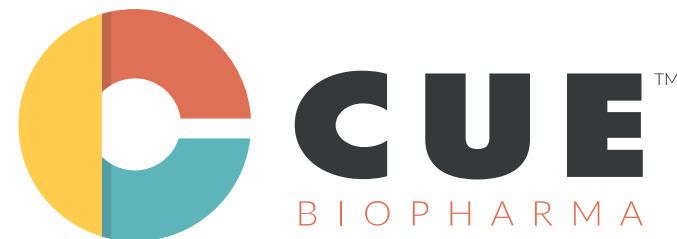


# Cue Biopharma, Inc.

## Q2 Earnings & Business Update

Nasdaq: CUE

August 19, 2024



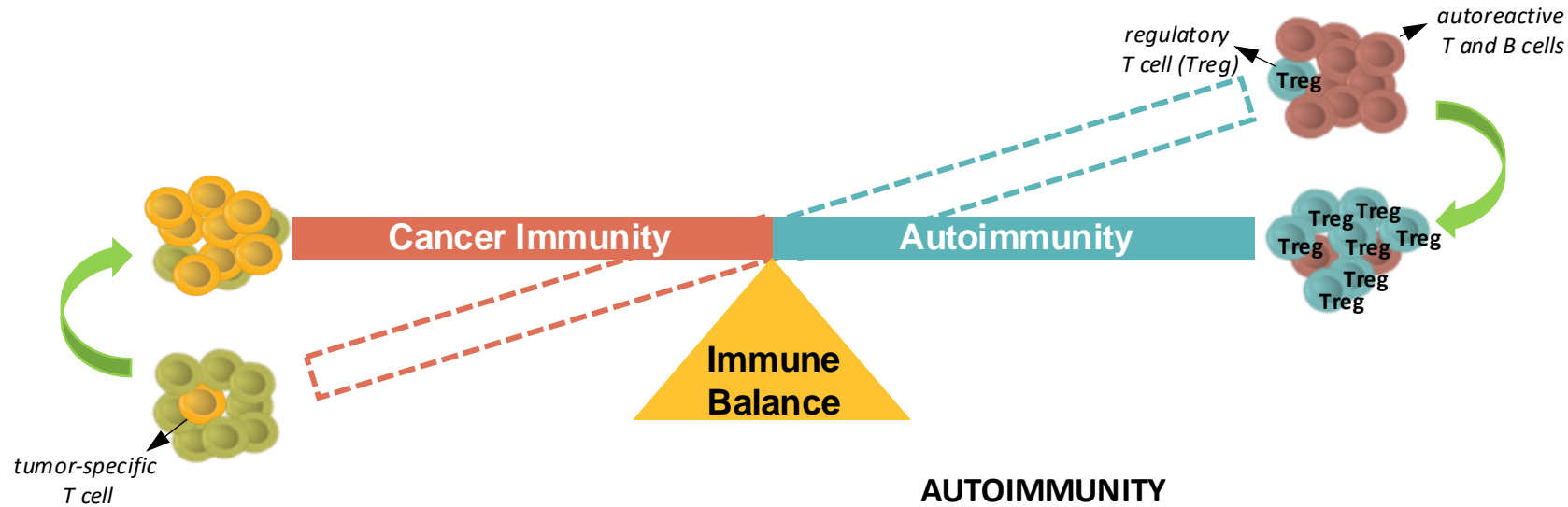
# Forward-Looking Statements Disclaimer

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# Immuno-STATs: Pipeline for Restoration of Immune Balance



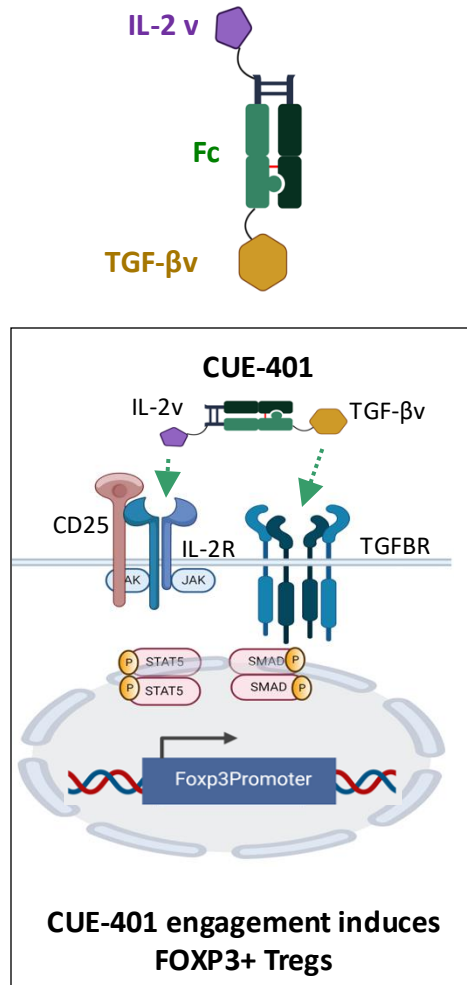
## ONCOLOGY

- **CUE-100 series** (IL-2 targeted to tumor-specific T cells)
  - **CUE-101 (HPV-E7)** (R/M HNSCC)
    - Efficacy: > **doubling of ORR & mPFS vs SoC**
    - Alignment with FDA on a registration path
  - **CUE-102 (Wilms' Tumor-1, WT-1)** (Ova., CRC, Gastric, Pancr.)
    - Ph 1a monotherapy dose escalation completed
    - Evidence of anti-tumor activity in several patients
  - Pre-clinical pipeline of Immuno-STATs targeting KRAS (G12D/V), MAGE-A4, MART-1, NY-ESO1, PRAME, etc.

