Spring 2024

Kyverna Therapeutics

HARNESSING THE POWER OF CELL THERAPY IN AUTOIMMUNE DISEASE

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Advancing the Science

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

MAY 2018

KYVERNA FOUNDED FOR AUTOIMMUNE DISEASES

JAN 2020

Kyverna develops anti-CD19 CAR T-cell autoimmunity hypothesis

FEB 2020

NATURE MEDICINE

BRUDNO[1]
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

MAY 2021

NIH

Exclusive license in autoimmunity

AUG 2021

NEJM

SCHETT[2]
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

SCHETT[3]
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 IND cleared

JUN 2023

Kyverna First CTA cleared

FIRST PATIENT TREATED WITH KYV-101

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

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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

Board of Directors

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

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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 revenue[2] 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**

Note: [1] National Institutes of Health (NIH) Autoimmune Diseases Coordinating Committee. Progress in Autoimmune Diseases Research (Publication No. 05–5140). March 2005. 14, Accessed date: October 25, 2022; [2] GlobalData; [3] Published literature through GlobalData market analysis reports and internal data

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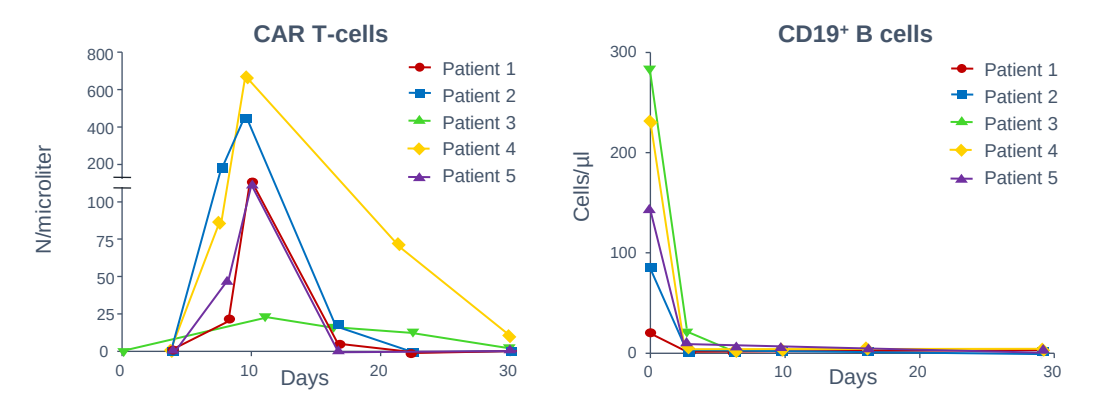
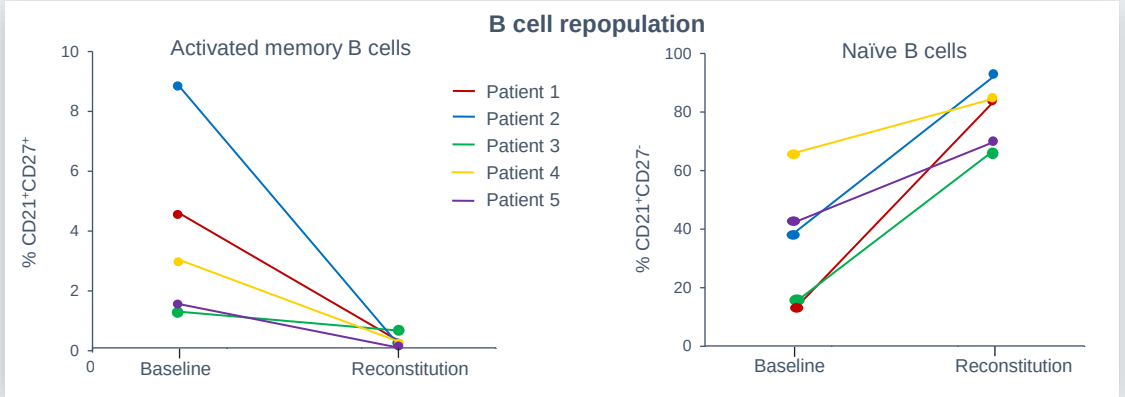
Clinical support for CAR T use in autoimmune patients

Based on third party academic data observed in SLE patients[1]

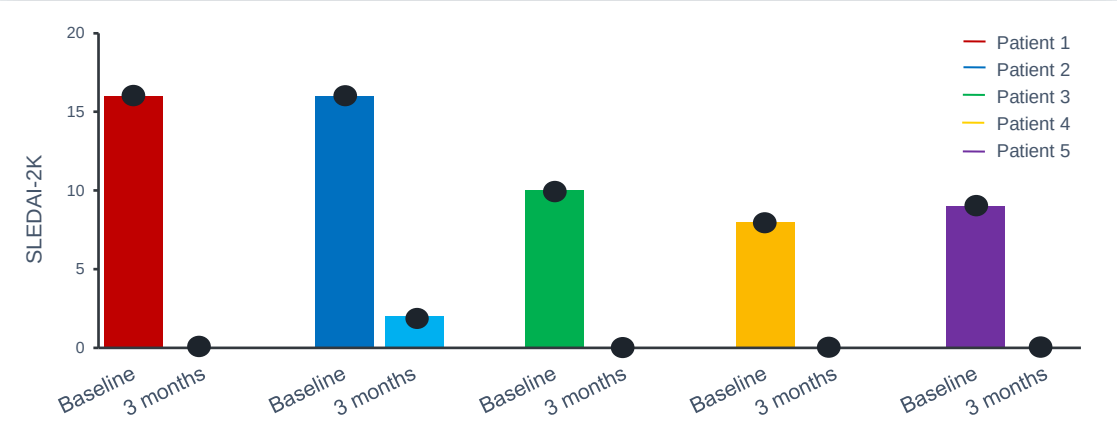
CAR T observed to expand *in vivo*, with deep depletion of B cells…



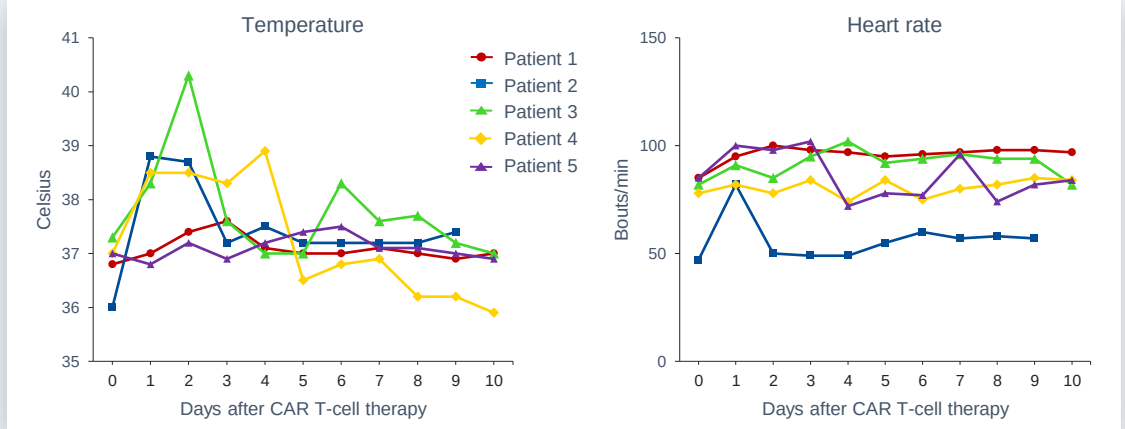
Drug-free remission was maintained during longer follow ups, even after the reappearance of naïve B cells



