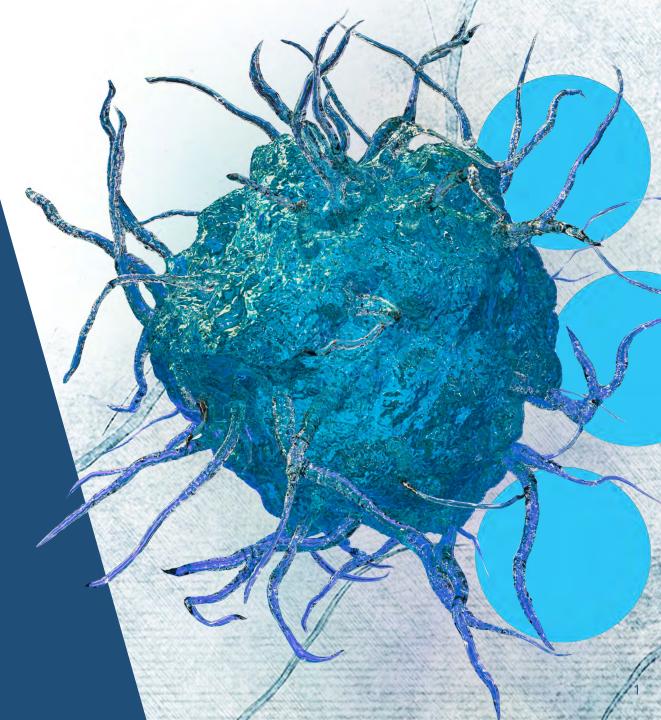
nkarta

NEXT GENERATION Natural Killer Cells Engineered to Beat Cancer



Forward looking statements

This presentation contains forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, regarding future events and the future results of the company that are based on current expectations, estimates, forecasts, and projections about the industry in which the company operates and the future of our business, future plans and strategies, projections, anticipated trends and events, the economy, and other future conditions, and the beliefs and assumptions of the management of the company. Words such as "address," "anticipate," "believe," "consider," "continue," "develop," "estimate," "expect," "further," "goal," "intend," "may," "plan," "potential," "project," "seek," "should," "target," "will," variations of such words, and similar expressions are intended to identify such forward-looking statements. Such statements reflect the current views of the company and its management with respect to future events and are subject to inherent risks, uncertainties, and changes in circumstances that are difficult to predict and may be outside our control. Therefore, you should not rely on any of these forward-looking statements. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, the company's actual results, performance, or achievements could differ materially from the results expressed in, or implied by, these forward-looking statements. Please see section entitled "Risk Factors" in our guarterly and periodic filings for a description of these risks and uncertainties. This presentation has been prepared by the company based on information it has obtained from sources it believes to be reliable. Summaries of documents contained in this presentation may not be complete. The company does not represent that the information herein is complete. The information in this presentation is current only as of the date on the cover, and the company's business or financial condition and other information in this presentation may change after that date. The company undertakes no obligation to update any forward-looking statements in order to reflect any event or circumstance occurring after the date of this presentation or currently unknown facts or conditions.



Pioneering the next revolution in cell therapy

Efficient, robust, next generation NK cell platform built for

Blood cancers and solid tumors

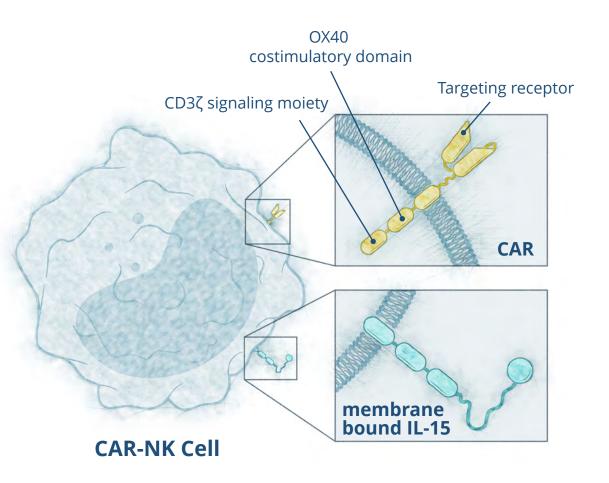
Allogeneic and off-the-shelf

Industrialized manufacturing

Outpatient administration

CO-LEAD PROGRAMS

NKX101: Phase 1 ongoing NKX019: patient dosing to start 2H 21



CRISPR

THERAPEUTICS

R

Cell therapy leaders

Complementary expertise

Global Collaboration to Develop Gene Edited Cell Therapies

GENOME ENGINEERING CAPABILITY

Best-in-class, clinically validated CRISPR gene editing

Ability to deploy up to 5 CRISPR/Cas9 gene edits in unlimited number of Nkarta product candidates

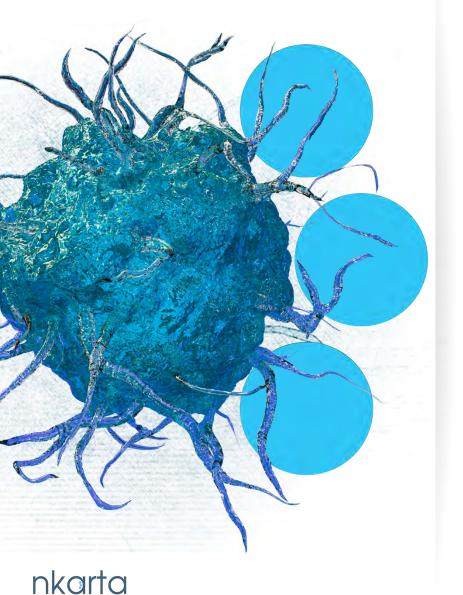
EXPERIENCED CLINICAL DEVELOPMENT PARTNER

