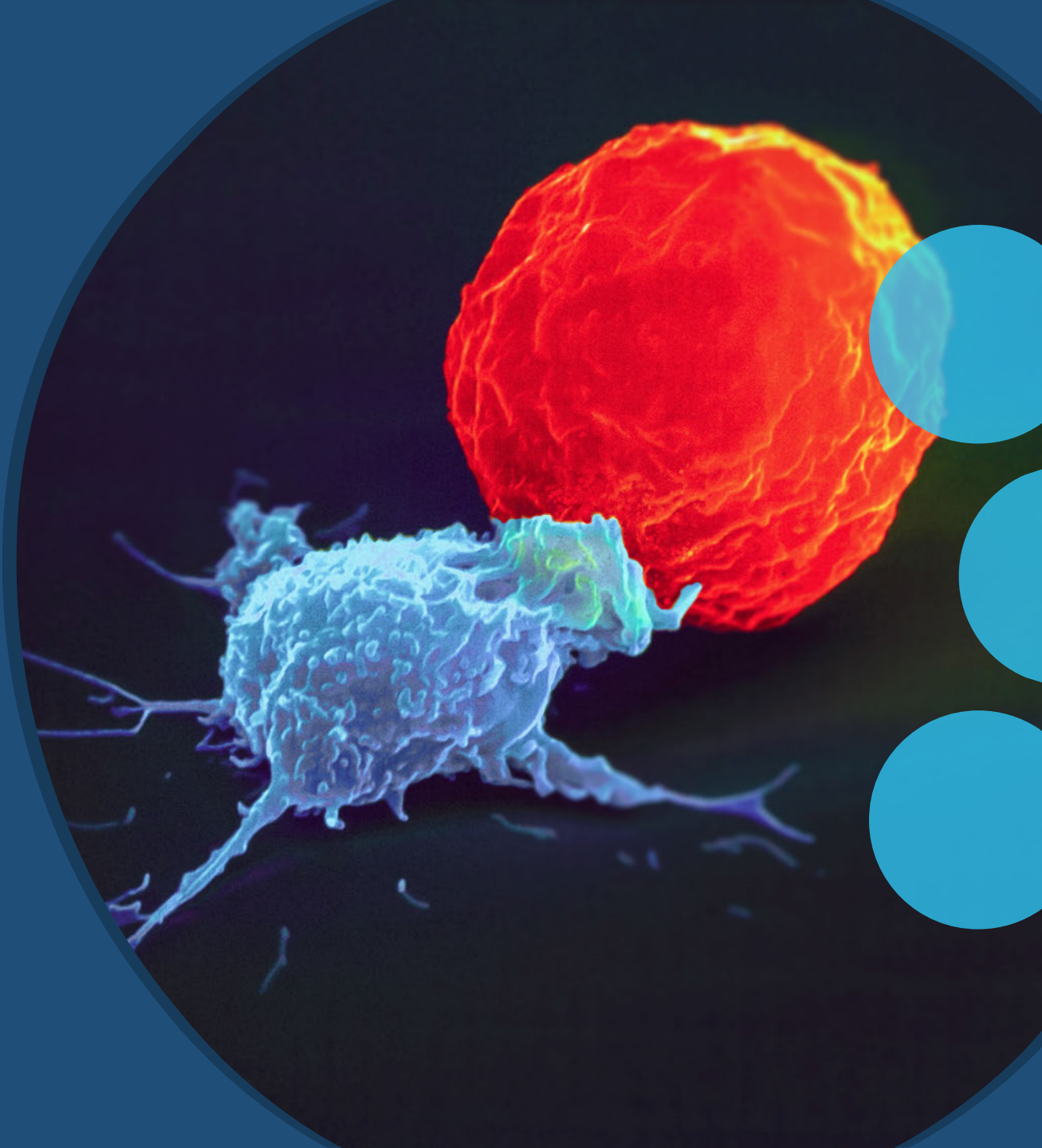




# Allogeneic Natural Killer Cells Engineered to Beat Cancer

June 4, 2020





# Forward looking statements

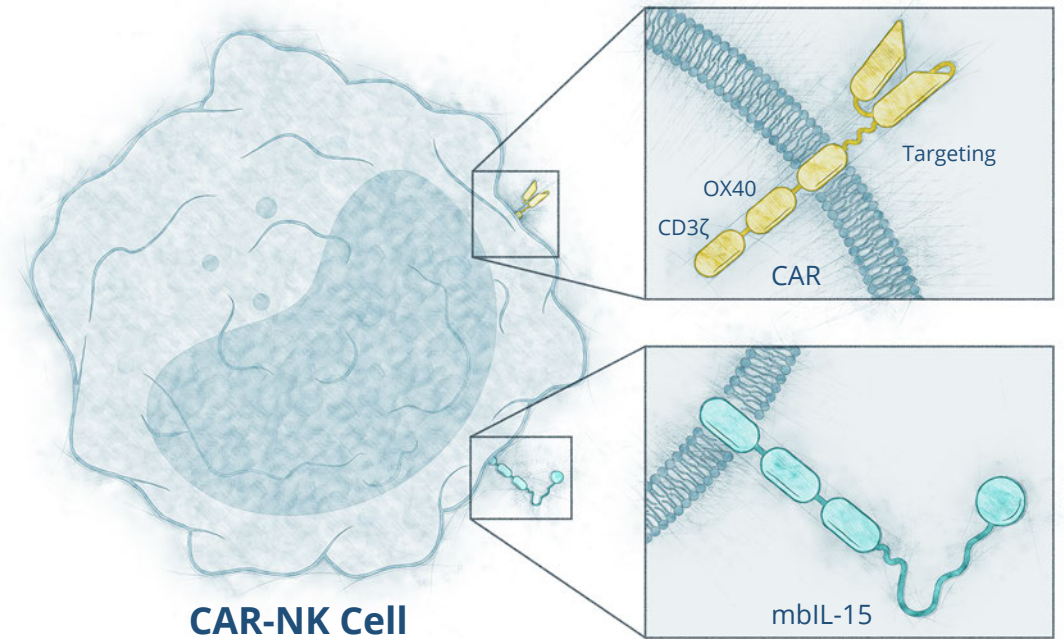
*This presentation is made pursuant to Section 5(d) of the Securities Act of 1933, as amended, and is intended solely for investors that are either qualified institutional buyers or institutions that are accredited investors (as such terms are defined under SEC rules) solely for the purpose of determining whether such investors might have an interest in a securities offering contemplated by Nkarta, Inc. Any such offering of securities will only be made by means of a registration statement (including a prospectus) filed with the SEC, after such registration statement becomes effective. No such registration statement has been publicly filed as of the date of this presentation. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.*

*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 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 certain risks, uncertainties, and assumptions. 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. 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.*

# Highlights: Nkarta engineered CAR-NKs

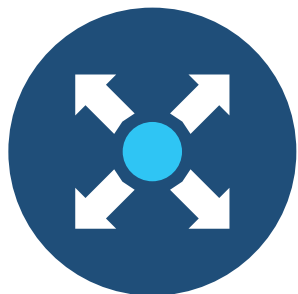
*Natural Killer cells are the cornerstone of innate immune surveillance*

- » Allogeneic and off-the-shelf with attractive cost of manufacturing
- » Proprietary expansion, persistence, tumor targeting and cryopreservation technologies
- » First IND submitted, next IND anticipated in 6 to 9 months
- » \$114M Series B with top healthcare investors



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

# Nkarta proprietary technologies



## Expansion

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



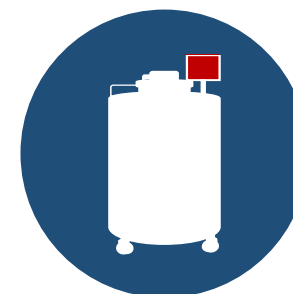
## Persistence

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



# 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)

**~600**  
Patients treated with non-engineered allogeneic NK cells

**~330**  
AML/MDS patients

**~100**  
R/R AML (non-transplant)

~34% aggregate CR rate

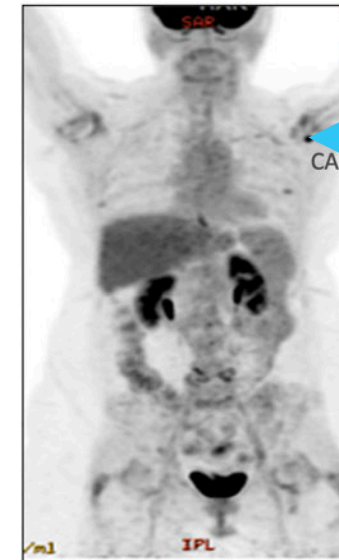
**MD Anderson study with CD19 CAR-NK cells**  
- Published in *New England Journal of Medicine*, Feb 2020