…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 symptoms[2]



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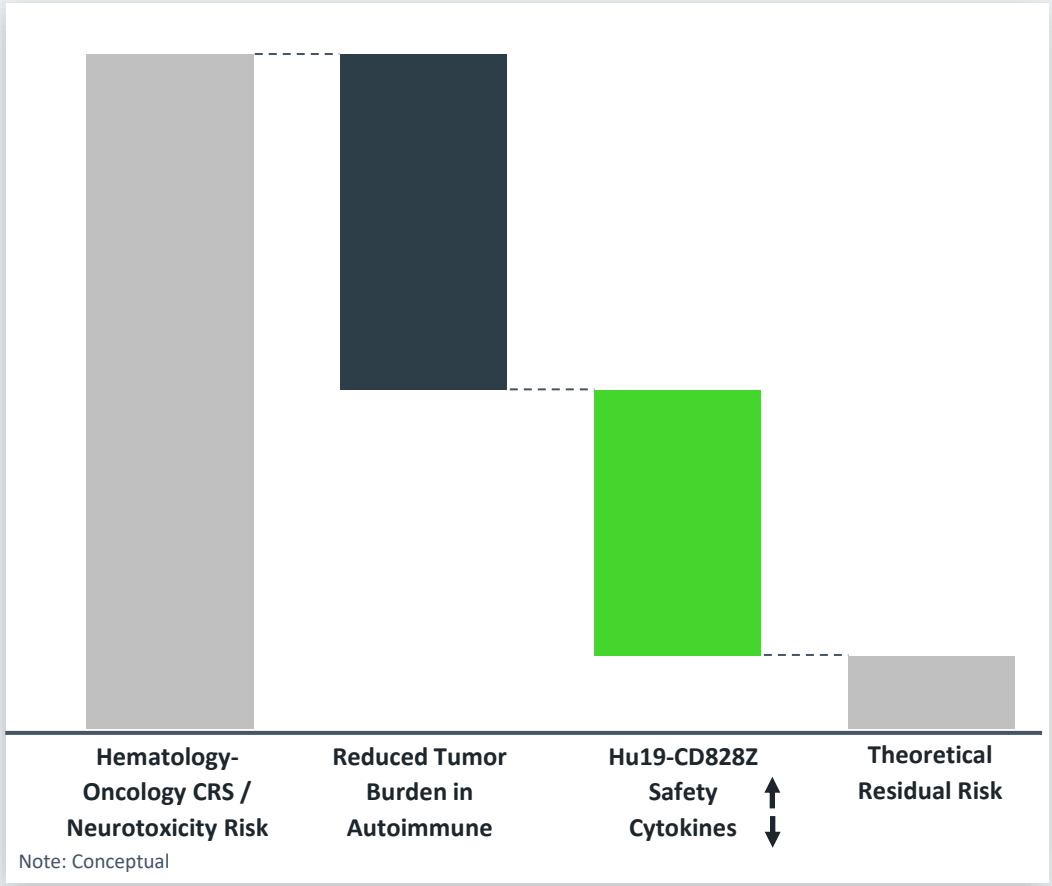
Opportunity to harness the power of CAR T-cell therapy in autoimmune disease

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

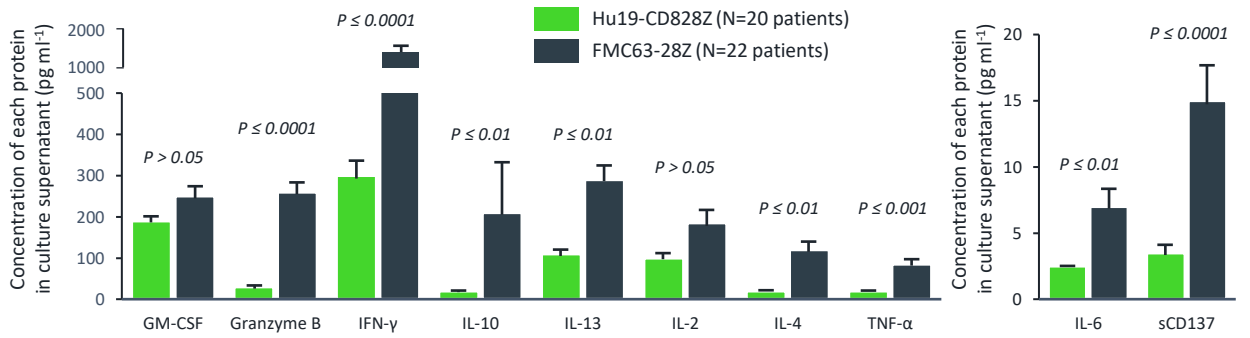
Conceptual Differences between Oncology and Autoimmune Disease Applications of CAR



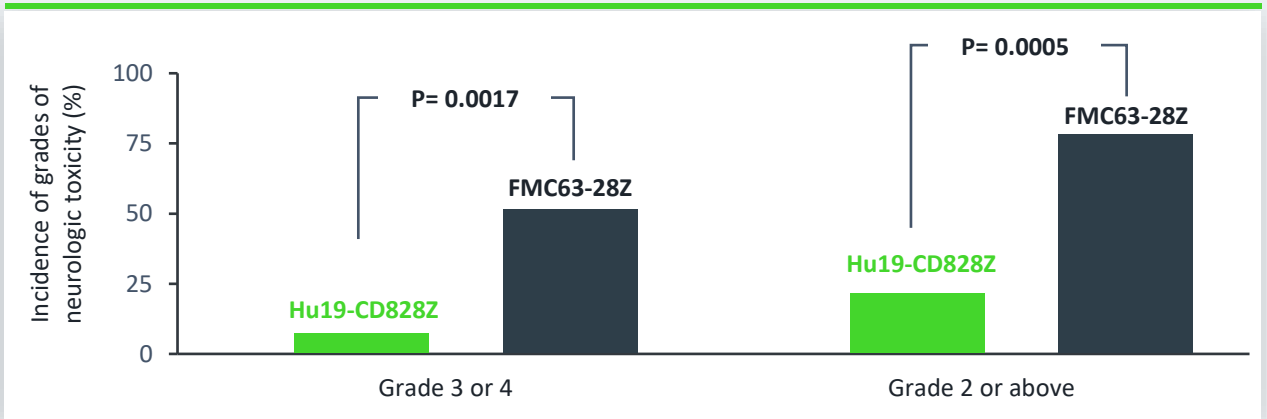
Note: Conceptual

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



Source: Brudno et al., Nature Medicine 2020; 26: 270-280

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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 (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
			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

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KYV-101

- Autologous CD19 CAR T

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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

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Broad development program for KYV-101 comprised of clinical trials and third party named patient activities

# of Patients	Identified	Consented	Apheresed	Dosed	28d Follow-up Complete
Total	**29**	**29**	**22**	**14**	**13**
Company-sponsored clinical trials	5	5	5	3	3
Investigator-initiated and named patient	24	24	17	11	10