Co-development and co-commercialization of CD70 CAR NK, CAR NK + CAR T, and option for a third early-pipeline target program

Leverage CD70 and allogeneic T cell expertise of CRISPR Therapeutics



They're called Natural Killer cells for a reason



Because	Therefore		
Innate power of NK cells to identify and kill transformed cells	Highly active, cytotoxic cells as foundation and starting material		
Low risk of GvHD	Naturally allogeneic		
Low risk of CRS and neurotoxicity	Potential for routine administration and broad outpatient access		
Predictable pharmacokinetics	Potential for flexible multi-dose and multi-cycle treatment		

Next gen platform enlists natural, healthy human NK immune cells for optimal product Donor selection for desired cell features

Process starts with highly active, cytotoxic, NK cells

Multiplex gene engineering to enhance immune cell performance Which allows for:



Potential for universal donors and master cell banks



Efficient manufacturing enables rapid, large-scale production



Well defined, high quality, consistent product



Staying Ahead of the Curve:

A Platform That Incorporates Multiple Next Generation Enhancements

nkarta

✓ <u>Armored cells</u> with membrane-bound IL-15 for persistence

- ✓ Multiplexed <u>CRISPR/Cas9 genome engineering</u>
- Enhanced expansion, persistence and TME resistance via <u>CISH deletion</u>
- <u>Cytokine activation</u> using IL-12, -15 and -18 to enhance anti-tumor activity persistence and memory-like properties
- Clinical trial designs include <u>multi-doses and multi-cycles</u> of treatment
- ✓ No requirement for cytokine support

Evolving body of clinical data validates NK approach

NKG2D and non-engineered NK cells

~30 clinical studies

Well tolerated and no GvHD (non-transplant)

600 ~330 AML/MDS patients

~100 R/R AML patients (non-transplant) ~34% aggregate CR rate

CD19

MD Anderson study with CD19 CAR-NK cells New England Journal of Medicine, Feb 2020

7 / 11 CRs

CRs in advanced B cell malignancies

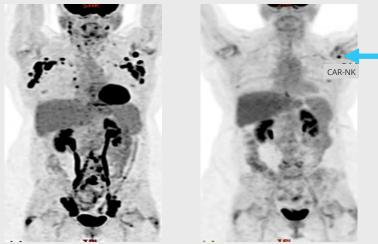
PRE-TREATMENT

DAY 30 POST CAR-NK

No reported CRS,

GvHD or

neurotoxicity



Patient achieved CR. CAR-NK cells traffic to sites of disease

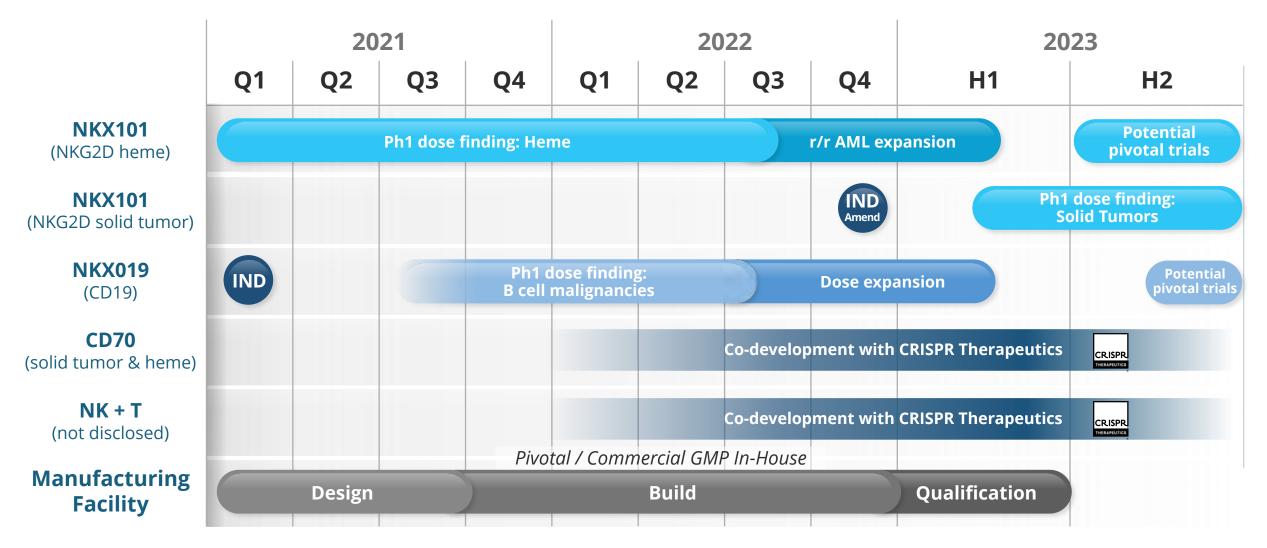


Supdate: ASH 2020 Activity and tolerability of engineered NK cells in multiple clinical studies

K. Rezvani, et al., N Engl J Med 2020, 382:545-553. DOI: 10.1056/NEJMoa1910607. Takeda Investor Day 2019. CRS: Cytokine release syndrome. GvHD: Graft versus host disease.

