Nkarta Announces Treatment of First Patient in First-in-Human Clinical Trial of Engineered NKG2D-Based NK Cell Cancer Immunotherapy NKX101

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First Multi-Center Clinical Trial to Investigate an Engineered NK Cell Targeting NKG2D

SOUTH SAN FRANCISCO, Calif., Nov. 12, 2020 (GLOBE NEWSWIRE) -- Nkarta, Inc. (Nasdaq: NKTX), a clinical-stage biopharmaceutical company developing engineered natural killer (NK) cell therapies to treat cancer, today announced that the first patient has been treated in the first-in-human Phase 1 clinical trial of NKX101 for the treatment of relapsed/refractory acute myeloid leukemia (AML) or higher risk myelodysplastic syndromes (MDS). The multi-center clinical trial is designed to evaluate safety, pharmacokinetics, and preliminary anti-tumor activity of NKX101.

NKX101 is the first investigational NK cell cancer immunotherapy engineered to express a chimeric activating receptor (CAR) targeting NKG2D. 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 and specifically expressed on cancer cells. With NKX101, NKG2D expression is increased by 10-fold and cytotoxic activity increased by 4-fold compared to non-engineered NK cells in preclinical models. NKX101 is also designed to express membrane-bound IL-15, which in preclinical models enhances the activity and persistence of the engineered NK cells. Nkarta's proprietary manufacturing processes enable the evaluation of cryopreserved NKX101, expanding trial access across multiple clinical centers.

"Despite recent treatment breakthroughs, AML patients who relapse after front-line therapy still have poor outcomes, underscoring the need for new treatment options for this aggressive and lethal blood cancer," said Carlos Bachier, M.D., Director of Cellular Therapy Research, Sarah Cannon Research Institute and Program Director for Sarah Cannon Center for Blood Cancer at TriStar Centennial Medical Center in Nashville, Tennessee, where the first patient has been treated. "To date, the significant clinical benefit achieved with CAR T cell therapies in the treatment of B cell lymphomas and acute lymphocytic leukemia has not extended to AML or other myeloid malignant disorders. The investigation of NKG2D-targeting and the tumor-killing potential of an engineered innate immune cell type is a promising new approach."

"An extensive body of academic research has already shown increased expression of NKG2D targets in AML and other cancers, and demonstrated clinical responses in relapsed/refractory AML patients who received non-engineered allogeneic NK cells in single center academic studies as treatment," said Kanya Rajangam, M.D., Ph.D., Chief Medical Officer of Nkarta. "With its amplified NKG2D targeting and enhanced NK cell engineering, NKX101 has the potential to improve upon this earlier clinical experience with non-engineered NK cells and to activate a deep and robust immune response in AML patients."

A poster on the design of the NKX101 clinical trial in progress has been accepted for presentation at the 2020 American Society of Hematology Annual Meeting and Exhibition, Abstract 1040, "A Phase 1 Study of NKX101, an Allogeneic CAR Natural Killer (NK) Cell Therapy, in Subjects with Relapsed/Refractory (R/R) Acute Myeloid Leukemia (AML) or Higher-Risk Myelodysplastic Syndrome (MDS)." Session 616, December 5, 2020.

About the Phase 1 Clinical Trial of NKX101 in Participants with Relapsed/Refractory Acute Myeloid Leukemia (AML) or Higher Risk Myelodysplastic Syndromes (MDS)
This First-in-Human Phase 1 study evaluates the safety, pharmacokinetics, and preliminary anti-tumor activity of NKX101, administered in a cycle of three weekly infusions following lymphodepletion, in adult patients living with relapsed/refractory AML or higher risk MDS. This single-arm, open-label, multi-center study consists of sequential dose-finding and dose-expansion. The safety of participants will be monitored by assessment of vital signs, physical examinations and laboratory tests. The clinical trial is designed to identify a recommended Phase 2 dose, and will evaluate cellular kinetics, pharmacodynamics, and preliminary anti-tumor activity using standard response criteria. Additional information is available on ClinicalTrials.gov, identifier NCT04623944.