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

PRE-TREATMENT



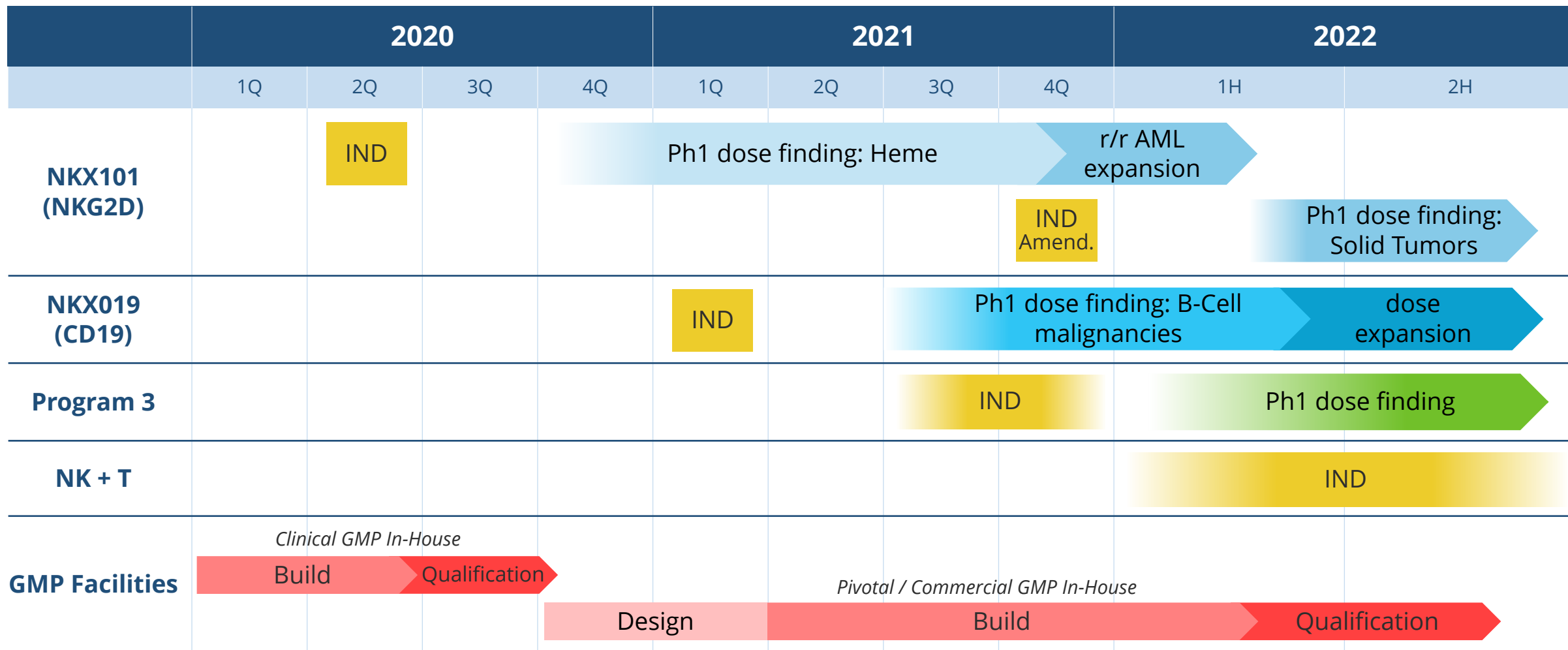
DAY 30 POST CAR-NK



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

Katayoun Rezvani, M.D., Ph.D., 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.

# Pipeline



# Leadership

## MANAGEMENT TEAM

**Paul Hastings**

President & CEO



genzyme

**Ralph Brandenberger, PhD**

VP, Technical Operations



Baxalta

geron



**Nadir Mahmood, PhD**

Chief Business Officer



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**Matthew Plunkett, PhD**

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**Kanya Rajangam, MD, PhD**

Chief Medical Officer



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geron

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Director



# Platform

# Nkarta CAR-NKs: engineered to enhance activity

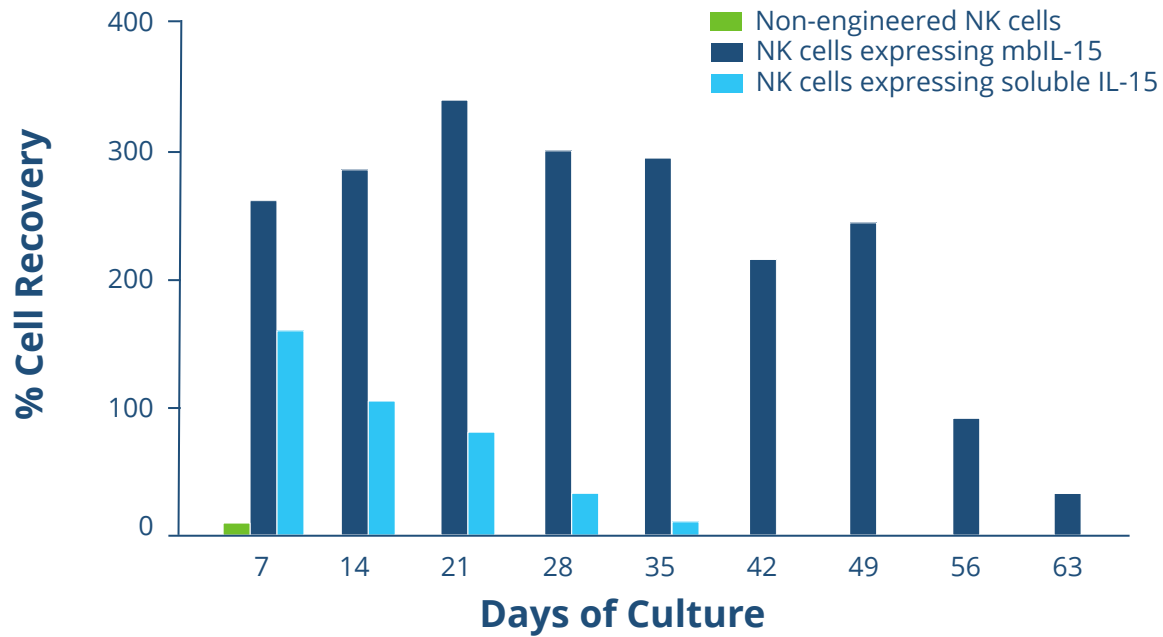
	APPROVED CAR-T THERAPIES	ALLO CAR-T THERAPIES	NK CELLS	CAR-NK CELLS
OPPORTUNITY FOR IMPROVED SOLID TUMOR ACTIVITY				✓
PERSISTENCE	✓✓	✓		✓
LOW GVHD RISK	✓	TBD	✓	✓
LOW RISK OF CRS OR NEUROTOXICITY			✓	✓
ALLOGENEIC, OFF-THE-SHELF MANUFACTURING		✓		✓
COST OF MANUFACTURING	+++	++	++	+

**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**



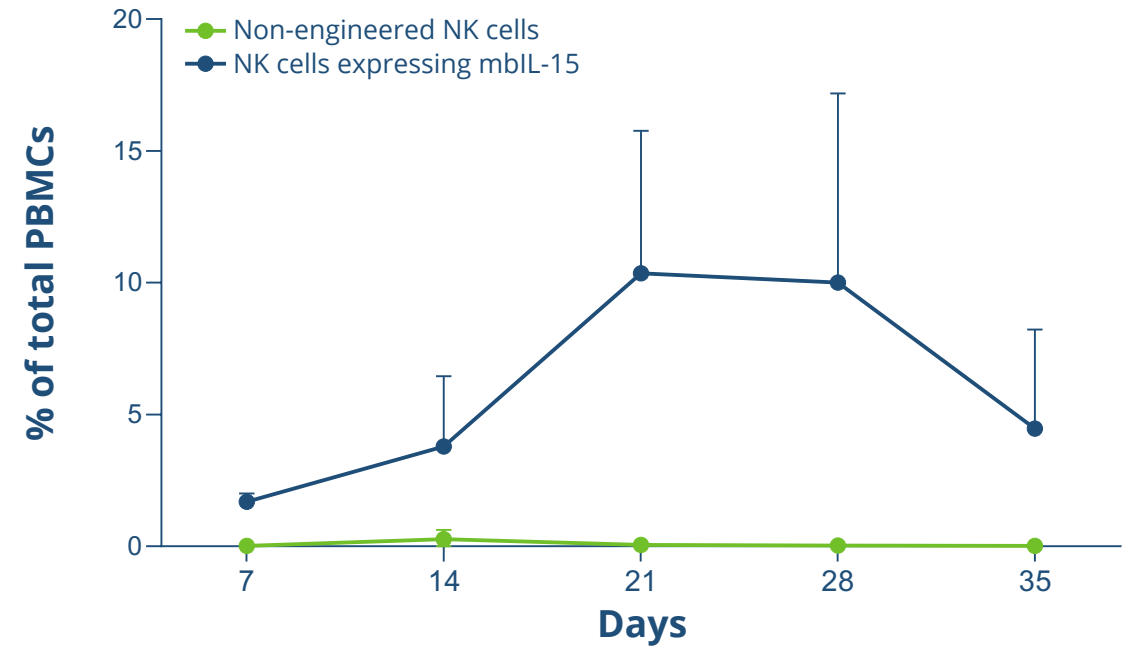
# Superior persistence from membrane bound IL-15

