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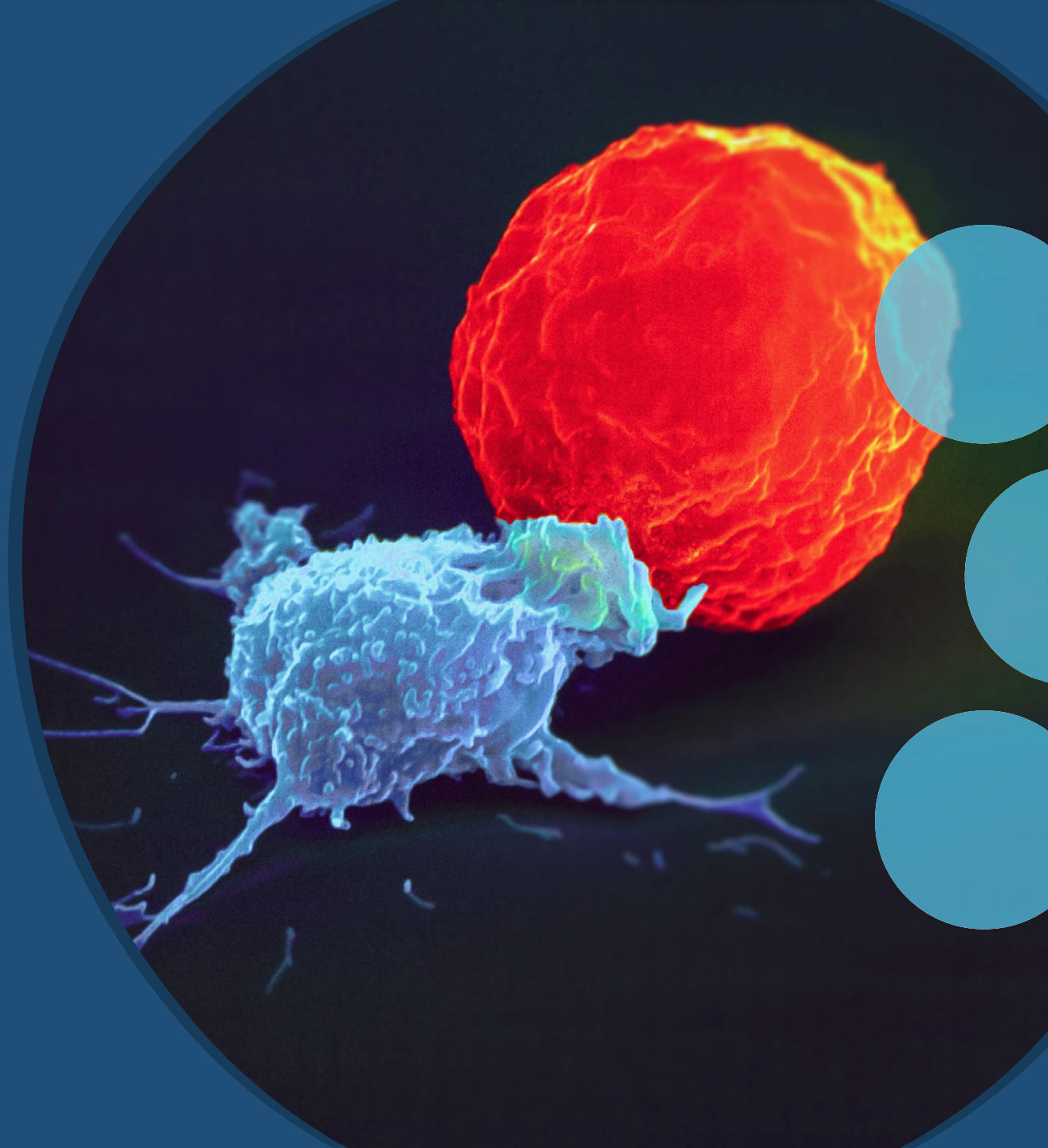
THERAPEUTICS

Allogeneic Natural Killer Cells Engineered to Beat Cancer

February 2020



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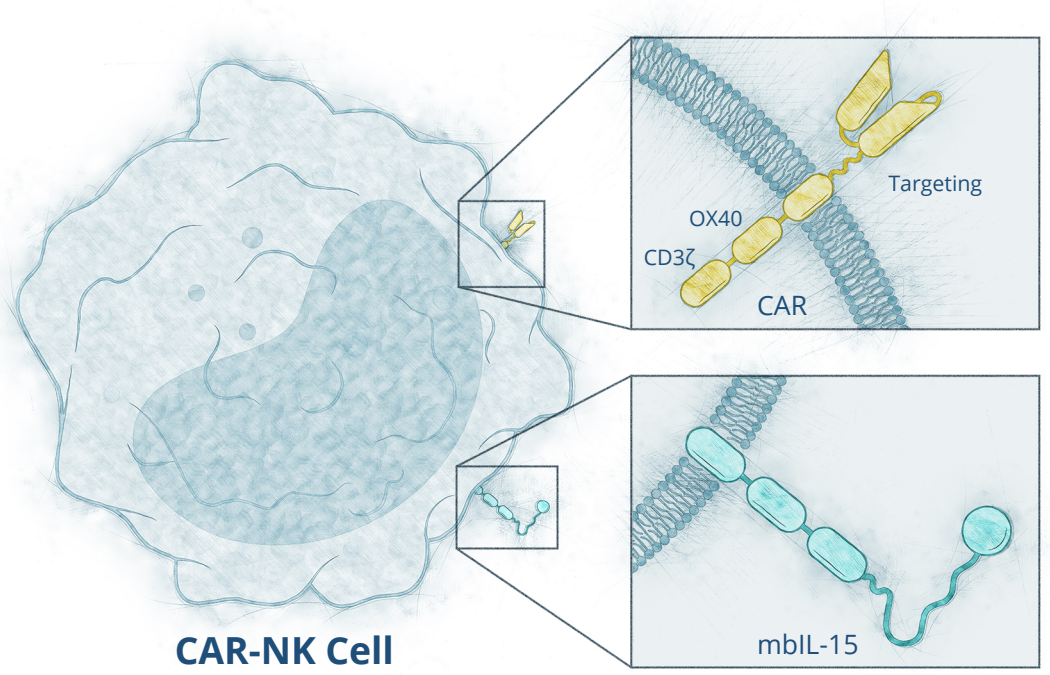
Highlights: Nkarta engineered CAR-NKs

Natural Killer cells are the cornerstone of innate immune surveillance

- Allogeneic and off-the-shelf with attractive cost of manufacturing
- Proprietary expansion, persistence, tumor targeting and cryopreservation technologies
- Three clinical programs expected to begin in next ~12 months
- $114M Series B with top healthcare investors



Targeting receptor, OX40 costimulatory domain, CD3ζ signaling moiety, membrane bound IL-15

