# Nkarta Presents New Preclinical Data from Engineered NK Cell Platform at SITC 36th Annual Meeting

November 12, 2021

SOUTH SAN FRANCISCO, Calif., Nov. 12, 2021 (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 Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting and Pre-Conference Programs.

"The data we presented at this year's SITC meeting showcase the rapid and continuous advancement of our NK cell platform and its potential to deliver pioneering off-the-shelf cell therapies," noted James Trager, PhD, Chief Scientific Officer of Nkarta. "Nkarta's ongoing research activities are designed to heighten the innate ability of NK cells to identify and kill tumor cells and to further build on our efficient and robust manufacturing process. Our findings reported at SITC support further exploration of CISH gene-knockout 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 SITC follow. Each poster will be available for download shortly after the presentation at https://www.nkartatx.com/publications/*

***Title:*** **A Combined Strategy of CD70 CAR Co-expression with Membrane-bound IL-15 and CISH Knockout Results in Enhanced NK Cytotoxicity and Persistence***
***Abstract Number and Type:*** **16439, oral**
***Poster Presentation Date and Time:*** **November 10, 2021, 2:40 p.m. ET**
This study illustrates multiple approaches to modify NK cells to target CD70, an antigen highly expressed in hematological malignancies and solid tumors, including renal cell carcinoma. Optimal CD70 chimeric antigen receptor (CAR) candidates were identified using high throughput screening approaches. 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 knockout of CISH and CD70 genes using the CRISPR/Cas9 system enhanced the persistence in culture and the cytotoxicity of the cells against multiple tumor cell lines. The knockout of CISH also supported the resistance of primary NK cells to suppressive elements active in the tumor microenvironment.

***Title:*** **CISH Gene-knockout Anti-CD70-CAR NK Cells Demonstrate Potent Anti-tumor Activity Against Solid Tumor Cell Lines and Provide Partial Resistance to Tumor Microenvironment Inhibition***
***Abstract Number and Type:*** **113, poster**
***Poster Presentation Date and Time:*** **November 12, 2021, 7:00 am – 8:30 pm ET**
Primary NK cells engineered with CD70 chimeric antigen receptor (CAR), membrane bound form of IL-15 (mbIL-15) and knockout of CISH and CD70 genes using the CRISPR/Cas9 system could be produced efficiently, demonstrating consistent knockout and transduction efficiency across donors. Memory like NK cell differentiation of the gene edited NK cells was achieved using a modified K562 stimulatory cell line expressing membrane-bound IL-15 and 4-1BBL with the addition of IL-12 and IL-18 during expansion. Various gene editing candidates were assessed; the knockout of CISH in particular enhanced not only tumor cell killing by CD70 CAR NK cells, but also their persistence in culture and resistance to suppressive molecules associated with the tumor microenvironment, such as TGFß and adenosine.

***Title:*** **Potentiating the Large-Scale Expansion and Engineering of Peripheral Blood-Derived CAR NK Cells for Off-the-Shelf Application**
***Abstract Number and Type:*** **151, poster**
***Poster Presentation Date and Time:*** **November 12, 2021, 7:00 am – 8:30 pm ET**
The study highlights novel methods for scaling the expansion of engineered NK cells to potentially supply a life cycle's worth of commercial off-the-shelf product from a single donor. The methods entail sequential pulses with a proprietary K562 stimulatory cell line in the presence of IL-2 and use of IL-12 and IL-18 to achieve differentiation into memory-like NK cells. When these methods were used to achieve cell expansion greater than even 2 billion-fold, CAR expression was increased on the NK cell surface, engineered cells with CISH gene knockout, CAR and mbIL-15 were preferentially enriched during expansion, and the chromosomal integrity of the cells was well maintained.

***Title:*** **KIR Haplotype Can Inform Donor Selection in the Production of Allogeneic Memory-Like CAR NK Cells for Clinical Application**
***Abstract Number and Type:*** **128, poster**
***Poster Presentation Date and Time:*** **November 13, 2021, 7:00 am – 8:30 pm ET**
Study findings suggest that the profile of activating and inhibitory KIR genes expressed by healthy donors' NK cells may serve as a future criterion for selecting donors whose NK cells can be engineered for enhanced cytotoxic activity. The optimal KIR profile may depend on the process used to generate NK cells. Engineered CD19 CAR NK cells whose expansion includes IL-12 and IL-18 added to a proprietary K562 stimulatory cell line containing mbIL-15 and 15-41BBL stimulatory cells showed enhanced potency and upregulation of NK memory associated cell surface markers and natural cytotoxicity markers. Finally, donor KIR haplotype correlated best with CAR NK activity in cells expanded in the presence of IL-12 and IL-18, showing that donor selection and expansion methods must be considered together for development of optimal CAR NK therapies.

* *Presented jointly with CRISPR Therapeutics*

**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, 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, but are not limited to, statements concerning Nkarta’s expectations regarding any or all of the following: the potential of Nkarta’s NK cell platform; the clinical application of CISH gene-knockout CD70 CAR NK cells; future criteria for donor selection; the efficiency and scalability of Nkarta’s manufacturing processes; Nkarta’s ability to develop manufacturing methods that produce a life cycle’s worth of commercial product from a single donor; Nkarta’s ability to build a pipeline of cell therapies; and the benefits of Nkarta’s cell engineering and manufacturing technologies. 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, filed with the SEC on November 10, 2021, 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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