

Cue Biopharma, Inc.

Corporate Update

Nasdaq: CUE

April 2024



CUETM
B I O P H A R M A

Forward-Looking Statements Disclaimer

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Agenda

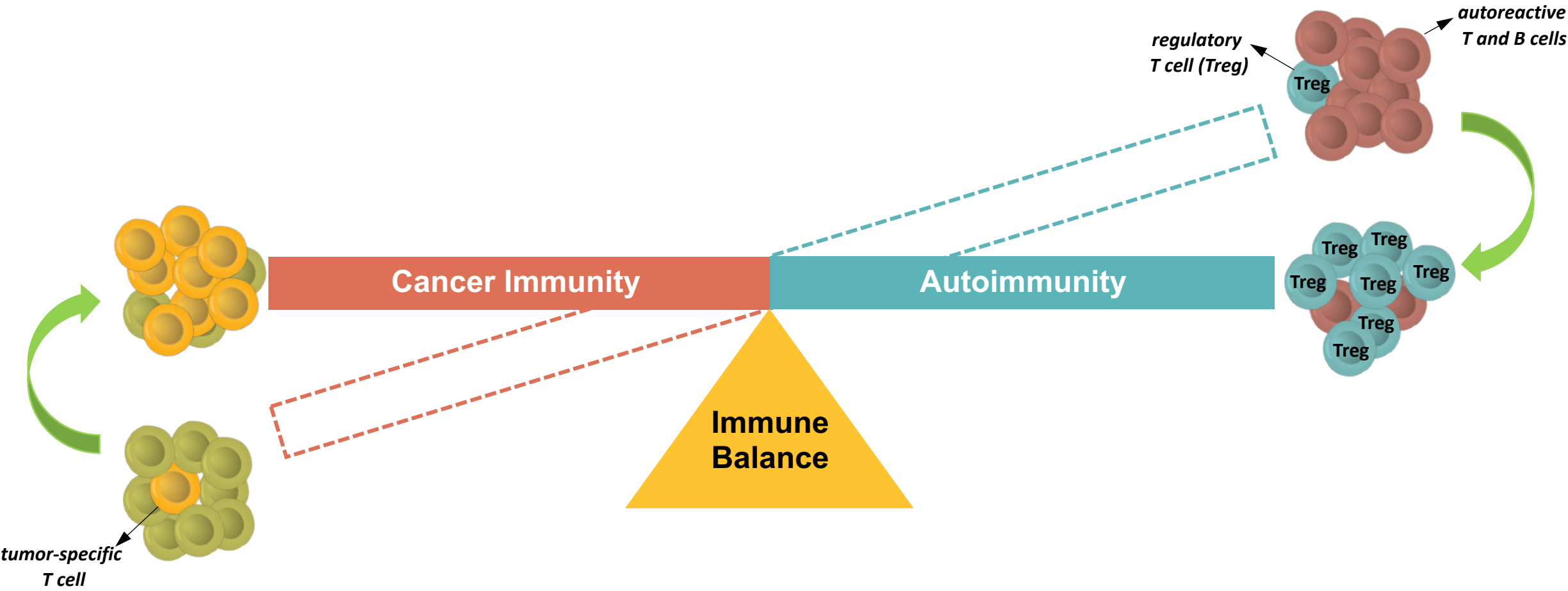
1. Platform Overview and Competitive Positioning – Dan Passeri, CEO
2. Approach and Asset Development – Anish Suri, CSO & President
3. Clinical Update – Matteo Levisetti, CMO
 - CUE-101
 - CUE-102
4. Autoimmune Programs – Anish Suri, CSO & President
5. Financial Update – Kerri-Ann Millar, CFO
6. Closing Remarks – Dan Passeri, CEO

Vision

Translating “Nature’s Cues” into breakthrough immunotherapies

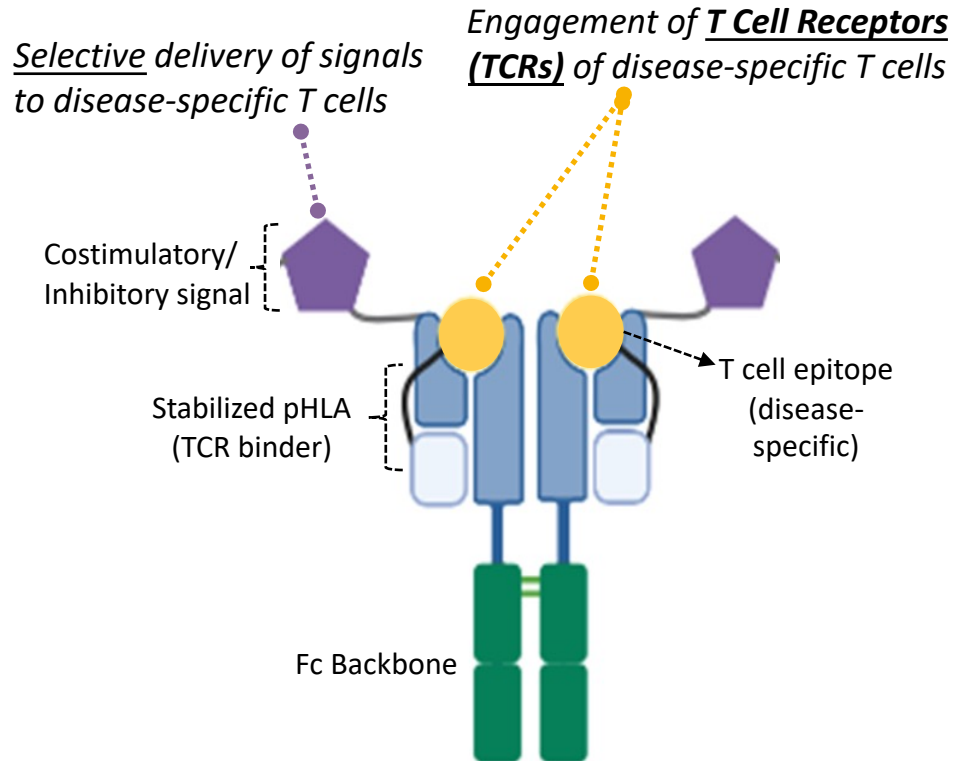
- ✓ Precision immunotherapy via a validated class of selective T cell engagers
- ✓ Clinical efficacy with paradigm shifting data
- ✓ Favorable tolerability
- ✓ Platform addresses significant unmet need in oncology and autoimmunity

Goal: Selective Modulation of Disease-Relevant Immune Cells while Preserving Patient Safety

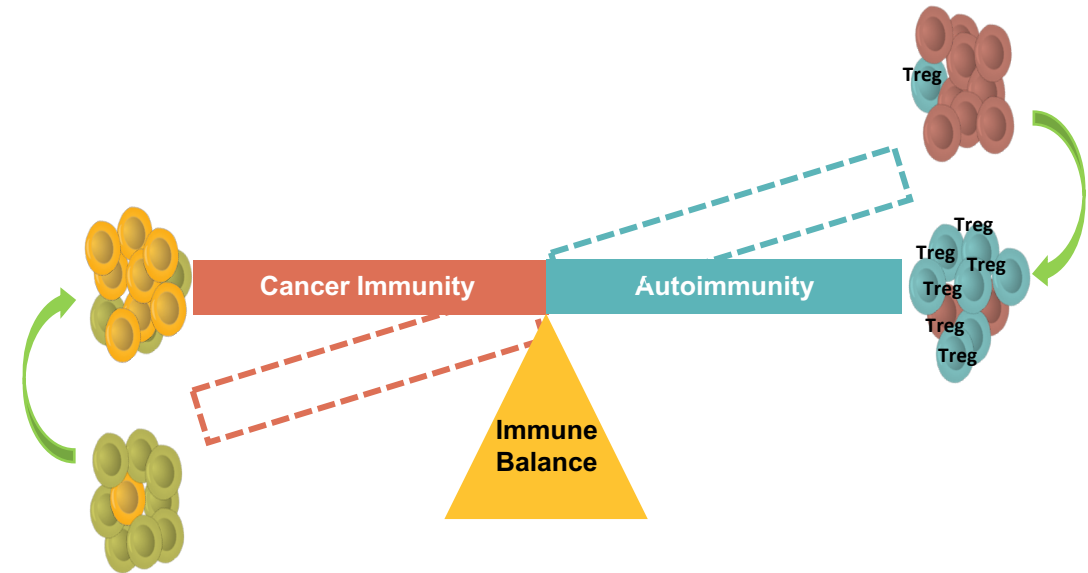


Immuno-STAT Platform: Selective Modulation of Disease-Relevant T Cells

Immuno-STAT™ Platform



Immuno-STATs avoid systemic immune activation (oncology) or broad immune suppression (autoimmunity)