Pipeline

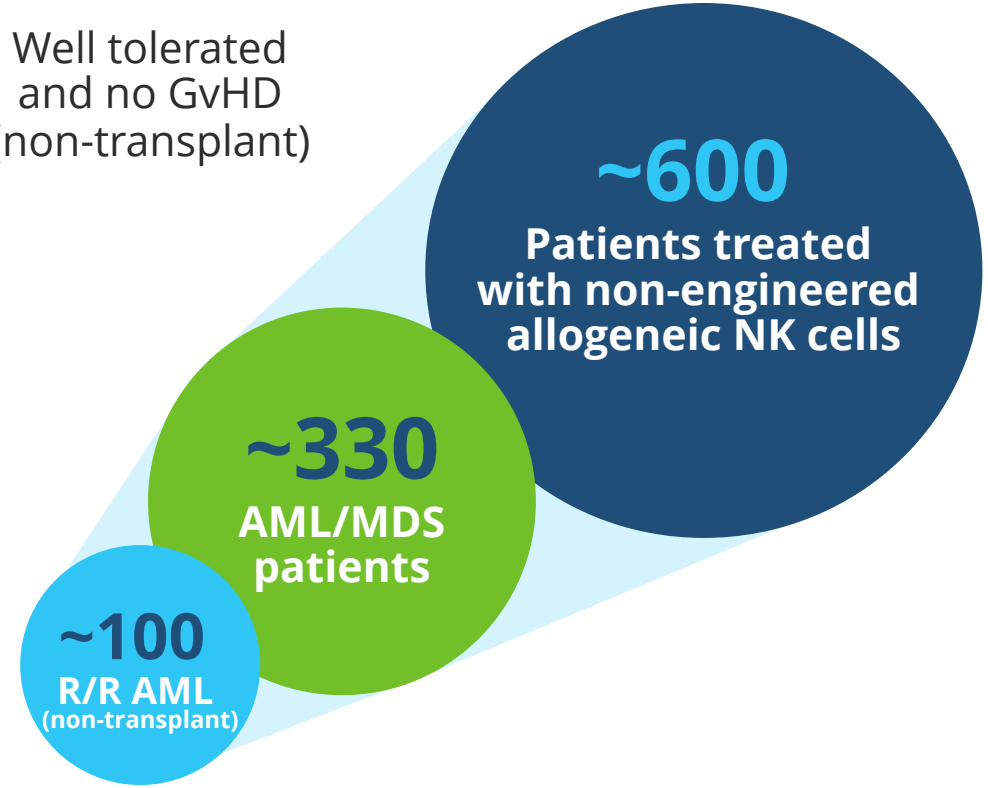
	INDICATION / THERAPEUTIC AREA	DISCOVERY	PRECLINICAL	PLANNED IND	PLANNED PHASE 1
NKX101 (NKG2D)	AML and higher-risk MDS (systemic i.v.)			*1Q20*	*3Q20*
	HCC/mCRC/ICC (locoregional i.a.)			*2Q20*	*4Q20*
NKX019 (CD19)	B-cell malignancies			*3Q20*	*1Q21*
PROGRAM 3	Oncology			*2021*	*2021*
NK + T	Oncology			*2022*	

AML: Acute myeloid leukemia. MDS: Myelodysplastic syndromes. HCC: Hepatocellular carcinoma. mCRC: Metastatic colorectal cancer. ICC: Intrahepatic cholangiocellular carcinoma. i.v.: intravenous (systemic) administration; i.a.: intra-arterial (locoregional) administration

Extensive clinical experience validates NK approach

Patients have been treated with non-engineered NK cells across ~30 studies

Well tolerated and no GvHD (non-transplant)

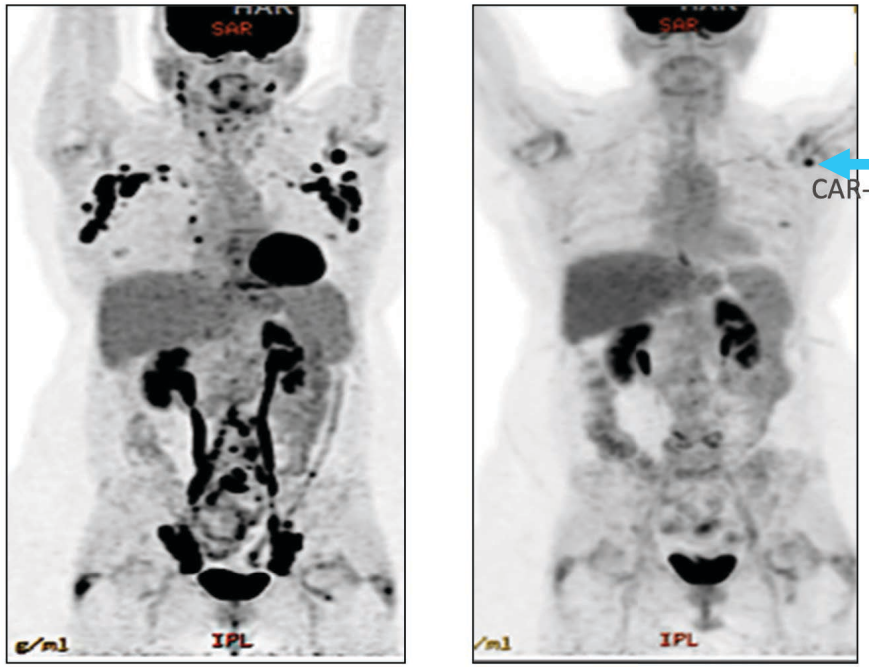


~34% aggregate CR rate

MD Anderson study with CD19 CAR-NK cells

- ✓ 7 / 11 CRs in patients with advanced B-cell malignancies
- ✓ No reported CRS, GvHD or neurotoxicity

PRE-TREATMENT | **DAY 30 POST CAR-NK**



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

Velluchamy 2017; Nkarta systematic literature review; Rezvani NEJM 2020; Takeda Oncology Investor Day 2019.
CR: Complete remission. CRS: Cytokine release syndrome. GvHD: Graft versus host disease.

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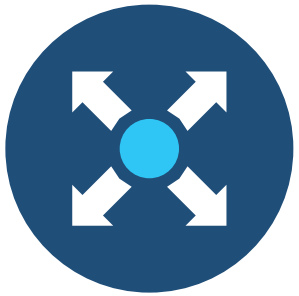
Platform

Nkarta proprietary technologies



Expansion

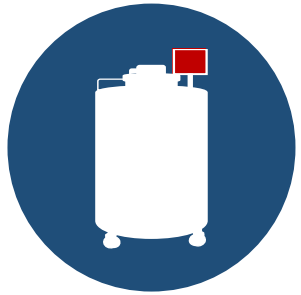
Co-culture with proprietary K562 stimulatory cell line to achieve high cell doses

