Preliminary Safety, PK/PD, and Clinical Activity of NKX019, an Allogeneic, CD19-Targeted, CAR NK Cell Therapy, in Systemic Sclerosis: Results From an Ongoing, Phase 1/2, Open-Label, Multicenter, Dose-Escalation/Optimization, Basket Study

Poster 1179

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Background

SSc is a progressive, debilitating disease that can severely impact quality of life

- Incidence and prevalence estimates of SSc in the US were 15.1 per 100,000 person-years and 25.9 per 100,000 people, respectively[1]
- SSc is a rare, heterogeneous autoimmune disease marked by inflammation, vasculopathy, and progressive fibrosis of the skin and internal organs[2,3]

Among connective tissue diseases, SSc carries the highest disease-specific mortality[4]

- Standardized mortality rates are up to 3.5 times higher in persons with SSc when compared to persons without SSc[5,6]
- Approximately 60% of disease-related deaths are attributed to ILD and PAH[7,8]

B cells are one of the central drivers of SSc pathology

- B cell dysregulation leads to chronic, uncontrolled inflammation[9–11]
- Due to its broad expression across B cell lineages, CD19 is a well-validated target to deplete pathogenic B cell populations[9]

Current treatments do not holistically address underlying disease

- Available therapies address symptoms, not the underlying disease, and can have serious safety and tolerability issues[12]

NKX019 Is an Investigational, Allogeneic, CD19-Targeted CAR NK Cell Therapy

Off-the-shelf availability — Advantage of allogeneic treatment

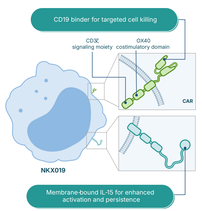
- Cryopreserved CAR NK cells available for delivery to the point of care
- Outpatient administration, with no patient leukapheresis or concern for manufacturing delays

Controllable dose — Supports dose refinement

- Predictable PK enables greater control of exposure[13]
- Rigorous dose-escalation and regimen-optimization strategy informed by safety, PK/PD, and clinical response data[14]

Favorable safety profile — Robust B cell depletion without immune cascade

- Across 79 patients as of September 18, 2026, NKX019 has demonstrated favorable safety and tolerability in oncology and autoimmune disease, particularly regarding IEC-associated adverse events



Objective

To report the safety, PK/PD, and clinical activity of NKX019 in patients with SSc during the dose-escalation phase of the NTRUST-2 study

Methods

- NTRUST-2 (NCT06733935) is an ongoing, phase 1/2, open-label, multicenter, dose-escalation/refinement, basket study of NKX019 in patients with B cell–mediated autoimmune diseases
- Patients washed out or reduced immunosuppressant or biologic background medications before LD preconditioning* during the dose-escalation phase. NKX019 was then administered at 1B, 2B, or 4B CAR NK cells/dose on Days 0, 3, and 7 (**Figure 1**)
- The current analysis used a September 18, 2026, data cutoff and focused on patients who received LD preconditioning with Flu/Cy, received 3 doses of NKX019, and had ≥1 post-baseline efficacy-evaluable assessment

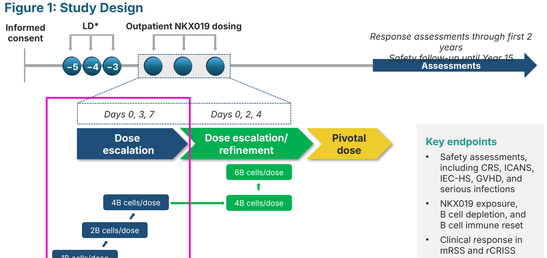
Key inclusion criteria

- Aged 18–75 years
- Met 2013 ACR/EULAR classification criteria
- Ten years or less since the first non-Raynaud symptom
- Met ≥1 of the following criteria:
  - Severe skin involvement (mRSS ≥30) or progressive active skin disease with mRSS ≥15
  - Moderate to severe ILD (FVC >45% and <70% of predicted) or DLCO corrected (>40% and <70% of predicted)

Key exclusion criteria

- Substantial medical concern, including severe dysfunction in major organ systems, immunodeficiencies, solid organ transplant, and use of cell therapies
- Moderate to severe PAH

Figure 1: Study Design



Key endpoints

- Safety assessments, including CRS, ICANS, IEC-HS, GVHD, and serious infections
- NKX019 exposure, B cell depletion, and B cell immune reset
- Clinical response in mRSS and rCRISS

