Nurix Therapeutics Presents Preclinical Data from Two Autoimmune and Inflammatory Disease Programs, NX-5948 and GS-6791, at ACR Convergence 2024

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Data demonstrate potential superiority of a targeted protein degradation strategy compared to kinase inhibition for both BTK and IRAK4 targets in select inflammatory and autoimmune diseases

SAN FRANCISCO, Nov. 17, 2024 (GLOBE NEWSWIRE) -- Nurix Therapeutics, Inc. (Nasdaq: NRIX), a clinical stage biopharmaceutical company developing targeted protein modulation drugs designed to treat patients with cancer and inflammatory diseases, today announced the presentation of preclinical data, including mechanism of action and relevant disease models, from two pipeline programs: NX-5948 and GS-6791. NX-5948 is Nurix's proprietary, orally available, brain penetrant Bruton's tyrosine kinase (BTK) degrader, which is being developed for the potential treatment of inflammation and autoimmune diseases in addition to its ongoing Phase 1b trial in patients with B-cell malignancies. GS-6791 is a selective, orally bioavailable degrader of interleukin-1 receptor-associated kinase 4 (IRAK4), which is being developed in collaboration with Gilead Sciences for the potential treatment of rheumatoid arthritis and other inflammatory diseases. These data were presented in two posters at ACR Convergence 2024, the annual meeting of the American College of Rheumatology (ACR), being held November 14–19, 2024, in Washington, D.C.

"The preclinical data presented at ACR Convergence underscore the exceptional potential of our targeted protein degradation strategy compared to kinase inhibition for both BTK and IRAK4, which are critical targets in inflammatory and autoimmune diseases, and support continued advancement of these drug candidates into clinical studies," said Arthur T. Sands, M.D., Ph.D., president and chief executive officer of Nurix. "These programs showcase the capability of Nurix's DELigase platform to generate potent best-in-class degrader drug candidates with the potential to deliver superior efficacy in several inflammatory diseases."

BTK mediates signaling downstream of the B cell receptor (BCR), toll-like receptors (TLRs), and Fc receptors (FcRs), making it an attractive therapeutic target in antibody-mediated autoimmune and inflammatory diseases. BTK has been shown to have both kinase and scaffold activities that are key to its function. Targeting BTK can reduce the production of new antibodies and mitigate the inflammation induced by existing antibodies, addressing key challenges in inflammatory and autoimmune diseases. In a poster titled: *NX-5948, a Clinical-Stage BTK Degrader, Achieves Deep Suppression of BCR, TLR, and FcR Signaling in Immune Cells and Demonstrates Efficacy in Preclinical Models of Arthritis and Other Inflammatory Diseases,* data illustrate the potential benefit of the BTK degrader NX-5948, which is equivalent or superior to inhibition of BTK across multiple mechanistic studies and models of inflammatory diseases. In primary B cells, NX-5948 promotes rapid degradation of BTK and more potently suppresses proximal BCR signaling and BCR- and TLR-mediated B cell activation than current BTK inhibitors under development. In a model of established collagen-induced arthritis, oral administration of NX-5948 achieves equal or superior improvement of clinical scores and deeper suppression of plasma cell numbers compared to BTK inhibitors. NX-5948 also demonstrates efficacy in several other models of inflammatory diseases including antibody-induced glomerulonephritis (a model of lupus nephritis), autoimmune lymphoproliferative syndrome (ALPS, a second model of lupus-like disease), passive cutaneous anaphylaxis (a model of allergic response including chronic spontaneous urticaria), and experimental autoimmune encephalitis (a model of multiple sclerosis).

IRAK4 plays a critical role in TLR- and interleukin-1 family receptor (IL-1R) signaling to induce inflammatory responses. Like BTK, IRAK4 has both kinase and scaffold functions, the latter of which have been shown to be particularly critical in IL-1 and TLR-mediated signaling across diverse cell types. GS-6791, a targeted protein degrader of IRAK4, provides a differentiated mode of action compared with inhibition of kinase activity.

In a poster titled: *IRAK4 Degrader GS-6791 Inhibits TLR and IL-1R-Driven Inflammatory Signaling, and Ameliorates Disease in a Preclinical Arthritis Model,* data demonstrate that GS-6791 is a potent degrader of IRAK4 *in vitro* and *in vivo* across a range of cell types. In PK/PD models GS-6791 inhibits IL-1- and TLR-induced cytokine release and results in deeper reduction of human B cell and synovial fibroblast cytokine responses compared to IRAK4 kinase inhibitors. In a preclinical model of arthritis, orally administered GS-6791 demonstrates robust, dose-dependent efficacy.

The poster presentations are available online in the Scientific Resources section of the Nurix Therapeutics website under Posters and Presentations.

About NX-5948: NX-5948 is an investigational, orally bioavailable degrader of BTK that is currently being evaluated in a Phase 1a/b clinical trial in adults with relapsed or refractory B-cell malignancies. Additional information on the Phase 1a/b clinical trial can be accessed at www.clinicaltrials.gov (NCT05131022).

About GS-6791 (previously NX-0479): GS-6791 is a potent, selective, oral IRAK4 degrader. Degradation of IRAK4 by GS-6791 has potential applications in the treatment of rheumatoid arthritis and other inflammatory diseases. Nurix's collaboration partner, Gilead Sciences, is responsible for conducting IND-enabling studies and advancing this program to clinical development.

About Nurix Therapeutics, Inc.

Nurix Therapeutics is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative small molecules and antibody therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer, inflammatory conditions, 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, clinical stage 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 activation of multiple immune cell types including T cell and NK cells. 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 the potential advantages and therapeutic benefits of NX-5948 and GS-6791 generally or as compared to inhibitors, the potential role of NX-5948 and GS-6791 in the treatment of inflammatory and autoimmune disease, the potential benefits and advantages of Nurix's scientific approach and DELigase™ platform, and the extent to which mechanistic studies and preclinical model data predict human efficacy, 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 ability of each party to perform its obligations under the Nurix-Gilead collaboration; (ii) whether the parties will be able to successfully conduct and complete preclinical development, clinical development and commercialization of any drug candidates under the Nurix-Gilead collaboration; (iii) the risks inherent in the drug development process, including the unexpected emergence of adverse events or other undesirable side effects during clinical development; (iv) uncertainties related to the timing and results of preclinical studies and clinical trials; and (v) other risks and uncertainties described under the heading "Risk Factors" in Nurix's Quarterly Report on Form 10-Q for the period ended August 31, 2024, 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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