Persistence

Expression of proprietary membrane bound IL-15 to enhance time in circulation

Targeting

Engineered for expression of optimized CARs



Cryopreservation

Maintains NK cell viability and potency

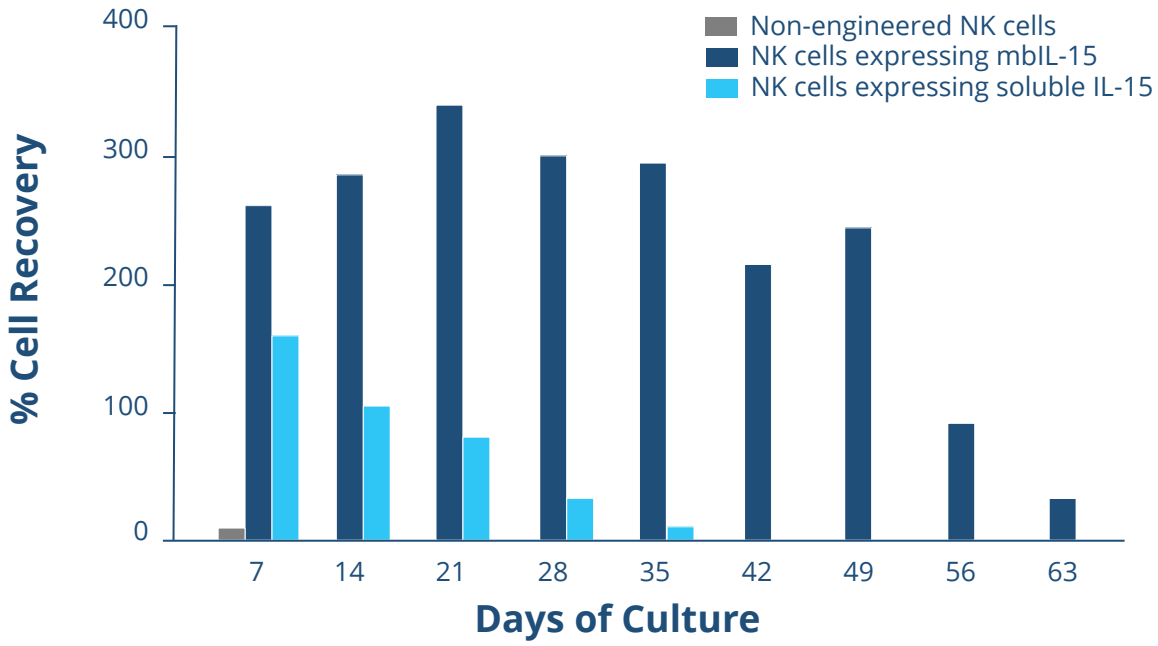
Nkarta CAR-NKs: engineered to enhance activity

	APPROVED CAR-T THERAPIES	ALLO CAR-T THERAPIES	NK CELLS	CAR-NK CELLS
ABILITY TO DISCRIMINATE HEALTHY VS. CANCER CELLS			✓	✓
PERSISTENCE	✓✓	✓✓		✓
OPPORTUNITY FOR IMPROVED SOLID TUMOR ACTIVITY				✓
LOW GVHD RISK	✓	✓	✓	✓
LOW RISK OF CRS OR NEUROTOXICITY		TBD	✓	✓
ALLOGENEIC, OFF-THE-SHELF MANUFACTURING		✓		✓
COST OF MANUFACTURING	+++	++	++	+

Nkarta's platform is designed to generate CAR-NKs engineered to address the limitations of current CAR-T therapies, including safety concerns, tumor targeting, manufacturing time and COGS

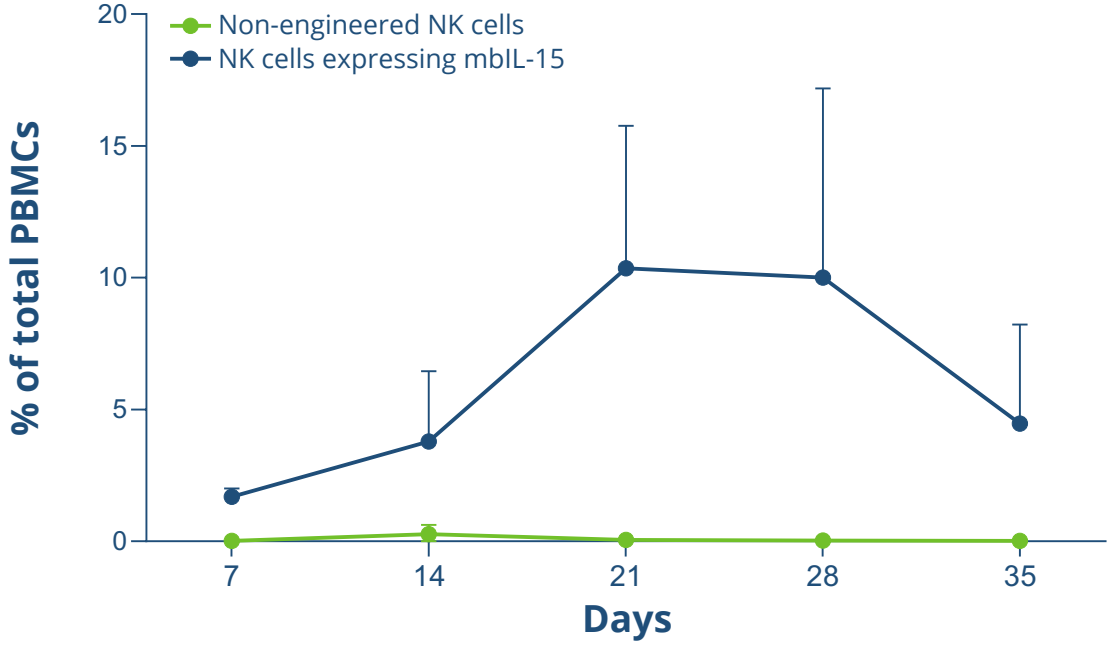
Superior persistence from membrane bound IL-15

