Cue Biopharma, Inc.

Corporate Update

Nasdaq: CUE

April 2024

Forward-Looking Statements Disclaimer

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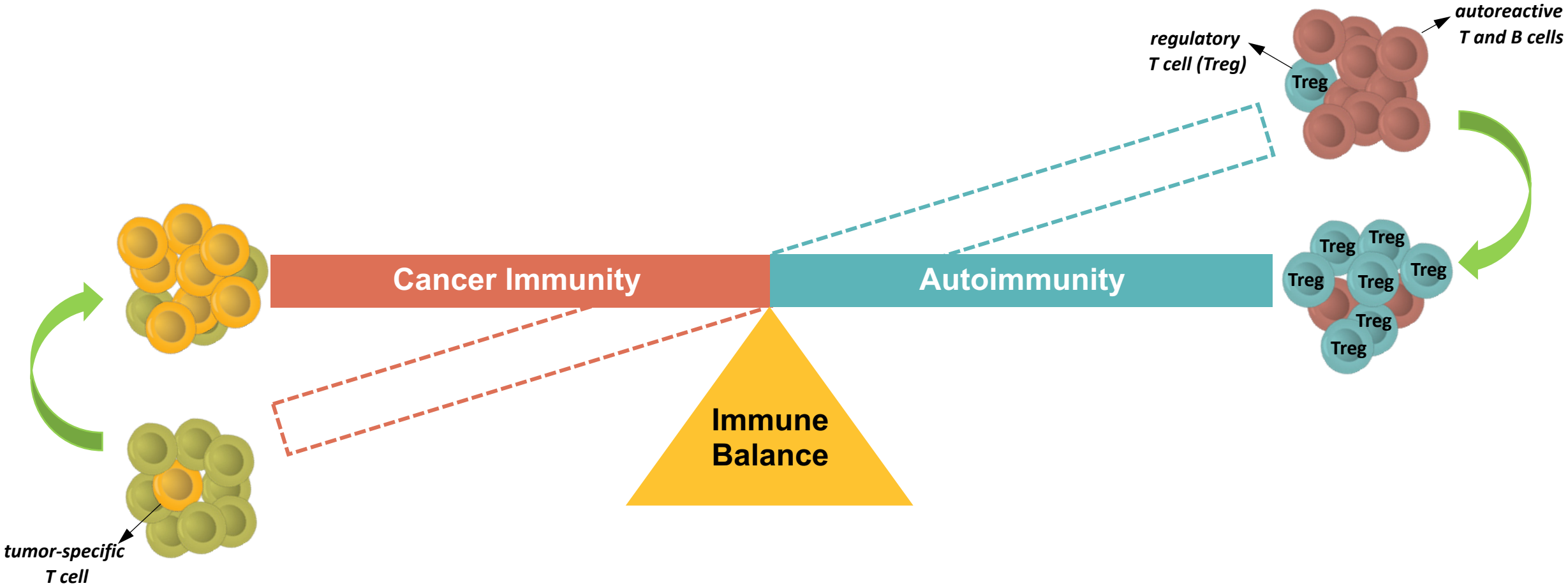
This presentation contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that are intended to be covered by the “safe harbor” created by those sections. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as “believe,” “expect,” “may,” “will,” “should,” “would,” “could,” “seek,” “intend,” “plan,” “goal,” “project,” “estimate,” “anticipate,” “strategy,” “future, “vision”, “likely” or other comparable terms, although not all forward-looking statements contain these identifying words. All statements other than statements of historical facts included in this presentation regarding our strategies, prospects, financial condition, operations, costs, plans and objectives are forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding our development plans for CUE-101 and the continued buildout of our pipeline, the sufficiency of our cash, cash equivalents and marketable securities to support the clinical development of CUE-101, anticipated results of our drug development efforts, including study results, our expectations regarding the timing of milestone events, regulatory developments and expected future operating results. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, our limited operating history, limited cash and a history of losses; our ability to achieve profitability; potential setbacks in our research and development efforts including negative or inconclusive results from our preclinical studies, our ability to secure required U.S. Food and Drug Administration (“FDA”) or other governmental approvals for our product candidates and the breadth of any approved indication; adverse effects caused by public health pandemics, including COVID-19, including possible effects on our operations and clinical trials; negative or inconclusive results from our clinical studies or serious and unexpected drug-related side effects or other safety issues experienced by participants in our clinical trials; delays and changes in regulatory requirements, policy and guidelines including potential delays in submitting required regulatory applications to the FDA; our reliance on licensors, collaborators, contract research organizations, suppliers and other business partners; our ability to obtain adequate financing to fund our business operations in the future; our ability to maintain and enforce necessary patent and other intellectual property protection, competitive factors, general economic and market conditions; and the other risks and uncertainties described in the Risk Factors and in Management's Discussion and Analysis of Financial Condition and Results of Operations sections of our most recently filed Annual Report on Form 10-K and any subsequently filed Quarterly Report(s) on Form 10-Q. Any forward-looking statement made by us in this presentation is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

