

Cue Biopharma, Inc.

Immune Responses, On Cue™

Nasdaq: CUE
February 2024



CUE™
B I O P H A R M A

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Vision

Translating “Nature’s Cues” into breakthrough immunotherapies

- ✓ Created selective T cell engagers for precision immunotherapy
- ✓ Demonstrated clinical efficacy with paradigm shifting data
- ✓ Platform modularity addresses significant unmet need in oncology and autoimmunity

Cue Biopharma's Therapeutic Platform has the Potential to Restore Immune Balance to Address Two Major Causes of Human Suffering and Mortality

Cancer

- 20 million new cases worldwide
- 2 million new cases in US in 2021 alone
- ~50% will result in R/M disease and ultimately death

Autoimmune Disease

- 4% of the world's population
- 24 million cases in the US
- Almost all decrease life expectancy

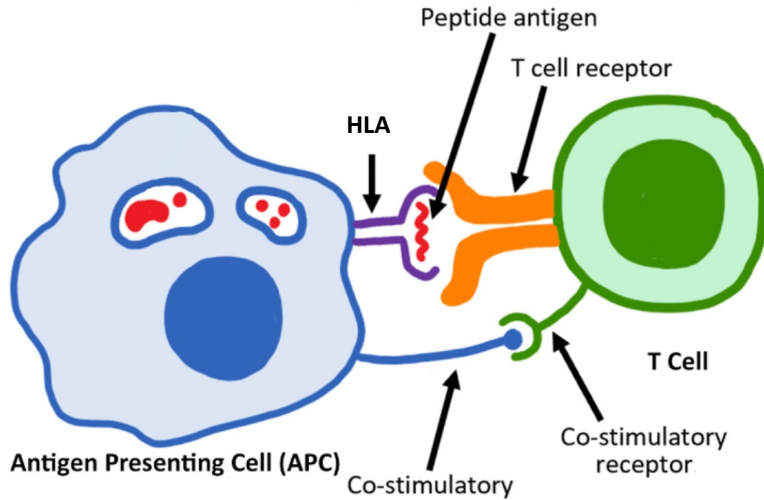
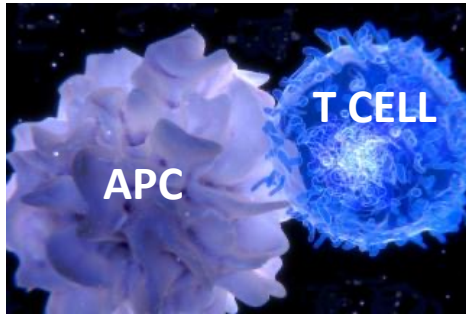
Inadequate protective immunity

Overt self-reactive immunity

Immune
Balance

Sources: 1. Pan American Health Organization & WHO; 2. Global Autoimmune Institute; 3. Dou et al Cell 187;3, 2024;

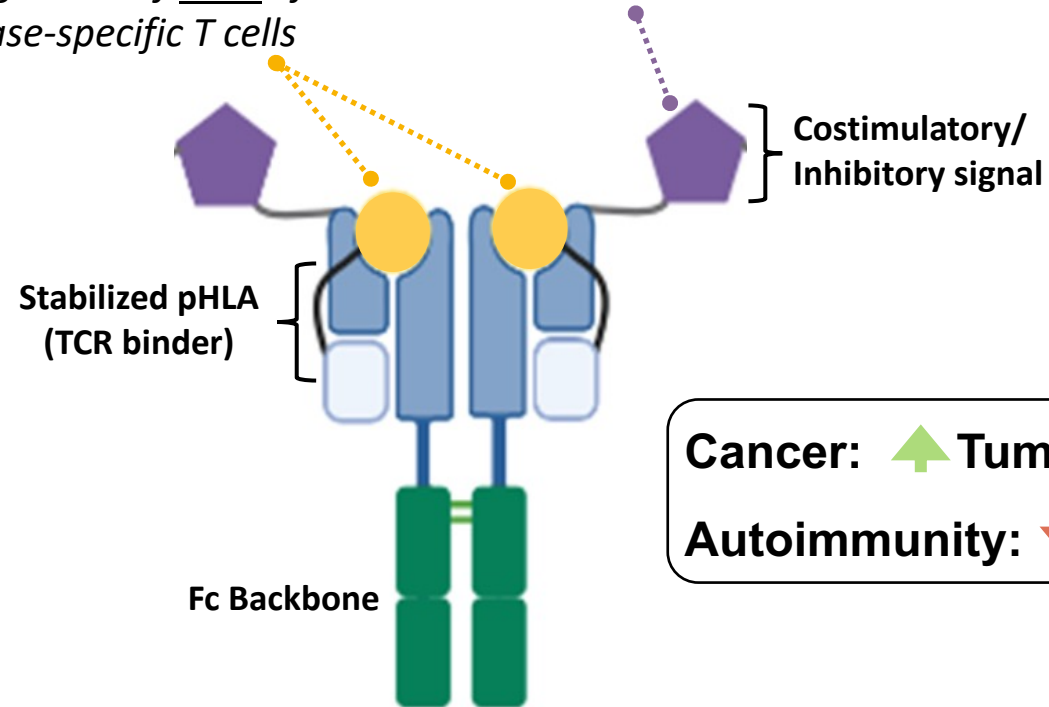
Immuno-STAT Platform: Turning Nature's Selectivity into Effective Drugs



Immuno-STAT™ Platform

Engagement of TCRs of disease-specific T cells

Selective delivery of signals to disease-specific T cells

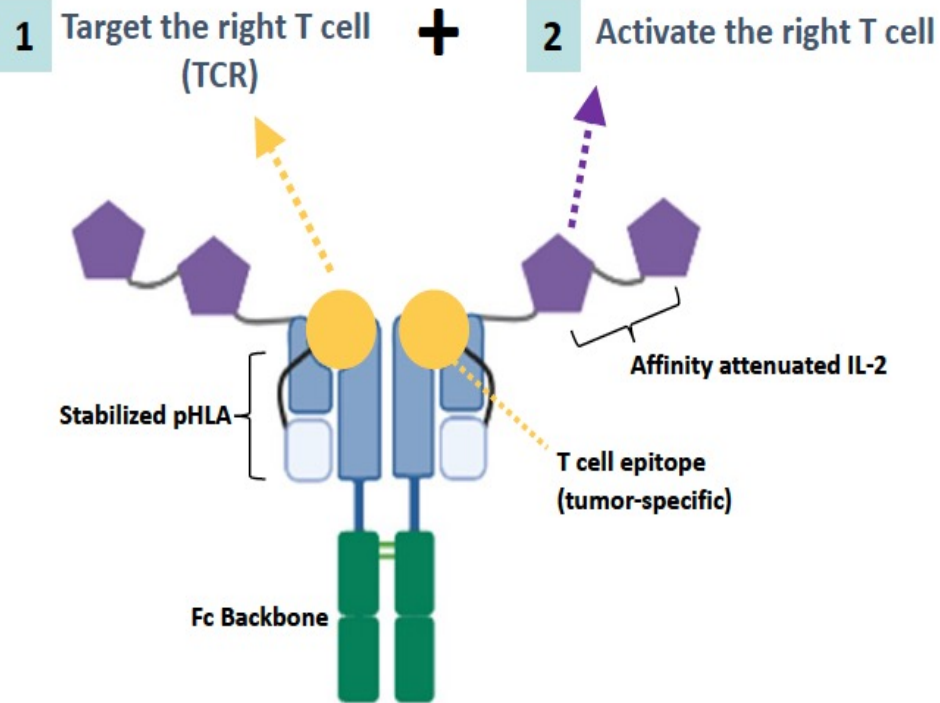


Cancer: Tumor-specific T cells
Autoimmunity: Pathogenic T cells



Oncology

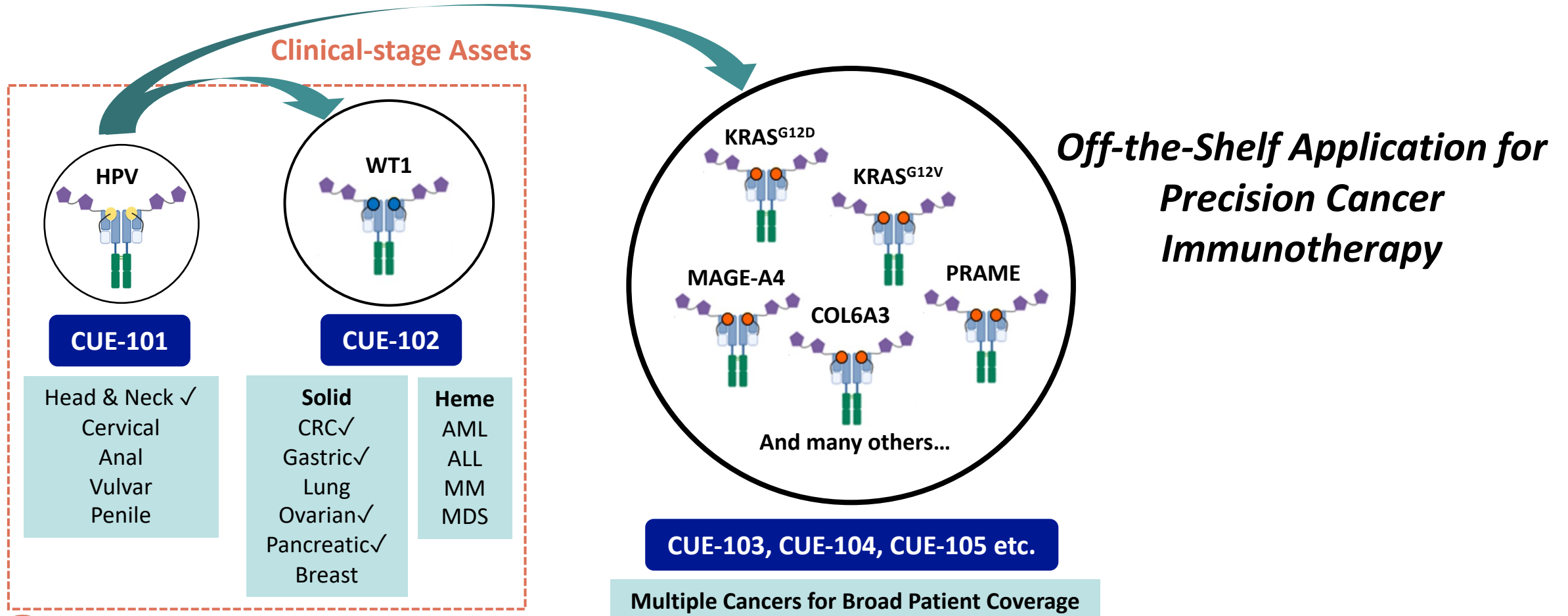
CUE-100 Series: Best-in-Class IL-2-based T Cell Engagers