In vitro persistence



Source: Imamura, Blood 2014

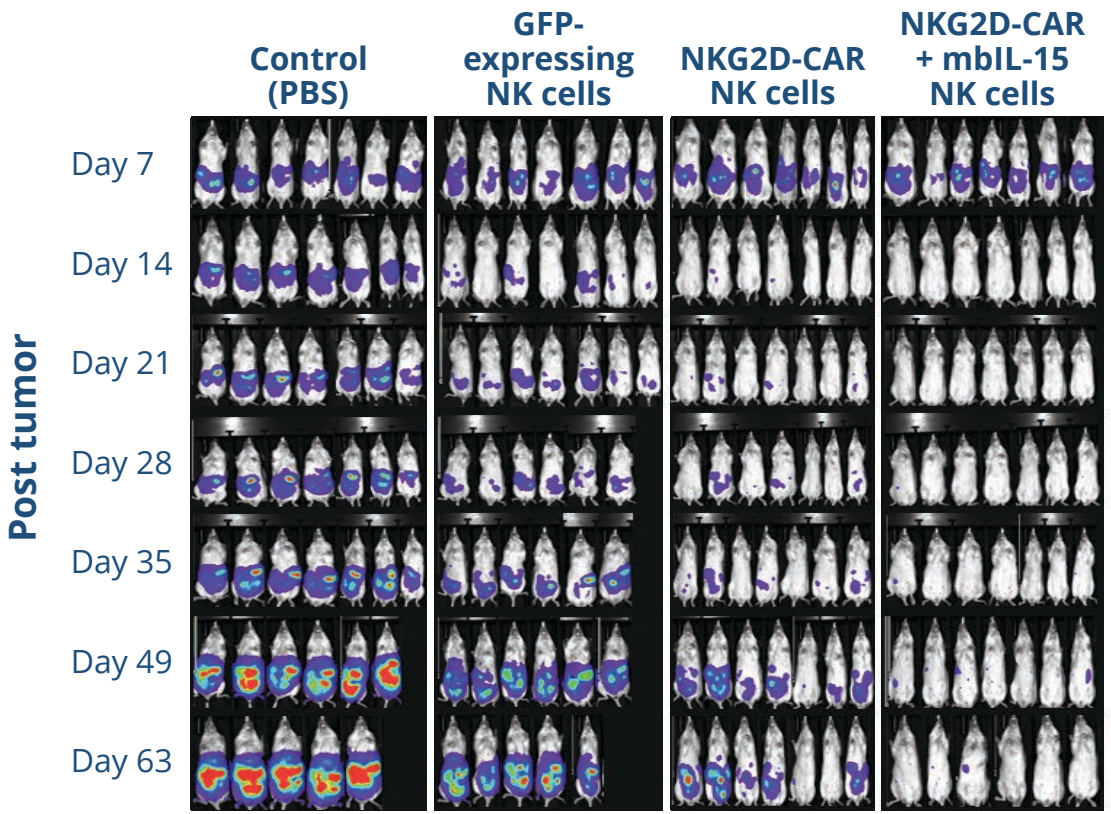
In vivo persistence and expansion in NSG mice

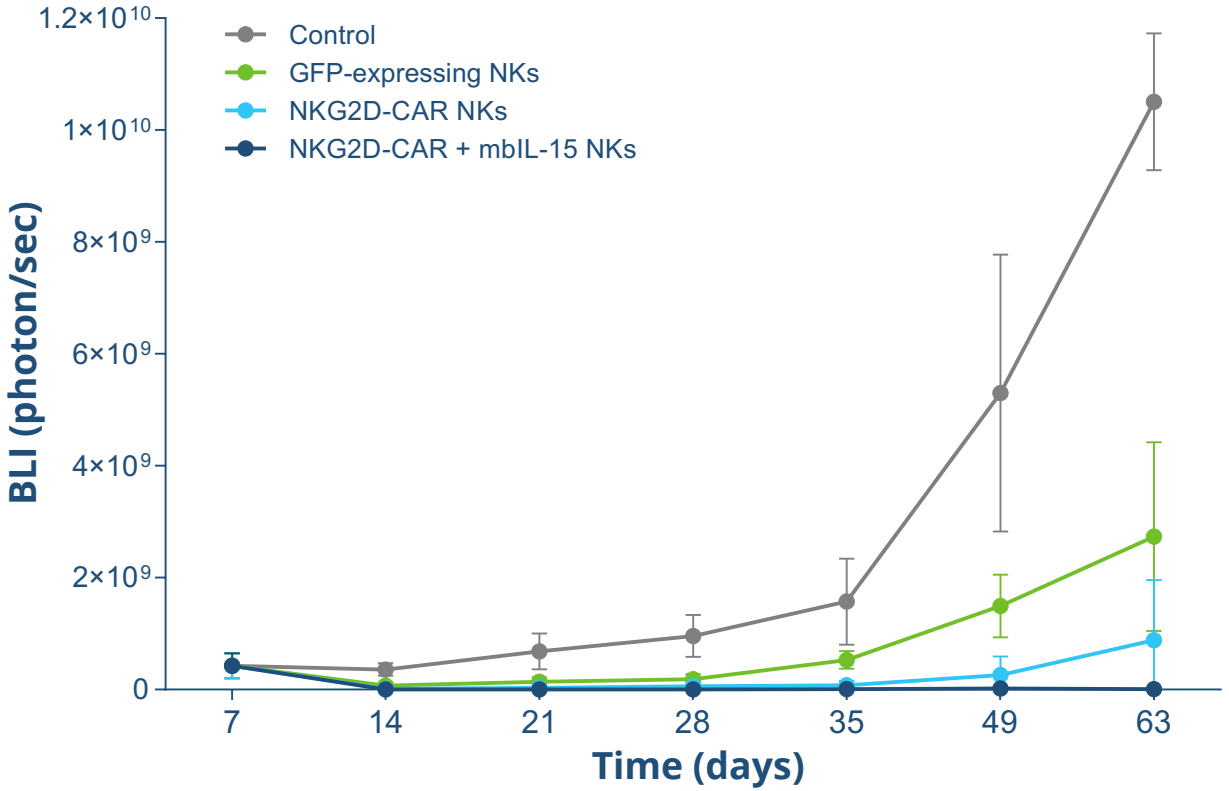


Source: Nkarta. N = 5 per arm.

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 activity





Source: Nkarta. U2OS osteosarcoma model; 3 x 10^6 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

Allogeneic, commercially-enabling manufacturing

1 Collect & Isolate

NK cells collected from healthy donors by leukapheresis.

2 Activate

NK cell expansion using proprietary stimulatory cells.

3 Engineer

Expanded NK cells are transduced to express mbIL-15 and CAR.

4 Expand

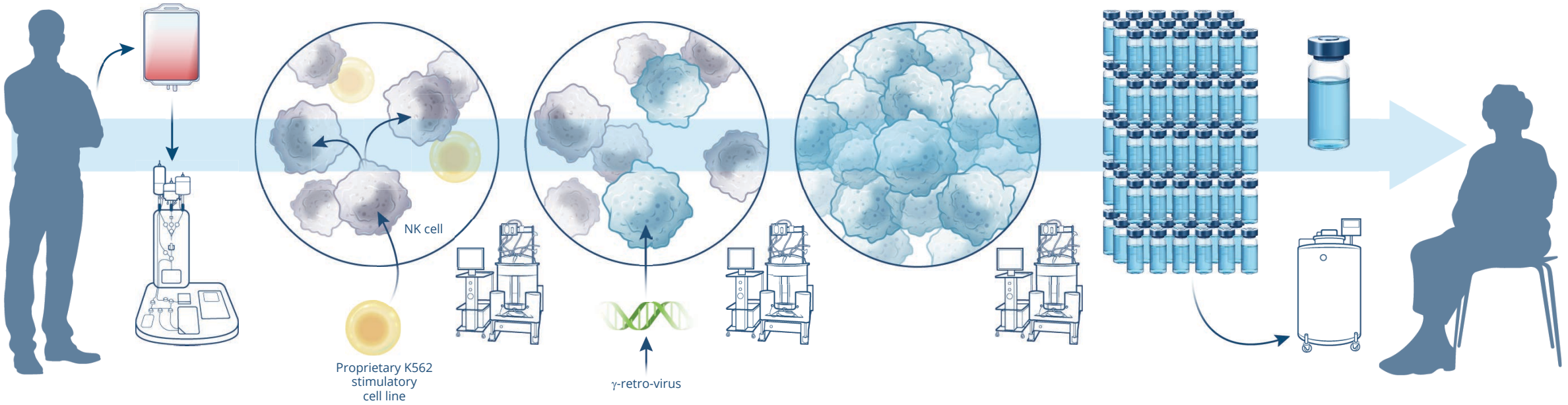
Continued expansion driven by mbIL-15.