## AUTOIMMUNITY

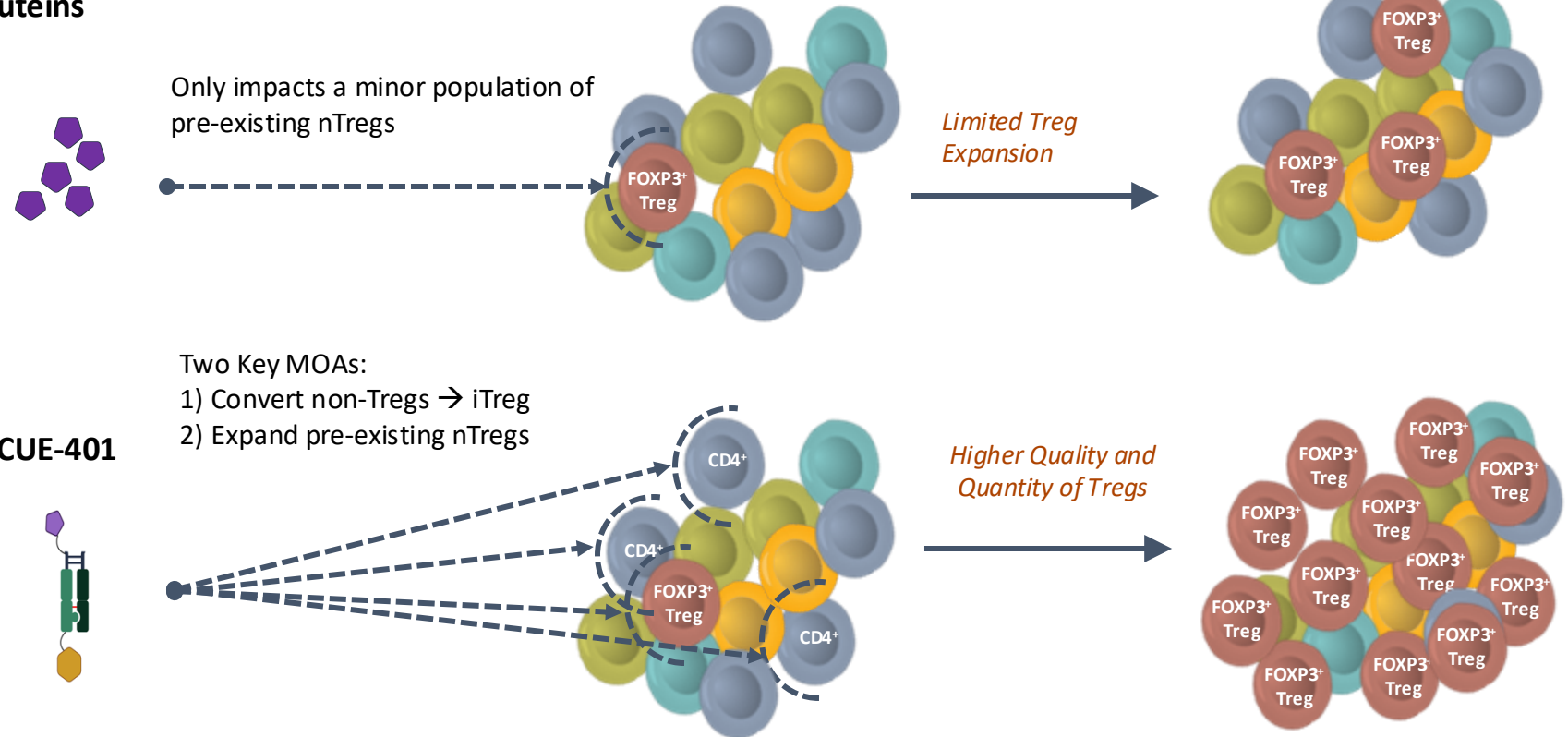
- **CUE-401 (Regulatory T cells, Tregs)**
  - Biologic for conversion and expansion of new Tregs
  - Broad applications in autoimmune and inflammatory diseases
  - Partnered with Ono Pharmaceuticals (option for 50% US rights)
- **CUE-500 Series (targeting autoreactive B cells)**
  - MoA: T cell-mediated B cell depletion
  - Potential for a biologic to achieve "CAR-T-like" efficacy
  - Broad applications in many autoimmune diseases

# CUE-401: IL-2/TGF- $\beta$ Bispecific for Treg Conversion and Expansion



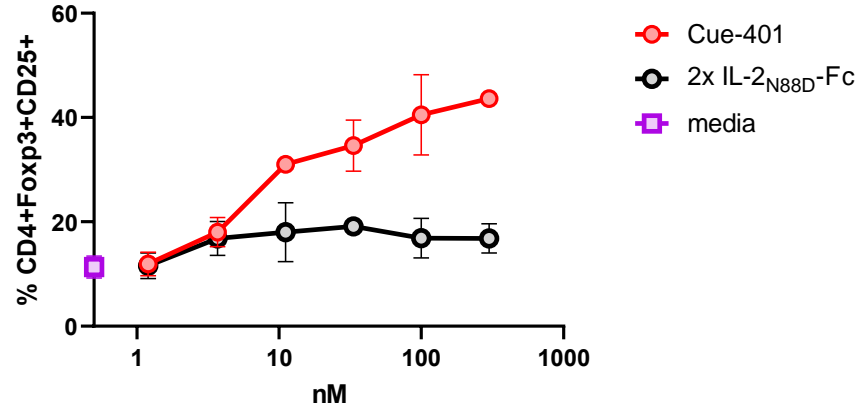
## CUE-401 vs. Competitive Molecules: Superior Differentiation

