in vivo CAR T cell therapy

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Disclosures

- Advisory Boards: AstraZeneca, Abbvie, BeiGene, Bristol Myers Squibb, Celgene, Gilead/Kite, Pfizer, Merck
- Research Funding: Bristol Myers Squibb
- Steering committee: BeOne

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Introduction

- Emerging next generation immunotherapy that engineers CAR T cells directly inside the patient's body
- Specialized delivery vehicles such as targeted lipid nanoparticles or lentiviral vectors are injected directly into the patient's body
- Early human trial in multiple myeloma (KLN-1010) has reported promising results
- Key hurdles to overcome:
  - Targeting precision
  - Safety
  - Long term durability

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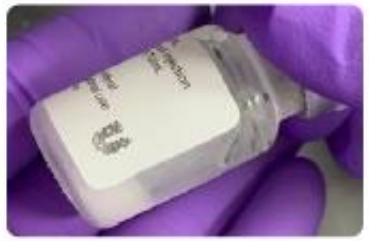
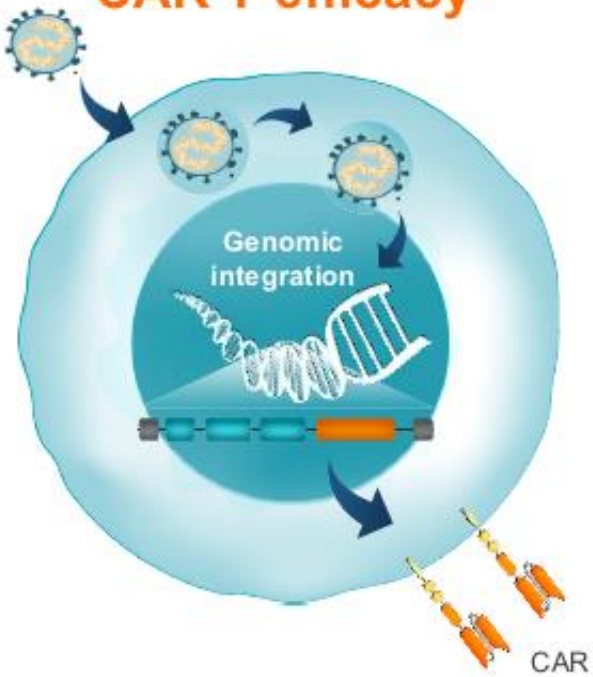
In vivo delivery addresses key challenges with *ex vivo* CAR therapies

	ACCESS	TREATMENT LOGISTICS	THERAPEUTIC EFFECT
Ex vivo	>20 days manufacturing vein to vein time **COSTLY TO SCALE AND MANUFACTURE**	Complex logistics • Apheresis • Lymphodepletion • CAR T infusion **LD W/ ASSOCIATED SIDE EFFECTS**	**Potential for Transformative CAR T efficacy**
In vivo	 On-demand availability **SCALABLE WITH LOW COGs**	 One-time infusion **NO LYMPHODEPLETION**	