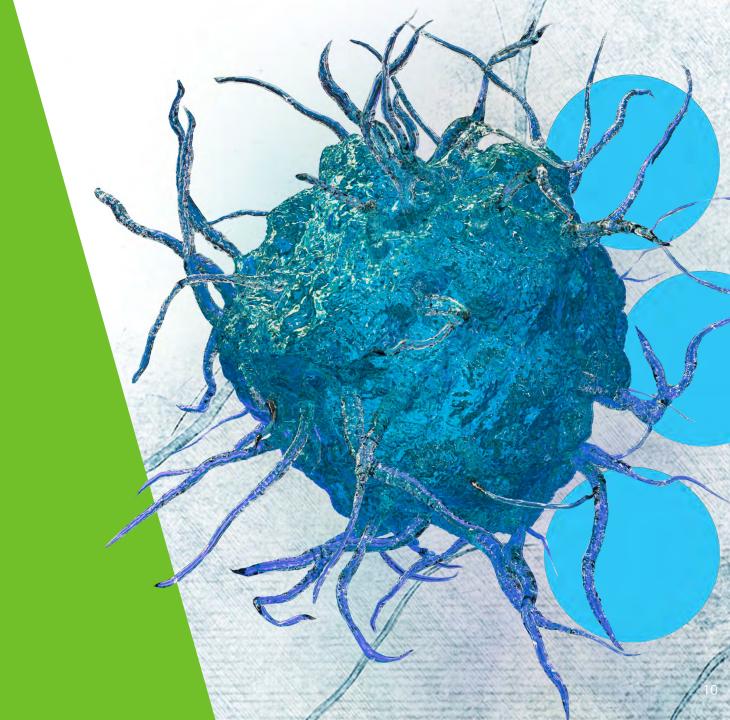


Platform-driven pipeline with multiple upcoming milestones





Platform





Harnessing the power and efficiency of healthy adult NK cells for the next revolution in cell therapy

CELL SOURCE

FEATURE	AUTOLOGOUS	IPSC	DONOR
MANUFACTURING	Highly difficult to scale	Complex NK differentiation and expansion over 4-8 weeks	Robust and scalable 2-week process starting with real NK cells
GENETIC ENGINEERING	Costly and inconsistent	Requires single cell isolation, extensive pre-clinical characterization	Consistent, cost-effective, and efficient
FINAL PRODUCT IDENTITY	Driven by process alone	Sensitive to control of differentiation at scale, subject to genetic drift	Highly consistent NK cell function and phenotype
POTENCY	Variable with starting material; Diminished cell killing capacity due to self recognition and NK cell dysfunction in cancer	Driven by process and genetic engineering	Donor selection, process, and engineering for optimal potency
PACKAGING AND DELIVERY	Limited doses/complex logistics	Cryopreserved and off-the-shelf	Cryopreserved and off-the-shelf



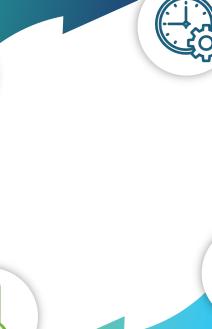
Proprietary technologies in place for a best-in-class NK cell platform

Expansion

Donor NK cells are cocultured with proprietary K562 stimulatory cell line to achieve **high cell numbers**

Cryopreservation

Freezing process maintains NK cell viability and potency to enable true off-the-shelf cell product



Persistence

NK cells are engineered for expression of proprietary **membrane bound IL-15** to enhance time in circulation

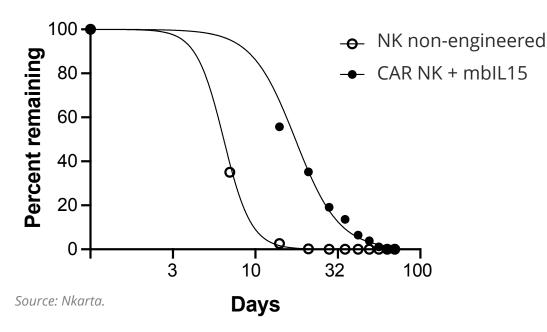


NK cells are engineered for expression of **optimized CARs**



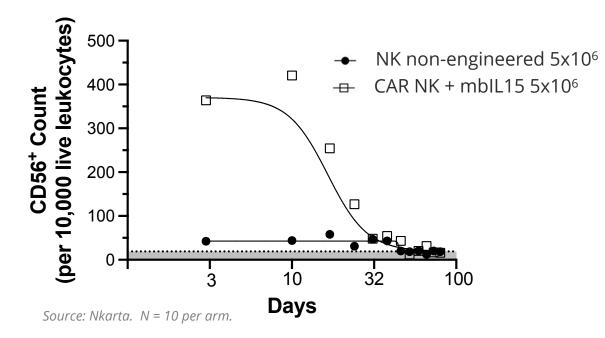
Superior NK cell persistence from membrane bound IL-15

IN VITRO PERSISTENCE



2-fold increase in exposure observed in vitro with a single administration

IN VIVO PERSISTENCE AND EXPANSION IN NSG MICE

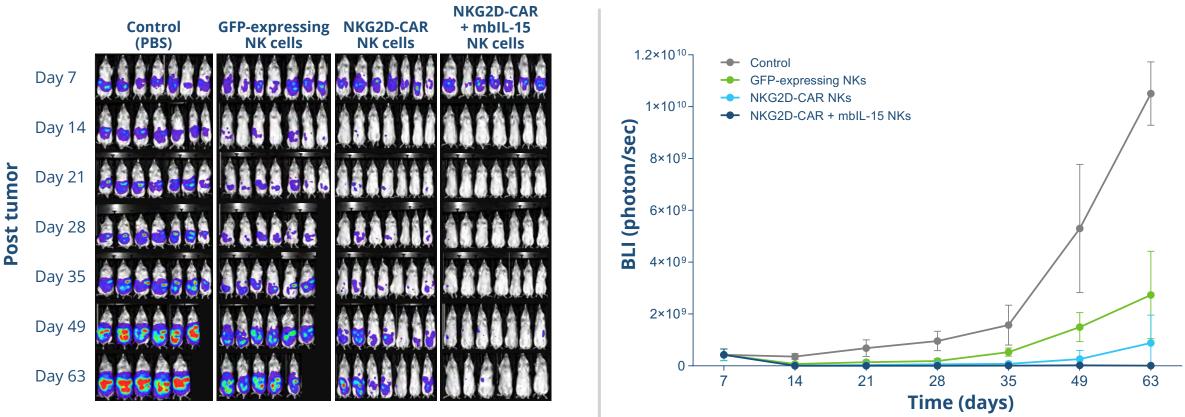


7-fold increase in exposure observed in vivo with a single administration

NK cells engineered to express membrane-bound IL-15 (mbIL-15) demonstrate superior persistence as compared to unmodified NK cells



