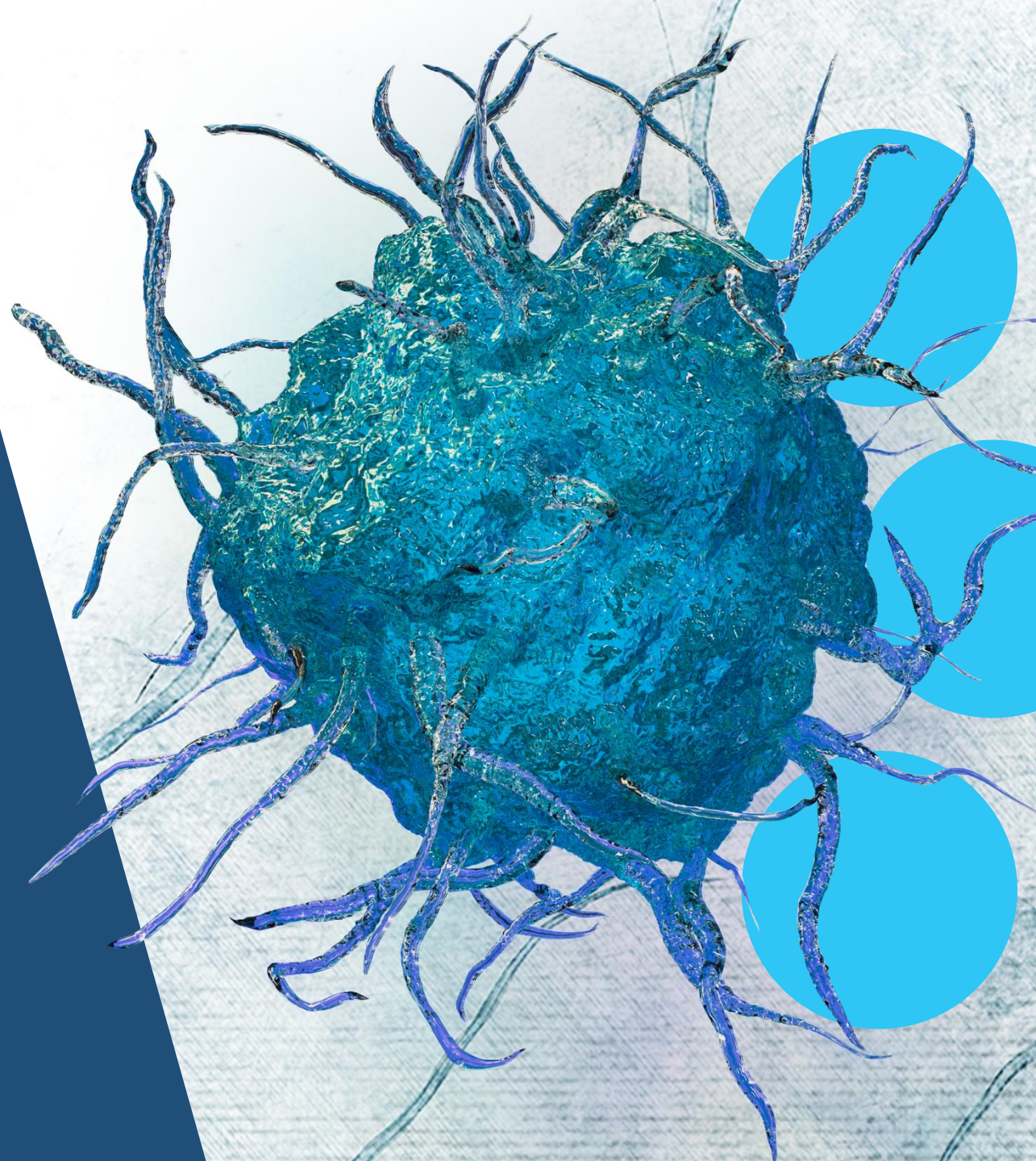
# Pioneering Engineered Natural Killer Cells

## Transforming the treatment of autoimmune disease



nkarta | April 2026

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Creating a Different Kind of Cell Therapy

