# CRG-023, A Novel Tri-specific CAR T Product Candidate Engineered To Prevent Antigen Escape And Sustain Durable Anti-tumor Functionality Against B-cell Malignancies

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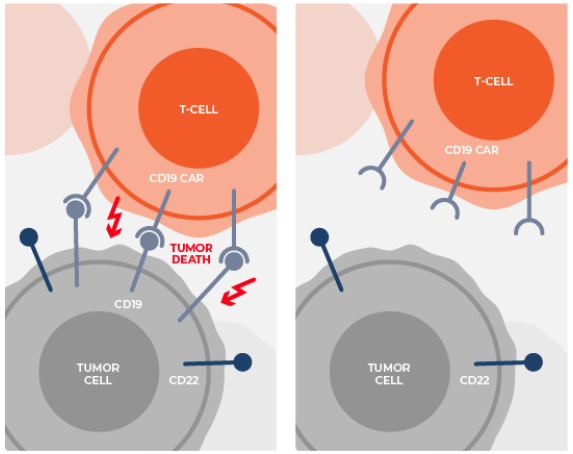
Acknowledgement of S. Zompì

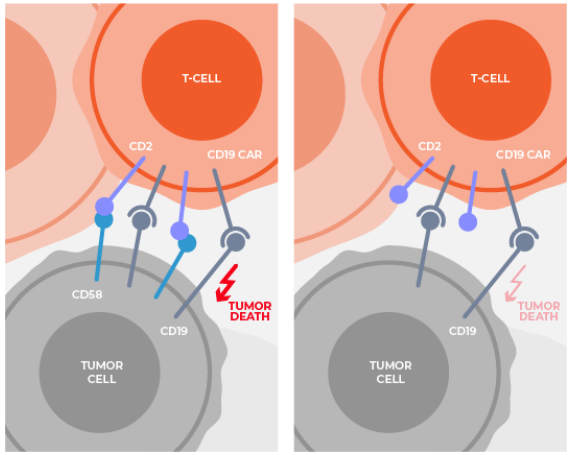
ASH abstract

# CRG-023, A Tri-specific CAR T Designed To Improve Patient Outcomes

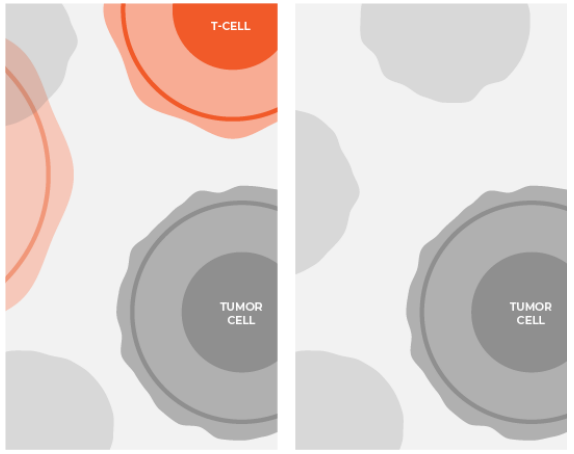
