



HER2-Targeted Dual Switch CAR-T Cells Enable Post-Infusion Control of Efficacy and Safety with Small Molecules

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American Society of Gene & Cell Therapy

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ASGCT 21st Annual Meeting

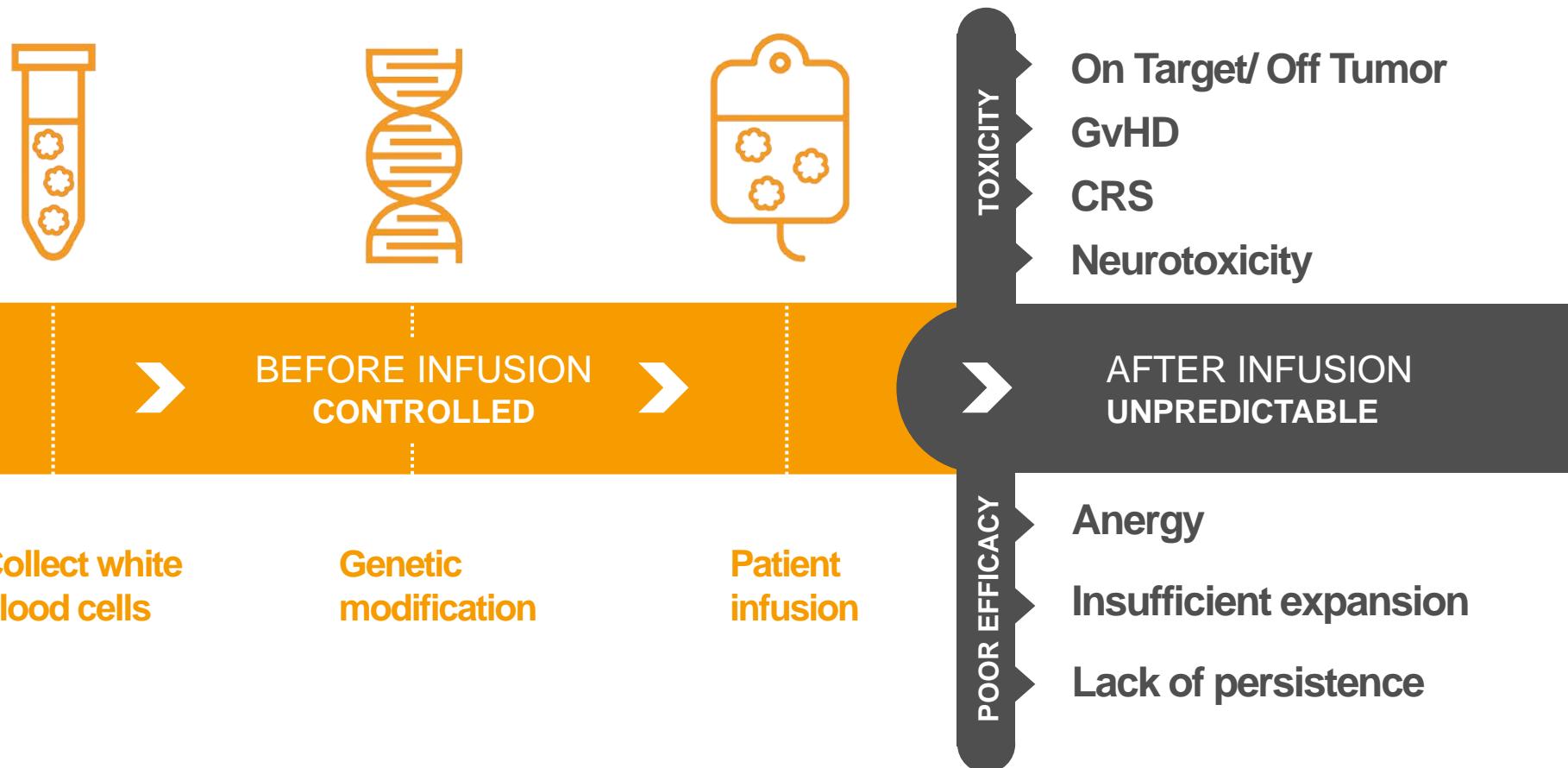
CHICAGO, ILLINOIS MAY 16-19



Disclosure: I am an employee of Bellicum Pharmaceuticals and receive salary, benefits, and equity

Challenges in CAR-T Cell Therapy

Most cell therapies can only be controlled **before** infusion, but **not after** infusion



