

June 2024

Kyverna Therapeutics

HARNESSING THE POWER OF CELL THERAPY
IN AUTOIMMUNE DISEASE



Lupus warrior

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Advancing the Science

5 years of dedication to autoimmune disease – focusing on patient impact

MAY 2018



Kyverna develops anti-CD19 CAR T-cell autoimmunity hypothesis

Kyverna First IND cleared



JAN 2020

**KYVERNA
FOUNDED**
FOR AUTOIMMUNE
DISEASES

NATURE MEDICINE

BRUDNO¹
February 2020

Nature Medicine
Article

Safety and Feasibility of Anti-CD19 CAR T Cells With Fully Human Binding Domains in Patients With B-Cell Lymphoma

Construct validation

FEB 2020

MAY 2021

NIH



Exclusive license in autoimmunity

AUG 2021

NEJM

SCHETT²
August 2021

New England Journal of Medicine
Correspondence

CD19-Targeted CAR T Cells in Refractory Systemic Lupus Erythematosus

Proof of concept in autoimmunity

SEP 2022

NATURE MEDICINE

SCHETT³
September 2022

Nature Medicine
Correspondence

Anti-CD19 CAR T Cells Therapy for Refractory Systemic Lupus Erythematosus

8 months treatment-free remission

NOV 2022

Kyverna First CTA cleared

**FIRST PATIENT
TREATED WITH
KYV-101**

JUN 2023

Note: Timeline not to scale; ¹ Brudno et al., Nature Medicine 2020; 26:270-280; ² Mougiakakos, Krönke, Völkl, Kretschmann, Aigner, Kharboutli, Böltz, Manger, Mackensen, and Schett, NEJM 2021; 385:567-569; ³ Mackensen et al., Nature Medicine 2022; 28: 2124-2132

Seasoned leadership team with significant CAR T and autoimmune experience

Leadership



Peter Maag, PhD
Chief Executive Officer



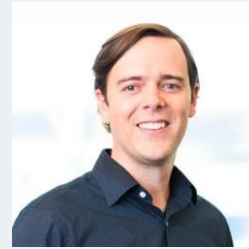
James Chung, MD, PhD
Chief Medical Officer



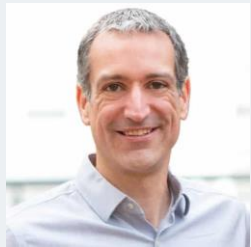
Karen Walker
Chief Technology Officer



Dominic Borie, MD, PhD
President, Research and Development



Ryan Jones, MBA
Chief Financial Officer



Tom Van Blarcom, PhD
Senior Vice President and Head of Research



Devin Murray
Senior Vice President, Partnerships and Alliances



Seshadri ("Sesha") Srinivasachari, MBA
Vice President, Program Lead



Benjamin Dewees, RAC
Vice President of Global Regulatory Affairs



Portia Serame
Vice President, Human Resources

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Beth Seidenberg, MD	Founding Managing Director, Westlake Village BioPartners; General Partner, Kleiner Perkins
Fred Cohen, MD	Co-Founder and Sr. Managing Director at Vida Ventures
Steve Liapis, PhD	Director, Northpond Ventures
Brian Kotzin, MD	Independent Director
Dan Spiegelman	Independent Director
Ian Clark	Chairperson and Director
Peter Maag, PhD	Chief Executive Officer

Scientific Advisors

Peter A. Merkel, MD, MPH	Chief of Rheumatology and Professor of Medicine and Epidemiology at the University of Pennsylvania
Ignacio Sanz, MD	Mason I. Lowance Professor of Medicine and Pediatrics, Chief of the Division of Rheumatology, and Director of the Lowance Center for Human Immunology at Emory University
Georg Schett, MD	Professor and Head of Department of Internal Medicine 3 at Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

Autoimmune diseases represent a large, under-served market

Autoimmune diseases prevalence high and increasing (80+ different diseases)

Autoimmune diseases affect 8% of people in the U.S.¹, with prevalence increasing YoY

Autoimmune disease large and growing market

Currently marketed products: >\$80B revenue² in 2021

Current treatments inadequate for patients long-term

Current therapies:

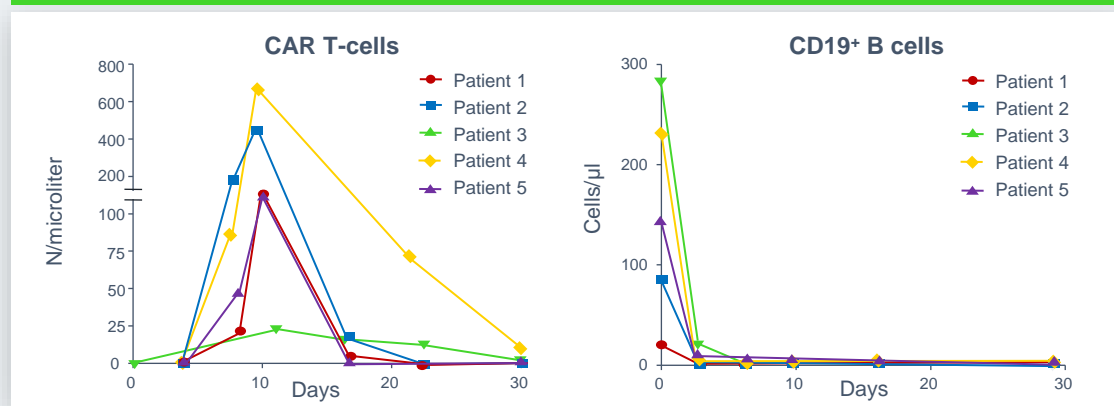
- Low rates of remission
- Serious long-term side effects

B Cell-Driven Diseases	Estimated Number of Diagnosed Patients in US + EU + Japan ³ as of 2022
Rheumatoid Arthritis	4,700,000
Multiple Sclerosis	1,520,000
Sjogren's disease	750,000
Systemic Lupus Erythematosus (SLE)	560,000
Systemic sclerosis	200,000
Lupus nephritis	160,000
Myasthenia gravis	160,000
Inflammatory myositis	120,000
ANCA-Associated Vasculitis	100,000
Neuromyelitis Optica	20,000
Total	~8.3 Million Patients

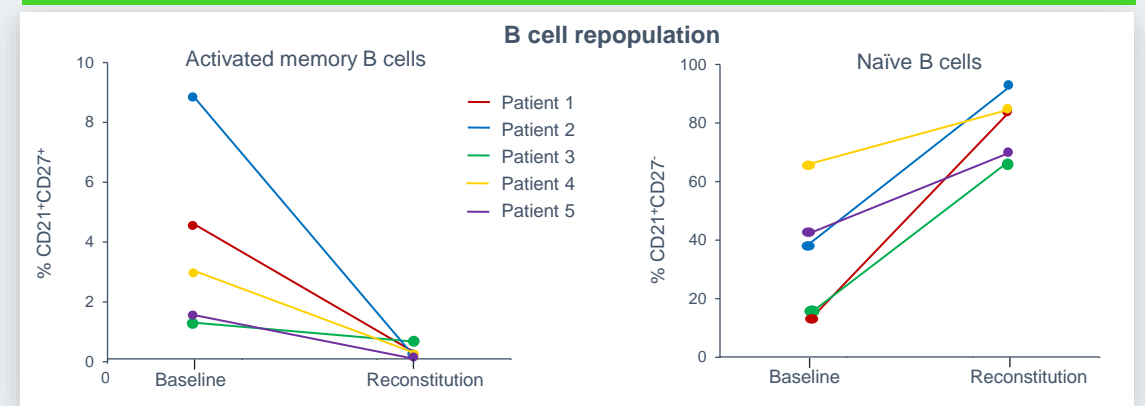
Clinical support for CAR T use in autoimmune patients

Based on third party academic data observed in SLE patients¹

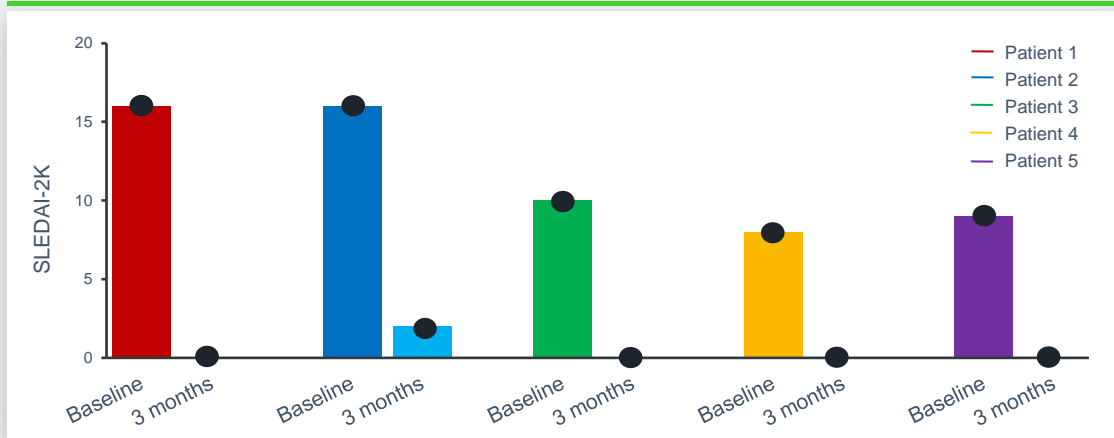
CAR T observed to expand *in vivo*, with deep depletion of B cells...