*LD preconditioning = a total of 90 mg/m² Flu as 30 mg/m²/day on Days −5, −4, and −3 and 1 g/m² Cy on Day −3. Patients with cytopenia at baseline may receive Cy alone as 1 g/m² Cy on Day −3. LD preconditioning is performed in an outpatient setting for both treatments. ACR, American College of Rheumatology; BL, billion; CRS, cytokine release syndrome; Cy, cyclophosphamide; DLCO, diffusing capacity of the lungs for carbon monoxide; EULAR, European Alliance of Associations for Rheumatology; Flu, fludarabine; FVC, forced vital capacity; GVHD, graft-versus-host disease; ICANS, immune effector cell-associated neurotoxicity syndrome; IDSMB, independent data safety monitoring board; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; ILD, interstitial lung disease;
LD, lymphodepletion; mRSS, modified Rodnan skin score; PAH, pulmonary arterial hypertension; rCRISS, revised Composite Response Index in Systemic Sclerosis.

Results

Table 1: Baseline Characteristics

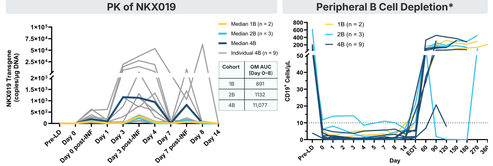
- Of the 34 patients treated with NKX019 in the NTRUST-2 study, 14 had SSc with a median disease duration of 4.6 years (range, 0.5–8.1 years; **Table 1**)
- All patients had active, treatment-refractory disease at baseline, and 9/14 (64.3%) patients received ≥3 prior treatments, including glucocorticoids (35.7%), cDMARDs (85.7%), rituximab (14.3%), and other therapies (71.4%)

Measure	Overall N = 14	Dose 4B n = 9	Dose 2B n = 3	Dose 1B n = 2
Age, median (range), years	51.5 (30–66)	52.0 (30–66)	55.0 (51–61)	38.5 (31–46)
Female, n (%)	10 (71.4)	7 (77.8)	1 (33.3)	2 (100.0)
Race and ethnicity, n (%)				
White	9 (64.3)	6 (66.7)	2 (66.7)	1 (50.0)
Black or African American	4 (28.6)	3 (33.3)	1 (33.3)	0
Asian	1 (7.1)	0	0	1 (50.0)
Hispanic or Latino	7 (50.0)	4 (44.4)	2 (66.7)	1 (50.0)
Disease duration,* median (range), years	4.6 (0.5–8.1)	5.3 (0.5–8.1)	2.9 (1.3–2.9)	4.1 (1.8–6.4)
SSc-specific autoantibody,† % positive				
ANA	85.7	77.8	100.0	100.0
Anti-Scl-70	35.7	55.6	0	0
Anti-RNA polymerase III	28.6	11.1	66.7	50.0
Baseline disease activity, median (range)				
mRSS	26.0 (12.0–46.0)	25.0 (19.0–46.0)	27.0 (18.0–32.0)	23.5 (12.0–35.0)
CGA score	70.5 (42.0–93.0)	70.0 (42.0–93.0)	75.0 (69.0–85.0)	70.0 (60.0–80.0)
PtGA score	64.0 (2.0–100.0)	66.0 (30.0–100.0)	52.0 (28.0–90.0)	36.0 (2.0–70.0)
HAQ-DI score	1.1 (0.0–2.3)	1.3 (0.0–2.1)	0.6 (0.1–2.3)	1.1 (0.1–2.0)
Presence of ILD, n (%)	10 (71.4)	6 (66.7)	2 (66.7)	2 (100.0)
FVC % predicted, median (range)	58.5 (43.0–104.0)	56.5 (43.0–104.0)	61.5 (51.0–72.0)	68.5 (63.0–74.0)
DLCO % predicted, median (range)	70.5 (40.8–96.0)	59.0 (40.8–86.0)	59.0 (59.0–59.0)	89.5 (83.0–96.0)
Number of prior treatments, n (%)				
1–2	5 (35.7)	3 (33.3)	1 (33.3)	1 (50.0)
≥3	9 (64.3)	6 (66.7)	2 (66.7)	1 (50.0)
Prior treatments,‡ n (%)				
Systemic GCs	5 (35.7)	4 (44.4)	1 (33.3)	0
cDMARDs	12 (85.7)	8 (88.9)	3 (100.0)	1 (50.0)
MMF (and derivatives)	9 (64.3)	7 (77.8)	2 (66.7)	0
Rituximab	2 (14.3)	2 (22.2)	0	0
Anti-fibrotics	1 (7.1)	1 (11.1)	0	0
Other§	10 (71.4)	6 (66.7)	2 (66.7)	2 (100.0)