Controllable CAR-T Cell Therapy

Bellicum's molecular switches allow control **after** infusion



BEFORE INFUSION
CONTROLLED



iC9

SAFETY
switch
to eliminate
toxic cells

AFTER INFUSION
CONTROLLED



iRMC

GO
switch
to activate
immune cells

Collect white
blood cells

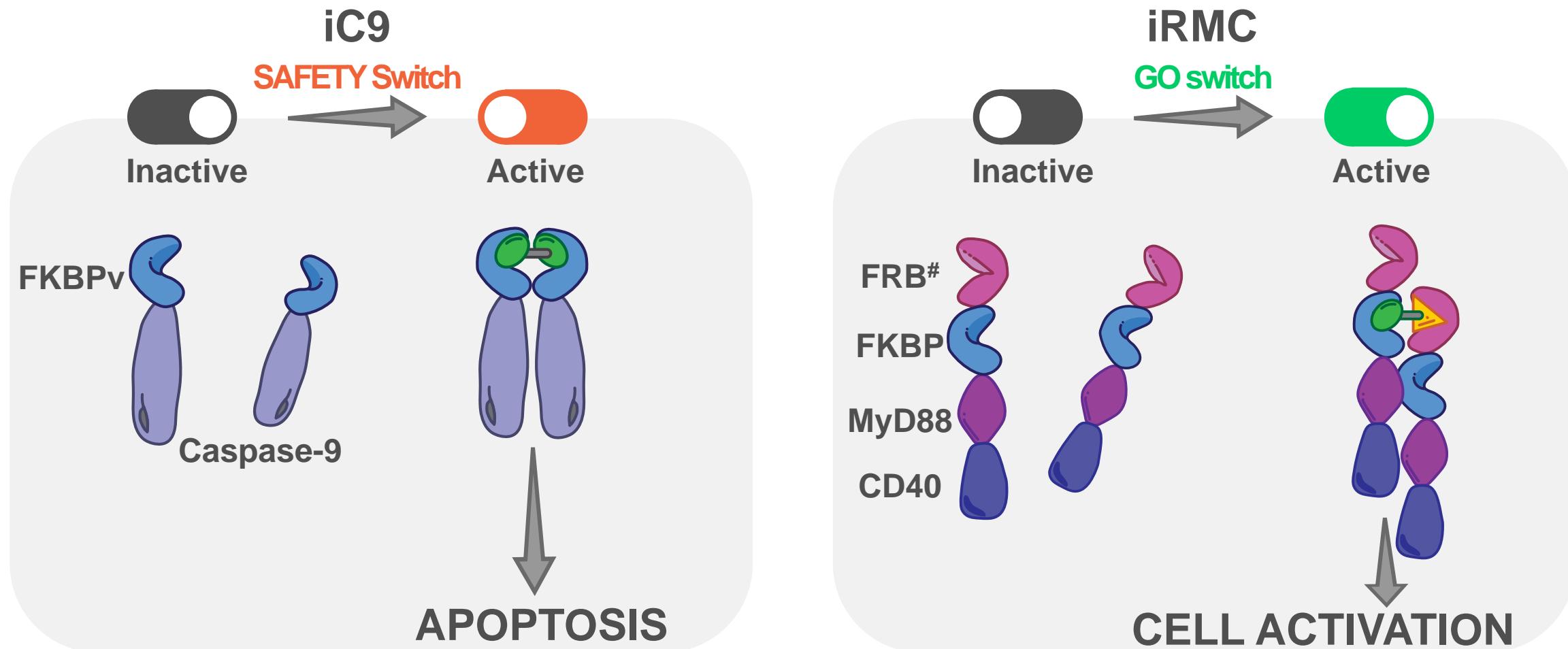
Genetic
modification

Patient
infusion

**Potential for
Improved
Benefit / Risk**

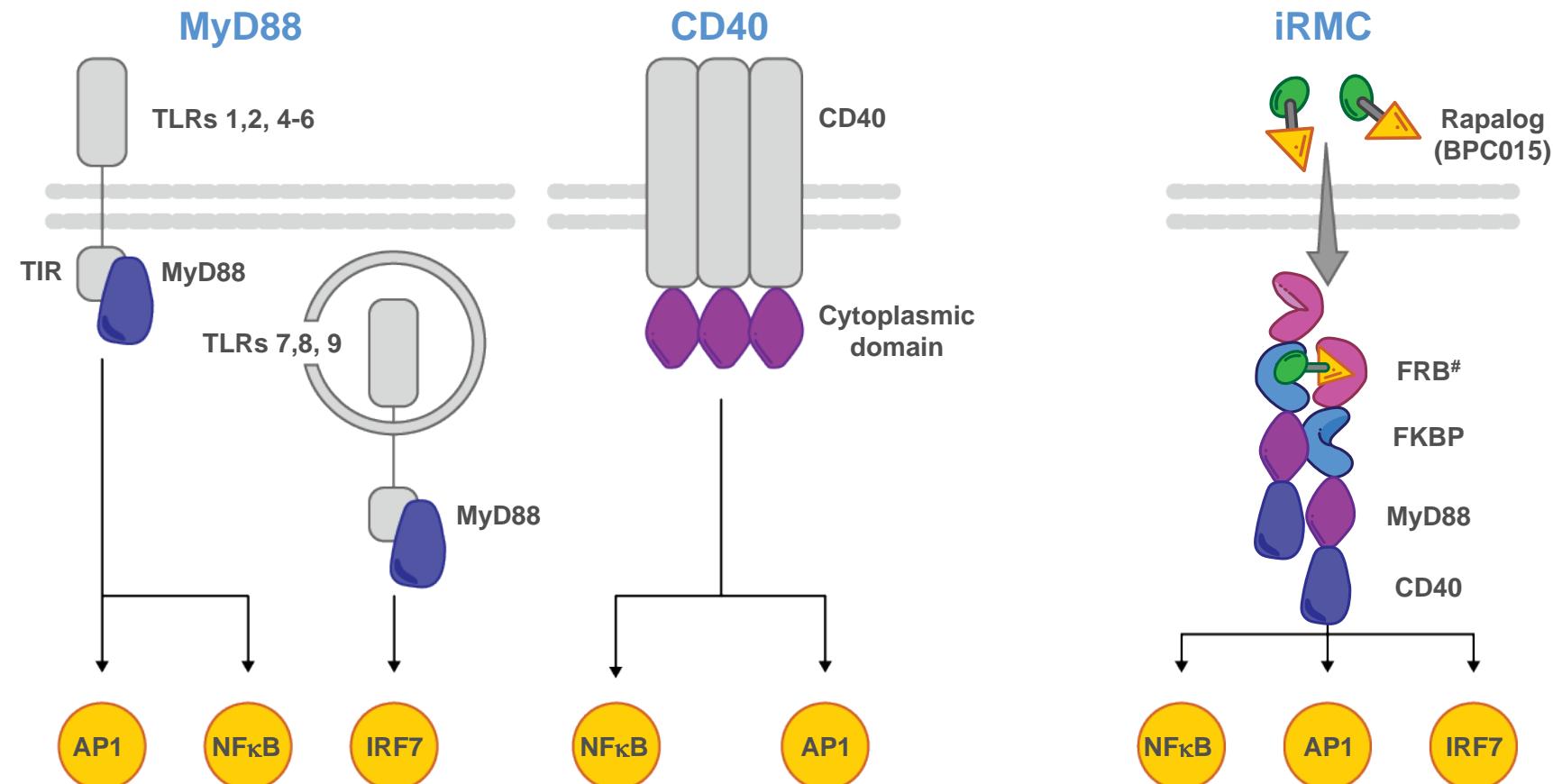
Dimerizer Switches

Dimerization of signaling proteins with dimerizers induce diverse biological outcomes