Note: As of Dec. 31, 2023

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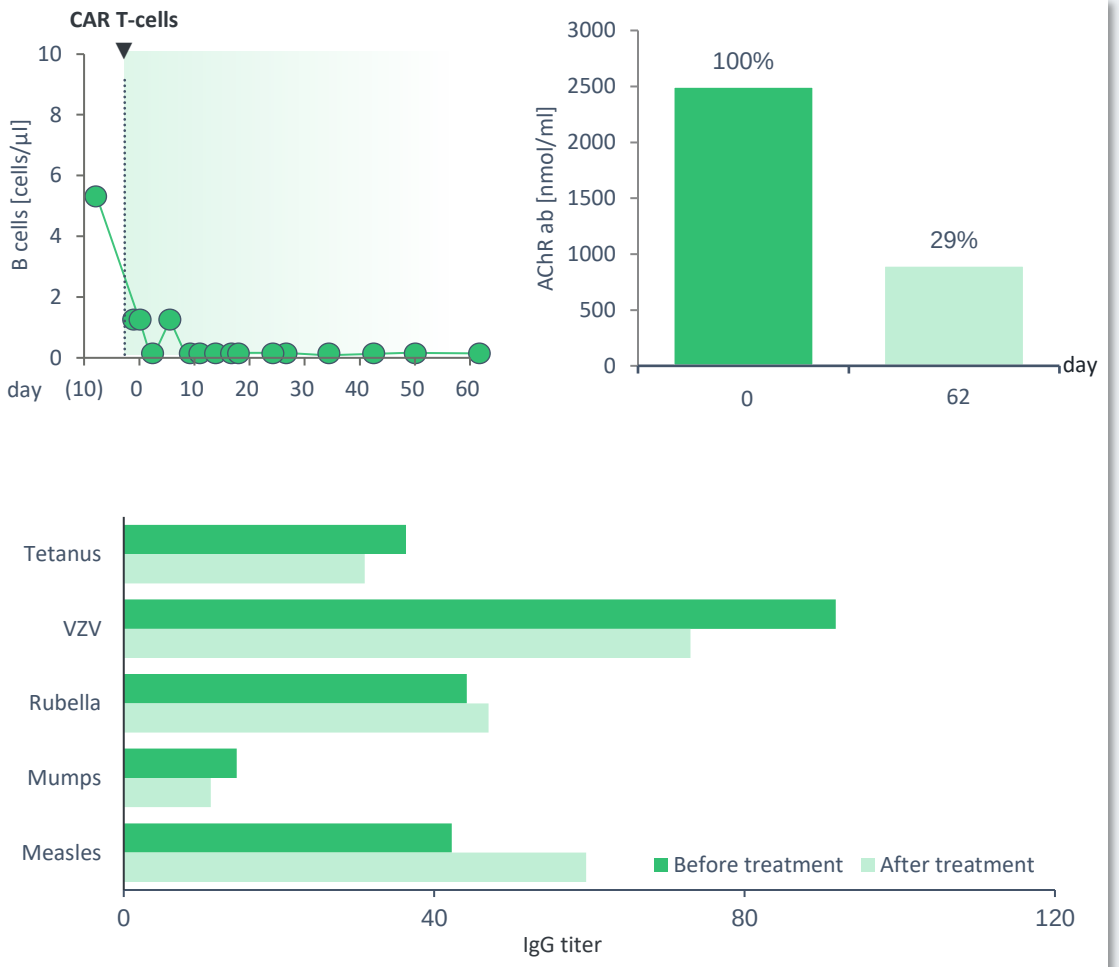
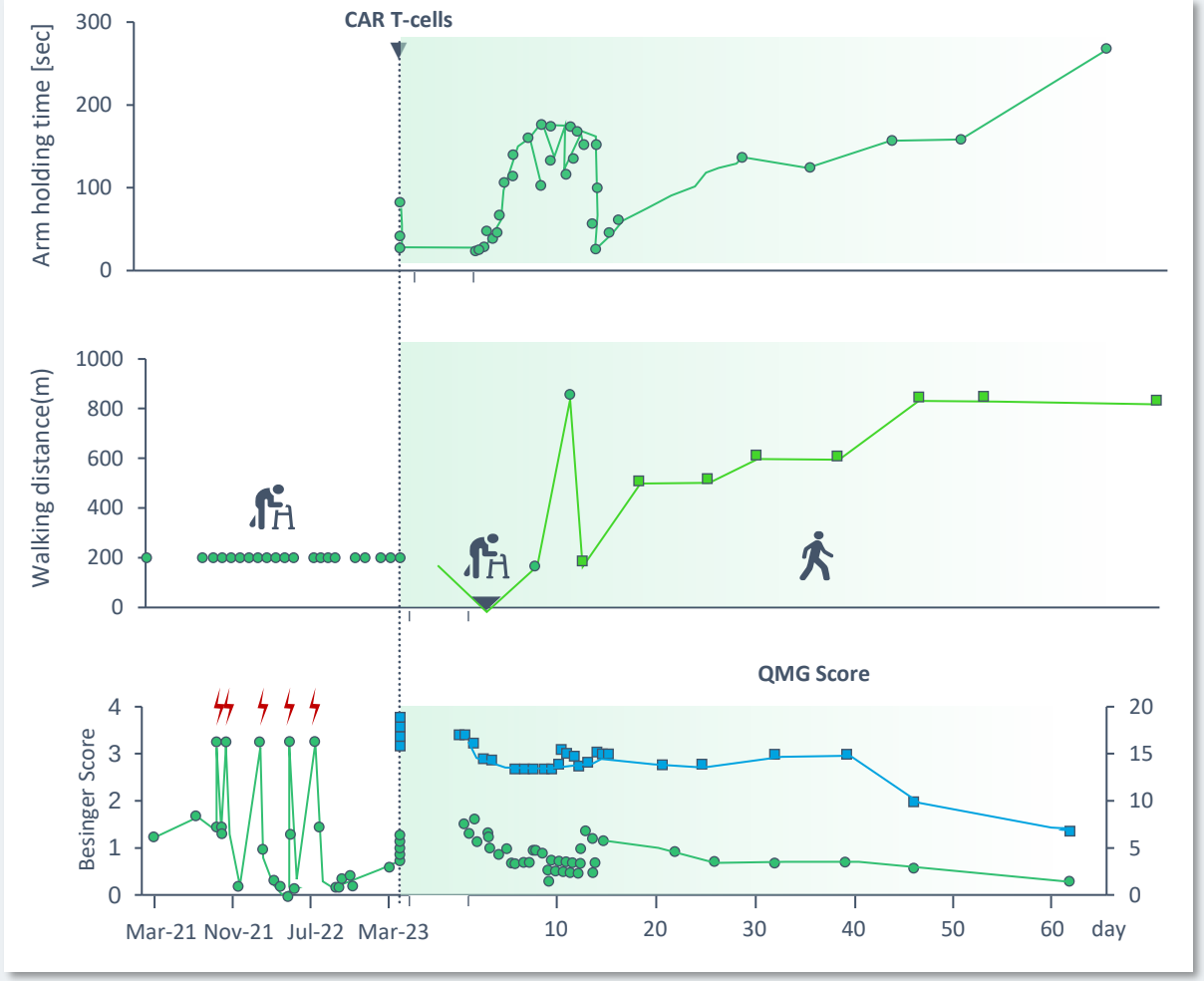
Myasthenia Gravis Named Patient #1 – Lancet Neurology

