

Clinical Program Update

25 April 2022

Clinical Data as of 21 April 2022

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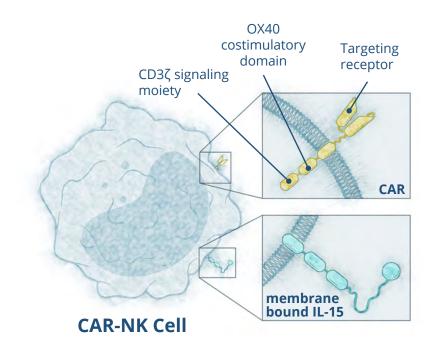
Best-in-class platform driving off-the-shelf CAR NK cell therapies

Co-lead programs in hematologic malignancies

NKX101

Targeting NKG2D ligands

- Phase 1 in r/r AML and higher-risk MDS
- Orphan Drug Designation
- NKG2D receptor is primary driver of NK cell activation and tumor killing



NKX019

Targeting CD19

- Phase 1 in r/r B cell malignancies
- Validated target
- Opportunity to differentiate from CAR T cells with broad patient access



NKX101 and NKX019: Well tolerated and highly active in heavily pre-treated r/r AML and r/r NHL patients, respectively

NKX101

- 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

NKX019

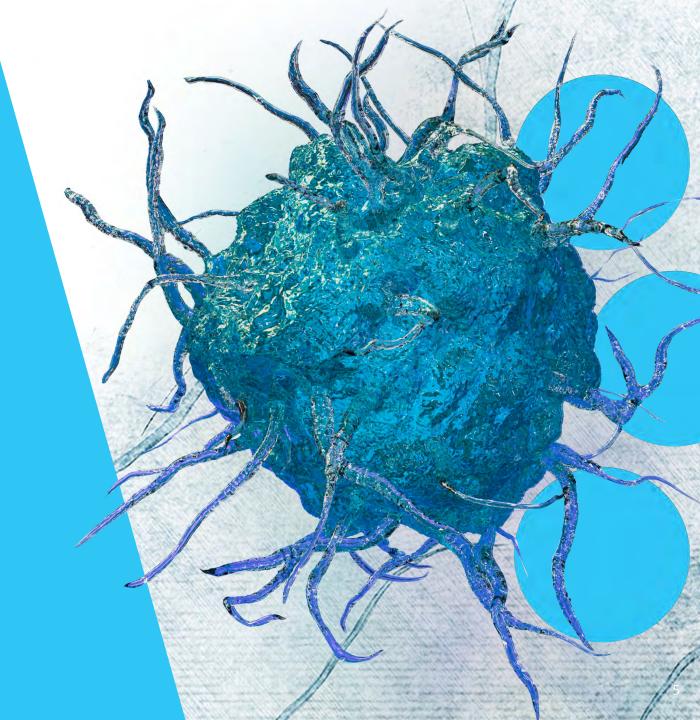
- No DLTs or cases of CRS, GvHD or neurotoxicity
- 5 of 6 patients responded (83%) and 3 of 6 patients achieved complete response (50%) in NHL at 1B cells x 3
 - Complete responses observed in multiple NHL histologies including DLBCL



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

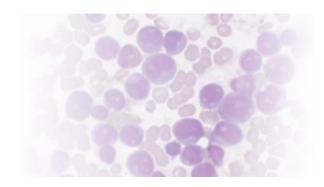
DLT, dose-limiting toxicity; CRS, cytokine release syndrome; GvHD, graft-versus-host disease; MRD-, minimal residual disease negative; DLBCL, diffuse large B cell lymphoma.

