Nkarta Announces IND Clearance of Investigator-Sponsored Trial in Myasthenia Gravis and Opening of Enrollment for Ntrust-2

December 5, 2024

Ntrust-2 open to enroll patients with systemic sclerosis, myositis and ANCA-associated vasculitis across three parallel cohorts

Investigator-Sponsored Trial (IST) expands the development of NKX019 to neuromuscular autoimmune disease myasthenia gravis

Patient dosing initiated and enrollment open in Ntrust-1 and IST of NKX019 in systemic lupus erythematosus

Clinical data from Ntrust-1 and Ntrust-2 planned for 2025

SOUTH SAN FRANCISCO, Calif., Dec. 05, 2024 (GLOBE NEWSWIRE) -- Nkarta, Inc. (Nasdaq: NKTX), a biopharmaceutical company developing engineered natural killer (NK) cell therapies, today announced the opening of Ntrust-2 to enrollment and the IND clearance for an investigator-sponsored trial (IST) that will evaluate NKX019, Nkarta's allogeneic, CD19-directed chimeric antigen receptor (CAR) NK-cell therapy, in patients with myasthenia gravis (MG). Ntrust-2, a multi-center clinical trial, will evaluate NKX019 across three parallel cohorts, including patients with systemic sclerosis (SSc, scleroderma), idiopathic inflammatory myopathy (IIM, myositis) and ANCA-associated vasculitis (AAV). The IST will be led by researchers at the University of California, Irvine and the University of Kansas Medical Center.

NKX019 is an allogeneic, off-the-shelf, chimeric antigen receptor (CAR) NK-cell therapy candidate engineered to deplete CD19-positive cells in B-cell mediated disease. The approach leverages the potential advantages of NK cell therapy, including rapid B-cell killing without the need for cell expansion, a lower risk of toxicities associated with rapid cell expansion, fludarabine-free lymphodepletion to reduce toxicity, and the added utility of on-demand dosing, including the opportunity for repeated dosing as needed.

"The expansion to these four autoimmune indications, in addition to continued execution across our existing clinical trials for lupus nephritis and systemic lupus erythematosus, speaks to the promise of our investigational NK cell therapy, NKX019, to provide a safe and accessible treatment option for people living with autoimmune disease," said Paul J. Hastings, CEO of Nkarta.

Ntrust-2 is a multi-center, open label, dose escalation clinical trial that builds on academic studies of durable, drug-free remissions in patients with autoimmune disease after CD19-targeted cell therapy. The trial will enroll patients with SSc, IIM or AAV into parallel cohorts. Per the trial protocol, patients receive NKX019 on Days 0, 3, and 7 following lymphodepletion with cyclophosphamide, an agent with an established safety profile across autoimmune diseases. The trial will assess the safety of NKX019 as well as its ability to enable long-term remissions via a "reset" of the immune system through the elimination of pathogenic B cells.

The dual-center, single-arm, open-label Phase 1 IST will be led by Ali A. Habib, M.D., Clinical Professor of Neurology at the University of California, Irvine (UCI), and other investigators.

"While the development of new therapies continues to improve outcomes for people living with myasthenia gravis, there remains considerable need for further improvements in clinical outcomes, as well as therapy administration. Most current therapies require ongoing and potentially life-long treatment. Cell therapy has the potential to move away from chronic dosing and change the treatment paradigm for people with myasthenia gravis," said Dr. Habib.

The IST is designed to enroll patients with myasthenia gravis and will evaluate safety and clinical outcomes. Translational and biomarker studies, including autoantibodies, cytokine profiles and pharmacokinetics are also planned. Patients will receive NKX019 on Days 0, 3 and 7 following single-agent lymphodepletion with cyclophosphamide.

Myasthenia gravis (MG) is an autoimmune disorder where communication between nerves and muscles is disrupted. The condition occurs when the immune system's B cells produce antibodies that block or damage the neuromuscular junction, leading to muscle weakness and fatigue. Symptoms fluctuate and vary in severity, and in more life-threatening cases, MG can affect muscles responsible for breathing. There is currently no cure for MG, and treatment typically requires chronic immunosuppressive medicines.