- ✓ **Generation of a Therapeutic Index for IL-2**
 - Selective targeting of IL-2 to tumor-specific T cells
- ✓ **Clinical Validation and PoC (>100 Patients Treated)**
 - Monotherapy efficacy in late-stage cancer patients
 - Greater than doubling of ORR and mPFS in combination with CPI
- ✓ **Favorable Tolerability Profile**
 - No capillary leak syndrome
 - No clinically significant cytokine release syndrome
 - Q3W dosing with up to 24 months on treatment
- ✓ **Strong Metrics of Manufacturability**
 - Antibody-based modular design, expression, CMC and COGS
 - Highly stable (DP stability >36 months)
- ✓ **Flexible Platform with Significant Regulatory Advantages**
 - Accelerated development of pipeline candidates
 - Opportunity to target many different cancers

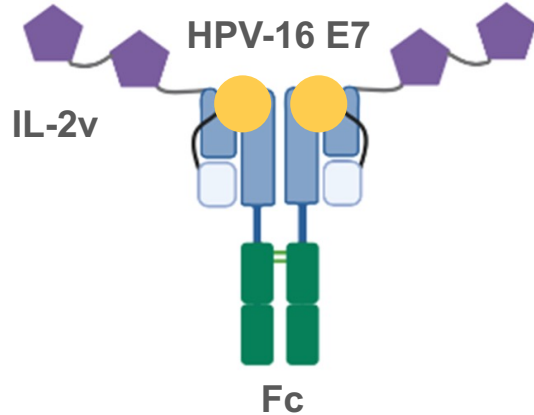
Platform Modularity Enables Targeting Many Different Cancers

Structural similarity creates potential regulatory and development efficiencies



CUE-101: Clinical Validation and Efficacy in HPV+ Head and Neck Cancer

CUE-101



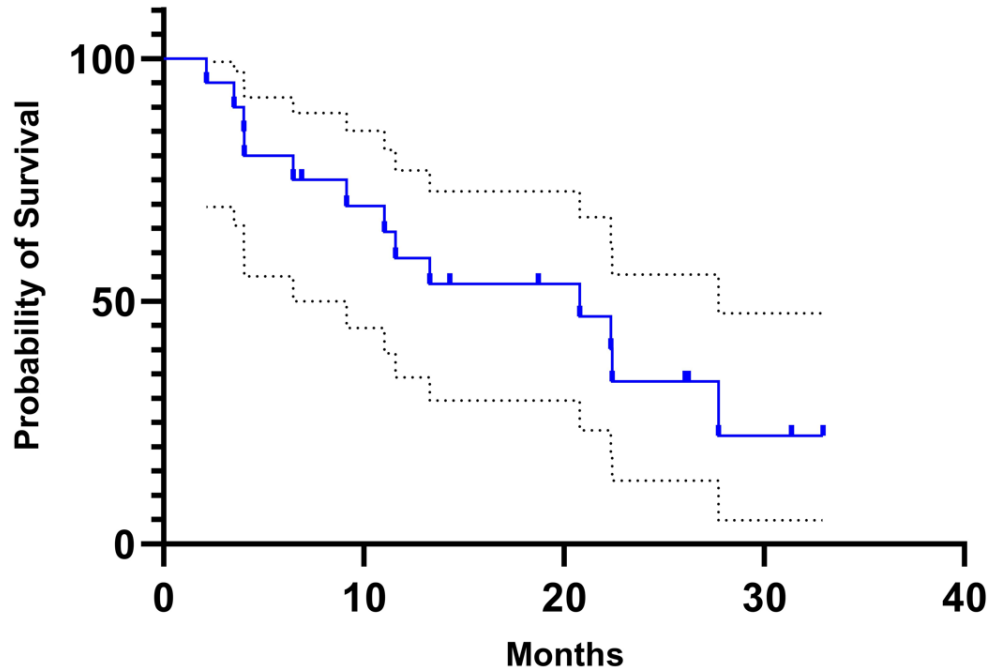
Abbreviations:
 mOS = Median Overall Survival
 SOC = Standard of Care
 ORR = Overall Response Rate
 mPFS = Median Progression Free Survival
 IST = Investigator Sponsored Study

	CUE-101	CUE-101 + KEYTRUDA	Locally Advanced	
	2L+ R/M	1L R/M	Neoadjuvant	Adjuvant
Status	Phase IA/IB Fully Enrolled Doubled mOS vs. SOC	Phase IA/IB Fully enrolled Doubled ORR and mPFS vs. SOC	IST Ongoing	IST Planned
Market Opportunity	~\$400M	~\$750M	~\$1.5-2.0B	

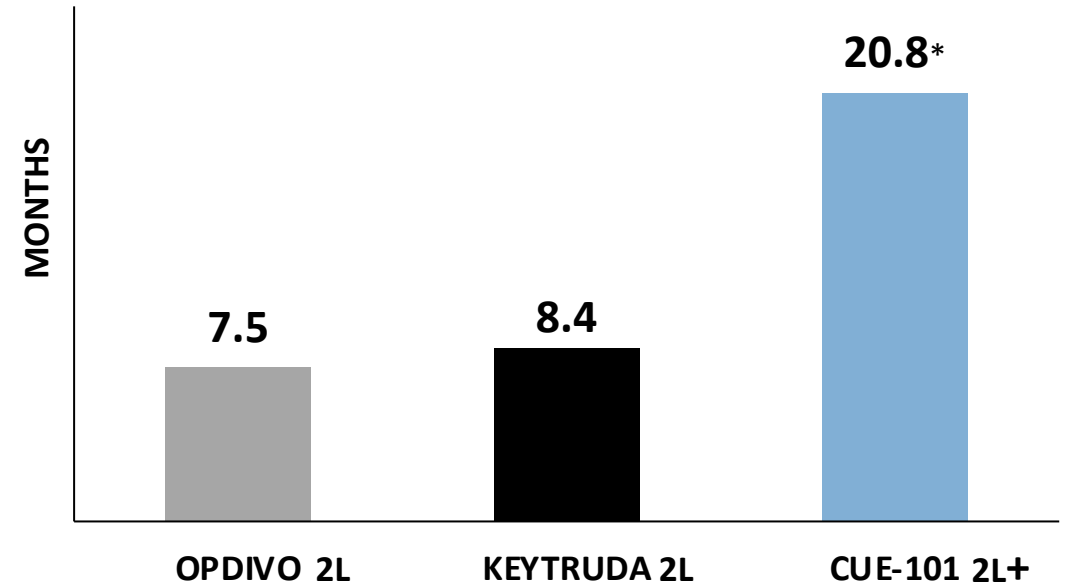
Source: based on 2024 analysis conducted by Trinity Life Sciences, peak revenue estimates

CUE-101 Monotherapy: Substantial Increase in Survival in 2L+ Patients

CUE-101 Survival Curve



CUE-101 Median Overall Survival vs. Anti-PD-1 Historical Benchmarks^{1,2}



Overall survival (months) in the 20 patients treated with CUE-101 monotherapy (4 mg/kg).