*From occurrence of the first non–Raynaud phenomenon symptom. †Autoantibody presence is calculated in all patients. Two of 14 (14.3%) patients were positive for ACAs. ‡At screening prior to LD preconditioning. §Other treatments included antimalarials, calcineurin inhibitors, Janus kinase inhibitors, biologics. ACA, anti-centromere antibody; ANA, antinuclear antibody; Anti-Scl-70, anti-topoisomerase I; B, billion; cDMARD, conventional disease-modifying antirheumatic drug; CGA, Clinician Global Assessment; DLCO, diffusing capacity of the lungs for carbon monoxide; FVC, forced vital capacity; GC, glucocorticoid; HAQ-DI, Health Assessment Questionnaire Disability Index; ILD, interstitial lung disease; LD, lymphodepletion; MMF, mycophenolate mofetil; mRSS, modified Rodnan skin score; PtGA, Patient Global Assessment; SSc, systemic sclerosis.

Figure 2: NKX019 Exposure and B Cell Depletion

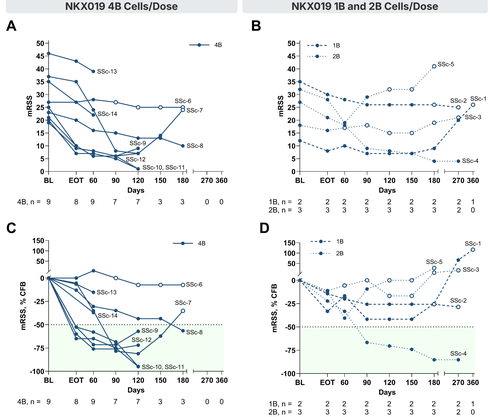
- At 4B cells/dose, treatment with NKX019 led to robust B cell depletion followed by reconstitution of the B cell compartment (**Figure 2**)
- PK data indicated dose-dependent increases in NKX019 exposure



†One patient did not have detectable B cells at baseline due to prior treatment with rituximab. One patient receiving 2B cells/dose received rituximab after NKX019 treatment and had a subsequent decline in B cells at Days 90–180. Ten cells/µL is the clinically reliable threshold for peripheral B cell depletion and is represented with a dotted line.[15] AUC, area under the curve; B, billion; DNA, deoxyribonucleic acid; EOT, end of treatment; GM, geometric mean; INF, infusion; LD, lymphodepletion preconditioning; PK, pharmacokinetics.

Figure 3: mRSS Over Time (A, B) and Percent CFB (C, D)

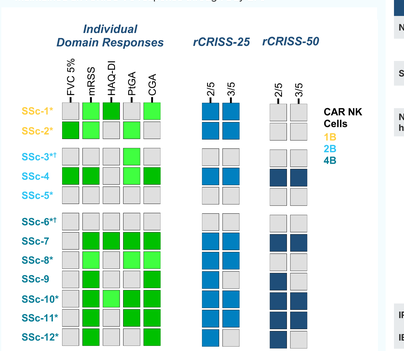
- Rapid and deep responses in mRSS were observed through Day 90 in patients receiving 4B cells/dose relative to lower dosing cohorts, suggesting a dose response (**Figure 3**)
- At Day 90, mRSS decreased in 6/7 (85.7%) patients receiving 4B cells/dose, with a median reduction of 15 points (range, 0–29 points)
- At Day 90, 5/7 (71.4%) patients receiving 4B cells/dose achieved an mRSS-50 response



Axis breaks were applied as needed for visualization purposes; no data points were excluded. Open circles indicate visits where administration of additional immunomodulatory agents (cDMARDs, IVIG, and/or rituximab) may have contributed to clinical efficacy. B, billion; BL, baseline; cDMARD, conventional disease-modifying antirheumatic drug; CFB, change from baseline; EOT, end of treatment; IVIG, intravenous immunoglobulin; mRSS, modified Rodnan skin score; SSc, systemic sclerosis.