Persistence and targeting to maximize anti-tumor activity

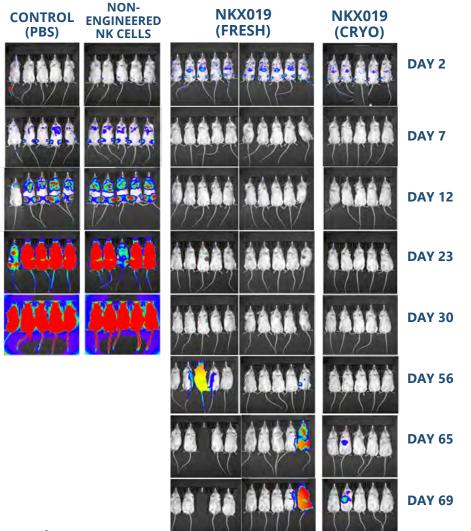


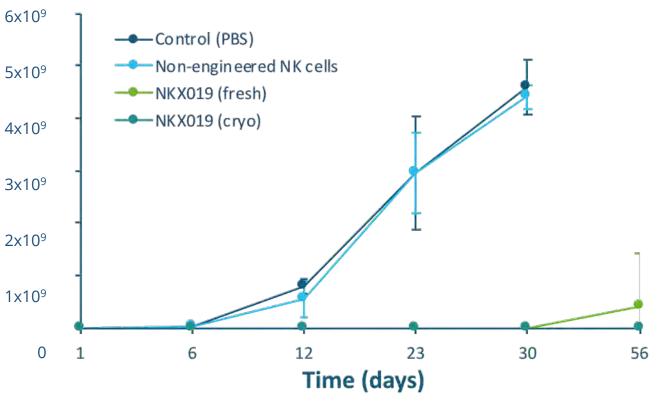
Source: Nkarta. U2OS osteosarcoma model; 3 x 10⁶ NK cells administered on D7. Graphical data at right are average BLI of mice above.

NK cells demonstrate enhanced tumor killing when engineered for targeting and mbIL-15 expression



Our cryopreserved products are highly cytotoxic



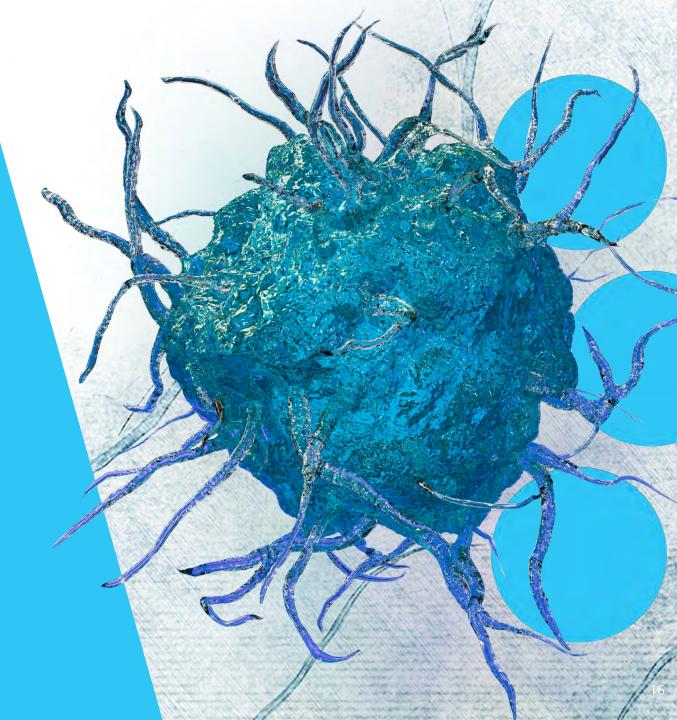


Nalm-6 lymphoma model. 107 cells administered one day post tumor. Graphical data above are an average of mouse luminescence at left. "Cryo" denotes cryopreserved then thawed NKX019.

NKX019 production under optimized conditions allows cryopreservation with retention of *in vivo* activity

