Nurix Therapeutics Presents Positive Preclinical Data at the AACR 2025 Annual Meeting from Multiple Orally Available, Brain Penetrant Degraders Against Three High Value Oncology Targets

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Nurix's lead BTK degrader, bexobrutideg, demonstrates exceptional efficiency, with a single molecule degrading approximately 10,000 copies of BTK per hour

BRAF degrader demonstrates broad activity across all three BRAF mutation classes

Aurora A kinase degraders demonstrate potential to address both enzymatic and scaffolding functions and promote tumor regression in brain and small cell lung cancer models

SAN FRANCISCO, April 25, 2025 (GLOBE NEWSWIRE) -- Nurix Therapeutics, Inc. (Nasdaq: NRIX), a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted protein degradation medicines, today announced multiple preclinical presentations at the American Association for Cancer Research (AACR) 2025 Annual Meeting supporting several programs, each with different drug targets for indications with central nervous system (CNS) involvement. The AACR Annual Meeting is being held from April 25-30, 2025, in Chicago, IL.

“The data we are presenting at AACR highlight the power of our DEL-AI platform to design and create potent, orally available degraders that overcome the limitations of inhibitors, target difficult to treat mutations, and access the CNS, a feature which is particularly important for patients whose tumor has metastasized to the brain,” said Gwenn M. Hansen, Ph.D., chief scientific officer of Nurix. “We look forward to advancing these programs in pursuit of novel therapeutic options for the benefit of patients living with cancer.”

In a poster titled: “*NX-5948 is a CNS-penetrant catalytic Bruton’s tyrosine kinase (BTK) degrader that breaks established design rules for CNS drugs,”* data were presented that highlight the unique physico-chemical properties of NX-5948, now called bexobrutideg, that differentiate it from traditional brain penetrant drugs. Bexobrutideg exhibits CNS exposure in several preclinical models and, most importantly, is detectable in the cerebrospinal fluid of patients where it has demonstrated clinically meaningful responses in patients with primary CNS lymphoma or chronic lymphocytic leukemia with CNS involvement. An important feature of protein degraders compared to small molecule inhibitors is their catalytic nature. In vitro experiments enabled calculation of the catalytic efficiency of bexobrutideg, demonstrating that a single molecule can degrade approximately 10,000 copies of BTK protein per hour at clinically relevant concentrations, which means that activity and efficacy can be achieved at much lower concentrations of a degrader as compared to an inhibitor.

In a second poster titled: *NRX-0305: a pan-mutant BRAF degrader with broad preclinical efficacy, brain penetrance, and synergistic potential with MEKi across class 1/2/3 BRAF-mutant cancers,* preclinical data were presented from Nurix’s differentiated BRAF degrader, NRX-0305, which degrades all three classes of mutant oncogenic BRAF proteins while sparing wildtype BRAF in healthy cells. Mutations in BRAF, a key component of the mitogen-activated protein kinase (MAPK) pathway, drive oncogenic transformation and are commonly found in a variety of cancers including melanoma, non-small cell lung cancer (NSCLC) and colorectal cancer (CRC). BRAF mutations are categorized into three mutational classes (Class 1-3). While approved BRAF inhibitors (BRAFi) provide survival benefit to Class 1 patients, drug durability and efficacy are limited by the emergence of primary and acquired resistance. Furthermore, patients who have progressed on BRAFi, especially in melanoma, frequently present with brain metastases, for which there are limited treatment options due to poor CNS penetrance of available drugs. New data demonstrate that BRAF degradation correlates with reduced tumor cell viability across a panel of clinically relevant BRAF mutations, supporting the role of degradation in driving antiproliferative effects. In disease models, data demonstrated broad anti-tumor efficacy of NRX-0305 across all three BRAF mutation classes and in tumors that are resistant to existing therapies. Specifically, NX-0305 demonstrated superior anti-tumor efficacy in a xenograft (PDX) model derived from a patient with a class 1 BRAF mutation whose tumor was resistant to both pembrolizumab + BRAFi compared to a competitor BRAF degrader CFT1946. In addition, the data showed anti-tumor efficacy as a single agent and in combination with MEKi in class 3 (G466V) NSCLC cell-derived xenograft (CDX) models.