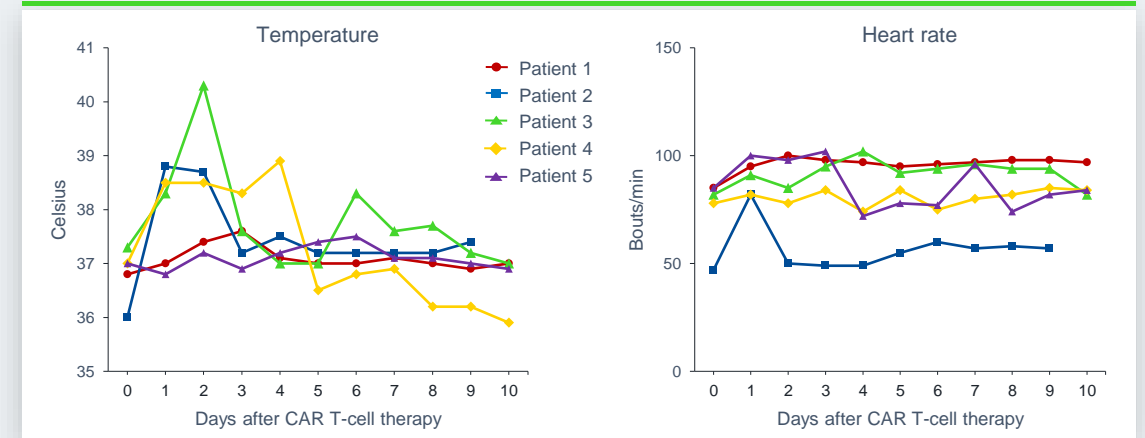
Drug-free remission was maintained during longer follow ups, even after the reappearance of naïve B cells



...with 100% remission observed based on SLE disease activity index after 3 months



...while being well-tolerated for 10 days post-treatment based on CRS symptoms²



Note: Mackensen et al., Nature Medicine 2022; 28: 2124-2132; ¹ Lupus nephritis commonly develops in patients with SLE; ² Cytokine release syndrome is generally measured using criteria defined by Lee DW, et al. Biol Blood Marrow Transplant. 2019;25:625-638

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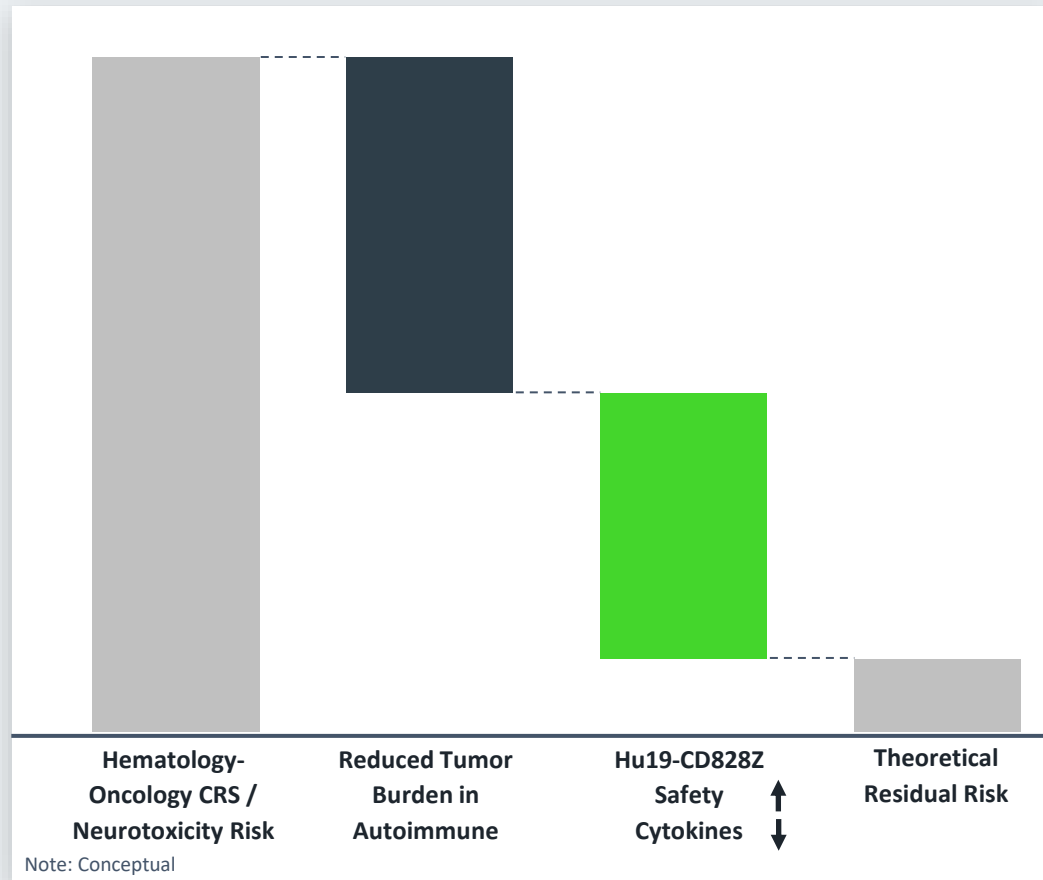
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Opportunity to harness the power of CAR T-cell therapy in autoimmune disease

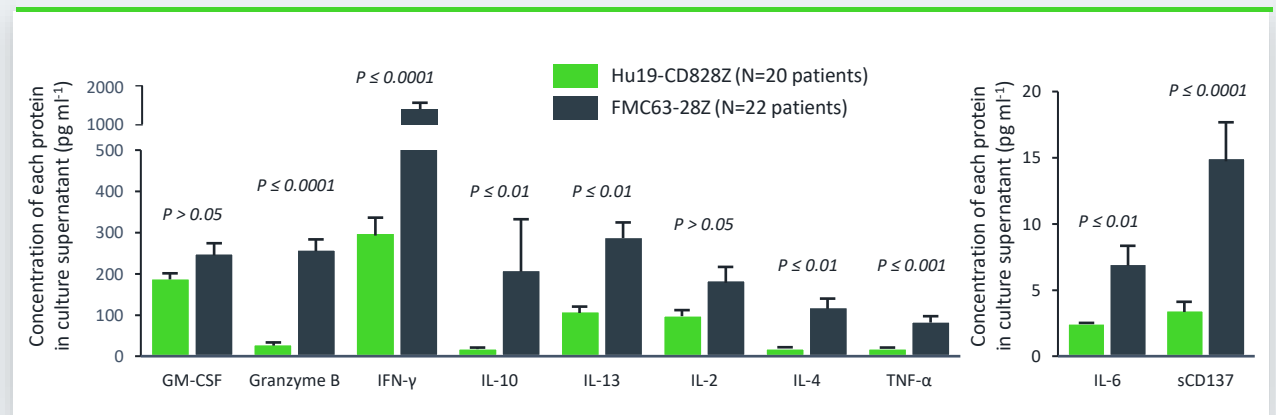
CAR construct experience from oncology; Hu19-CD828Z is the construct found in KYV-101 and KYV-201