## *In vitro* persistence



Source: Imamura, Blood 2014

## *In vivo* persistence and expansion in NSG mice

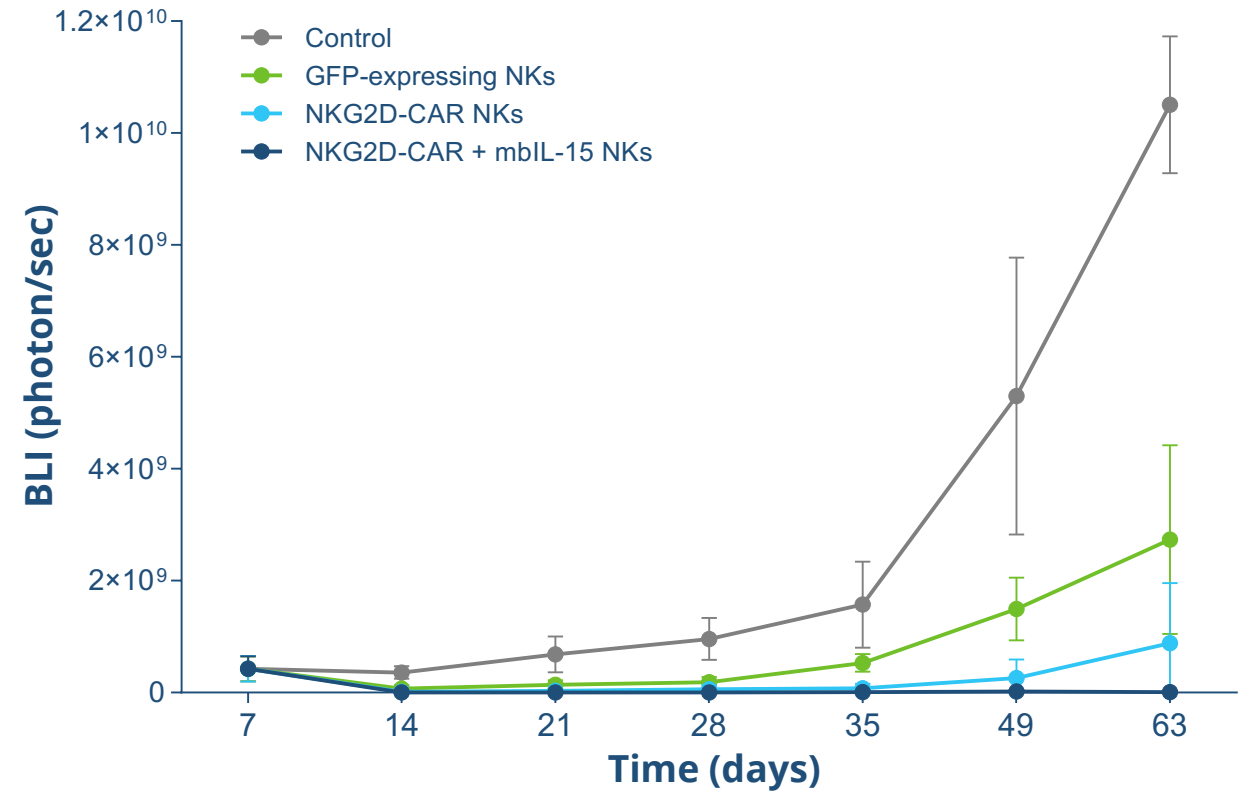
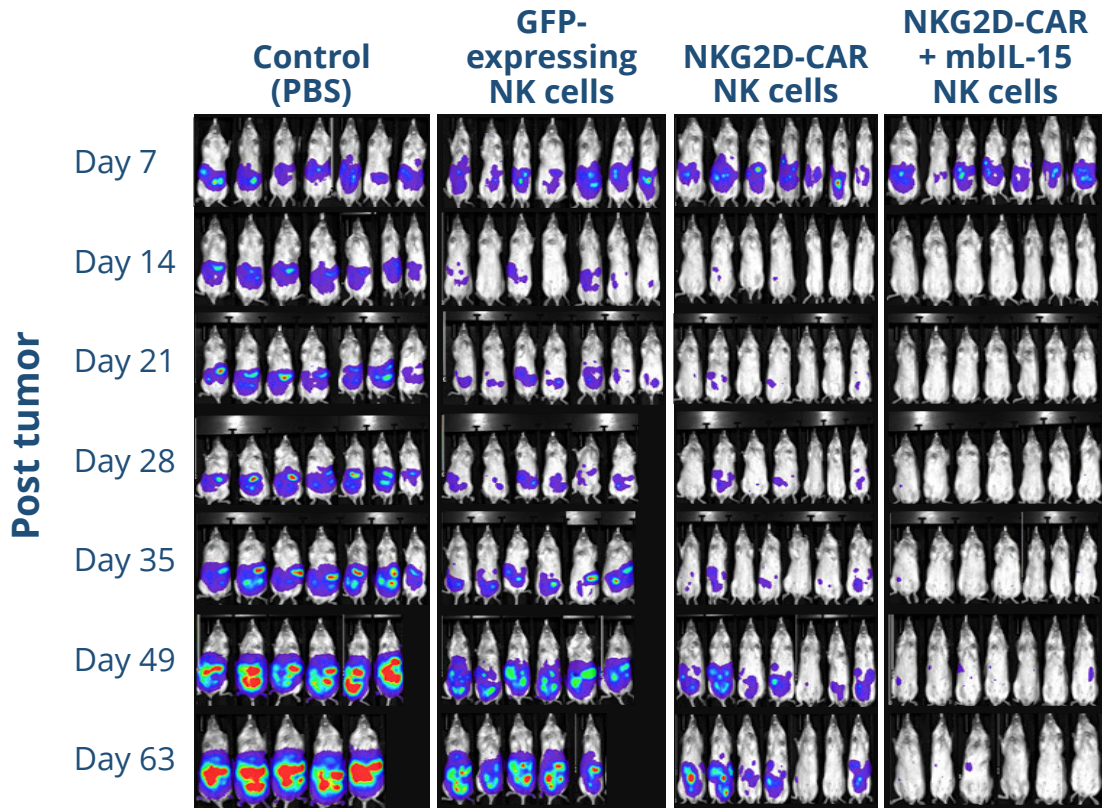


Source: Nkarta. N = 5 per arm.

**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



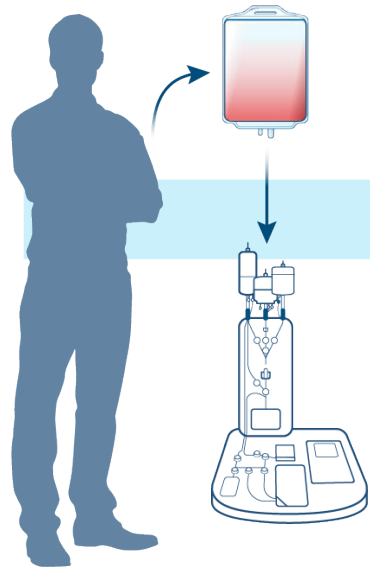
Source: Nkarta. U2OS osteosarcoma model;  $3 \times 10^6$  NK cells administered on D7. Graphical data at right are average BLI of mice above.