Inducible MyD88/CD40

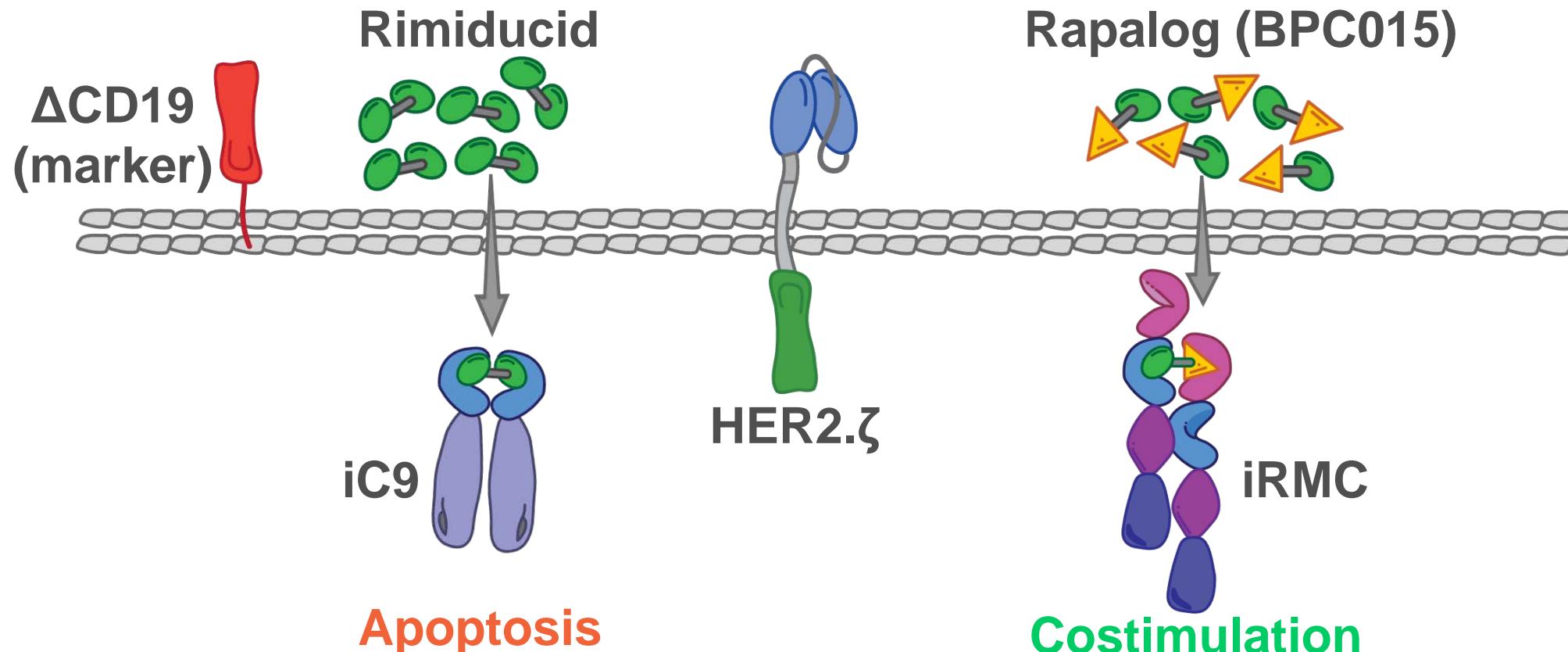
Co-opting MyD88 and CD40 signaling pathways to generate inducible costimulation



Proinflammatory cytokines, Type I IFNs, Proliferation
Other immune functions

HER2 DS CAR-T Design

Vectors encode 1st gen HER2-CAR, iRMC costim, iC9 safety, and CD19 selection marker

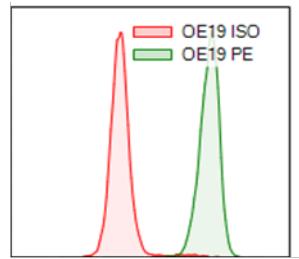


HER2 DS CAR-T Eliminate Target Cells and Proliferate Efficiently

iRMC inducible costimulation enhances HER2 DS CAR-T

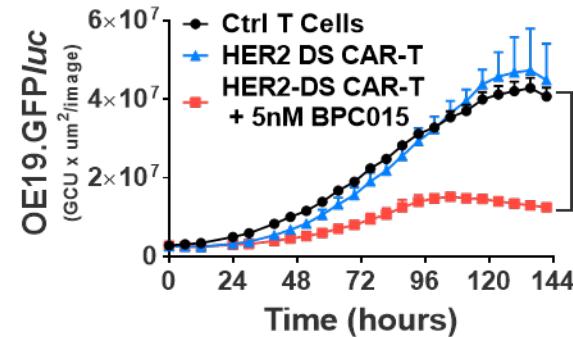


OE19 (HER2⁺) E:T

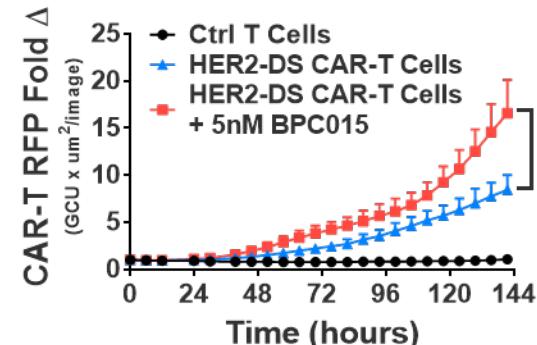


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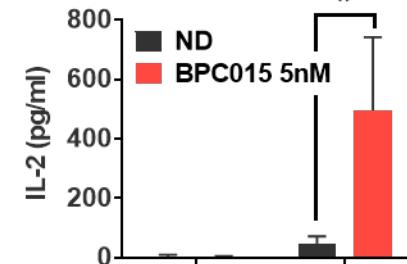
Target Cells



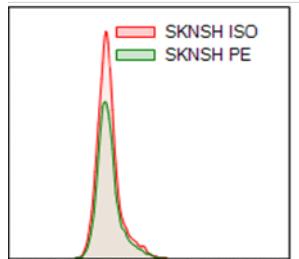
T Cells



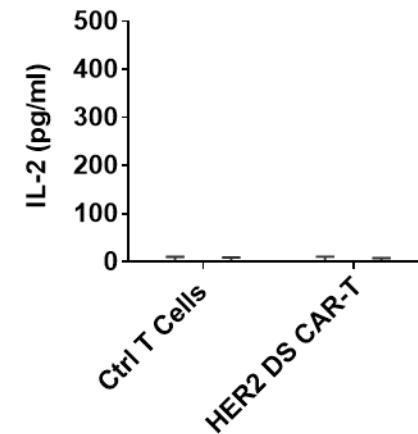
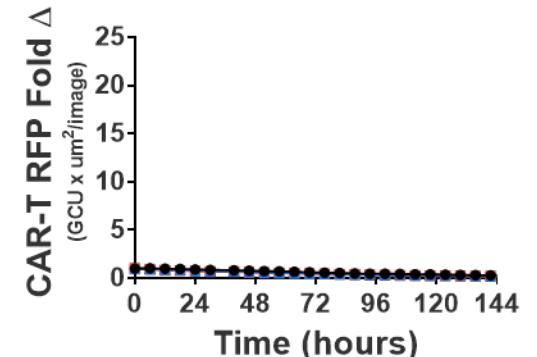
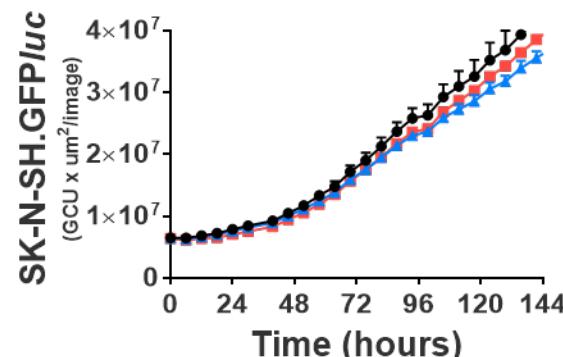
IL-2