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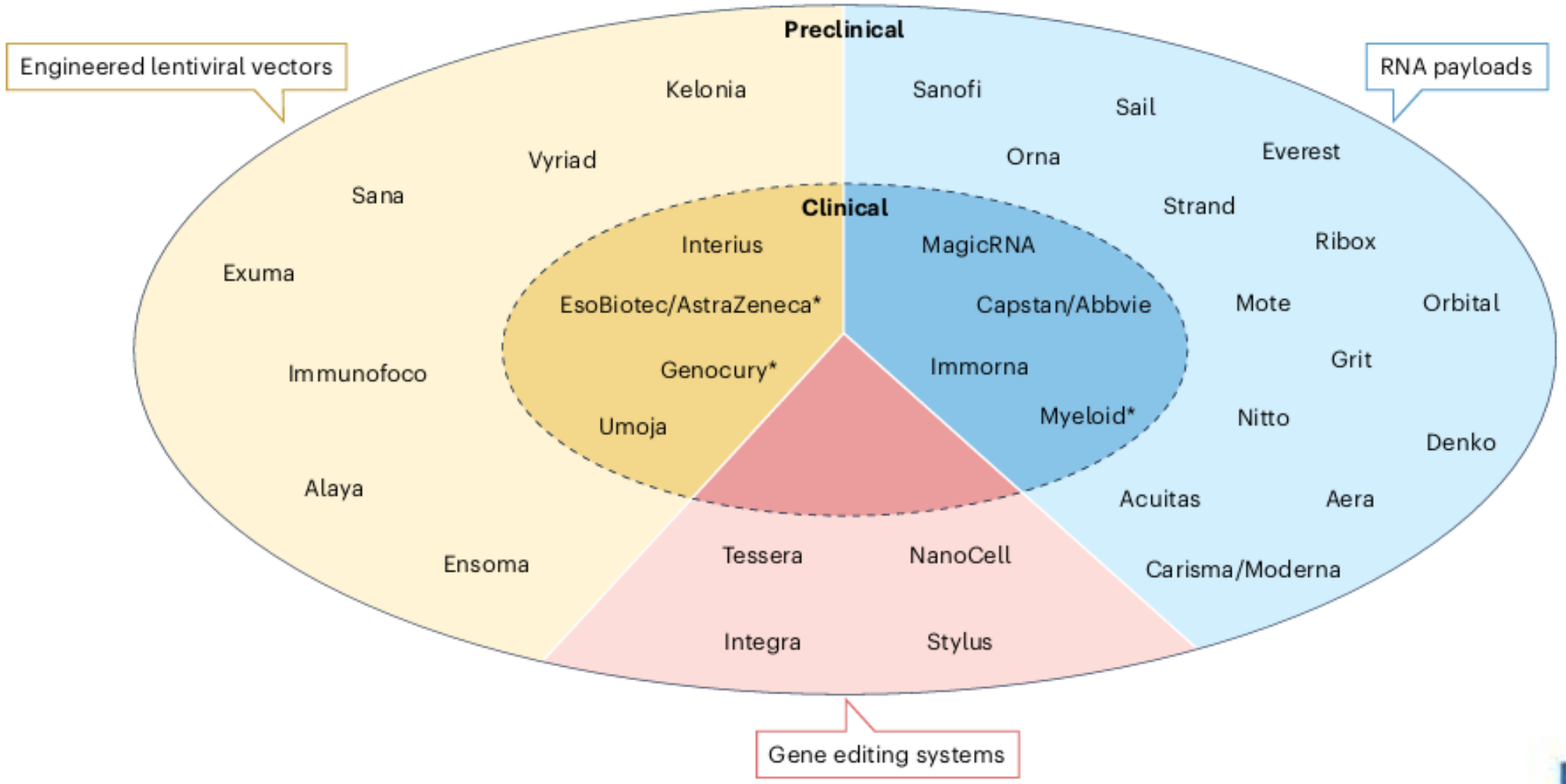
The rapidly evolving, in vivo CAR therapy ecosystem



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Pre-clinical work and trials in progress

Table 1 | Lentiviral-based in vivo CAR-T cell platforms in development

Company	Targeting mechanism	Therapeutic payloads	Lead indications	Preclinical evidence	Development stage
Interius BioTherapeutics	Anti-CD7 scFv-decorated particles (T cell and natural killer cell engineering)	Anti-CD20 CAR, anti-CD19 CAR	B cell malignancies, autoimmunity	Proof of principle in mice and NHPs[84]	Clinical (phase I enrolling in 2024 with anti-CD20 CAR)[78,85]
Umoja Biopharma/ Abbvie	Multi-domain anti-CD3, CD80, CD58 decorate particles (T cell engineering)	Anti-CD19 CAR, anti-CD22 CAR, anti-CD20 CAR	B cell malignancies, autoimmunity	Proof of principle in mice and NHPs[81,88,91]	Clinical (phase I initiated in 2024 with anti-CD19 CAR, the others in 2024, 2026)[90]
Shenzen Genocury Ltd	Anti-CD3 decorated particles	Anti-CD19 CAR	B cell malignancies	Not disclosed	Investigator-sponsored trial, first responder in a patient with lymphoma[95,96]
EsoBiotec/Astra Zeneca	Targeted lentiviral particles	Anti-BCMA CAR, undisclosed	Multiple myeloma, autoimmunity, solid tumours	Proof of principle in mouse model[95]	Phase I initiation in 2025, first clinical response in myeloma, acquisition[98,101,148]
Kelonia	Anti-CD3 decorated particles	Anti-BCMA CAR	Multiple myeloma	Proof of principle in mice and NHPs[102,103]	Phase I initiation mid 2025
Sana	Anti-CD8 fusogen-decorated particles	Anti-CD19 CAR	Undisclosed	Proof of principle in mice and NHPs[78,109,111]	Undisclosed
Ensoma	CD46-targeted viral-like particles (multilineage)	Anti-HER2 CAR	Multiple solid tumours	Proof of principle in preclinical models[112]	Undisclosed
Exuma Biotec	CD3-targeted lentiviral vector	Anti-CD19 CAR	B cell malignancies	Proof of principle, mouse models[114]	Undisclosed

BCMA, B cell maturation antigen; CAR, chimeric antigen receptor; NHP, non-human primate.