5 Cryopreserve

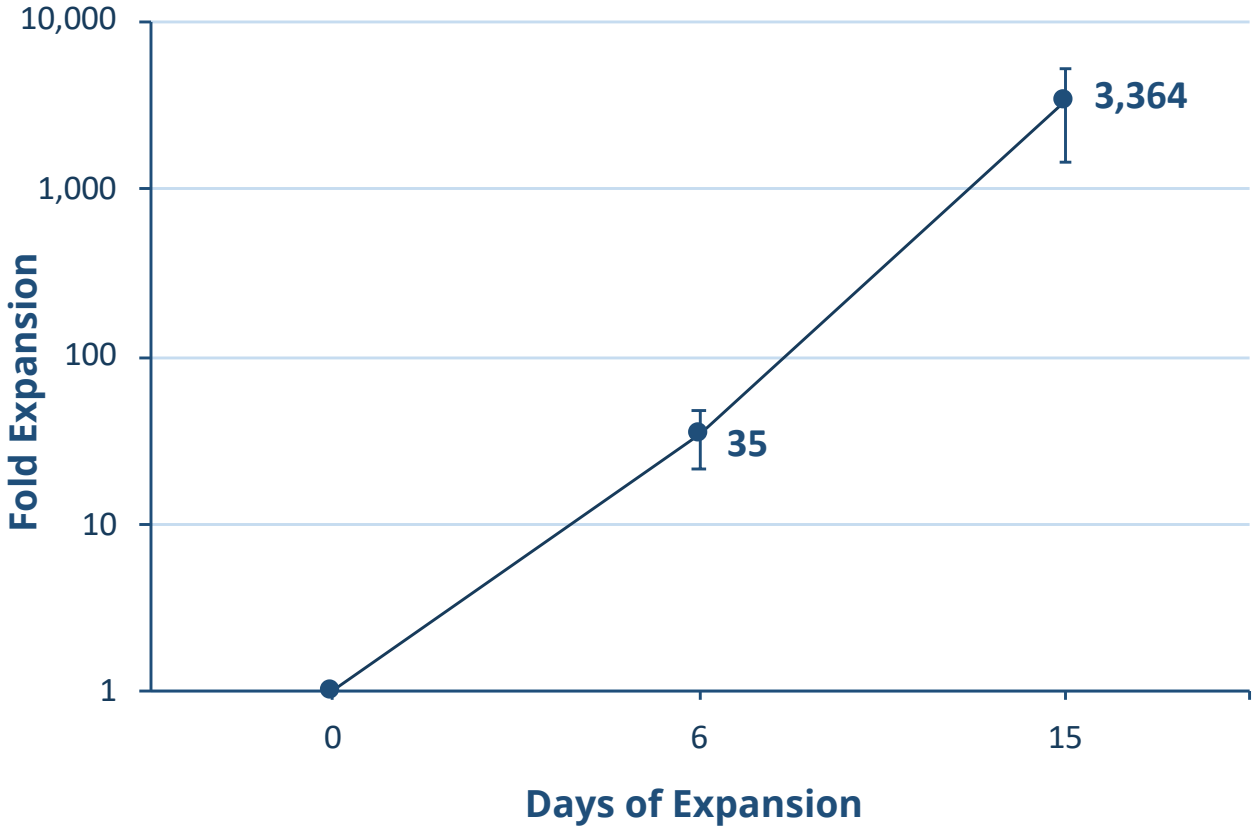
Harvesting and cryopreservation of final cell product.

6 Thaw & Administer

NK product candidate is thawed for off-the-shelf administration to patients.



Proprietary expansion to enable large 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.

- Extensive optimization enables truly off-the-shelf products
- Currently constructing in-house cGMP manufacturing suite
- Projected cost of commercial manufacturing at peak: ~$2,000 / dose (500 doses / batch)

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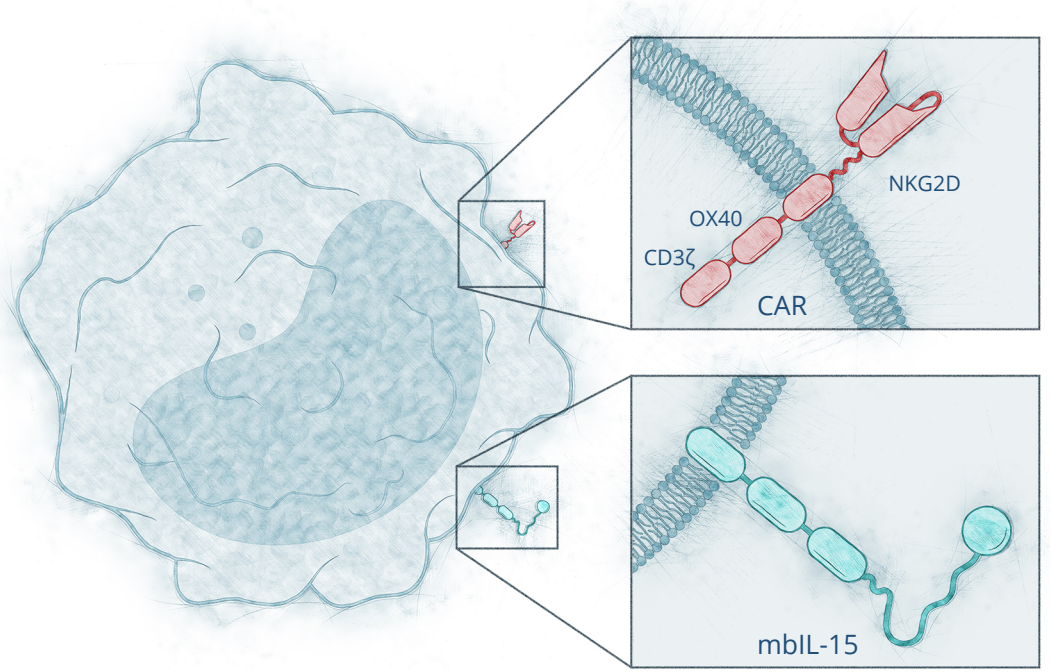
Pipeline

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



NKX101: NKG2D activating receptor, OX40 costimulatory domain, CD3ζ signaling moiety, membrane bound IL-15

