Nkarta Presents New Preclinical Data from Engineered NK Cell Platform at AACR Annual Meeting 2022

April 8, 2022

SOUTH SAN FRANCISCO, Calif., April 08, 2022 (GLOBE NEWSWIRE) -- Nkarta, Inc. (Nasdaq: NKTX), a biopharmaceutical company developing engineered natural killer (NK) cell therapies to treat cancer, today announced the presentation of four preclinical data abstracts focused on its natural killer cell platform and pipeline at the American Association for Cancer Research (AACR) Annual Meeting 2022.

"The data we presented at this year's AACR meeting highlight the breadth and diversity of our scientific efforts, as we continue to expand our ability to deliver off-the-shelf cell therapies with the potential to disrupt the cancer treatment landscape," said James Trager, PhD, Chief Scientific Officer of Nkarta. "Our research activities are designed to extend the capabilities of NK cells, to lay the groundwork for further pipeline programs - including our pioneering NK+T cell program - and to implement cutting edge translational methods to support our ongoing clinical programs. Our findings reported at AACR further support exploration of multiply edited CD70 CAR NK cells for clinical application, one focus of our ongoing collaboration with our partners at CRISPR Therapeutics."

Details of the preclinical poster presentations at AACR follow. Posters are available for download on the Nkarta website (https://www.nkartatx.com/publications/) and on the AACR e-poster website (https://cattendee.abstractsonline.com/meeting/10517).

Presented jointly with CRISPR Therapeutics:

Title: **CBLB, CISH and CD70 multiplexed gene knockout with CRISPR/Cas9 enhances cytotoxicity of CD70-CAR NK cells and provides greater resistance to TGF-β for cancer immunotherapy**
Session Category: **Immunology**
Session Title: **Preclinical Immunotherapy**
Abstract Number: **5512**

This study illustrates gene editing approaches that enhance the ability of NK cells to target CD70, an antigen highly expressed in a variety of malignant settings, including renal cell carcinoma (RCC) and adenocarcinoma. Editing targets included cytokine inducible SH2-containing protein (CISH) and the E3 ubiquitin ligase CBLB, both negative regulators of NK cell function. Preclinical results showed that a combined editing and engineering strategy to armor primary NK cells via co-expression of the CD70 CAR and a membrane bound form of IL-15 (mbIL-15), together with a triple knockout of CISH, CBLB and CD70 genes using the CRISPR/Cas9 system enhanced anti-tumor activity against renal cell carcinoma (RCC) solid tumor cell lines and provide greater resistance to TGF-β mediated inhibition. These data support the further exploration of CD70/CISH/CBLB triple gene knockout CD70 CAR NK cells for clinical application.

Nkarta presentations:

Title: **Surveying surface antigen expression in multiple myeloma preclinical models**
Session Category: **Tumor Biology**
Session Title: **Nonclinical Models of Cancer**
Abstract Number: **6004**

Multiple myeloma (MM) is a progressive hematological cancer with a 5-year survival rate of 53%. Novel therapeutic strategies are being developed to target specific MM surface antigens. Yet, changes in antigen expression through MM progression are poorly understood in the clinic and have not been well characterized in preclinical models. Data presented in this study highlighted antigen expression differences in MM cells when analyzed in mouse tissue compared to in vitro culture. Like the widely variable expression observed between patients, BCMA and CD138 were differentially expressed in the mouse bone marrow between MM models. Commonly targeted antigens in MM also vary kinetically in vivo and can be measured and tracked using flow cytometry. The present findings also support the use of specific cell lines when assessing BCMA, CD38 and CD138-specific immunotherapies or combinatorial approaches to MM treatment.

Title: **Development of multiomics approaches to evaluate NKG2D ligand dynamics and anti-tumor immune responses during CAR-NK treatment**
Session Category: **Clinical Research Excluding Trials**
Session Title: **Immuno-oncology**
Abstract Number: **5187**

NKX101 is an investigational NK cell therapy engineered to overexpress a chimeric receptor consisting of NKG2D ectodomain, costimulatory signaling motifs, and a membrane-bound form of IL-15. NKX101 is currently under clinical evaluation for treatment of relapsed/refractory acute myeloid leukemia (AML) and higher risk myelodysplastic syndrome (MDS). To better understand patterns of response to NKX101, we describe the development of several key translational methods, including (i) a single-cell (sc) RNAseq approach to assess gene expression pattern changes in NKX101 and patient cells, (ii) a multiplex IHC panel to monitor NKG2D-ligand expression by cancer cells, and (iii) an ELISA method to detect shed NKG2D-ligand in serum. Employing multiplex IHC and digital image analysis, we found that membrane bound NKG2D-ligands are upregulated in AML and HCC compared to age-matched normal tissue controls. Lastly, using in-house developed ELISAs, we determined that shed NKG2D-ligands can be successfully detected in serum isolated from patients with MDS. Taken together, these assays provide methods for evaluation of NKG2D-ligand dynamics as well as the detection and phenotypic analysis of CAR-NK and immune cell populations in clinical samples.

Title: **Immune masking strategies to extend the pharmacokinetics of allogeneic cell therapies**
Session Category: **Immunology**
Session Title: **Preclinical Immunotherapy**
Abstract Number: **5511**

Development of immune evasion strategies are underway to improve the pharmacokinetics of allogeneic cell therapies by engineering them to avoid host vs. graft disease, where allogeneic NK and T cells are rapidly targeted by the patient's own immune system. Hypoimmune strategies are particularly important for the development of allogeneic products containing mixed NK and T cell populations to minimize product cell fratricide. A conventional method for preventing host T rejection of allogenic T cells, is to combine knockout (KO) β-2 microglobulin (β2M) to diminish expression of MHC class I proteins with overexpression of nonclassical MHC class I protein, HLA-E, to evade host NK cell rejection. This study evaluated the effectiveness of HLA-E and other molecules in β2M deficient T cells for inhibiting NK cell cytotoxicity. Concurrently, a high throughput platform was developed to screen NK inhibitory peptides and synthetic ligands to identify novel immune masking strategies for extending allogeneic cell therapy persistence for broad patient populations.

The study showed that the benefit of HLA-E expression in suppressing NK cell cytotoxicity is highly correlated with the expression of NKG2A on the host NK cells. Viral peptides were potent suppressors of NK cell activity, and less dependent on donor NKG2A expression. These data support further exploration of different immune masking strategies in order to extend the pharmacokinetics of allogeneic cell therapies.

About Nkarta
Nkarta is a clinical-stage biotechnology company advancing the development of allogeneic, off-the-shelf natural killer (NK) cell immunotherapies 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.

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: the future impact of Nkarta's research activities; the clinical application of multiply edited CD70 CAR NK cells; Nkarta's ability to build and advance a pipeline of cell therapies for the treatment of cancer; and the potential of Nkarta's current and future product candidates to disrupt the cancer treatment landscape. 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; 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; the complexity of the manufacturing process for CAR NK cell therapies; 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 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