Nkarta Updates Clinical Progress of CAR-NK Cell Therapy NKX101 for Patients with Relapsed or Refractory Acute Myeloid Leukemia

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- Encouraging antileukemic activity seen with NKX101 in patients with AML, including several with high-risk features, using a modified lymphodepletion incorporating Ara-C (cytarabine)
- In patients with r/r AML treated with a three-dose regimen of NKX101 at 1.5 billion cells per dose after fludarabine/Ara-C for lymphodepletion, n=6
    - 4 of 6 patients achieved complete response (67% CR/CRi, 50% CR rate)
    - 2 CRs with MRD negativity
    - 1 patient deepened response to MRD negative CRi with additional cycles
- NKX101 was well tolerated across dose-levels and lymphodepletion regimens
- Expansion cohort incorporating Ara-C based lymphodepletion expected to be the basis of NKX101 development moving forward
- Updated clinical data from NKX101 program expected in 1H 2024
- Conference call scheduled for today, June 27, at 8:00 a.m. ET

SOUTH SAN FRANCISCO, Calif., June 27, 2023 (GLOBE NEWSWIRE) -- Nkarta, Inc. (Nasdaq: NKTX), a biopharmaceutical company developing engineered natural killer (NK) cell therapies, today announced positive updated data from its Phase 1 study of NKX101 to treat patients with relapsed or refractory (r/r) acute myeloid leukemia (AML). NKX101 is an allogeneic, off-the-shelf cell therapy candidate comprising NK cells derived from healthy donors and engineered to target NKG2D ligands on cancer cells.

Four of six patients in one dose expansion cohort achieved a best composite complete response (67% CR/CRi rate) after receiving at least one cycle of NKX101. In this cohort, a cycle consisted of three weekly doses of NKX101 at 1.5 billion cells per dose after treatment with fludarabine (Flu) and Ara-C (cytarabine) for lymphodepletion. Ara-C is an established and important drug in the treatment of AML across treatment lines, including first line therapy. Exposure to Ara-C is also known to upregulate NKG2D ligands, potentially increasing sensitivity of cancerous cells to NK-cell mediated killing. Data from the NKX101 study suggest Ara-C has the potential to be an effective agent for lymphodepletion.

“Patients with relapsed or refractory AML have few treatment options, and novel approaches are urgently needed. Traditional chemotherapy is often unable to drive deep remissions in this setting, and many patients cannot tolerate it,” said Carlos Bachier, M.D., Medical Director of Research and Cellular Therapy, Sarah Cannon Transplant & Cellular Therapy Program at Methodist Hospital in San Antonio, Texas. “NKX101 following lymphodepletion with fludarabine and Ara-C had encouraging anti-tumor activity in a small number of patients with difficult to treat relapsed/refractory AML. This activity, together with its tolerable safety profile, merits further study of NKX101.”

“NK cell therapy has long held promise for patients with AML, and these latest results highlight our continued progress towards delivering on that promise with NKX101,” said David R. Shook, M.D., Nkarta’s Chief Medical Officer. “While these data are early and in a small number of patients, the response rate exceeds the rate observed with even the latest approved agents and highlights the potential advantages of lymphodepletion using Flu/Ara-C.”

Nkarta expects to enroll 12 to 20 additional patients in the expansion cohort using Flu/Ara-C lymphodepletion of the Phase 1 clinical trial and provide a clinical update in the first half of 2024. Nkarta also plans to introduce protocol changes intended to standardize criteria for retreatment and consolidation and simplify study logistics for enrolled patients.

Evaluating NKX101 in r/r acute myeloid leukemia
NKX101 is an allogeneic, cryopreserved, off-the-shelf cancer immunotherapy candidate that uses donor-derived NK cells engineered to target NKG2D ligands on cancer cells. NKX101 is being evaluated in a dose-escalation Phase 1 study as a multi-dose, multi-cycle cellular therapy in patients with r/r AML. As of June 10, 2023, a total of 36 patients with r/r AML were enrolled, compared to 17 at the previous update of April 21, 2022.

Thirty patients with r/r AML were treated with NKX101 after lymphodepletion with fludarabine and cyclophosphamide (Flu/Cy), through dose finding and a separate dose expansion cohort. The majority (17/30, 57%) of patients had poor risk disease. The patients in these cohorts were heavily pre-treated, with 2 median lines of therapy (range 1-12) and 27/30 (90%) having been treated with venetoclax.

A separate, expansion cohort enrolled 6 patients who received lymphodepletion with Flu/Ara-C followed by 3 weekly doses of NKX101 at 1.5 billion cells per dose. This cohort included 5/6 (83%) patients with poor risk disease and other additional high-risk clinical features such as early relapse after allogeneic hematopoietic cell transplant (HCT) and chemo-refractory disease. The patients in this cohort were also heavily pre-treated, with 2 median lines of therapy (range 1-3) and all having been previously treated with venetoclax-containing regimens. Today’s announcement is the first time that results from the Flu/Ara-C cohort are being presented.

Safety in NKX101
NKX101 was well tolerated. No dose-limiting toxicities were observed across all cohorts. The safety profile of NKX101 was consistent across both lymphodepletion regimens. The emerging safety profile of NKX101 is positively differentiated from those of many cell therapies.

In patients with r/r AML that received lymphodepletion with Flu/Cy (Table 1), limited CAR T-like toxicities were observed, including 5 (12%) ≤grade 2 infusion reactions, 5 (12%) cases of ≤grade 2 cytokine release syndrome (CRS), 1 case of grade 2 immune effector cell-associated neurotoxicity

syndrome (ICANS), and no graft-versus-host disease (GvHD). The most common higher-grade adverse events were myelosuppression - a condition resulting in fewer red blood cells, white blood cells and platelets, as well as infection, which are common in this patient population post lymphodepletion.