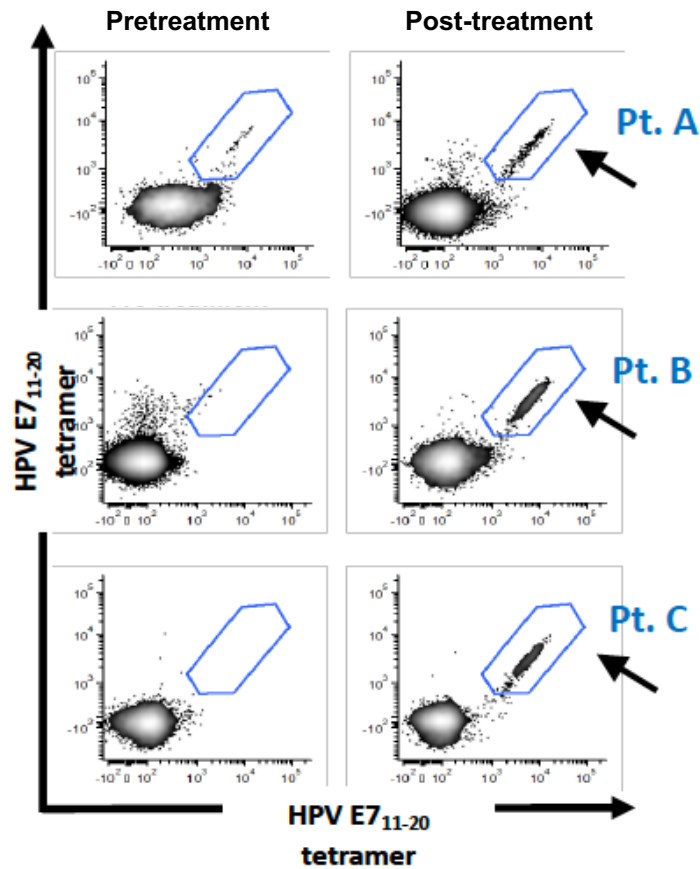
Data Extract: 06-Feb-2024

*Kaplan-Meier estimate of median OS 20.8 months [95% CI; 10.0, NA]

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

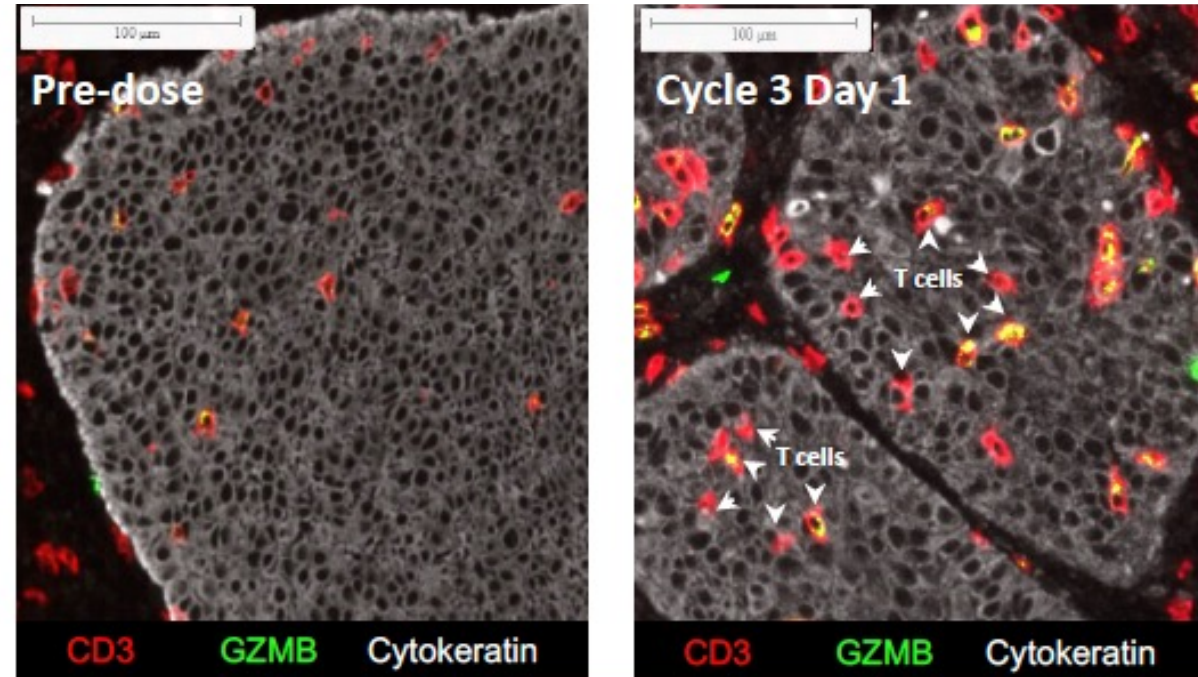
CUE-101 Monotherapy: Tumor-Specific T Cell Expansion and Infiltration

Tumor-specific T cell Expansions



Examples of E7-specific T cell expansions in blood at different time-points from 3 subjects treated with CUE-101 at the RP2D dose of 4mg/kg

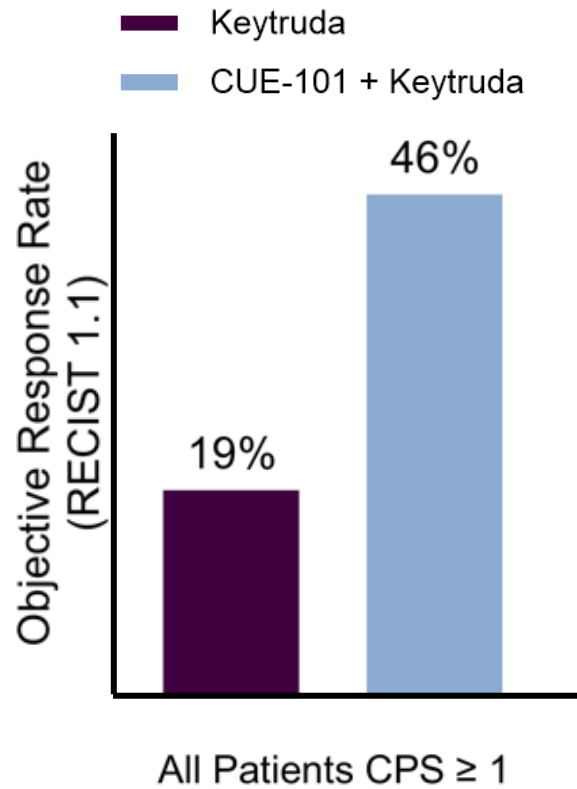
T cell infiltration into tumors post-CUE-101 treatment



CD3 = T cells
GZMB = Granzyme B

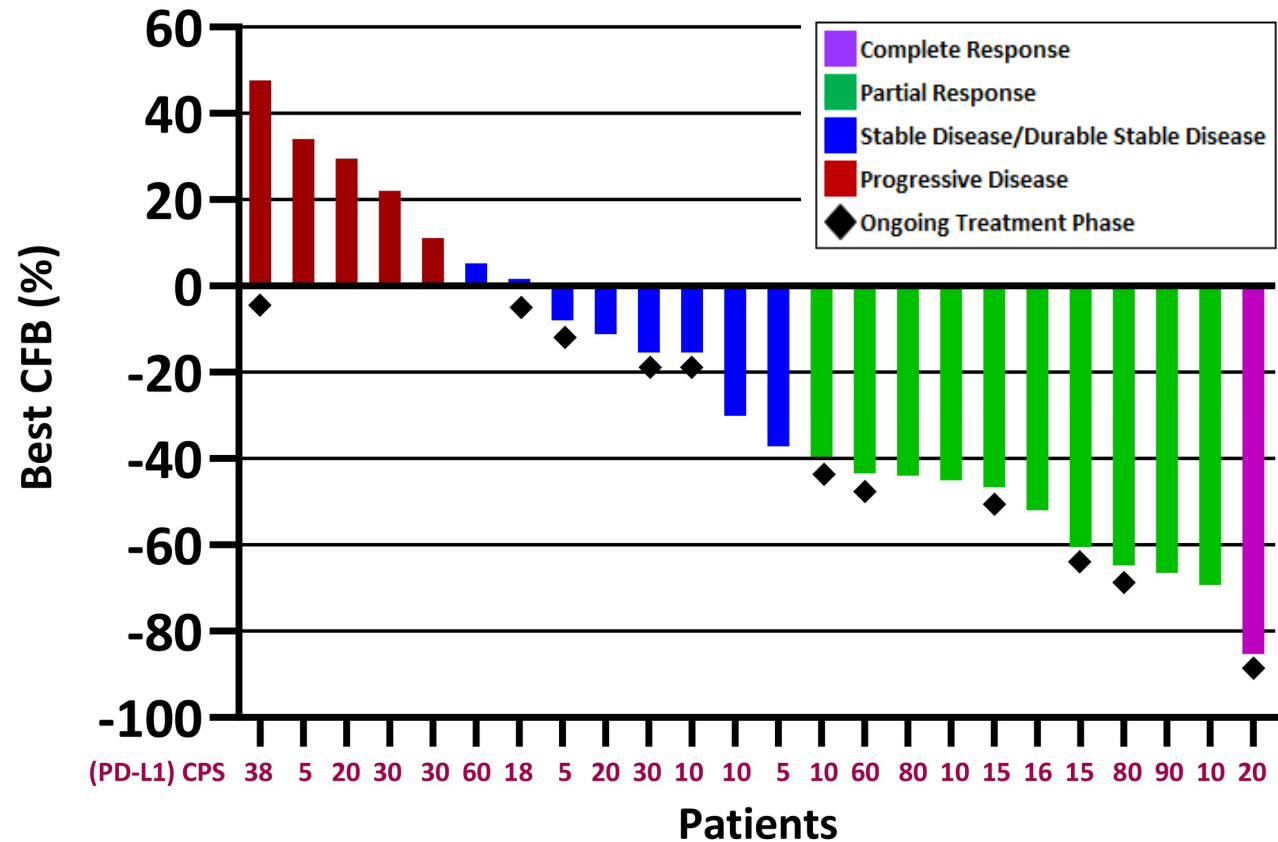
CUE-101 + Keytruda: Potential Best-in-Class 1L Regimen for Patients with HPV+ R/M HNSCC

Overall Response by RECIST: ORR=11/24 (46%); DCR 18/24 (75%)



(1) KEYNOTE 048 Study; Burtness B et al, Lancet 2019; (2) Harrington et al, J Clin Oncol 2022.