CD25-biased IL-2 muteins



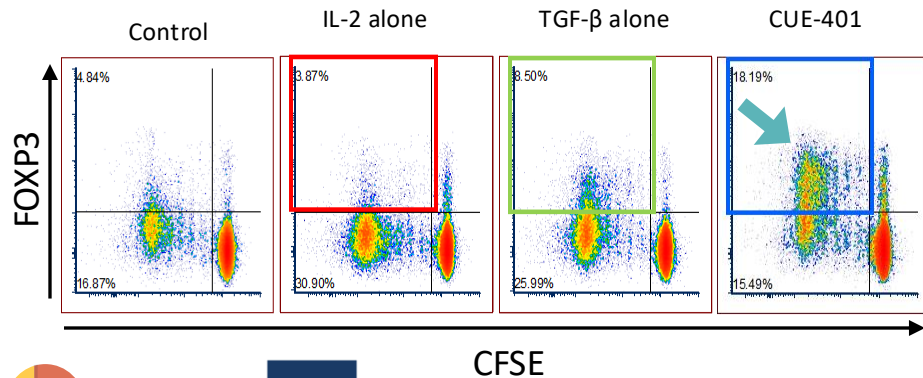
# CUE-401: Differentiated MoA and In Vivo Efficacy

Human MLR (GVHD): Treg Expansion  
CUE-401 vs IL-2 munein

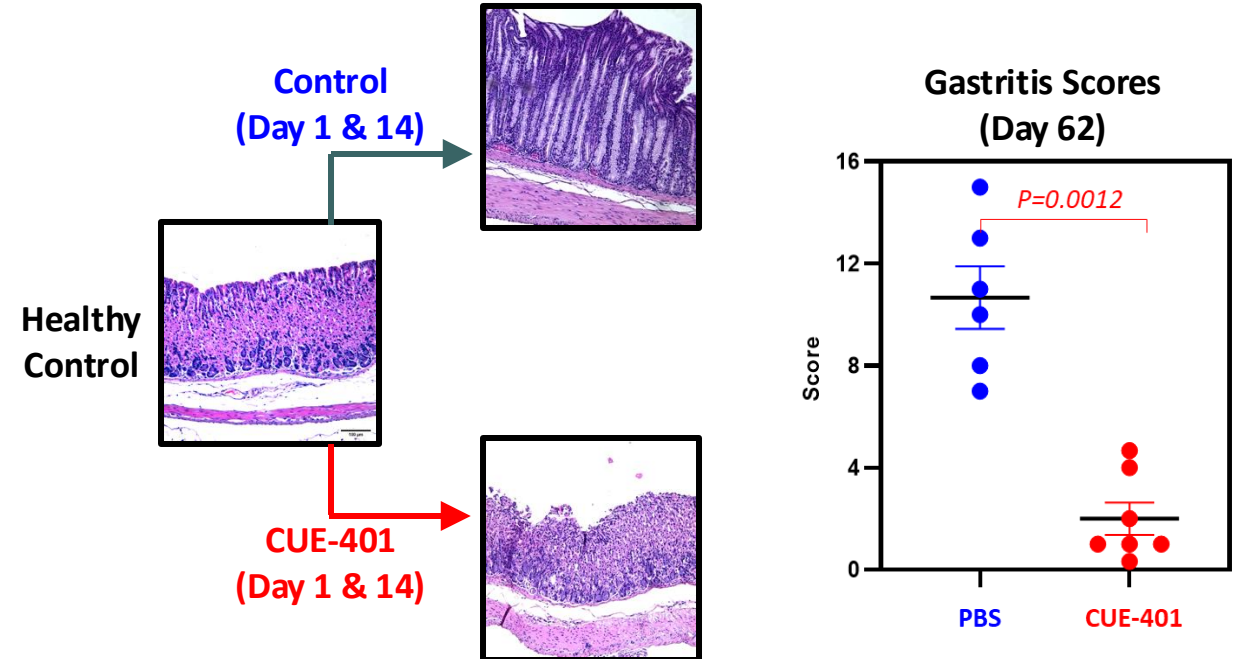


## CUE-401 MoA:

Treg differentiation requires both IL-2 and TGF- $\beta$  signals



*Short-term treatment with CUE-401 results in significant long-term protection from gastritis and tissue destruction*

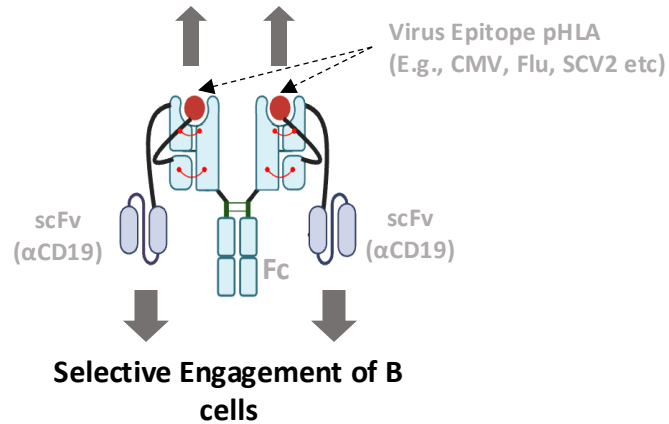


Source: Sponsored Research Collaboration with Dr. Richard DiPaolo, St. Louis University