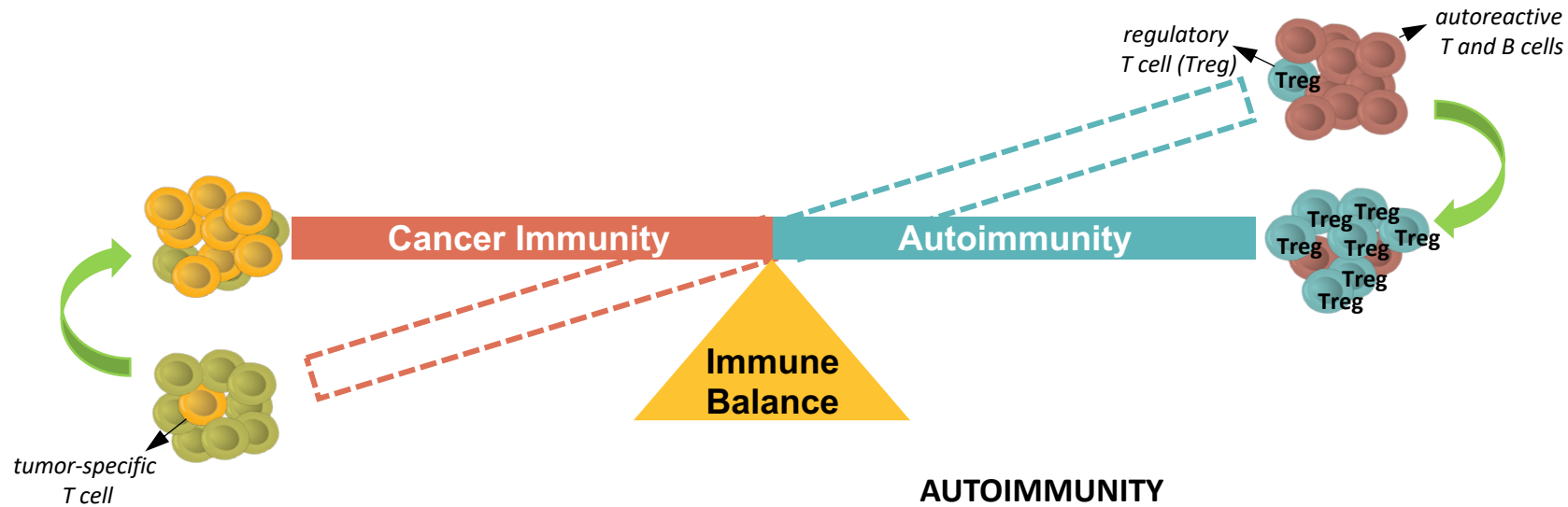


Cancer: ↑ Tumor-specific T cells

Autoimmunity: ↑ Regulatory T cells (Tregs)

 ↓ Deplete Pathogenic B cells

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

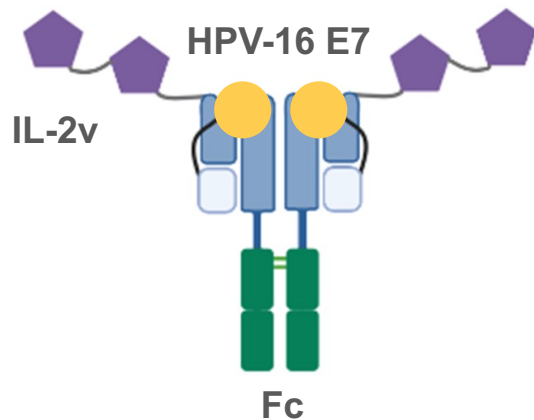
- **CUE-401 (Regulatory T cells, Tregs)**
 - Biologic for conversion and expansion of new Tregs
 - Broad applications in autoimmune and inflammatory diseases
 - Partnered with Ono Pharmaceuticals (option for 50% US rights)
- **CUE-500 Series (targeting autoreactive B cells)**
 - MoA: T cell-mediated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

A large, glowing, spherical object resembling a virus or a cluster of cells, centered on a teal background with a white horizontal band. The object is composed of many small, interconnected parts, giving it a textured, crystalline appearance. It is surrounded by a faint, circular glow. The background is a solid teal color, with a white horizontal band across the middle. The overall aesthetic is clean and scientific.

CUE-101

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

CUE-101



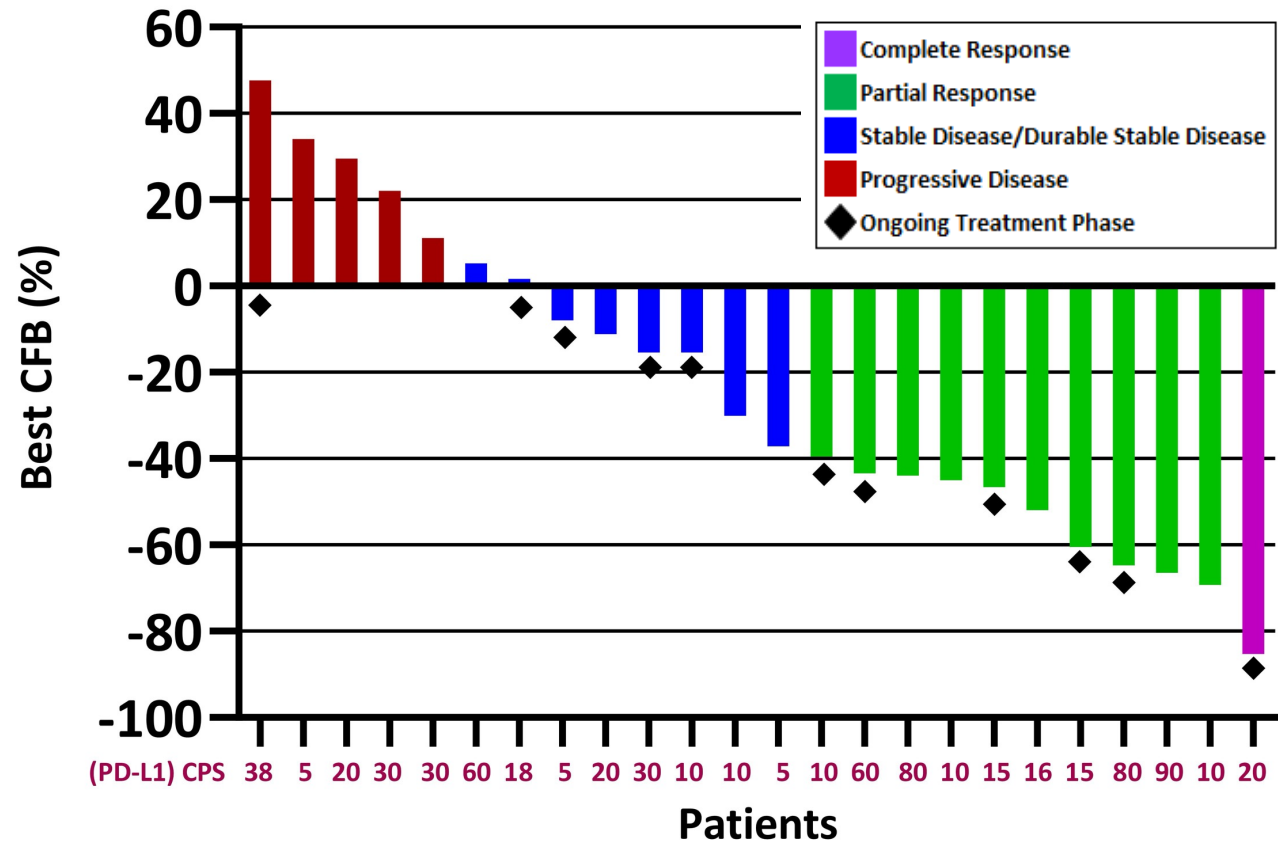
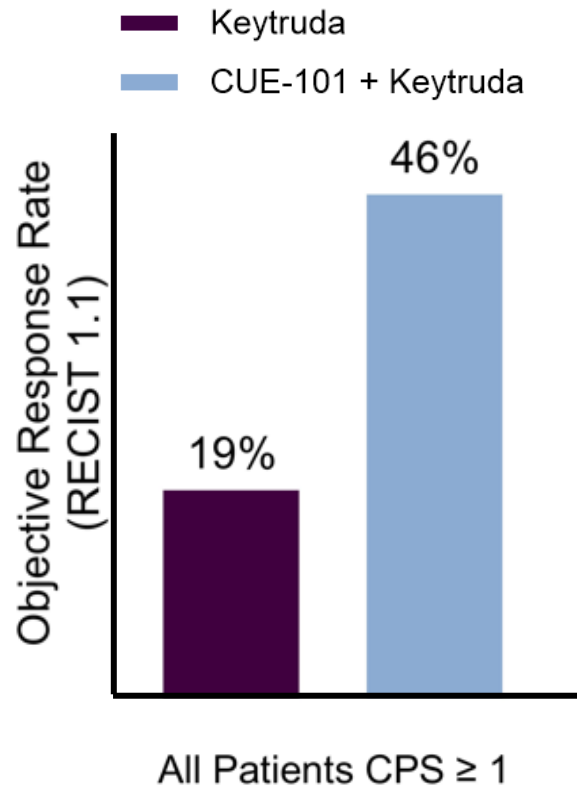
Abbreviations:
 mOS = Median Overall Survival
 SOC = Standard of Care
 ORR = Overall Response Rate
 mPFS = Median Progression Free Survival
 IST = Investigator Sponsored Study

	Locally Advanced			
	2L+ R/M	1L R/M	Neoadjuvant	Adjuvant
Status	CUE-101 Phase IA/IB Fully Enrolled Doubled mOS vs. SOC	CUE-101 + KEYTRUDA Phase IA/IB Fully enrolled Doubled ORR and mPFS vs. SOC	IST Ongoing	IST Planned
Market Opportunity	~\$400M	~\$900M	~\$1.5-2.0B	

