Nkarta Receives FDA Clearance of IND Application for NKX019 in Lupus Nephritis

October 17, 2023

New pipeline program builds on academic studies of durable, drug-free remissions in patients with autoimmune disease after CD19-targeted cell therapy

NKX019, an allogeneic CAR NK cell therapy targeting CD19+ B cells, could modify refractory autoimmune disease while maintaining NK-driven safety profile

Off-the-shelf accessibility and proprietary engineering could eliminate burdens of autologous products and may enable differentiating conditioning regimen

Resource prioritization and cost reductions expected to extend cash runway by one year into 2026 to support important clinical data readouts in 2024

Estimated cash and cash equivalents of $278.4 million as of September 30, 2023

Conference call scheduled for today, October 17, 8:00 am ET

SOUTH SAN FRANCISCO, Calif., Oct. 17, 2023 (GLOBE NEWSWIRE) -- Nkarta, Inc. (Nasdaq: NKTX), a biopharmaceutical company developing engineered natural killer (NK) cell therapies, today announced the clearance of an Investigational New Drug (IND) application by the U.S. Food and Drug Administration (FDA) to evaluate NKX019, its allogeneic, CD19-directed CAR NK cell therapy candidate, for the treatment of lupus nephritis.

“We believe that NKX019, as an NK cell-based approach, has the potential to distinguish itself in the growing field of cell therapy for autoimmune diseases through improved access and tolerability. Off-the-shelf availability reduces patient burden and eliminates the need for costly infrastructure and treatment delays required for autologous cell therapies. Our proprietary engineering may also improve safety through a reduced need for lymphodepletion. NKX019 is active immediately and is self-sustaining, without the need for large cytokine surges from preparative chemotherapy,” noted David R. Shook, M.D., Chief Medical Officer of Nkarta. “Patients with severe autoimmune diseases such as lupus nephritis need safe and novel therapies. We will continue to work closely with leading investigators to bring the promise of cell therapy to patients in need to explore this potentially transformative therapeutic approach.”

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by abnormal B cell function and autoantibody production and results in a range of clinical manifestations including organ damage and an increased risk of death. Lupus nephritis (LN) is among the most severe manifestations of SLE. Approximately 40 percent of the estimated 200,000 patients in the U.S. diagnosed with SLE will develop LN. Up to 30 percent of patients with LN progress to end stage kidney disease, which can be fatal unless dialysis or a kidney transplant is received.(1)

The multi-center, open label, dose escalation clinical trial will assess the safety and clinical activity of NKX019 in patients with refractory LN. Patients will receive a three-dose cycle of NKX019 at 1 billion or 1.5 billion cells per dose on Days 0, 7 and 14 following lymphodepletion (LD) with single agent cyclophosphamide (cy), an agent with an established safety profile in SLE and LN. The study is designed to enroll up to 12 patients, with the first patient expected to be enrolled in the first half of 2024.

“The potential of cell therapy to reset the immune system and provide long-term, drug-free remissions for patients with severe autoimmune disease may represent the biggest medical breakthrough in the last 50 years of rheumatology,” said Roberto Caricchio, M.D., the Myles J. McDonough Chair in Rheumatology, Professor of Medicine, and Chief of the Division of Rheumatology in the Department of Medicine at the University of Massachusetts Chan Medical School. “Patients with lupus nephritis have limited treatment options, and the early results with cell therapy suggest that we may be defining a new era of treatment.”

Corporate Updates
Nkarta also announced cost containment measures designed to extend its projected cash runway by one year into 2026, funding its operations well beyond the multiple clinical data updates expected in 2024. Nkarta estimates that, as of September 30, 2023, it had cash, cash equivalents, restricted cash, and investments of $278.4 million. This figure is preliminary and subject to completion of Nkarta’s financial closing procedures. The decrease in forecasted spend includes a reduction in and re-allocation of headcount combined with a stringent cap on future headcount growth, planned centralization of operations to a single location and early success in the optimization of Nkarta’s manufacturing platform.

The company expects to announce clinical updates from its three pipeline programs in 2024: NKX101 (AML) in the first half of 2024, NKX019 (NHL) in mid-2024 and NKX019 (AID) in 2024. Nkarta will evaluate options to advance each program with additional investment on the basis of those data readouts.

“The clearance of Nkarta’s IND for NKX019 in lupus nephritis is an important achievement for Nkarta, and we feel NK cell therapy is ideally suited for the treatment of autoimmune disease,” said Paul J. Hastings, President and CEO of Nkarta. “Nkarta is well-capitalized with runway that extends into 2026 and beyond key data readouts across the three programs. We plan to remain disciplined about our expenditures as we focus on execution and the multiple opportunities for near- and long-term value creation.”

“We’ve taken the unfortunate but necessary step to streamline our workforce and reconfigure our R&D approach to be in the best position to advance our multiple cell therapies programs,” Hastings continued. “We are grateful to the talented and committed members of our team who will be departing Nkarta. I thank each of them personally for their dedication to Nkarta and our mission to bring accessible and life-changing cell therapies to patients in need.”

