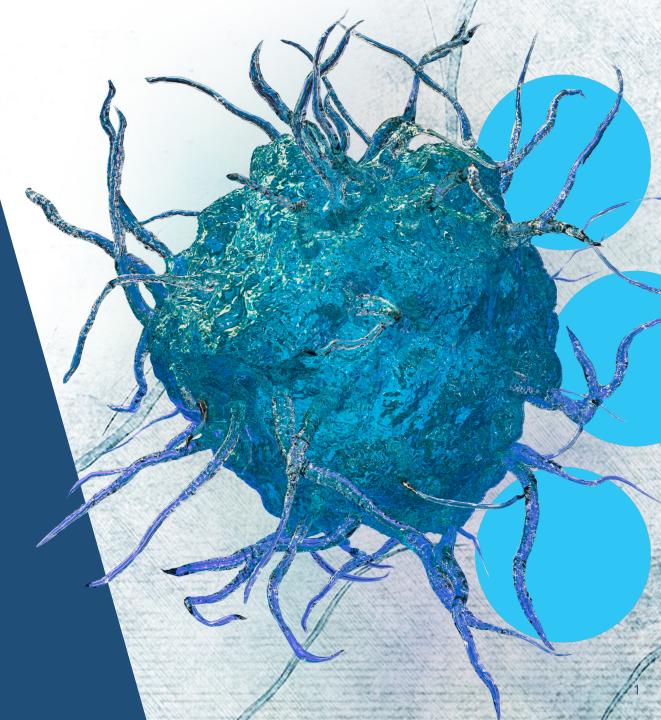
# nkarta

# 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 annual, guarterly and other filings with the Securities and Exchange Commission for a description of these risks and uncertainties.

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# Pioneering the next revolution in cell therapy

## Next generation NK cell platform built for

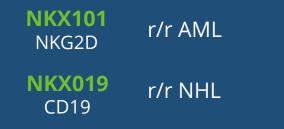
**Blood cancers and solid tumors** 

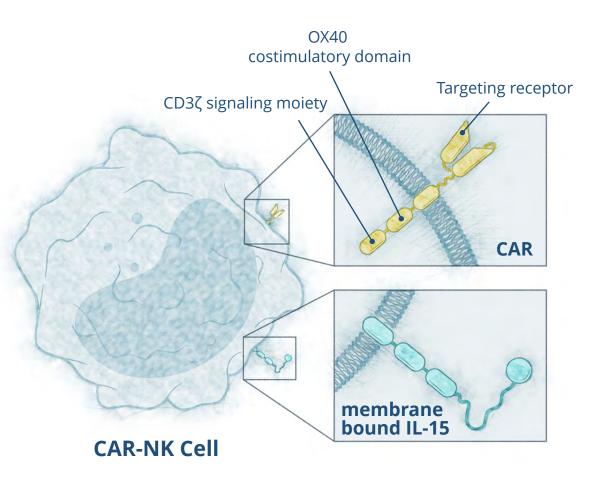
Allogeneic and off-the-shelf

Industrialized manufacturing

**Outpatient administration** 

## Recent Updates from Co-Lead Programs





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

Predictable pharmacokinetics with low risk of CRS and neurotoxicity

## Which allows for:



Potential for universal donors and master cell banks





Well defined, high quality, consistent product



Potential for flexible multi-dose and multicycle treatment, and outpatient administration

## **CRISPR** THERAPEUTICS

## nkarta THERAPEUTICS

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

Staying Ahead of the Curve:

A Platform That Incorporates Multiple Next Generation Enhancements ✓ <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 gene edits, including <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

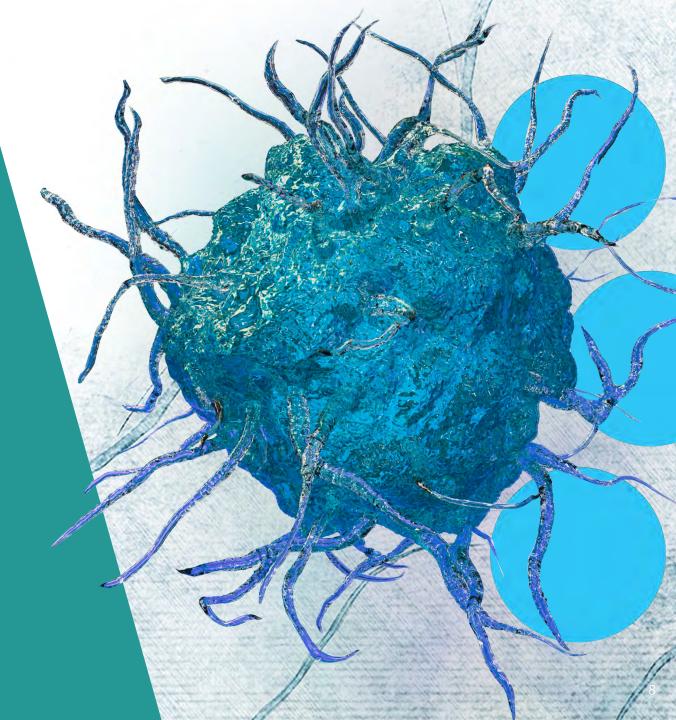
# Platform-driven pipeline with co-lead NK cell candidates advancing in hematologic malignancies