Source: based on 2024 analysis conducted by Trinity Life Sciences, peak US and EU-5 revenue estimates

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%)



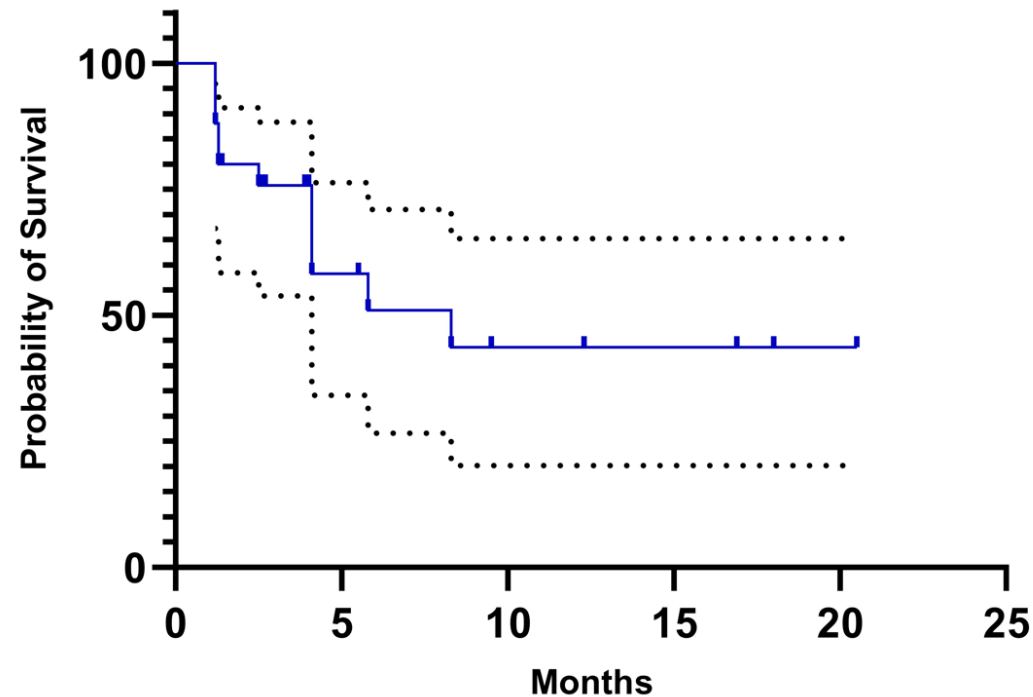
(1) KEYNOTE 048 Study; Burtness B et al, Lancet 2019; (2) Harrington et al, J Clin Oncol 2022.

1L = First line; CPS = Combined Positive Score

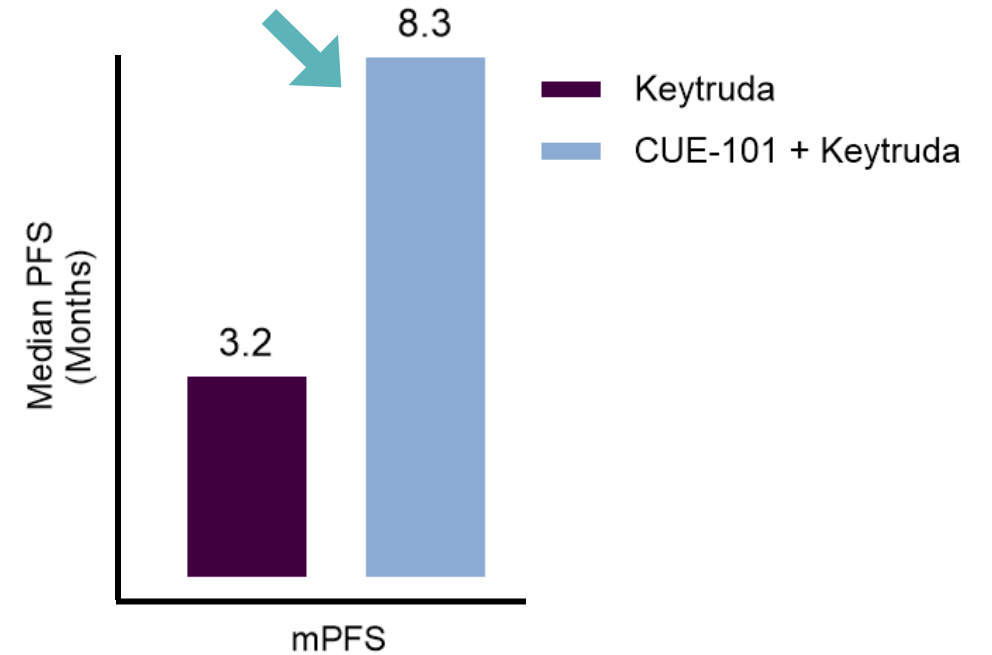
Data Extract: 06-Feb-2024. Includes 24/25 patients in Response Evaluable Population

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

CUE-101 + Keytruda Progression Free Survival



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



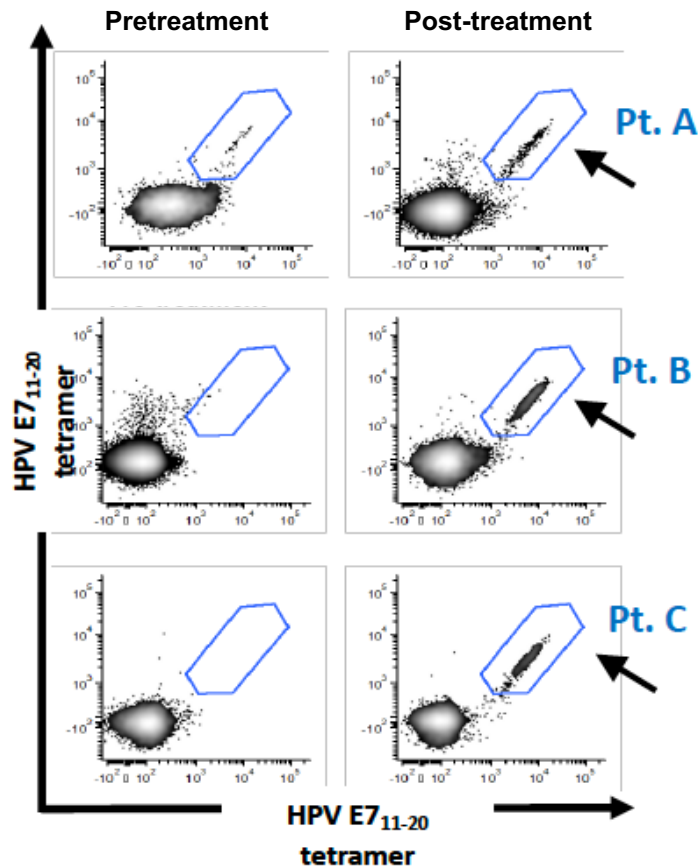
Kaplan-Meier estimate of median PFS 8.3 months [95% CI; 5.0, NA] in the 25 patients treated with CUE-101 (4 mg/kg) + Keytruda combination therapy.

* Cross-study comparison to KEYNOTE 048 Study; Burtneess B et al, Lancet 2019

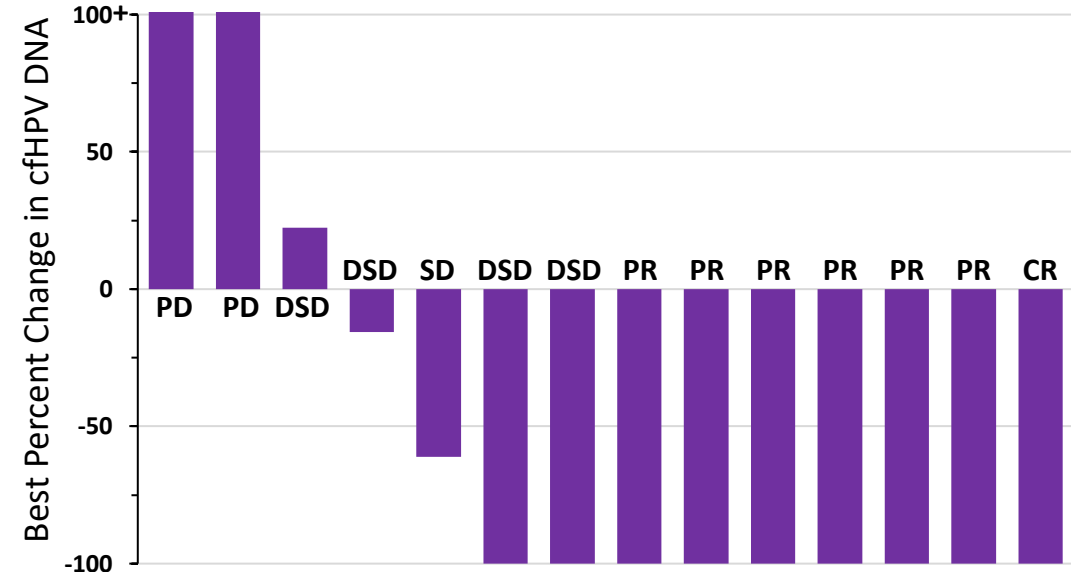
Data Extract: 06-Feb-2024.