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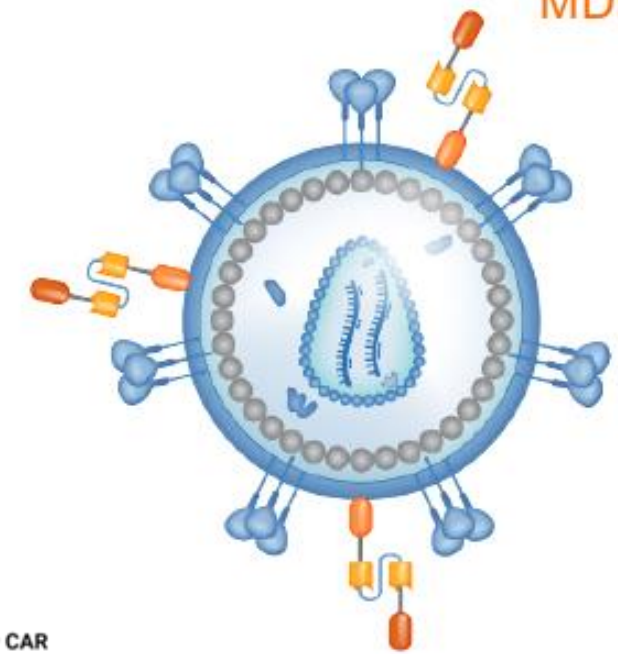
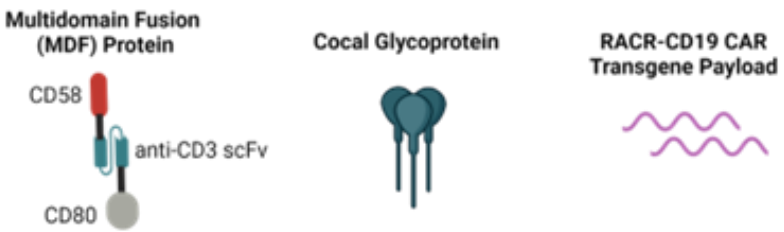
Particle surface engineering includes the Multidomain Fusion (MDF) protein for T cell-specific binding and activation signals and Cocal for internalization and payload delivery



MDF

1) T cell-specific binding
2) T cell activation signals

Cocal fusion glycoprotein



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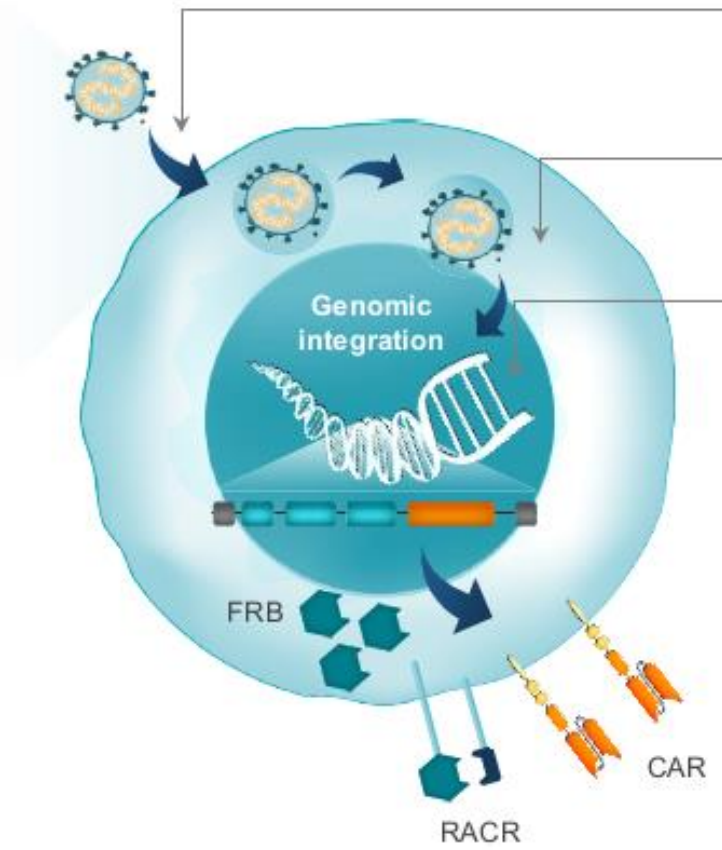
Umoja's integrated platforms enable *in vivo* CAR T therapies

- VivoVec™ surface engineering (Multi Domain Fusion [MDF] protein and Cocal) engages T-cell receptor and co-stimulation[1] for optimized T cell activation and transduction
- Proprietary rapamycin-activated cytokine receptor (RACR) for expansion and potency
- Dedicated manufacturing facility located in Louisville, CO