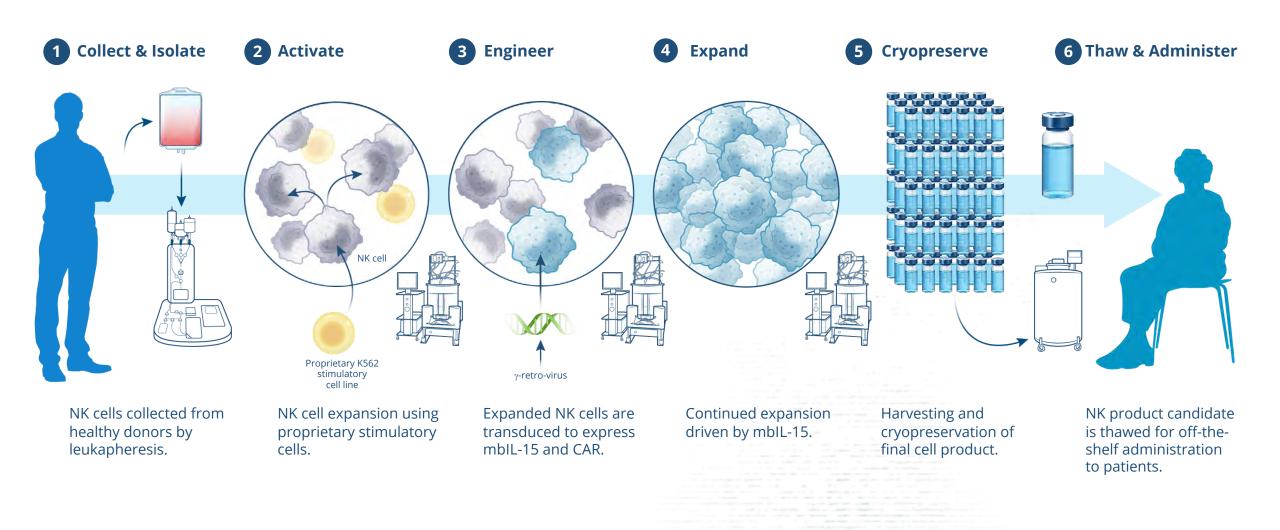


Manufacturing



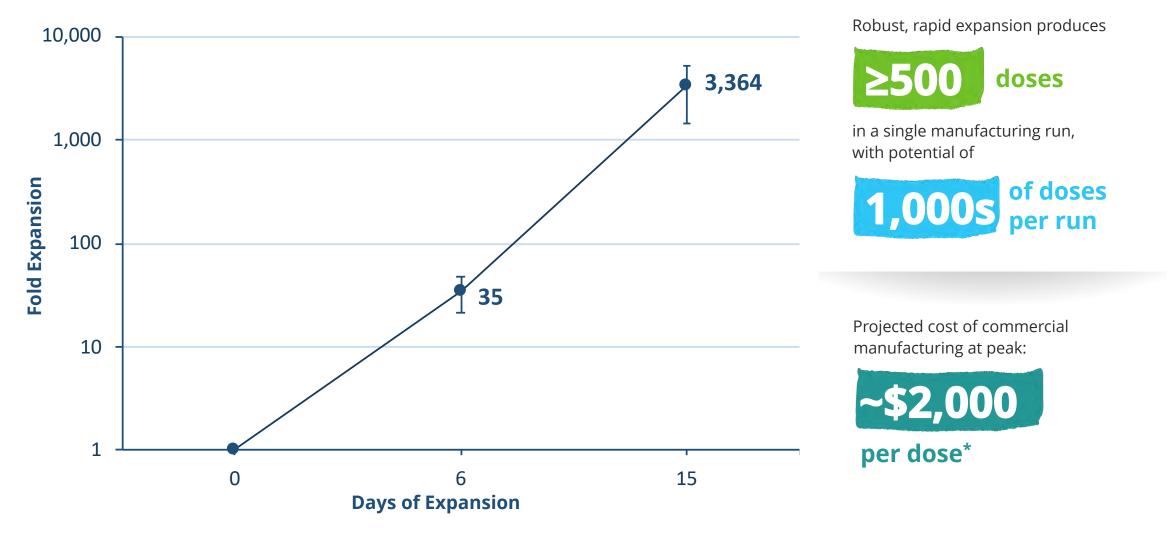


A powerful and efficient process for off-the-shelf products





Proprietary expansion enables industrial-scale manufacturing





Data above are from the process development of NKX019 for cGMP manufacturing and are an average of 5 expansions from 4 different donors.



In-house manufacturing to control process and production

CLINICAL GMP FACILITY

Multi-product facility to support clinical development

Clinical production expected to start in 2021

FUTURE COMMERCIAL-SCALE FACILITY

Design and engineering process initiated

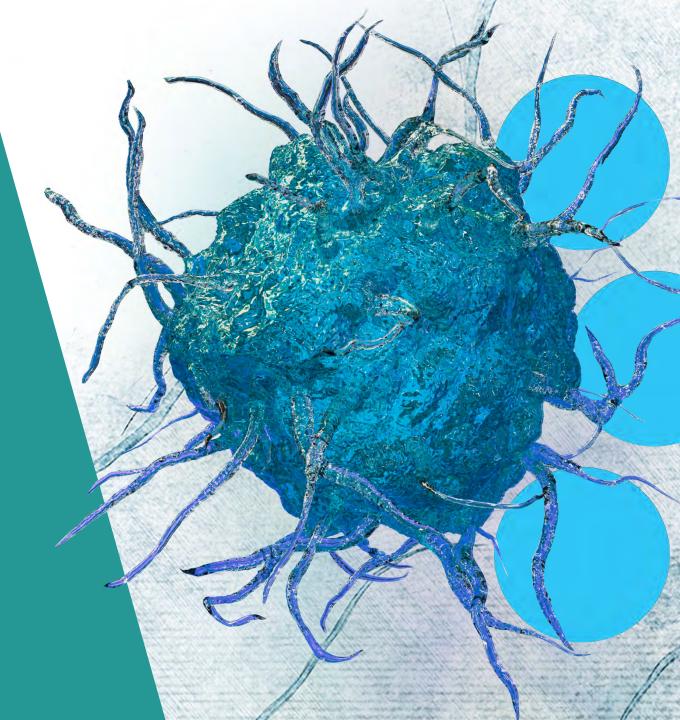
Facility expected to supply pivotal trials of NKX101 and NKX019