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



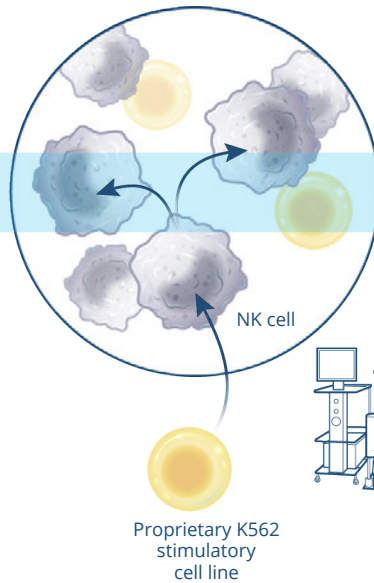
# Allogeneic, commercially-enabling manufacturing

## 1 Collect & Isolate



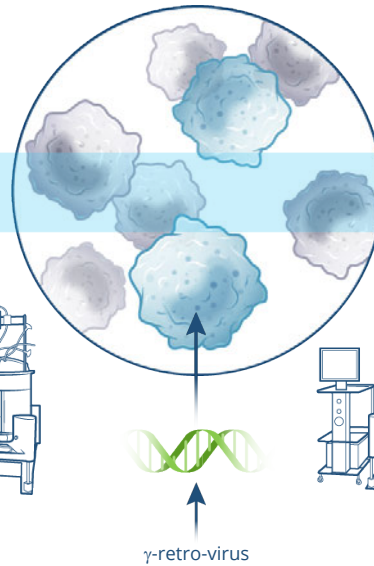
NK cells collected from healthy donors by leukapheresis.

## 2 Activate



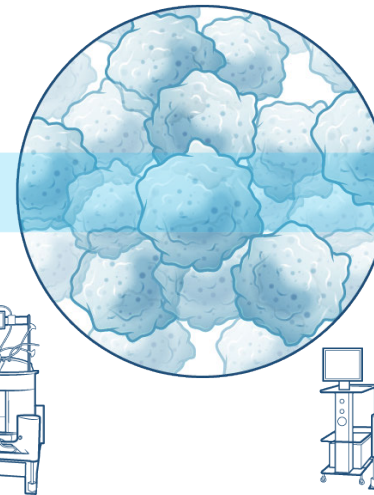
NK cell expansion using proprietary stimulatory cells.

## 3 Engineer



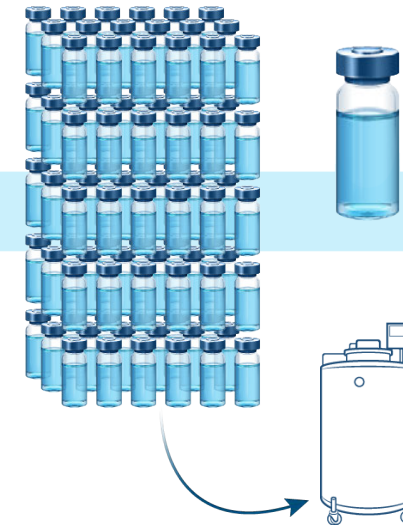
Expanded NK cells are transduced to express mbIL-15 and CAR.

## 4 Expand



Continued expansion driven by mbIL-15.

## 5 Cryopreserve



Harvesting and cryopreservation of final cell product.

