financial and business matters; our current and prospective drug candidates; the planned timing and conduct of our clinical trial programs for our drug candidates, preclinical activities, research and development costs, current and prospective collaborations; the potential advantages of our DELigase® platform and drug candidates; the extent to which our scientific approach and DELigase® platform may potentially address a broad range of diseases; the estimated size of the market for our drug candidates; and the timing and success of the development and commercialization of our anticipated drug candidates. Forward-looking statements reflect Nurix's current beliefs, expectations, and assumptions regarding the future of Nurix's business, future plans and strategies, its development plans, its preclinical 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) risks and uncertainties related to Nurix's ability to advance its drug candidates, obtain regulatory approval of and ultimately commercialize its drug candidates; (ii) the timing and results of preclinical and clinical trials; (iii) Nurix's ability to fund development activities and achieve development goals; (iv) the impact of the COVID-19 pandemic on Nurix's business, clinical trials, financial condition, liquidity and results of operations; (v) Nurix's ability to protect intellectual property and (vi) other risks and uncertainties described under the heading "Risk Factors" in Nurix's Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 16, 2021, Nurix's Quarterly Report on Form 10-Q filed with the SEC on October 14, 2021, 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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