Program (Target)	Indication	Research	IND-Enabling	Clinical	Status
<b>NKX101</b> (NKG2D)	r/r AML	0	0	O	Phase 1 Ongoing
<b>NKX019</b> (CD19)	r/r NHL	0	0	O	Phase 1 Ongoing
<b>NKX101</b> (NKG2D)	Solid Tumors	0	O		IND Amendment 1H 2023
<b>NKX70</b> (CD70)	Heme & Solid Tumors	0			Collaboration CRISPR
<b>NK + T</b> (Undisclosed)	Undisclosed	0			

Manufacturing Facilities	Design / Engineering	Construction / Validation	Production	Status
<b>Clinical GMP</b> South San Francisco, CA	0	0	-0	Supplying NKX019 for Phase 1
<b>Pivotal and Commercial</b> South San Francisco, CA	0			Construction Beginning 2022



## Platform





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

#### **Expansion**

Donor NK cells are co-cultured 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

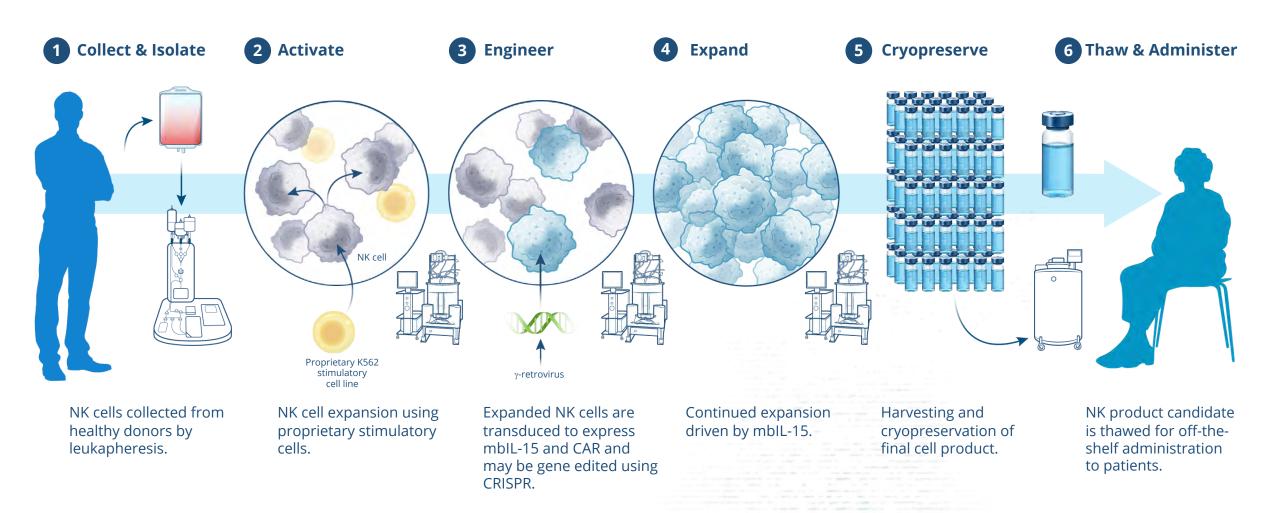
## Targeting

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

## **Gene Editing**

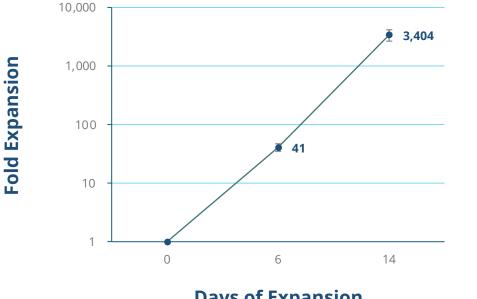
NK cells are gene edited to enhance cytotoxicity and improve resistance to suppression by tumor microenvironment

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



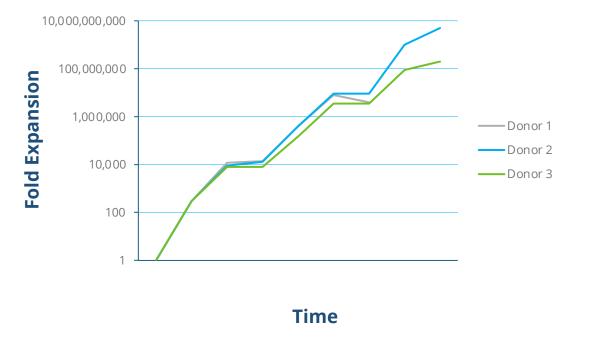
## Proprietary expansion and engineering enable industrial-scale manufacturing

#### **Current process supporting dose escalation** trials: >3 thousand-fold expansion



**Days of Expansion** 

## Potential future scalability could achieve >2 billion-fold expansion



Data are from NKX019 expansions at current manufacturing scale for clinical supply.

Data presented at SITC 2021: Potentiating the Large-Scale Expansion and Engineering of Peripheral Blood-Derived CAR NK Cells for Off-the-Shelf Application, J. Trager, Abstract 151.