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





AML is a rapidly progressing leukemia with a poor prognosis



Cancer of immature blood cells or "blasts" in the bone marrow

- Treatment requires multiple rounds of intensive chemotherapy
- Most patients will ultimately relapse, even after prior CR
- Patients unfit for intensive chemotherapy may achieve CR with venetoclax but eventually relapse

Treatment Options - r/r AML

Low response rate with traditional chemotherapy

12 to 18% CR rate

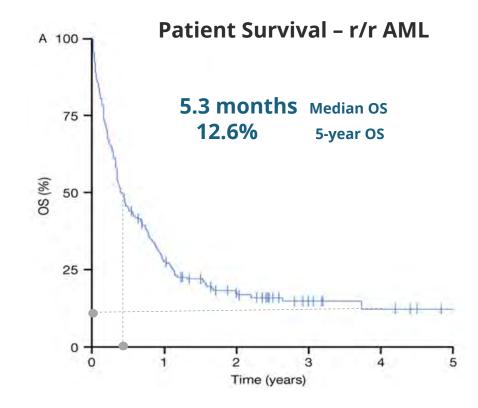
• Approximately 50% of patients have targetable mutations (FLT3, IDH1/2)

19 to 25% CR rate

 Long-term remission often depends on HCT in patients who are fit enough to receive it

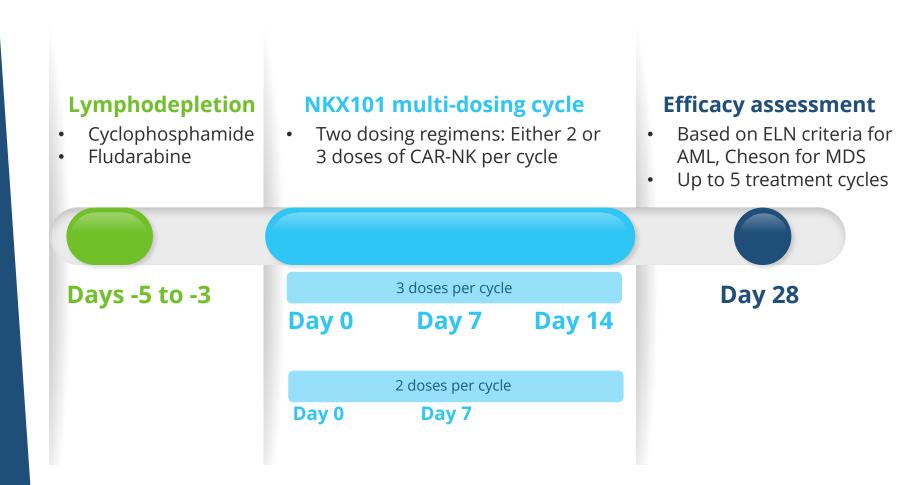
Pre-transplant CR improves outcomes





NKX101 Phase 1 Trial Design

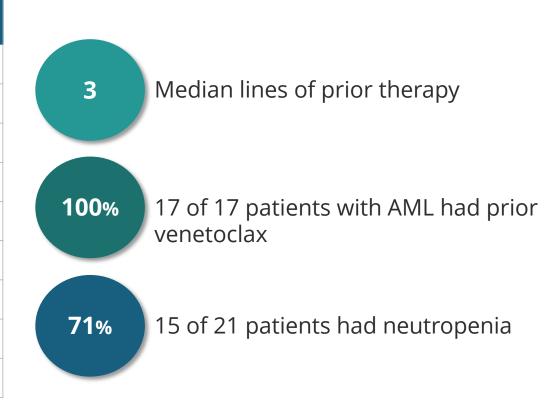
- High-risk pre-treated patient population
 - r/r AML or higher risk
 MDS, ≥1 therapy
 - Must have received targeted therapy, where approved
 - Pre- and post-allogeneic transplant
- Key Objectives
 - Safety and tolerability
 - Anti-tumor activity
 - Pharmacokinetics





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 ⁹ /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 [^]	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 / 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 / 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%)	



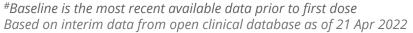
Based on interim data from open clinical database as of 21 Apr 2022

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 [#]	Best post-NK response	
1.5B × 3	13%	PD	3/5 CR
	8%	CR (MRD-)	at highest
1B × 3	16%	CR (MRD+) 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	
100M × 3	30%	PR	
	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.