NKG2D: ligands enriched in tumors, demonstrated responses

NKG2D ligand expression is documented in multiple tumor types

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

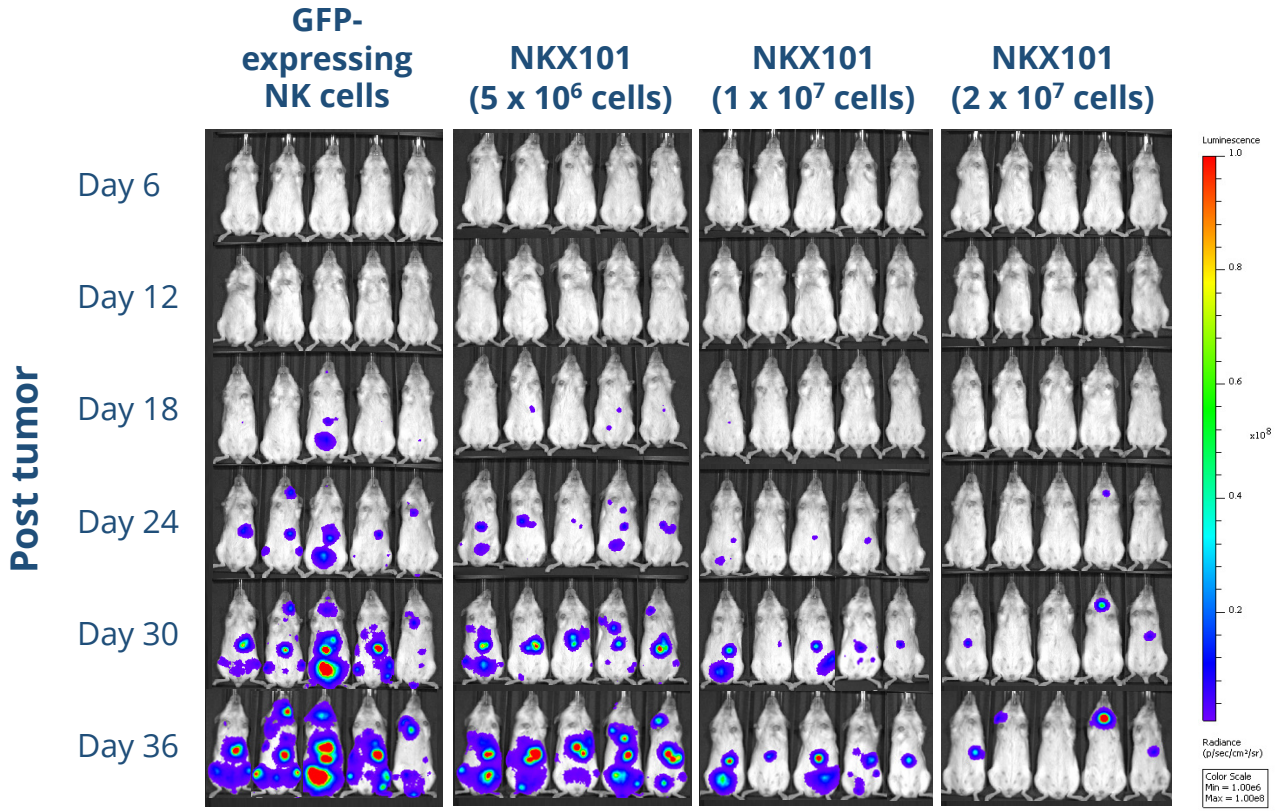
Clinical responses observed in R/R AML with non-engineered allo-NKs validate NKG2D

STUDY	RESPONSES*
Bachanova, *Crit Rev Oncog* 2014, A+B cohort	**9 / 42 (21%)**
Bachanova, *Crit Rev Oncog* 2014, 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: Acute myeloid leukemia (AML)

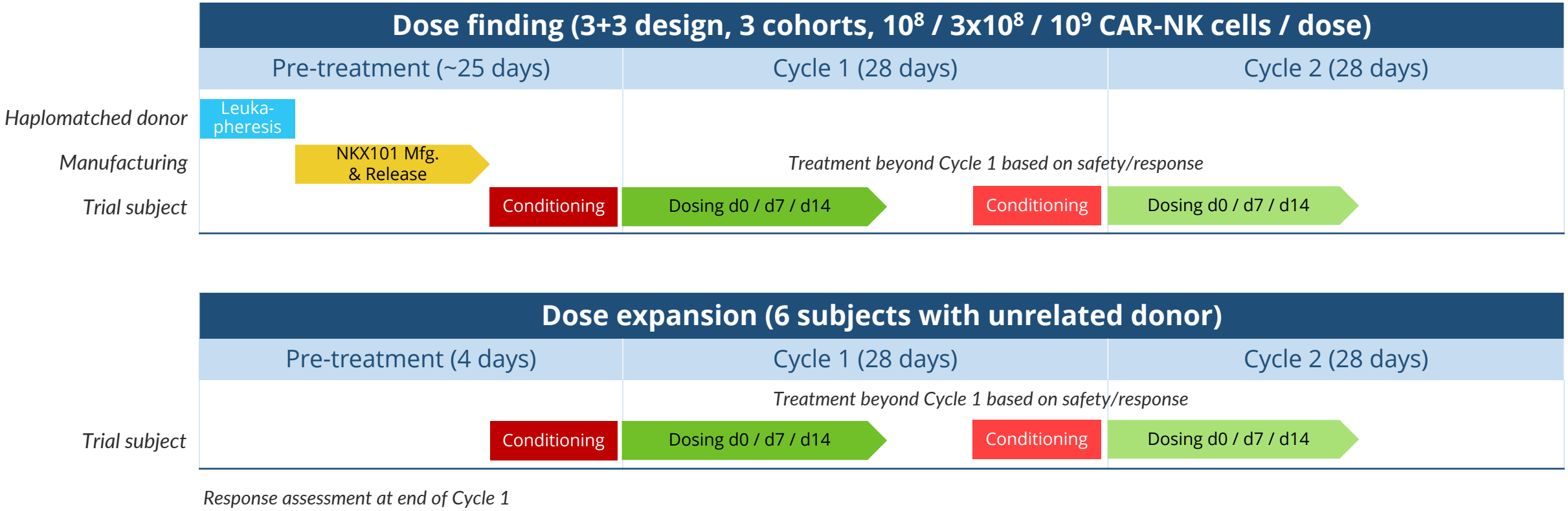
- AML US incidence: ~21K / yr
  - 5-year survival rate ~28%
- NKG2D targets are over-expressed in AML blasts
- Clinical activity with non-engineered NKs
- Positive pre-IND meeting May 2019
- Phase 1 in r/r AML and higher-risk MDS expected to commence 3Q20