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## In-house manufacturing to control process and production

#### **CLINICAL GMP FACILITY**

Multi-product facility

Support early clinical trials and research

Manufacturing NKX019 for Phase 1 clinical trial

## **FUTURE COMMERCIAL-SCALE FACILITY**

88,000 sq ft facility in South San Francisco

Combined manufacturing hub and company headquarters

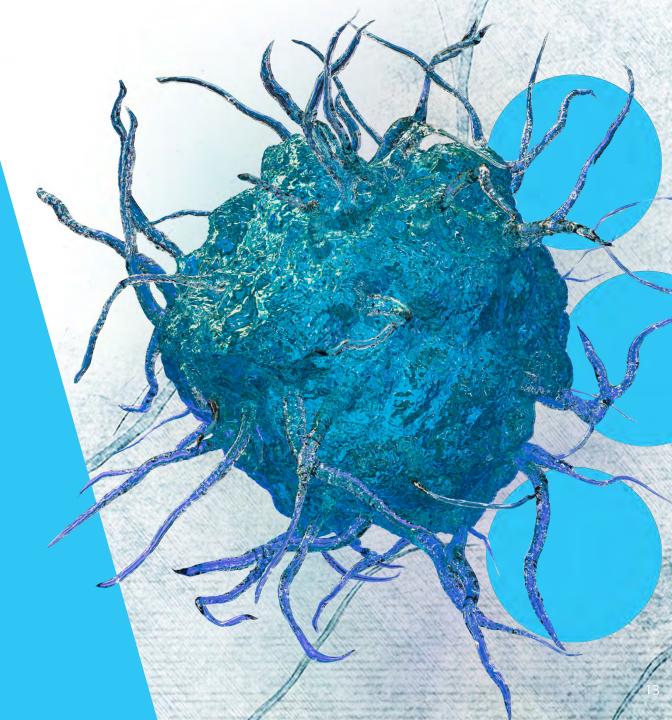
Expected to supply pivotal trials and early commercial

Construction to start Summer 2022



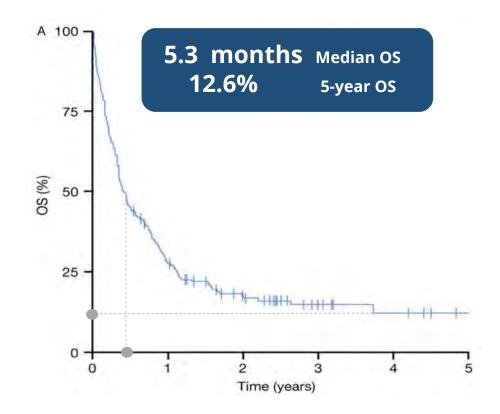
## NKX101 for the Treatment of Relapsed/Refractory AML and Higher-Risk MDS





## **R/R AML has limited treatment options and poor outcomes**

- Low response rate with traditional chemotherapy
  - 12 to 18% CR rate
- Approximately 50% of patients have targetable mutations (*FLT3*, *IDH1/2*)
  - 19 to 25% CR rate
- Long-term remission often depends on HCT in patients who are fit enough to receive it
  - Pre-transplant CR improves outcomes



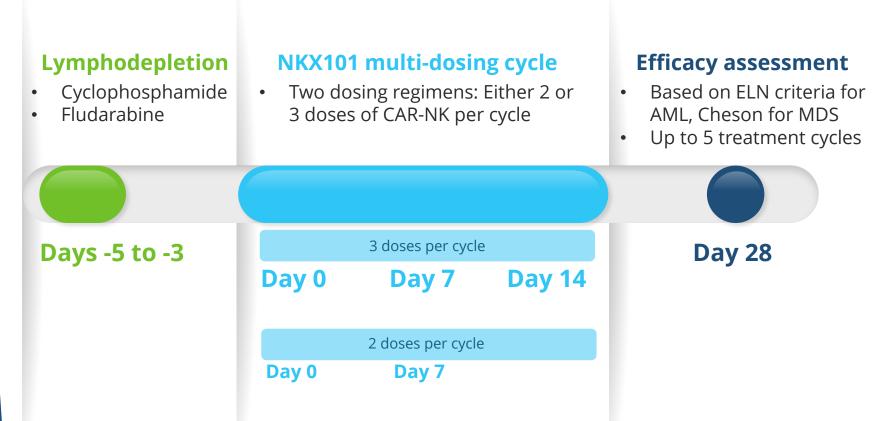
Roboz, 2014; Faderl, 2012; Ravandi; 2015; Patel 2012; Xospata USPI; Tibsovo USPI; Idhifa USPI; Brandwein, 2020 *CR, complete response; USPI, U.S. Prescribing Information; HCT, Hematopoietic stem cell transplantation.* 



#### **Patient Survival – Historical Control**

## NKX101 Phase 1 Trial Design

- High-risk pre-treated patient population
  - r/r AML or higher risk MDS, ≥1 therapy
  - Must have received targeted therapy, where approved
  - Pre- and post-allogeneic transplant
- Key Objectives
  - Safety and tolerability
  - Anti-tumor activity
  - Pharmacokinetics