LENTIVIRAL PARTICLE SUSPENSION



1a T cell binding

1b T cell activation and co-stimulation

VivoVec surface engineering

2 Transduction and payload genome integration

lentiviral vector

3 CAR T cell generation in the patient's body

RACR-Controlled CAR T cell expansion and persistence

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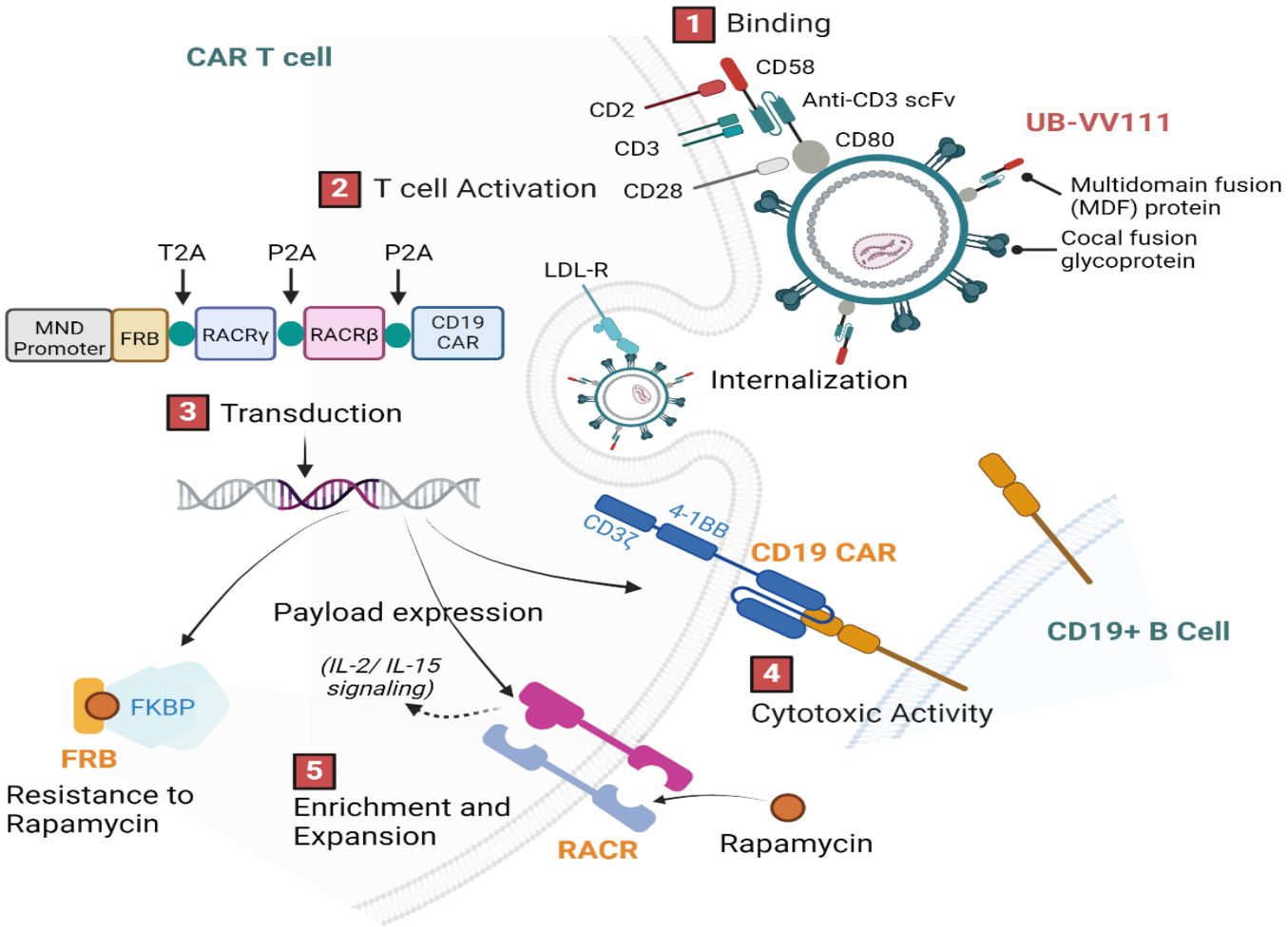
UB-VV111 PRODUCT SCHEMATIC AND PROPOSED MECHANISM OF ACTION