**Harnessing** NK cells – the immune system's first responders – to make cell therapy safer

**Creating** an off-the-shelf product that can be administered in a community setting

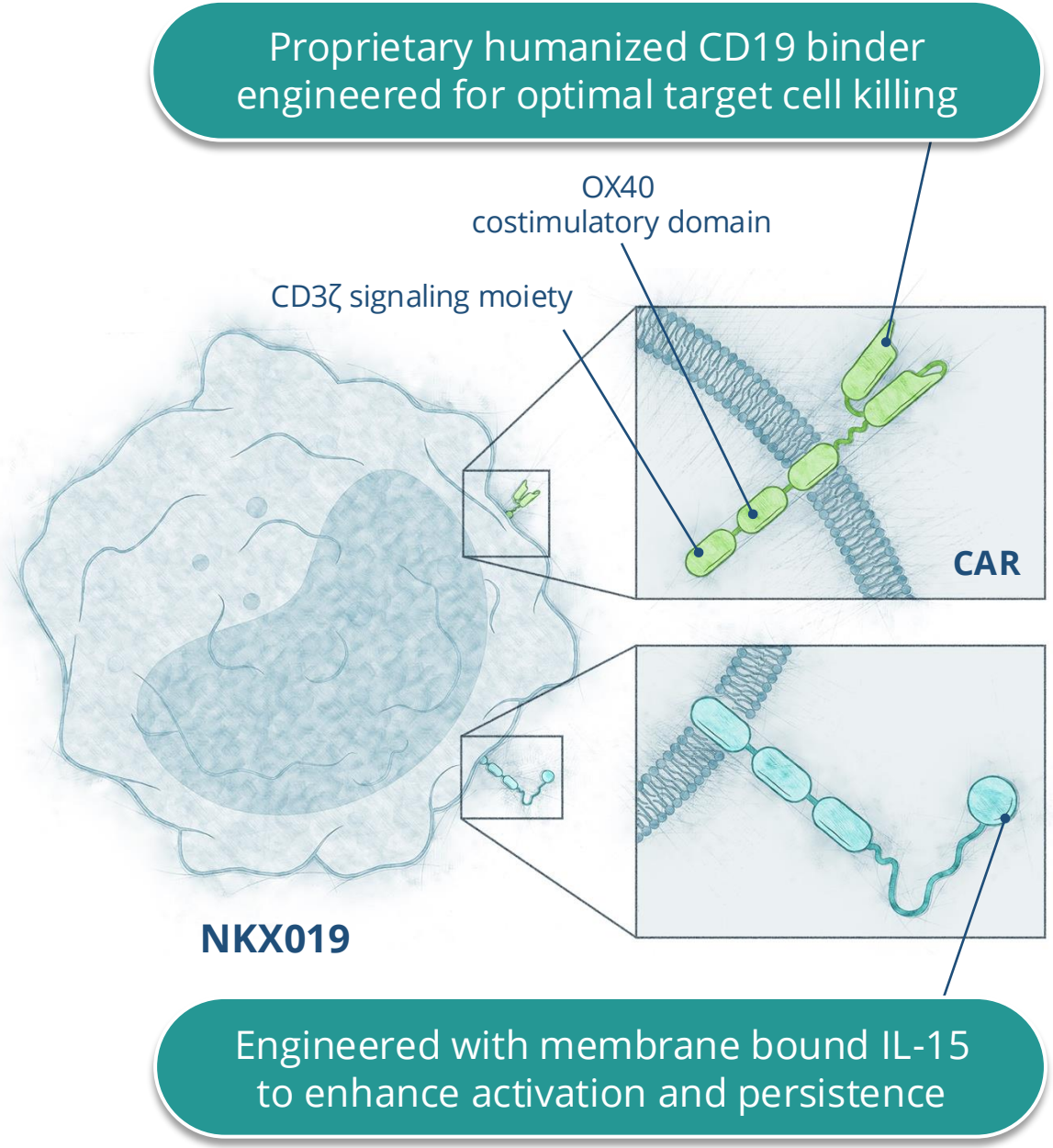
**Pioneering** donor-derived, scalable NK cells to broaden access for autoimmune patients

# Safely Harnessing NK Cells' Natural Killing Ability

Healthy, pre-screened donors provide off-the-shelf availability

Suitable for outpatient dosing (and redosing, if needed) in community-based settings

No immune effector cell-associated neurotoxicity syndrome (ICANS) or life-threatening cytokine release syndrome (CRS)[1]

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1: Dickinson, et al. *EHA.* 2023.

# Challenging the Treatment Paradigm for Autoimmune Disease

**Autoimmune disease driven by pathologic B cells is a major unmet need**

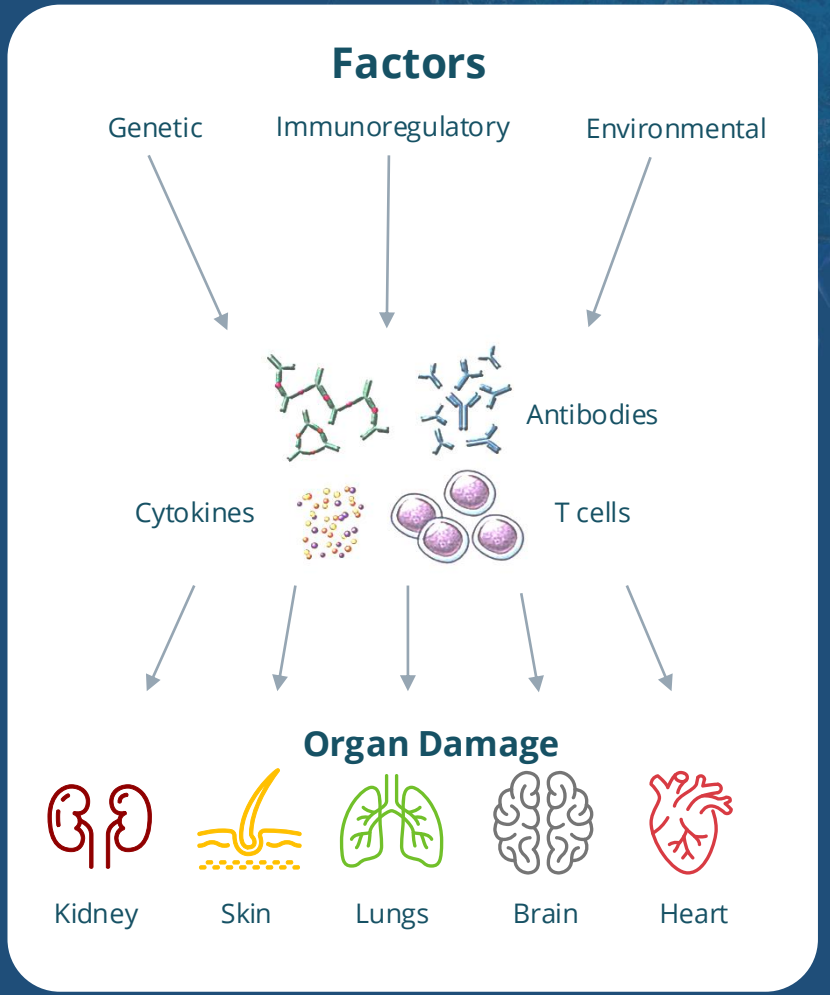
- Estimated 7 million U.S. patients[1]

**Treatment with long-term immune suppression is often inadequate and limited by toxicity[2]**

- Patient care is predominantly outpatient
- Chronic medications without disease remission

**CD19-directed CAR cell therapy has challenged the current treatment paradigm**

- Drug-free remissions >2 years after a single treatment in academic trials[3]