## Antigen escape




## Loss of co-stimulation




## Lack of T-cell persistence




**Multi-specificity**

Expression of three specific chimeric antigen receptors

**New Co-Stim Technology**

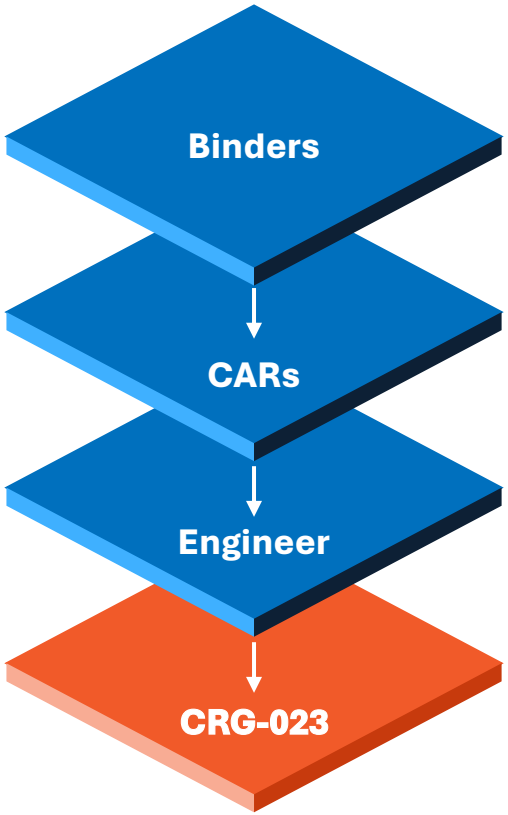
CAR-Engineered, CD2 technology

**Design & Engineering**

New human binders, optimized CAR design, multi-cistronic engineering

# CRG-023 Expresses Three Independent CARs, Targeting CD19, CD20, CD22

## Functional optimization