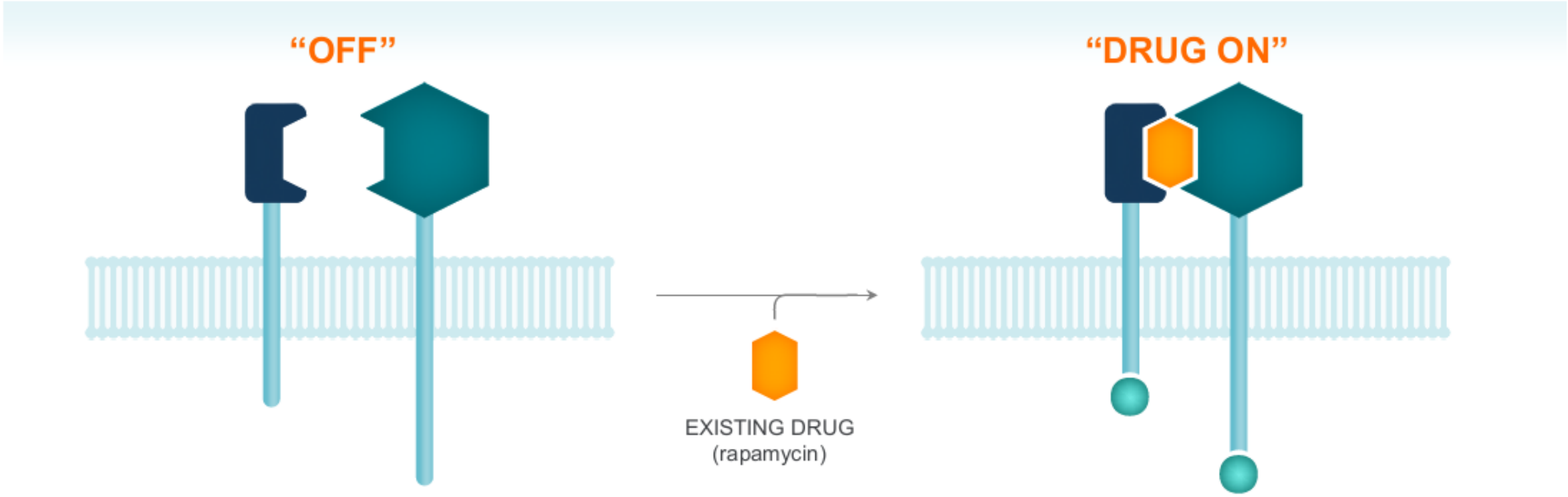


- UB-VV111 selectively binds, activates, and transduces T cells in vivo to generate CAR T cells that express an anti-CD19 CAR and the RACR system
- Mediated through MDF (binding/activation) and internalization (cocal)
- UB-VV111-generated anti-CD19 CAR T cells mediate antigen-specific cytotoxic activity, cytokine secretion, and proliferation in response to CD19-positive target cells
- Expression of RACR provides intracellular IL-2/IL-5 signals following rapamycin administration to selectively enrich and expand CAR T cells in vivo. The FRB domain of the RACR system prevents mTOR inhibition in CAR T cells by sequestering rapamycin-FKBP complexes

RACR is unique in the *in vivo* CAR T industry

"Drug On" switch: Mechanism that enhances T cell expansion and persistence

- Key integrated technology that serves to replace T cell enhancing effects of lymphodepletion