Modular design for future expansion to meet commercial demands



Pipeline





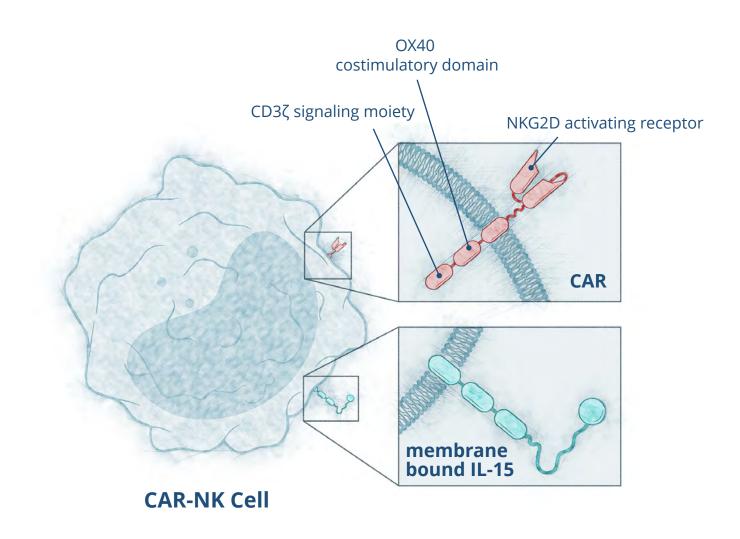
NKX101: CAR-NK targeting NKG2D ligands

NKG2D receptor is primary driver of NK cell activation and tumor killing

>10x increase in NKG2D expression vs. non-engineered NK cells

OX40 selected based on superiority vs. other costimulatory domains

Targets of NKG2D are selectively over-expressed in cancer cells





NKG2D: ligands in multiple tumors, responses in AML

NKG2D ligand expression is documented in multiple tumor types

TUMOR TYPE	REFERENCE
AML, ALL, CML, CLL	Hilpert, <u>J Immunol 2012</u>
MULTIPLE MYELOMA	<u>Carbone, Blood 2005</u>
HCC	<u>Kamimura, J Hep 2012</u>
BREAST	<u>de Kruijf, BMC Can 2012</u>
OVARIAN	<u>McGilvray, Int J Can 2010</u>
LUNG	Okita, Can Imm Immunother 2016
COLON	McGilvray, CCR 2009
MELANOMA	<u>Vetter, J Inv Derm 2002</u>
OSTEOSARCOMA	Lu, Neoplasma 2008
GLIOMA	Weiss, CCR 2018

Clinical responses observed in R/R AML with non-engineered allo-NKs validate NKG2D

STUDY	RESPONSES*
<u>Bachanova, <i>Crit Rev Oncog</i> 2014</u> , A+B cohorts	9 / 42 (21%)
<u>Bachanova, <i>Crit Rev Oncog</i> 2014,</u> C cohort	8 / 15 (53%)
Curti, Blood 2011	1 / 5 (20%)
Kottaridis, PLOS One 2015	1 / 1 (100%)
Miller, Blood 2005	5 / 19 (26%)
Romee, Sci Transl Med 2016	5 / 9 (56%)
Rubnitz, Pediatr Blood Cancer 2015	6 / 12 (50%)
OVERALL	35 / 103 (34%)

*AML responses in patients with morphologic disease at baseline as reported in individual trials, patients with CR at study entry excluded from summary. The 35 responses include 20 CR, 12 CRi, 2 CRp and 1 MLFS.



NKX101: Rationale in acute myeloid leukemia (AML)

NKG2D TARGETS ARE OVER-EXPRESSED in AML blasts

CLINICAL ACTIVITY with non-engineered NKs

UNMET NEED:

nkarta

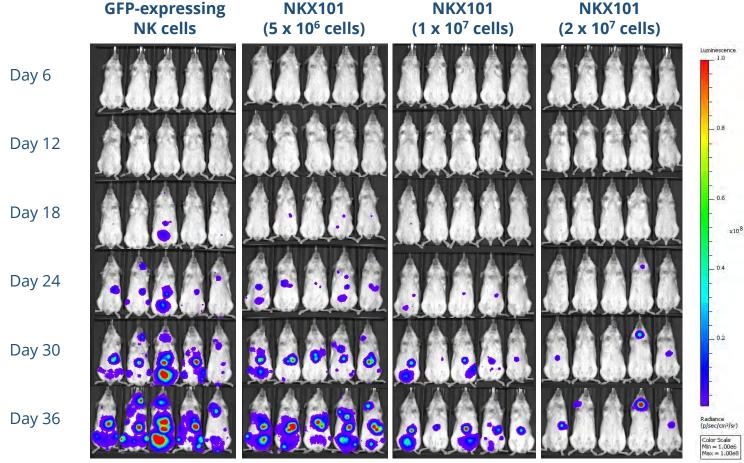
THERAPEUTICS

• AML US incidence: ~21K / yr

Post tumor

5-year survival rate ~28%

Sources: SEER database; Veluchamy, Front Immunol 2017; Brayer ASH 2018; Hilpert, J Immunol, 2012



THP-1 xenograft model treated with a single dose of NK cells (i.v.) 2 days after tumor injection

NKX101 Trial Design

- Modified 3+3 design
- 3 dose levels
- Multi-dosing
 - Regimen A: 3 doses/cycle
 - Regimen B: 2 doses/cycle
- Total CAR-NK cells per cycle: 300 M, 900 M or 3 B
- Potential for multiple treatment cycles lymphodepletion + multi-dose NKX101
- Off-the-shelf and haplorelated product

Single-arm two-part multi-center Phase 1 study evaluating safety and efficacy of NKX101 in r/r AML and higher-risk MDS patients

Lymphodepletion

Cyclophosphamide (300 mg/m²) and Fludarabine (30mg/m²) daily for 3 days

NKX101 multi-dosing cycle

Two dosing regimens: 2 or 3 doses per cycle Total exposure: 300M, 900M or 3B per cycle

Efficacy assessment

Further treatment cycle(s) with FDA concurrence

Day 0
Reg A: Dose 1Day 7
Reg A: Dose 2Day 14
Reg A: Dose 3Day 28Day 0
Reg B: Dose 1Day 7
Reg B: Dose 2Day 14
Reg A: Dose 3Day 28