1L = First line; CPS = Combined Positive Score

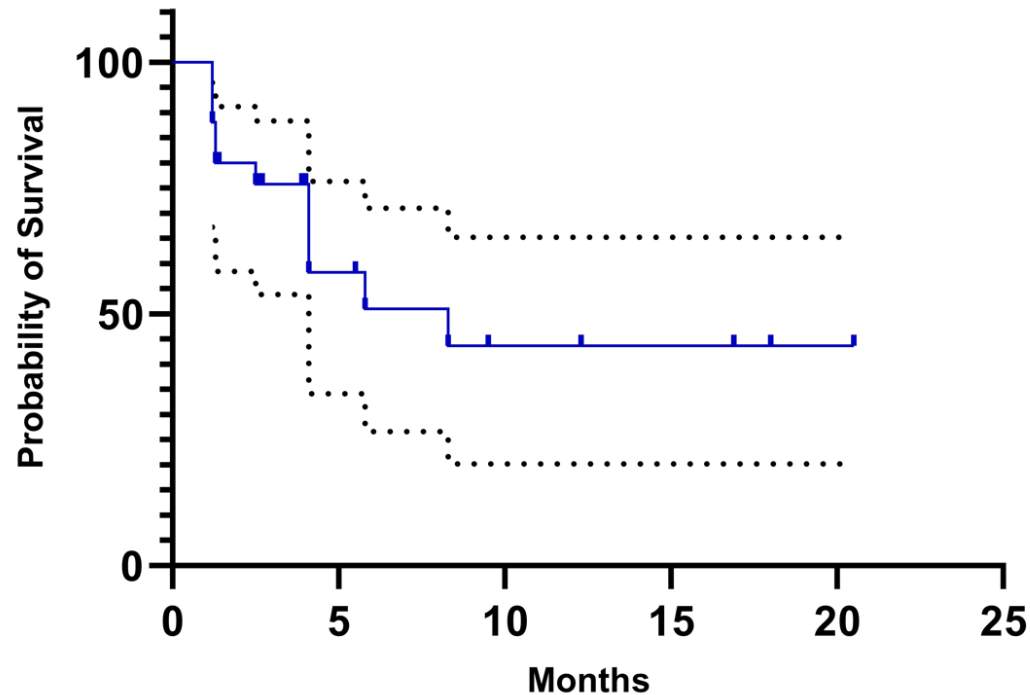


Data Extract: 06-Feb-2024. Includes 24/25 patients in Response Evaluable Population

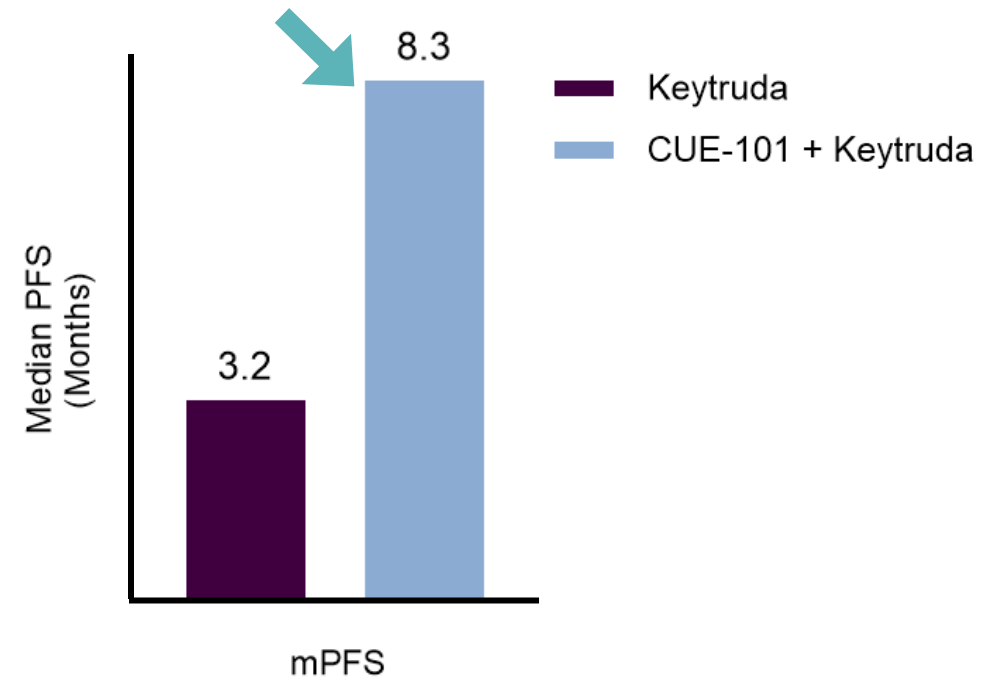
CUE-101 + Keytruda: Notable Increase of PFS in 1L Patients

(cross-study comparison of historical benchmark)

CUE-101 + Keytruda Progression Free Survival



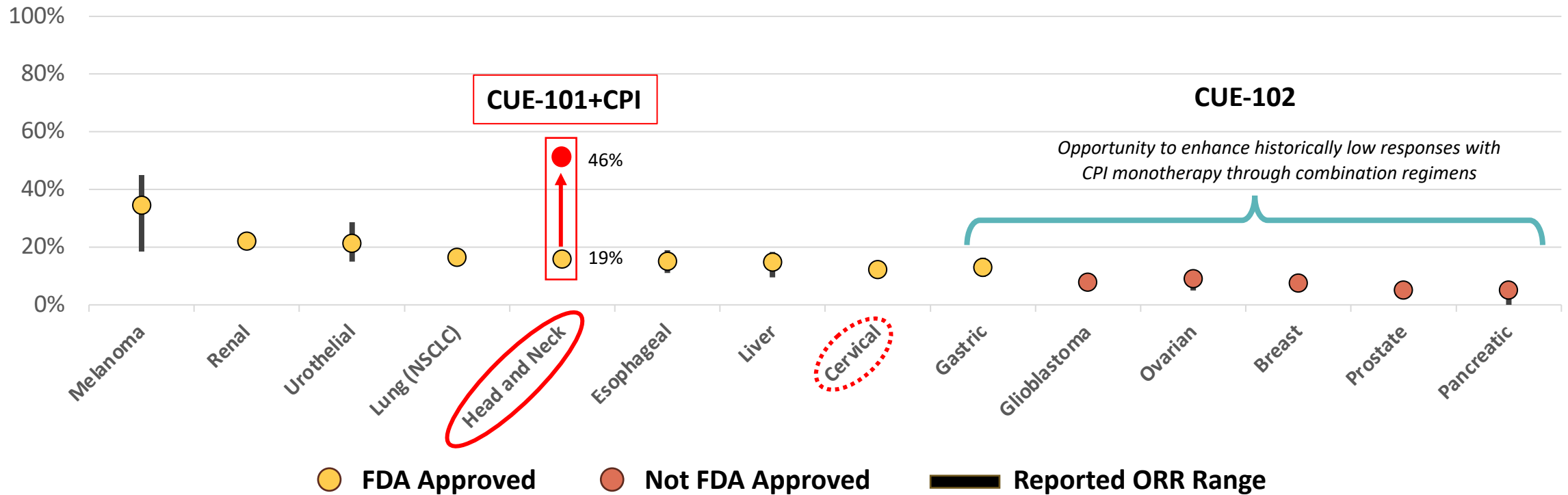
CUE-101 + Keytruda Median PFS vs. Anti-PD-1 Historical Benchmark*



Kaplan-Meier estimate of median PFS 8.3 months [95% CI; 5.0, NA] in the 25 patients treated with CUE-101 (4 mg/kg) + Keytruda combination therapy.

Immuno-STATs: Expanding Patient Reach and Enhancing Efficacy for CPIs

Reported Overall Response Rate with PD-1/PD-L1 Monotherapy ¹



Demonstrated enhancement of response through synergy of Immuno-STATs with PD-1 inhibitor

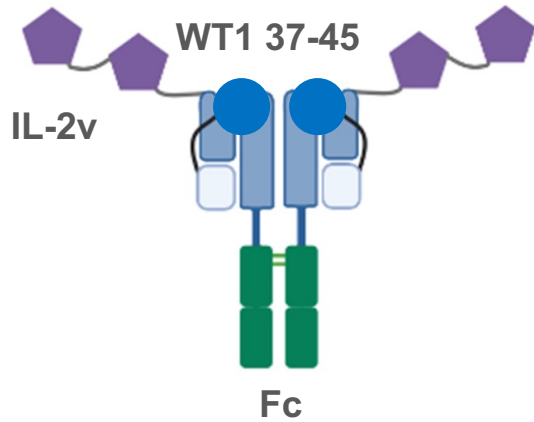
Source: 1) Mao et al. Cancer Immunol Immunotherapy. 2023 Jul;72(7):2483-2498. Doi: 10.1007/s00262-023-03441-3. Epub 2023 Apr 6.