Conceptual Differences between Oncology and Autoimmune Disease Applications of CAR

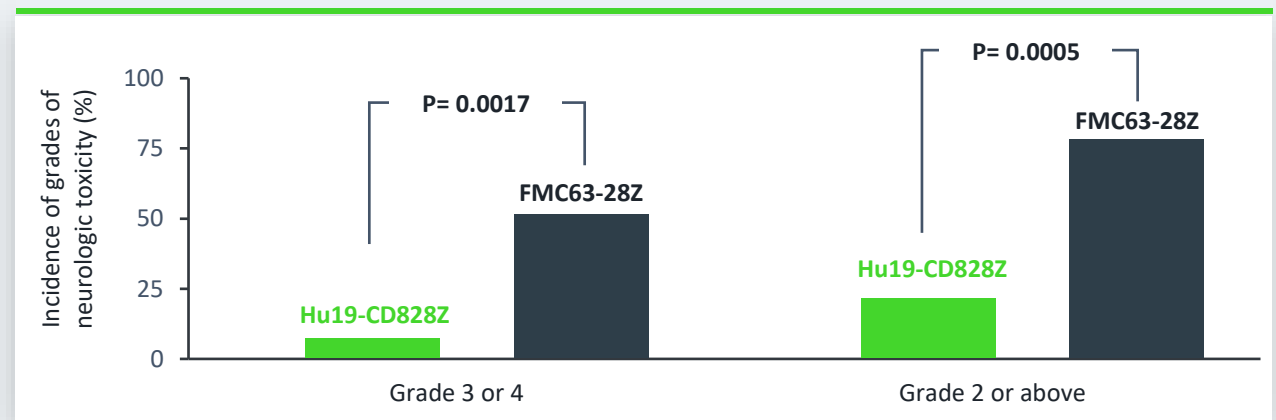


Hu19-CD828Z Phase 1 by NIH with 20 B cell Lymphoma Patients

Reduced Cytokine Production in Oncology Observed Compared to YESCARTA® Construct



Reduced Neurologic Toxicity Observed Compared to YESCARTA® Construct



Our pipeline of CAR T-cell therapies for autoimmune diseases

Technology	Candidates	Target	Indication	Discovery / Validation	Preclinical	Clinical Phase 1	Clinical Phase 2	Clinical Phase 3	Partnership / Commercial Rights	Key Milestone Achieved
CAR T	KYV-101 Rheumatology	CD19	Lupus nephritis	KYSA-1 Phase 1/2 (US) KYSA-3 Phase 1/2 (EU)					kyverna.	KYSA-1: IND cleared 11/22 Fast Track 05/23 KYSA-3: CTA cleared 06/23
			Systemic sclerosis	KYSA-5 Phase 1/2 (US)					kyverna.	IND cleared 10/23
	KYV-101 Neurology	CD19	Myasthenia gravis	KYSA-6 Phase 2 (US)					kyverna.	IND cleared 11/23 Fast Track 12/23 ODD 04/24
			Multiple sclerosis	KYSA-7 Phase 2 (US)					kyverna.	IND cleared 12/23 Fast Track 01/24
CRISPR / Cas9 Allogeneic	KYV-201	CD19	Multiple indications						kyverna. Intellia THERAPEUTICS	
CAR T & Other Approaches	Multiple	Multiple	IBD & other indications						kyverna.	

Note: Inflammatory bowel disease/IBD includes Crohn's disease and ulcerative colitis

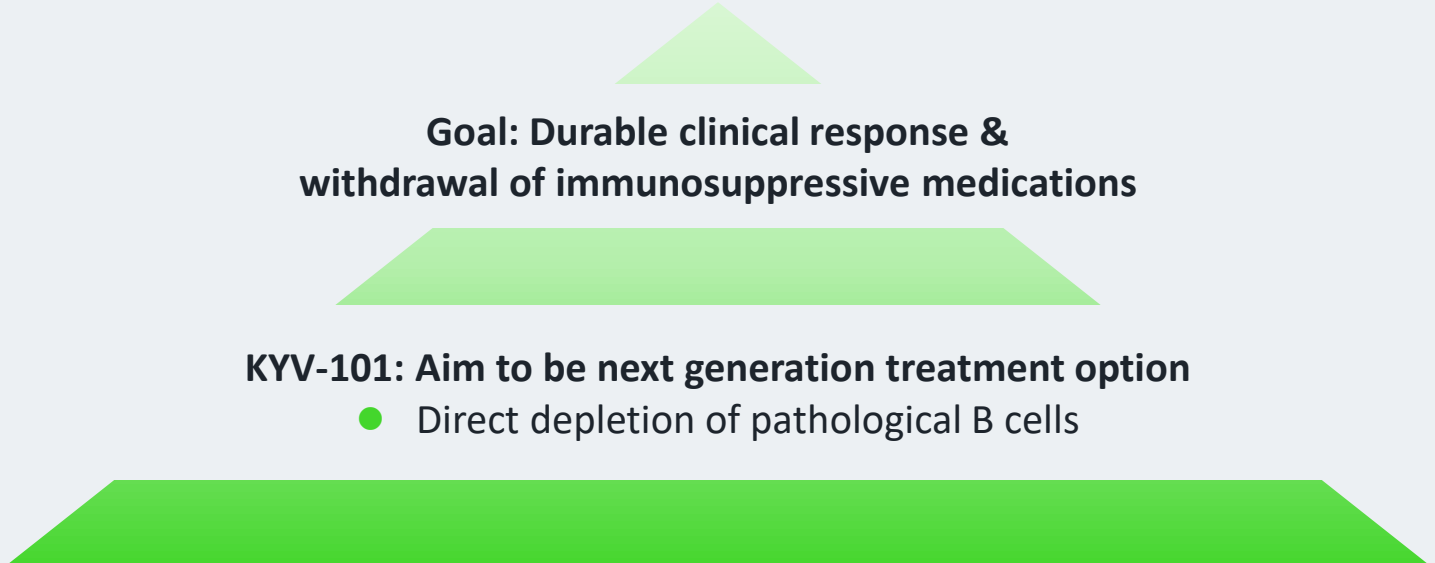
Note: Fast track designation does not assure that we will experience a faster development process, regulatory review or regulatory approval process compared to conventional FDA procedures

KYV-101

+ Autologous CD19 CAR T



KYV-101 – CD19 CAR T-cell therapy for autoimmunity



Goal: Durable clinical response & withdrawal of immunosuppressive medications

KYV-101: Aim to be next generation treatment option

- Direct depletion of pathological B cells

KYV-101: Potential for differentiated therapeutic profile

- Clinical support for therapeutic activity
- Reduced immunogenicity (fully human)
- Potentially reset disease-contributing B cells with a single treatment

KYV-101: Track record of favorable safety in multiple settings to date

- Designed to reduce levels of cytokine release
- Reduced neurotoxicity and CRS observed in oncology trial
- Expected to avoid standard-of-care toxicities

Note: CRS = cytokine release syndrome

A Diverse Set of Indications Across Neurology and Rheumatology

The First 20 Patients

	Rheumatology		Neurology					
	LN	SSc	MS	MG	SPS	MG+SPS	MG+LEMS	AIE
Patients dosed ¹	6	1	3	4	1	1	3	1
Dose	50M, 100M	100M	100M	100M	100M	100M	100M	100M
Age	18-55	53	36-47	24-75	69	61	33-45	34
Male:Female	3:3	1:0	2:1	1:3	0:1	0:1	0:3	1:0
Years since diagnosis	2-26	4	4-23	1-11	9	14	5-6	<1
Prior therapies	6-10	1	1-2	3-7	4	7	6-9	4

(1) Internal data from KYSA-1, KYSA-3, and investigator-reported named patient experience with 28-day follow up as of March 31, 2024.