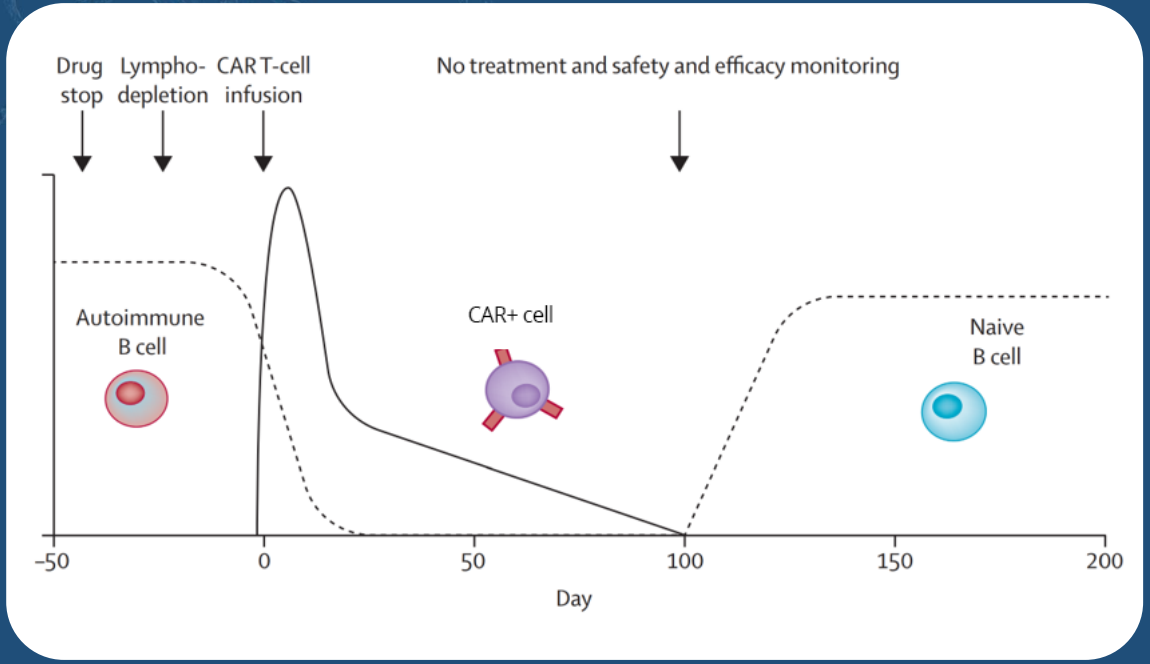



Adapted from: Tsokos, *NEJM*. 2011; 365:2110-2121.

*CAR: chimeric antigen receptor*

1: Canaccord Genuity. 14 Nov 2023.
2: Diana Paredes-Ruiz, *Expert Rev Clin Imm.* 20(4), 359–373.
3: Mueller, et al. *NEJM.* 2024; 390:687–700.

# Cell Therapy Has Shown the Ability to Bring About Drug-Free Remission in Autoimmune Patients




Adapted from: Schett, et al, *Lancet*. 2023; 402: 2034-2044.

## Transient B-cell suppression can provide durable disease control

- CAR+ cells rapidly eliminated
- Post-treatment recovery with naïve B cells may lead to an “immune reset”

## Drug-free remissions were achieved after a single treatment across multiple indications in academic trials[1]

- Systemic lupus erythematosus/lupus nephritis
- Idiopathic inflammatory myopathy (myositis)
- Systemic sclerosis (scleroderma)

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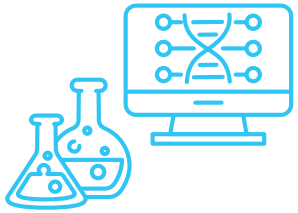
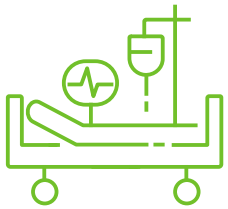
1: Mueller, et al. *NEJM.* 2024; 390:687-700.

# Logistical Burdens and Toxicity Have Limited CAR T Cell Therapy's Adoption



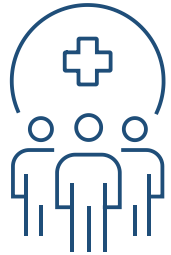
## Autologous CAR T logistical and manufacturing challenges hamper accessibility

- Apheresis and cell processing facilitated by oncology/BMT providers
- Delay in patient treatment while CAR T cells are manufactured
- Higher manufacturing failure rates are a drawback for autologous CAR T cells



## CAR T cell toxicity profile creates dependency on additional specialists

- Rapid *in vivo* expansion of CAR T cells produces high levels of proinflammatory cytokines, resulting in potential for high-grade CRS and ICANS needing ICU support



## Standard of care therapy for autoimmune disease is predominantly outpatient

- Cell therapy often requires prolonged inpatient monitoring
- Achieving more widespread adoption of cell therapy will require deeper partnerships between specialist community care providers and patients

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*BMT: bone marrow transplant; CAR: chimeric antigen receptor; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome; ICU: intensive care unit*

# CAR NK Cells May Be Ideally Suited to Treat Autoimmune Disease

**Off-the-shelf, allogeneic CAR NK cells may offer superior safety and accessibility without compromising clinical activity**

- ✓ On-demand, off-the-shelf availability for autoimmune patients
- ✓ Limited *in vivo* expansion means low risk low-grade CRS or ICANS

**Established proof of concept for CD19 CAR NK in autoimmune disease[1]**

- ✓ B-cell depletion and immune reset achieved in relapsed/refractory SLE
- ✓ Low disease activity or remission in 75% of patients at 6 months
- ✓ No ICANS of any grade and only low-grade CRS

