Nkarta Announces Positive Preliminary Dose Finding Data for Two Lead Engineered Natural Killer Cell Programs

April 25, 2022

NKX101 – 3 of 5 patients with relapsed / refractory AML treated with a three-dose regimen consisting of 1B or 1.5B CAR NK cells per dose achieved complete response with full hematologic recovery (60% CR rate); 2 of 3 CRs are MRD negative

NKX019 – 5 of 6 patients with relapsed / refractory NHL treated with a three-dose regimen consisting of 1B CAR NK cells per dose achieved response (83% ORR) and 3 of 6 achieved complete response (50% CR rate); responses included DLBCL

No cytokine release syndrome (CRS), neurotoxicity or graft versus host disease (GvHD) reported for either program

Higher dose regimen of 1.5 billion x 3 doses of CAR NK cells is being evaluated in both programs

Updated data will be submitted for presentation at a future medical meeting

Conference call scheduled for today, April 25 at 8:00 am ET

SOUTH SAN FRANCISCO, Calif., April 25, 2022 (GLOBE NEWSWIRE) -- Nkarta, Inc. (Nasdaq: NKTX), a biopharmaceutical company developing engineered natural killer cell therapies to treat cancer, today announced positive preliminary Phase 1 data from independent dose finding studies of its two lead chimeric antigen receptor (CAR) natural killer (NK) cell therapy candidates, NKX101 and NKX019, in two distinct groups of hematologic malignancies.

“We’re excited to see our CAR NK co-lead candidates, NKX101 and NKX019, show such striking early single-agent activity in heavily pretreated patient populations, with an exceptional safety profile without the side effects associated with CAR T cell therapies,” said Paul J. Hastings, President and CEO of Nkarta. “These encouraging data across multiple indications further validate Nkarta’s best-in-class NK cell platform, as we seek to transform cancer treatment by bringing together the safety advantages of NK cells with an off-the-shelf modality designed to make the benefits of cell therapy accessible in a community setting.”

In the first trial, evaluating NKX101, in relapsed / refractory (r/r) acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), three of five patients with heavily pre-treated AML who received the higher dose level in a three-dose regimen achieved a complete response (60% CR) with hematologic recovery, with two of the three responses MRD (minimal residual disease) negative. There is currently no standard of care for these patients.

In the second trial, evaluating NKX019, in r/r B cell malignancies, three of six patients treated at the higher dose level in a three-dose regimen showed a complete response (50% CR), including one patient with aggressive diffuse large B cell lymphoma (DLBCL) and one patient with mantle cell lymphoma (MCL). In both trials, no dose limiting toxicity was observed and there were no CAR T like adverse events of any grade.

Nkarta continues to enroll patients in three-dose regimens of 1.5 billion NK cells per dose in the dose finding portions of the NKX101 and NKX019 trials. Data from both programs, including additional follow-up and updates on the higher dose cohorts, will be submitted for presentation at a future medical meeting.

Evaluating NKX101 in r/r acute myeloid leukemia
NKX101 is an allogeneic, cryopreserved, off-the-shelf cancer immunotherapy candidate that uses 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 monotherapy in patients with r/r AML and higher-risk MDS.

As of April 21, 2022, 21 patients were enrolled and dosed, 17 with a diagnosis of AML and four with MDS. Patients were heavily pre-treated and had received a median of three prior lines of therapy (range of 1 to 12). All patients with AML had received prior treatment with venetoclax. At baseline, the median percentage of blast cells in bone marrow was 27% (range of 3 to 85%).

“Relapsed/refractory acute myeloid leukemia (AML) is a historically hard-to-treat disease, and given the lack of effective treatments, people with cancer and those who treat them are faced with few options,” said Marcello Rotta, M.D., Colorado Blood Cancer Institute (CBCI), a part of the Sarah Cannon Cancer Institute at Presbyterian/St. Luke’s Medical Center, and investigator in the NKX101 clinical trial. “Complete responses with corresponding MRD negativity in r/r AML using engineered NK cells, as seen in these preliminary findings, is encouraging. We look forward to leading further investigation to better understand the full potential of a CAR NK approach.”