Note: LN, lupus nephritis; SSc, systemic sclerosis; MG, myasthenia gravis; MS, multiple sclerosis; SPS, stiff person syndrome; LEMS, Lambert-Eaton myasthenic syndrome; AIE, anti-DAGLA autoimmune encephalitis

Early KYV-101 CAR-related safety data consistent with other CAR T-cell therapies across autoimmune and oncology indications

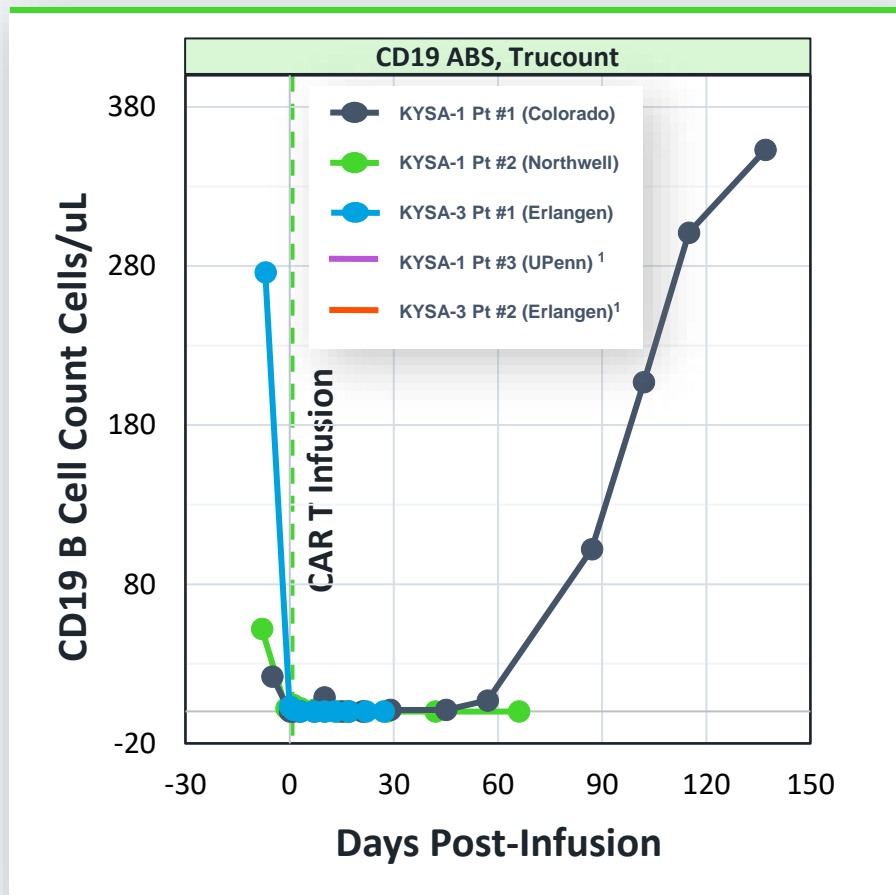
Source	Indication	N	Any Grade CRS	Any Grade ICANS ^a	CRS Grade ≥3	ICANS Grade ≥3
KYV-101 experience¹	Rheum & Neuro	20	17	1	0	0
Schett Group case series ²	SLE, IIM, SSc	15	9	1	0	0
Hu19-NIH Ph1 Lymphoma study ³	DLBCL, FL, BL, MCL	20	18	NR ^d	2	1
ZUMA-1 (axi-cel) ⁴	DLBCL 3L	101	94	65	13	28
TRANSCEND (liso-cel) ⁵	DLBCL 3L	268	122	95	11	32 ^b
JULIET (tisa-cel) ⁶	DLBCL 3L	115	85	69	26 ^c	22

- CAR T-cell therapies are associated with class effects, including CRS and ICANS, which may be potentially serious or life-threatening, but generally resolve within the first month of treatment and are manageable with close monitoring by a treating physician

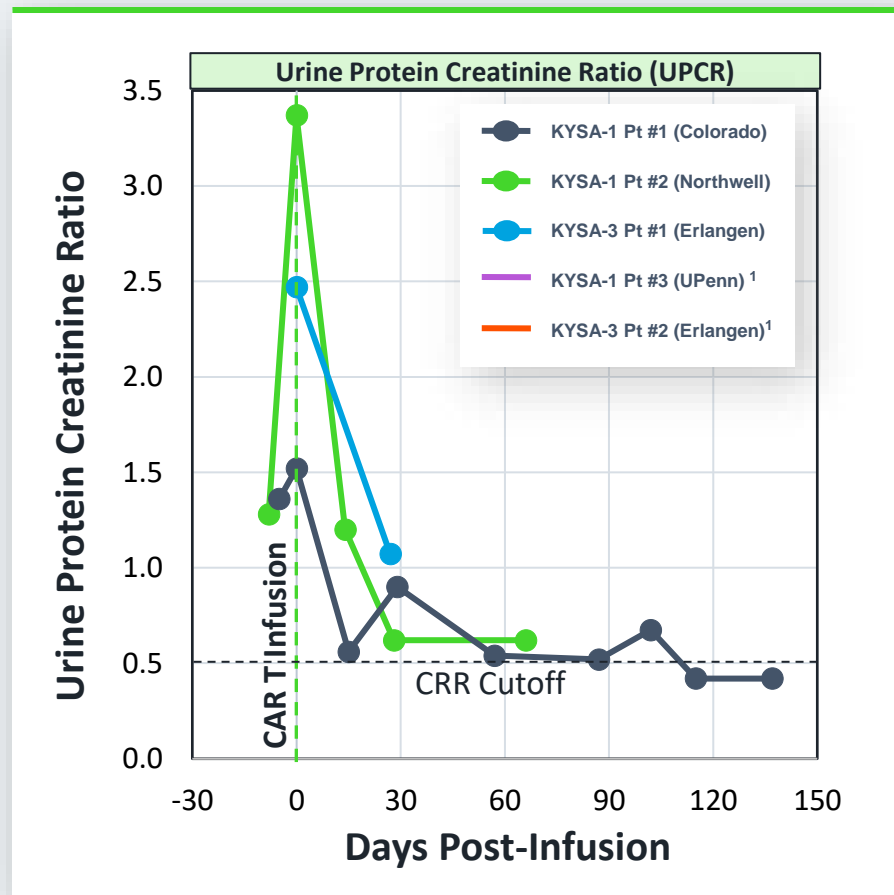
(1) Internal data from KYSA-1, KYSA-3, and investigator-reported named patient experience with 28-day follow up as of March 31, 2024. (2) Muller et al., NEJM, 2024. (a) References 3-6 are reported as neurological toxicities. (b) reported at 12% of 268 patients. (c) reported as 23% of 115 patients. Sources: (3) Brudno, et al, Nature Medicine, 2020, (4) Neelapu S.S., et al, NEJM, 2017, (5) BREYANZI prescribing information, (6) KYMRIAHA prescribing information; Abbreviations: MG, myasthenia gravis; LN, lupus nephritis; MS, multiple sclerosis; SPS, stiff person syndrome; DE, anti-DAGLA autoimmune encephalitis; SSc, systemic sclerosis; IgG4RD, IgG4 related disease; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; BL, Burkitt's lymphoma; MCL, mantle cell lymphoma; SLE, systemic lupus erythematosus; IIM, idiopathic inflammatory myopathies; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; NR, not reported, (d) Grade 1 neurological AEs were not recorded in this trial. Three subjects had Grade 2 ICANS, and 16 patients had Grade <2 ICANS. These limited observations are derived from separate clinical settings, and with respect to the autoimmune data are based primarily on information from case reports rather than clinical trials. They do not represent head-to-head comparisons of CD19 CAR T-cell treatment in autoimmune indications as compared to oncology indications. Future clinical trials may not confirm the clinical safety observations discussed in these case reports and studies.