CUE-101 MoA: Tumor-Specific T Cell Expansion and Biomarker/Response

Tumor-specific T cell Expansions

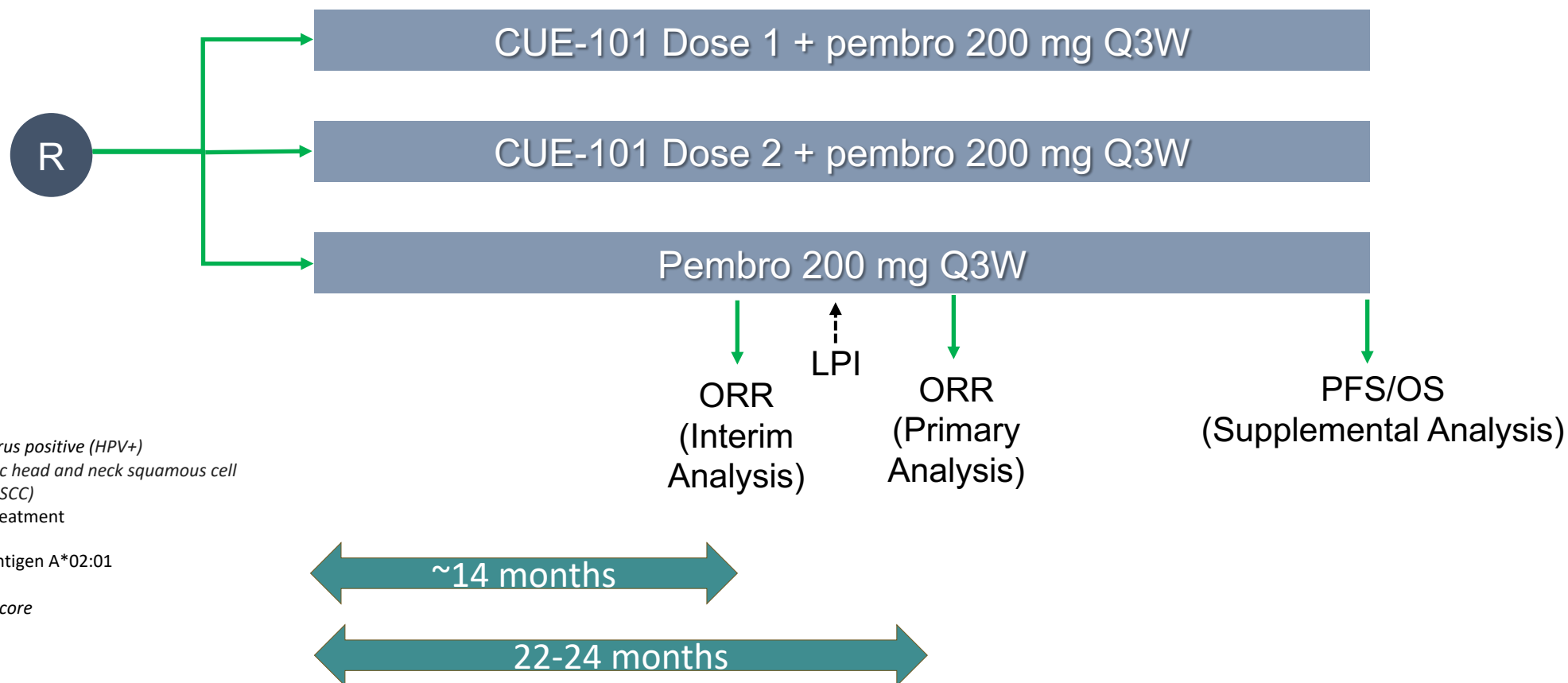


Reduction in Cell-Free HPV DNA Correlates with Response



- All tested patients treated with CUE-101 plus pembro combination with RECIST-determined PRs or CR achieve ~100% reduction in circulating cell-free HPV DNA
- ~100% reduction in cell-free HPV DNA also observed in multiple patients with durable stable disease as classified by RECIST

Phase 2, randomized, controlled study of CUE-101 in combination with pembrolizumab compared with pembrolizumab alone as first-line treatment of patients with recurrent/metastatic (R/M) HPV+ HNSCC



- RM HPV+ HNSCC
*Human papillomavirus positive (HPV+)
recurrent/metastatic head and neck squamous cell
carcinoma (R/M HNSCC)*
- No prior systemic treatment
- HLA-A*02:01
*Human leukocyte antigen A*02:01*
- CPS ≥ 1
Combined positive score

Significant Value Inflection Readout by Randomized Phase 2 CUE-101 Trial

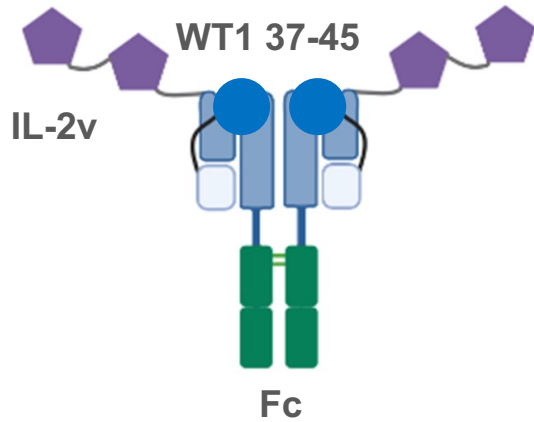
- **CUE-101-01 combination data compelling compared to historical, published metrics of clinical benefit**
- **Randomized Phase 2 study of CUE-101 +/- pembrolizumab provides:**
 - Confirmation of CUE-101 dose for Phase 3 study
 - Estimation of treatment effect (ORR and PFS) to inform Phase 3 study design and sample size
 - Increased confidence in probability of success in registrational trial
- **Potential new SOC in patients with HPV+ R/M HNSCC**
- **Further increases probability of success of future combos of CUE-100 series ISTs + CPI**



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*

2L+
R/M

Regimen

CUE-102

Status

- ✓ Dose Escalation Fully Enrolled
- ✓ Favorable Tolerability
- ✓ Emerging Signals of Activity
- ✓ Expansion cohorts enrolling