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

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

NKX101: Heme dose finding and expansion



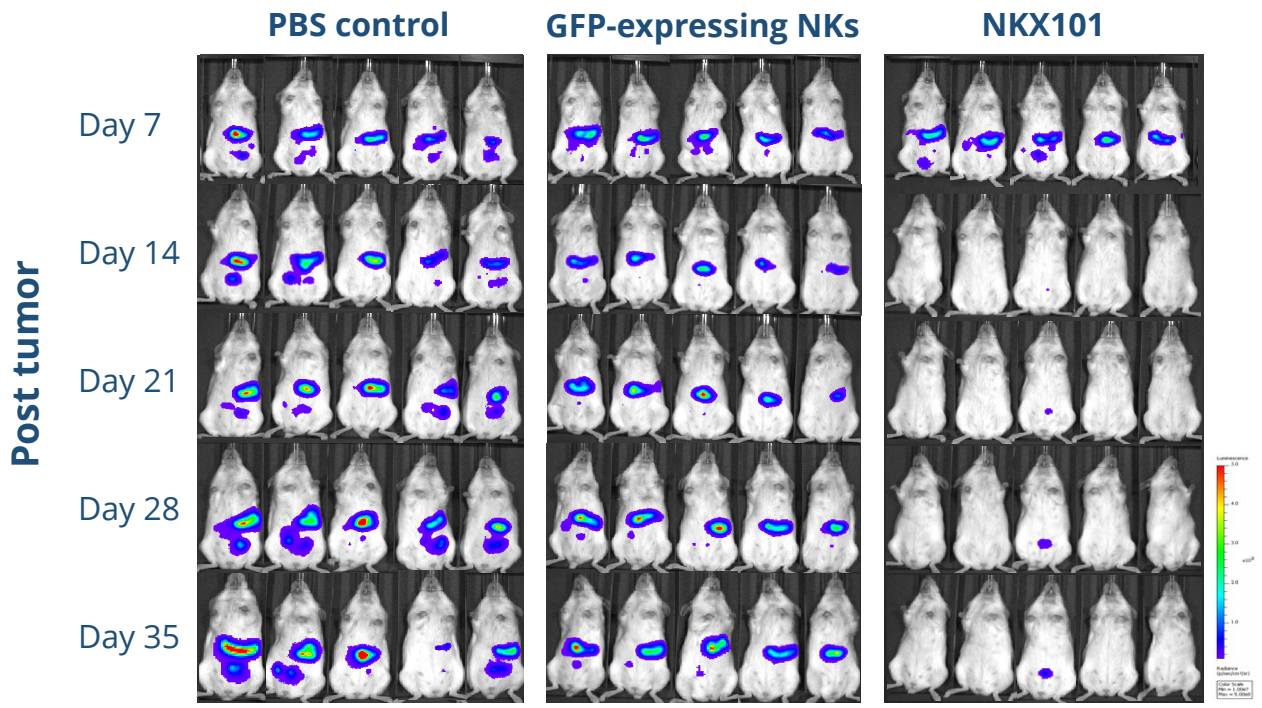
Response assessment at end of Cycle 1

In addition to haplomatched subjects, the dose expansion cohort is designed to evaluate subjects treated with off-the-shelf NKX101 – our expectation for pivotal trials and commercial use

NKX101: 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

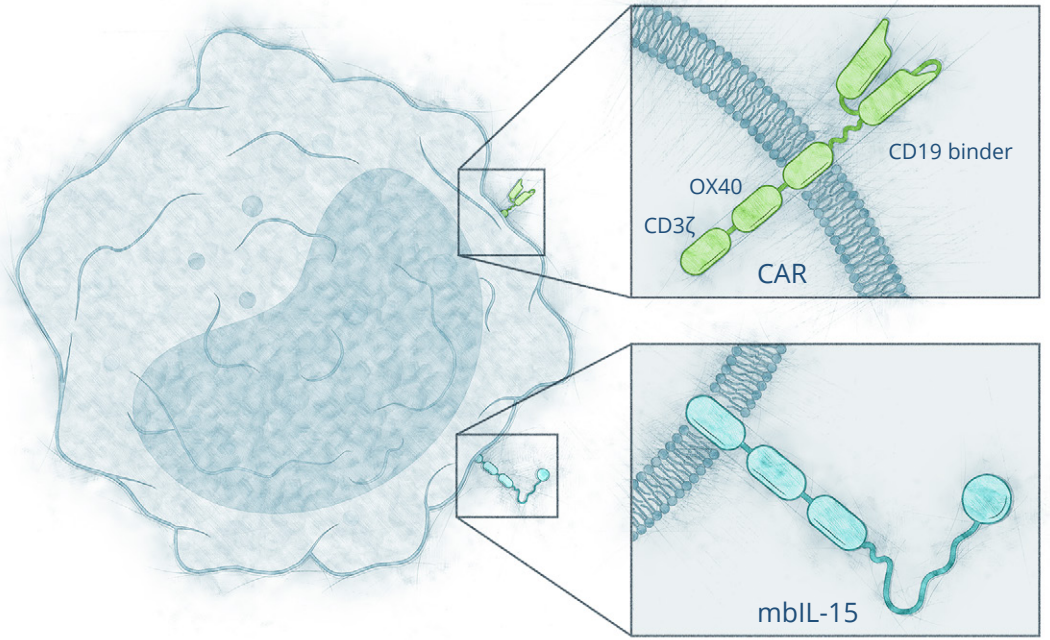


SNU449 HCC xenograft model
3 x 10^6 NK cells injected at day 7 post-tumor

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; planned 3Q20 IND

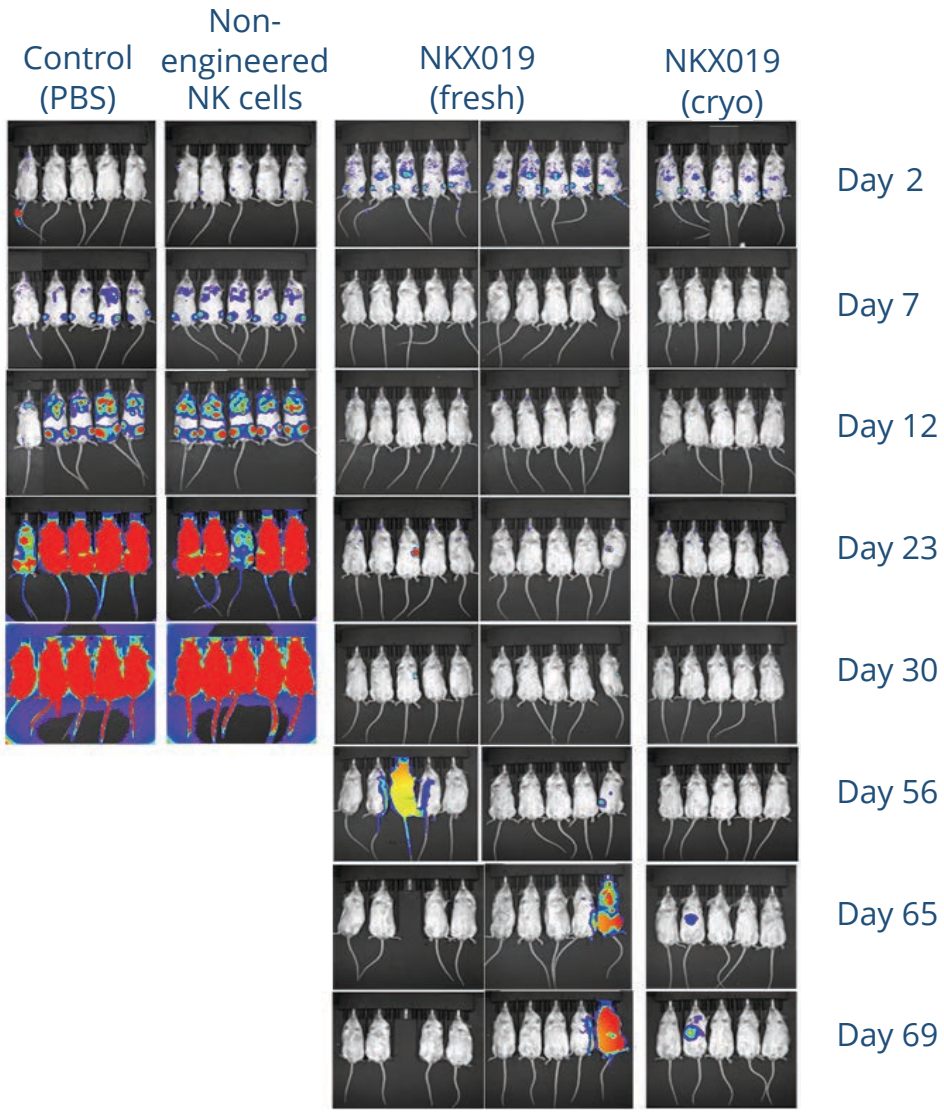
- Large opportunity after CAR-T approvals:
  - Gr3+ CRS: 13–49%
  - Gr3+ neurotoxicity: 18–31%
  - Limited number of specialized sites can treat
  - 9–34% of patients in pivotal trials didn't receive cells (primarily due to mfg. challenges)
- Rezvani (MDACC / Takeda) CAR19-NK:
  - 7 / 11 CRs in patients with B-cell malignancies (median 4 prior rounds Tx)
  - No reported CRS, GvHD or neurotoxicity
- Allogeneic, off-the-shelf product
- Expecting a well-tolerated safety profile