Safety in NKX101
NKX101 was well tolerated. No dose-limiting toxicities were observed. Toxicities associated with engineered chimeric antigen receptor (CAR) T cell treatments were not observed at any dose, including cytokine release syndrome, graft-versus-host disease, and immune effector cell-associated neurotoxicity (ICANS). The most common higher-grade adverse events were myelosuppression - a condition resulting in fewer red blood cells, white blood cells and platelets, and infection, which are common in this patient population post lymphodepletion. Two patients experienced Grade 2 infusion reactions, transient fever and fluid responsive hypotension. (See table 1.) The emerging safety profile of NKX101 is positively differentiated from those of many cell therapies.

NKX101 Safety (Table 1)

≥ G3 AEs in > 1 subject	Total (N=21)
Hematologic Events	
Thrombocytopenia	10 (48%)
Febrile neutropenia	8 (38%)
Neutropenia	7 (33%)
Anemia	6 (29%)
White blood cell count decreased	2 (10%)
Leukocytosis	2 (10%)
Infections	
Pneumonia	5 (24%)
Sepsis	2 (10%)
Other	
Hypoxia^	4 (19%)
Fatigue	2 (10%)

Treatment emergent adverse events regardless of relationship based on interim data from open clinical database as of 21 Apr 2022
^ In the setting of febrile neutropenia/pneumonia

Clinical Activity in NKX101
Twenty-one patients who received NKX101 were assessed (See table 2.) In the two highest dose-level cohorts (3 doses of 1 billion cells or 3 doses of 1.5 billion cells), 3 of 5 patients with AML achieved a complete response (60% CR) with hematologic recovery. Two of the 3 reported complete responses were MRD (minimal 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. For all cohorts in the dose finding portion, 8 of 17 patients with AML achieved an overall response (47% ORR) and 3 of 17 achieved a complete response with hematologic recovery (18% CR). Four patients with MDS were treated, with no response observed.

NKX101 Clinical Activity (Table 2)

	AML: ORR *(CR, CRi, MLFS, PR)*	**AML: CR**	**MDS: ORR** *(CR, marrow CR, PR)*
NKX101 – 3 doses / cycle (Day 0, 7, 14)			
1.0B / 1.5B x 3	3/5 (60%)	**3/5 (60%)** **2/3 MRD-**	0/2 (0%)
100M / 300M x 3	4/6 (67%)	0/6 (0%)	No patients treated
Overall Responses	7/11 (64%)	3/11 (27%)	0/2 (0%)
NKX101 – 2 doses / cycle (Day 0, 7)			
1.5B x 2	0/3 (0%)	0/3 (0%)	No patients treated
150M / 450M x 2	1/3 (33%)	0/3 (0%)	0/2 (0%)
Overall Responses	1/6 (17%)	0/6 (0%)	0/2 (0%)

Evaluating NKX019 in r/r B cell malignancies

NKX019 is an allogeneic, cryopreserved, off-the-shelf cancer immunotherapy candidate that uses NK cells engineered to target the B-cell antigen CD19, a clinically validated target for B-cell cancer therapies. The NKX019 Phase 1 study is evaluating the safety and anti-tumor activity of NKX019 as a multi-dose, multi-cycle monotherapy in patients with r/r B cell malignancies.

As of April 21, 2022, 13 patients were enrolled and dosed. Ten patients entered the study with a diagnosis of non-Hodgkin lymphoma (NHL), 5 of which were aggressive large B cell lymphoma (LBCL). Patients had received a median of 4 prior lines of therapy (range of 2 to 7). To date, enrollment has included patients with aggressive disease presentations and extensive lesions throughout the body. Patients were enrolled at clinical trial sites in Australia (10) and the United States (3).

“The curative potential of CAR T cell therapy is truly remarkable, but many eligible patients are still not cured, and the safety and logistical challenges of approved autologous CAR T therapy are barriers,” said Michael Dickinson, M.D., Lead, Aggressive Lymphoma disease group, Clinical Haematology, Peter MacCallum Cancer Centre and Royal Melbourne Hospital, and investigator in the NKX019 trial. “The NKX019 trial exemplifies the continued progress of our field. NKX019 showed clear activity, in patients with a range of NHL histologies, without the sort of toxicities expected of other cellular therapies, supporting continued exploration of this CAR NK candidate.”

Safety in NKX019
NKX019 was well tolerated. No dose-limiting toxicities were observed. Toxicities associated with CAR T cell treatments were not observed at any dose, including cytokine release syndrome, graft-versus-host disease, and ICANS. The most common higher-grade adverse events were myelosuppression - a condition resulting in fewer red blood cells, white blood cells and platelets, which is common in this patient population post lymphodepletion. (See table 3.) One patient experienced Grade 1 infusion reactions. The emerging safety profile of NKX019 is positively differentiated from those of many cell therapies.