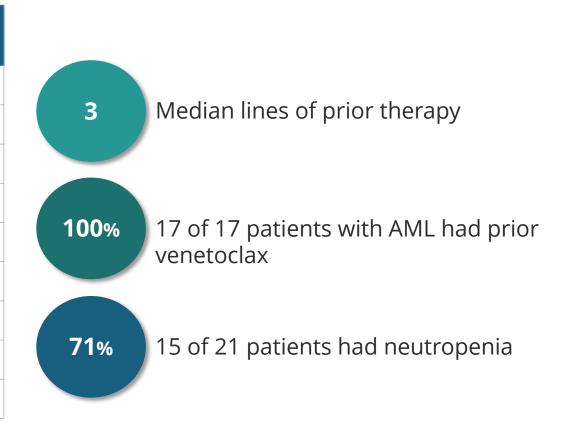


#### nkarta THERAPEUTICS



## NKX101 patients were heavily pre-treated and multiplyrelapsed with poor prognosis

Characteristics	Total (N=21)
Age, median (range)	60 (22 - 76)
Diagnosis, AML/MDS, n	17/4
Baseline ECOG 1, n	12
Months since diagnosis, median (range)	13 (2 – 54)
Baseline blast %, median (range)	27 (3 - 85)
Baseline ANC <1 × 10 <sup>9</sup> /L	15
Median prior lines of therapy (range)	3 (1 - 12)
Prior allogeneic transplant, n	4
Prior venetoclax, n	20



ANC: absolute neutrophil count; ECOG: Eastern Cooperative Oncology Group. Based on interim data from open clinical database as of 21 Apr 2022



## NKX101 was well-tolerated across all regimens and dose levels

## • No dose-limiting toxicities

- Currently enrolling cohort at 1.5 billion cells × 3 doses
- Myelosuppression and infection consistent with lymphodepletion and underlying disease were the most common higher-grade toxicities
  - Two patients with Grade 2 infusion reactions, transient fever, chills, fluid responsive hypotension

## No CAR T-like toxicities observed at any dose

- No cytokine release syndrome
- No ICANS/ neurotoxicity
- No graft-versus-host disease

≥ G3 AEs in > 1 subject	Total (N=21)
Hematologic Events	
Thrombocytopenia	10 (48%)
Febrile neutropenia	8 (38%)
Neutropenia	7 (33%)
Anemia	6 (29%)
White blood cell count decreased	2 (10%)
Leukocytosis	2 (10%)
Infections	
Pneumonia	5 (24%)
Sepsis	2 (10%)
Other	
Hypoxia <sup>^</sup>	4 (19%)
Fatigue	2 (10%)

\*Treatment emergent adverse events regardless of relationship Based on interim data from open clinical database as of 21 Apr 2022 ^ In the setting of febrile neutropenia/pneumonia

ICANS: Immune Effector Cell- Associated Neurotoxicity Syndrome.

# Favorable dose response to both increased number of cells / dose and number of doses / cycle in AML

	AML: ORR (CR, CRi, MLFS, PR)	AML: CR	MDS: ORR (CR, marrow CR, PR)
NKX101 – 3 doses	5 / cycle (Day 0, 7, 14)		
1B / 1.5B x 3	3/5 (60%)	3/5 (60%) 2/3 MRD-	0/2 (0%)
100M / 300M x 3	4/6 (67%)	0/6 (0%)	No patients treated
Overall Responses	7/11 (64%)	3/11 (27%)	0/2 (0%)
NKX101 – 2 doses	5 / cycle (Day 0, 7)		
1.5B x 2	0/3 (0%)	0/3 (0%)	No patients treated
150M / 450M x 2	1/3 (33%)	0/3 (0%)	0/2 (0%)
Overall Responses	1/6 (17%)	0/6 (0%)	0/2 (0%)

## 3/5 CRs (60%), including 2 MRD- observed at highest dose levels in 3-dose regimen in AML

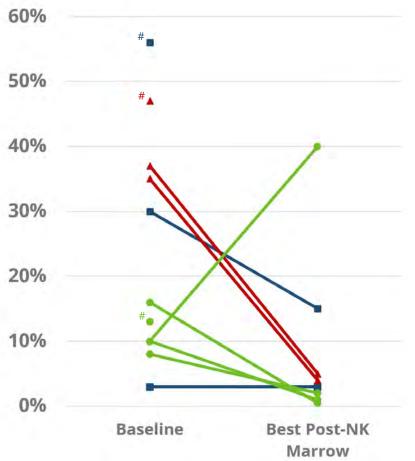
Based on interim data from open clinical database as of 21 Apr 2022

AML, acute myeloid leukemia; CR, complete response; CRi; complete response with incomplete hematologic recovery; HR-MDS, higher-risk myeloid disease syndrome; MLFS, morphological leukemia-free state; MRD-, minimal residual disease negative; ORR, overall response rate; PR, partial response.



# NKX101 drives AML blast reduction at all dose levels in 3 dose regimen with some patients achieving MRD-

Dose Level	Baseline marrow blasts <sup>*</sup>	Best post-NK response	
1.5B × 3	13%	PD	3/5 CR
	8%	CR (MRD-)	at highest
1B × 3	16%	<b>CR (MRD+)</b> MLFS end of Cycle 1, CR end of Cycle 2	doses in go-forward
	10%	PD	3-dose
	10%	CR (MRD-)	regimen
	35%	MLFS	
300M × 3	37%	MLFS	
	47%	PD	
	30%	PR	
100M × 3	56%	PD	
	3%	MLFS	



