



Nurix Therapeutics Presents Positive Clinical Results from its Novel BTK Degradar (NX-2127) at the 64th American Society of Hematology (ASH) Annual Meeting

December 12, 2022

Treatment with NX-2127 provides clinically meaningful responses in heavily pretreated chronic lymphocytic leukemia (CLL) patients regardless of Bruton's tyrosine kinase (BTK) mutational status

BTK mutations conferring resistance to both covalent and non-covalent BTK inhibitors remain susceptible to degradation by NX-2127

Nurix will host a Key Opinion Leader (KOL) webinar event at 9:30 pm ET today to review data presented at ASH and progress in its degrader portfolio

SAN FRANCISCO, Dec. 12, 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, today presented additional positive clinical data from its Phase 1 clinical trial of NX-2127 in two oral sessions by Anthony Mato, M.D., MSCE, former director of the Chronic Lymphocytic (CLL) Program at Memorial Sloan Kettering Cancer Center, and Omar Abdel-Wahab, M.D., Chair of Sloan Kettering Institute (SKI) Molecular Pharmacology Program at Memorial Sloan Kettering Cancer Center. NX-2127 is a once daily, oral, investigational new drug that combines BTK degradation with immunomodulatory activity. The podium presentations took place at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition which is being held in New Orleans, Louisiana.

"These early Phase 1 data demonstrate that NX-2127 effectively degrades BTK resulting in clinically meaningful responses independent of prior treatments or BTK mutational status and offering a potential new treatment modality for patients who have otherwise exhausted other approved and emerging treatment options," said Robert J. Brown, M.D., Nurix's executive vice president of clinical development.

The data presented by Dr. Mato demonstrate that treatment with NX-2127 results in sustained BTK degradation and clinically meaningful responses in heavily pretreated patients with relapsed/refractory CLL independent of prior treatments or BTK mutational status. These presentations included preliminary data from 36 adults with relapsed/refractory B-cell malignancies enrolled in the Phase 1a/b study, including 23 patients with CLL who had undergone and failed a median of five prior therapies including a BTK inhibitor. Approximately 78% of this group had previously received both BTK and BCL2 inhibitors and 35% had been treated with the non-covalent BTK inhibitor pirtobrutinib. Of the CLL patients, 48% had one or more identified BTK resistance mutations prior to treatment with NX-2127. Following treatment with NX-2127 in this heavily pretreated CLL population, sustained BTK degradation and decreased B cell activation were observed regardless of prior treatment and baseline BTK mutation status with an overall response rate (ORR) of 33% (95% CI 12–62%). As of September 21, 2022, the data cut-off date, the median follow up was 5.6 months (0.3 to 15.7 months), and 14 of 23 patients remained on treatment. Importantly, the safety profile of NX-2127 was consistent with prior results from the Phase 1a portion of the trial and reports for BTK-targeted therapies in heavily pretreated patients with B cell malignancies.

"We are excited by the growing body of data generated in our Phase 1a/1b clinical trial of NX-2127 which highlights the significant differentiation and potential advantages of BTK degradation over BTK inhibition, especially in the setting of resistance to existing therapies," said Arthur T. Sands, M.D., Ph.D., president and chief executive officer of Nurix. "We continue to explore the promise of this first-in-class targeted protein degrader of BTK as we enroll additional CLL patients in the ongoing expansion cohort and continue to enroll patients with non-Hodgkin lymphoma in the dose escalation. We look forward to additional clinical updates in 2023."

The presentation by Dr. Abdel-Wahab highlighted critical scientific findings underlying the emergence of new BTK inhibitor resistance mutations that lack BTK's enzymatic function but still drive tumor growth. These so-call "kinase deficient" and "kinase dead" mutations underscore the importance of BTK's scaffolding function, which is uniquely addressable by the BTK degrader modality. In the presentation, five different clinically emergent BTK resistance mutations were analyzed and categorized as kinase proficient, kinase deficient, or kinase dead, each conferring a different spectrum of resistance to available therapies. NX-2127 was found to be broadly active against all these mutations. These findings translated into clinically meaningful BTK degradation in the Phase clinical 1 trial and clinical activity independent of baseline BTK mutations.

Webcast details

The live KOL webinar event, which will begin at 8:30 pm CT (9:30 pm ET) on Monday, December 12, 2022, and the subsequent replay, will be available in the Investors section of the Nurix website under [Events and Presentations](#).

About the Phase 1, Study of NX-2127

The multicenter Phase 1 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 is being 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), Waldenström 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 NX-2127

NX-2127 is a novel bifunctional molecule that degrades Bruton's tyrosine kinase (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.

About Nurix

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 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 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 the tolerability, safety profile, therapeutic potential and other advantages of NX-2127; the planned timing and conduct of the clinical trials for 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. 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-2127 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-2127 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 macroeconomic conditions, including as a result of the COVID-19 pandemic, inflation and rising interest rates 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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