# CUE-500 Series: Selective T Cell Engagers for B Cell Depletion

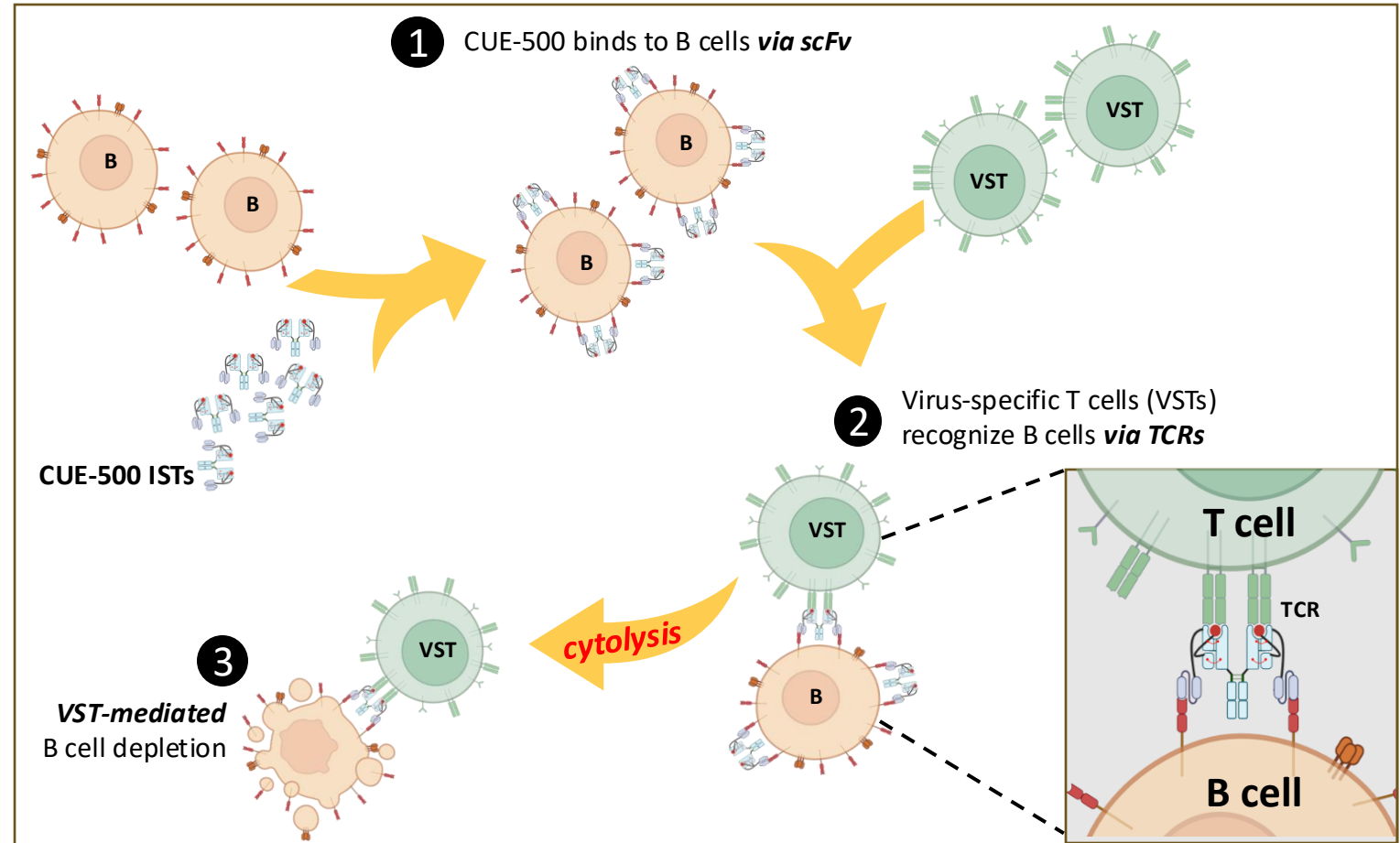
## Selective Engagement of Virus-Specific T Cells (VSTs)



## Advantages of VSTs over other T cells:

- ✓ Trained memory killer T cells
- ✓ Present in high frequency in peripheral (diseased) tissue<sup>1,2,3,4</sup>
- ✓ Rapid serial killing function
- ✓ Avoids broad immune activation
- ✓ No x-reactivity towards self-tissue

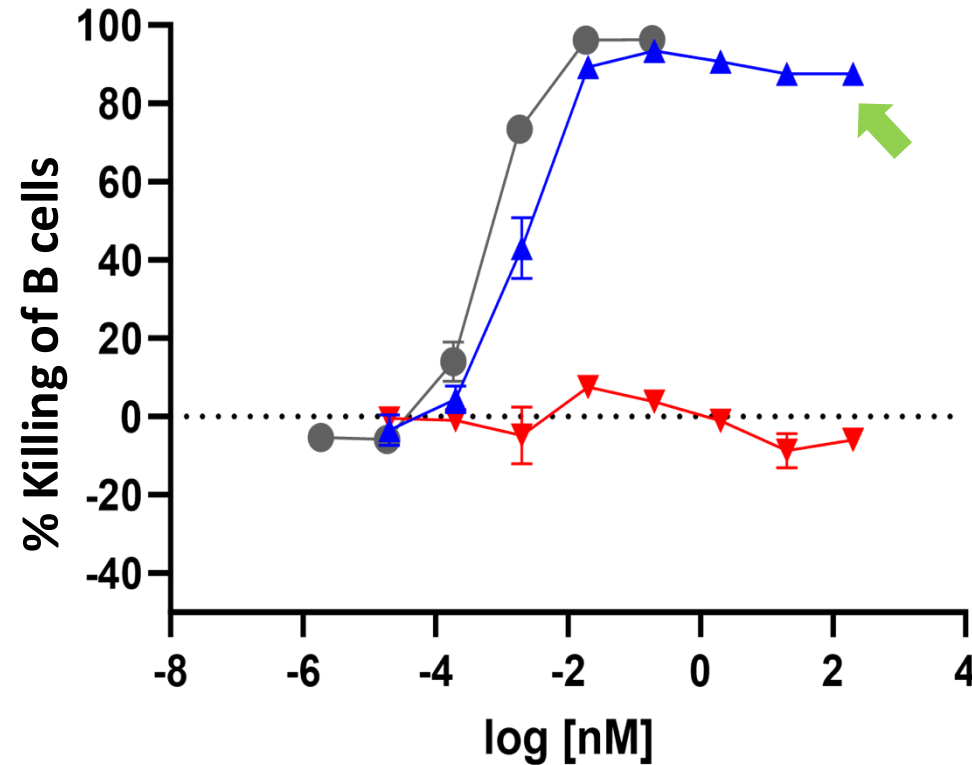
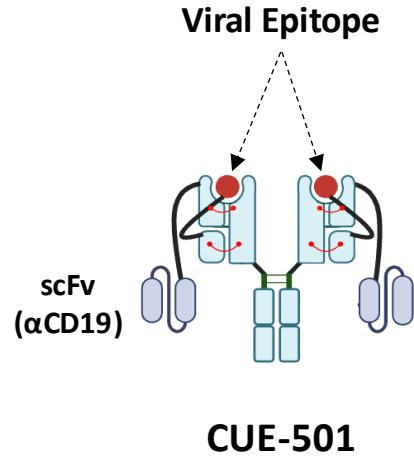
1. Poon et al., Cell Rep. 2021 Nov 30;37(9):110071
2. Tan et al., Arth. Res. 2000
3. Scotte et al., Eur. Jour. Imm 1999
4. Turcinov et al., Arth. Rheum. 2023