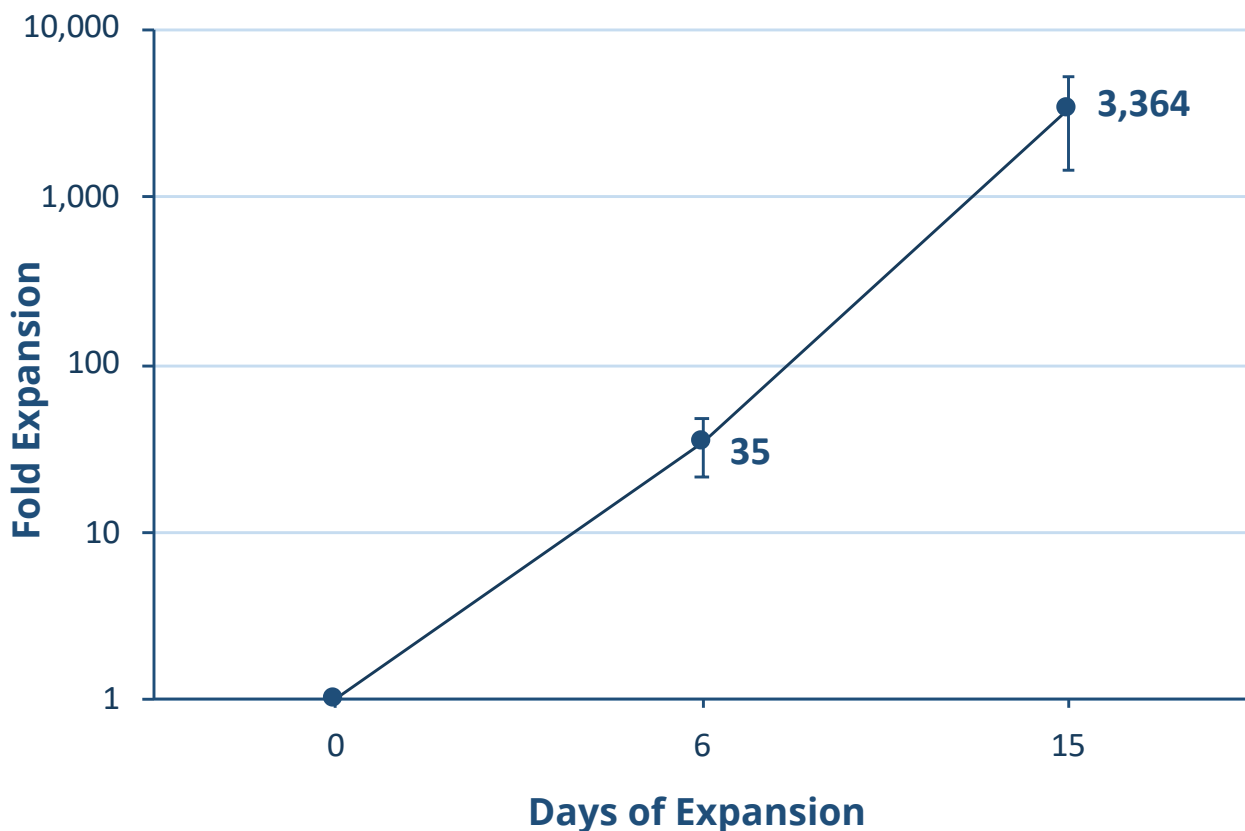
## 6 Thaw & Administer



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



# Proprietary expansion to enable large scale manufacturing

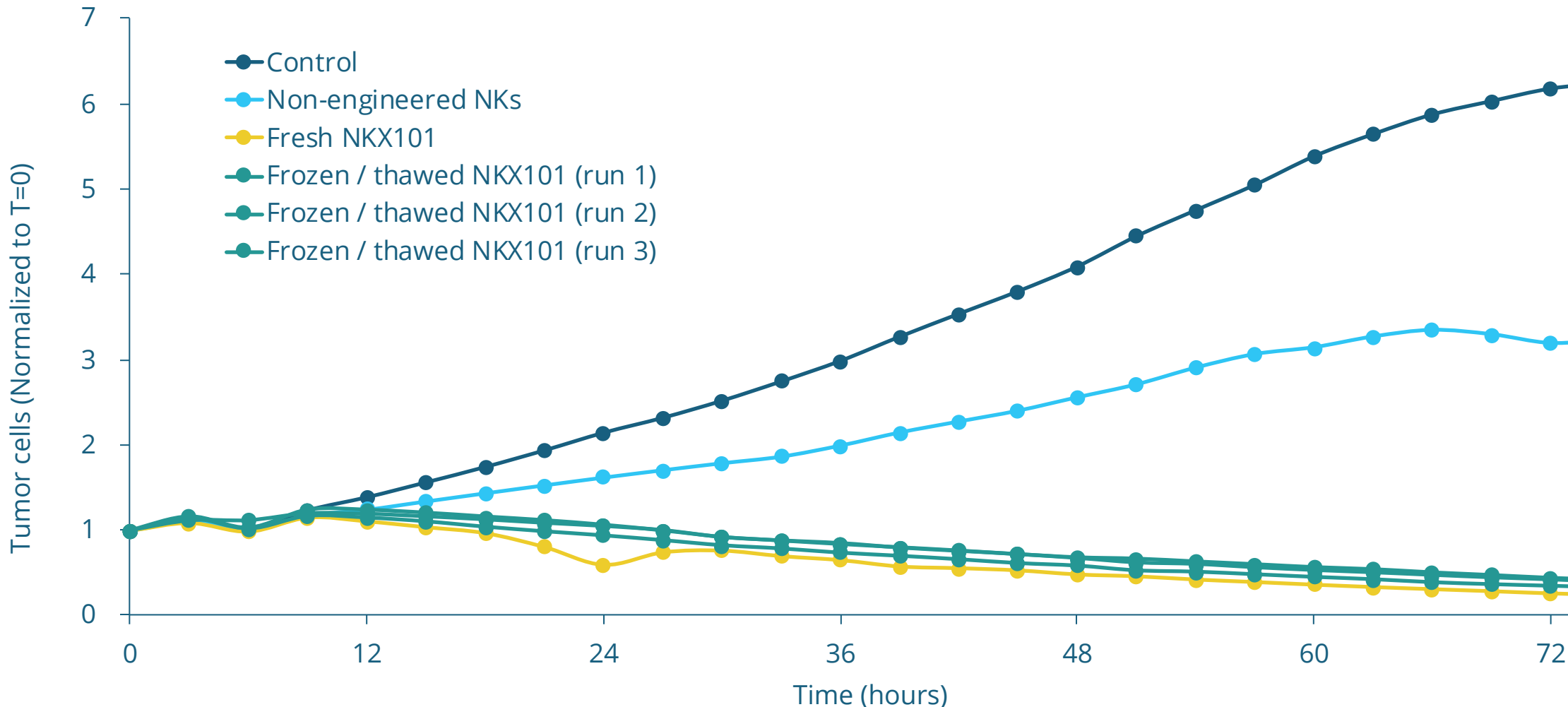


*Data above are from the process development of NKX019 for cGMP manufacturing and are an average of 5 expansions from 4 different donors.*

- » 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)



# Cryopreserved NKX101 retains *in vitro* cytotoxicity

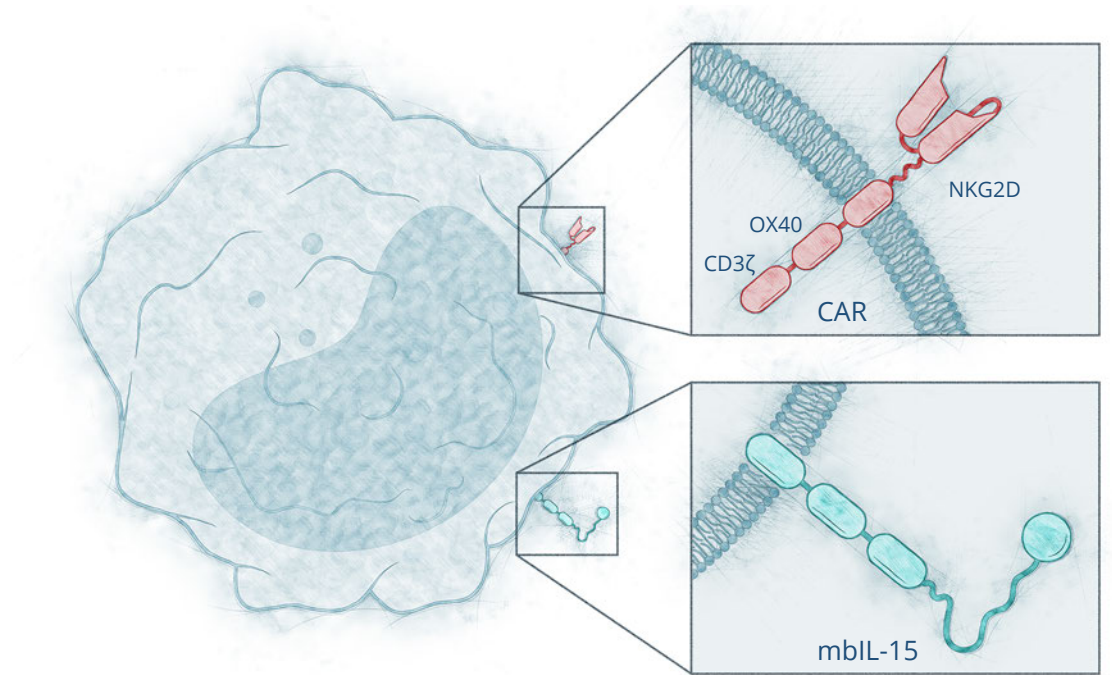


**Cryopreserved NKX101 retains cytotoxicity similar to fresh NKX101 in a long-term assay**

# 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	<a href="#">Hilpert, <i>J Immunol</i> 2012</a>
MULTIPLE MYELOMA	<a href="#">Carbone, <i>Blood</i> 2005</a>
HCC	<a href="#">Kamimura, <i>J Hep</i> 2012</a>
BREAST	<a href="#">de Kruif, <i>BMC Can</i> 2012</a>
OVARIAN	<a href="#">McGilvray, <i>Int J Can</i> 2010</a>
LUNG	<a href="#">Okita, <i>Can Imm Immunother</i> 2016</a>
COLON	<a href="#">McGilvray, <i>CCR</i> 2009</a>
MELANOMA	<a href="#">Vetter, <i>J Inv Derm</i> 2002</a>
OSTEOSARCOMA	<a href="#">Lu, <i>Neoplasma</i> 2008</a>
GLIOMA	<a href="#">Weiss, <i>CCR</i> 2018</a>

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

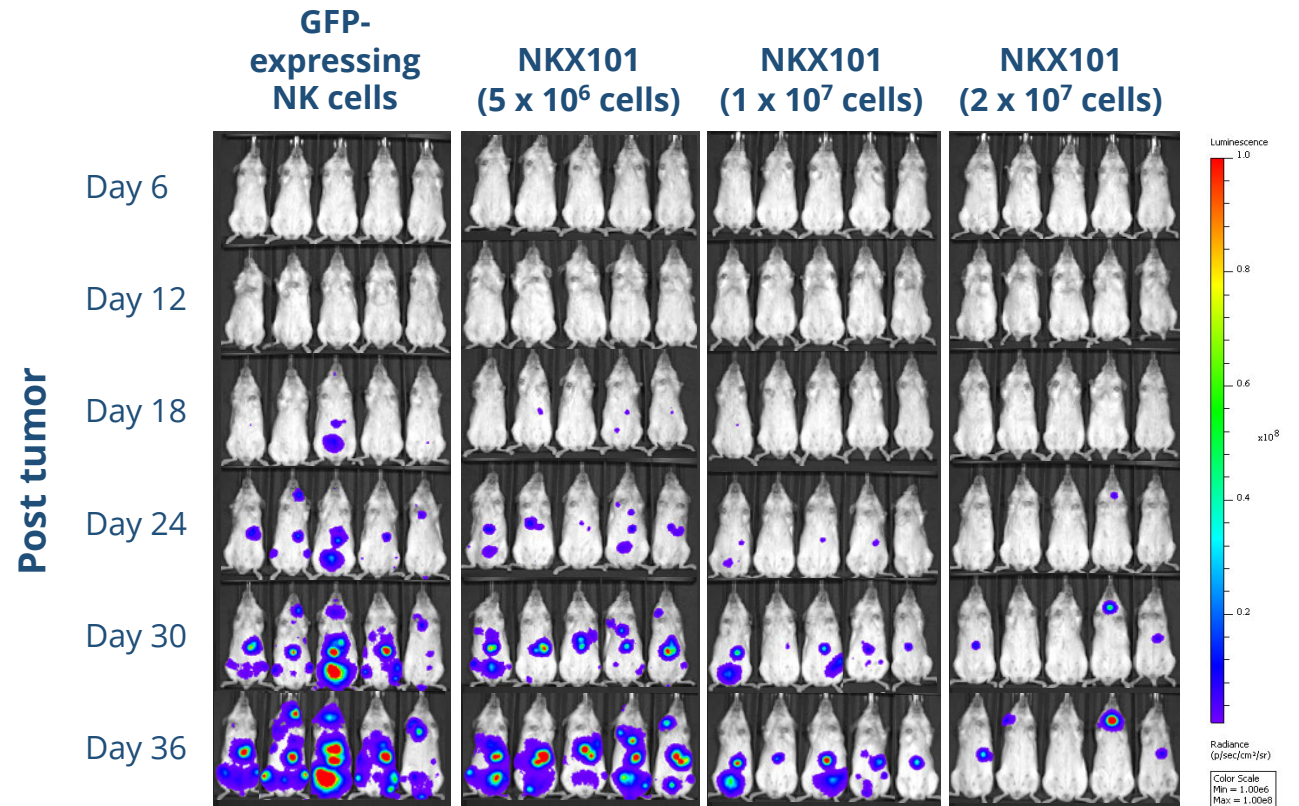
STUDY	RESPONSES*
<a href="#">Bachanova, <i>Crit Rev Oncog</i> 2014</a> , A+B cohort	9 / 42 (21%)
<a href="#">Bachanova, <i>Crit Rev Oncog</i> 2014</a> , C cohort	8 / 15 (53%)
<a href="#">Curti, <i>Blood</i> 2011</a>	1 / 5 (20%)
<a href="#">Kottaridis, <i>PLOS One</i> 2015</a>	1 / 1 (100%)
<a href="#">Miller,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