CUE-102

CUE-102: Second Clinical Program Targeting WT1-Positive Cancers

CUE-102



99% sequence identity to CUE-101

- FDA cleared CUE-102 IND with no additional tox studies
- FDA cleared CUE-102 dose-escalation to start at the clinically active dose of 1 mg/kg, expediting clinical development

*Colorectal
Gastric
Ovarian
Pancreatic*



Regimen

CUE-102

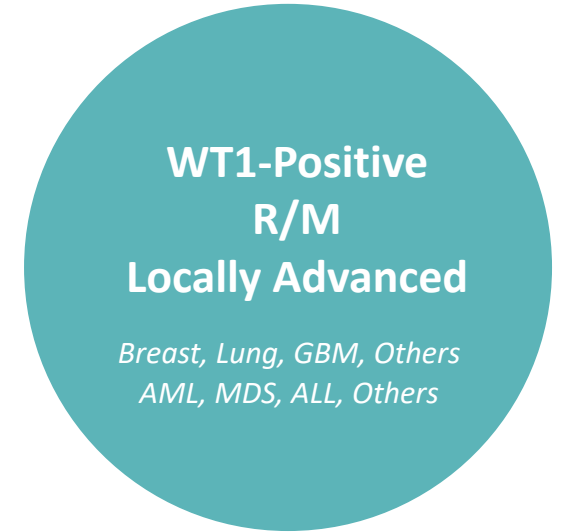
Status

Phase IA/IB

Dose Escalation Fully Enrolled
Favorable Tolerability
Emerging Signals of Activity

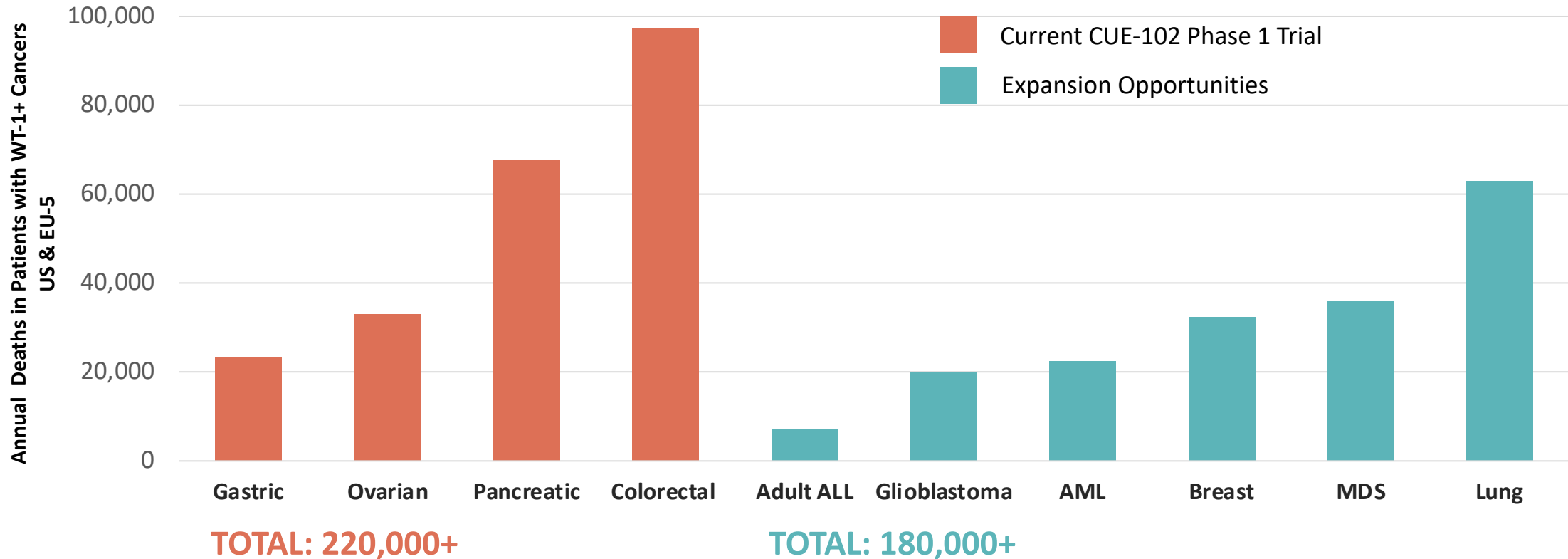


CUE-102 +/- SoC



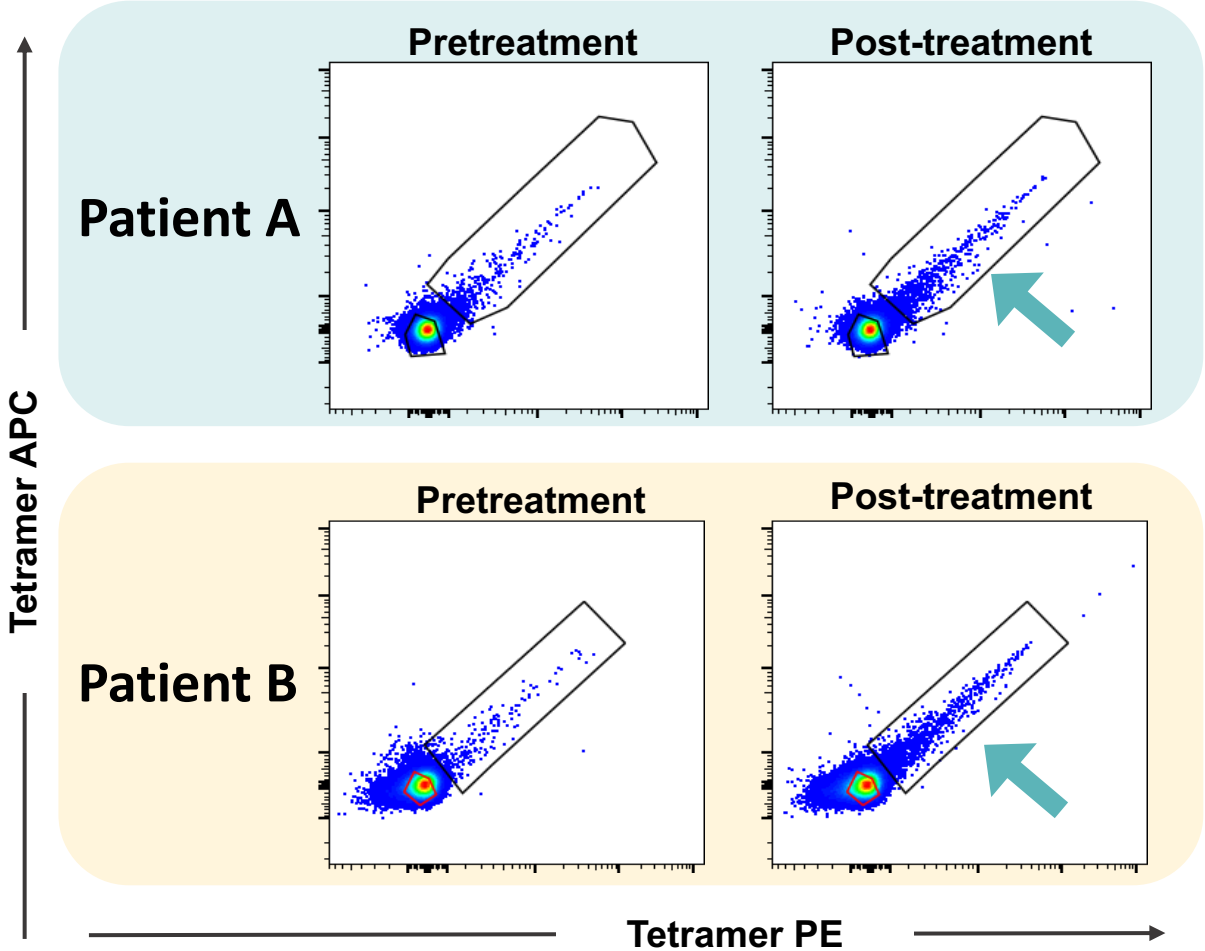
**WT1-Positive
R/M
Locally Advanced**
*Breast, Lung, GBM, Others
AML, MDS, ALL, Others*

Significant Unmet Need in Patients with WT1-Positive Cancers



Sources: 1. Trinity Life Sciences 2. Globocan 2020; 3. SEER; 4. Qi XW et al. *Sci Rep.* 2015 Mar 9;5:8924. doi: 10.1038/srep08924; 5. Naitoh K et al. *Anticancer Research* July 2016, 36 (7) 3715-3724, 6. Xiang C et al. *Hematology.* 2023 Mar 27: doi10.1080/16078454.2023.2254557, 7. Jiang Y et al. *Oncotarget.* 2018 Mar 23 doi: 10.18632/oncotarget.23671

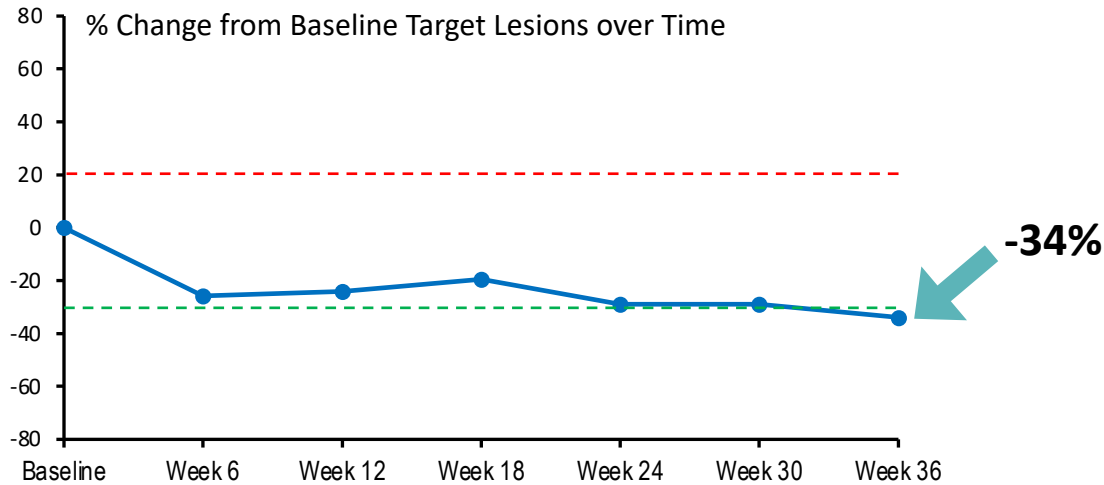
Selective Expansion of WT1-Specific T Cells Demonstrated in Patients