Phase IA/IB

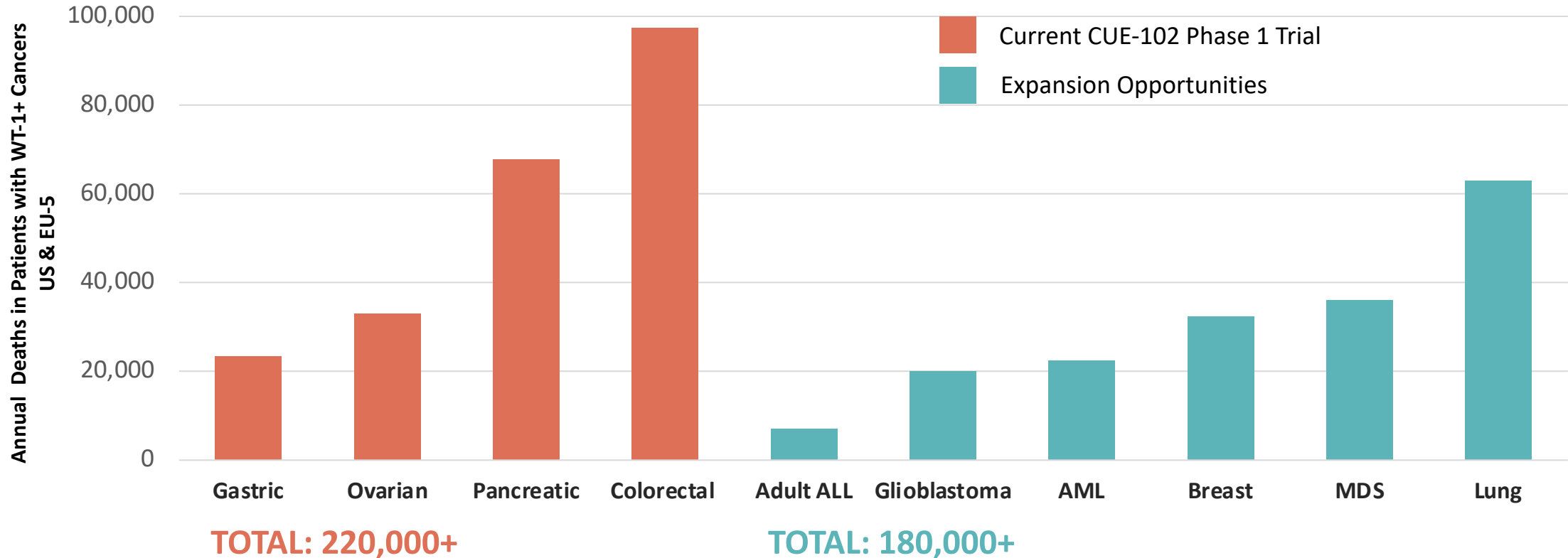
1L
R/M

CUE-102 +/- SoC

WT1-Positive
R/M
Locally Advanced

*Breast, Lung, GBM, Others
AML, MDS, ALL, Others*

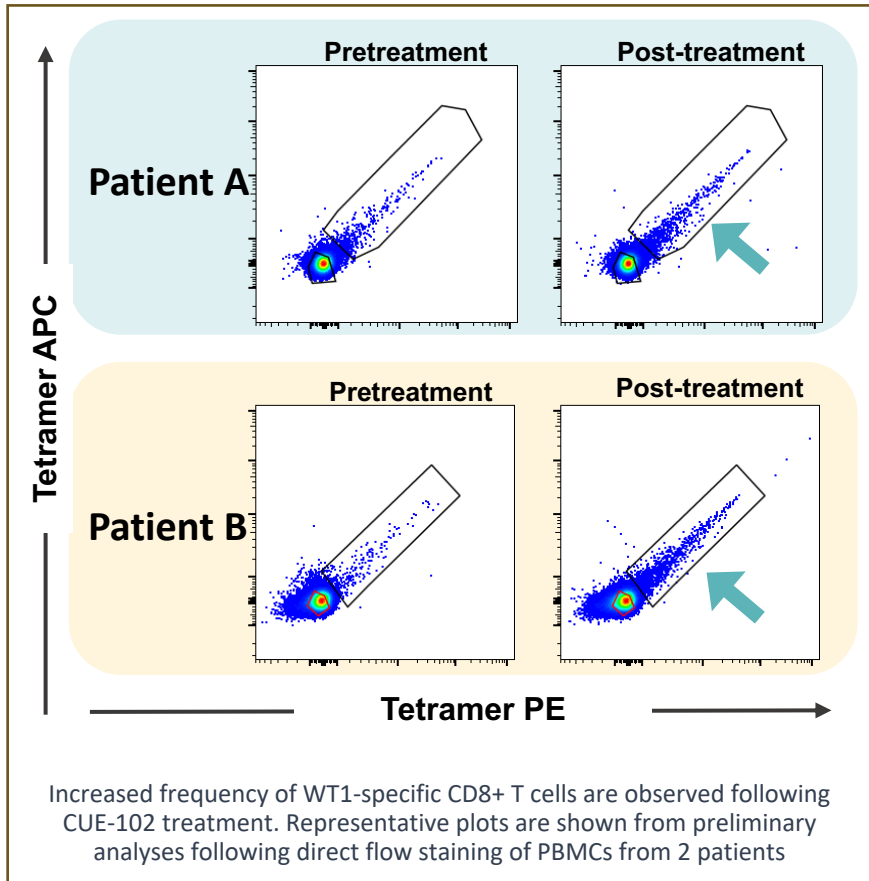
Significant Unmet Need in Patients with WT1-Positive Cancers



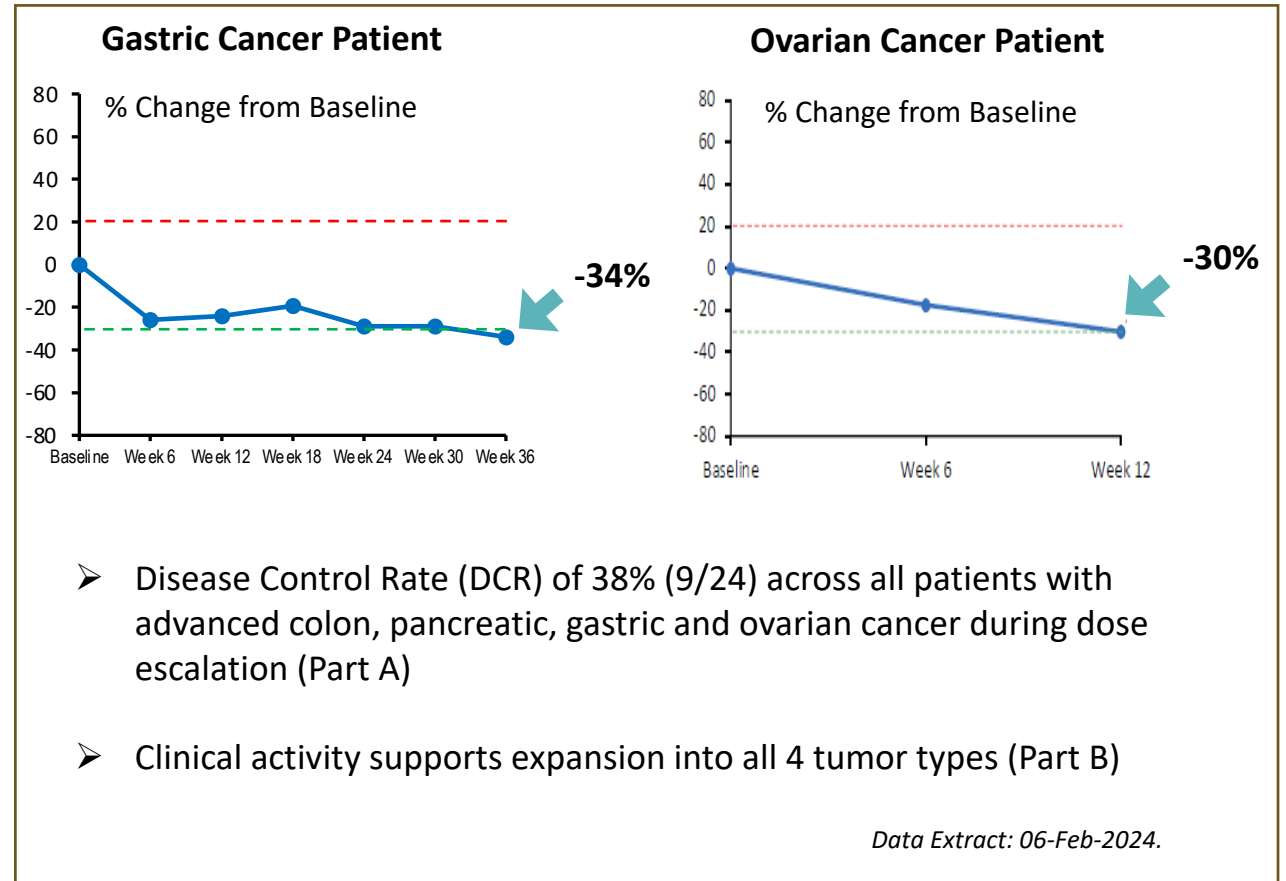
Sources: 1. Trinity Life Sciences 2. Globocan 2020; 3. SEER; 4. Qi XW et al. *Sci Rep.* 2015 Mar 9;5:8924. doi: 10.1038/srep08924; 5. Naitoh K et al. *Anticancer Research* July 2016, 36 (7) 3715-3724, 6. Xiang C et al. *Hematology.* 2023 Mar 27: doi10.1080/16078454.2023.2254557, 7. Jiang Y et al. *Oncotarget.*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

CUE-102 Treatment: Selective T cell Expansion and Tumor Reductions

Selective Expansion of WT-1-specific T cells

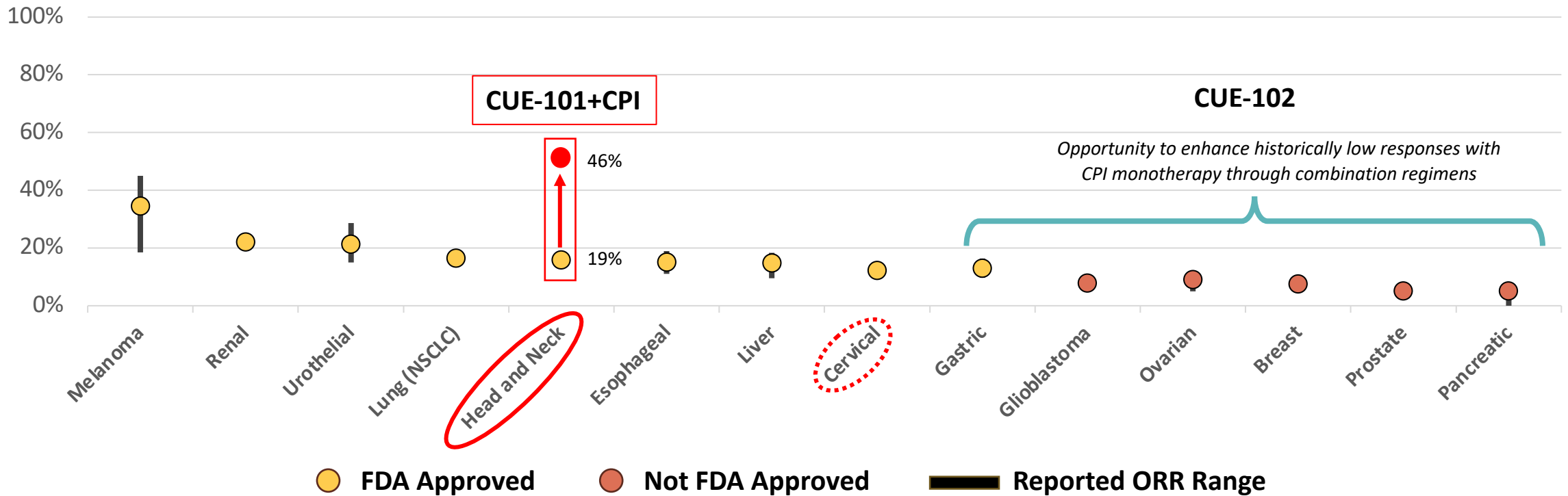


Examples of Tumor Reductions in CUE-102-treated Patients



CUE-100 Series: Potential to Expand Patient Reach and Enhance 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.