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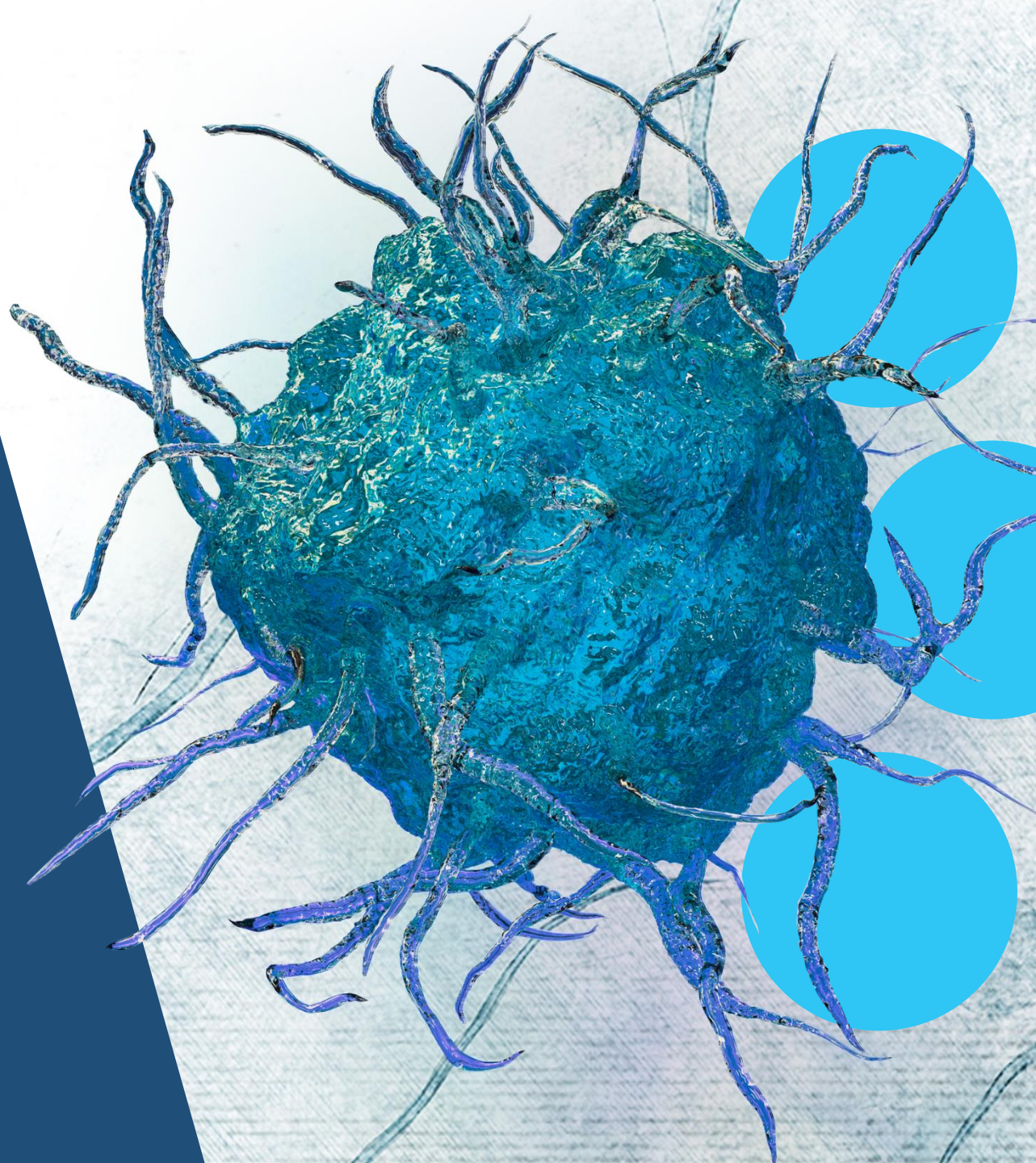
*CAR: chimeric antigen receptor; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome; SLE: systemic lupus erythematosus*

1: Gao, et al. *Lancet*. 2025; 406:2968–2979.

CD19 CAR NK

# NKX019



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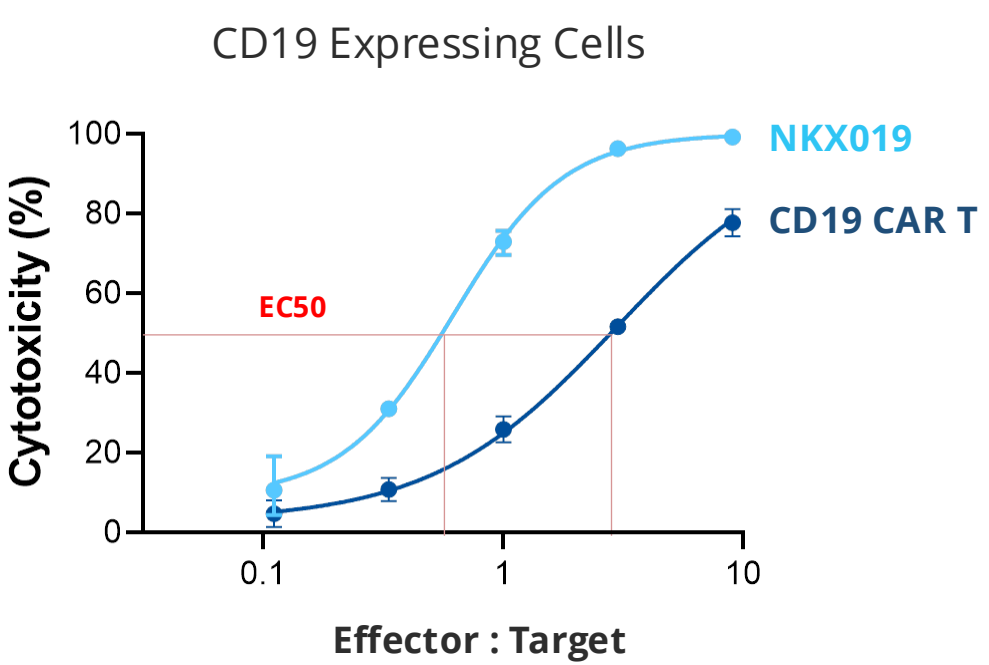
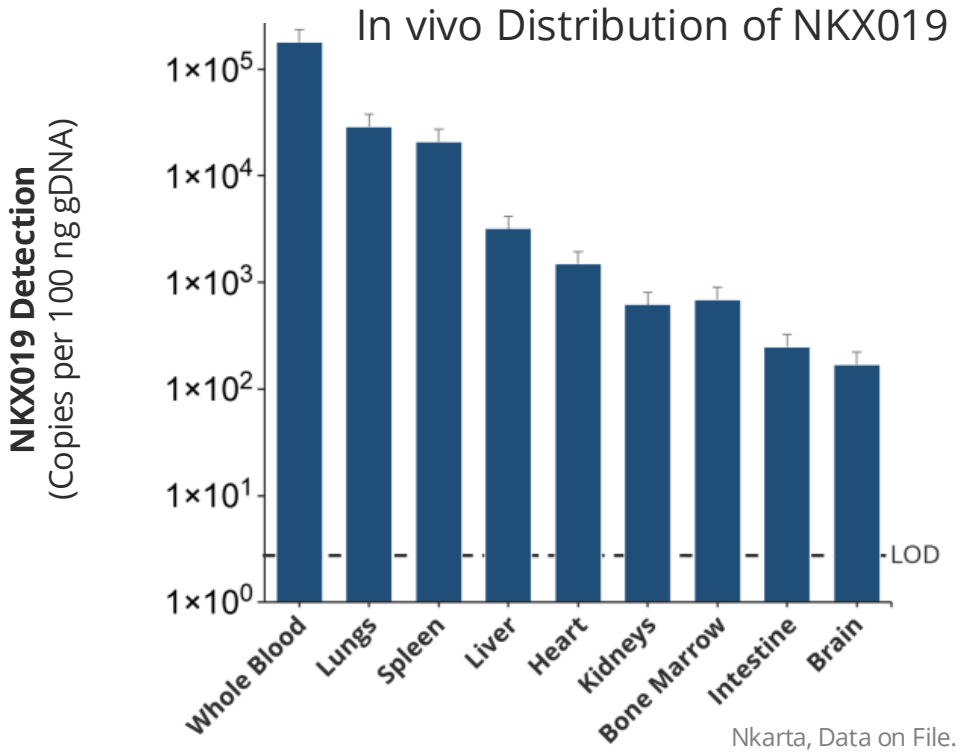
# NKX019 Exhibits Superior Killing of CD19+ Cells Compared to CAR T Therapy