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



Note: Named patient data; Haghikia A, et al. Anti-CD19 CAR T cells for refractory myasthenia gravis. The Lancet: Neurology 2023. 22(12):1104-1105

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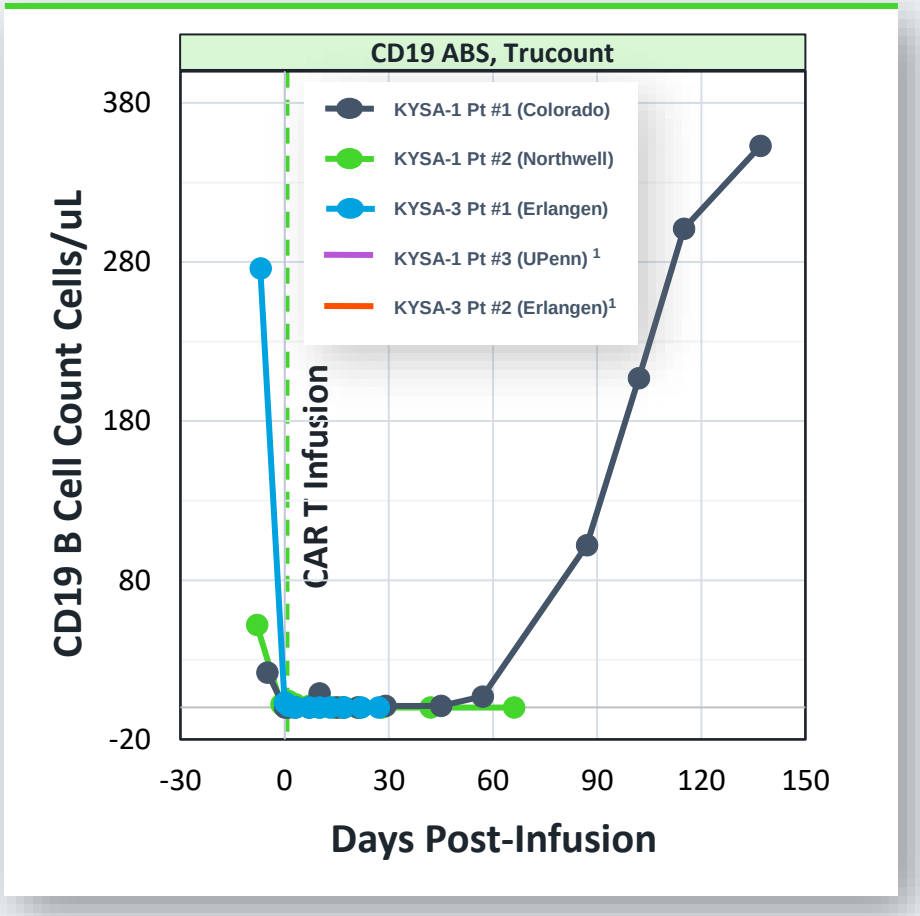
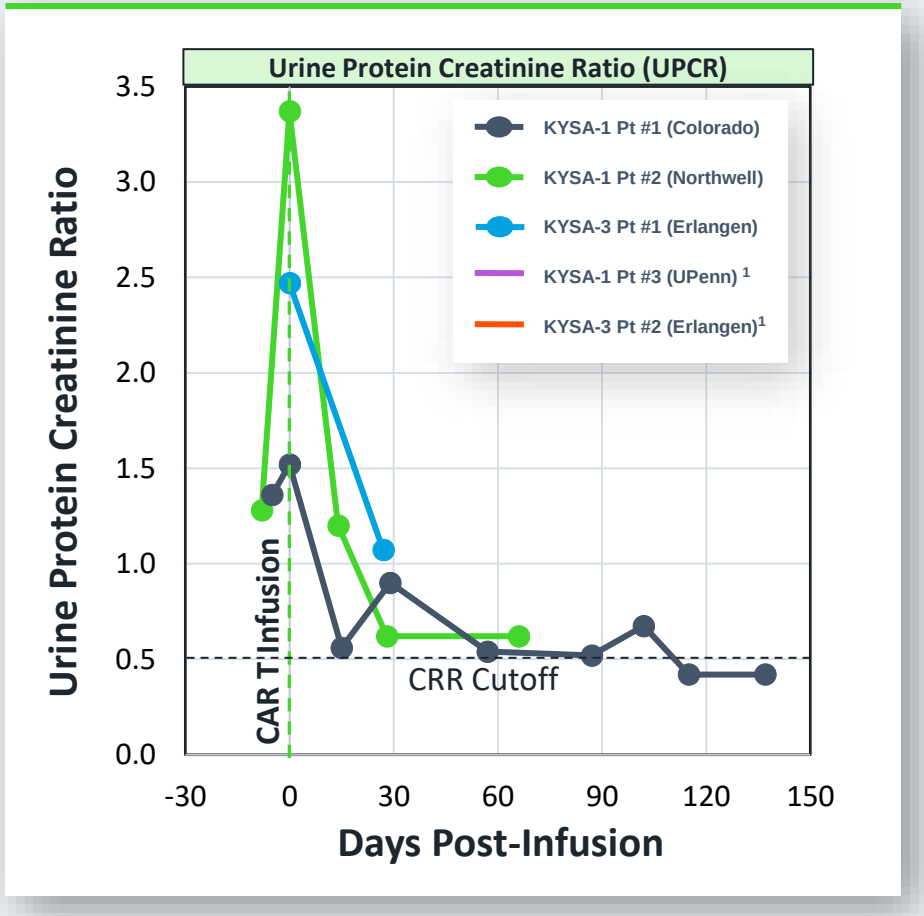
Promising initial results in KYSA-1 and KYSA-3 multi-center clinical studies in lupus nephritis

Pharmacodynamic Activity and Return of B Cells



Improvement in Proteinuria



Note: data available as of 12/31/2023; [1]KYSA-1 Pt #3 and KYSA-3 Pt#2 enrolled and apheresed but not yet dosed as of 12/31/2023