through engineering and screening

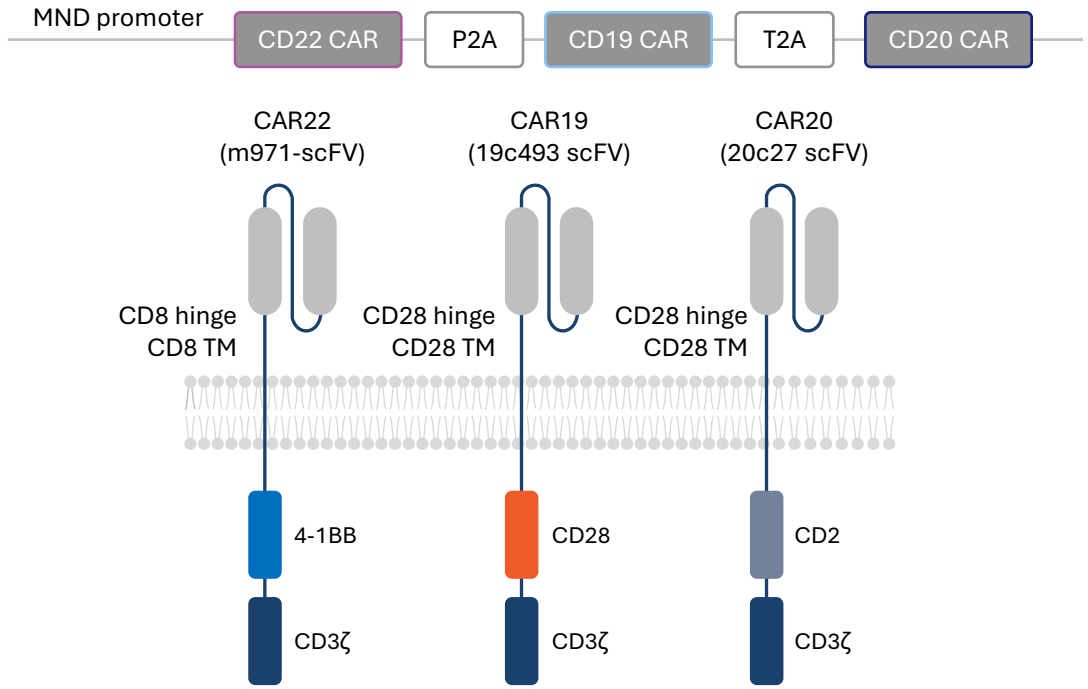



**Novel, human scFvs** from antibody discovery campaigns for **CD19** and **CD20**

Top **CD19 and CD20 binders** as mono-specific CARs

Top CARs in **bi- and tri-** format to determine vector compatibility

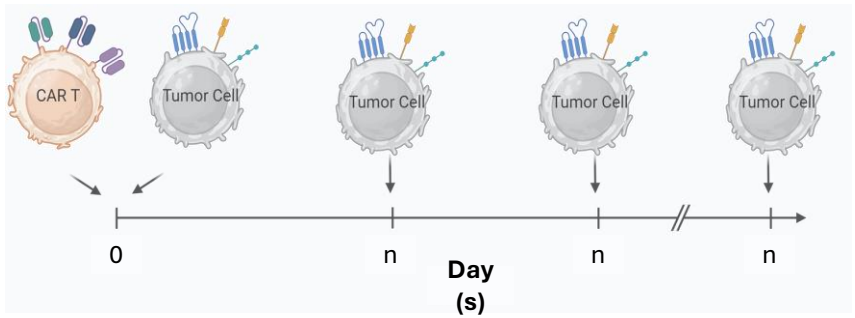
## Single Lentiviral Vector

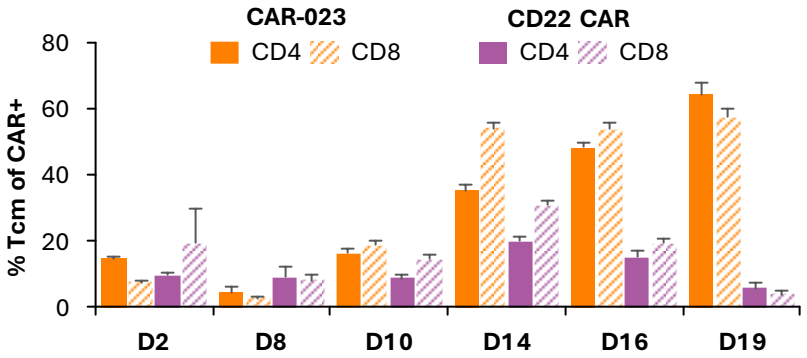



Three different co-stimulatory domains
Novel CD2 co-stim