Nkarta, Data on File.

**NKX019 exhibits superior killing in B cell tumor cells, including against low CD19-expressing cells[1]**

**NK cells traffic throughout the body, including to traditionally privileged sites[2]**

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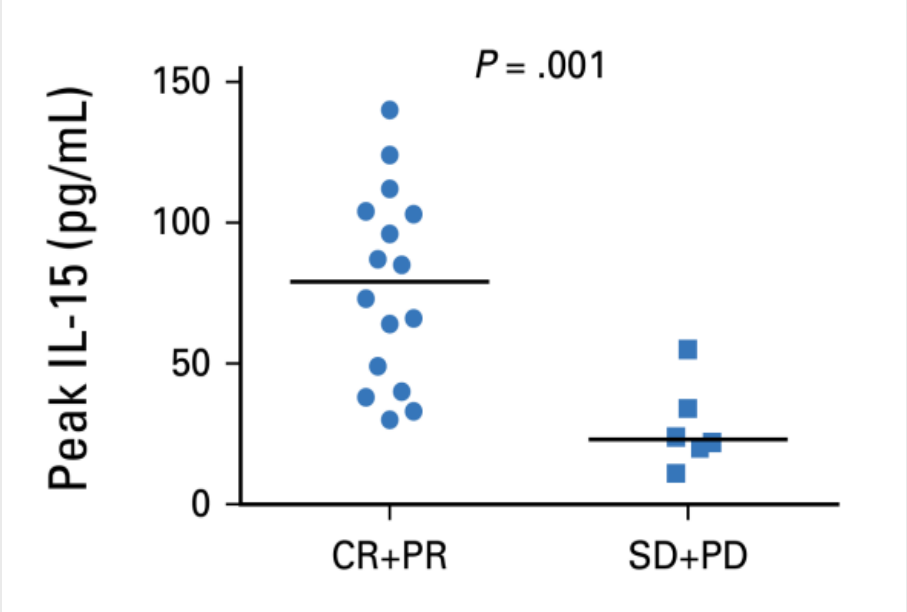
*Nalm6 cells engineered to express varying levels of CD19 were obtained from R. Majzner, Stanford*
*Effector : Target is the ratio of NK or T cells to tumor cells.*


1: Dickinson, et al. *Blood.* 2021; 138 (Suppl 1): 3868.
2: Peng, et al. *Clin Rev Allergy Immunol.* 2014; 47 (2): 119.

# NKX019 Clinical Responses Achieved without Increasing Proinflammatory Cytokines

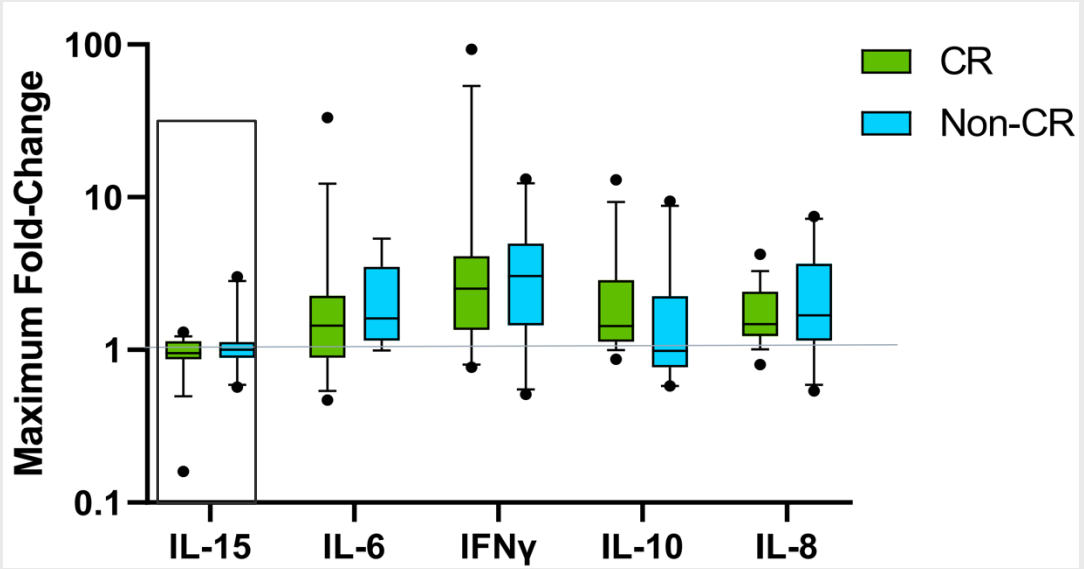
## No ICANS or Life-Threatening CRS Observed in Nkarta NKX019 Oncology Study[1]

CAR T clinical responses are associated with significant increases in serum cytokines




Kochenderfer, et al. *J Clin Oncol.* 2017; 35 (16): 1803.