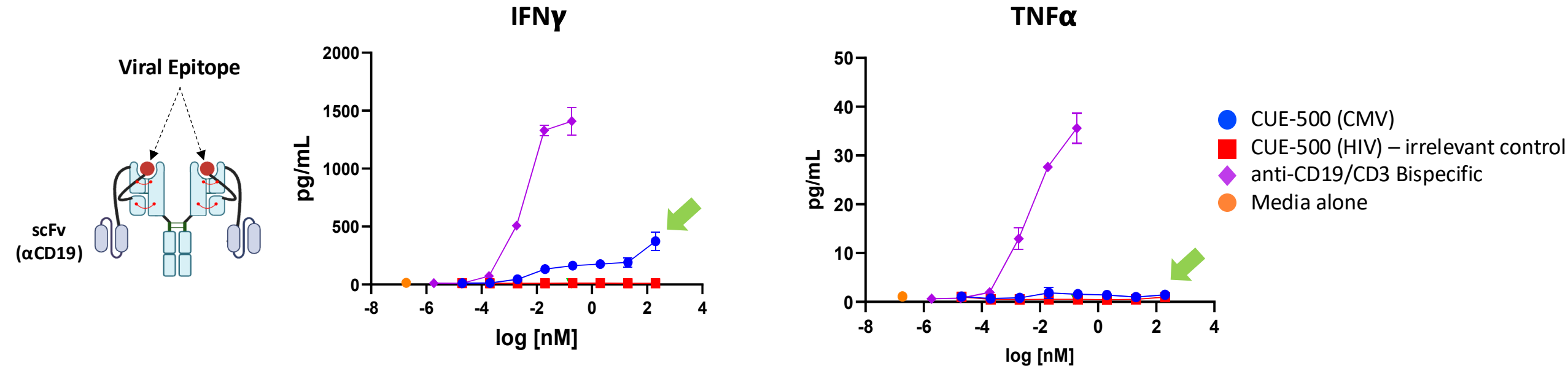
**Note:** CUE-500 series leverages a derisked, validated framework via the oncology clinical experience

# CUE-501: Potent and Selective B Cell Killing

CUE-501 selectively redirects CMV-specific memory CD8+ T cells to kill human B cells



# CUE-501 vs. Bispecific Pan T Cell Engagers: Significant Reduction in Cytokine Release



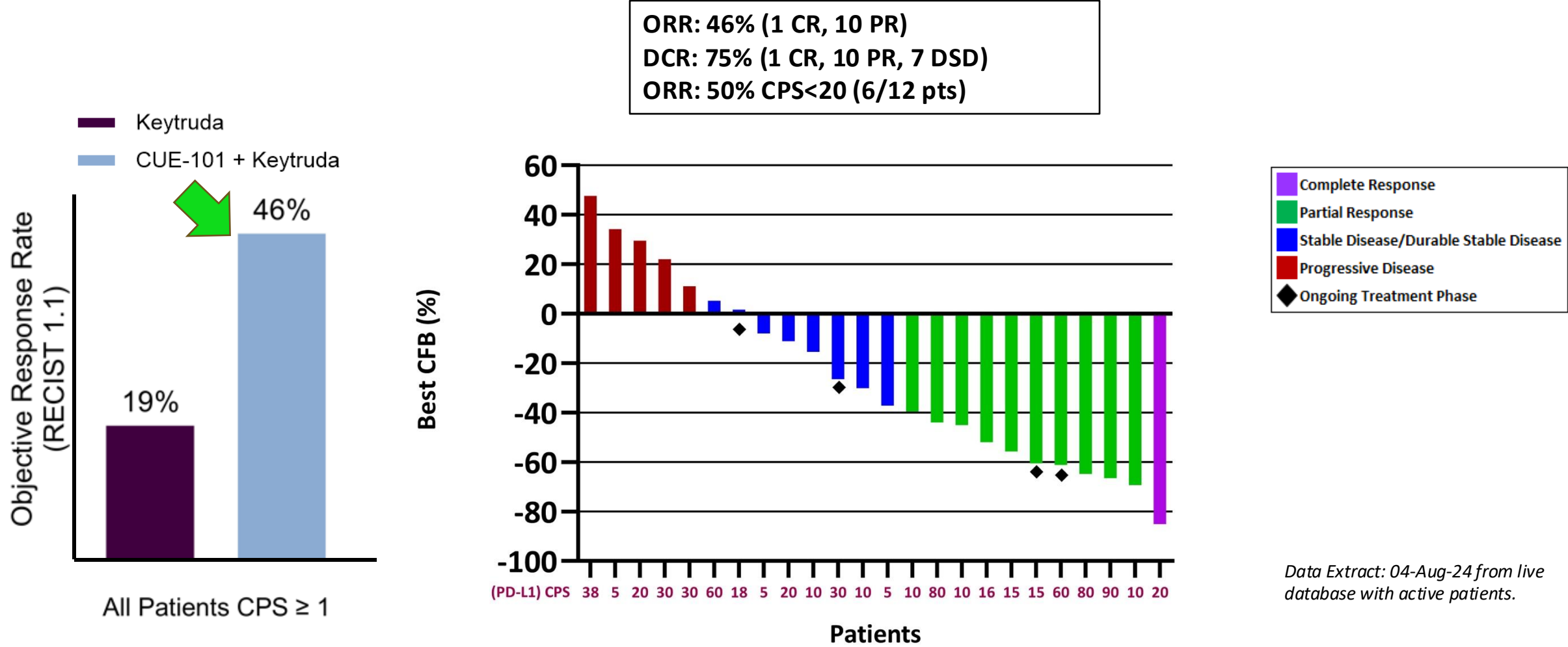
*CUE-501 redirects CMV-specific memory CD8+ T cells to kill human B cells with reduced cytokine production relative to anti-CD3/CD19 bispecific*