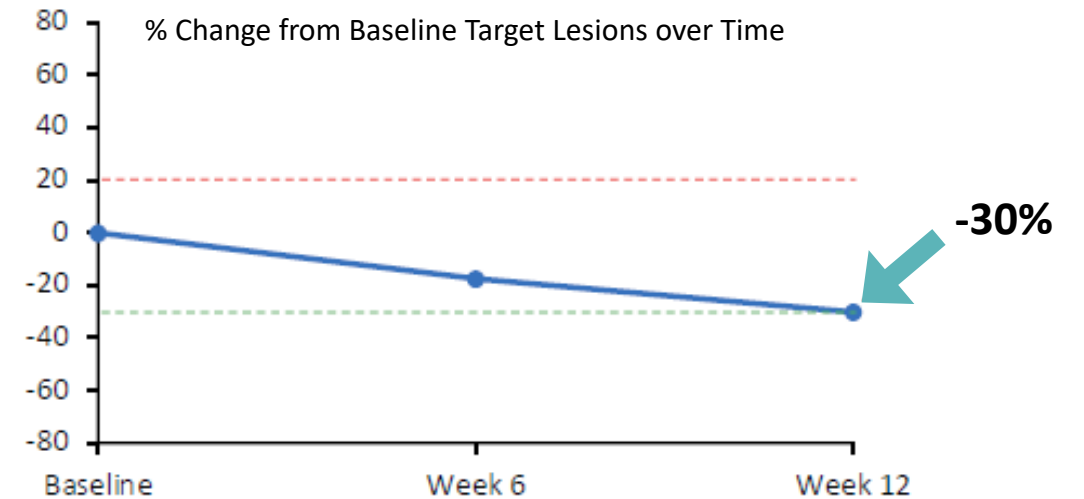
Increased frequency of WT1-specific CD8+ T cells are observed following CUE-102 treatment. Representative plots are shown from preliminary analyses following direct flow staining of PBMCs from 2 patients

CUE-102 Treatment: Reductions in Target Tumors

Gastric Cancer Patient



Ovarian Cancer Patient



- Disease Control Rate (DCR) of 38% (9/24) observed across patients with advanced colon, pancreatic, gastric and ovarian cancer during dose escalation (Part A)
- Clinical activity supports expansion into all 4 tumor types (Part B)

Data Extract: 06-Feb-2024.

CUE-100 Series: IL-2 Immunotherapy with Breakthrough Potential

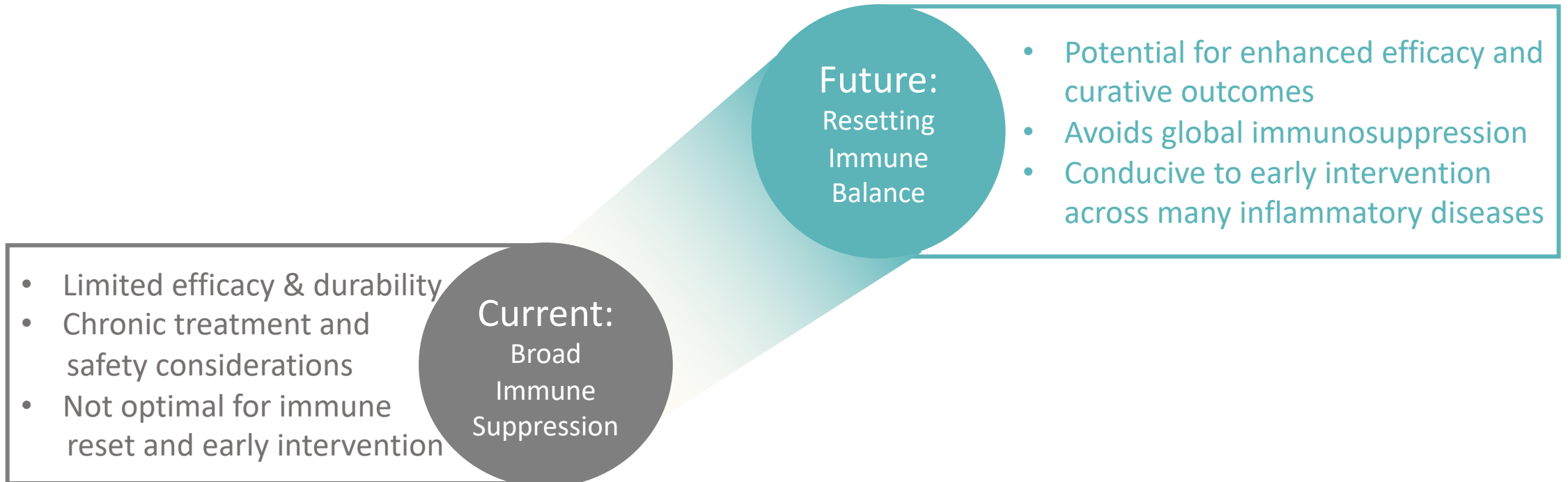
- ✓ **Clinical Efficacy:** Selective targeting of IL-2 to tumor-specific T cells achieves significantly greater efficacy without compromising patient safety
- ✓ **Registration Path (CUE-101):** Clear alignment on next steps following recent FDA interaction
- ✓ **Platform Derisking:** Provides significant regulatory advantages and clinical development efficiencies for future CUE-100 series candidates
- ✓ **Platform Modularity:** Creates significant market expansion opportunities and cost efficiencies
- ✓ **Multiple Paths:** In large solid tumor markets as early as 1L with exploration of adjuvant / neoadjuvant approaches
- ✓ **Partnering Opportunities:** Across assets and regions



Autoimmune Disease

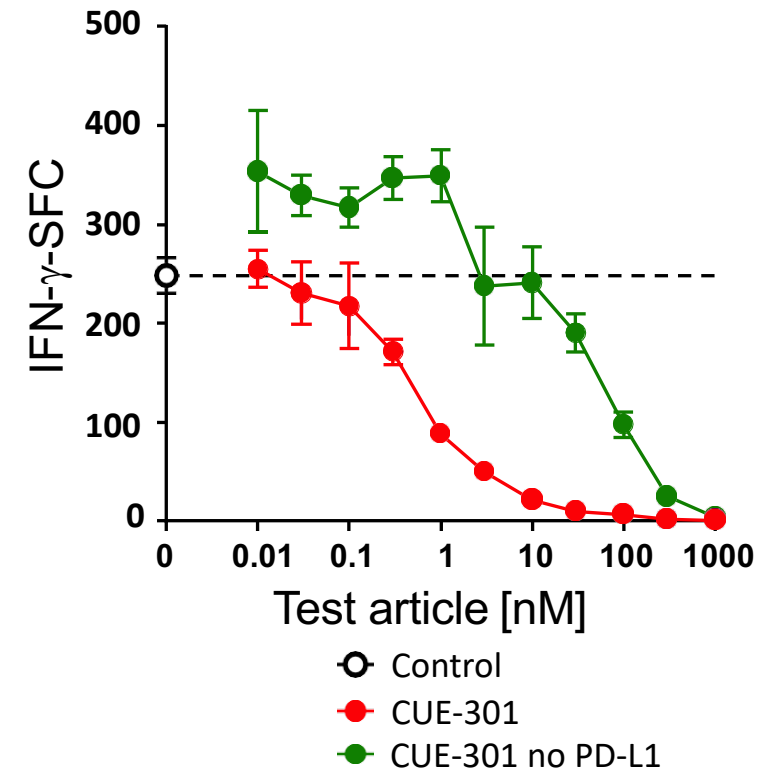
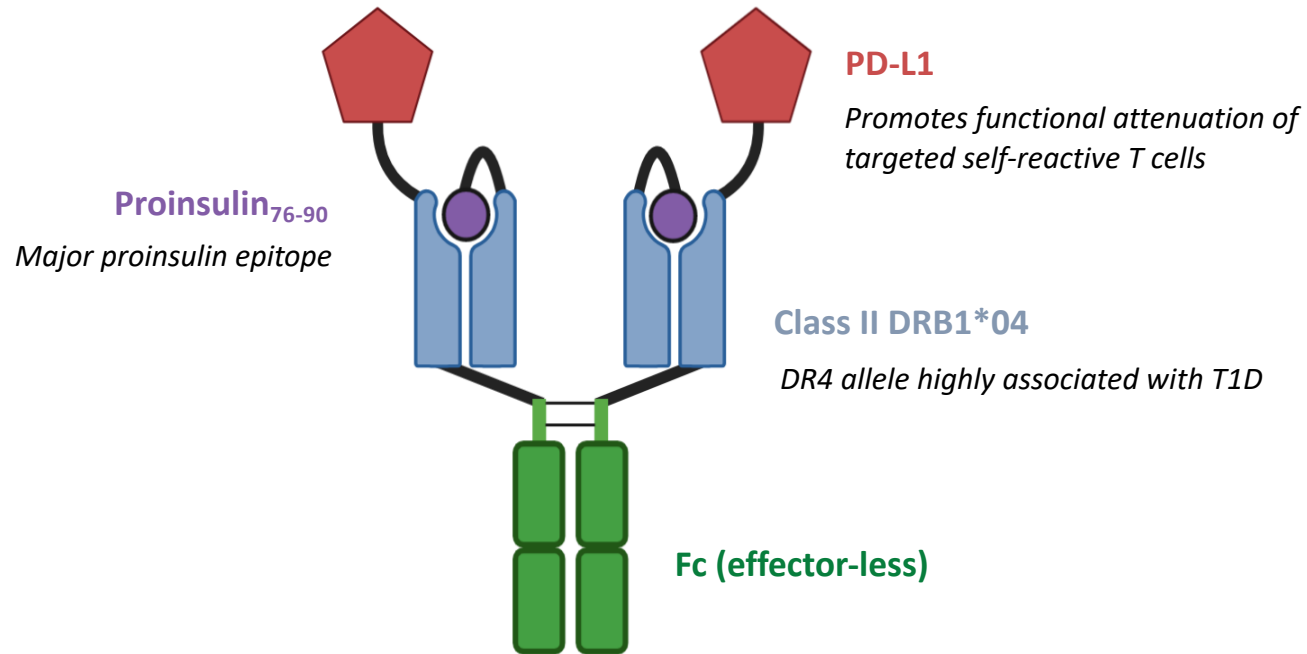
Resetting Immune Balance for Autoimmune and Inflammatory Diseases