Vision

Translating “Nature’s Cues” into breakthrough immunotherapies

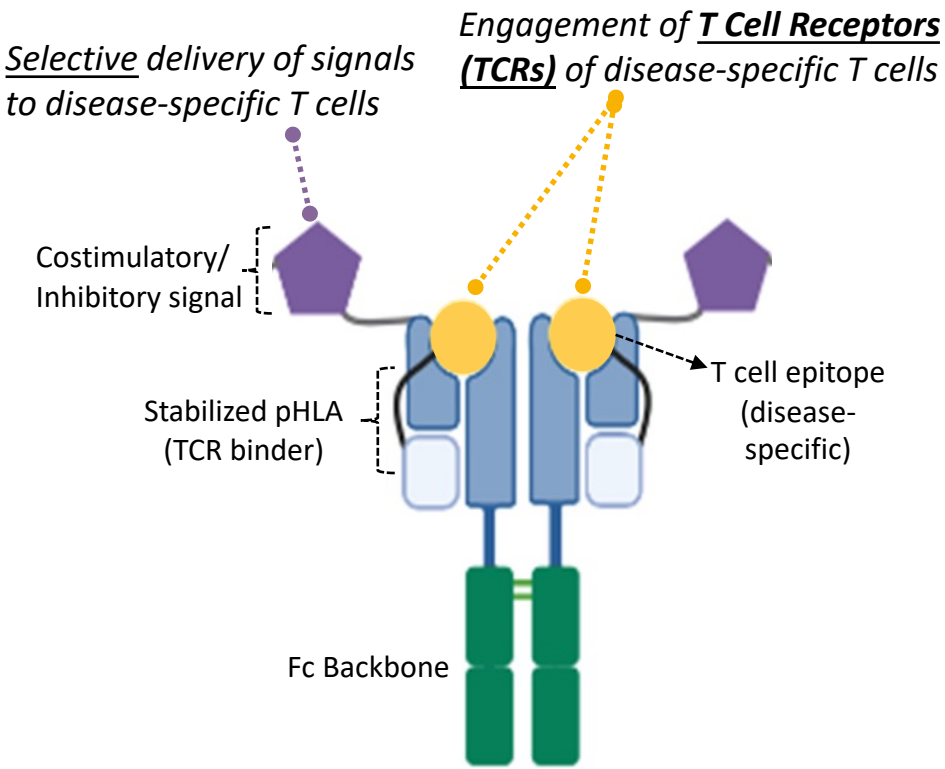
- ✓ Precision immunotherapy via a validated class of *selective* T cell engagers
- ✓ Clinical efficacy with paradigm shifting data
- ✓ Favorable tolerability
- ✓ Platform addresses significant unmet need in oncology and autoimmunity