# CUE-500 Series: Significant Superior Differentiation

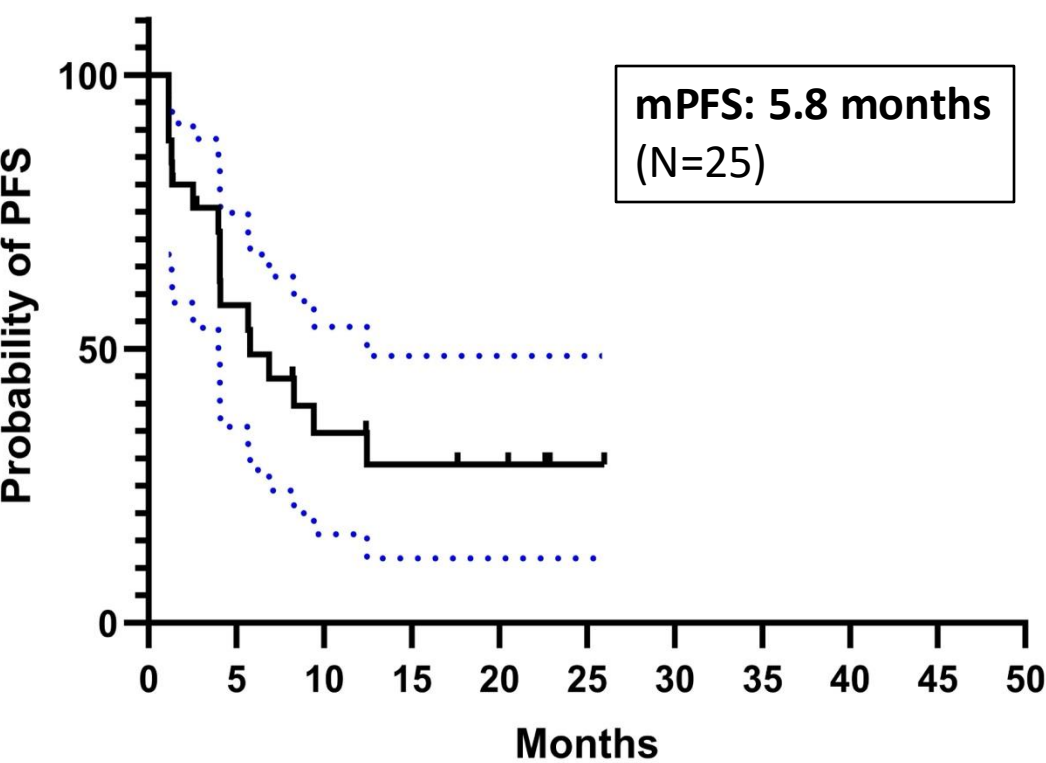
	CAR-T Cell Therapy	Pan TCE Molecules (e.g., anti-CD3/CD19)	CUE-500 TCE
<b>Selective activation of trained virus-specific killer T cells (“effector VST cells”)</b>	X	X	✓
<b>Takes advantage of effector VST cells present in circulation and diseased tissue</b>	X	X	✓
<b>Avoid broad/systemic immune activation</b> (CRS, ICANS, other toxicities, including self-reactivity)	X	X	✓
<b>Off-the-shelf administration and amenable to sub-cutaneous dosing</b>	X	✓	✓
<b>Avoid patient pre-conditioning regimens and enable out-patient administration</b>	X	✓	✓
<b>Manufacturing and supply chain</b>	Complex	Standard biologic	Standard biologic