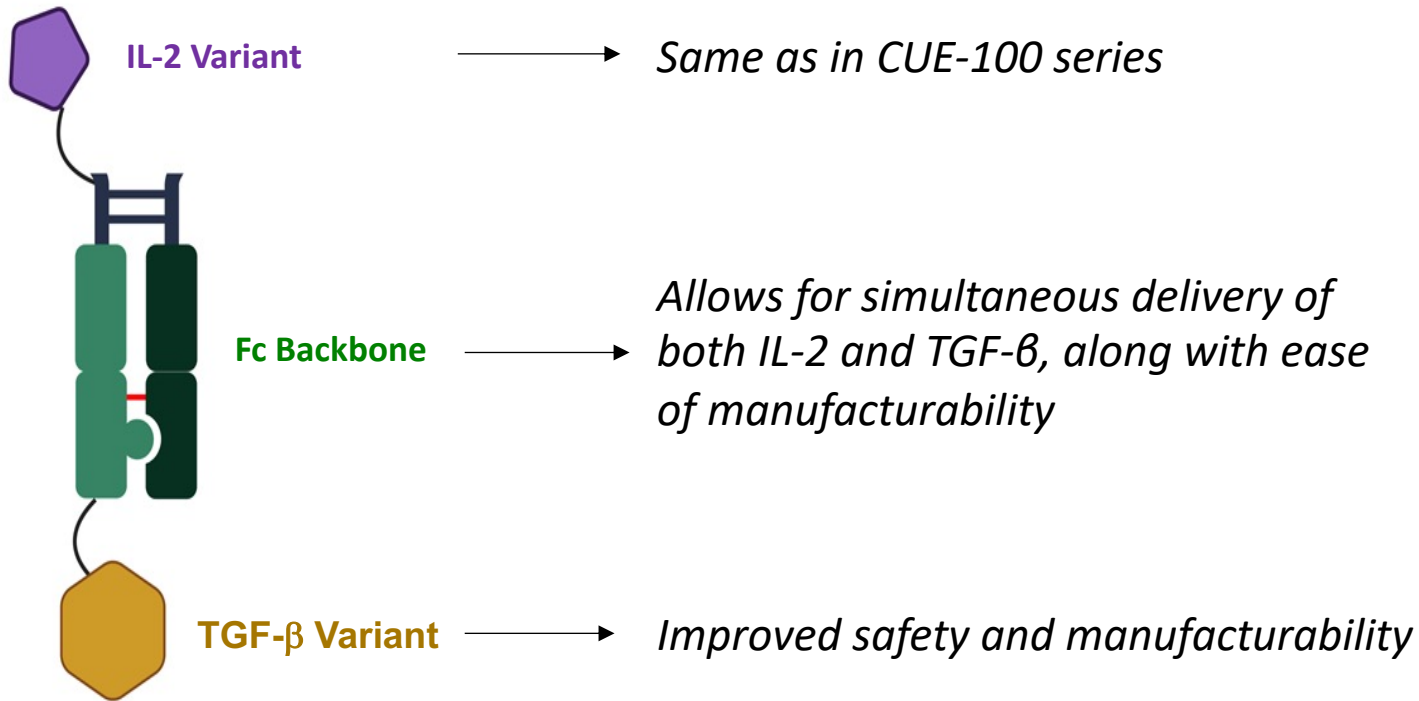
A microscopic image of a cell, likely a Treg cell, with a bright, glowing nucleus. The cell is surrounded by a complex network of cytoplasm and organelles, all rendered in shades of teal and light blue. The background is a soft, out-of-focus teal color.

Autoimmune Diseases

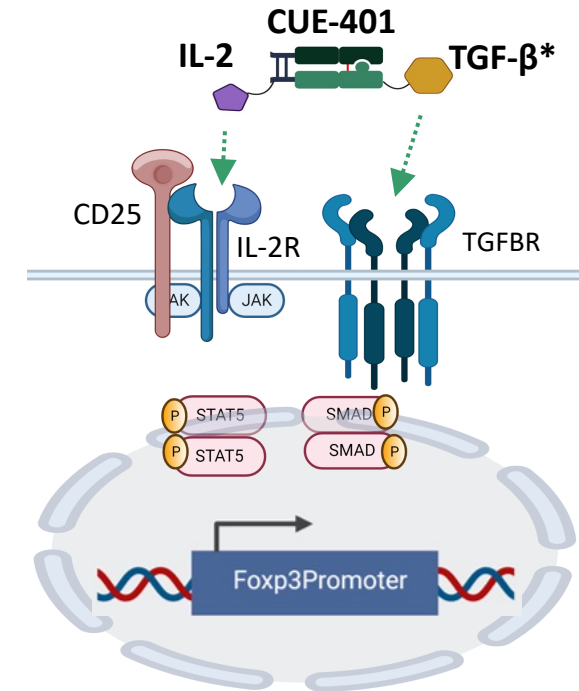
CUE-401 – Conversion and Expansion of NEW Tregs

CUE-401: Designed for Conversion and Expansion of Tregs

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



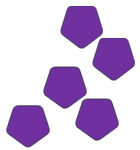
CUE-401 results in induction of FOXP3+ Tregs



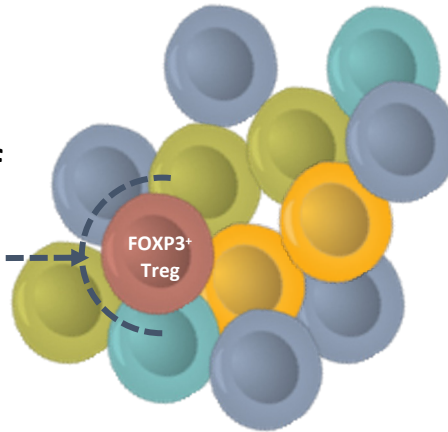
**Ono Pharmaceutical funding ongoing research activities through preclinical option period
Cue retains a 50% co-development and co-commercialization right in the US market**

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

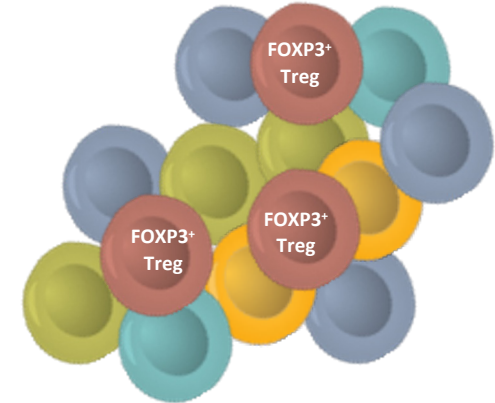
CD25-biased
IL-2 muteins



Focus on a minor population of
pre-existing nTregs



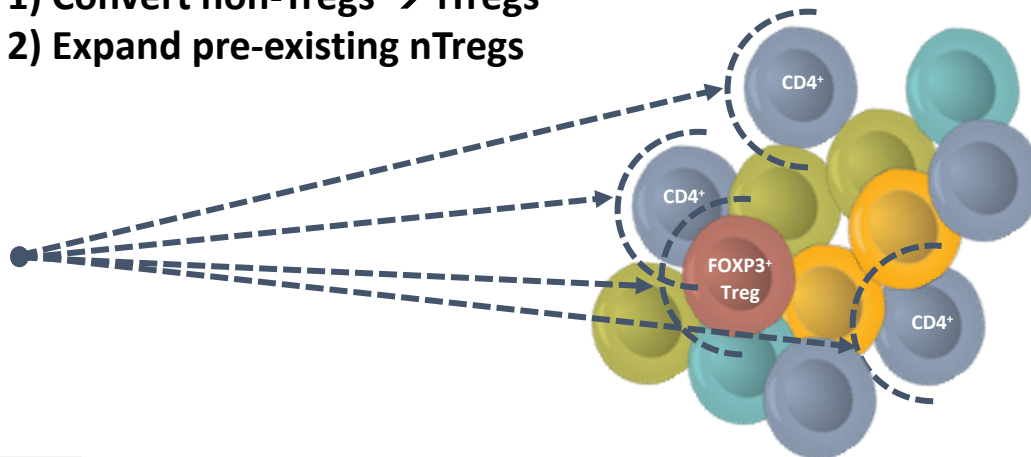
Limited Treg
Expansion



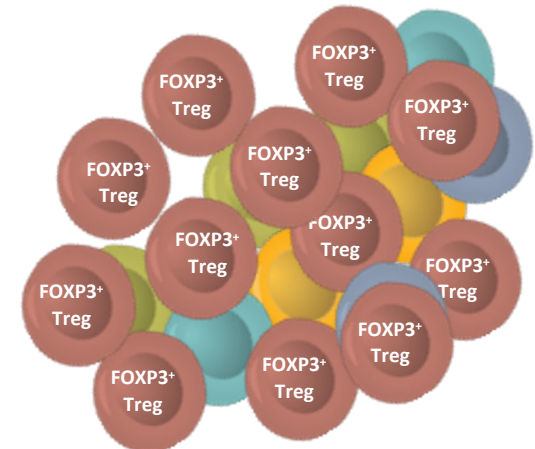
Two Key MOAs:

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

CUE-401

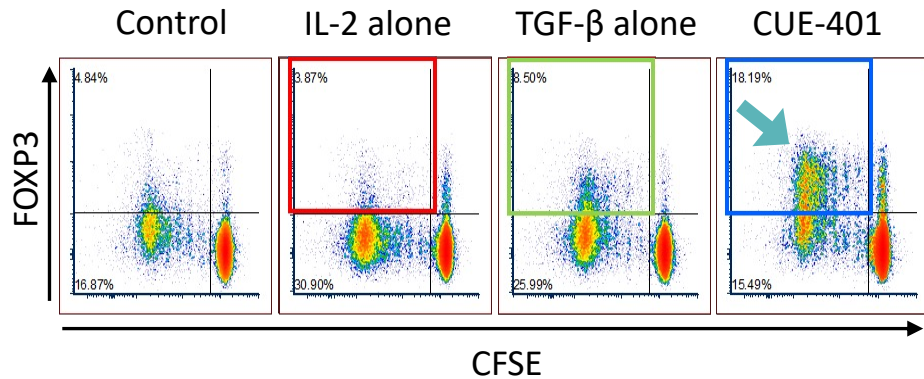


Greater Treg
Frequency

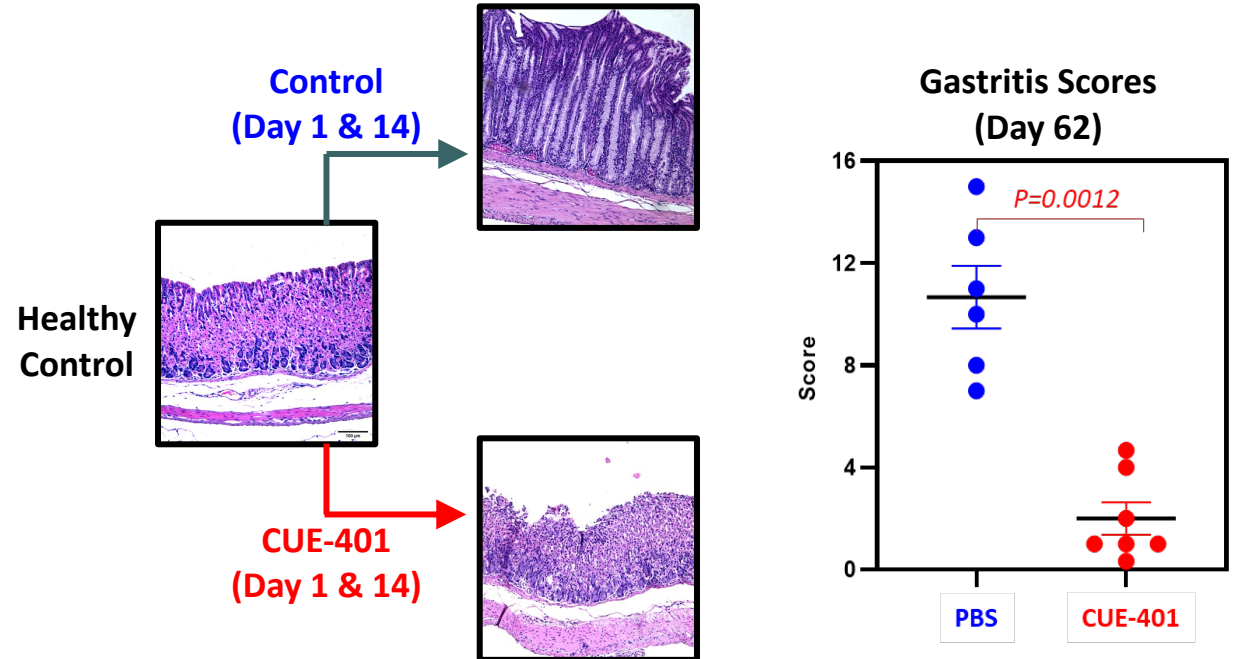


CUE-401: Mechanism of Action and In Vivo Efficacy

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



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

A microscopic image of a cell, likely a B cell, is shown in shades of teal and white. The cell's surface is highly textured and irregular. A horizontal white band is superimposed across the center of the image, containing the text. The background is a dark teal color with some light-colored speckles.

CUE-500 Series

***Biologics for B cell Depletion in Autoimmune and
Inflammatory Diseases***

T Cell-Mediated B Cell Depletion: Established Efficacy in Oncology and Encouraging Results from Initial CAR-T Trials in Autoimmunity

CAR-Ts Targeting B Cells in Oncology

APPROVED CAR T-CELL THERAPIES

BRAND NAME	GENERIC NAME	TARGETED DISEASE
Kymriah™	tisagenlecleucel	Follicular Lymphoma, Diffuse Large B-cell Lymphoma, or Lymphoblastic Leukemia
Yescarta™	axicabtagene ciloleucel	Follicular Lymphoma or Diffuse Large B-cell Lymphoma
Tecartus™	brexucabtagene autoleucel	Mantle Cell Lymphoma or Acute Lymphoblastic Leukemia
Breyanzi®	lisocabtagene maraleucel	Large B-cell Lymphoma
Abecma®	idecabtagene vicleucel	Relapsed or Refractory Multiple Myeloma
Carvykti™	ciltacabtagene autoleucel	Relapsed or Refractory Multiple Myeloma

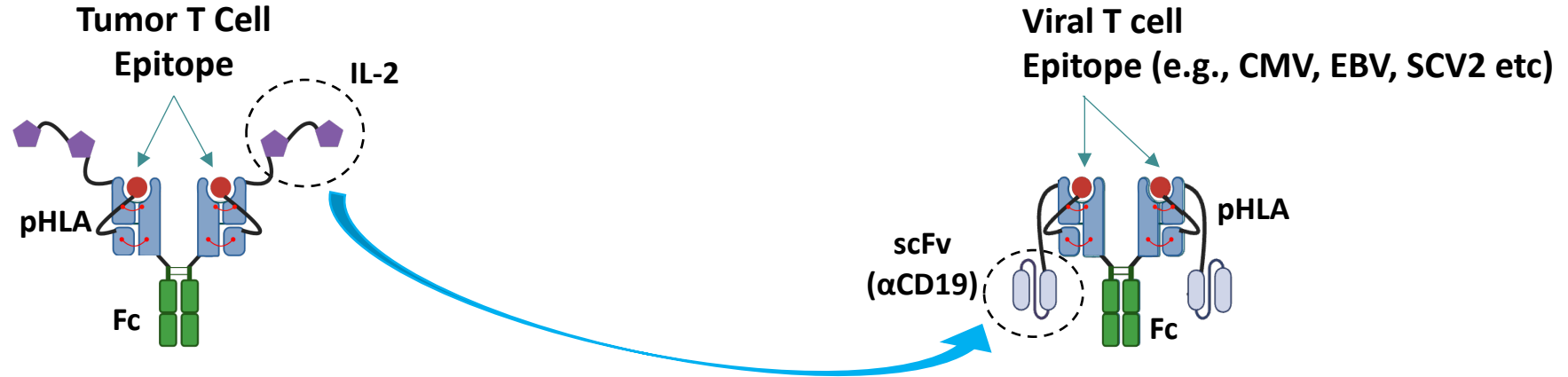
CAR-Ts Targeting B Cells in Autoimmunity



CD19 CAR T-Cell Therapy in Autoimmune Disease — A Case Series with Follow-up

Company	Target	Status/Indication ¹
Novartis	CD19	Ph1/2 in lupus
Cartesian Tx	BCMA	Ph2 in MG
BMS	CD19	Ph1 in lupus
Cabaletta Bio	CD19	Ph1 in lupus
Gracell	CD19 & BCMA	Ph1 in lupus
Kyverna	CD19	Preclinical

T Cell-Mediated B Cell Depletion: CUE-500 Series Leverages a Derisked, Validated Framework



CUE-100 series (Oncology)