"RACR" switch components are expressed along with a CAR

STAT ACTIVATION
for enhanced persistence/potency
"drug on" control for safety

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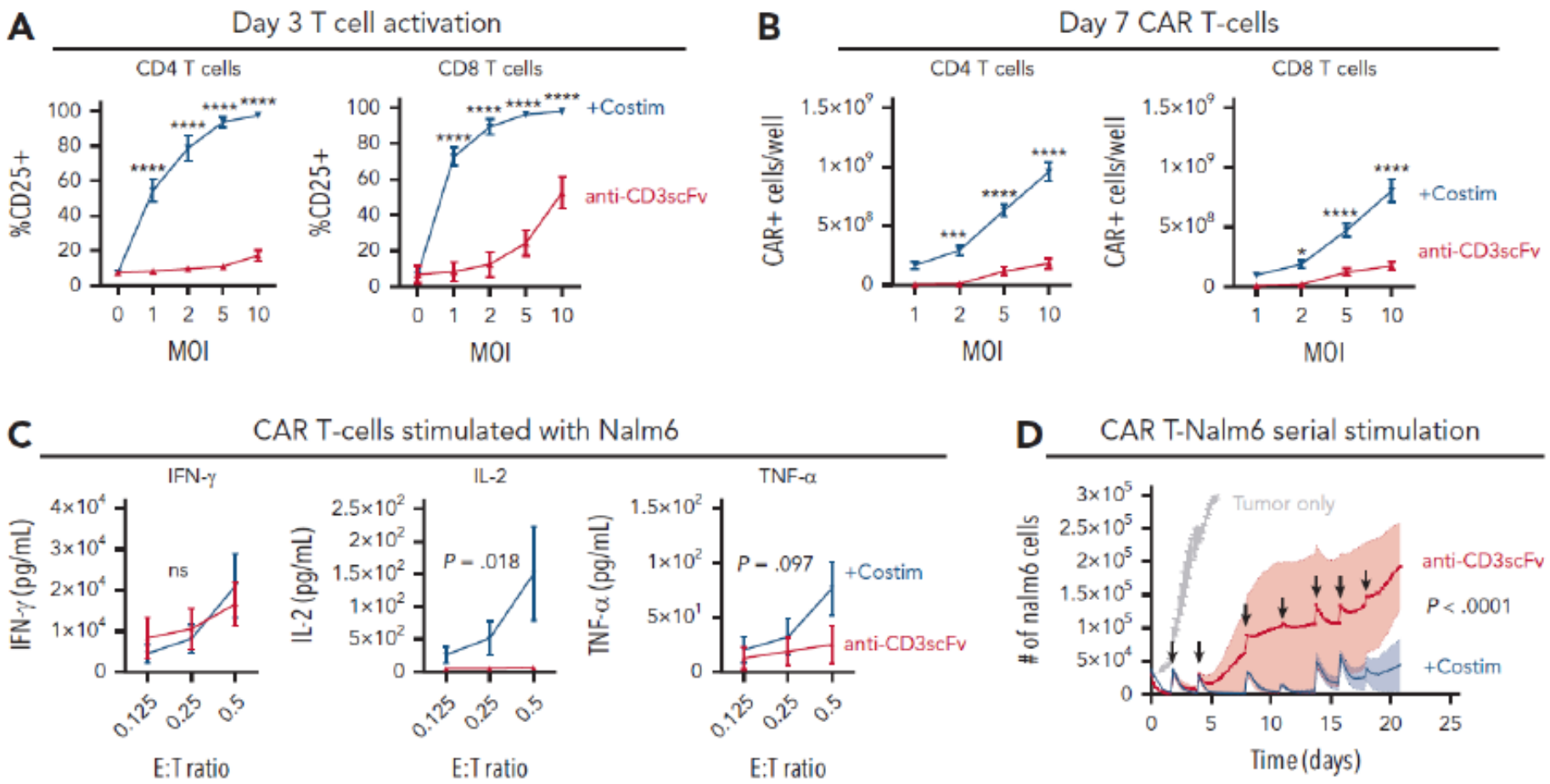
Preclinical data support VivoVec mechanism of action