Promising initial results in KYSA-1 and KYSA-3 multi-center clinical studies in lupus nephritis

Pharmacodynamic Activity and Return of B Cells

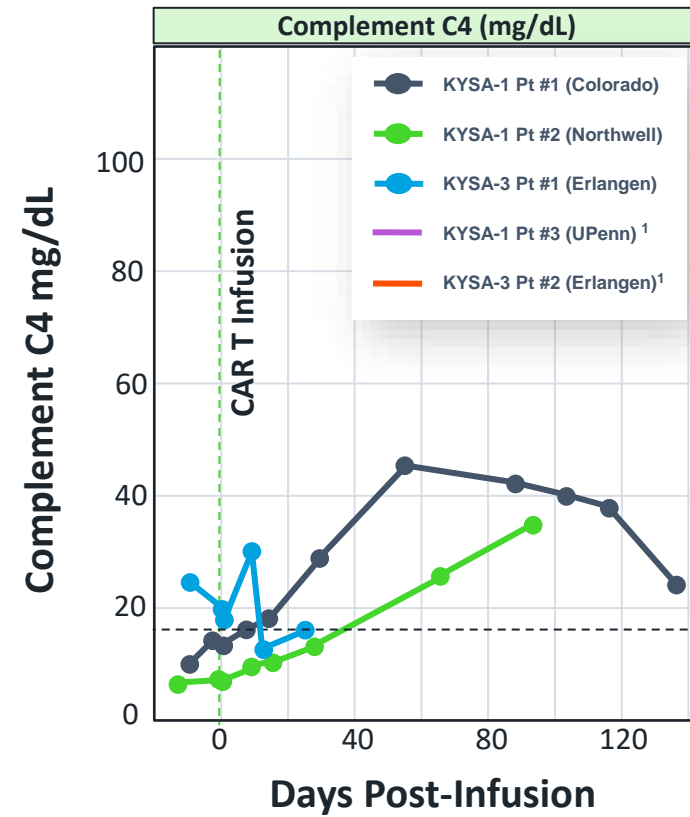
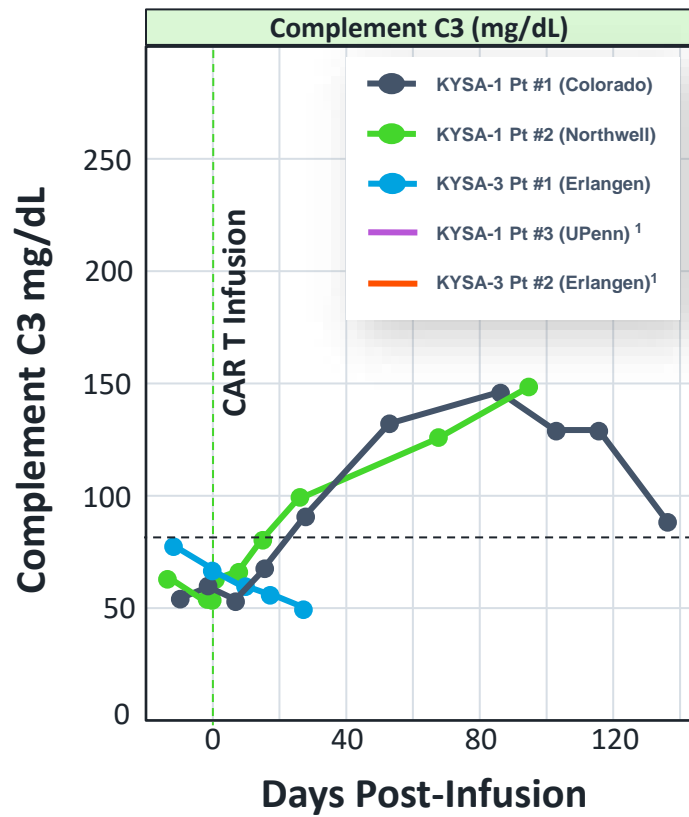
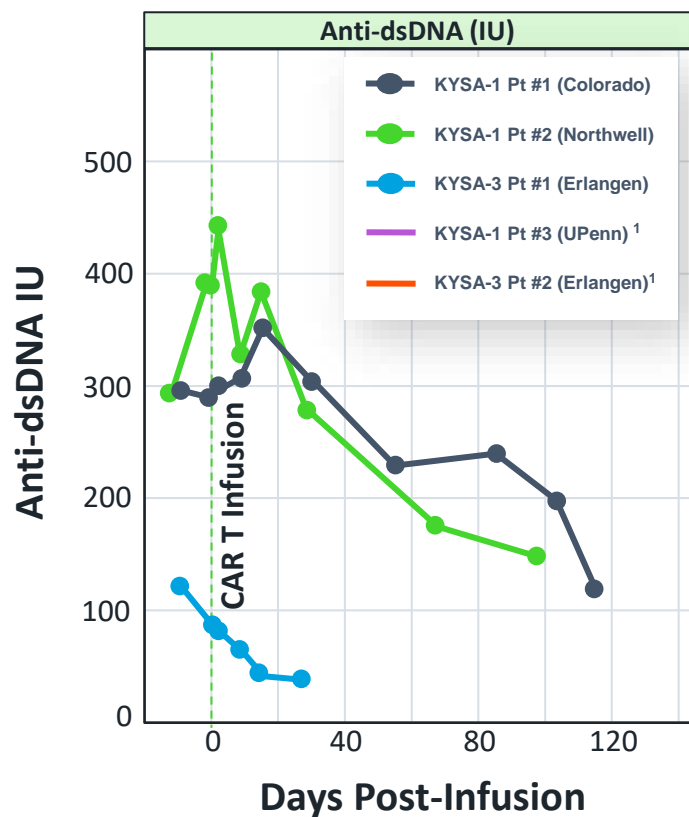