On Tuesday, April 29, 2025, Nurix scientists will also present data from the company’s ongoing collaboration sponsored by Alex’s Lemonade Stand Foundation (ALSF), a leading funder of pediatric cancer research, to develop a drug to potentially treat aggressive childhood cancers including neuroblastoma and medulloblastoma. As part of the collaboration, Nurix has identified a panel of selective, orally bioavailable degraders of Aurora A kinase (AURKA), an oncogene frequently overexpressed in these pediatric cancers and in adult solid tumors and hematologic malignancies. While several AURKA inhibitors are effective in

preclinical tumor models, this activity has failed to translate into clinical efficacy, which may be explained by recent studies that found that AURKA has kinase-independent scaffolding functions that are not effectively blocked through enzymatic inhibition. In an oral presentation titled "*Identification of selective, orally bioavailable Aurora A degraders for treatment of pediatric and adult cancers*," Nurix will highlight preclinical data from studies of NRX-4972, an orally bioavailable and highly selective brain penetrant AURKA degrader. The data demonstrate that daily oral administration of NRX-4972 resulted in downregulation of MYCN as well as induction of DNA damage, apoptosis, and G2/M arrest, the latter set of effects being more pronounced in the context of degradation rather than AURKA inhibitor, which translated into significant efficacy in a model of neuroblastoma. Data comparing AURKA degradation to inhibition in a second efficacy model will be included in the upcoming oral presentation on Tuesday, April 29, 2025.

About Bexobrutideg (NX-5948)
Bexobrutideg is an investigational, orally bioavailable, brain penetrant, small molecule degrader of BTK. Bexobrutideg is currently being evaluated in a Phase 1a/b 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 NRX-0305
NRX-0305 is a potent, selective, and orally bioavailable mutant-specific BRAF degrader that Nurix is exploring for use in oncology. Nurix has reported preclinical data demonstrating potent anti-tumor activity in multiple cell line-derived and patient-derived xenograft disease models representing Class I, Class II and Class III B-RAF mutations. Anti-tumor activity was also observed in the setting of CNS disease and treatment-resistance, suggesting the potential for utility across a broad range of solid tumor types.

About Aurora A Kinase
Aurora A kinase (AURKA) is an oncogene frequently overexpressed in adult solid tumors, hematologic malignancies, and pediatric cancers. Several AURKA inhibitors are effective in preclinical tumor models, but this activity has failed to translate into clinical efficacy. To address the limitations of inhibitors, Nurix has designed bifunctional targeted protein degraders of AURKA that enable removal of both enzymatic and scaffolding functions.

About Nurix Therapeutics, Inc.

Nurix Therapeutics is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of targeted protein degradation medicines, the next frontier in innovative drug design aimed at improving treatment options for patients with cancer and inflammatory diseases. Nurix's wholly owned, clinical stage pipeline includes degraders of Bruton's tyrosine kinase (BTK), a B-cell signaling protein, and inhibitors of Casitas B-lineage lymphoma proto-oncogene B (CBL-B), an E3 ligase that regulates activation of multiple immune cell types including T cells and NK cells. Nurix also is advancing multiple potentially first-in-class or best-in-class degraders and degrader antibody conjugates (DACs) in its preclinical pipeline. Nurix's partnered drug discovery pipeline consists of preclinical stage degraders of IRAK4 and STAT6, as well as multiple additional programs under collaboration agreements with Gilead Sciences, Inc., Sanofi S.A. and Pfizer Inc., within which Nurix retains certain options for co-development, co-commercialization and profit sharing in the United States for multiple drug candidates. Powered by a fully AI-integrated discovery engine capable of tackling any protein class, and coupled with unparalleled ligase expertise, Nurix's dedicated team has built a formidable advantage in translating the science of targeted protein degradation into clinical advancements. Nurix aims to establish degrader-based treatments at the forefront of patient care, writing medicine's next chapter with a new script to outmatch disease. Nurix is headquartered in San Francisco, California. For additional information visit http://www.nurixtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and other federal securities laws. Any statements contained herein that do not describe historical facts, including, but not limited to, statements regarding Nurix's plans and expectations for, and the potential benefits of, its drug candidates and preclinical programs; and the potential benefits of protein degraders as compared to protein inhibitors, are forward-looking statements that involve risks and uncertainties that could cause actual results to differ materially from those discussed in such forward-looking statements. 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 and preclinical studies; (iii) whether Nurix will be able to fund its research and development activities and achieve its research and development goals; (iv) 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; (v) whether Nurix will be able 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 quarter ended February 28, 2025, and subsequent filings with the SEC. Any of these risks and uncertainties could materially and adversely affect Nurix's business and results of operations, which could, in turn, have a significant and adverse impact on Nurix's stock price. Nurix cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. Nurix undertakes no obligation to update publicly any forward-looking statements to reflect new information, events or circumstances after the date they were made or to reflect the occurrence of unanticipated events.

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