\*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)

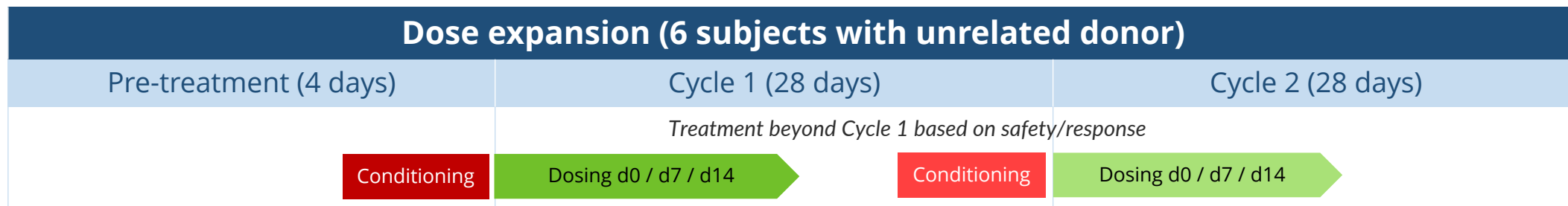
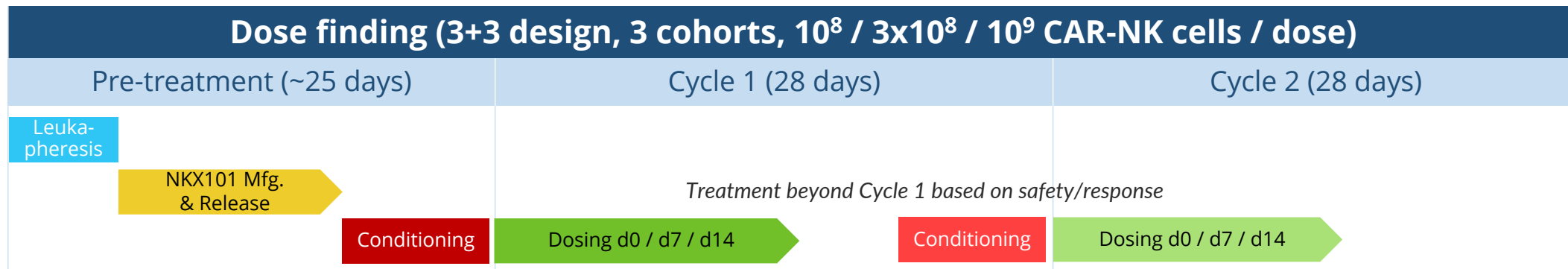
- » AML US incidence: ~21K / yr
  - 5-year survival rate ~28%
- » NKG2D targets are over-expressed in AML blasts
- » Clinical activity with non-engineered NKs
- » IND filed in May 2020
- » Phase 1 in r/r AML and higher-risk MDS: FPI expected 4Q20



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



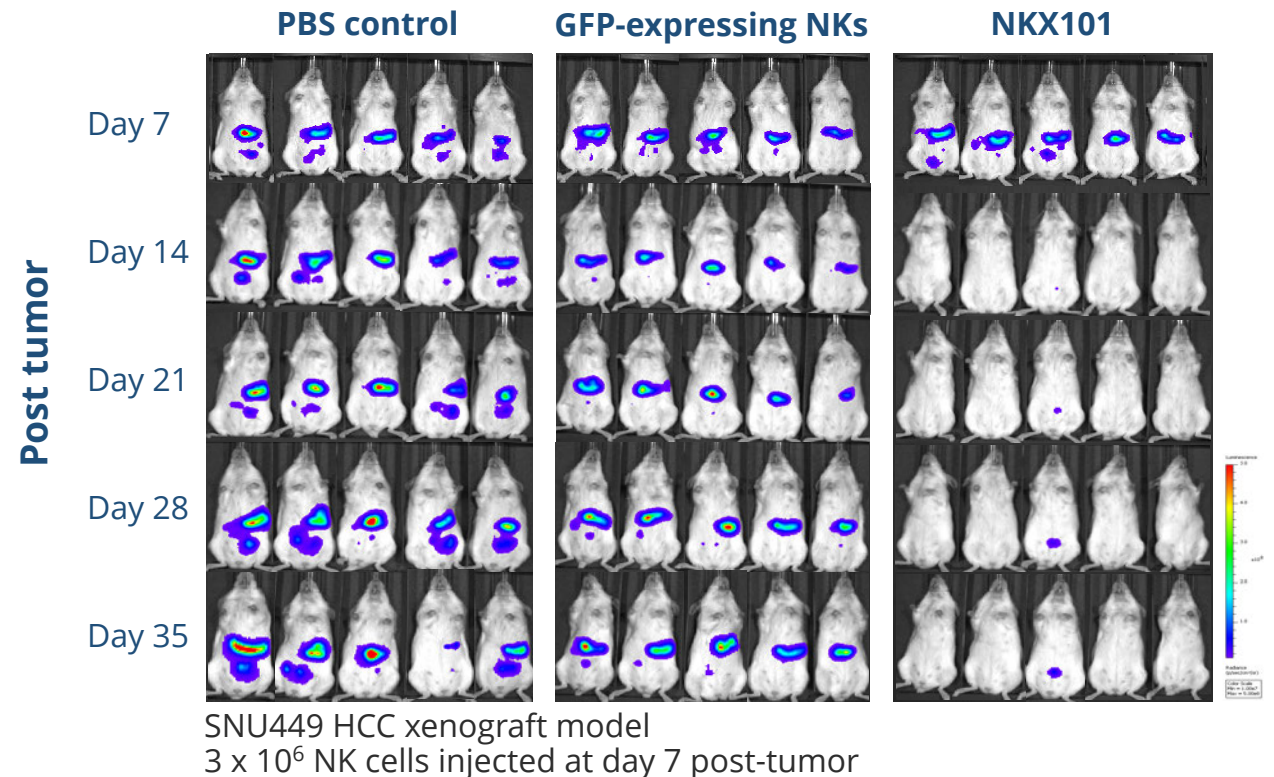
Response assessment at end of Cycle 1

**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<sup>o</sup> liver cancer or liver metastases

## NKX101 activity in NSG mice

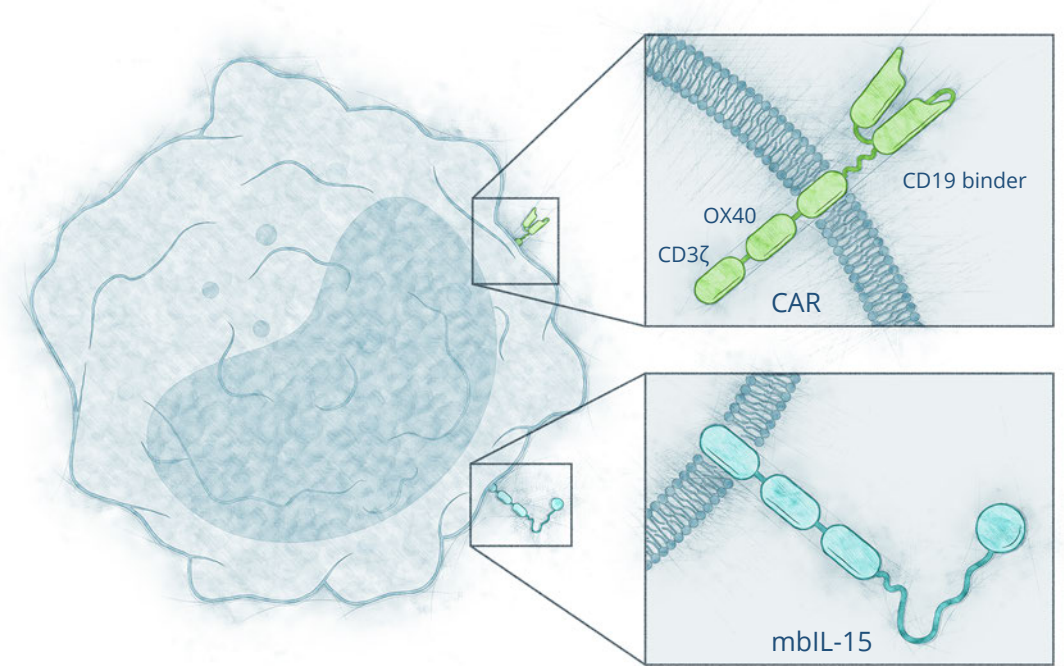


HCC: Hepatocellular carcinoma. CRC: Colorectal cancer. Sources: SEER database; Sun Act Pharm Sin 2015; Kamimura, J Hepatology, 2012; Kamiya et. al, Cancer Immunol Res 2016; Qin 2017