Clinical Program Updates for NKX101 in AML

In June 2023, Nkarta reported updated Phase 1 clinical trial results for NKX101, its allogeneic, off-the-shelf CAR NK cell therapy candidate engineered to target NKG2D ligands, which are overexpressed on cancer cells. In the cohort of patients with relapsed or refractory (r/r) AML who received treatment cycles with a three-dose regimen of NKX101 at 1.5 billion cells per dose after LD with fludarabine (flu) and cytarabine (Ara-C), four of six patients achieved complete response (CR/CRi); three responses were MRD negative.

Nkarta continues to expect enrollment of 12 to 20 additional patients in the cohort using flu/Ara-C for LD, and enrollment is ongoing. A clinical update that includes preliminary safety and response data from these additional patients is expected in the first half of 2024. Nkarta also plans to present an update at a medical meeting in late 2023 that includes follow-up data on the six patients from the June 2023 report.

As previously discussed, the NKX101 clinical protocol was amended to enable retreatment and consolidation. As part of ongoing scale-up and optimization of manufacturing across its platform, Nkarta also successfully filed a manufacturing process change amendment with the FDA. The focus of the process change was to enhance product yield to meet anticipated clinical demand and prepare for potential commercial scale manufacturing. After pausing for inventory buildup, patient enrollment resumed with material generated with the optimized manufacturing process.

Clinical Program Update for NKX019 in NHL
Nkarta announced today the opening of a new cohort in its Phase 1 study of NKX019 in r/r NHL. The new cohort introduces a compressed dosing schedule, where patients receive NKX019 doses on Days 0, 3 and 7 following standard LD with flu and cy. In previous cohorts, NKX019 has been administered on Days 0, 7 and 14 following LD. This schedule is designed to intensify exposure to NKX019 in the first week after LD, when internal data suggest that NKX019 exposure is highest. The new cohort will target patients (n=6) with large B-cell lymphoma (LBCL), including those who have received prior CD19-directed CAR-T cell therapy. Nkarta may also use data from this cohort to inform future dosing strategies across its platform.

In December 2022, Nkarta announced the opening of three dose expansion cohorts to evaluate NKX019 monotherapy and NKX019 in combination with rituximab in patients with LBCL. Preliminary results from these cohorts did not meet Nkarta's expectations, based on the clinical experience of NKX019 in the dose finding portion of the Phase 1 study. As a result, Nkarta is no longer enrolling patients in these dose expansion cohorts. Preliminary data from the dose compression cohort are expected mid-2024. Nkarta plans to evaluate the results from this cohort before committing additional resources to the NHL program.

(1) CDC Fact Sheet for Lupus: https://www.cdc.gov/chronicdisease/resources/publications/factsheets/lupus.htm; Parikh 2020, Am J Kidney Dis. 76(2):265-281; Pryor 2021, Rheum Dis Clin North Am. 47(1): 41–53; Mahajan 2020, Lupus, 29(9): 1011-1020.

Conference Call Information
Nkarta management will discuss its program in autoimmune disease and other corporate updates on Tuesday, October 17, at 8:00 a.m. ET. To access the live webcast, please register online on the Investors section of Nkarta's website. An archived webcast will be available on the Company's website approximately two hours after the event.

About NKX019
NKX019 is an allogeneic, cryopreserved, off-the-shelf immunotherapy candidate that uses natural killer (NK) cells derived from the peripheral blood of healthy adult donors. It is engineered with a humanized CD19-directed CAR for enhanced cell targeting and a proprietary, membrane-bound form of interleukin-15 (IL-15) for greater persistence and activity without exogenous cytokine support. CD19 is a biomarker for normal B cells as well as those implicated in autoimmune disease and B cell-derived malignancies.

About NKX101
NKX101 is an allogeneic, cryopreserved, off-the-shelf cancer immunotherapy candidate that uses natural killer (NK) cells derived from the peripheral blood of healthy donors. It is engineered with a chimeric antigen receptor (CAR) targeting NKG2D ligands on tumor cells. NKG2D, a key activating receptor found on naturally occurring NK cells, induces a cell-killing immune response through the detection of stress ligands that are widely expressed on cancer cells. NKX101 is also engineered with a membrane-bound form of interleukin-15 (IL15) for greater persistence and activity without exogenous cytokine support.

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 NKX101 and NKX019; the therapeutic potential, accessibility, tolerability and safety profile of NK cell therapies, including NKX101 for the treatment of cancer and NKX019 for the treatment of autoimmune disease, such as lupus nephritis, and cancer; the potential advantages of CAR NK cell therapies and NKX019, in particular, over other cell therapies for the treatment of autoimmune disease; plans and timelines for the future availability and presentation of NKX101 and NKX019 clinical data; Nkarta's plans to reduce future spend; and Nkarta's estimated cash position and expected cash runway.

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 its two lead product candidates, NKX101 and NKX019; that Nkarta may be delayed in initiating, enrolling or completing any 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; the complexity of the manufacturing process for CAR NK cell therapies; the availability of components and supplies necessary for

the conduct of our clinical trials; and Nkarta's ability to implement cost reduction measures as planned.

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 June 30, 2023, filed with the SEC on August 10, 2023, 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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