# CUE-101 + Keytruda in 1L HPV+ R/M HNSCC – Key Differentiation: Enhanced Clinical Benefit in Patients with CPS ≥1

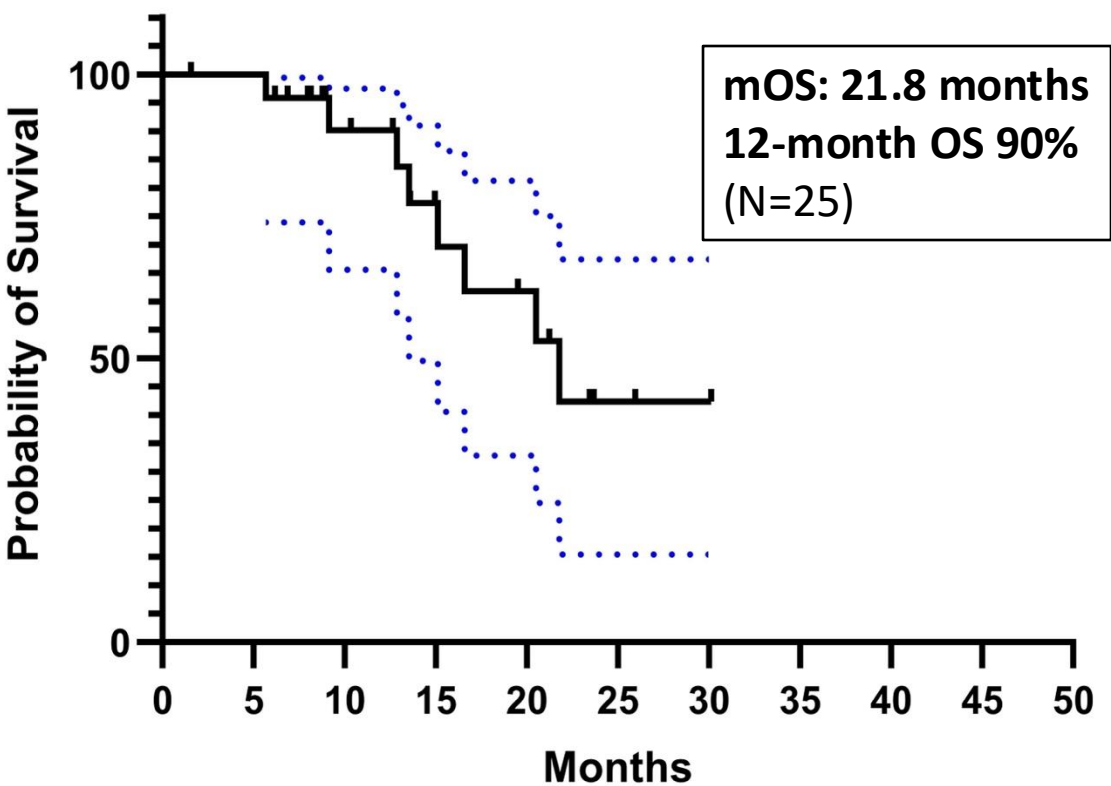


# Substantial Enhancement of PFS and Marked Increase in OS in 1L R/M HNSCC (CPS ≥ 1)

Progression Free Survival 4 mg/kg Combination Therapy



Overall Survival 4 mg/kg Combination Therapy

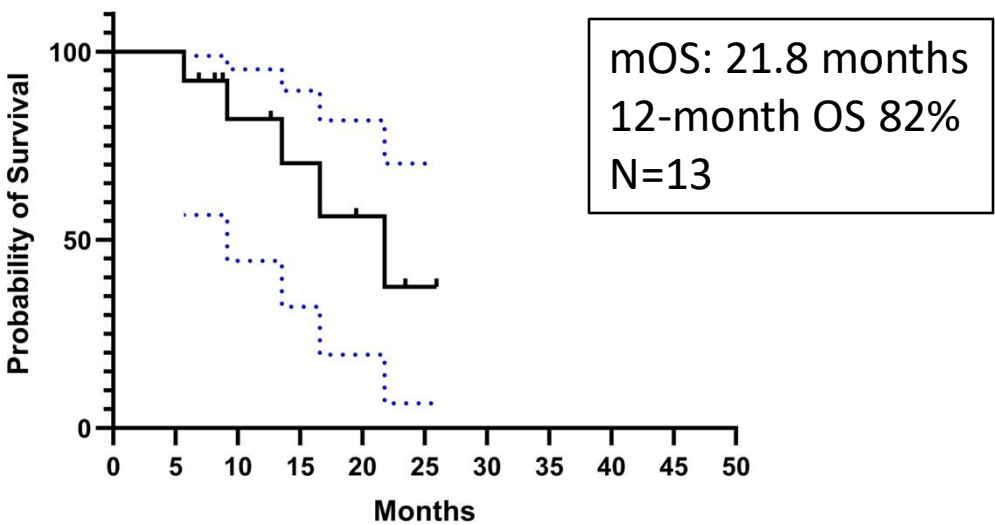


Data Extract: 04-Aug-24 from live database with active patients.

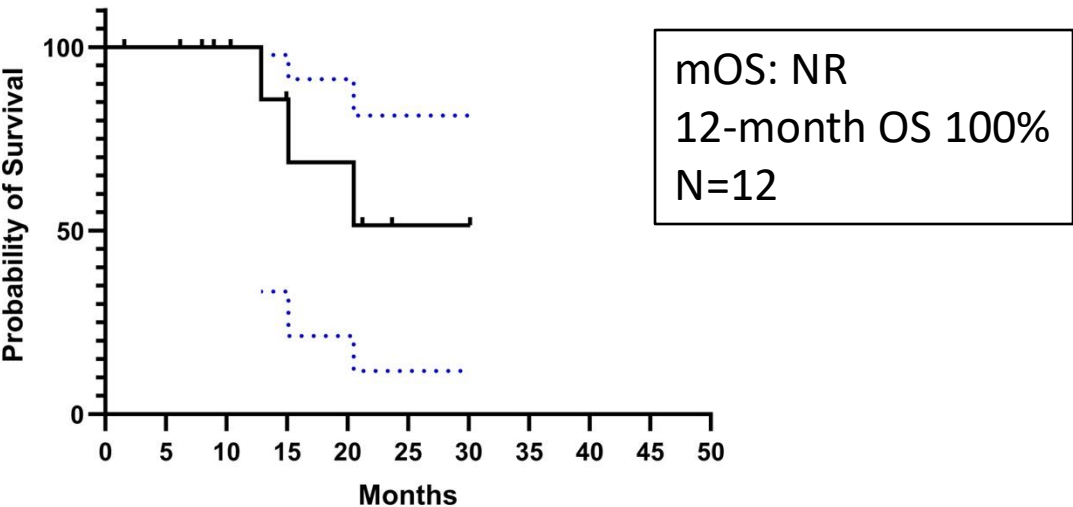
# CUE-101 4 mg/kg + Pembrolizumab in 1L R/M HNSCC:

## Marked Increase in Survival in CPS-low and CPS-high Patients

Overall Survival 4 mg/kg Combination Therapy CPS 1-19



Overall Survival 4 mg/kg Combination Therapy CPS ≥ 20

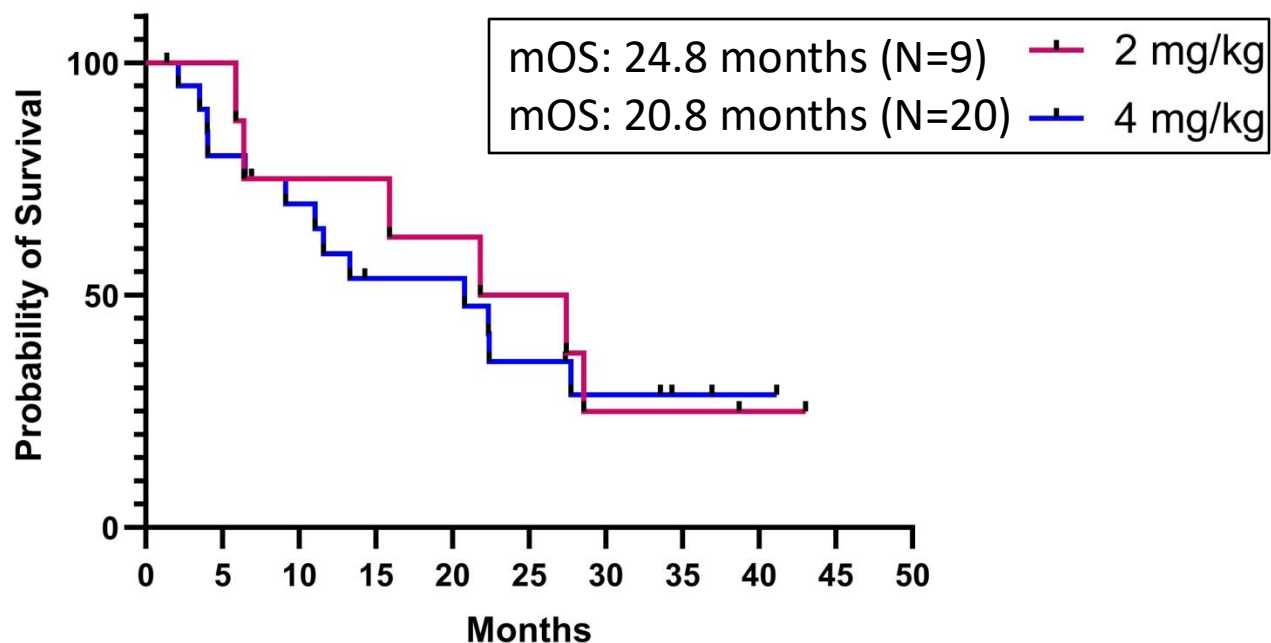


	PD-L1 CPS 1-19		PD-L1 CPS ≥ 20	
	Pembro Mono <sup>1</sup>	CUE-101 + Pembro	Pembro Mono <sup>1</sup>	CUE-101 + Pembro
Median OS (months)	10.8	21.8	14.8	Undefined
12-Month OS rate	44%	82%	56%	100%

1. Burtress JCO 2022      Data Extract: 04-Aug-24 from live database with active patients.

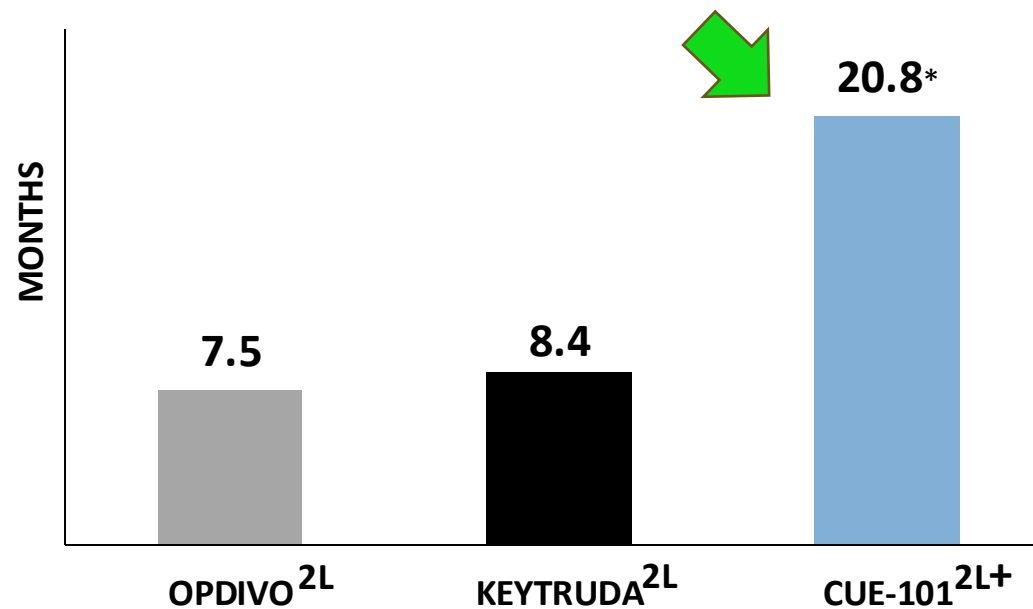
# CUE-101 Monotherapy in 2L+ R/M HNSCC: Notable Increase in Survival Observed at 2 and 4 mg/kg

Overall Survival 2 mg/kg & 4 mg/kg Monotherapy



1. Ferris et al Checkmate 141 NEJM 375;19, 2016
2. Cohen et al KEYNOTE-040 Lancet, 2018

CUE-101 Median Overall Survival vs. Anti-PD-1 Historical Benchmarks<sup>1,2</sup>



Data Extract: 04-Aug-24 from live database with active patients.

# Mission

## Translating “Nature’s Cues” into breakthrough immunotherapies

- ✓ Goal of establishing new standards of care for unmet needs in oncology and autoimmunity with potential for large market opportunities
- ✓ Clinically validated oncology programs with potential "best-in-class" T cell engagers demonstrate favorable tolerability and efficacy:
  - Provides significant risk reduction for entire Immuno-STAT™ platform
  - Clinical data continuing to mature
- ✓ Advancing preclinical autoimmune programs to target multiple diseases with potential for significant value creation:
  - **CUE-401:** Unique bispecific for induction & expansion of regulatory T cells  
Partnered with Ono Pharmaceutical (*Cue Biopharma has option to co-develop in U.S.*)
  - **CUE-501:** Novel biologic for B cell depletion in autoimmune diseases
- ✓ Implementing business model to mitigate capital access risk via partnerships for sustainable shareholder value potential



# Thank you

Translating “Nature’s Cues” into  
breakthrough immunotherapies