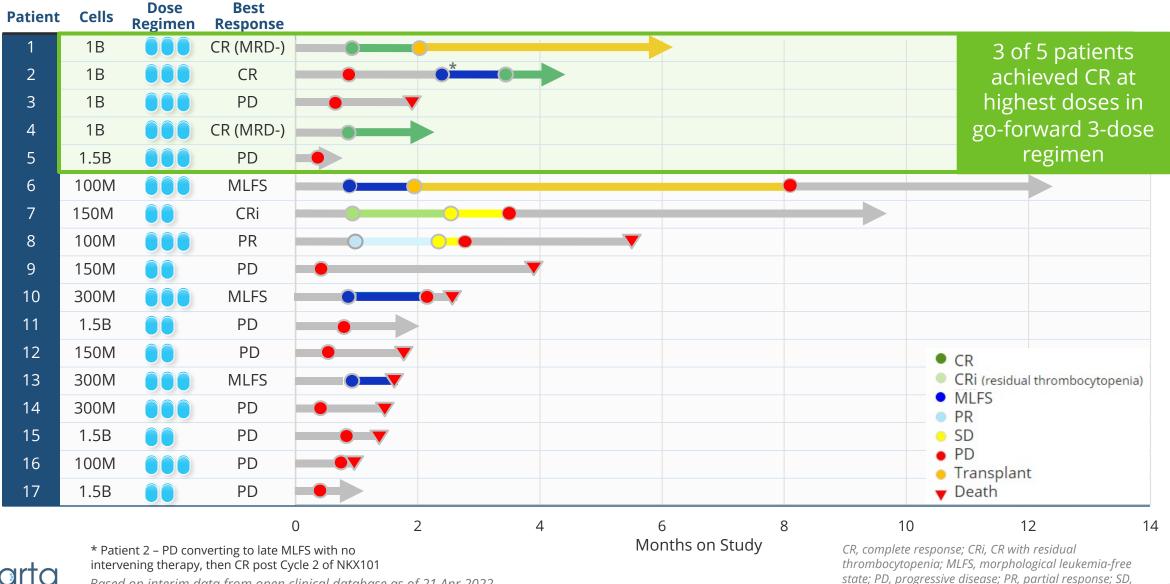
*MLFS, morphologic leukemia free state; MRD-, minimal residual disease negative; MRD+, minimal residual disease positive; PR, partial response; PD, progressive disease. #* PD, Peripheral blast progression



\*Baseline is the most recent available data prior to first dose Based on interim data from open clinical database as of 21 Apr 2022

THERAPEUTICS

## NKX101 demonstrated clinical activity across dose levels in AML



Based on interim data from open clinical database as of 21 Apr 2022

stable disease.

## **Case Study: Molecular remission following NKX101**

#### **Patient Profile**

- 68-year-old male
- **AML** with *IDH1* mutation
- Refractory to 4 prior lines of therapy, including venetoclax, ivosidenib and gemtuzumab
- At study entry, 8% blasts by morphology with 25% del(20q) by FISH

#### Efficacy

#### Post- Cycle 1 assessment

- CR, MRD- via FISH
- Normocellular marrow

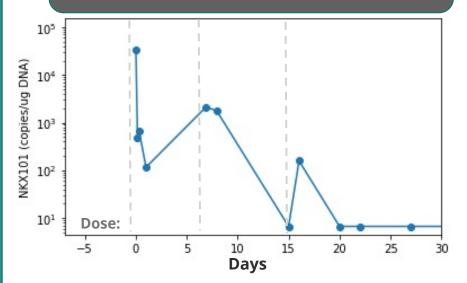
#### Safety

- Well tolerated
- ≥ Grade 3 events, anemia, neutropenia, decreased platelet count

## Follow up

- Underwent consolidative HCT
- In CR 6 months after treatment with NKX101

NKX101 detected after every dose 3 doses of 1 billion CAR NK cells per dose Expected NK-like PK and clearance Day 20



Based on interim data from open clinical database as of 21 Apr 2022 FISH, fluorescence in situ hybridization; HCT, hematopoietic cell transplant; MRD-, minimal residual disease negative.

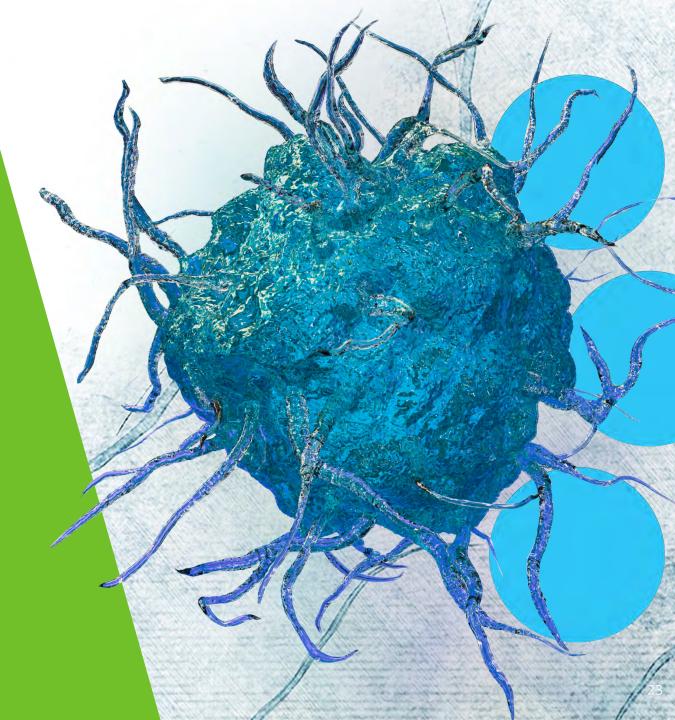


# Summary: NKX101 was well-tolerated and highly active in heavily pre-treated AML patients

- No DLTs or cases of CRS, GvHD or neurotoxicity
- 3 of 5 patients achieved CR (60%) in r/r AML at highest two dose levels in 3-dose regimen
  - 2 out of 3 CRs were MRD negative
- Responses and blast reduction observed across dose levels
  - Dose response
  - Deepening of response with additional cycle
- Next steps
  - Dosing of AML patients at 1.5B cells x 3 in dose escalation study
  - Potential for approval in r/r AML with single arm expansion cohort data
  - Potential to move to earlier lines in combination
  - Next data update 2H 2022