# CAR-023 Sustained Anti-tumor Activity And Central Memory Phenotype In Long Term, Serial Stimulation Assays

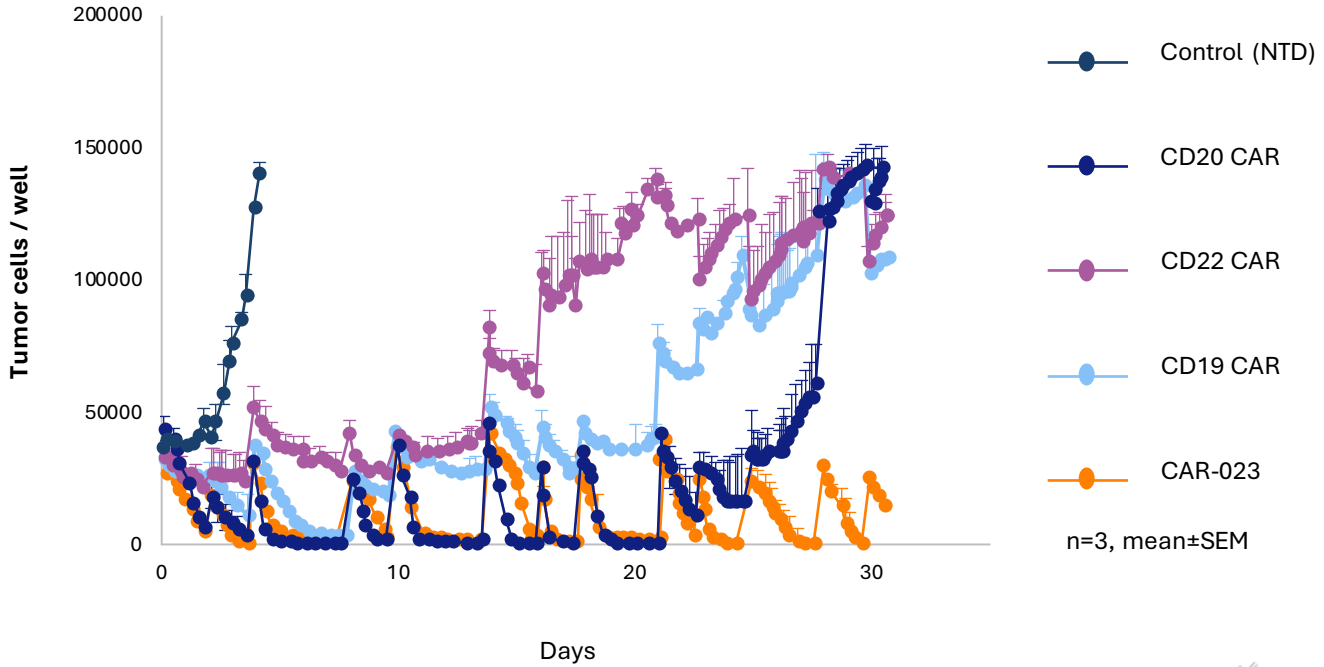
## Serial Stimulation Assay




Tcm based on CD62L and 45RO n=2, mean±SEM

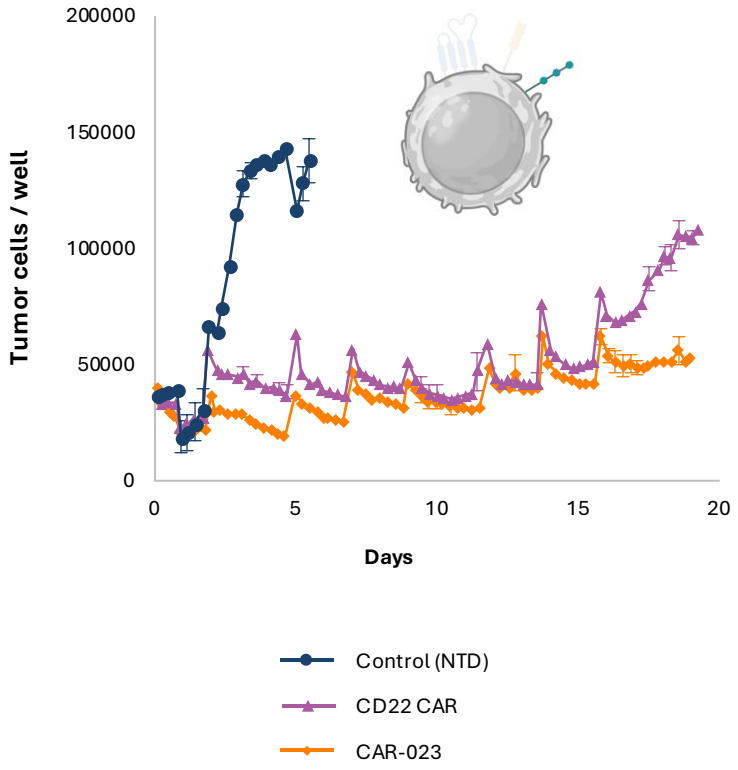
## Serial Stim w/ Raji (CD19+, CD20+, CD22+)



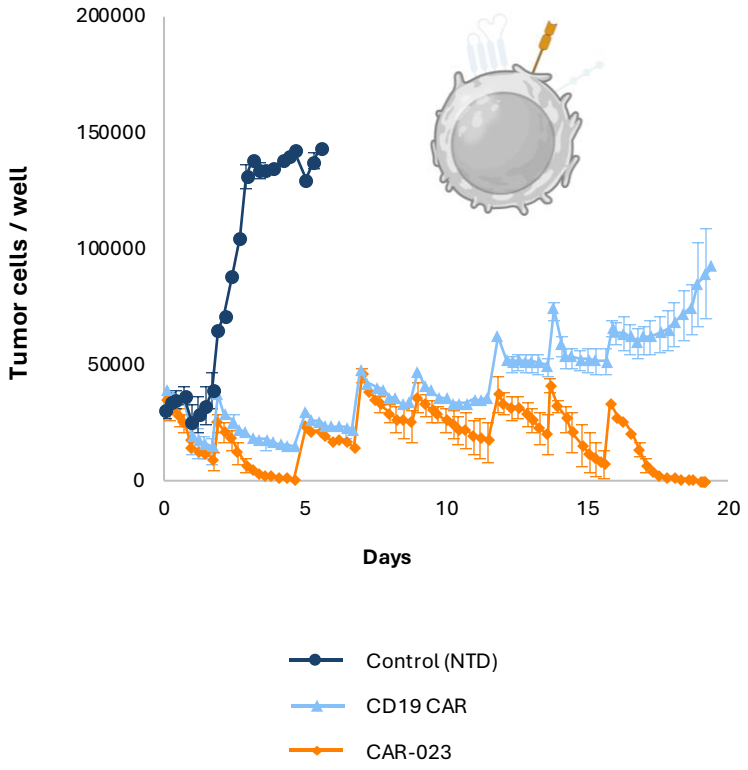

CAR-023 CAR T cells are research produced and representative of CRG-023 product candidate