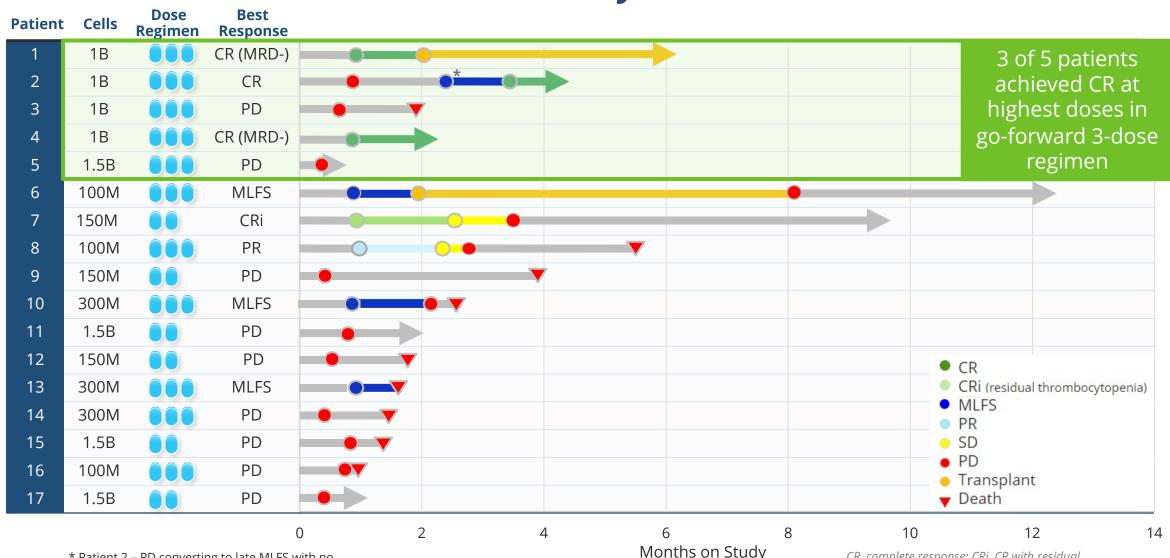


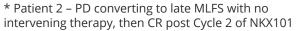


^{60%} 50% 40% 30% 20% 10% 0% Baseline Best Post-NK Marrow

^{*} PD, Peripheral blast progression

NKX101 demonstrated clinical activity across dose levels in AML





CR, complete response; CRi, CR with residual thrombocytopenia; MLFS, morphological leukemia-free state; PD, progressive disease; PR, partial response; SD, 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

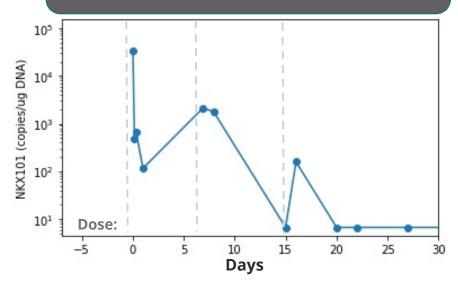
Safety

- 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





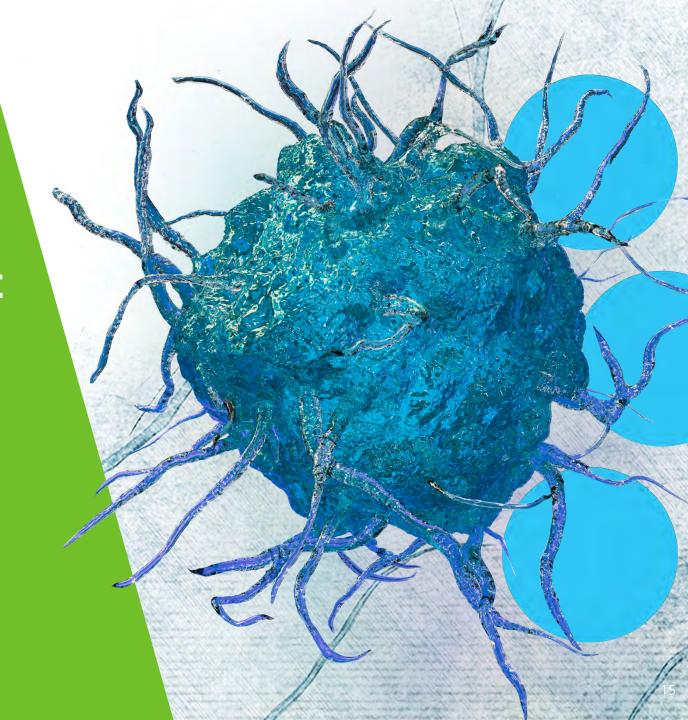
Based on interim data from open clinical database as of 21 Apr 2022 FISH, fluorescence in situ hybridization; HCT, hematopoietic cell transplant; MRD-, minimal residual disease negative.