Safety Table 1 – Patients treated with fludarabine / cyclophosphamide lymphodepletion

Grade 3+ AEs in ≥10% of patients	**Total (n=30)**
Hematologic Events	
Thrombocytopenia	18 (60%)
Anemia	16 (53%)
Neutropenia	13 (43%)
Febrile neutropenia	8 (27%)
White blood cell count decreased	5 (17%)
Leukocytosis	4 (13%)
Infections	
Pneumonia	3 (10%)
Other	
Hypoxia^	4 (13%)
Fatigue	3 (10%)
Hypotension	3 (10%)

Treatment emergent adverse events regardless of relationship based on interim data from open clinical database as of 10 June 2023

^ In the setting of febrile neutropenia/pneumonia

In patients with r/r AML in the expansion cohort using Flu/Ara-C lymphodepletion (Table 2), there were no observations of CRS, ICANS or GvHD of any grade. Myelosuppression and infection remained the most common higher-grade adverse events. However, there were no >grade 3 infections, and no treatment-associated fatalities.

Safety Table 2 – Patients treated with fludarabine / Ara-C lymphodepletion

Grade 3+ AEs in >1 patient	**Total (n=6)**
Hematologic Events	
Anemia	3 (50%)
Febrile neutropenia	3 (50%)
Neutropenia	3 (50%)
Thrombocytopenia	2 (33%)
Lymphocyte count decreased	2 (33%)
WBC decreased	2 (33%)
Infections	
Sepsis	3 (50%)

Clinical Activity in NKX101

In patients with r/r AML that received Flu/Ara-C lymphodepletion, 4 of 6 achieved CR/CRi (67% CR/CRi rate) and 3 of 6 achieved a complete response with hematologic recovery (50% CR rate). Two of the 4 reported complete responses were MRD (measurable residual disease) negative. MRD negativity is broadly viewed as an important quantitative measure of disease burden in AML and is associated with increased disease-free survival and decreased risk of recurrence. One patient with MRD positive CR underwent allogeneic HCT and remains in CR at 4 months. Another patient with CR has no detectable disease by flow cytometry and additional MRD testing is pending. Flu and Ara-C are often combined with other chemotherapies, such as idarubicin and mitoxantrone in r/r AML, and such combinations (e.g. FLAG-Ida) have been used as a part of comparator arms in multiple registrational studies, with CR rates between 10-12%.

In patients with r/r AML that received Flu/Cy lymphodepletion, and the highest doses of NKX101 (3 weekly doses at 1 billion or 1.5 billion cells per dose), 4 of 18 achieved CR/CRi (22% CR/CRi rate) and 3 of 18 achieved a complete response with hematologic recovery CR (17% CR rate). There were no CRs at the lower doses of NKX101.

Conference Call Information

Nkarta management will discuss the NKX101 results on Tuesday, June 27, at 8:00 a.m. ET. To access the live webcast, please register online on the Investors section of Nkarta's website: https://ir.nkartatx.com/events-and-presentations. An archived webcast and accompanying slides will be available on the Company's website approximately two hours after the event.

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. To learn more about the NKX101 clinical trial in adults with AML, please visit ClinicalTrials.gov.

About the NKX101 Trial
This Phase 1 clinical trial evaluates the safety and anti-tumor activity of NKX101 as a multi-dose, multi-cycle cellular therapy following lymphodepletion in patients with r/r AML. Patients must have received at least one prior therapy, and patients diagnosed with a disease mutation must have received a targeted therapy, where approved.

Patients in the NKX101 Phase 1 trial received either fludarabine / cyclophosphamide lymphodepletion or fludarabine /Ara-C lymphodepletion followed by NKX101. Patients received doses of 100 million, 300 million, 1 billion or 1.5 billion NK cells three times in the 3-dose regimen, or doses of 150 million or 1.5 billion NK cells two times in the 2-dose regimen. Based on tumor response and tolerability assessment, patients were eligible to receive additional treatment cycles. Disease assessment was performed by investigator review according to the ELN response criteria.

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 anti-tumor activity and intended for broad access in the outpatient treatment setting. For more information, please visit the company's website at www.nkartatx.com.

Forward-looking statements
Forward-looking statements include, among others, statements of Nkarta's future expectations, plans and prospects. These may include statements concerning Nkarta's expectations regarding any or all of the following: the therapeutic potential, tolerability and safety profile of NKX101; plans and timelines for the availability and presentation of NKX101 clinical data; plans and timelines for the continued and future clinical development and commercial potential of NKX101; and the potential advantages of using fludarabine/cytarabine (Ara-C) as lymphodepletion for NKX101. These forward-looking statements are based on current information, assumptions and expectations that are subject to change and involve a number of risks and uncertainties that may cause actual results to differ materially from those contained in the forward-looking statements.

Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more data on existing patients become available. The clinical trial program is ongoing, and the final results may be materially different from those reflected in any interim data we report. Further, others, including regulatory agencies, may not accept or agree with Nkarta's assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and the value of the company in general. In addition, the information Nkarta chooses to publicly disclose regarding a particular study or clinical trial is typically a summary of extensive information, and you or others may not agree with what Nkarta determines is the material or otherwise appropriate information to include in Nkarta's disclosure, and any information Nkarta determines not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or business.

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 March 30, 2023, filed with the SEC on May 11, 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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