Evolution in Disease Management



CUE-301: Designed for Selective Inhibition of Autoreactive T Cells

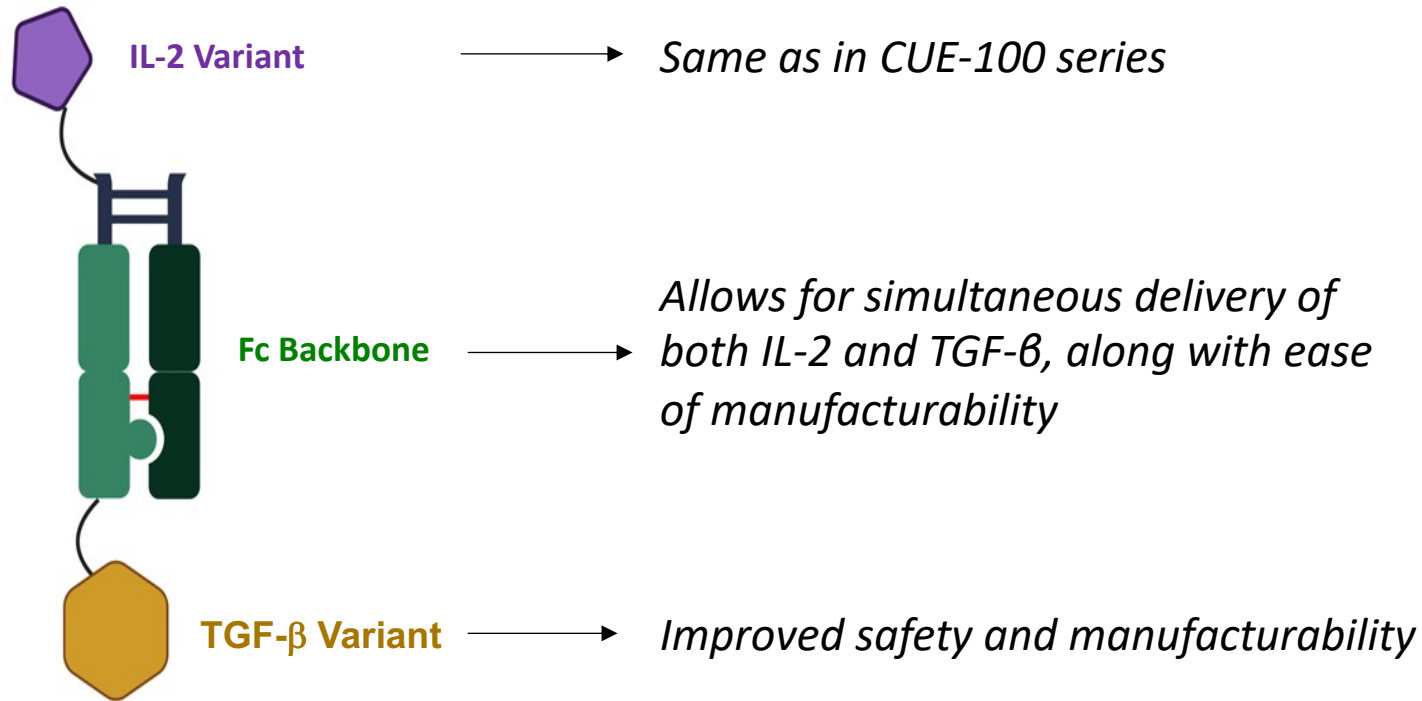
PoC with modulation of Proinsulin-specific T cells in T1D



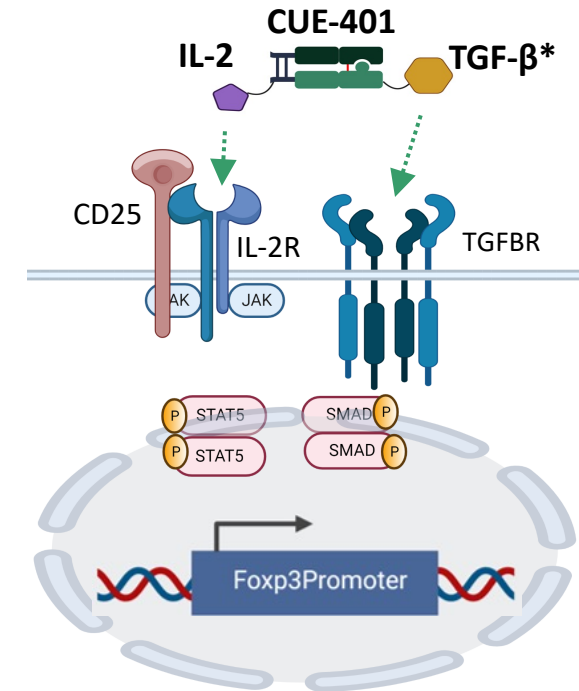
Established datasets provide PoC for further characterization of Immuno-STAT platform in modulating autoreactive T cells to intercept autoimmune disease (Celiac, MS, RA, etc.)

CUE-401: Designed for Selective Treg Induction and Expansion

CUE-401 MOA can be broadly developed for many different autoimmune diseases



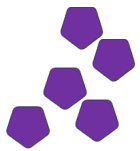
CUE-401 results in induction of FOXP3+ Tregs



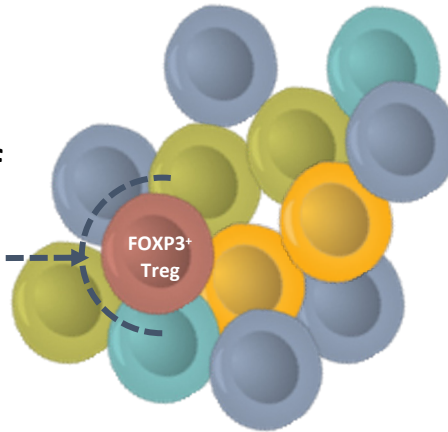
Ono Pharmaceutical funding ongoing research activities through preclinical option period
Cue retains a 50% co-development and co-commercialization right in the US market