Improvement in Proteinuria



KYSA-1 and KYSA-3 Study of KYV-101 in Lupus Nephritis

Additional markers of improved disease activity

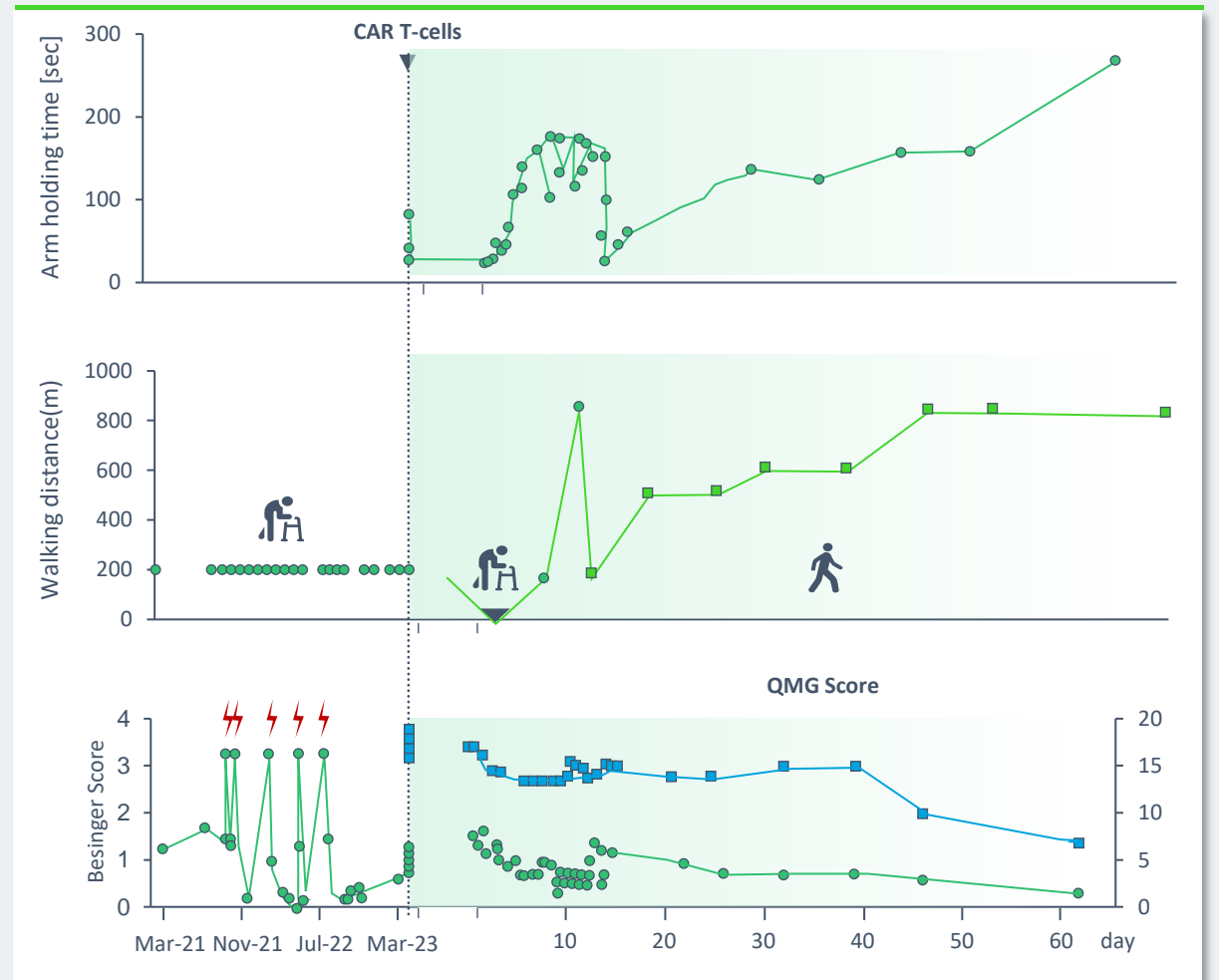
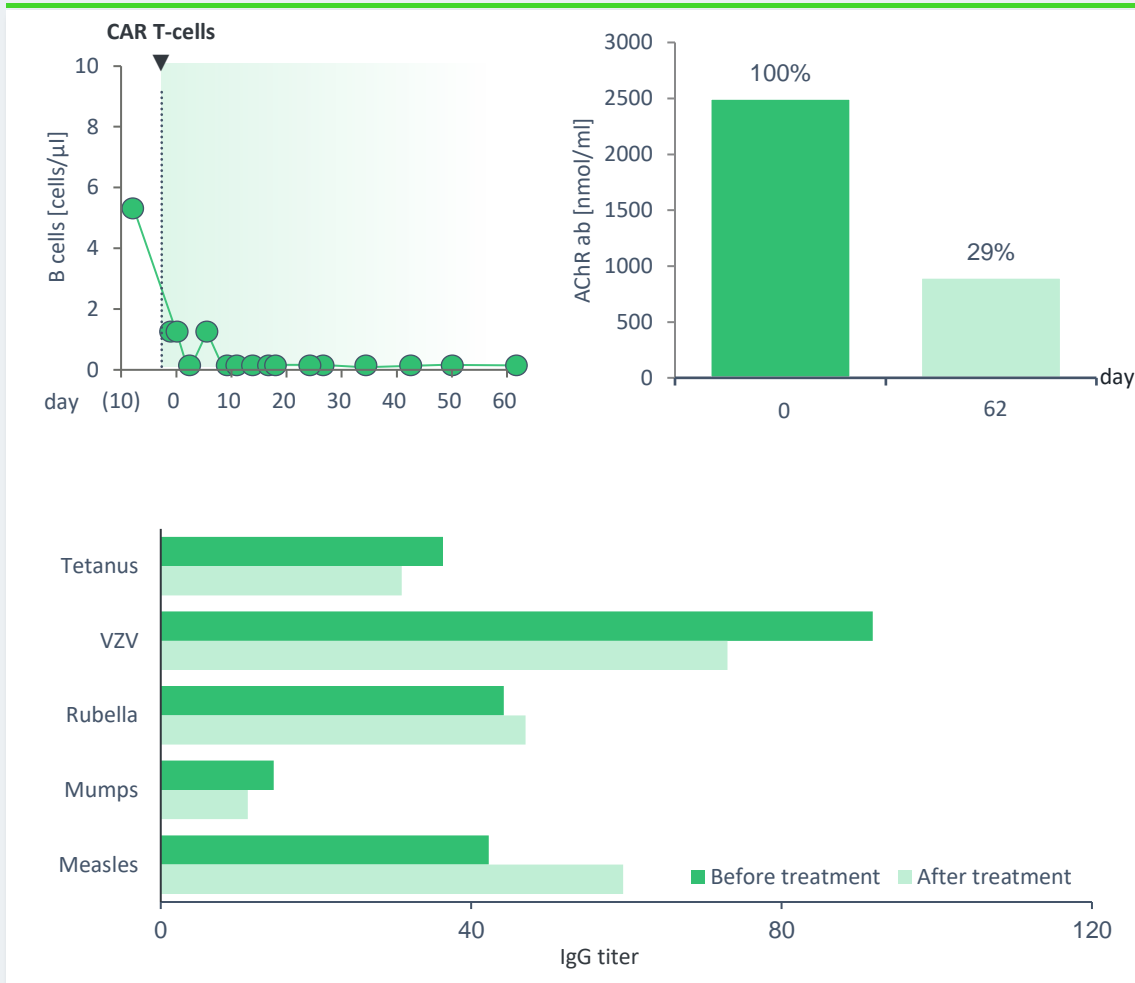


Myasthenia Gravis Named Patient #1 – Lancet Neurology

Within 60 days of infusion, observed improved symptoms and mobility

Observed dramatic reduction in AChR-ab serum levels, while maintaining antibody titers

After 5 ICU admissions in 18 months, improvement in QMG score and mobility observed



Published Case Reports – MED

KYV-101 Experience in Multiple Sclerosis

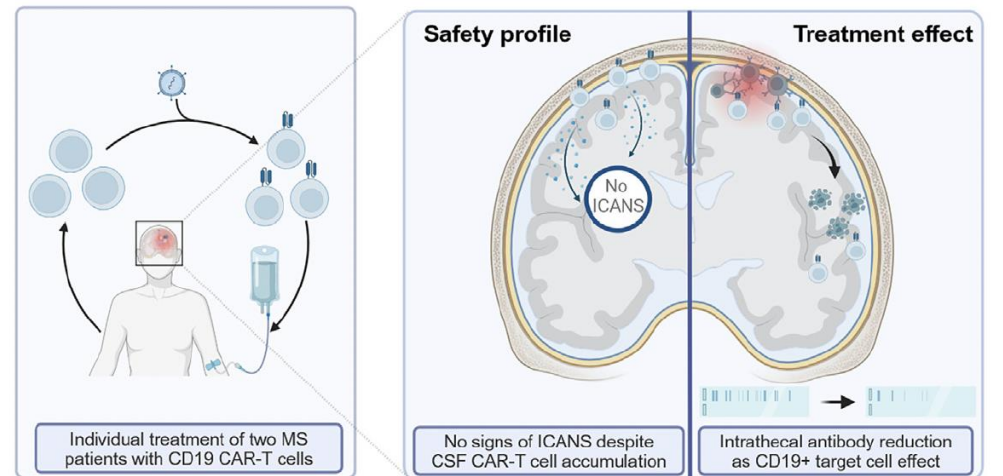
Med

CellPress
OPEN ACCESS

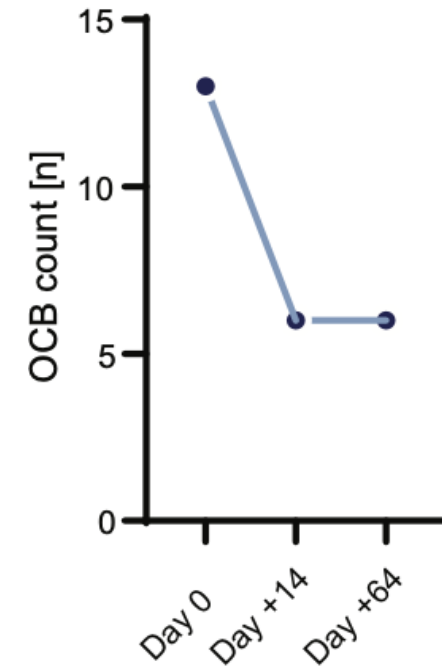
Case Report

CD19-targeted chimeric antigen receptor T cell therapy in two patients with multiple sclerosis

Felix Fischbach,^{1,6} Johanna Richter,^{2,6} Lena Kristina Pfeffer,^{1,6} Boris Fehse,² Susanna Carolina Berger,² Stefanie Reinhardt,¹ Jens Kühle,³ Anita Badbaran,² Kristin Rathje,² Nico Gagelmann,² Dominic Borie,⁴ Johan Seibel,⁵ Francis Ayuk,² Manuel A. Friese,¹ Christoph Heesen,^{1,*} and Nicolaus Kröger^{2,7,*}

