Nurix Therapeutics Presents New Preclinical Data Supporting NX-2127 and DeTIL-0255 Clinical Programs at the American Association for Cancer Research Annual Meeting

April 8, 2022

Studies provide insight into bifunctional molecular mechanism and first in vivo demonstration of immunomodulatory imide drug (IMiD) activity of NX-2127, resulting in robust tumor cell killing

Animal models of adoptive cell therapy support the use of NX-0255 in the production of an investigational drug-enhanced TIL therapy, DeTIL-0255

SAN FRANCISCO, April 08, 2022 (GLOBE NEWSWIRE) -- Nurix Therapeutics, Inc. (Nasdaq: NRIX), a clinical stage biopharmaceutical company developing targeted protein modulation drugs, today announced the presentation of preclinical data that support the clinical development of investigative therapies NX-2127 and DeTIL-0255, for the treatment of B-cell malignancies and solid tumors, respectively, at the American Association for Cancer Research (AACR) Annual Meeting. The meeting is being held from April 8-13, 2022 in New Orleans, LA.

“Our data presentations at the AACR meeting highlight the breadth and potential of our protein modulation platform to create therapies that could be transformative for patients with cancer,” said Gwenn M. Hansen, Ph.D., Nurix’s chief scientific officer. “These presentations showing the unique activity of two proprietary small molecule protein modulators, NX-2127 and NX-0255, provide clear scientific rationale supporting our ongoing clinical programs for NX-2127 in B-cell malignancies and DeTIL-0255 for solid tumors. We plan to provide clinical updates from both programs in the second half of 2022.”

In a poster presentation entitled: *Concurrent degradation of BTK and IMiD neosubstrates by NX-2127 enhances multiple mechanisms of tumor killing (Abstract 1126)*, Nurix scientists present data that demonstrate the bifunctional activity of NX-2127 to degrade Bruton’s tyrosine kinase (BTK) and immunomodulatory imide drug (IMiD) neosubstrates, Aiolos and Ikaros. These data provide support for the application of NX-2127’s unique combination of BTK degradation and IMiD activity as a therapy for B-cell malignancies with potentially enhanced efficacy over the individual therapy classes alone.

Additional details include:

- Efficient BTK degradation was observed in a range of B-cell lymphoma lines notably a cell line that expresses the most common BTK inhibitor (BTKi)-resistance mutation found in the clinic (C481S).
- In a model of diffuse large B-cell lymphoma, data demonstrate that once-daily oral dose of NX-2127 promoted BTK and Aiolos degradation leading to complete tumor regression.
- NX-2127’s IMiD activity was demonstrated by the ability to degrade Aiolos and Ikaros in resting primary human T cells, enhancing IL-2 secretion, which serves as a marker of T cell activation. The potent degradation of Ikaros by NX-2127 in mantle cell lymphoma cells lines directly correlates to its superior anti-tumor activity.
- NX-2127 treatment of B-cell lymphoma lines resulted in superior tumor cell killing activity compared to IMiDs and BTKis including a C481S BTKi resistant line.
- NX-2127 treatment resulted in downregulation of genes that are important for DNA replication, DNA repair, and cell cycle progression in tumor cells which may be a contributing factor to the robust tumor cell killing activity observed.
- NX-2127 treatment also demonstrated strong upregulation of CD1c expression, a marker for antigen presenting cells, which may lead to enhanced recognition of certain tumor cells by T cells.

“Our data provide mechanistic insight into the dual BTK-degrading and IMiD activities of NX-2127 and highlight the potential advantages of orally available NX-2127 over current therapeutic options for the treatment of B-cell malignancies,” said Robert J. Brown, M.D., Nurix’s executive vice president of clinical development. “We believe that the combination of BTK degradation, which is effective against BTK inhibitor resistant mutants, with IMiD activity can potentially provide a superior treatment option addressing significant unmet needs of patients suffering from B-cell malignancies.”

In a second poster entitled: *Ex-vivo inhibition of CBL-B with a novel small molecule inhibitor, NX-0255, enhances persistence and anti-tumor activity of adoptively transferred CD8+ T cells in mouse tumor models (Abstract 573),* Nurix scientists present data that demonstrate that adding the CBL-B inhibitor NX-0255 during ex-vivo expansion of tumor-specific T cells leads to a cell therapy that can confer a more durable anti-tumor response. These results support the use of NX-0255 in the production of an investigational drug-enhanced TIL therapy, DeTIL-0255, which is currently in a Phase 1 clinical trial.

Additional details include:

- Mice treated with T-cells cultured with a combination of NX-0255 and IL-2 demonstrated superior anti-tumor activity and survival vs. T cells cultured with NX-0255 or IL-2 alone.
- T-cells cultured with NX-0255 persisted longer in circulation.
- The addition of NX-0255 increased the frequency and absolute numbers of less exhausted CD8+ memory T-cells, increasing their in vivo persistence and ability to infiltrate the tumor.

All presentations and posters will be available for registered attendees for on-demand viewing on the AACR website on April 8, 2022 at 1:00 PM ET. The posters are also available on the Events and Presentations page of the Investors section of Nurix's website.

About NX-2127
NX-2127 is a novel bifunctional molecule that degrades Bruton's tyrosine kinase (BTK) and IMiD neosubstrates. NX-2127 is currently being evaluated in a Phase 1a/1b clinical trial in patients with relapsed or refractory B cell malignancies. Initial data from the Phase 1a dose-escalation portion of the study demonstrated clinically meaningful degradation of BTK in all patients, including in a chronic lymphocytic leukemia patient with significant mutations in the BTK gene associated with resistance to standard of care BTK inhibitors. Nurix expects to present additional data from this study in the second half of 2022. Additional information on the clinical trial can be accessed at www.clinicaltrials.gov (NCT04830137).

About NX-0255
NX-0255 is an inhibitor of Casitas B-lineage lymphoma proto-oncogene B (CBL-B) designed to enhance the function of ex vivo expanded T cells for adoptive cell transfer. Nurix has an open Phase 1 clinical trial to evaluate NX-0255-treated TILs (DeTIL-0255) in adults with gynecological malignancies. Nurix anticipates dosing the first patient in the first half of 2022 and providing a clinical update from the run-in portion of the study in the second half of 2022. Additional information on the clinical trial can be accessed at www.clinicaltrials.gov (NCT05107739).

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 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; the planned timing for the provision of clinical updates and initial findings from our clinical studies; the potential advantages of our DELigase™ platform and drug candidates; and the extent to which our scientific approach and DELigase™ platform may potentially address a broad range of diseases. 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 and clinical 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 studies 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 for the fiscal year ended November 30, 2021, Nurix's Quarterly Report on Form 10-Q for the fiscal period ended February 28, 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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