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



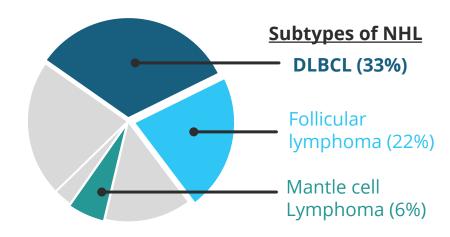


Non-Hodgkin lymphomas are cancers derived from B cells and include aggressive and indolent forms

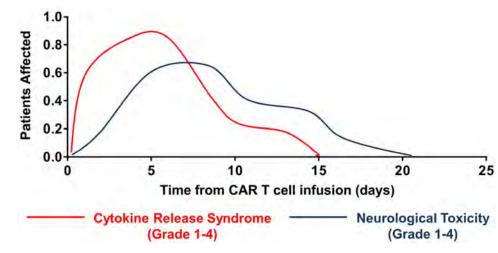
- All forms express B-cell antigens, such as CD19
- DLBCL has a poor prognosis and r/r disease is especially challenging
 - 32-54% CR rate in r/r LBCL with CAR T cells
 - Other salvage therapies median OS of ~6 months

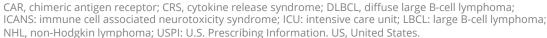
Safety and accessibility limit widespread CAR T use

- Toxicities are common and life-threatening
 - Over 25% of patients require ICU admission
 - Grade 3+ CRS: 13-49%, Grade 3+ ICANS: 18-31%
- Limited number of specialized sites
- 9-34% of patients in pivotal trials did not receive cells



CAR T toxicity observed in 60 to 80% of patients

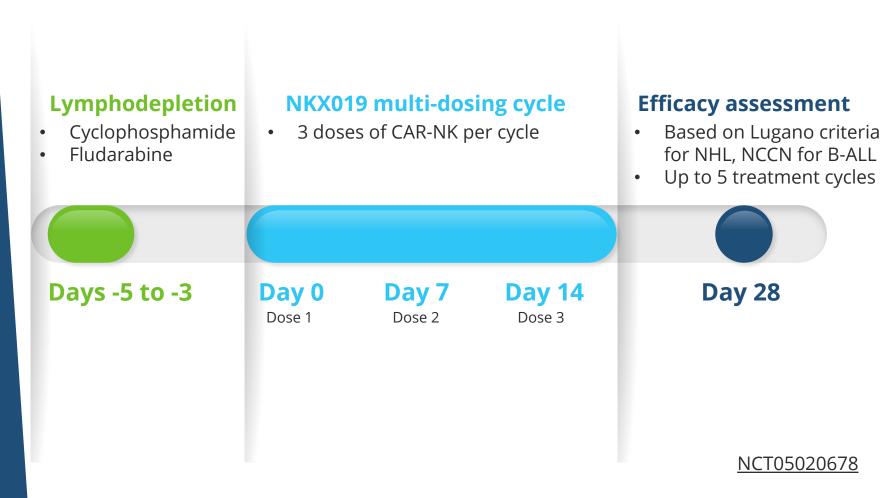






NKX019 Phase 1 Trial Design

- High-risk, high-need patient population
 - r/r NHL, CLL and B-ALL
 - ≥2 prior therapies
 - CAR T naïve
- Key Objectives
 - Safety and tolerability
 - Anti-tumor activity
 - Pharmacokinetics