## NKX019 for the Treatment of Relapsed/Refractory B-Cell Malignancies





## CD19 is a validated target with approved CAR T cell therapies, but safety and accessibility limit widespread use

0.0

- 32 to 54% CR rate in LBCL with approved autologous CAR T-cell products
- Toxicities are common and life-threatening, often requiring hospitalization and ICU care
  - Over 25% of patients require ICU admission
  - Grade 3+ CRS: 13 to 49%
  - Grade 3+ ICANS/neurotoxicity: 18 to 31%
- Logistic challenges
  - Limited number of specialized sites
  - 9 to 34% of patients in pivotal trials did not receive cells

YESCARTA USPI; KYMRIAH USPI; BREYANZI USPI; Azoulay et al, 2020; Locke, Moffitt 2017 CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome, ICANS: immune cell associated neurotoxicity syndrome, ICU: intensive care unit, LBCL: large B-cell lymphoma, USPI: U.S. Prescribing Information.

## Long 1.0 0.8-0.6-0.4-0.2-

10

Cytokine Release Syndrome

(Grade 1-4)

CAR T toxicity observed in 60 to 80% of patients

Time from CAR T cell infusion (days)

15

25

20

**Neurological Toxicity** 

(Grade 1-4)

## NKX019 Phase 1 Trial Design

- High-risk, high-need patient population
  - r/r NHL, CLL and B-ALL
  - $\geq 2$  prior therapies
  - CAR T naïve
- Key Objectives

arta

- Safety and tolerability
- Anti-tumor activity
- Pharmacokinetics

## Lymphodepletion

- Cyclophosphamide
- Fludarabine

## NKX019 multi-dosing cycle

• 3 doses of CAR-NK per cycle

#### **Efficacy assessment**

- Based on Lugano criteria for NHL, NCCN for B-ALL
- Up to 5 treatment cycles

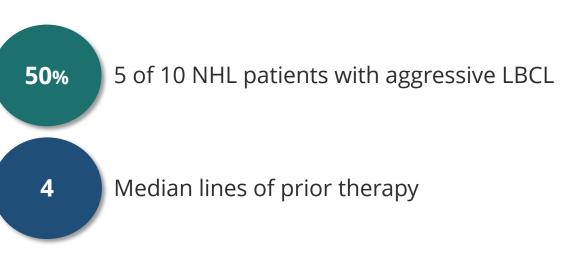
# Days -5 to -3 Day 0 Day 7 Day 14 Day 28

#### NCT05020678

CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; B-ALL, B cell acute lymphocytic leukemia; NHL, non-Hodgkin lymphoma.

# Mirroring real-world CAR T, NKX109 patients were heavily pre-treated, with a poor prognosis

Characteristic	Total (N=13)	
Age, median (range)	54 (21-82)	
Baseline ECOG 1	7	
Australia/US	10/3	
Diagnosis		
Large B cell lymphoma <sup>#</sup>	5	
Follicular lymphoma	3	
Marginal zone lymphoma	1	
Mantle cell lymphoma	1	
B-cell acute lymphoblastic leukemia	3	
Prior lines of therapy, median (range)	4 (2 - 7)	



Based on interim data from open clinical database as of 21 Apr 2022



## NKX019 was well-tolerated across all dose levels

- No dose-limiting toxicities up to 1 billion cells x 3 dose level
  - Currently enrolling cohort at 1.5 billion cells × 3 doses
- Myelosuppression consistent with LD was the most common higher-grade toxicity
  - One patient with Grade 1 infusion reaction, transient fever
- No CAR T-like toxicities at any dose
  - No cytokine release syndrome
  - No ICANS/ neurotoxicity
  - No graft-versus-host disease



≥ G3 AEs in > 1 subject	Total (N=13)
Hematologic Events	
Neutropenia	9 (69%)
Thrombocytopenia	5 (38%)
Febrile neutropenia	3 (23%)
Anemia	2 (15%)

\*Treatment emergent adverse events regardless of relationship Based on interim data from open clinical database as of 21 Apr 2022

## Favorable dose response in aggressive NHL with increased dose of NKX019

	NKX019 300M cells x 3 doses		NKX019 1B cells x 3 doses	
	ORR (CR, PR) CR		ORR (CR, PR)	CR
All NHL	2/4 (50%)	1/4 (25%)	5/6 (83%)	3/6 (50%)
LBCL#	1/3 (33%)	0/3 (0%)	1/2 (50%)	1/2 (50%)
MCL	No patients treated	No patients treated	1/1 (100%)	1/1 (100%)
FL	1/1 (100%)	1/1 (100%)	2/2 (100%) [2 PR]	0/2 (0%)
MZL	No patients treated	No patients treated	1/1 (100%)	1/1 (100%)
B-ALL	0/1 (0%)	0/1 (0%)	0/2 (0%)	0/2 (0%)

#LBCL includes 4 DLBCL and 1 FL3b

- 5/6 ORR (83%), including 3/6 CRs (50%) observed at highest dose level in NHL
- CRs observed in multiple histologies

ALL, acute lymphoblastic leukemia; CR, complete response; FL, follicular lymphoma; IR, indeterminant response; LBCL, large B-cell lymphoma; MCL, mantle zone lymphoma; NHL, non-Hodgkin lymphoma; ORR, overall response rate; PR, partial response.