Preliminary data from Ntrust-1 and Ntrust-2 are anticipated in 2025. As previously announced, a first patient was dosed in Ntrust-1, a clinical trial of NKX019 for the treatment of lupus nephritis, and in an IST of NKX019 for the treatment of systemic lupus nephritis led by researchers at the Columbia University Irving Medical Center. Both studies remain open to enrollment.

About Systemic Sclerosis
Systemic sclerosis (SSc, scleroderma) is a progressive autoimmune disease characterized by inflammation and hardening in the skin and other areas of the body including blood vessels and vital organs, especially the lungs. Aberrant immune responses involving autoantibodies induce an inflammatory response in normal tissues that causes the body to produce excess collagen, leading to tight, hard tissue and injury to blood vessels. There are approximately 100,000 people in the U.S. living with SSc. There are no available treatments to halt or reverse the disease process. Approved therapies focus primarily on disease symptoms and can involve significant side effects.

About Myositis
Idiopathic inflammatory myopathy (IIM, myositis) is a group of autoimmune disorders characterized by inflammation, weakness, muscle damage, pain, and compromised quality of life. The disease can affect vital organs and be life-threatening. Across the three major subtypes thought to be driven by B cells, dermatomyositis (DM), immune-mediated necrotizing myopathy (IMNM) and anti-synthetase syndrome (ASyS), there are an estimated 50,000 people in the U.S. living with the disease. Despite approved therapies, many people with myositis have refractory disease.

About ANCA-associated Vasculitis
Anti-neutrophilic cytoplasmic autoantibody (ANCA) vasculitis is an autoimmune disease characterized by severe, systemic damage to small blood vessels. ANCAs attach to neutrophils, a type of white blood cell, and cause the neutrophils to attack small blood vessels walls, causing inflammation. Inflamed vessels may rupture or become blocked, leading to clinical symptoms and a systemic inflammatory response. Patients may have disease-related complications, such as life-threatening damage to the kidneys, lungs and other organs, as well as toxicities associated with treatment, such as long-term use of immunosuppressants like glucocorticoids. It is estimated that approximately 140,000 people in the U.S. are living with vasculitis.

About SLE
Systemic lupus erythematosus (SLE) is an autoimmune disease that causes the body's immune system to attack its own tissues. The dysregulated immune system produces antibodies that can affect various organs, including the skin, joints, kidneys, heart, and brain. Symptoms can include fatigue, joint pain, or severe life-threatening organ disease. SLE can cause lupus nephritis (LN), a severe complication that affects the kidneys.

About the Ntrust Clinical Trials in Autoimmune Disease
Ntrust-1 and Ntrust-2 are multi-center, open label, dose escalation clinical trials that build on academic studies of durable, drug-free remissions in patients with autoimmune disease after CD19-targeted cell therapy. Both trials will assess the safety of NKX019 in people living with autoimmune diseases as well as its ability to enable long-term remissions via a "reset" of the immune system through the elimination of pathogenic B cells. Per the trial protocols, patients receive three-dose cycles of NKX019 at 1 billion or 1.5 billion cells per dose following single-agent lymphodepletion with cyclophosphamide, an agent with an established safety profile across autoimmune diseases. Leveraging the engineering of NKX019, no patients in either trial will receive supplemental cytokines or antibody-based therapeutics. This approach is designed to evaluate the single-agent activity of NKX019 and facilitate a more rapid path to regulatory approval.

In the Ntrust-1 study (NCT06557265), patients with refractory lupus nephritis receive three-dose cycles of NKX019 following lymphodepletion. Patients in Ntrust-1 may also receive additional cycles to restore response.

Ntrust-2 will enroll patients with systemic sclerosis (scleroderma), idiopathic inflammatory myopathy (myositis), and ANCA-associated vasculitis (AAV) into parallel cohorts, and NKX019 will be dosed on Days 0, 3, and 7, a regimen that may be advantageous across all Nkarta clinical trials. Each trial is designed to initially enroll up to 12 patients.