# NKX019: CD19 targeted CAR-NK; IND 1Q21

- » 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
- » Phase 1 in B cell malignancies
  - Off-the-shelf NKX019
  - $3 \times 10^8$  starting dose, 2 dose finding cohorts
  - Several dose expansion cohorts thereafter

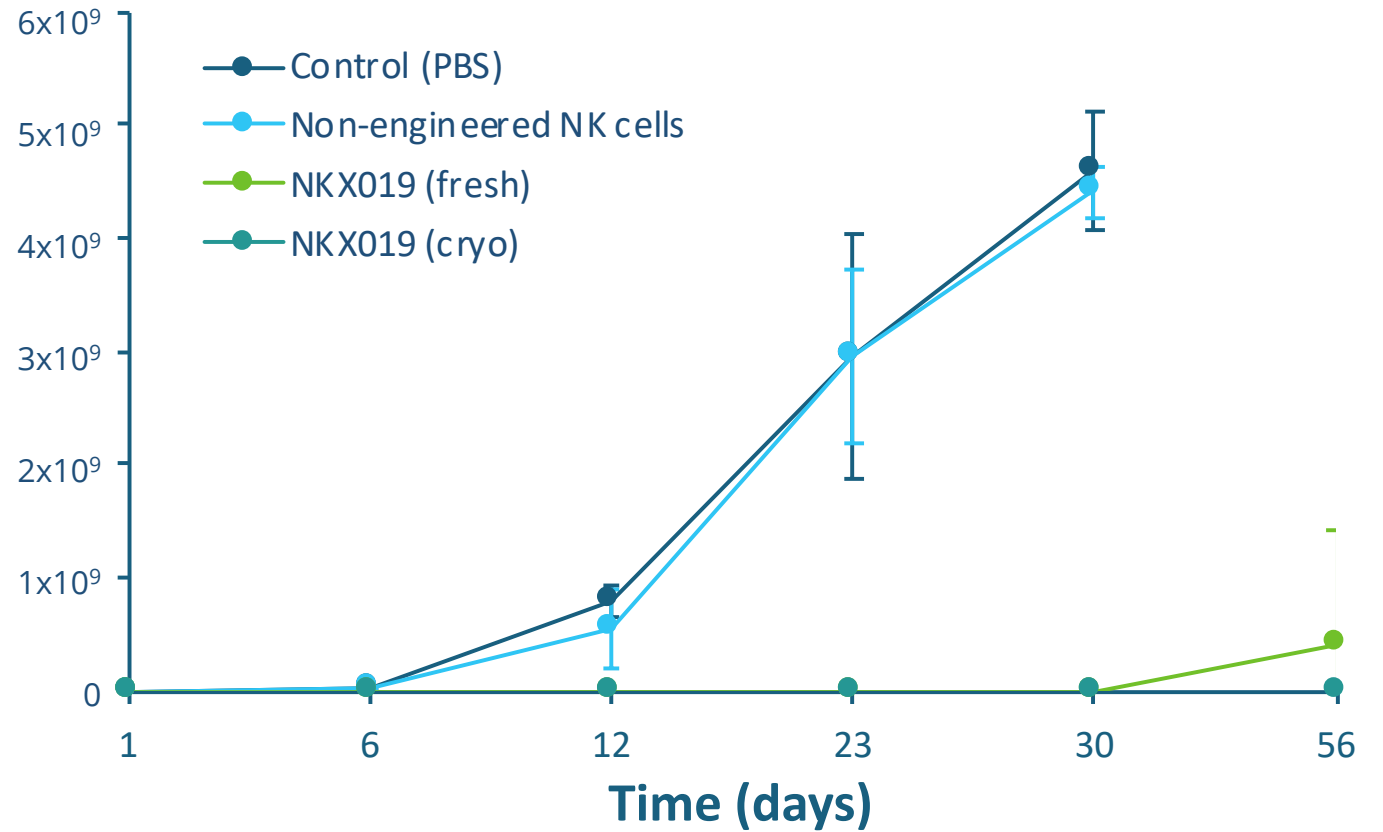
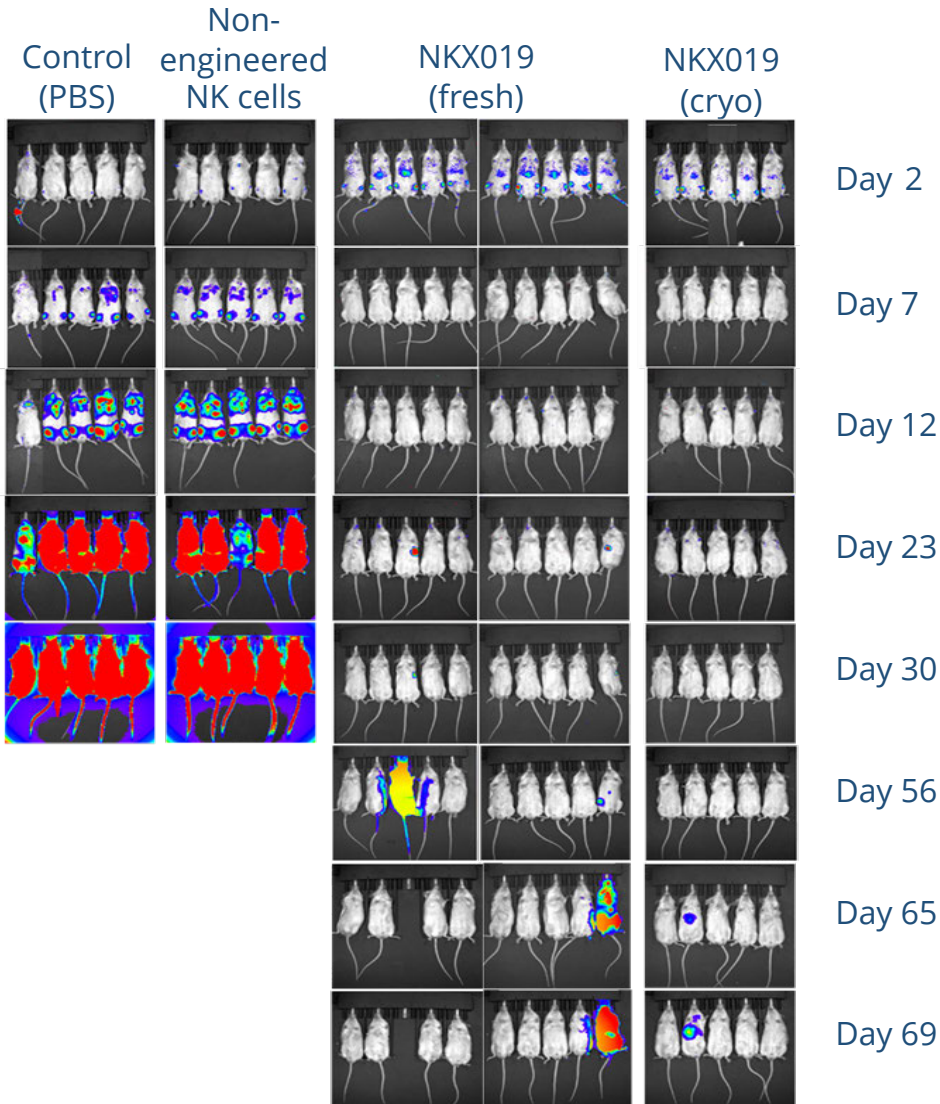


**NKX019: Proprietary CD19 binder, OX40 costimulatory domain, CD3ζ signaling moiety, membrane bound IL-15**

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<sup>7</sup> 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**



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 to ~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

# Financial and investors

- » Samsara BioCapital led \$114 million Series B financing in August 2019
- » March 31, 2020 cash, cash equivalents, s/t investments:
  - ~\$90 million (*pro forma* for Series B 2<sup>nd</sup> Tranche expected in June 2020)
  - Sufficient to late 2021 (expected)
- » Leading investor syndicate

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CONNECTING INVESTORS TO INVENTORS