# CAR-023 Sustained Anti-tumor Function When Activated By Single Antigen

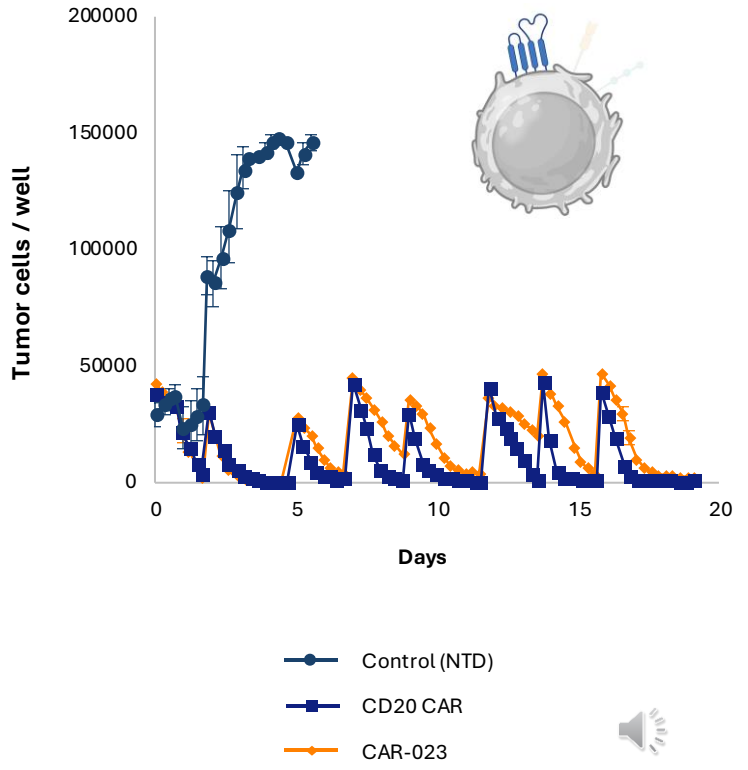
**Serial Stim w/ Raji**
(CD19$^{-}$, CD20$^{-}$, **CD22$^{+}$**)