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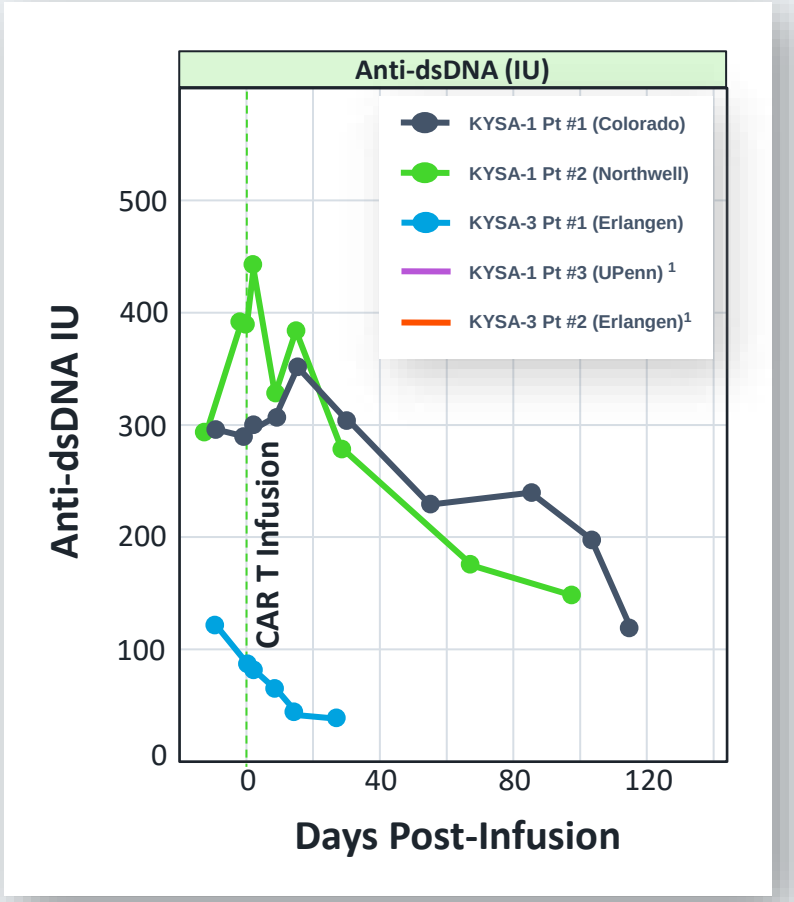
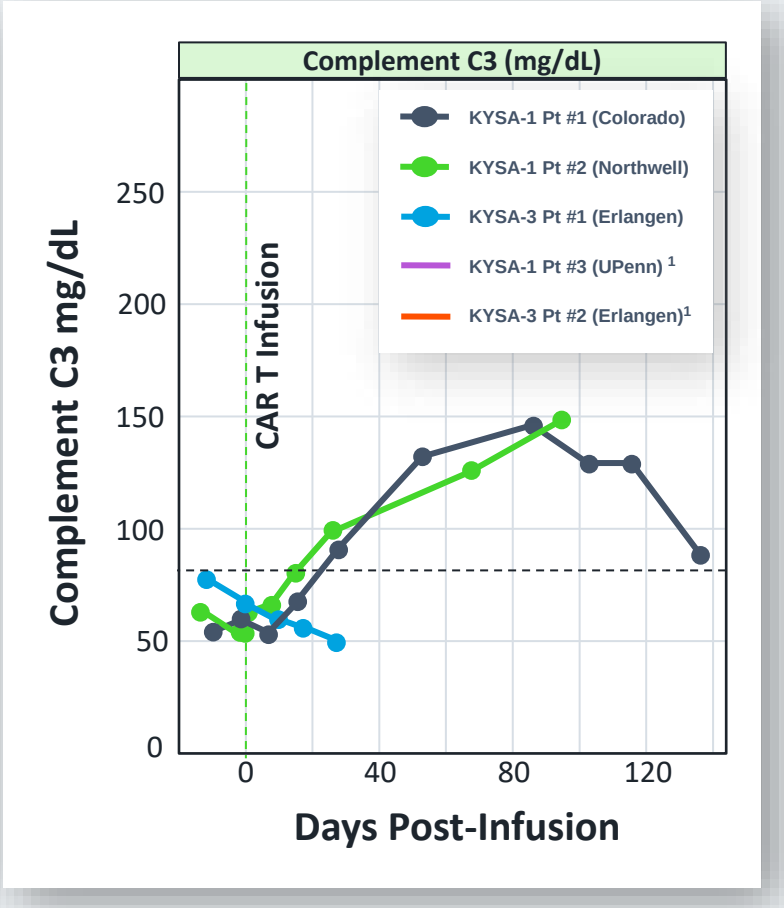
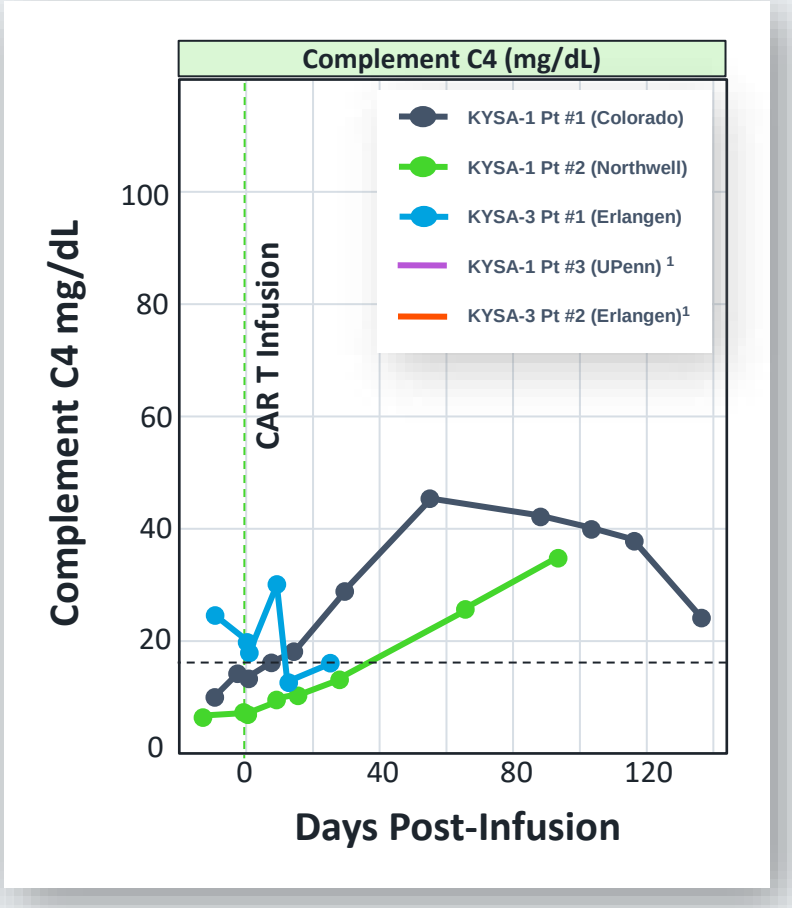
KYSA-1 and KYSA-3 Study of KYV-101 in Lupus Nephritis
Additional markers of improved disease activity







Note: data available as of 12/31/2023; [1]KYSA-1 Pt #3 and KYSA-3 Pt#2 enrolled and apheresed but not yet dosed

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

Source	Indication	N	Any Grade CRS[a]	Any Grade ICANS[b]	CRS Grade ≥3	ICANS[b] Grade ≥3
KYV-101 experience[1]	**MG, LN, MS, SPS, DE**	**13**	**10**	**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[c]	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
JULIET (tisa-cel)[6]	DLBCL 3L	115	85	69	26	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

Note: CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome; BL = Burkitt lymphoma; DLBCL = diffuse large B cell lymphoma; FL = follicular lymphoma; MG = myasthenia gravis; MCL = mantle cell lymphoma; SLE = systemic lupus erythematosus; SSc = systemic scleroderma; [a] Data for reference 6 reported using Penn, rather than Lee, criteria for CRS; [b] Data for references 3, 4, 5, and 6 reported as neurologic toxicities; [c] Grade 1 neurological toxicity was not recorded in this trial. Three subjects had Grade 2 neurologic toxicity, and 16 patients had Grade <2 neurologic toxicity; [1] Internal data from first two patients in KYSA-1 and named patient data and safety data for patients with 28 days of follow-up as of 12/31/2023; [2] Taubmann J, et al. ACR 2023. Abstract 0783. Arthritis Rheumatol. 2023; 75 (suppl 9); [3] Brudno JN, et al. Nat Med. 2020;26:270-280; [4] Neelapu SS, et al. NEJM 2017;377:2531-44; [5] BREYANZI® (lisocabtagene maraleucel) Prescribing Information 2023, Bristol-Myers Squibb; [6] KYMRIAH® (tisagenlecleucel) Prescribing Information 2022, Novartis Pharmaceuticals