CUE-401: Quantitatively & Qualitatively Superior to IL-2 Muteins

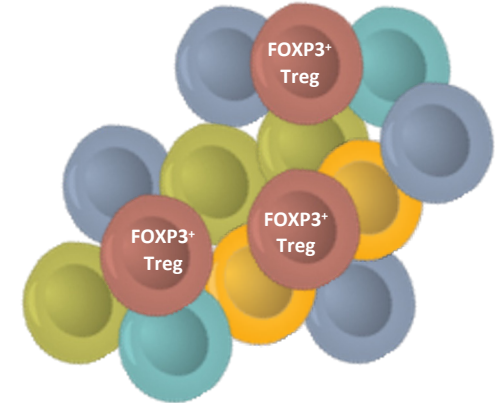
CD25-biased
IL-2 muteins



Focus on a minor population of
pre-existing nTregs



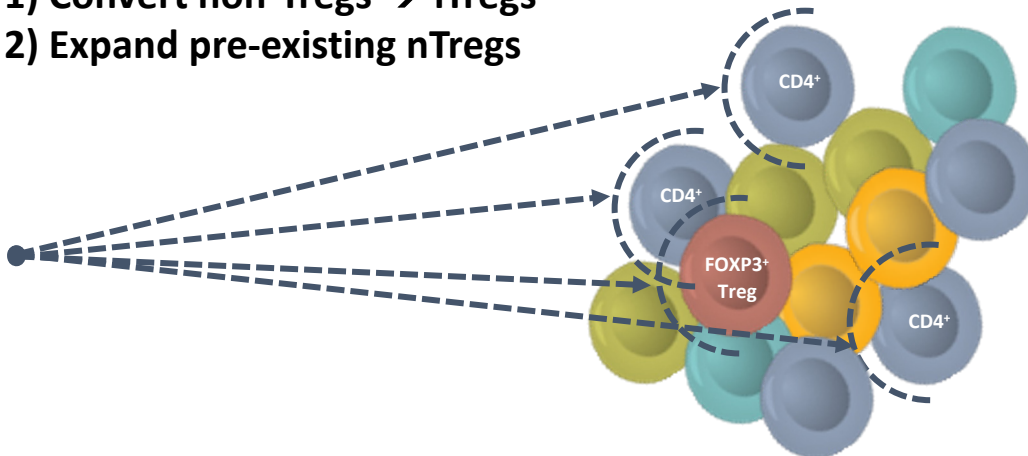
Limited Treg
Expansion



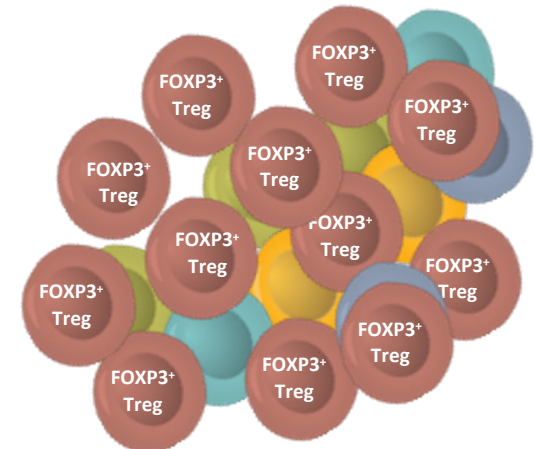
Two Key MOAs:

- 1) Convert non-Tregs → iTregs
- 2) Expand pre-existing nTregs

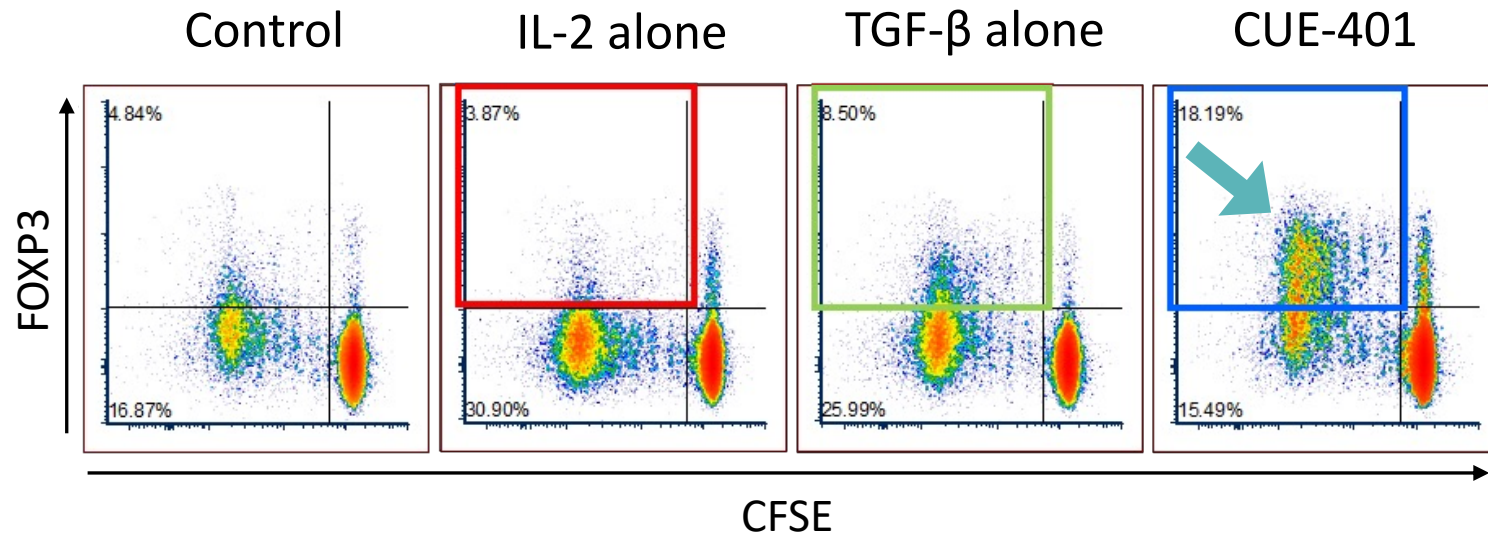
CUE-401



Greater Treg
Frequency

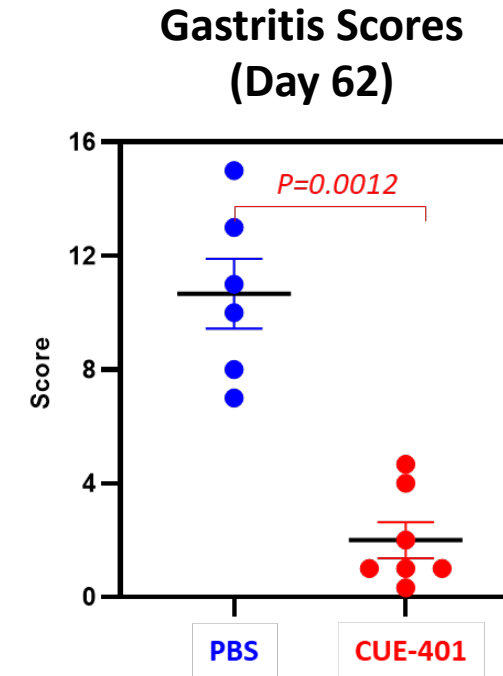
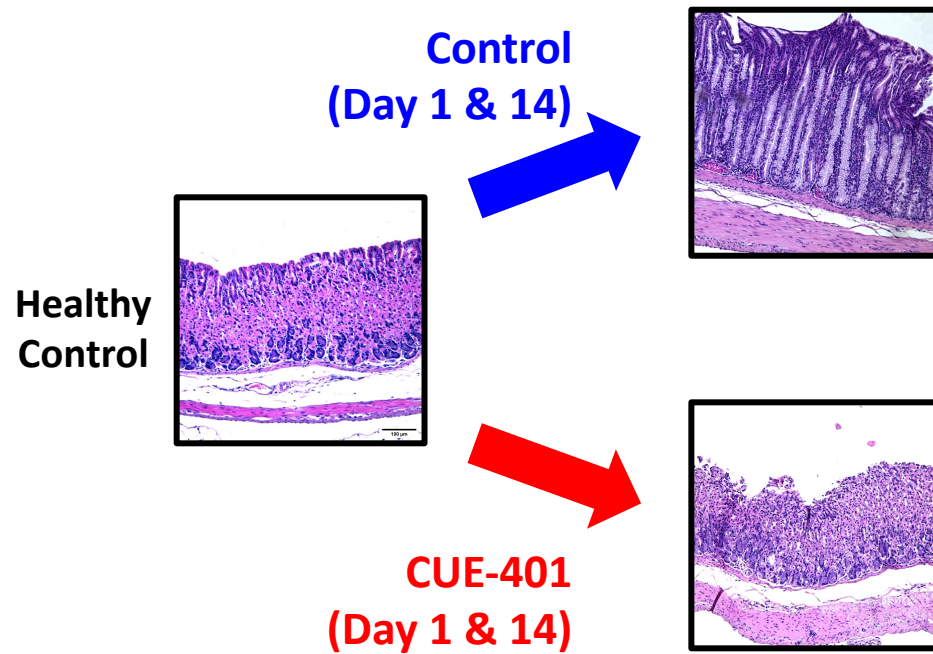


CUE-401 Harnesses Multiple Signals to Induce Tregs



CUE-401 provides both IL-2 and TGF- β activating signals that are necessary for iTreg differentiation

CUE-401 Treatment: Protection from Autoimmune Gastritis



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

Immuno-STAT Platform: Positioned for Near-term Value Inflection

Milestones	
CUE-101 Monotherapy	1Q 2024: Registration Path Defined in Alignment with FDA
CUE-101 + Pembrolizumab	1H 2024: Provide Ph1B Readout Mid 2024: Define Ph2/3 Registration Trial
CUE-101 Neoadjuvant (IST) CUE-101 Adjuvant (IST)	Mid 2024: Translational Biomarker Readout 1H 2024: Initiate Adjuvant IST
CUE-102 Monotherapy	1Q 2024: Initiate Dose Expansion (CRC) 2Q 2024: Initiate Dose Expansion (PC,GC,OV) 2H 2024: Provide Ph1B Readout
CUE-401	1H 2024: Prioritized Candidate Selection 2H 2024: Ono Clinical Candidate Option Decision 2H 2024: Cue Co-Development Option Decision
Immuno-STAT Program(s) (oncology & autoimmunity)	2024: Execute Strategic Partnership(s)

Investment Summary

- **Established clinical PoC with our two lead oncology programs**
 - Well characterized safety, tolerability, and efficacy both as monotherapy and combination therapy
- **Clinical data sets generated to date have the potential to shift the treatment paradigm**
 - Demonstrated meaningful increases in OS, ORR and mPFS
- **Multiple applications of novel platform have potential to address some of the largest pharma markets in the US**
 - Solid tumors and large autoimmune disease indications
- **Modular platform provides multiple paths to value creation**
 - Structural similarity provides regulatory advantages and capital efficiencies to develop numerous immunotherapies
 - Partnering opportunities across platform and regions

Thank you

Translating “Nature’s Cues” into
breakthrough immunotherapies



CUETM
B I O P H A R M A