SK-N-SH (HER2⁻)



1:5

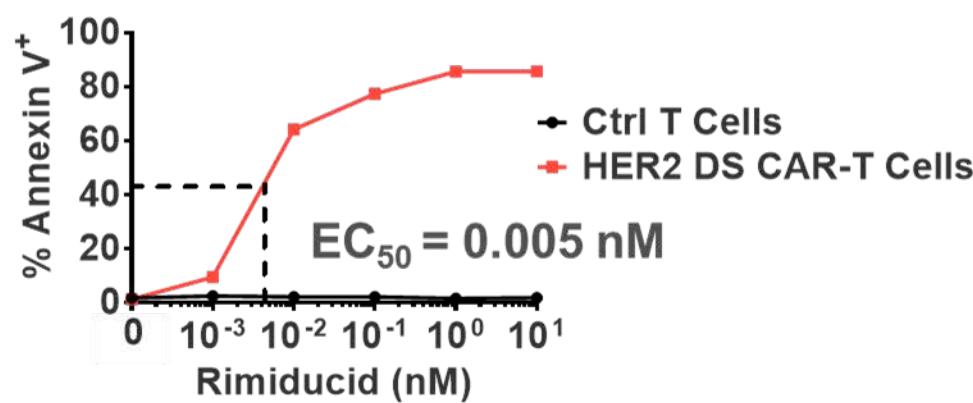


Activation of iC9 Induces Apoptosis in HER2 DS CAR-T

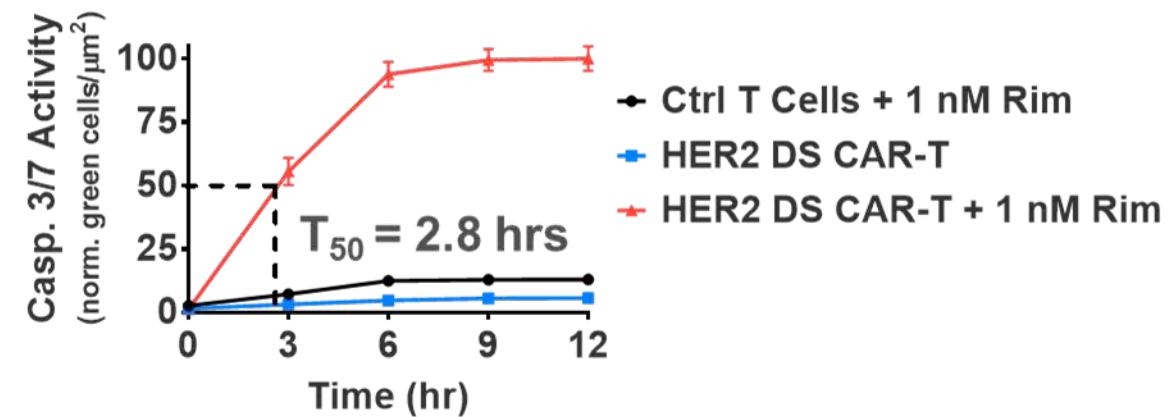
Rimiducid induced apoptosis is sensitive and rapid



Annexin V

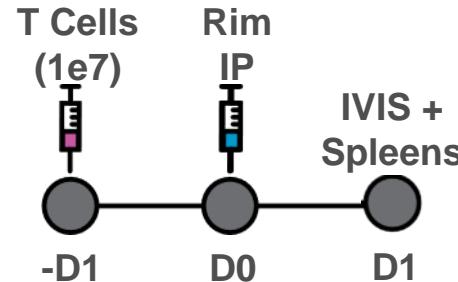


Caspase 3/7



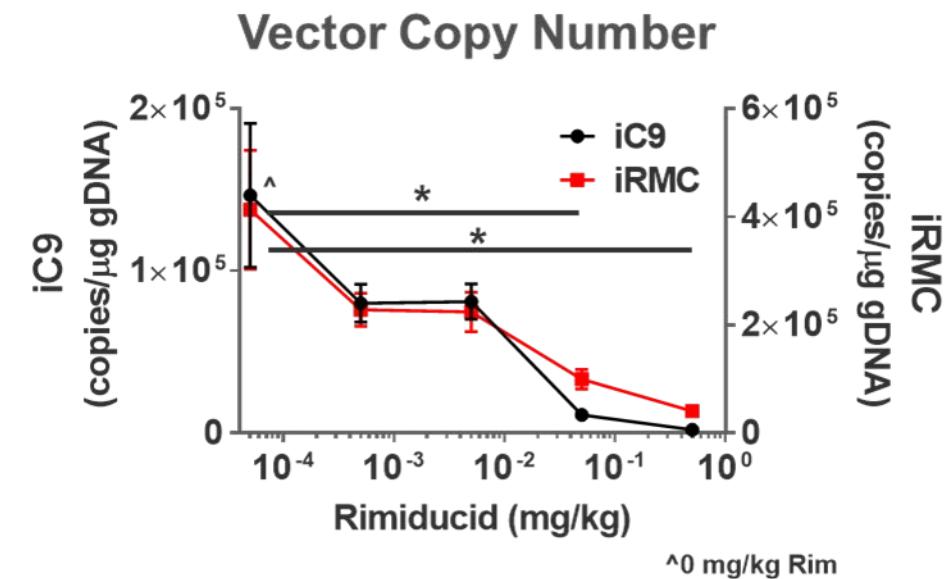
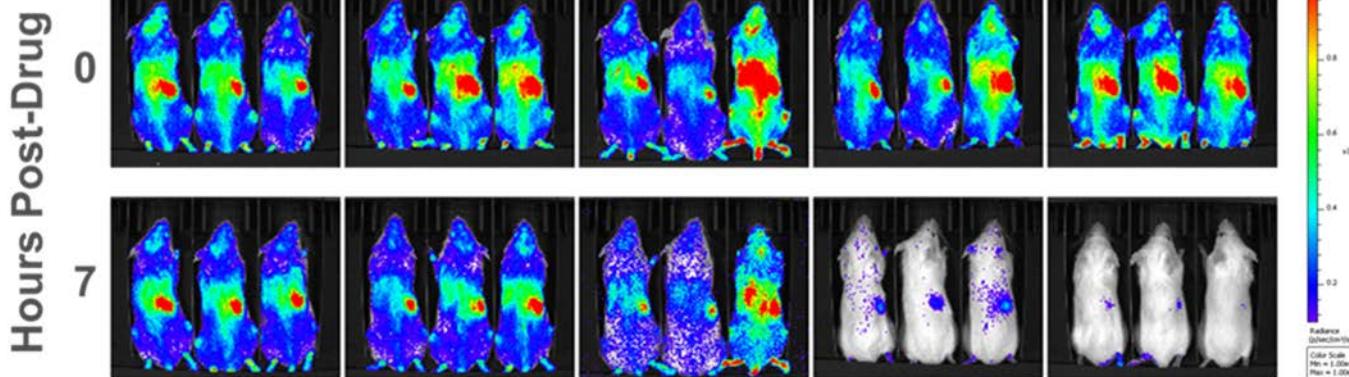
HER2 DS CAR-T Elimination In Vivo with Rimiducid