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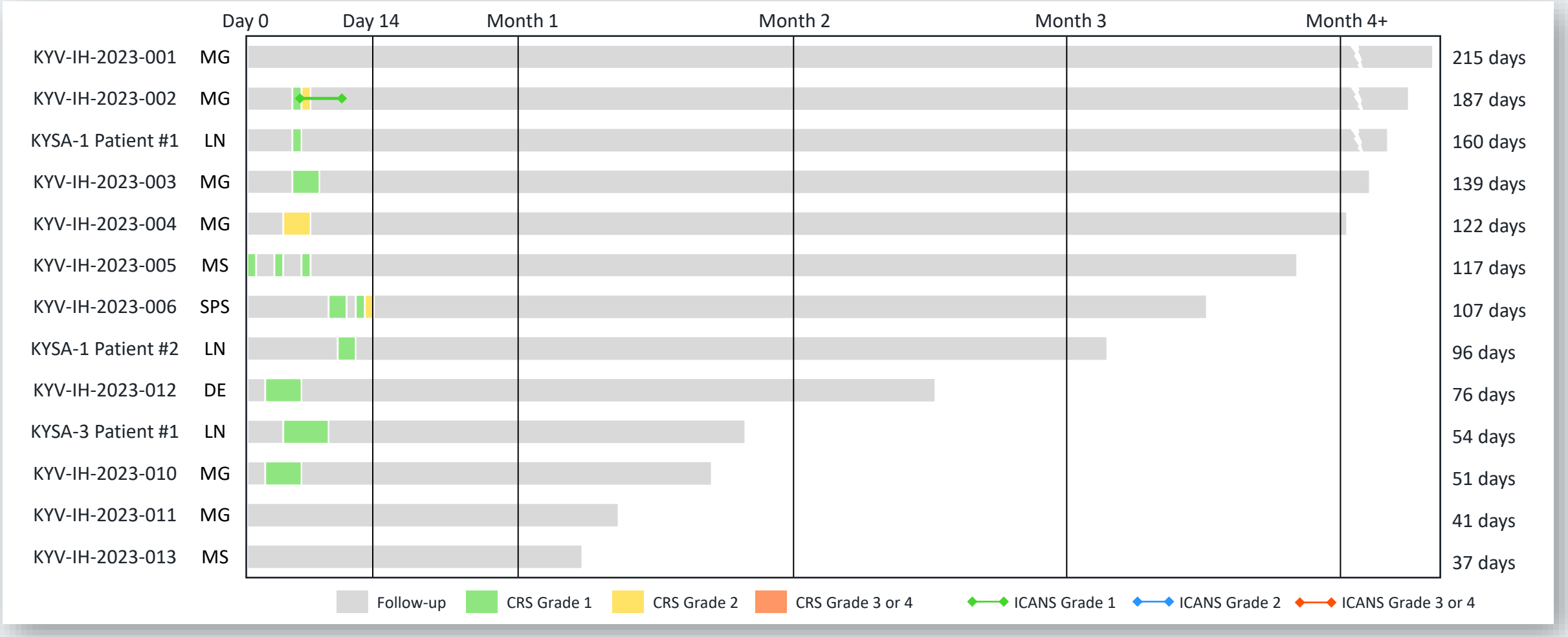
CAR-related safety events observed in patients in Kyverna-sponsored clinical trials and named patient activities have been readily manageable (No CRS or ICANS Grade ≥3)

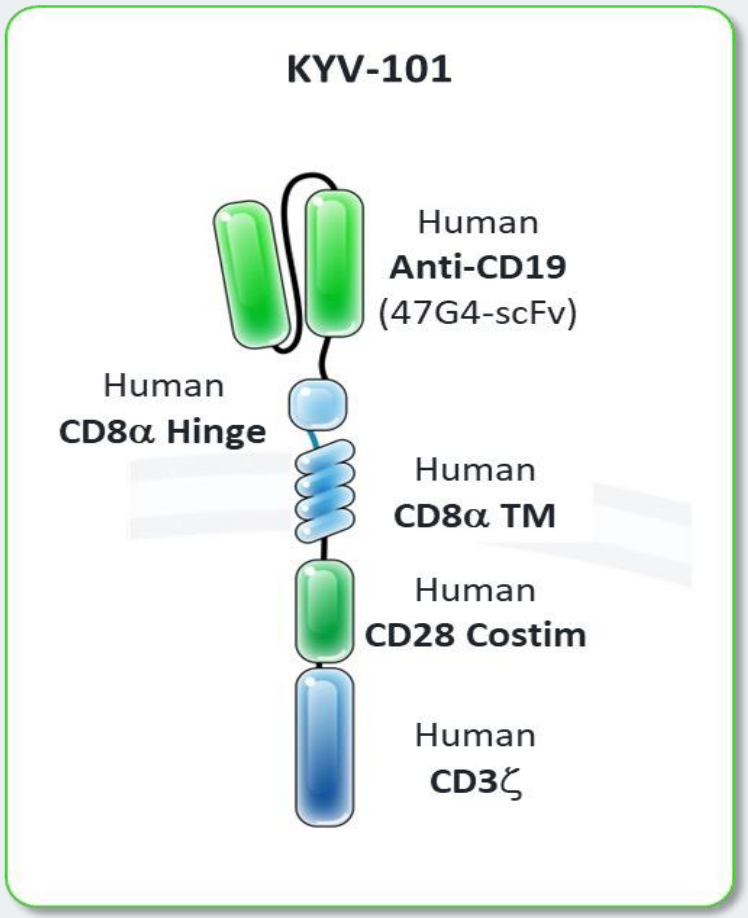
Time from infusion as of Dec 31, 2023



Note: Data as reported by sites as of 12/31/2023; Patient KYV-IH-2023-008 is not shown due to the short follow-up; myasthenia gravis (MG), multiple sclerosis (MS), stiff person syndrome (SPS), lupus nephritis (LN), anti-DAGLA encephalitis (DE)

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



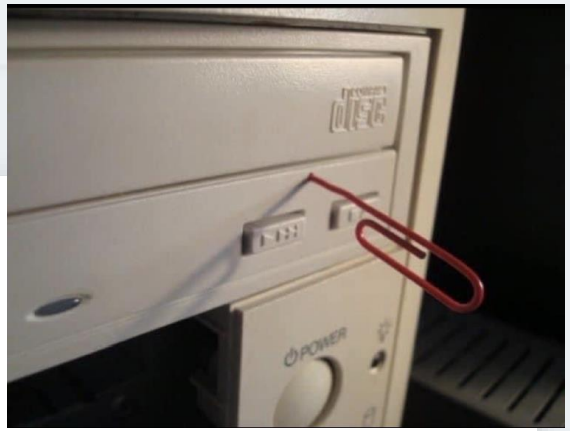
Engineered for improved safety profile[1]

- 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 setting[2]