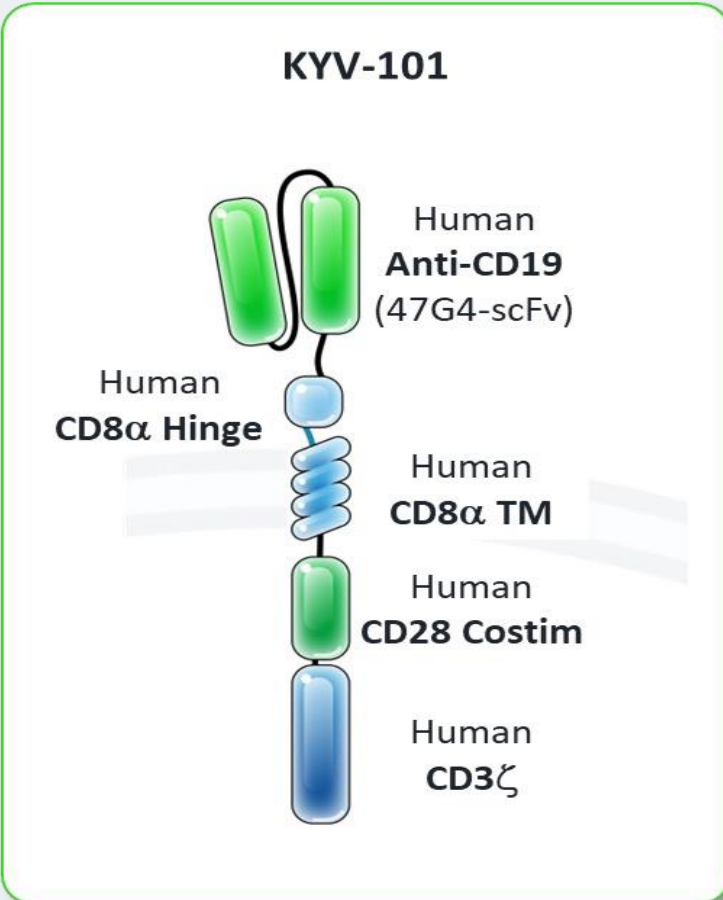


Evidence of Biologic Activity by Demonstrated Decrease in OCBs



KYV-101 is an autologous CD19 CAR T with a favorable safety profile observed in oncology setting

Believed to have properties appropriate for use in autoimmune diseases



Engineered for improved safety profile¹

- Developed at the NIH to improve upon axicabtagene ciloleucel (YESCARTA®)
- Structurally distinct in key aspects
 - Fully human single-chain fragment variable compared with murine
 - CD8α hinge and TM domains compared with CD28 hinge and TM domains

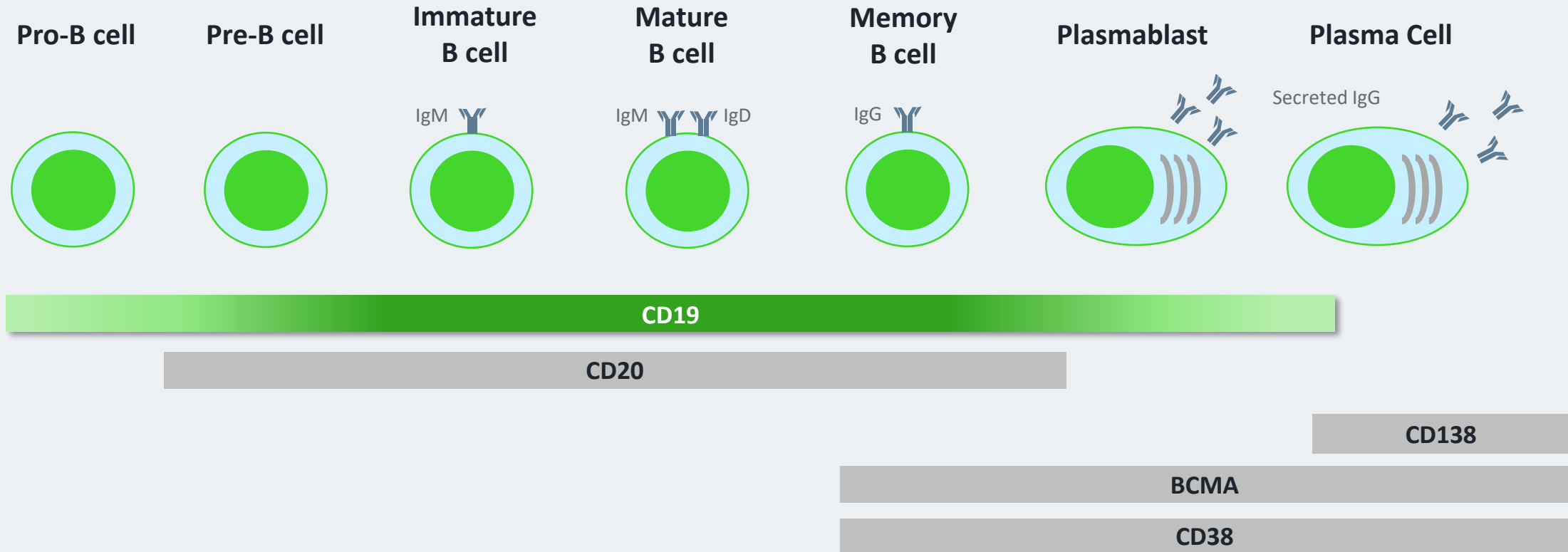
Design validated by clinical improvement observed in oncology setting²

- 20 patients with B cell lymphoma treated in Phase 1 trial by NIH
- Similar CAR T-cell expansion and clinical efficacy to YESCARTA® construct
- Improved safety profile observed relative to YESCARTA® construct
 - Lower levels of cytokine release, lower levels of clinical toxicity (e.g., neurotoxicity)
 - Lower immunogenicity

Program underway with NIH to generate in vivo data

Note: ¹ Alabanza et al., Molecular Therapy 2017, 25:2452-2465; ² Brudno et al., Nature Medicine 2020; 26:270-280

CD19 expressed on broader range of B cell subsets compared with CD20












CD19-targeted depletion of B cells eliminates the broadest range of B cell subsets while sparing long-lived plasma cells, the reservoir of established humoral immunity

Several Kyverna-sponsored trials and investigator-initiated trials for KYV-101 underway

Program	Indication	Country	IND/CTA Submission		Comments
			Cleared	In Process	
KYV-101	LN	US	✓		
		Germany	✓		
	SSc		✓		
	MG	US	✓		
	MS		✓		
KYV-101 IIT	MS		✓		Stanford IIT
				✓	UCSF IIT
	Undisclosed	US	✓		UMass IIT
	Dermatomyositis		✓		Stanford IIT
	Basket		✓		UPenn IIT

Site Partnerships Drive Innovation at Kyverna

Named Patient, IIT, and Collaborations

	Neurology	Rheumatology	Biomarkers	Lymphodepletion
 Perelman School of Medicine University of Pennsylvania		✓	✓	
 Stanford MEDICINE School of Medicine	✓	✓	✓	✓
 UCSF School of Medicine	✓		✓	
 CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN		✓	✓	✓
 Friedrich-Alexander-Universität Erlangen-Nürnberg		✓	✓	
 hhu Heinrich Heine Universität Düsseldorf		✓	✓	
 UKE HAMBURG	✓		✓	
 RUB	✓		✓	
 OTTO VON GUERICKE UNIVERSITÄT MAGDEBURG	✓	✓	✓	✓



KYV-201

+ Allogeneic CD19 CAR T

KYV-201 is a potential best-in-class allogeneic CD19 CAR T cell therapy for B cell-driven autoimmune diseases