Figure 4: rCRISS-25 and rCRISS-50 Responses at Day 90

- Five of 7 (71.4%) patients receiving 4B cells/dose with ≥3 months of follow-up achieved an rCRISS-50 or higher response at Day 90 (**Figure 4**)
- Six of 7 (85.7%) patients receiving 4B cells/dose with ≥3 months of follow-up achieved a rCRISS-25 or higher response at Day 90
- All patients with an rCRISS response demonstrated improvement in mRSS and/or FVC
- The patient with the longest follow-up in the 2B cells/dose cohort maintained an rCRISS-70 response through Day 270



An rCRISS response required improvement in ≥2 of 5 (2/5) or ≥3 of 5 (3/5) measures. *Denotes patients with ILD. †Indicates visits where administration of additional immunomodulatory agents (cDMARDs, IVIG, and/or rituximab) may have contributed to clinical efficacy. B, billion; CAR, chimeric antigen receptor; cDMARD, conventional disease-modifying antirheumatic drug; CGA, Clinician Global Assessment; FVC, forced vital capacity; HAQ-DI, Health Assessment Questionnaire Disability Index; ILD, interstitial lung disease; IVIG, intravenous immunoglobulin; mRSS, modified Rodnan skin score; NK, natural killer; PtGA, Patient Global Assessment; rCRISS, revised Composite Response Index in Systemic Sclerosis; SSc, systemic sclerosis.

Table 2: Safety Assessments in Patients Receiving 1B, 2B, or 4B Cells/Dose of NKX019

- NKX019 has no reported events of CRS, ICANS, IEC-HS, GVHD, related serious infections, or deaths (**Table 2**)
- One patient developed a NKX019-related hematologic event requiring intervention (neutropenia [7.1%])

Measure, n (%)	Overall N = 14	Dose 4B n = 9	Dose 2B n = 3	Dose 1B n = 2
NKX019-related AEs	7 (50.0)	4 (44.4)	1 (33.3)	2 (100)
Grade ≥3 events	2 (14.3)	1 (11.1)	0	1 (50.0)
Serious NKX019-related AEs	1 (7.1)*	0	0	1 (50.0)*
Serious infections	0	0	0	0
NKX019-related Grade ≥3 hematologic events				
Neutropenia	1 (7.1)	1 (11.1)	0	0
Received G-CSF	1 (7.1)	1 (11.1)	0	0
Febrile neutropenia	1 (7.1)*	0	0	1 (50.0)*
Received G-CSF	0	0	0	0
Prolonged cytopenias (>28 days)	0	0	0	0
Received G-CSF	0	0	0	0
Received blood transfusion	0	0	0	0
IRRs	1 (7.1)	1 (11.1)	0	0
IEC-associated AEs				
CRS	0	0	0	0
ICANS	0	0	0	0
IEC-HS	0	0	0	0
GVHD	0	0	0	0
Death	0	0	0	0

*One patient receiving 1B cells/dose experienced a serious NKX019-related AE of febrile neutropenia. AE, adverse event; B, billion; CRS, cytokine release syndrome; G-CSF, granulocyte colony-stimulating factor; GVHD, graft-versus-host disease; ICANS, immune effector cell–associated neurotoxicity syndrome; IEC, immune effector cell; IEC-HS, immune effector cell–associated hemophagocytic lymphohistiocytosis-like syndrome; IRR, infusion-related reaction.

Conclusions

Safety and PK/PD

- NKX019 was well tolerated overall at all doses
- No CRS, ICANS, IEC-HS, GVHD, or deaths were reported
- Robust peripheral B cell depletion was observed following NKX019 infusion, particularly in patients who received 4B cells/dose

Clinical activity

- Five of 7 (71.4%) patients receiving 4B cells/dose with ≥3 months of follow-up achieved an mRSS-50 response, indicating ≥50% improvement in their mRSS
- Five of 7 (71.4%) patients receiving 4B cells/dose with ≥3 months of follow-up achieved rCRISS-50 responses in 2 or more domains
- Preliminary NKX019 data in SSc demonstrate a well tolerated safety profile and encouraging clinical activity in the 4B cohort; further investigation is warranted

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Abbreviations

B, billion; CAR, chimeric antigen receptor; CD3ζ, CD3 zeta chain; cDMARD, conventional disease-modifying antirheumatic drug; CRS, cytokine release syndrome; Cy, cyclophosphamide; Flu, fludarabine; FVC, forced vital capacity; GVHD, graft-versus-host disease; ICANS, immune effector cell-associated neurotoxicity syndrome; IEC, immune effector cell; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; IL, interleukin; ILD, interstitial lung disease; LD, lymphodepletion; mRSS, modified Rodnan skin score; NK, natural killer; PAH, pulmonary arterial hypertension; PD, pharmacodynamic; PK, pharmacokinetic; rCRISS, revised Composite Response Index in Systemic Sclerosis; SSc, systemic sclerosis.

Disclosures

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Disclaimer: Preliminary data from an ongoing study as of the September 18, 2026, data cutoff. NKX019 is an investigational product candidate that has not been approved by the FDA or any other regulatory authority.

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