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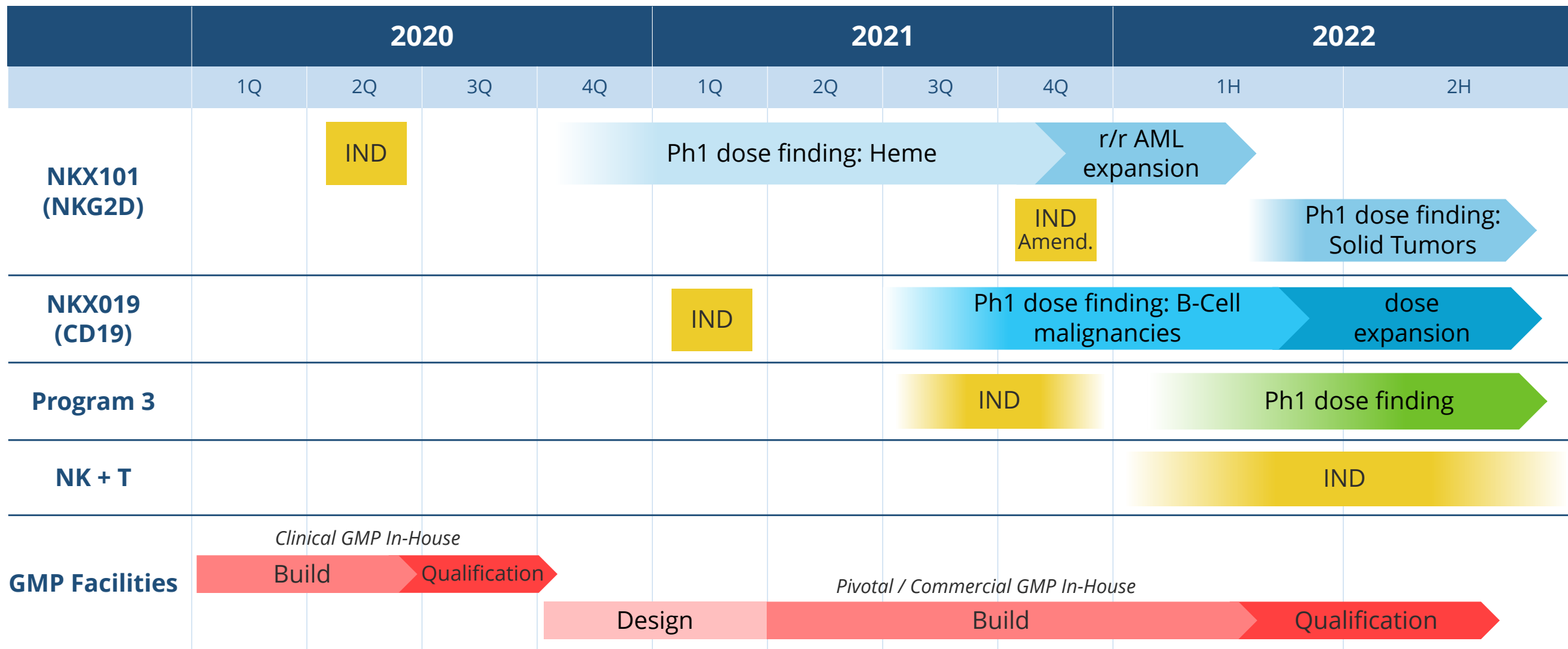
**novo**  
holdings

**RACAPITAL**

  
**SAMSARA**  
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# Expected upcoming milestones

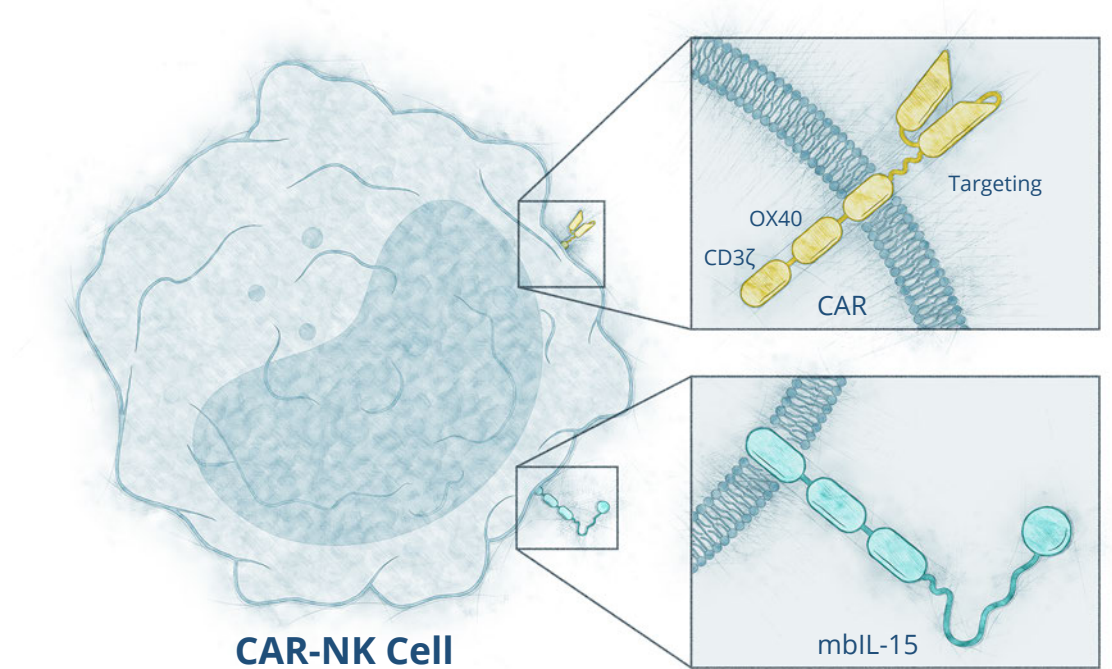




# Nkarta: Leaders in NK cell therapy

*Natural Killer cells are the cornerstone of innate immune surveillance*

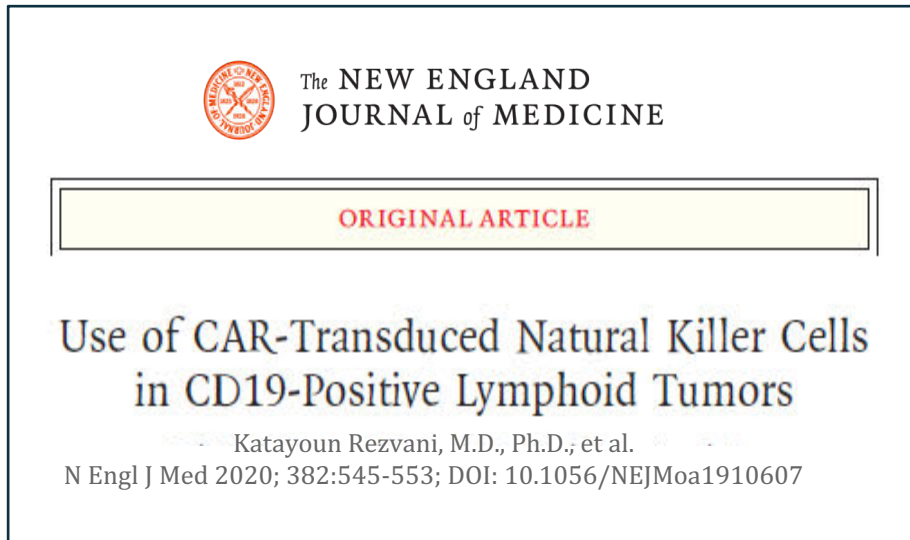
- » Allogeneic and off-the-shelf with attractive cost of manufacturing
- » Proprietary expansion, persistence, tumor targeting and cryopreservation technologies
- » First IND submitted, next IND anticipated in 6 to 9 months
- » Multiple data readouts in 2021 and 1H22 expected to drive value



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

# Appendix

# Foundational clinical study validates NK cell approach



**Independent clinical study  
demonstrated clinical activity and  
tolerability of CAR-NK cells**

- » Single-site study at MD Anderson Cancer Center
- » CAR-NK cells targeting CD19
  - Sourced from umbilical cord blood
  - Engineered to express anti CD-19 CAR, IL15 and iC9
  - Only freshly prepared cells delivered to patients
- » 11 subjects with relapsed/refractory disease
  - 5 CLL, 2 DLBCL, 1 follicular (Gr 3B), 3 transformed follicular
  - Median 4 lines of prior therapy
- » 8/11 responses within 30 days of single infusion
  - 7 CR, 1 PR
  - 5/8 responders received post-remission therapy
- » No reported CRS / neurotoxicity / GVHD