NKX101 demonstrates anti-tumor activity in solid tumors

LIVER & BILE CANCER US INCIDENCE: ~42K / YR 5-year survival rate ~18%

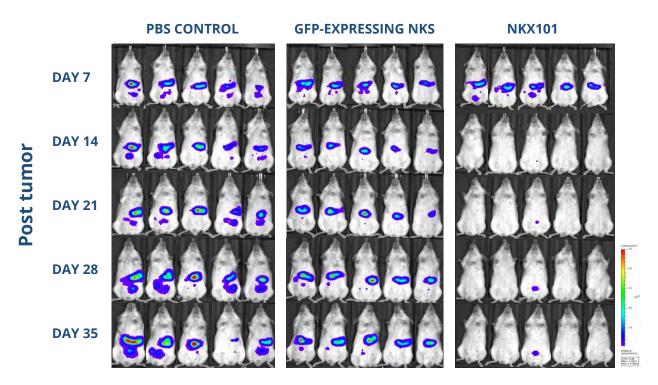
NKG2D TARGETS OVER-EXPRESSED on HCC and CRC cells

NK CELLS ARE IMPORTANT IN LIVER immunity and tumor surveillance

ACTIVITY OF NON-ENGINEERED NK cells in HCC/ICC: 3/16 PRs

PLANNED PHASE 1: LOCOREGIONAL delivery using SOC technique in 1° liver cancer or liver metastases

NKX101 activity in NSG mice



SNU449 HCC xenograft model 3 x 10⁶ NK cells injected at day 7 post-tumor

HCC: Hepatocellular carcinoma. CRC: Colorectal cancer. Sources: SEER database; Sun Act Pharm Sin 2015; Kamimura, J Hepatology, 2012; Kamiya et. al, Cancer Immunol Res 2016; Qin 2017



NKX019: CD19 targeted CAR-NK

UNMET NEED REMAINS DUE to SAFETY, SPEED, ACCESS of APPROVED CD19 CAR-T THERAPIES

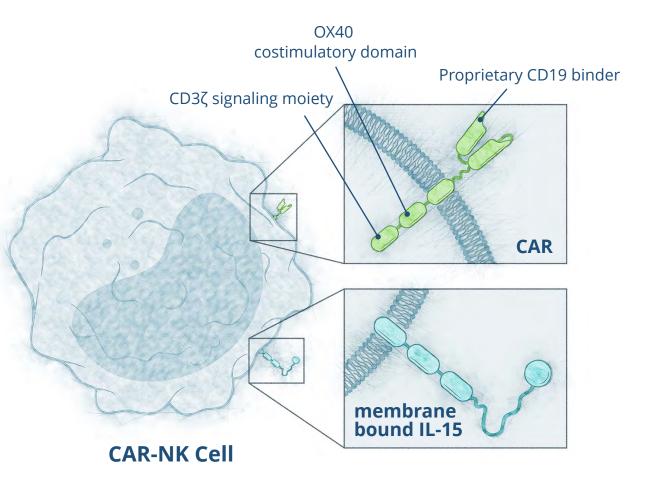
- Gr3+ CRS: 13–49%; Gr3+ neurotoxicity: 18–31%
- Limited number of specialized sites can treat
- 9–34% of patients in pivotal trials didn't receive cells (primarily due to mfg. challenges)

IL-12 and IL-18 EXPANSION ENHANCES *IN VITRO* and *IN VIVO* CYTOTOXICITY and PERSISTENCE

• In combination with Nkarta's NKSTIM feeder NK expansion platform

PATIENT DOSING EXPECTED TO START IN 2H 2021

• Phase 1 in B cell malignancies



Sources: Kymriah® and Yescarta® package inserts; Rezvani NEJM 2020. Per NEJM publication, CR/SD patient achieved a CR for Richter's transformation and SD for underlying CLL. <u>Trager SITC</u> <u>2019.</u>



NKX019 kills tumors with high or low levels of CD19 expression

100-100-**NKX019 NKX019** Cytotoxicity (%) Cytotoxicity (%) 80· 80. CD19 CAR-T 60-60-CD19 CAR-T 40. 40. 20-20 C 0 0.1 10 0.1 10 **Effector : Target Effector : Target**

Low CD19 Expressing Cells

NKX019 can achieve high levels of cytotoxicity even when tumor cells express low levels of CD19 antigen, whereas CD19-targeted T cells are not as efficacious



Nalm6 cells engineered to express varying levels of CD19 were obtained from R. Majzner, Stanford CD19 CAR-T cells: express construct used in Kymriah® Effector : Target is the ratio of NK or T cells to tumor cells

High CD19 Expressing Cells

NKX019 Trial Design

- Modified 3+3 design
- 2 dose levels
- 300M, 1B CAR NK cells per dose
- 3 doses per cycle
- Potential for multiple treatment cycles
- Off-the-shelf product only
- Dose finding followed by multiple dose expansion cohorts

Single-arm multi-center Phase 1 study evaluating safety and efficacy of NKX019 in patients with r/r B cell malignancies