## NKX019 drove responses in every NHL subtype treated

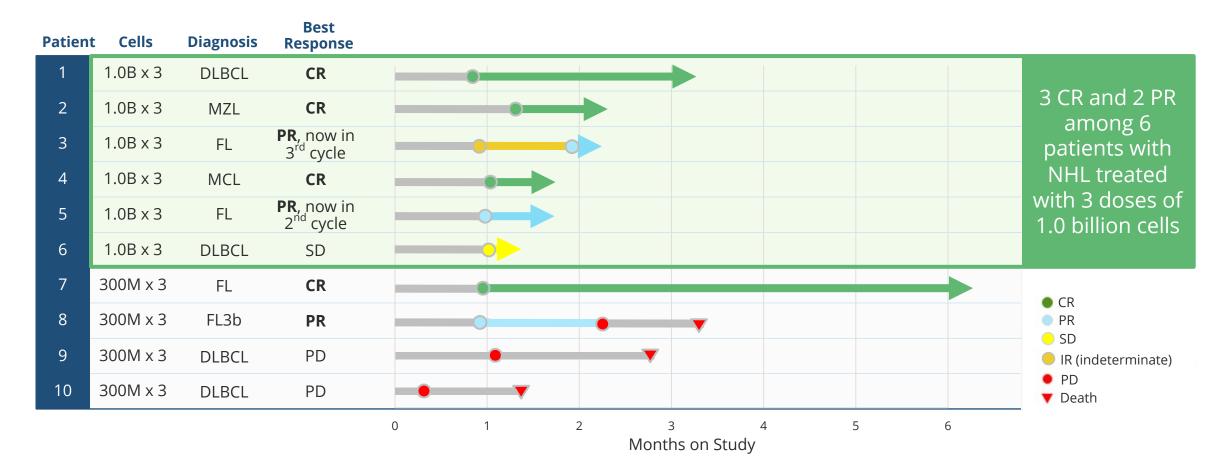
Dose Level	Diagnosis	Baseline Disease	Best Response
	DLBCL	Nodal	CR
	MCL	Nodal, marrow	CR
	FL	Nodal, liver, Spleen	PR, now in 3 <sup>rd</sup> cycle
1B x 3	MZL	Nodal, extra-nodal	CR
	FL	Nodal	PR, now in 2 <sup>nd</sup> cycle
	DLBCL	Liver, bone, marrow	SD, now in 2 <sup>nd</sup> cycle
	FL	Nodal, spleen	CR
300M x 3	FL3b	Nodal, liver, Spleen	PR
	DLBCL	Bulky nodal, liver, extra-nodal	PD
	DLBCL	Nodal, spleen	PD

- Dose response observed
- Responses observed after single cycle and across indolent and aggressive histologies
- All CRs are ongoing
- Protocol includes consolidation of CR
- Outpatient administration allowed after 1<sup>st</sup> cycle

Based on interim data from open clinical database as of 21 Apr 2022

*CR, complete response; DLBCL, diffuse large B cell lymphoma; FL, follicular lymphoma; FL3b, follicular lymphoma Grade 3b; IR, indeterminate response using LYRIC refinement; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; PR, partial response; PD, progressive disease.* 

## NKX019 provides rapid responses, including complete responses



Based on interim data from open clinical database as of 21 Apr 2022

aNHL, aggressive NHL; CR, complete response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; iNHL, indolent NHL; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; NHL, non-Hodgkin's lymphoma; PD, progressive disease; PR, partial response; SD, stable disease.



#### NKX019

# Case studies: Single cycle, rapid complete responses with NKX019 across doses in r/r NHL

#### **Patient Profile**

- 73-year-old female with extensive high-risk FL
- Relapsed after Rbendamustine, refractory to experimental BCL2i