Rimiducid activation of iC9 is titratable for controlled safety



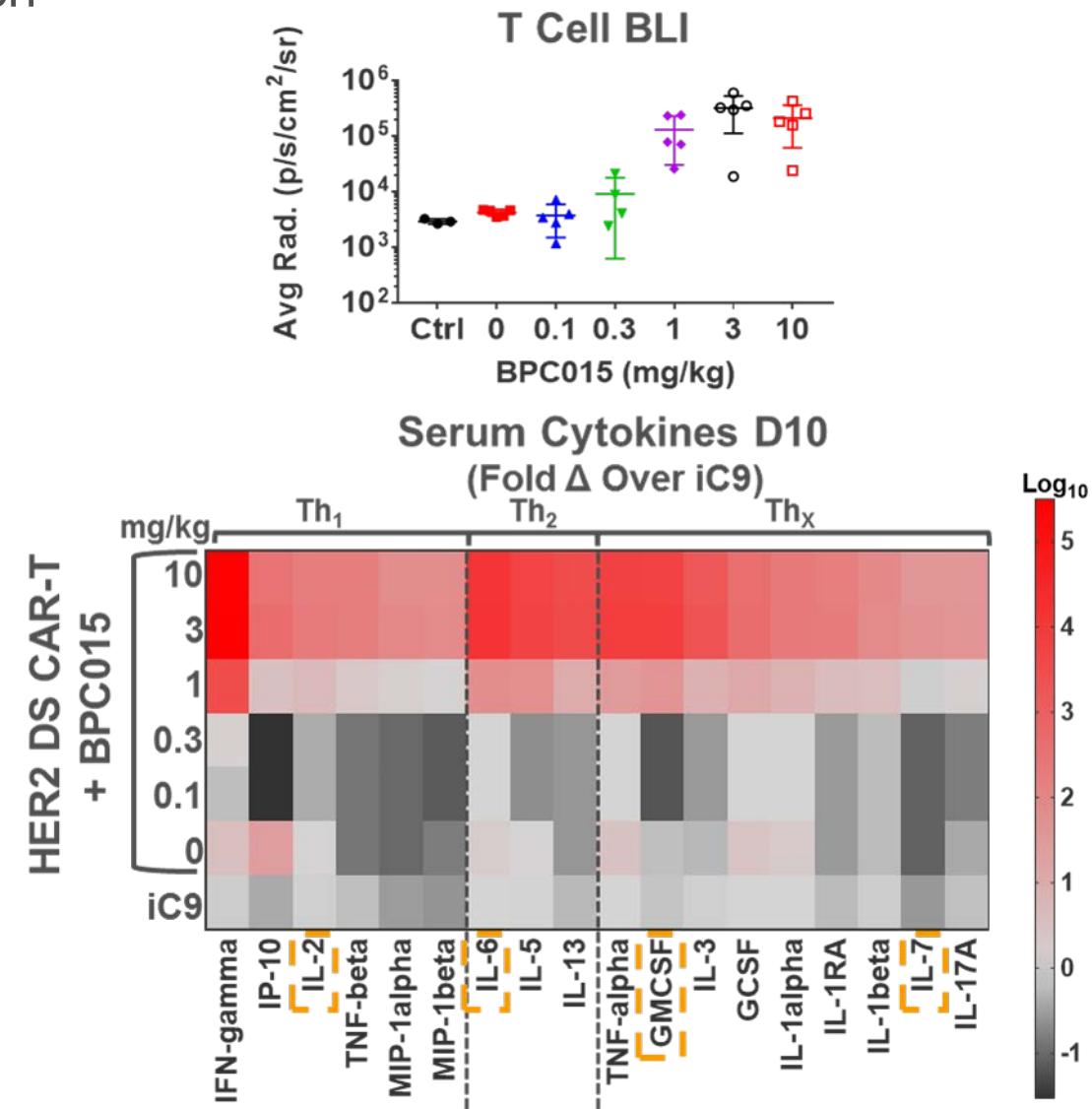
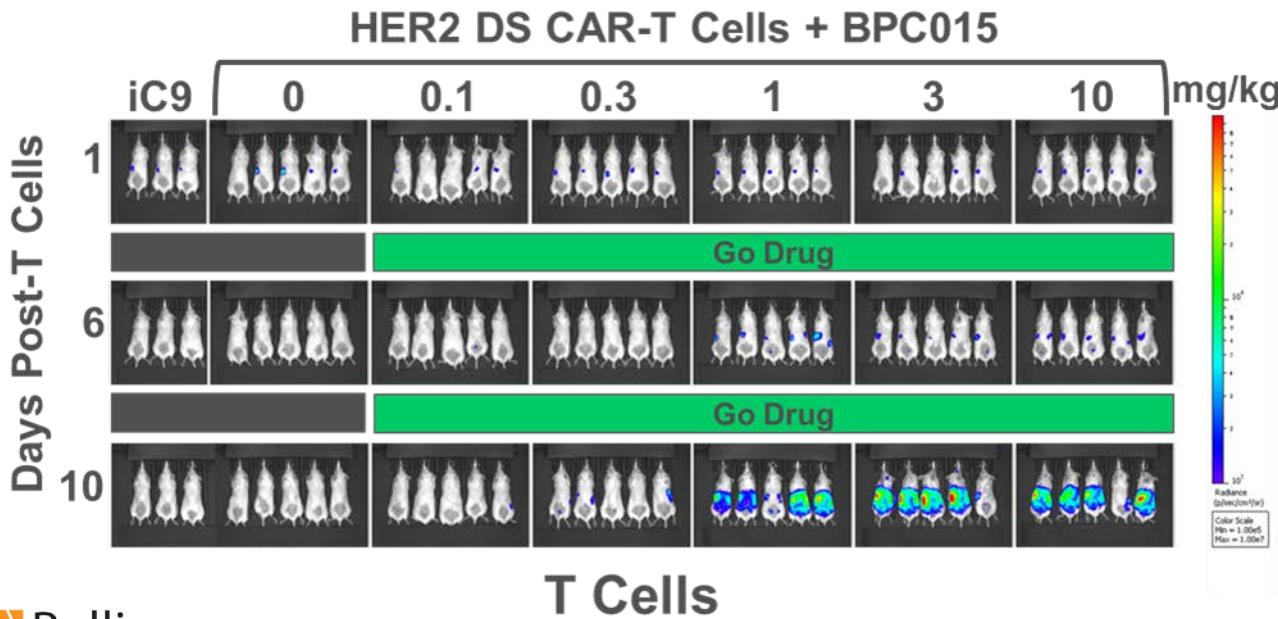
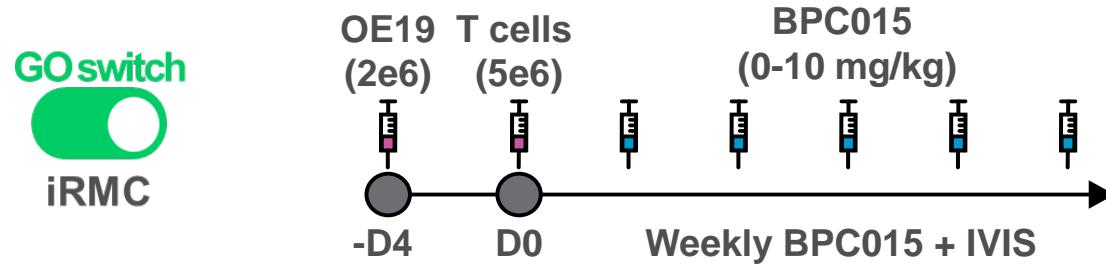
HER2 DS CAR-T Cells (GFP/luc)

