Nurix Therapeutics Presents Data at the American Association for Cancer Research (AACR) Annual Meeting Highlighting Activity of its BTK Targeted Protein Degraders, NX-2127 and NX-5948, against a Broad Range of BTKi Resistance Mutations

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Oral presentation features structural disclosure and preclinical characterization of NX-2127, Nurix's lead BTK degrader for the treatment of B-cell malignancies

Poster presentation highlights specificity and potency of NX-5948 and superior cellular activity of both NX-2127 and NX-5948 against BTKi resistance mutations compared to other published BTK degraders

SAN FRANCISCO, April 17, 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 announced presentations covering its targeted protein degradation programs, including the structural disclosure of NX-2127 and new preclinical data for NX-2127 and NX-5948, highlighting their superior activity against acquired mutations in Bruton's tyrosine kinase (BTK), a key therapeutic target in the treatment of B-cell malignancies. These data are being presented at the American Association for Cancer Research (AACR) Annual Meeting which is being held from April 14-19, 2023, in Orlando, FL.

"Our presentations at the AACR meeting highlight the features of our targeted BTK degraders that enable them to uniquely address a broad group of acquired BTK inhibitor resistance mutations," said Arthur T. Sands, M.D., Ph.D., president and chief executive officer of Nurix. "Nurix is leading the field in developing a superior class of Targeted Protein Degrader drug candidates that have broad capabilities against both wild-type BTK and across all mutations thus far tested with the potential to provide a new treatment modality for patients for whom existing options have failed."

Details of the AACR Presentations
In a poster presentation entitled *NX-5948 promotes selective, sub-nanomolar degradation of inhibitor-resistant BTK mutants,* preclinical data were presented demonstrating the potent tumor cell-killing activity of Nurix's BTK degraders (NX-5948 and NX-2127) against a broad range of acquired BTK inhibitor resistance mutations and their superiority compared with other reported degraders. Specifically, NX-5948 was shown to target and promote potent degradation of the V416L, T474I, and L528W BTKi resistance mutations that reduce or eliminate the activity of next-generation non-covalent inhibitors of BTK, such as pirtobrutinib. The broad range of activity of NX-2127 and NX-5948 against BTK mutations relative to BTK inhibitors and other BTK degraders provides further mechanistic rationale for the ongoing clinical trials in patients with advanced B cell malignancies.

"The presentations at the AACR and ACS meetings illustrate Nurix's approach which combines rational drug-design principles with a deep understanding of the biochemistry of E3 ligases and the pharmacodynamics of targeted protein degraders," noted Gwenn Hansen, Ph.D. , Nurix's chief scientific officer. "Our unique drug discovery expertise enables us to design targeted protein modulators that can address one or more key therapeutic targets, combining activities into a single molecule, which may have advantages in certain diseases."

The mechanistic basis for overcoming mutational resistance is supported by data demonstrating that NX-5948 binds BTK and the E3 ligase cereblon cooperatively, enabling it to maintain a stable ternary complex and retain degradation activity against certain BTKi resistance mutations despite a reduction in binding affinity to mutant BTK proteins. BTK degradation by NX-5948 was shown to be highly selective in proteomics assessments with no significant off-target activity identified in primary T cells, TMD8 cells, or MM-1R cells treated with NX-5948.

In an oral presentation entitled *First Disclosure of NX-2127, an oral targeted degrader of Bruton's tyrosine kinase (BTK) with concurrent immunomodulatory activity for the treatment of B-cell malignancies*, the structure of NX-2127 was disclosed to the broader oncology audience at AACR following its initial disclosure in an oral presentation at the American Chemical Society Spring meeting on March 29, 2023. The presentation also included the preclinical characterization and initial pharmacokinetic and pharmacodynamic data in humans.

All presentations and posters are available for registered attendees for on-demand viewing on the AACR website. Nurix's AACR presentations are also available on the Posters and Presentations section of the scientific resources page of the Nurix website.

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. Additional information on the ongoing clinical trial can be accessed at www.clinicaltrials.gov (NCT04830137).

About NX-5948
NX-5948 is an investigational, orally bioavailable, small molecule degrader of BTK that, differentiated from NX-2127, has been designed as a single target degrader. 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 Nurix Therapeutics, Inc.
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 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 plans, prospects and strategies; our current and prospective drug candidates; the planned timing for the provision of clinical updates and initial findings from our clinical studies; the potential advantages of our drug candidates; and the extent to which our 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) 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 clinical trials; (iii) Nurix's ability to fund development activities and achieve development goals; (iv) the impact of macroeconomic conditions 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 Quarterly Report on Form 10-Q for the fiscal quarter ended February 28, 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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