#### Efficacy

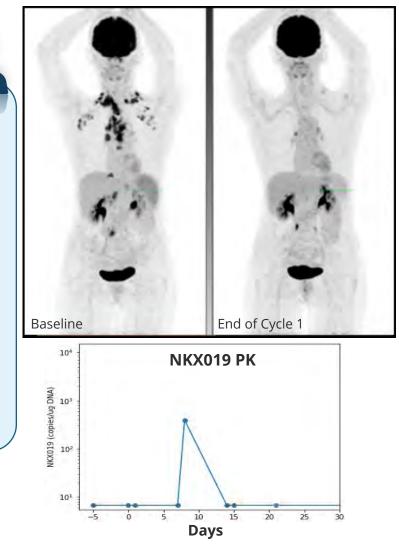
• CR after 1 cycle of 300M cells x 3

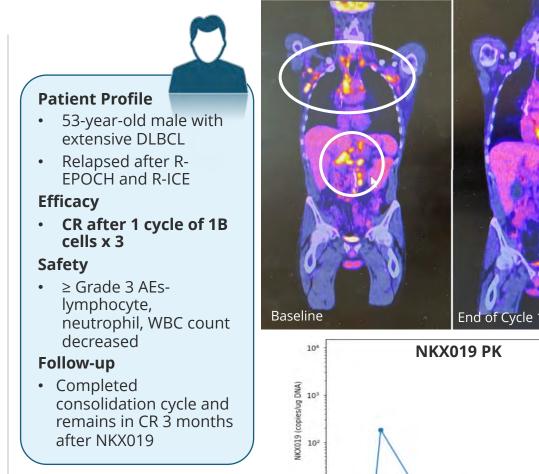
#### Safety

• No  $\geq$  Grade 3 AEs

#### Follow-up

• Remains in CR 6 months after NKX019





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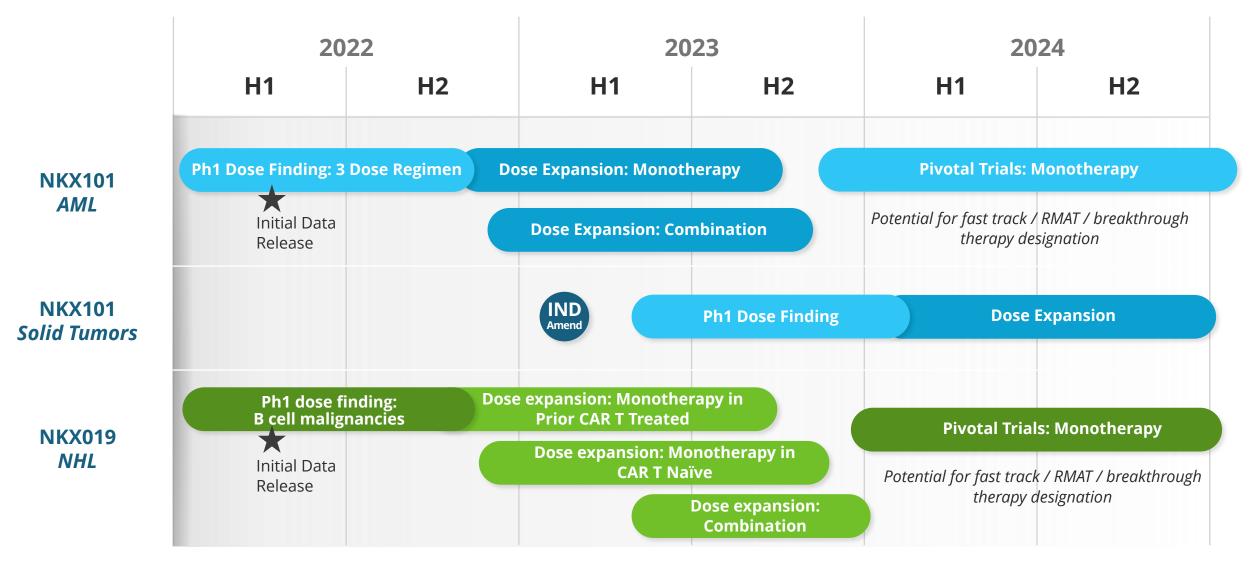


# NKX019 shows compelling preliminary activity and safety in NHL with the potential to address multiple unmet needs

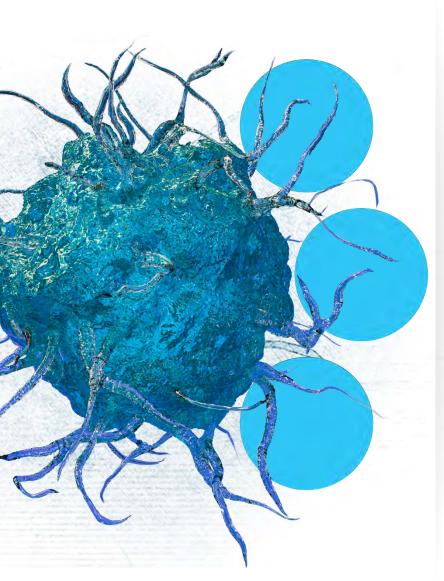
- No DLTs or cases of CRS, GvHD or neurotoxicity
- 5 of 6 patients responded (83% ORR) and 3 of 6 patients achieved complete response (50% CR) in NHL at 1B cells × 3 dose level
  - Complete responses observed in multiple NHL histologies including DLBCL
- Durability of at least 5 months with one patient at lowest dose of 300M cells x 3
- Next steps
  - Potential to improve and deepen responses with higher dose of 1.5B cells x 3
  - Planned expansion cohorts in both CAR T treated and CAR T naïve LBCL
  - Potential combination studies in expansion cohorts
  - Next data update 2H 2022



## Potential upcoming milestones for clinical programs







# Emerging clinical data from both NKX101 and NKX019 programs validate the Nkarta platform

- Allogeneic and off-the-shelf therapies available on demand
- Additional updates for NKX101 and NKX019 in 2H 2022
  - Growing pipeline with in-house manufacturing
  - Significant progress toward fulfilling our mission:

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