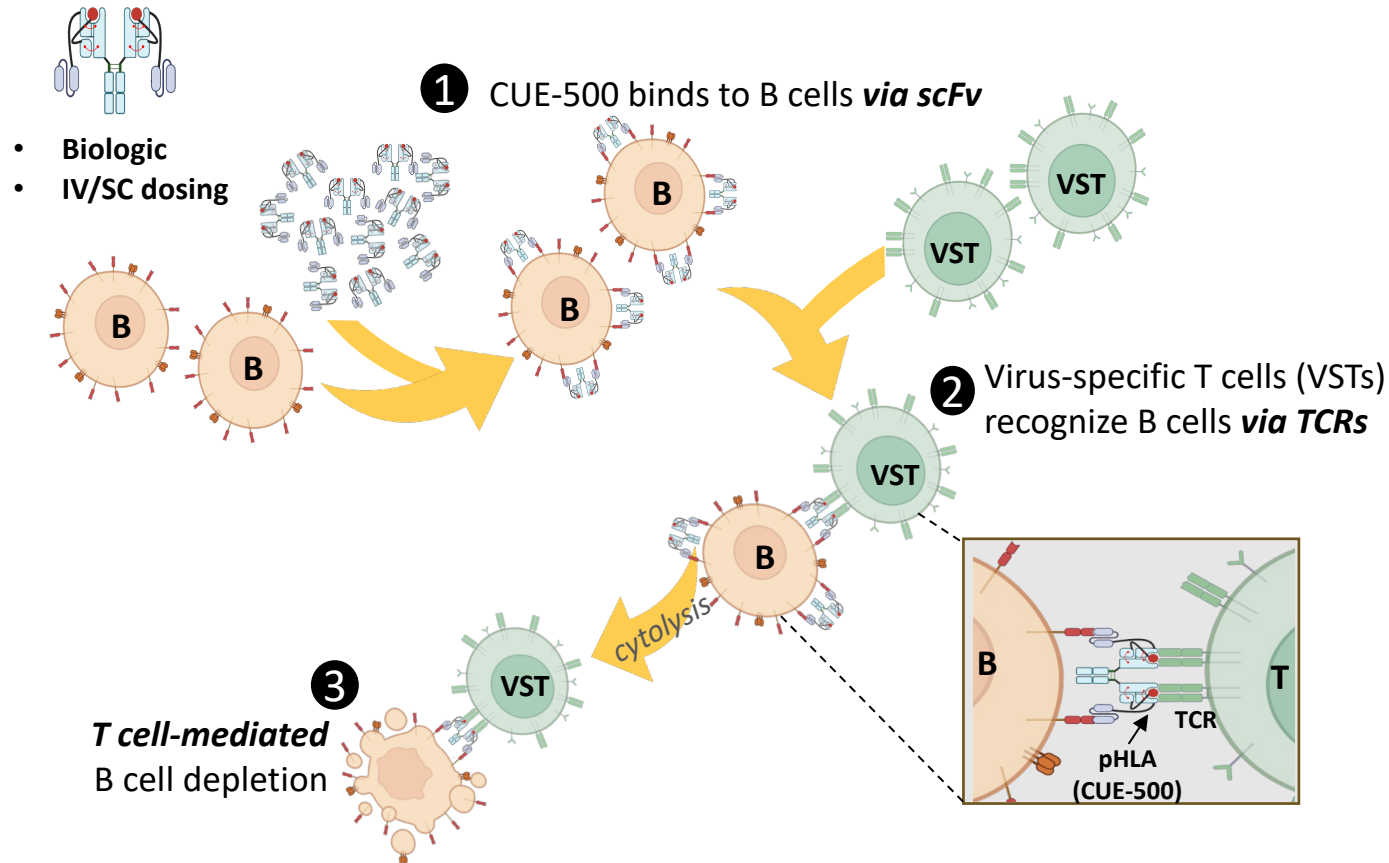
Selective Targeting of IL-2 to Tumor-Specific T cells

- ✓ Clinical Validation and Platform De-risking
 - ✓ MonoTx Efficacy (> doubling of mOS)
 - ✓ CPI Combo Efficacy (> doubling ORR and mPFS)
 - ✓ Alignment with FDA on a registration path
- ✓ Highly manufacturable with attractive COGS
- ✓ Favorable tolerability (Over 100 patients dosed; no MTD)
- ✓ No clinically-relevant immunogenicity

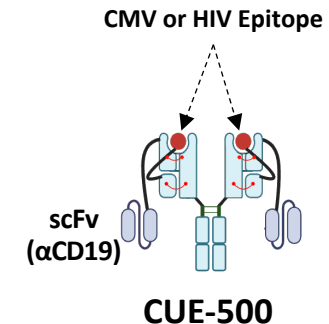
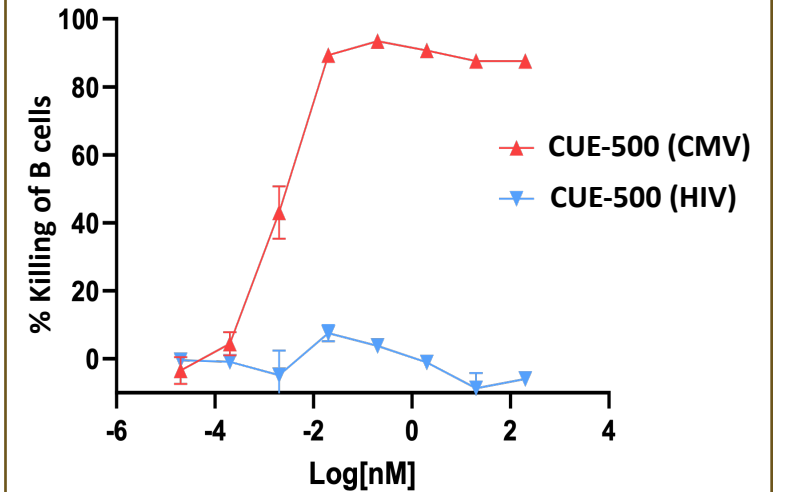
CUE-500 series

Engaging Virus-Specific T Cells (VSTs) to Deplete B Cells

CUE-500 Series: Mechanism of Action and Selective B Cell Killing

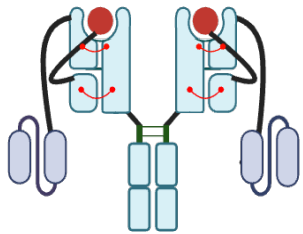


CUE-500: B Cell Killing by CMV-Specific Memory CD8+ T Cells



Market Opportunity: Breadth of B Cell Mediated Autoimmune Diseases (and Cancers) Represents Pipeline in a Product

CUE-500 Series



Biologic for paradigm-shifting treatment of numerous autoimmune diseases

➤ Autoimmunity:

- **Neuro-Inflammation** (MS, Myasthenia Gravis, Chronic inflammatory demyelinating polyradiculoneuropathy, NMO)
- **Rheumatology** (SLE, RA, Myositis, ANCA-vasculitis)
- **Hematology** (Immune thrombocytopenic purpura, Autoimmune hemolytic anemia, Antiphospholipid syndrome)
- **T1D and Endocrine** (Graves, Thyroiditis)
- **Dermatology** (Pemphigus, Bullous pemphigoid, Vitiligo)

➤ Transplantation:

- **Solid-organ transplants** (Ablation of donor-reactive allo Abs)

➤ Severe Allergies:

- **E.g., Food allergies** (Ablation of allergen-reactive B cells)

➤ Oncology:

- **B cell Malignancies** (MM, DLBCL, NHL, CLL, MCL, etc.)

CUE-500 Differentiation: MoA Offers Distinctive Advantages over mAbs, T Cell Engagers and Cell Therapy Modalities

	Ab-Mediated ADCC (e.g., Rituxan, Kesimpta, etc.)	CAR T Cell Therapy (e.g., YTB323, CABA-201, etc.)	Pan T Cell Engagers (e.g., Blincyto, CD3/CD20)
Effector Cell	NK cells	Engineered T cells	Endogenous T cells
Key Attributes	<ul style="list-style-type: none"> Autoimmunity: Clinical efficacy with limited durability 	<ul style="list-style-type: none"> Autoimmunity: Early data demonstrates robust efficacy and durability 	<ul style="list-style-type: none"> Autoimmunity: Limited experience
Challenges	<ul style="list-style-type: none"> Limited durability Variable efficacy Reliant on Fc function and polymorphisms (low vs high responders) Potential for broad immune activation 	<ul style="list-style-type: none"> Autologous with complex manufacturing process/supply chain Requires pre-conditioning regimens and in-patient administration Toxicity Risks: CRS and neurotoxicity 	<ul style="list-style-type: none"> High risk for activation of autoreactive T cells Toxicity Risks: CRS and neurotoxicity MoA may not be suitable for long-term treatment

CUE-500 Series
Off-the-shelf biologic designed to selectively engage and redirect virus-specific “killer” memory T cells for B cell depletion

Financial Overview December 31, 2023



\$48.5M

Cash & Cash Equivalents



\$5.5M Full Year 2023

Collaboration Revenue



\$34.4M

Working Capital



47.2M

Common Shares Outstanding

Summary of Corporate Development Milestones

ONCOLOGY: Strategic Transaction to Enhance Capacity

- ✓ CUE-101 Randomized Ph 2 study: confirmation of enhanced efficacy of [ISTs + CPI] vs [CPI SoC]
 - *interim analysis @ 14 months and ORR/mPFS analysis @ 22-24 months*
- ✓ CUE-101+CPI Combo: Potential for new SoC in 1L R/M HNSCC patients
- ✓ Positions ISTs as the solution for expanding patient reach and efficacy for CPIs
- ✓ Places CUE in strong position as a partner of choice for CPI franchises
 - *CUE-102 patient expansion positions combos with CPI in large indication segments where CPIs have failed*

Autoimmunity: Proof of Concept for Transformative/Breakthrough Approach

- ✓ CUE-400: Treg induction and expansion for broad applications in many autoimmune diseases
 - *Partnered with Ono Pharmaceutical with 50% US market option retained by Cue*
 - *Clinical Candidate Selection (milestone)*
 - *IND Filing (milestone)*
- ✓ CUE-500: best-in-class opportunity with novel biologic for T cell-mediated B cell depletion
 - *Competitive with CAR-Ts, and differentiated from ADCC and pan T cell engagers*

Summary of Strategic Positioning

- **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
 - Have potential to “revitalize” CPI sector and enhance market reach
 - Validated platform modularity and scalability
- **Multiple novel platform applications with the potential to address some of the largest pharma markets in the US and Global**
 - Solid tumors and large autoimmune disease indications
- **Modular platform enables potential for multiple value creation opportunities**
 - Structural similarity provides potential regulatory advantages and capital efficiencies to develop numerous immunotherapies
 - Multiple potential partnering opportunities across platform and geographic regions

Thank you

Translating “Nature’s Cues” into
breakthrough immunotherapies



CUE™
B I O P H A R M A