VivoVec binds, activates, and transduces in a T cell-specific manner



Nicolai et al Blood 2024

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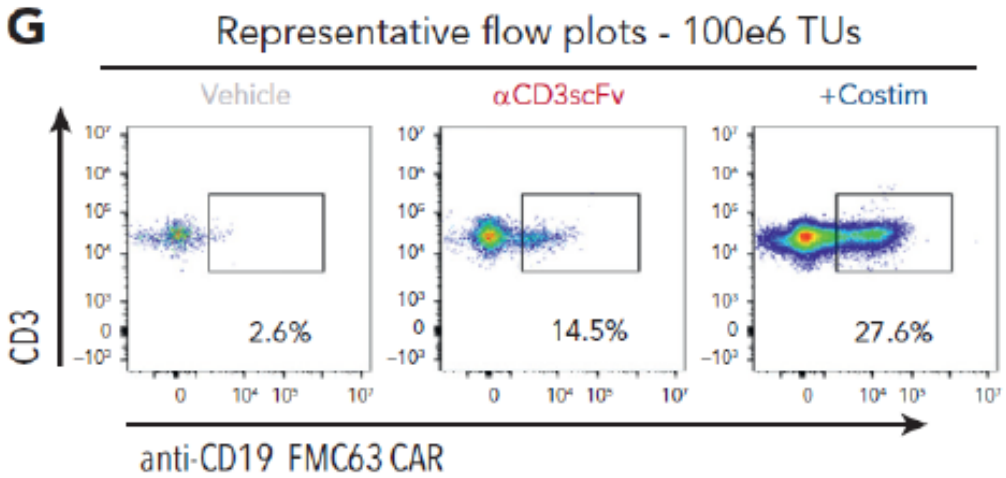
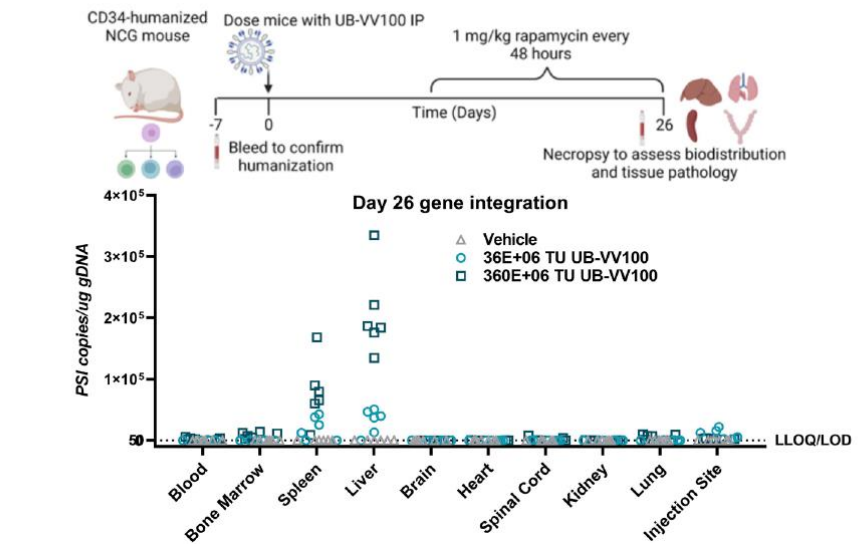
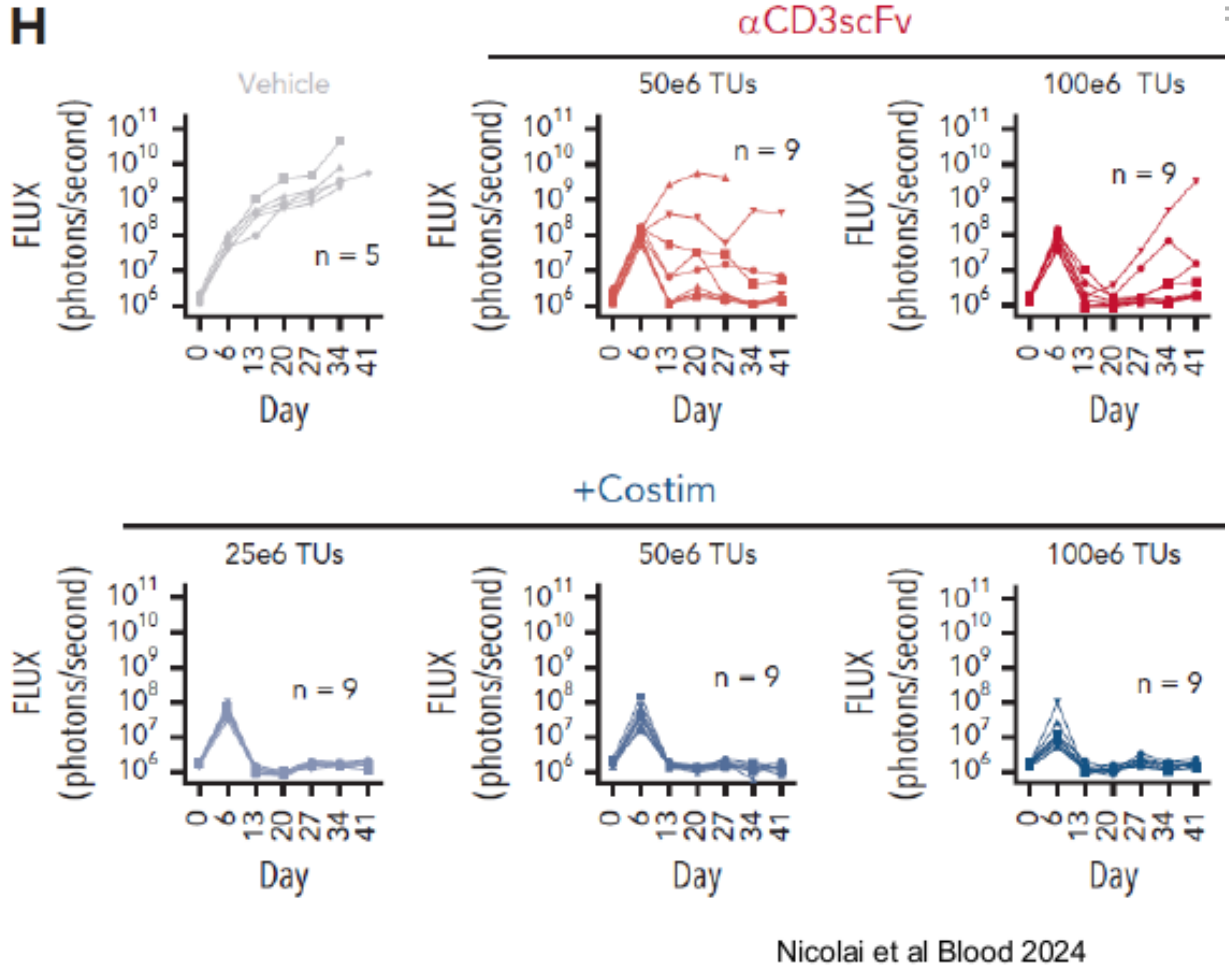
In vivo preclinical data demonstrate potent CAR T cell expansion and tumor control with MDF-enabled VivoVec particles in murine models