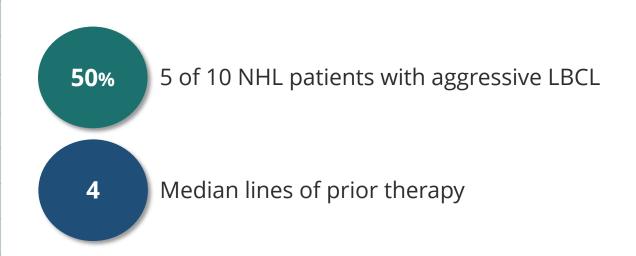




CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; B-ALL, B cell acute lymphocytic leukemia; NHL, non-Hodgkin lymphoma.

Mirroring real-world CAR T, NKX019 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 [#]	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

LD: lymphodepletion, ICANS: Immune Effector Cell- Associated Neurotoxicity Syndrome.



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

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 rd cycle
1B x 3	MZL	Nodal, extra-nodal	CR
	FL	Nodal	PR , now in 2 nd cycle
	DLBCL	Liver, bone, marrow	SD, now in 2 nd cycle
	FL	Nodal, spleen	CR
300M x 3	FL3b	Nodal, liver, Spleen	PR
	DLBCL	Bulky nodal, liver, extra-nodal	PD
	DLBCL	Nodal, spleen	PD

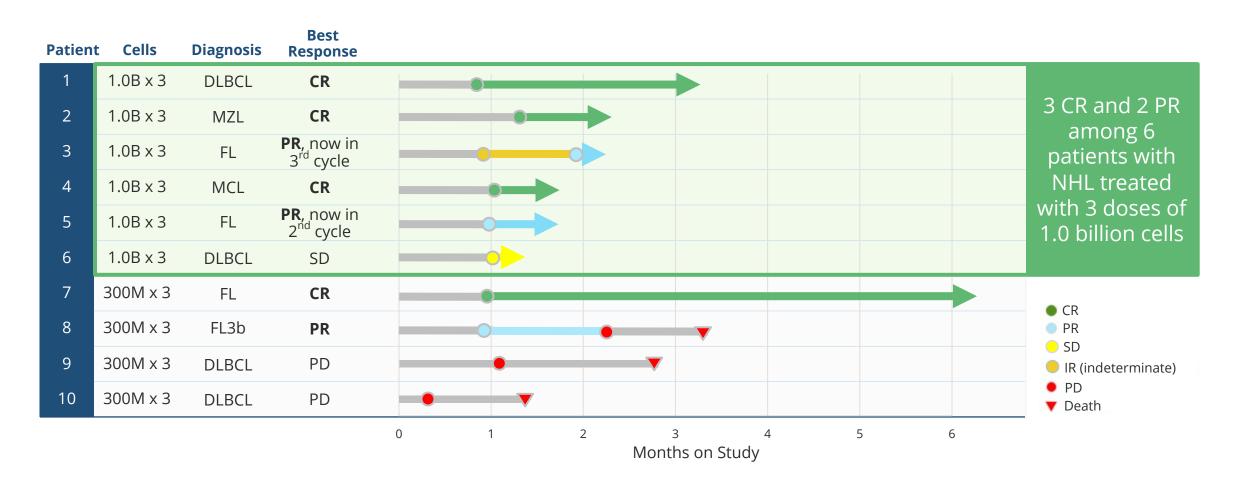
- Dose response observed
- Responses observed after single cycle and across indolent and aggressive histologies
- All CRs are ongoing
- Protocol includes consolidation of CR
- Outpatient administration allowed after 1st cycle

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.