Rimiducid (mg/kg)



Controlled Expansion of HER2 DS CAR-T In Vivo

Titration of BPC015 controls HER2 DS CAR-T expansion



HER2 DS CAR-T Eradicate Tumors In Vivo



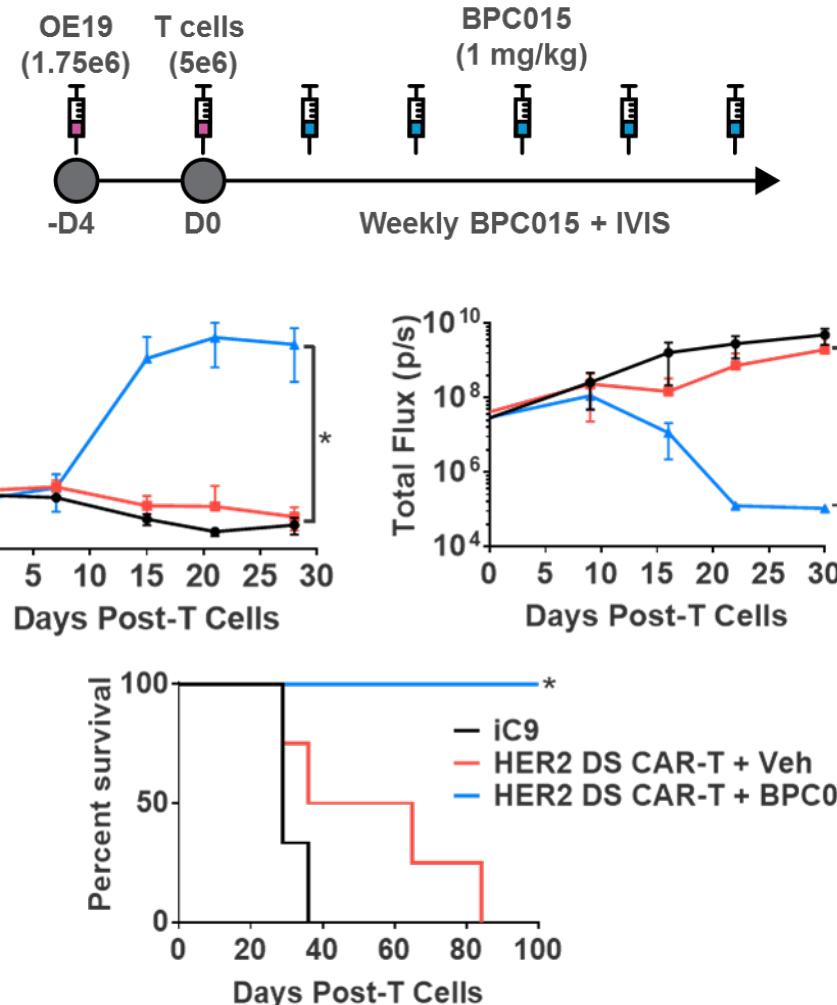
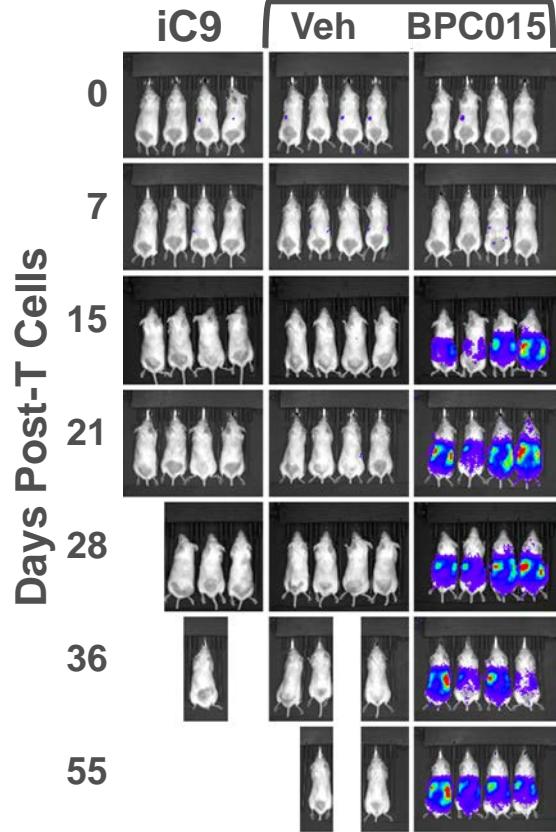
Activation of iRMC mediates CAR-T expansion and tumor clearance