NKX019 does not require serum cytokine elevation for CR in NHL




Nkarta. Data on File.

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*CR: complete response; NHL: non-Hodgkin lymphoma; PR: partial response; SD: stable disease; PD: progressive disease*
*IL-15: interleukin-15; IL-6 interleukin-6; IFNγ: interferon gamma; IL-10: interleukin-18; IL-8: interleukin-8*

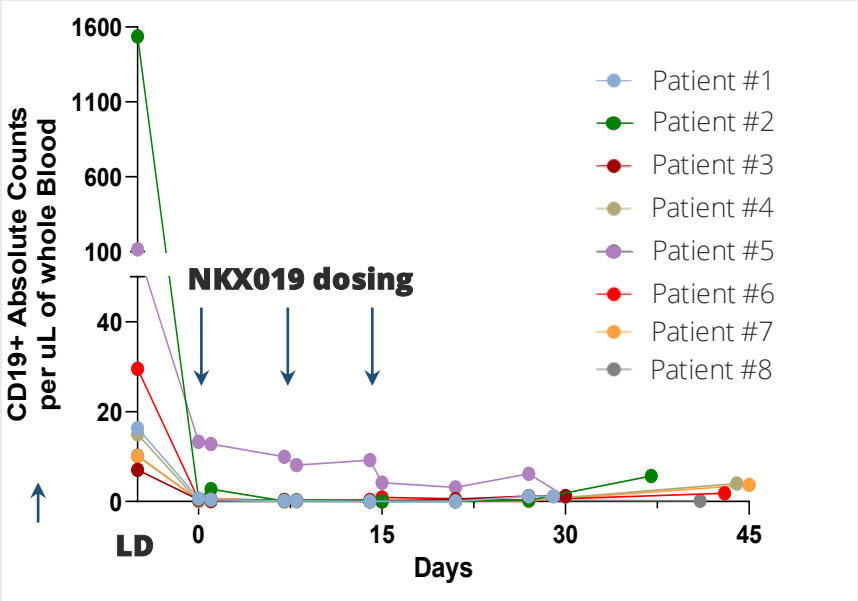
1: Hill, et al. Pan Pacific Lymphoma Meeting. 2024.

# NKX019 Depleted and Reset the B Cell Compartment in NHL Patients

## Patient samples from NHL trial show that NKX019 effectively eliminates CD19+ cells from circulation

Deep suppression achieved by 30 days following a single cycle of treatment (LD + 3 doses NKX019)

**Peripheral CD19+ counts after one cycle of NKX019 in NHL**

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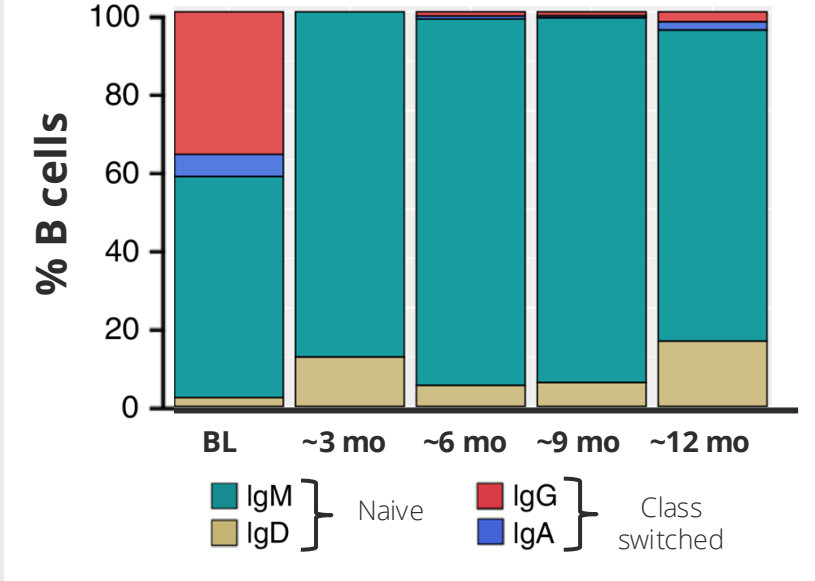
## B-cell isotypes are reset after NKX019 treatment in NHL trial

Naïve B cells (IgM and IgD) class switch after activation to express IgG and IgA, a requirement for autoantibodies[1]

Little to no recovery of autoantibody-producing plasmablasts or memory B cells following treatment

**Case study: Baseline to 12-month follow-up**




Nkarta. Data on File.

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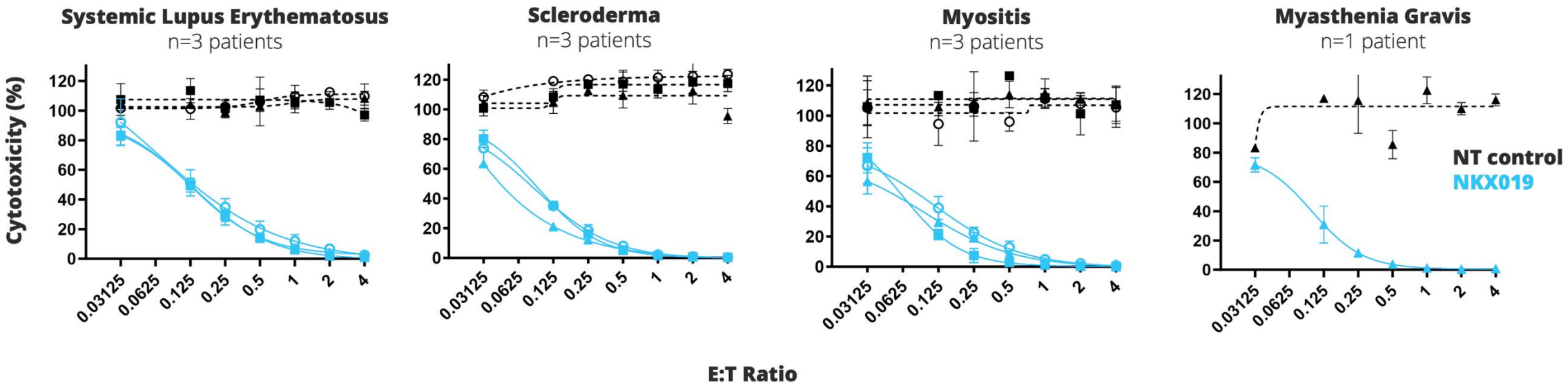
1: Liu, et al. *Autoimmunity.* 2004; 37 (6-7): 431.