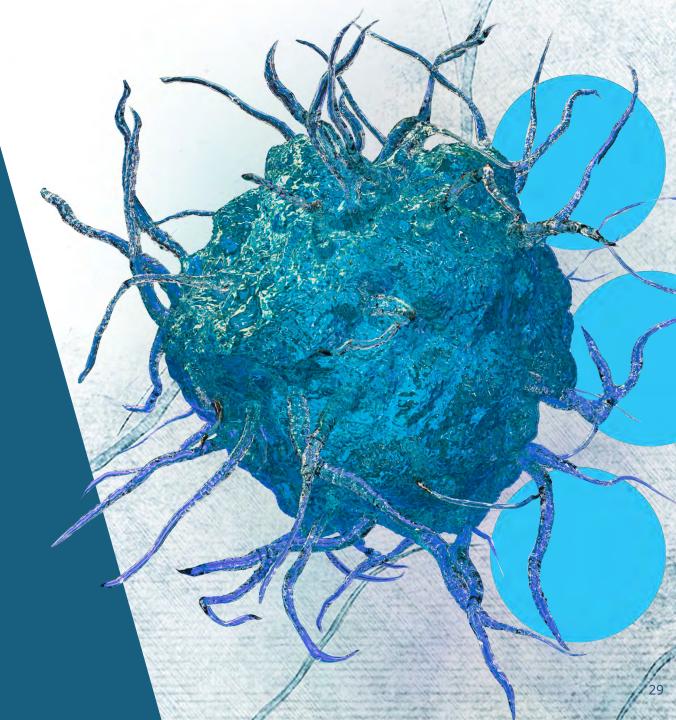
Lymphodepletion

Cyclophosphamide (300 mg/m²) and Fludarabine (30mg/m²) daily for 3 days NKX019 dosing cycle Total exposure per cycle: 900M or 3B

Efficacy assessment Up to 5 treatment cycles

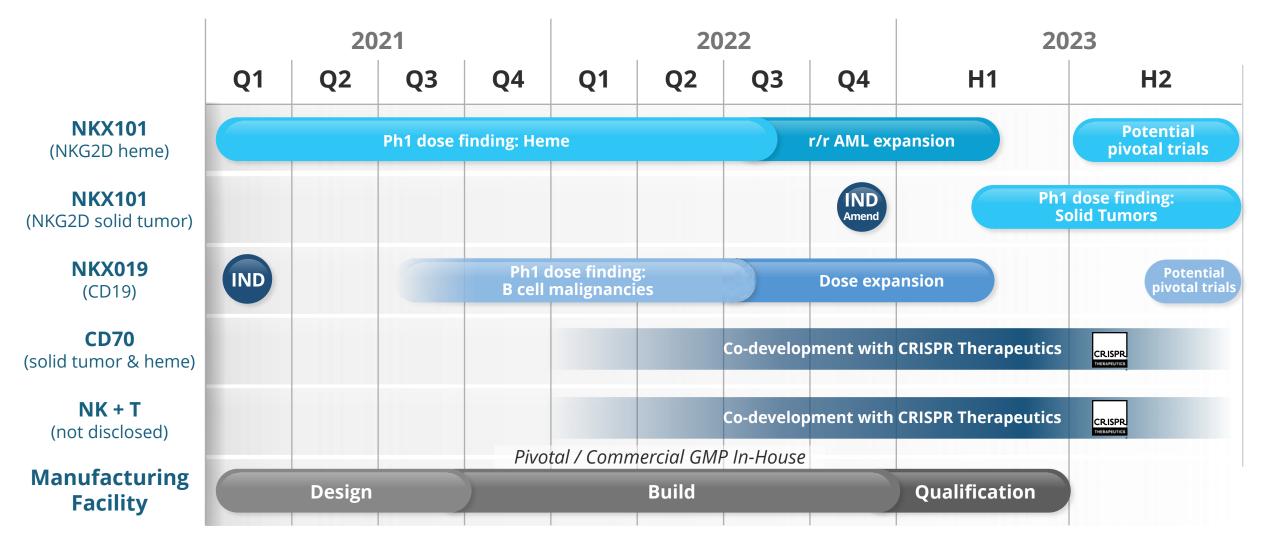
Day 0
Dose 1Day 7
Dose 2Day 14
Dose 3Day 28

Corporate





Platform-driven pipeline with multiple upcoming milestones





Pioneering the next revolution in cell therapy

Efficient and robust next generation NK cell platform for blood cancers and solid tumors

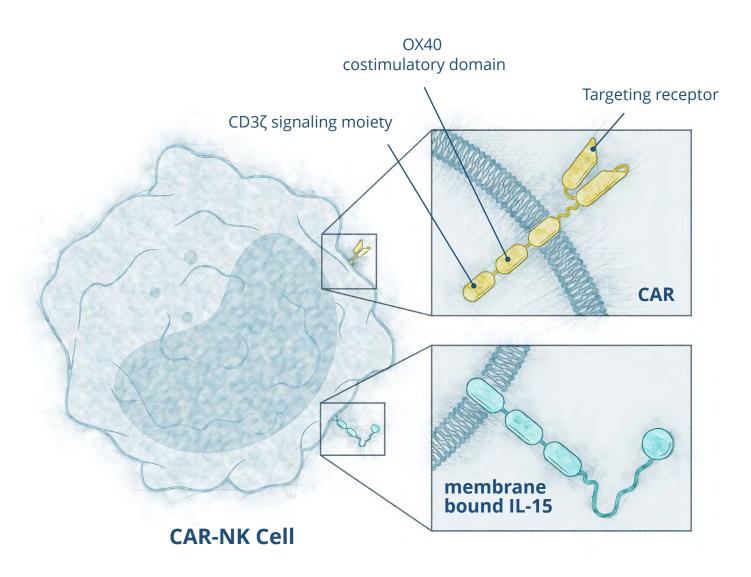
Allogeneic and off-the-shelf products

Industrialized manufacturing

Developed for outpatient administration

Co-lead programs

- NKX101: Phase 1 ongoing
- NKX019: FPI expected 2H 21





Our Vision and Mission

OUR VISION

To be the leading company delivering innovative, accessible cell therapies for cancer patients, their caregivers and families

OUR MISSION

We strive to discover, develop and deliver novel off-the-shelf NK cell therapy product candidates that have a profound impact on cancer patients





Thank you!