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

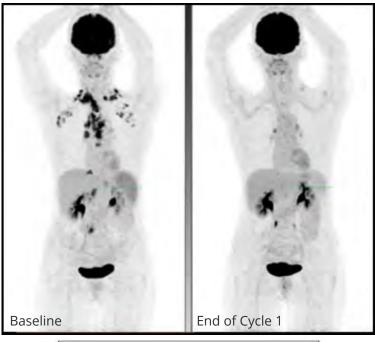
 CR after 1 cycle of 300M cells x 3

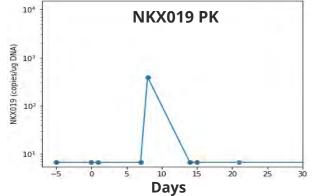
Safety

• No ≥ Grade 3 AEs

Follow-up

 Remains in CR 6 months after NKX019







Patient Profile

- 53-year-old male with extensive DLBCL
- Relapsed after R-EPOCH and R-ICE

Efficacy

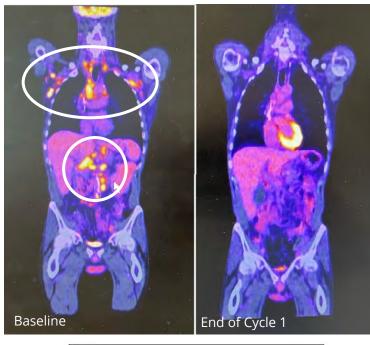
 CR after 1 cycle of 1B cells x 3

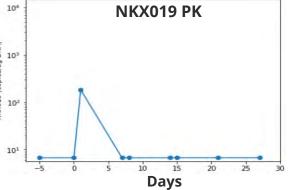
Safety

 ≥ Grade 3 AEslymphocyte, neutrophil, WBC count decreased

Follow-up

 Completed consolidation cycle and remains in CR 3 months after NKX019





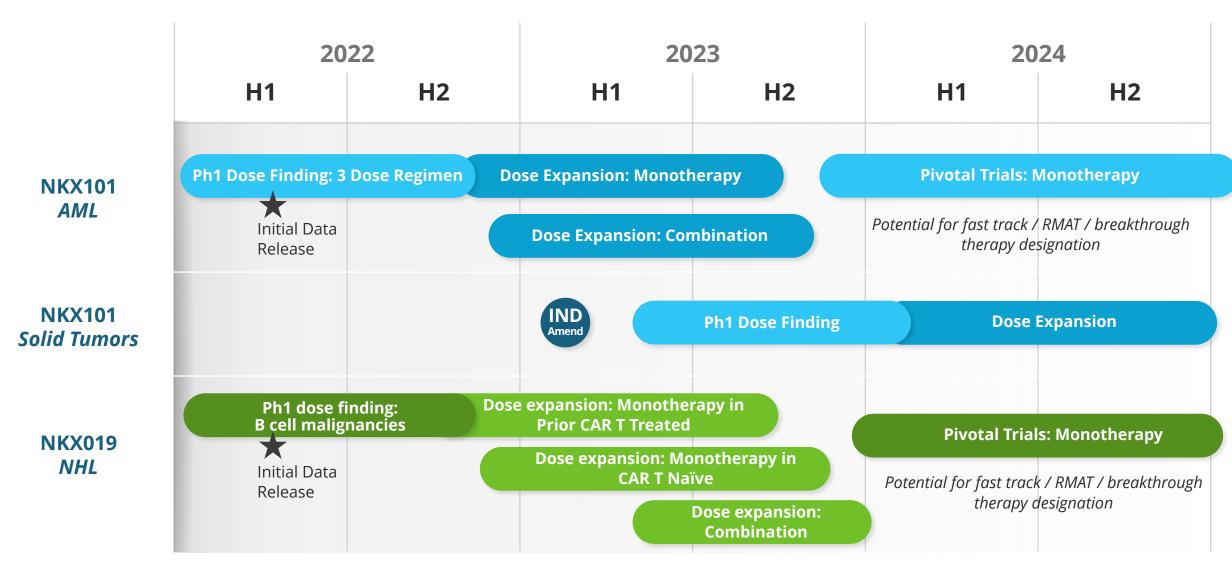


NKX019 shows compelling preliminary activity and safety in NHL with the potential to address multiple unmet needs

- 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

- Promising preliminary activity with favorable safety profiles
- ✓ Allogeneic and off-the-shelf therapies available on demand
- Potential to pursue accelerated regulatory pathway options, earlier line combination regimens for both programs
- ✓ Significant progress toward fulfilling the mission to:

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