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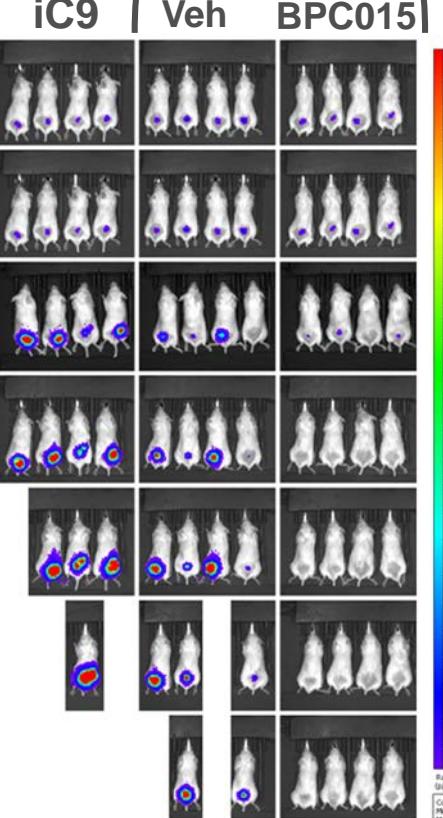
T Cells

HER2 DS CAR-T



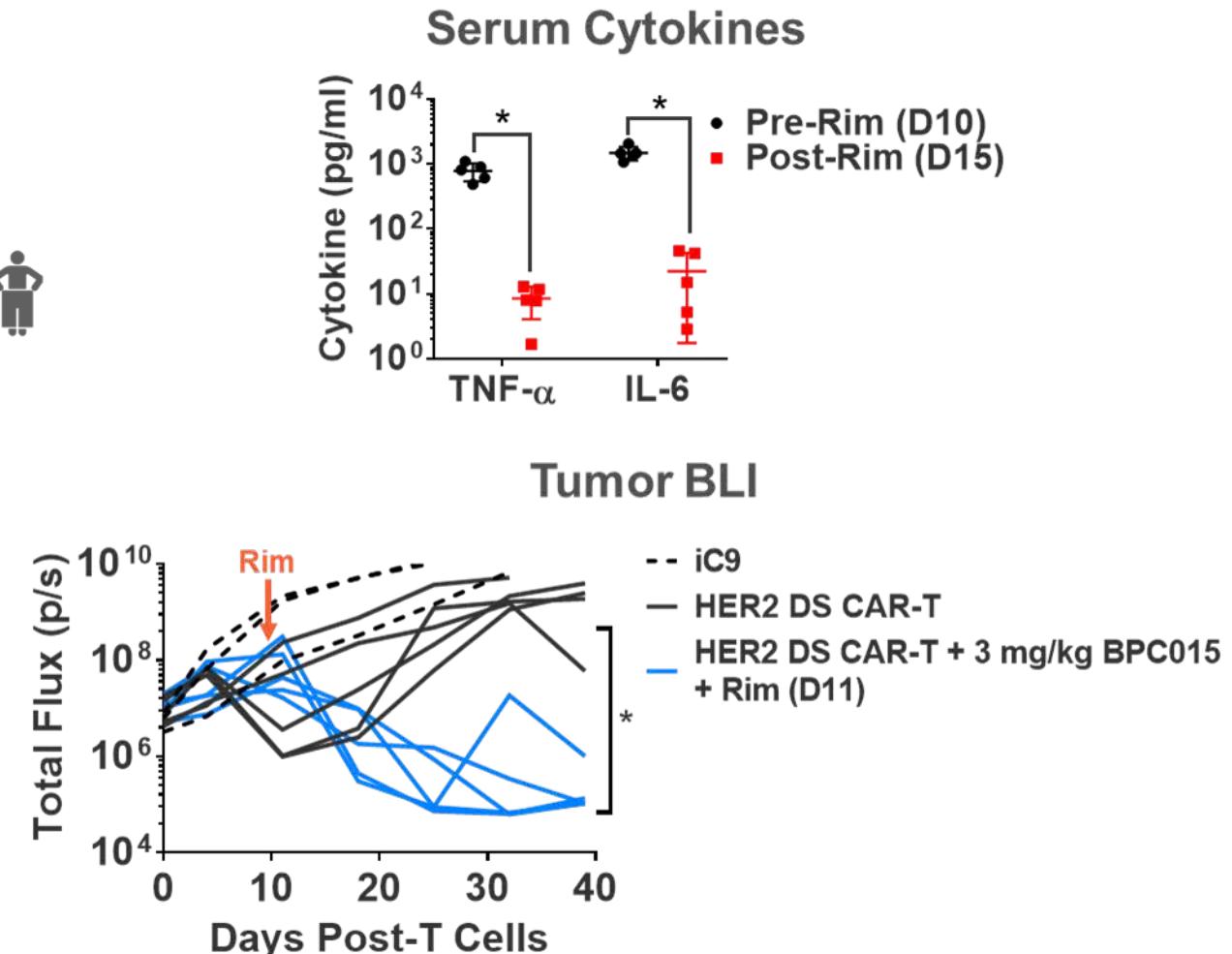
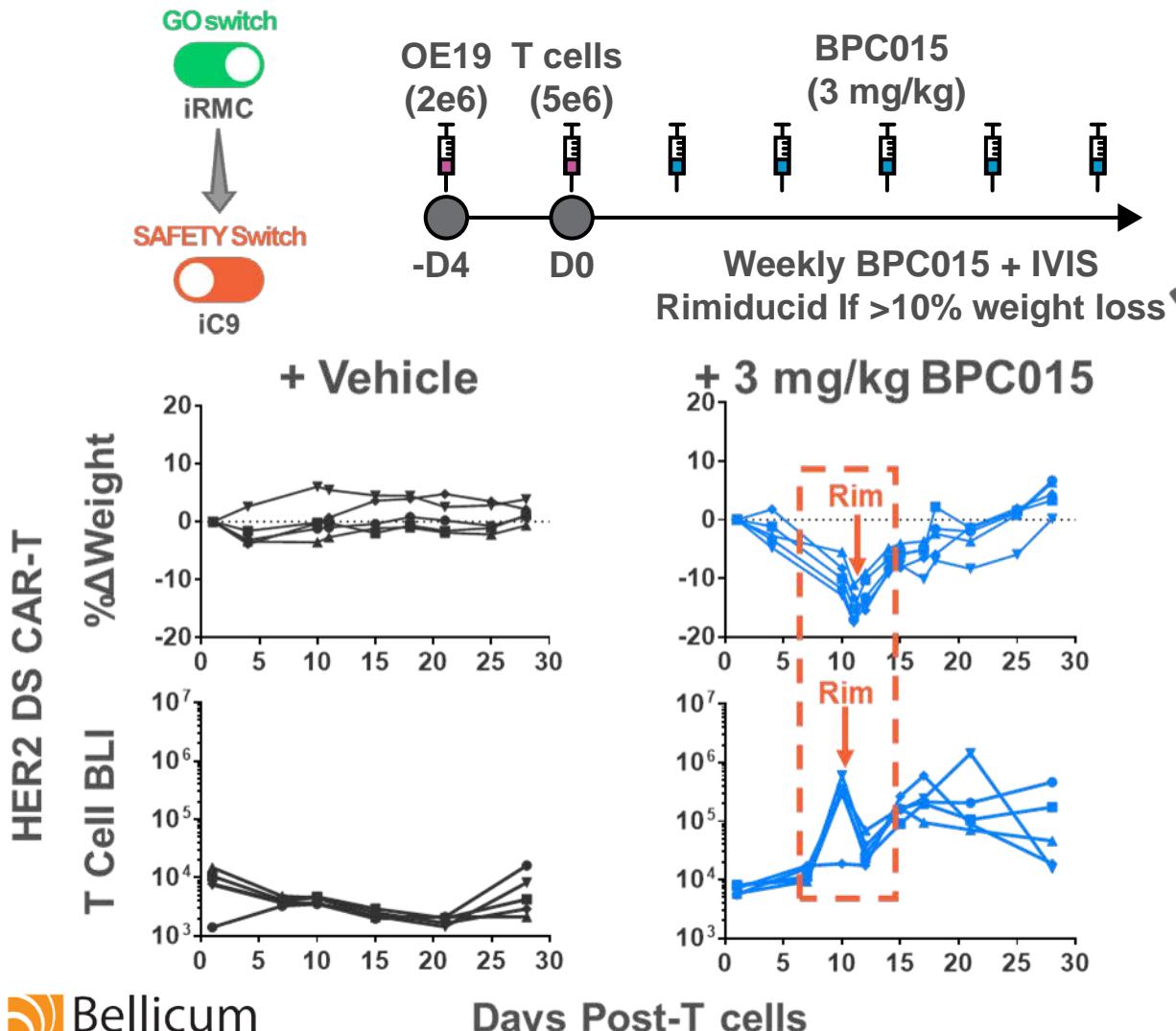
OE19.GFP/luc Tumors