NXK019 Safety (Table 3)

≥ G3 AEs in > 1 subject	Total (N=13)
Hematologic Events	
Neutropenia	9 (69%)
Thrombocytopenia	5 (38%)
Febrile neutropenia	3 (23%)
Anemia	2 (15%)

Treatment emergent adverse events regardless of relationship based on interim data from open clinical database as of 21 Apr 2022

Clinical Activity in NXK019

Thirteen patients who received NKX019 were assessed. (See table 4.) Five of 6 patients with NHL in the cohort receiving 3 doses of 1 billion cells achieved a response (83% ORR), and 3 of 6 achieved a complete response (50% CR rate). For all cohorts in the dose finding portion, 7 of 10 evaluable patients with NHL achieved an objective response (70% ORR) and 4 of 10 achieved a complete response (40% CR). Three patients with ALL were treated, with no response observed.

NXK019 Clinical Activity (Table 4)

	NKX019 - 300M cells x 3 doses		NKX019 - 1B cells x 3 doses	
	ORR *(CR, PR)*	**CR**	**ORR** *(CR, PR)*	**CR**
All NHL	**2/4 (50%)**	**1/4 (25%)**	**5/6 (83%)**	**3/6 (50%)**
LBCL	1/3 (33%)	0/3 (0%)	1/2 (50%)	1/2 (50%)
MCL	No patients treated	No patients treated	1/1 (100%)	1/1 (100%)
FL	1/1 (100%)	1/1 (100%)	2/2 (100%) [2PR]	0/2 (0%)
MZL	No patients treated	No patients treated	1/1 (100%)	1/1 (100%)
B-ALL	0/1 (0%)	0/1 (0%)	0/2 (0%)	0/2 (0%)

About the NKX101 Trial

NKX101 is an allogeneic, cryopreserved, off-the-shelf cancer immunotherapy candidate that uses natural killer (NK) cells engineered to target NKG2D ligands on cancer cells. The dose-finding portion of the NKX101 Phase 1 study evaluates the safety and anti-tumor activity of NKX101 as a multi-dose, multi-cycle monotherapy following lymphodepletion in patients with r/r AML and higher-risk MDS. 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 a cycle of treatment consisting of fludarabine/ cyclophosphamide lymphodepletion followed by either a three-dose regimen where NKX101 cells were given on Days 0, 7, and 14; or a two-dose regimen where the cells were given on Days 0 and 7. 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, 450 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 for patients with AML and Cheson response criteria for patients with MDS.

About the NKX019 Trial

NKX019 is an allogeneic, cryopreserved, off-the-shelf cancer immunotherapy candidate that uses natural killer (NK) cells engineered to target the B-cell antigen CD19, a clinically validated target for B-cell cancer therapies. The dose-finding portion of the NKX019 Phase 1 study evaluates the safety and anti-tumor activity of NKX019 as a multi-dose, multi-cycle monotherapy following lymphodepletion in patients with r/r B cell malignancies. Patients must have received at least two prior therapies. Patients who received prior autologous CAR-T therapy were not eligible.

Patients in the NKX019 trial received a cycle of treatment consisting of fludarabine/cyclophosphamide lymphodepletion followed by NKX019 cells in a three-dose regimen where cells were given on Days 0, 7, and 14. Patients received doses of 300 million or 1 billion cells three times in a cycle. 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 2014 Lugano response criteria for patients with NHL and NCCN response criteria for patients with ALL.

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 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 or MDS, please visit ClinicalTrials.gov.

About NKX019

NKX019 is an allogeneic, cryopreserved, off-the-shelf cancer 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 tumor 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 and malignant B cells, and it is a validated target for B cell cancer therapies. To learn more about the NKX019 clinical trial in adults with advanced B cell malignancies, please visit ClinicalTrials.gov.

About Nkarta

Nkarta is a clinical-stage biotechnology company advancing the development of allogeneic, off-the-shelf natural killer (NK) cell therapies for cancer patients. 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 regarding the future clinical development, tolerability, safety profile, accessibility, and therapeutic potential of Nkarta's product candidates. 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 Annual Report on Form 10-K for the quarter ended December 31, 2021, filed with the SEC on March 17, 2022, 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.

Nkarta Media/Investor Contact:
Greg Mann
Nkarta, Inc.
gmann@nkartatx.com