- 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

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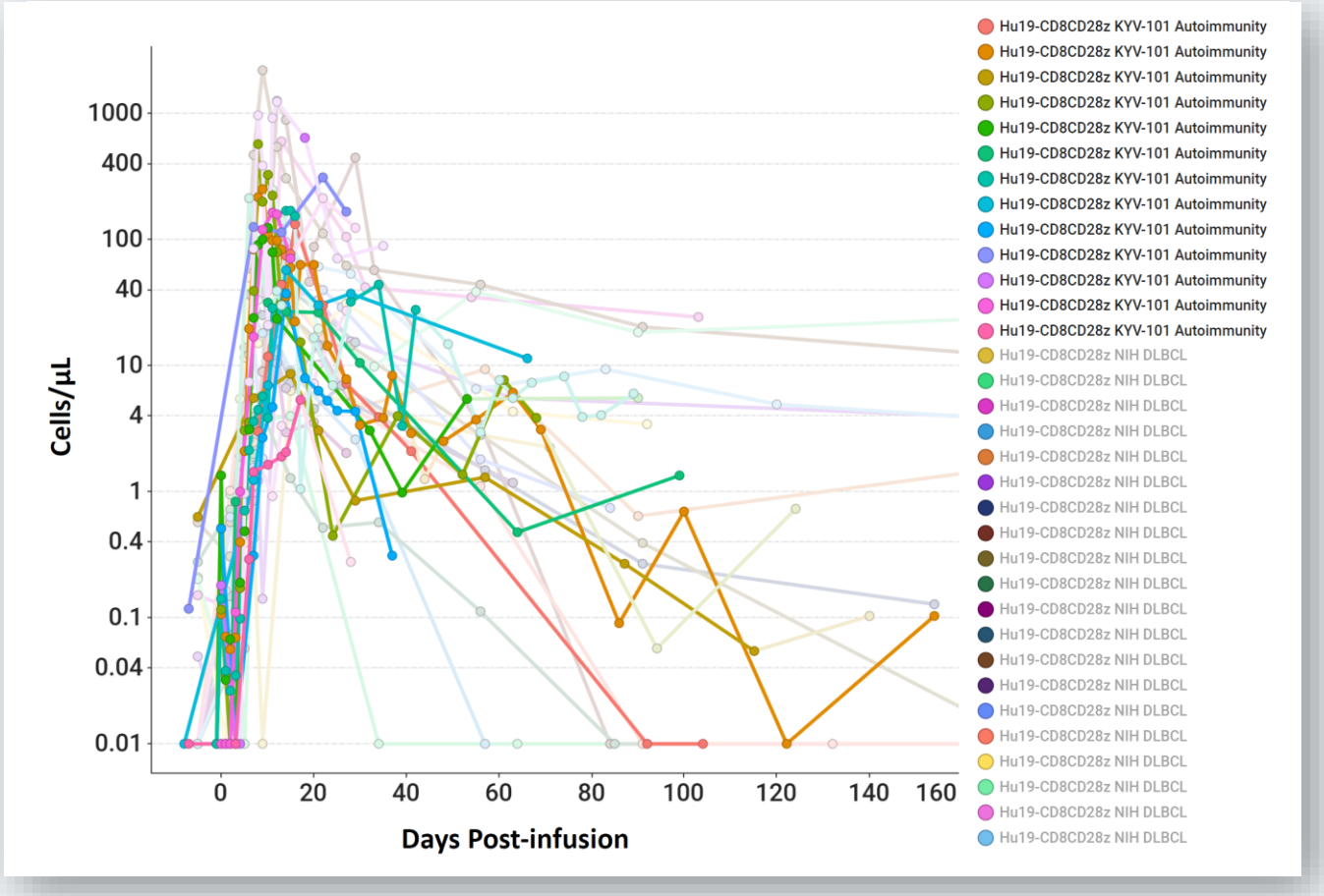
KYV-101 CAR T expansion in patients in Kyverna-sponsored clinical trials and named patient activities to date consistent with NIH oncology results



Comparison assumes close approximation between ddPCR (NIH) and FACS based data (KYV-001-001)[1]

Note: [1] Brudno et al., Nature Medicine 2020; 26:270-280; Internal data from first two patients in KYSA-1 and named patient data ("KYV-IH") as of December 31, 2023

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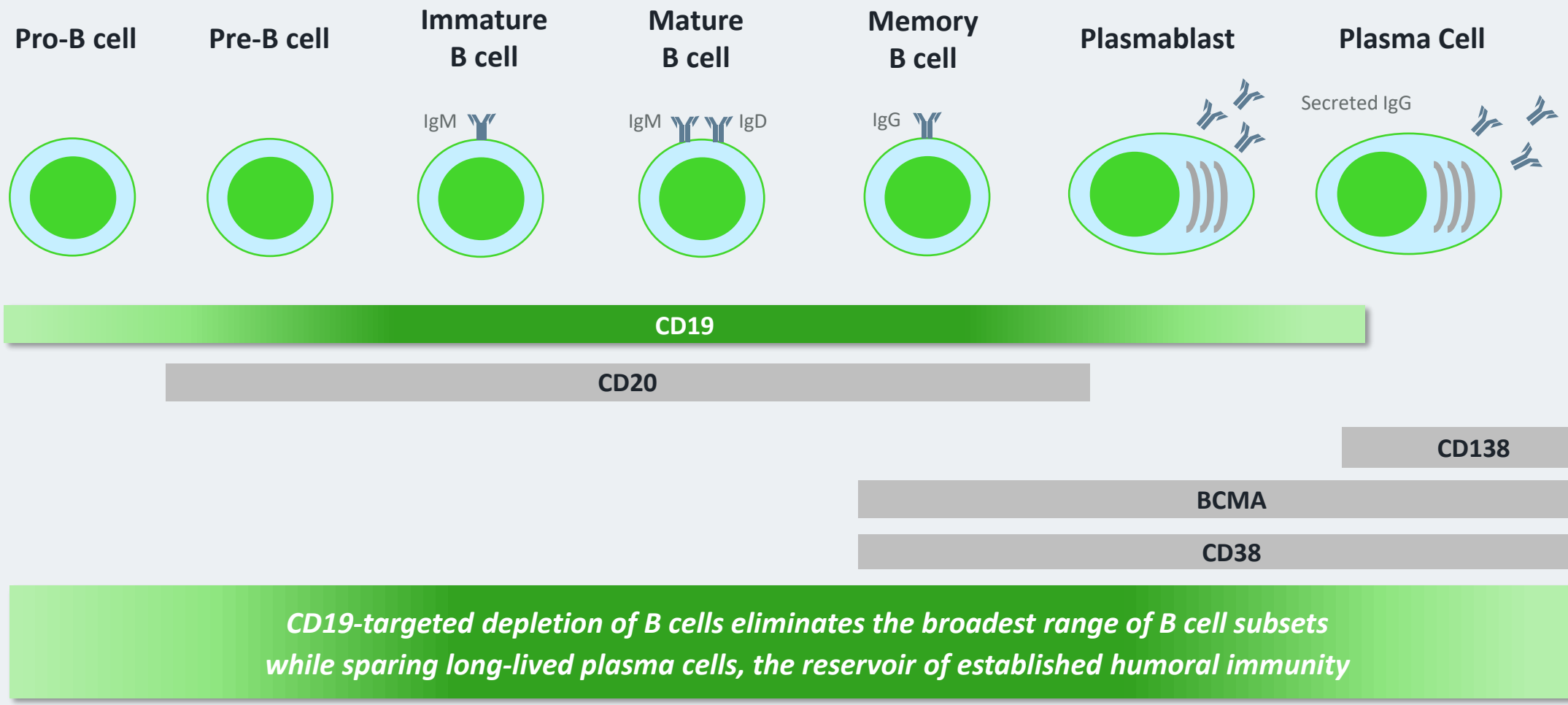
CD19 expressed on broader range of B cell subsets compared with CD20