**Serial Stim w/ Raji**
**(CD19$^{+}$**, CD20$^{-}$, CD22$^{-}$)

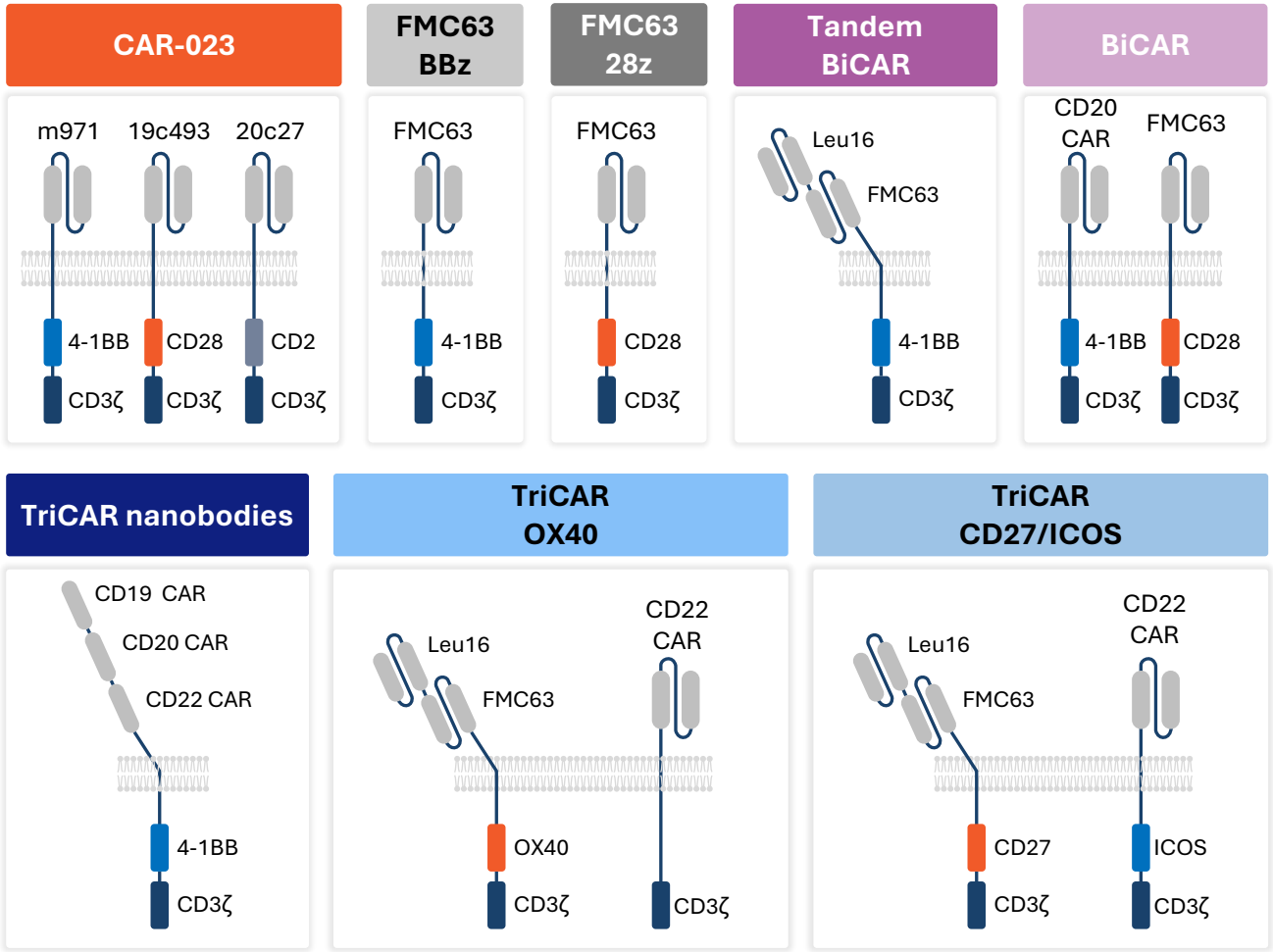


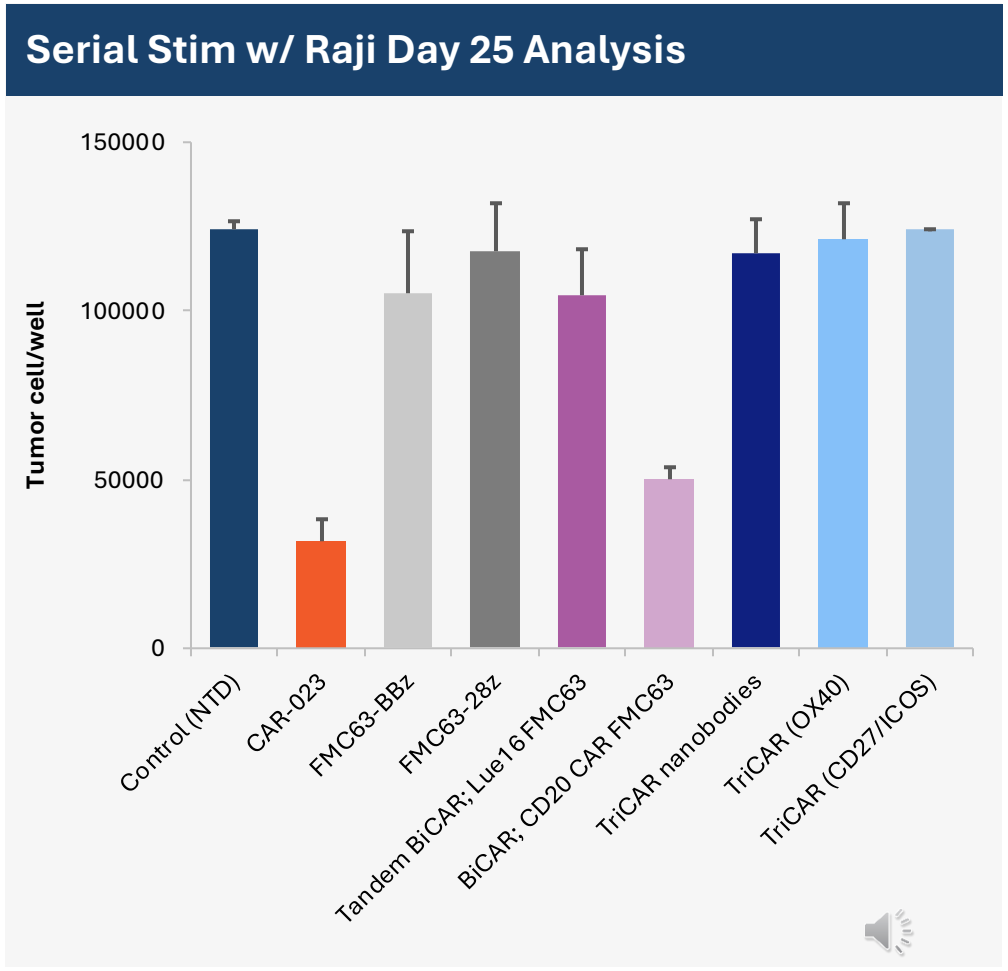

**Serial Stim w/ Raji**
(CD19$^{-}$, **CD20$^{+}$**, CD22$^{-}$)




n=3, mean±SEM

# CAR-023 had Sustained Tumor Control Relative to Benchmarks

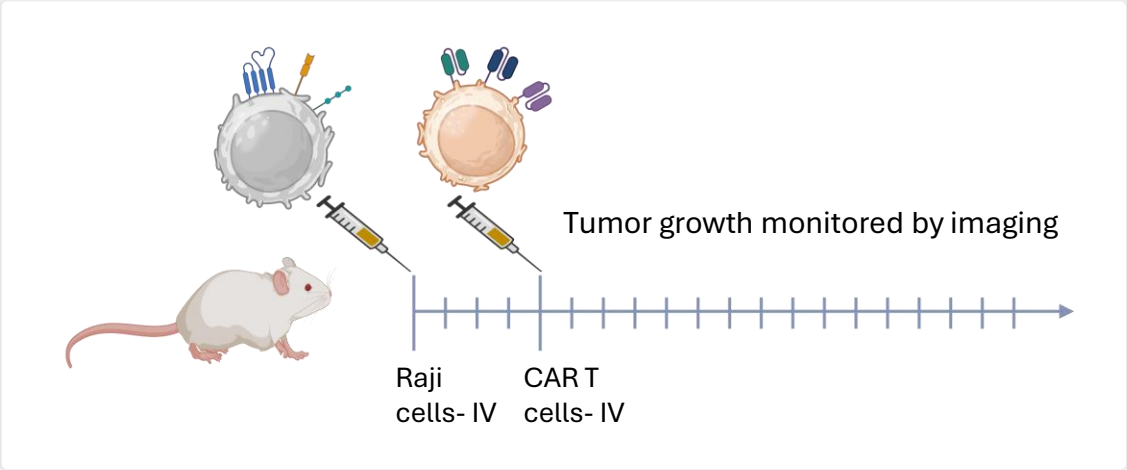


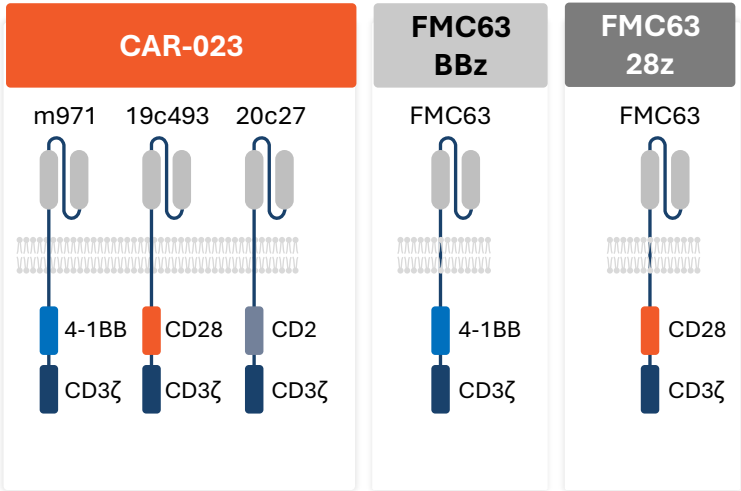



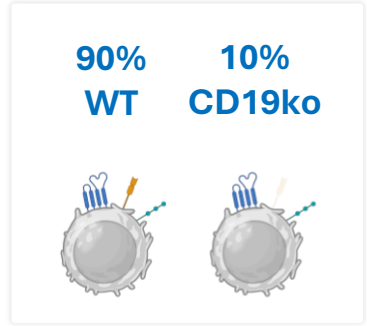

**FMC63 – CD19 scFv** | **Leu16 – CD20 scFv**

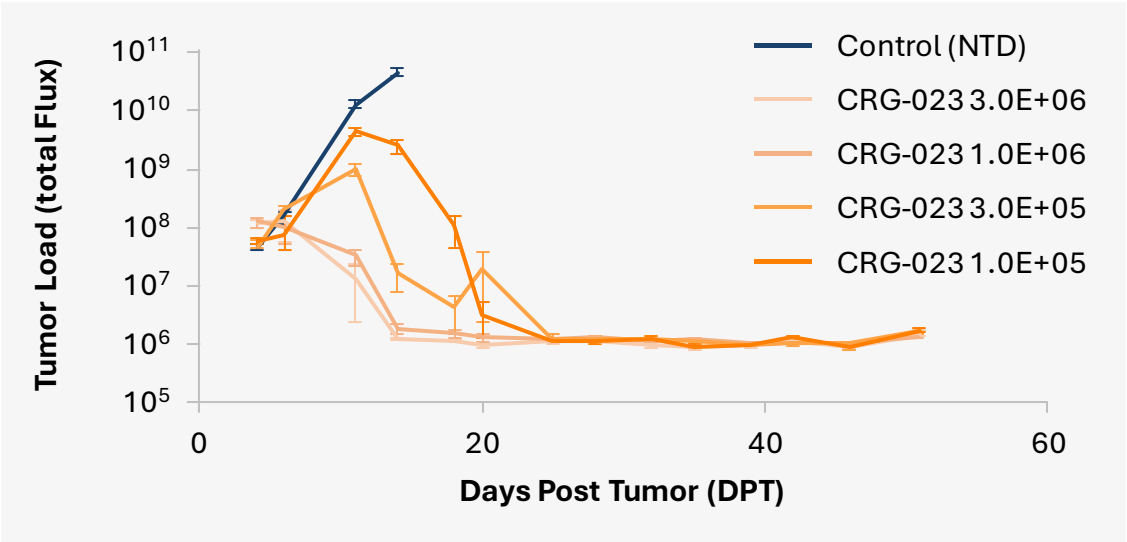