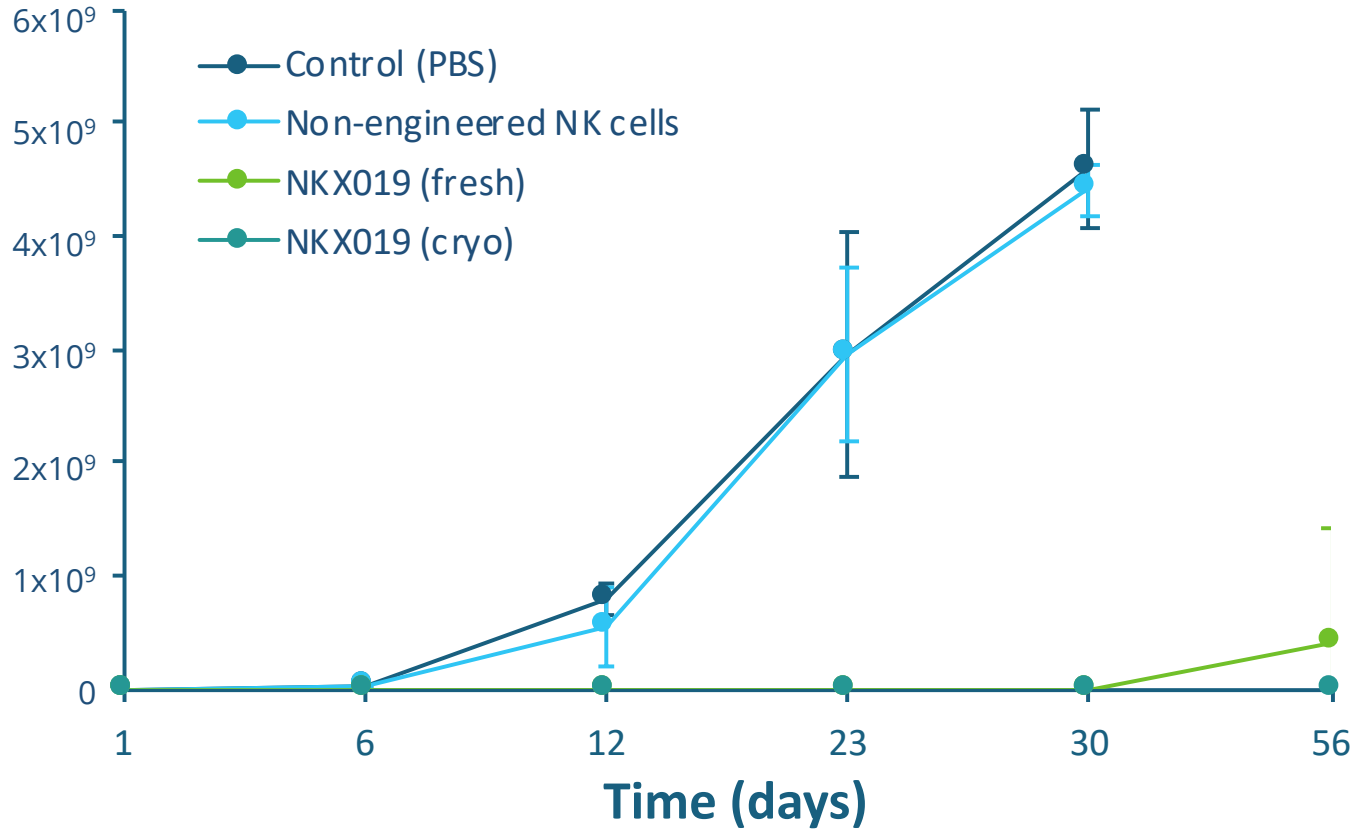


NKX019: Proprietary CD19 binder, OX40 costimulatory domain, CD3ζ signaling moiety, membrane bound IL-15

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.

NKX019: Activity in lymphoma model





Nalm-6 lymphoma model. 10^7 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

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Corporate

Intellectual property

PLATFORM

NK cell expansion
- Multiple issued patents and pending applications
- Compositions and methods of expansion/treatment
- Expiry ~2024 to ~2038

NK cell persistence
- Allowed US application and multiple pending OUS applications
- Expiry ~2035

Pipeline
- Provisional applications
- Compositions & treatment methods
- Expiry ~2039 to 2040

NKX101

NKG2D target
- Issued US patents and multiple pending US/OUS/PCT applications
- Claims to various NKG2D targeting constructs & treatment methods
- Expiry ~2034–2039

Local NKX101 delivery
- Provisional applications
- Local delivery to tumors
- Expiry ~2039

Combo Therapy
- Provisional applications
- NKG2D construct + adjunct therapy
- Expiry ~2039

NKX019

CD19
- Provisional applications
- Cells expressing tumor-targeting receptor & cytotoxic effector
- Expiry ~2040

Leadership

MANAGEMENT TEAM

Paul Hastings
President & CEO

Ralph Brandenberger, PhD
VP, Technical Operations

Nadir Mahmood, PhD
Chief Business Officer

Matthew Plunkett, PhD
Chief Financial Officer

Kanya Rajangam, MD, PhD
Chief Medical Officer

James Trager, PhD
Chief Scientific Officer

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Director

Financial and investors

- Samsara BioCapital led $114 million Series B financing in August 2019
- Projected capital into late 2021: after expected POC for NKX101 and NKX019
- Leading investor syndicate

Expected upcoming milestones