# NKX019 Targets and Kills CD19+ Cells Across Multiple Autoimmune Indications

**In vitro studies using blood samples from individuals with various autoimmune diseases show consistent B cell killing by NKX019.**

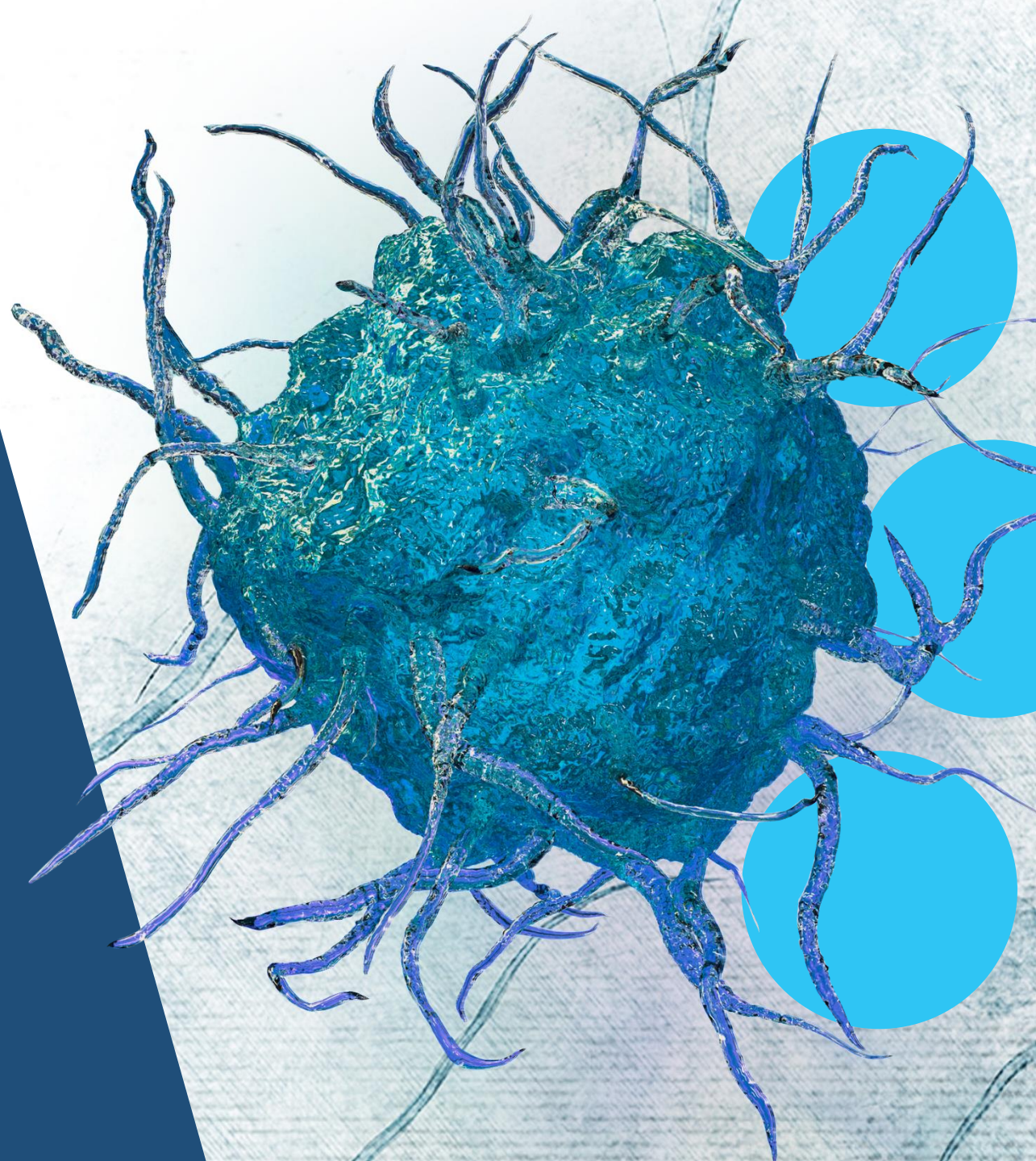



***E:T Ratio - Effector : Target is the ratio of NK cells to tumor cells.***

Nkarta. Data on File.

ONGOING CLINICAL TRIALS

# NKX019



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# NKX019
## CD19 CAR NK

**Trials in Progress**

**Ntrust-1**
Lupus Nephritis & Primary Membranous Nephropathy

**Ntrust-2**
Scleroderma, Myositis, ANCA-Associated Vasculitis & Rheumatoid Arthritis

**Investigator-Sponsored Trial**
Systemic Lupus Erythematosus

**Investigator-Sponsored Trial**
Myasthenia Gravis

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# Cohesive Study Objectives Across NKX019 Clinical Trials

## Primary

Safety and tolerability of NKX019 in the treatment of B-cell mediated autoimmune diseases