n=2, mean±SEM

# CRG-023 Demonstrated Impressive In Vivo Efficacy At Low CAR T Doses And In Antigen Escape Models

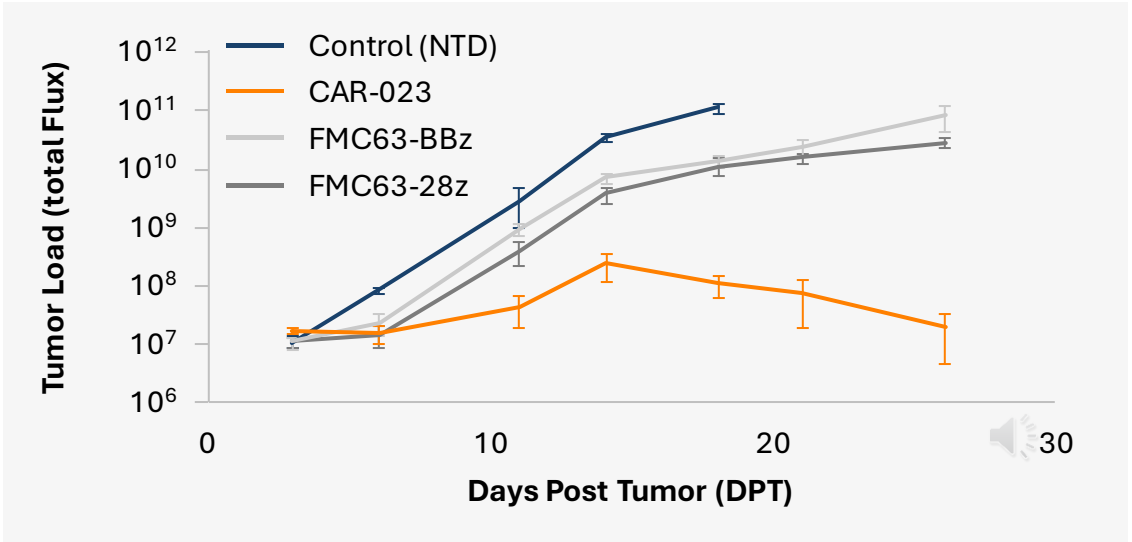


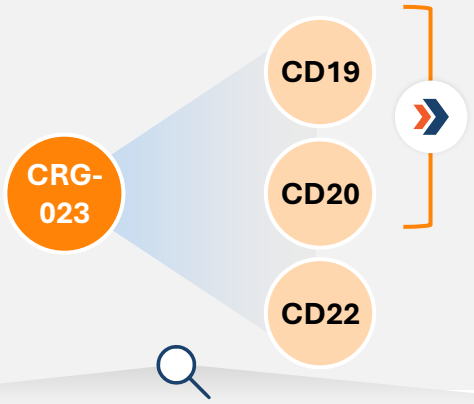

n=10mice/group; 1 representative of 3 donors




n=5mice/group

# CRG-023 Results Showed Enhanced Durable Activity Against Pre-clinical Lymphoma Models

CRG-023 is a tri-specific, tri-cistronic CAR T cell product candidate engineered to target CD19, CD20, and CD22




New binders for CD19, CD20 and a CD2 co-stimulatory domain were design features added to enhance CAR-mediated activity

Durable anti-lymphoma activity was observed in vivo, even at the lowest dose levels assessed and in antigen loss models

CAR-023 had durable anti-tumor activity *in vitro* when tumor cells expressed three, two or even one antigen

CAR-023 outperformed benchmark controls

Mechanistic insights inform preclinical data to support the planned IND