About the Investigator-Sponsored Clinical Trial of NKX019 for Generalized Myasthenia Gravis
The single-arm, open-label Phase 1 investigator-sponsored clinical trial is designed to enroll patients with generalized myasthenia gravis, and will evaluate safety and clinical outcomes. Translational and biomarker studies, including autoantibodies, cytokine profiles and pharmacokinetics are planned. Patients will receive NKX019 following single-agent lymphodepletion with cyclophosphamide. The clinical trial is being co-led by Ali A. Habib, M.D., Clinical Professor of Neurology at the University of California, Irvine, and other investigators.

About the Investigator-Sponsored Clinical Trial of NKX019 for Systemic Lupus Erythematosus
The single-center, single-arm, open-label Phase 1 investigator-sponsored clinical trial is designed to enroll up to 6 patients with systemic lupus erythematosus, regardless of renal involvement, and will evaluate safety and clinical outcomes in a potentially different population than Ntrust-1. Translational and biomarker studies, including autoantibodies, cytokine profiles and pharmacokinetics are also planned. Patients receive NKX019 following single-agent lymphodepletion with cyclophosphamide. The clinical trial (NCT06518668) is being led by Anca D. Askanase, M.D., M.P.H., Director, Lupus Center at Columbia University Irving Medical Center and the Director of Rheumatology Clinical Trials.

About NKX019
NKX019 is an allogeneic, off-the-shelf on-demand cell therapy candidate designed to deplete CD19-positive B cells, a therapeutic effect which may enable a "reset" of the immune system with the potential for durable remission without chronic therapy in people living with autoimmune disease. NKX019 uses natural killer (NK) cells derived from the peripheral blood of healthy adult donors. It is engineered with a humanized CD19-directed chimeric antigen receptor (CAR) for enhanced cell targeting and a proprietary, membrane-bound form of interleukin-15 (IL-15) for greater persistence and activity. Nkarta is evaluating NKX019 in multiple autoimmune conditions.

About Nkarta
Nkarta is a clinical-stage biotechnology company advancing the development of allogeneic, off-the-shelf natural killer (NK) cell therapies. By combining its cell expansion and cryopreservation platform with proprietary cell engineering technologies and CRISPR-based genome engineering capabilities, Nkarta is building a pipeline of future cell therapies engineered for deep therapeutic activity and intended for broad access in the outpatient treatment setting. For more information, please visit the company's website at www.nkartatx.com.

Cautionary Note on Forward-Looking Statements
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "anticipates," "believes," "expects," "intends," "plans," "potential," "projects," "would" and "future" or similar expressions are intended to identify forward-looking statements. Examples of these forward-looking statements include, but are not limited to, statements concerning Nkarta's expectations regarding any or all of the following: Nkarta's position, plans, strategies, and timelines for the continued and future clinical development and commercial potential of NKX019 (including the plans for the investigator-sponsored clinical trial in myasthenia gravis and the future availability and disclosure of clinical data and other updates from Nkarta's clinical trials); and the therapeutic potential, accessibility, tolerability, advantages, and safety profile of NK cell therapies, including NKX019 for the treatment of autoimmune diseases, such as lupus, systemic sclerosis, myositis, vasculitis, and myasthenia gravis.

Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties include, among others: Nkarta's limited operating history and historical losses; Nkarta's lack of any products approved for sale and its ability to achieve profitability; the risk that the results of preclinical studies and early-stage clinical trials may not be predictive of future results; Nkarta's ability to raise additional funding to complete the development and any commercialization of its product candidates; Nkarta's dependence on the clinical success of NKX019; that Nkarta may be delayed in initiating, enrolling or completing its clinical trials; competition from third parties that are developing products for similar uses; Nkarta's ability to obtain, maintain and protect its intellectual property; Nkarta's dependence on third parties in connection with manufacturing, clinical trials and pre-clinical studies; and the complexity of the manufacturing process for CAR NK cell therapies.

These and other risks and uncertainties are described more fully in Nkarta's filings with the Securities and Exchange Commission ("SEC"), including

the “Risk Factors” section of Nkarta’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, filed with the SEC on November 7, 2024, and Nkarta’s other documents subsequently filed with or furnished to the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Except to the extent required by law, Nkarta undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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