Adapted from Jejeune et al, Front Immunol 2020;11:762

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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	US	✓		
	MG		✓		
	MS		✓		
KYV-101 IIT	MS	US	✓		Stanford IIT
				✓	UCSF IIT
	Undisclosed		✓		UMass IIT
	Dermatomyositis		✓		Stanford IIT
	Basket		✓		UPenn IIT

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KYV-201

- Allogeneic CD19 CAR T

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

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- **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

Intellia THERAPEUTICS

- **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

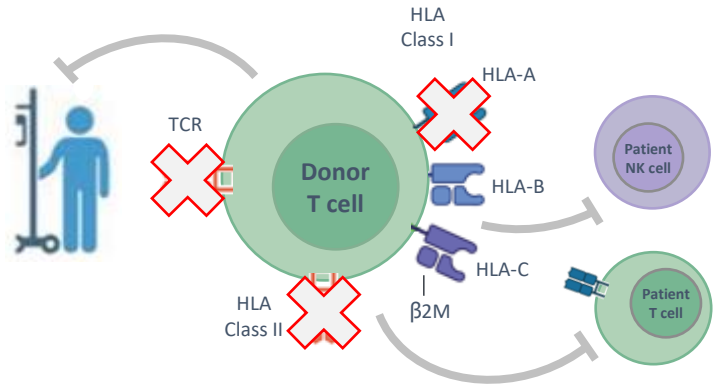
KYV-201 protection from T cells supports potential for longer-term persistence

Differentiated allogeneic platform based 3 genetic deletions

TCR KO + HLA-A KO + pan HLA Class II

Genetic deletion of the TCR avoids GvHD
TRAC KO

Partial genetic deletion of HLA inhibits NK cells
HLA-A-KO



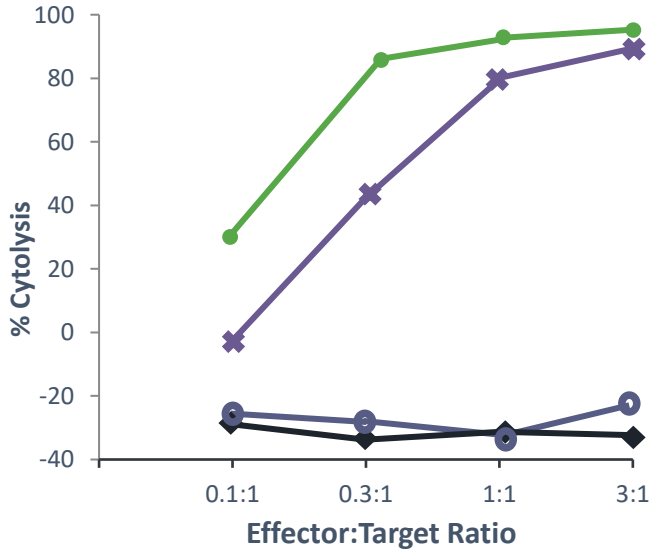
Intellia THERAPEUTICS

Match remaining HLA Class I alleles between donor and patient
HLA-B and HLA-C matching

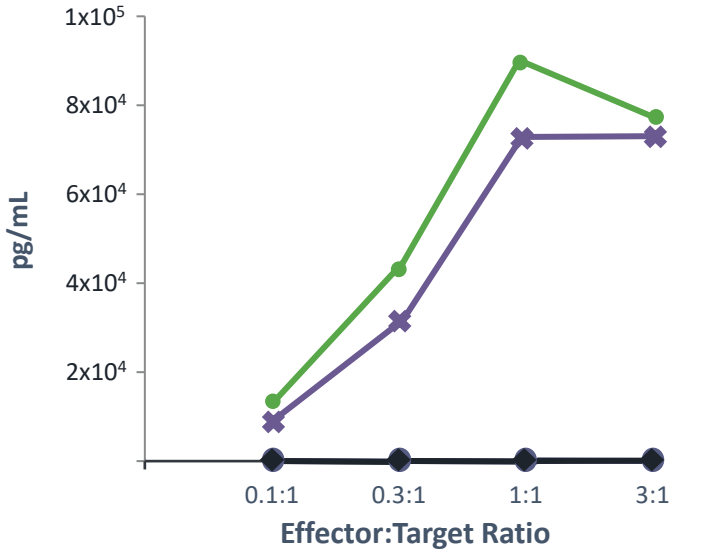
KYV-201 demonstrates robust CAR-mediated activity against CD19+ cells

Similar to HLA Class I deficient b2M KO[1]

Dose-Dependent Cytotoxicity



Dose-Dependent IFNγ Secretion



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

WT
CAR only
KO only
KYV-201

Note: [1] Internal data

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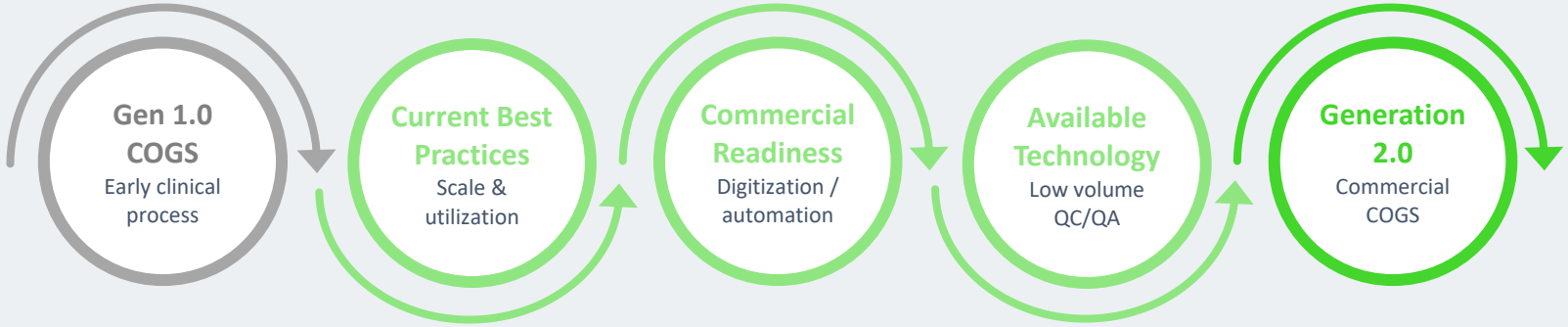
Kyverna's Ingenui-T process leverages expertise from industry leaders to target pharma-like COGS

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	• **ElevateBio's BaseCamp** for process development and cell product manufacturing • **Oxford Biomedica** supply agreement, enabling use of **LentiVector**	✓	✓	
Pharma-like COGS	• Foundation of **industry-best practices** • ElevateBio and other processes to **streamline COGS**	✓	✓	✓

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Kyverna's cash runway expected to fund operations into 2026, with several expected 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

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