## Secondary

Clinical activity, immunogenicity and pharmacokinetics

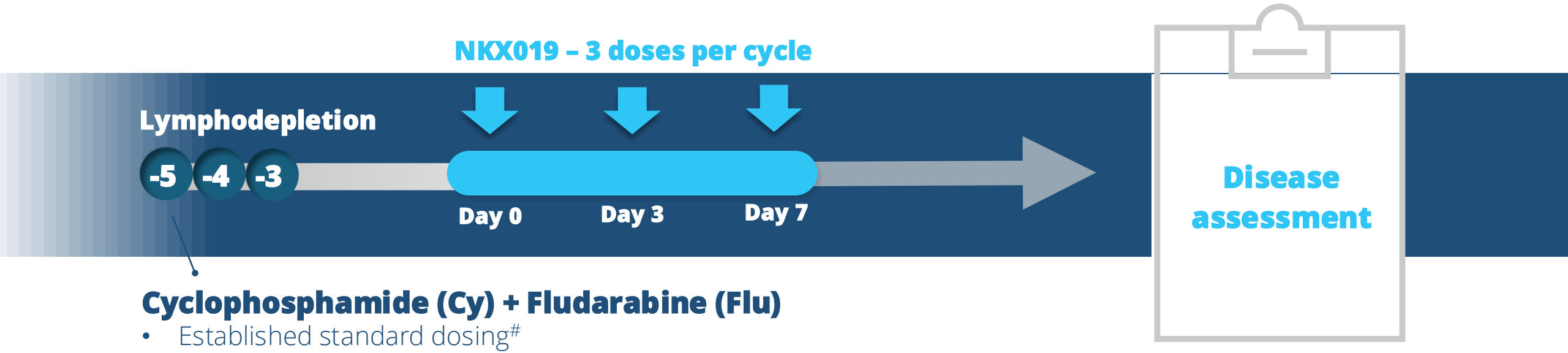
## Exploratory

Autoantibodies, pharmacodynamics and cytokine profile

# NKX019 Treatment Schema

## Dose escalation to 4B CAR+ NK cells per dose

- **Outpatient** administration enables expanded treatment in community settings*
- **Redosing option** (if needed) to deepen or restore patient response*




## Cyclophosphamide (Cy) + Fludarabine (Flu)

- Established standard dosing#
- Dose optionality for cy-only for patients with cytopenia
- Outpatient administration

*Indicates changes to be implemented under protocol amendments following submission to and approval by the FDA and Institutional Review Boards (IRBs) at participating clinical trial sites.

#LD= Flu total 90 mg/m$^2$ as 30 mg/m$^2$/day on Days -5, -4, and -3 and Cy total 1 g/m$^2$ as 1 g/m$^2$/day on Day -3. Cytopenic participants may receive Cy alone total 1 g/m$^2$ as 1 g/m$^2$/day on Day -3.

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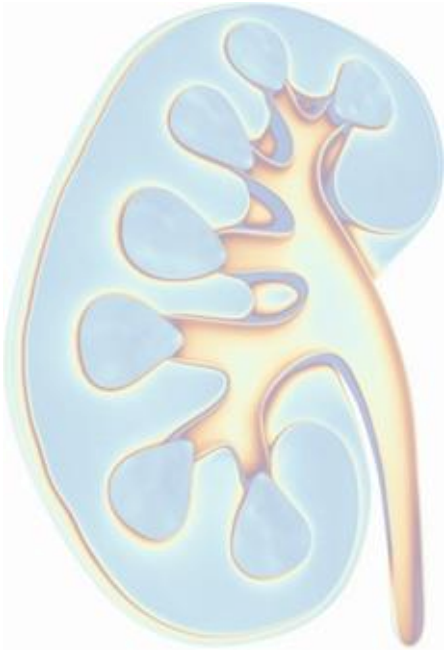
1: Hill, et al. Pan Pacific Lymphoma Meeting. 2024.

# Ntrust-1: Phase 1 Clinical Trial

## Patients with refractory lupus nephritis (LN) or primary membranous nephropathy (pMN)



**Key Eligibility:** Adults (18-75 yo) who have tried standard of care and still have active disease with proteinuria

**LN**

US prevalence: ~60,000

2019 ACR Criteria

Class III or IV LN by renal biopsy

anti-ANA, anti-dsDNA or anti-Smith

**pMN**

US prevalence: ~30,000

Active pMN by renal biopsy

Positive anti-PLA2R or other pMN autoantibody

**Study Status:** Enrolling in 4B cell dose cohort; Initial clinical update expected in 2026

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*ANA: antinuclear antibodies; dsDNA: double stranded deoxyribonucleic acid; PLA2R: phospholipase A2 receptor*

# Ntrust-2: Phase 1 Clinical Trial

## Patients with refractory systemic sclerosis (SSc), inflammatory myopathy (IM), ANCA-associated vasculitis (AAV) and rheumatoid arthritis (RA)

**Key Eligibility:** Adults (18-65 yo) who have tried standard of care and still have active or progressive disease

| **SSc** | **IM** | **AAV** | **RA** |
|---|---|---|---|
| US prevalence: ~85,000 | US prevalence: ~50,000 | US prevalence: ~70,000 | US prevalence: ~130,000 |
| 2013 ACR/EULAR criteria<br>Skin and/or lung disease | 2017 ACR/EULAR criteria<br>Positive myositis antibody<br>No other cause of myositis | 2022 ACR/EULAR criteria<br>PR3-ANCA or MPO-ANCA antibody positive | 2010 ACR/EULAR criteria<br>RF or ACPA positive<br>Active joint disease |

**Study Status:** Enrolling in 4B cell dose cohort;
Initial clinical update expected in 2026

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*PR3-ANCA: proteinase 3 anti-neutrophil cytoplasmic antibodies; MPO-ANCA: myeloperoxidase anti-neutrophil cytoplasmic antibodies*

# Investigator-Sponsored Trials

## Patients with refractory systemic lupus erythematosus (SLE) and myasthenia gravis (MG)

**SLE with or without lupus nephritis**

US prevalence: ~200,000

SLEDAI Criteria
Class III, IV, +/- V LN by renal biopsy
anti-ANA, anti-dsDNA or anti-Smith

**Key Eligibility:** Adults (18-65 yo) who have refractory disease despite standard of care

**MG**

US prevalence: ~100,000

MGFA Class II-IV disease
AChR and/or MuSK antibody

**Key Eligibility:** Adults (18-80 yo) who have refractory disease despite standard of care

**Study Status:** Enrollment ongoing

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*AChR: acetylcholine receptor; MGFA: Myasthenia Gravis Foundation of America; MuSK: muscle specific kinase*

# Summary

Focused on clinical trial execution

Several indications being evaluated in the clinic to allow multiple shots on goal

Ntrust-1
Ntrust-2

Data updates from Ntrust-1 and Ntrust-2 expected at medical meeting in 2026

Cash runway into 2029 to enable achievement of clinical milestones

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