About AML and MDS
Acute Myeloid Leukemia (AML) is a rapidly progressing blood cancer caused by abnormalities of myeloid cells, a cell type in the bone marrow that would normally develop into different types of blood cells. AML usually worsens rapidly and can lead to death if not treated. Despite recent advancements, an unmet need for novel treatment options remains high. Only approximately one in four patients with AML survive longer than five years. Patients with AML have a high rate of disease relapse after a treatment response. Due to age and comorbidities, not all patients are eligible to receive intensive chemotherapy, leaving them with limited treatment options. Once relapsed or refractory to front-line therapy, patients have limited treatment options. The worldwide incidence of AML was estimated to be more than 119,500 cases in 2017.* In the United States, there will be an estimated 19,940 new cases of AML in 2020, with an estimated 11,180 deaths resulting from the disease.**

Myelodysplastic Syndromes (MDS) are a group of bone marrow disorders in which the blood-forming cells in the bone marrow do not produce enough healthy blood cells. Some patients with MDS have too many young, immature blood-making cells in the bone marrow. The median overall survival rate of higher risk MDS patients is 0.8 to 3.0 years. There is currently no curative treatment for patients who relapse after front-line therapy or do not respond to front-line therapy. MDS can progress to AML in about one-third of patients.

*Ming Yi et al, J Hematol Oncol. 2020; 13: 72; **National Institutes of Health, Cancer Stat Facts, accessed 11 Nov 2020.

About NKX101
NKX101 is an investigational, off-the-shelf cancer immunotherapy that uses natural killer (NK) cells derived from the peripheral blood of healthy donors and engineered with membrane-bound IL15 and 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. By engineering NKX101 with the proprietary NKG2D-based CAR, the ability of NK cells to recognize and kill tumor cells in pre-clinical models is increased significantly compared to non-engineered NK cells. The addition of membrane-bound IL15, a proprietary version of a cytokine for activating NK cell growth, has been shown in pre-clinical models to enhance the proliferation, persistence and sustained activity of NK cells. A multi-center Phase 1 clinical trial of NKX101 in patients with relapsed/refractory acute myeloid leukemia (AML) or higher risk myelodysplastic syndromes (MDS) is currently enrolling. Additional information about the clinical trial is available on ClinicalTrials.gov, identifier NCT04623944.

About Nkarta's NK Cell Technologies

Nkarta has pioneered a novel discovery and development platform for the engineering and efficient production of allogeneic, off-the-shelf natural killer (NK) cell therapy candidates. The approach harnesses the innate ability of NK cells to recognize and kill tumor cells, and builds upon the important advances in cellular immunotherapy and chimeric antigen receptor (CAR) biology. To enhance the intrinsic activity of NK cells, Nkarta genetically engineers the cells with a CAR that consists of a targeting receptor designed to recognize and bind to specific proteins on the surface of cancerous cells. This receptor is fused to co-stimulatory and signaling domains to amplify cell signaling and NK cell cytotoxicity. Upon binding the target, NK cells become activated and release cytokines that enhance the immune response and cytotoxic granules that lead to killing of the target cell. All of Nkarta's NK cell therapy candidates are engineered with a membrane-bound IL15, a proprietary version of a cytokine known for activating NK cell growth, to enhance the persistence and activity of the NK cells.

Nkarta's manufacturing process generates an abundant supply of NK cells that, at commercial scale, is expected to be significantly lower in cost than other current allogeneic and autologous cell therapies. Key to this efficiency is the rapid expansion of donor-derived NK cells using a proprietary NKSTIM cell line, leading to the production of hundreds of individual doses from a single manufacturing run. The platform also features the ability to freeze and store CAR NK cells for an extended period of time and is designed to enable immediate, off-the-shelf administration to patients at the point of care.

About Nkarta

Nkarta is a clinical-stage biotechnology company advancing the development of allogeneic, off the shelf natural killer (NK) cell therapies for cancer. By combining its cell expansion and cryopreservation platform with proprietary cell engineering technologies, Nkarta is building a pipeline of cell therapy candidates generated by efficient manufacturing processes, which are engineered to enhance tumor targeting and improve persistence for sustained activity in the body. 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 statements concerning Nkarta's expectations regarding: Nkarta's growth, strategy, progress and timing of its preclinical studies and clinical trials for NKX101; the mechanism of action and activity of Nkarta's product candidates, including the activity of NKX101 in AML patients; NKX101's potential as a treatment for AML; the size of the AML market; the efficiency and cost of Nkarta's manufacturing processes; the number of doses generated from a manufacturing run; and the proprietary nature of Nkarta's technology. 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 ability to raise additional funding to complete the development and any commercialization of its product candidates; Nkarta's dependence on the success of its co-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; and risks relating to the impact on our business of the COVID-19 pandemic or similar public health crises.

These and other risks are described more fully in Nkarta's filings with the Securities and Exchange Commission ("SEC"), including the "Risk Factors" section of Nkarta's final prospectus for its initial public offering, filed with the SEC on July 13, 2020, Nkarta's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2020, filed with the SEC on August 20, 2020, and our 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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