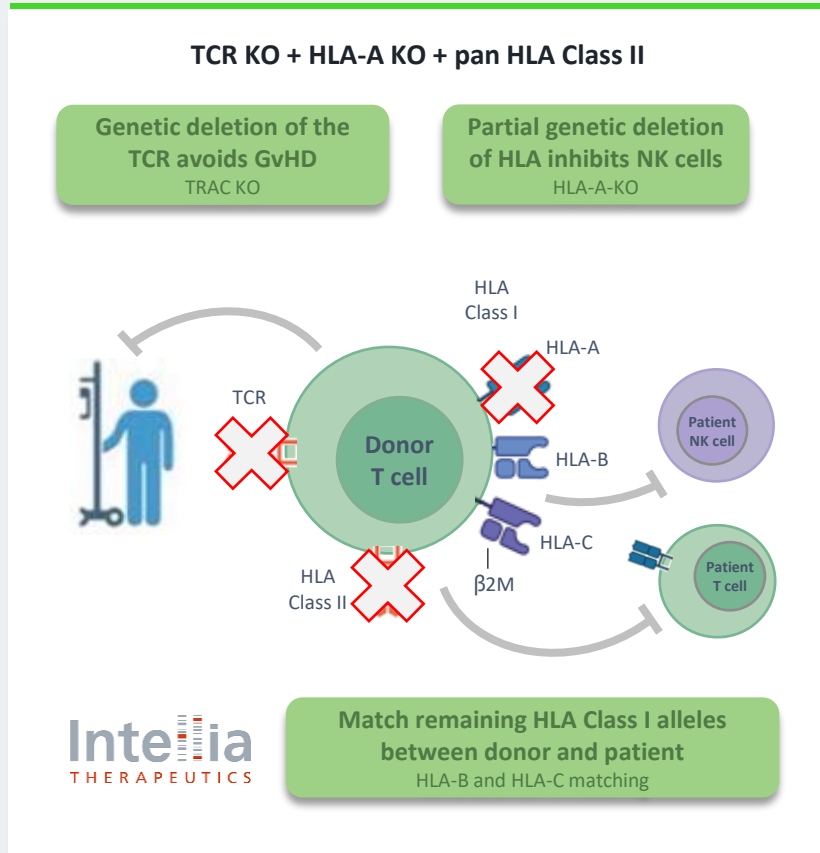
- **Potential novel CD19 CAR with clinical experience – utilizing same CAR as KYV-101**
 - Desirable CAR for B cell-driven autoimmune indications
- **Deep expertise in autoimmune disease**
 - Seasoned clinical development team with autoimmune disease experts and immunologists
- **Cell therapy development expertise**
 - Research, technical operations, clinical operations all led by experts in cell therapy



- **A leader in clinical applications of gene editing**
 - Recognized innovator in bringing solutions to patients; one of the first *in vivo* gene edited products in clinic
- **A leading allogeneic platform**
 - Platform designed to address limitations of autologous treatment manufacturing process
 - Proprietary approach enabled by lipid technology
- **Substantial genomics and analytical capabilities**
 - Demonstrated capabilities to screen and select ideal guides to ensure safety

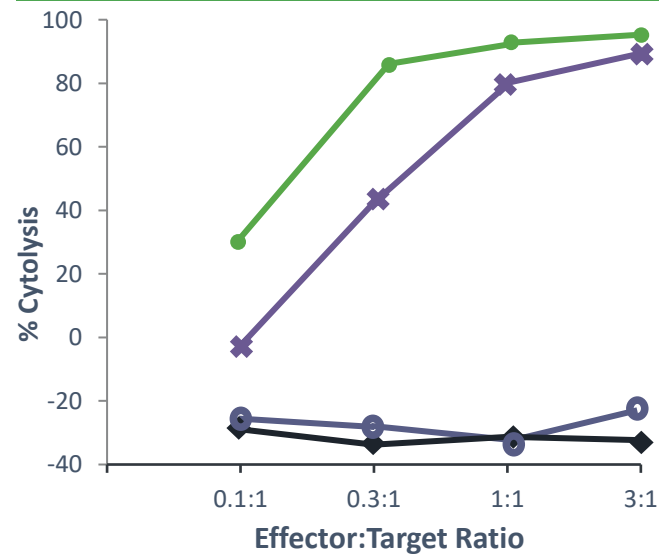
KYV-201 protection from T cells supports potential for longer-term persistence

Differentiated allogeneic platform based 3 genetic deletions



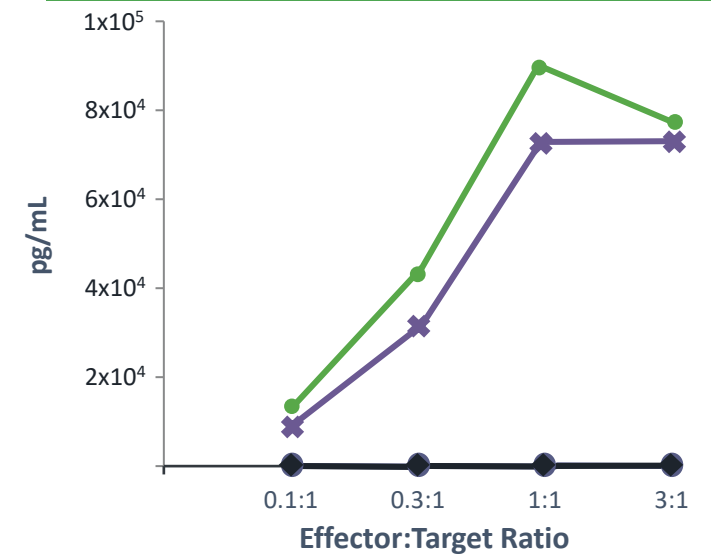
KYV-201 demonstrates robust CAR-mediated activity against CD19⁺ cells Similar to HLA Class I deficient b2M KO¹

Dose-Dependent Cytotoxicity



24h incubation with NALMS target cells
Representative of 3 donors
WT = Mock (unedited), untransduced
KO only = HLA-A / CIITA / TRAC KO
CAR only = CAR LV
KYV-201 = HLA-A / CIITA / TRAC KO + CAR LV

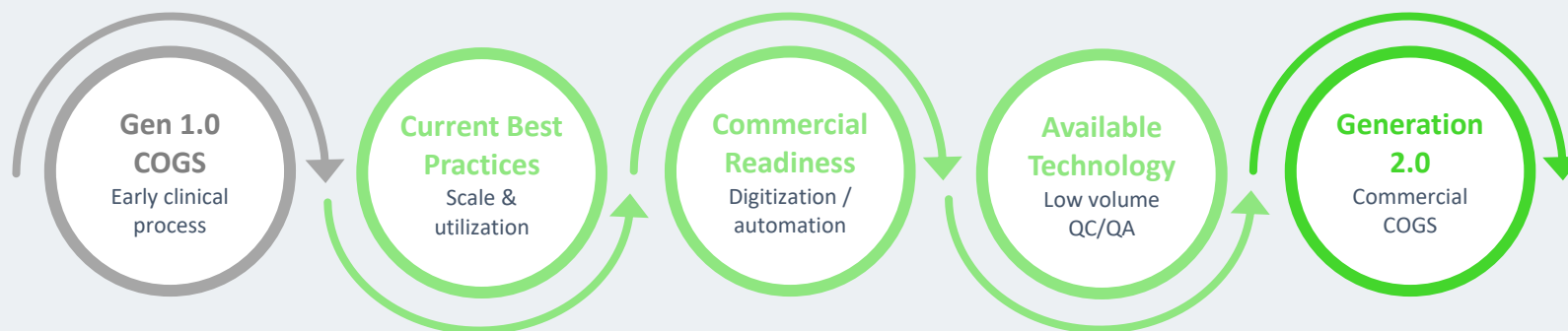
Dose-Dependent IFN γ Secretion



Note: ¹ Internal data

Kyverna's Ingenui-T process leverages expertise from industry leaders to target pharma-like COGS

Evolution of the Autologous Process: KYV-101 Gen 1.0 to Ingenui-T



Capturing unrealized value Gen 1.0 – Gen 2.0: Ingenui-T concept work packages

- | | | |
|---|--|-------------------|
| 1 | Cell isolation | kyverna. internal |
| 2 | Modernized cell process | elevatebio |
| 3 | Low volume fill for highly active dose | elevatebio |
| 4 | Low volume analytics w/ safety tests | TBD |
| 5 | Digitization | TBD |

Key Component	Kyverna's Approach	COGS	Supply Chain	Speed
Manufacturing and supply chain partnerships	<ul style="list-style-type: none"> ElevateBio's BaseCamp for process development and cell product manufacturing Oxford Biomedica supply agreement, enabling use of LentiVector 	✓	✓	
Pharma-like COGS	<ul style="list-style-type: none"> Foundation of industry-best practices ElevateBio and other processes to streamline COGS 	✓	✓	✓

Kyverna's strong balance sheet expected to fund several near-term catalysts

Clinical and named patient experience across multiple indications, multiple geographies, and multiple KOLs

Clinical data from open label studies, with updates at EULAR, ECTRIMS and ACR

Regulatory progress in **rheumatology and neurology** in US and Europe

Potential low-cost manufacturing progress via Ingenui-T

Allogeneic approach progress with KYV-201



kyverna™