HER2 DS CAR-T



Induction and Resolution of Toxicity in HER2 DS CAR-T

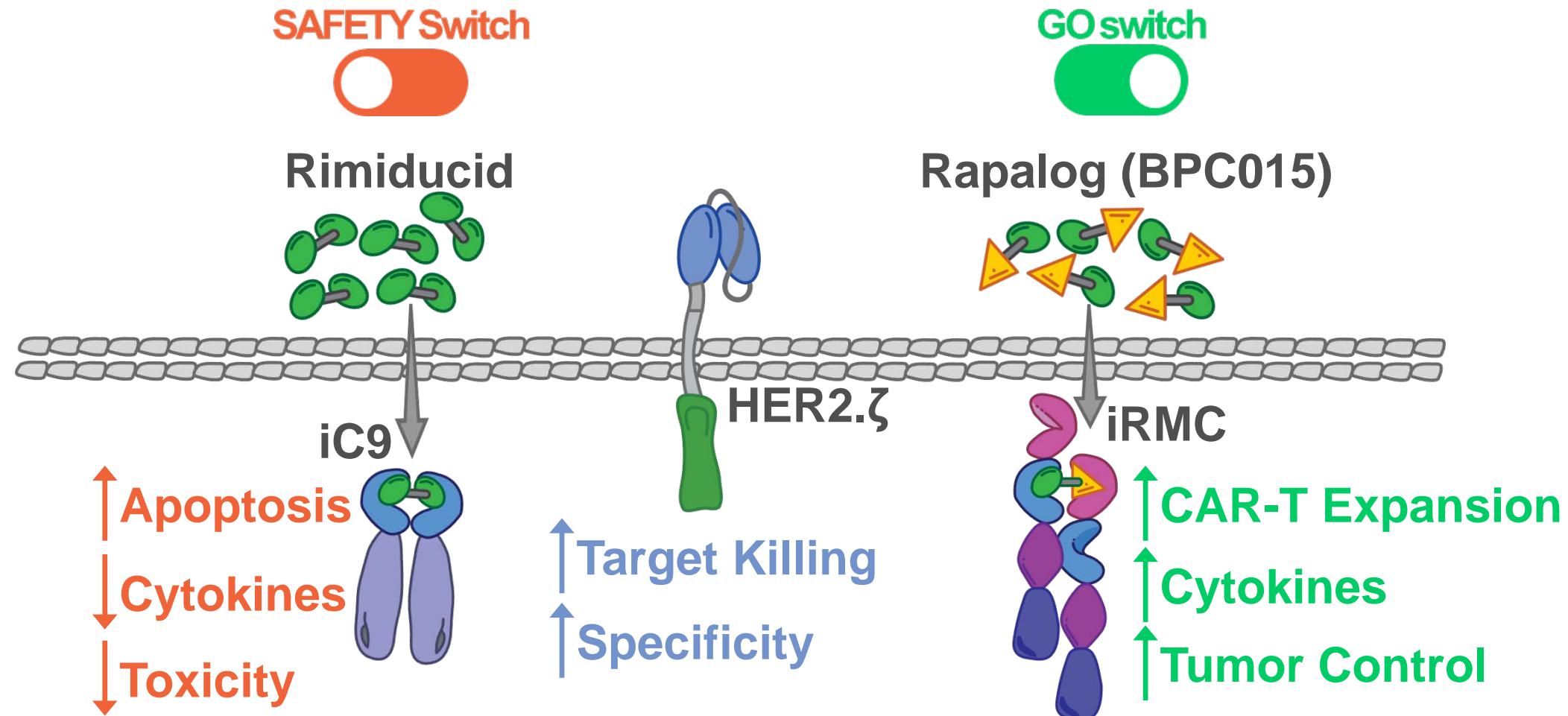
Resolution of acute toxicity with Rimiducid retains tumor control



* p<0.007

Summary HER2 DS CAR-T Cells

Control of CAR-T cells post-infusion



Acknowledgements

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- Margie Harris
- Mice

Vector Production

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