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UB-VV111-01: Staged exploration of dose, route of administration (ROA), and combination with rapamycin

- Stage 1:
  - Dose finding of UB-VV111 monotherapy in **r/r DLBCL / CLL (CAR T naïve or exposed)**
  - Independent in intranodal (IN) and intravenous (IV) ROAs
  - Maximally tolerated dose (MTD) is established in either/both ROAs
- Stage 2:
  - Addition of rapamycin to UB-VV111 monotherapy in either/both ROAs

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Eligibility criteria

- Age ≥18
- R/R DLBCL/CLL
  - CAR T naïve: must have had ≥2 prior lines of therapy (including CD20 Mab and anthracycline chemo for DLBCL; BTKi and/or BCL2i for CLL)
  - CAR T exposed: need to confirm D19 expression
- ECOG 0-1
- Measurable disease
- Good organ function and counts, including LVEF ≥40%, ALC ≥200

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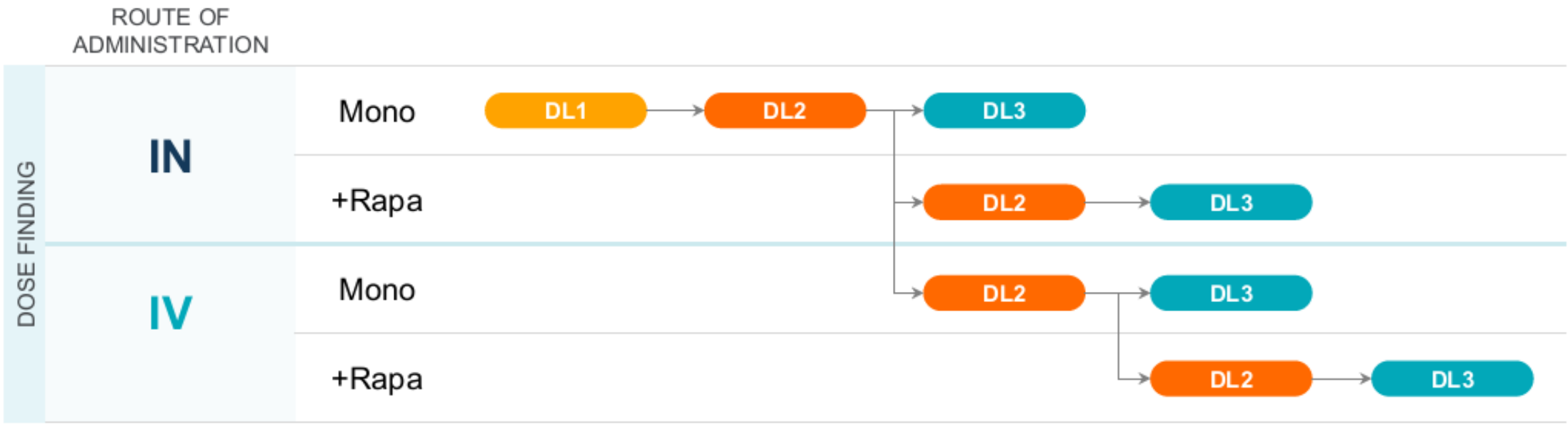
UB-VV111 INVICTA-1 Protocol Design

Enrollment is progressing well; enrollment staggered for safety

INDICATIONS: 3L+ DLBCL and CLL



- Dose escalation proceeds in both routes of administration with and without rapamycin

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Umoja Pipeline: Executing On Our Founding Vision

Programs in multiple large market indications supported by internal manufacturing

THERAPEUTIC AREA	PROGRAM	TARGET(S)	INDICATION(S)	PRE-CLINICAL	PHASE 1	PHASE 2
WHOLLY OWNED PROGRAMS						
Hematology	**UB-VV400**[1]	CD22	NHL			
	UB-VV500	BCMA x GPRC5D	Multiple Myeloma		Q4 2026	
Autoimmune	**UB-VV410**[1] *No RACR*	CD22	Lupus Nephritis			
Solid Tumors	**UB-VV1000**	Undisclosed	Solid Tumor Indication (undisclosed)			
PARTNERED PROGRAMS WITH abbvie						
Hematology	**UB-VV111**	CD19	NHL, CLL			
	UB-VV800	Undisclosed	Hematology			

[1] Phase 1 trials are China IIT run by our partner IASO; Umoja owns rights outside of Greater China

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Conclusions

- As a revolutionary cancer treatment strategy, in vivo CAR-T cell therapy provides benefits compared with traditional ex vivo CAR-T cells such as overcoming the complex, costly and time-consuming manufacturing processes.

- Could be the ideal therapeutic alternative to off-the-shelf CAR-T cells.

- Potential to be useful in oncology as well as autoimmune disorders.

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Thank you for your attention!

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