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

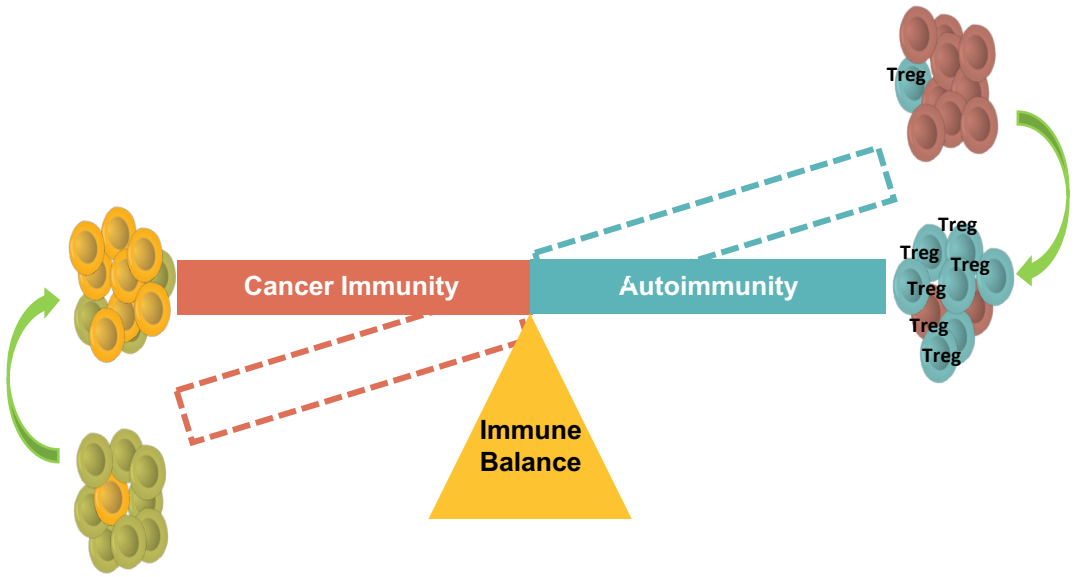


Immuno-STAT Platform: *Selective* Modulation of Disease-Relevant T Cells

Immuno-STAT™ Platform



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

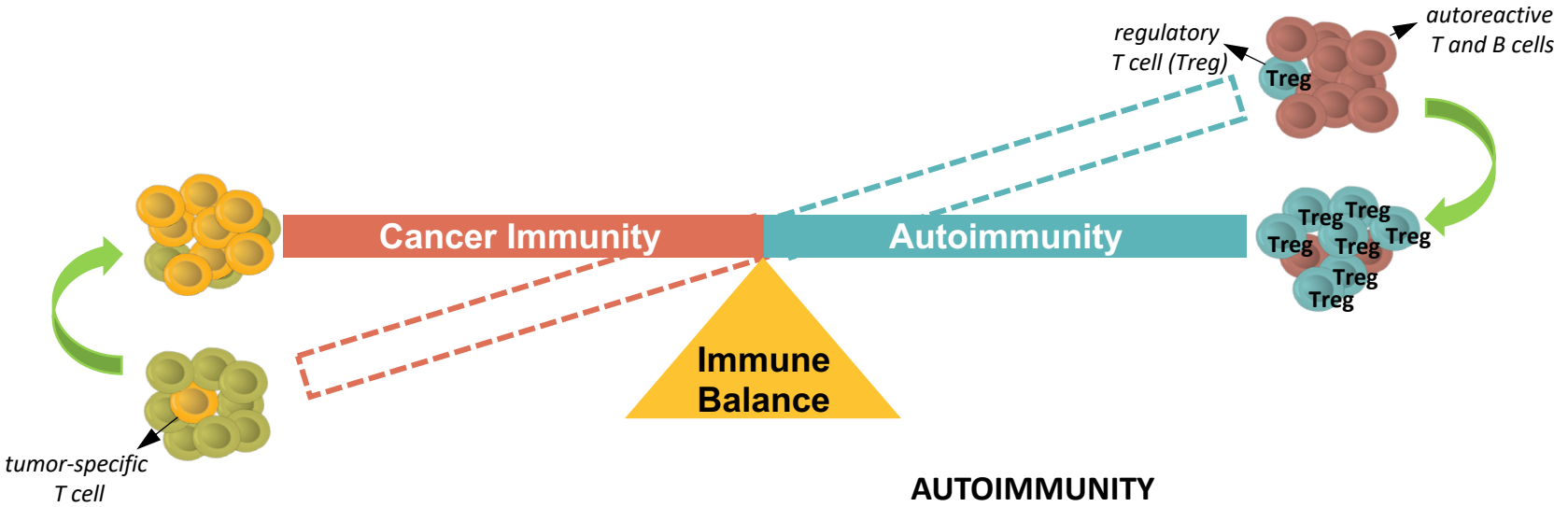


Cancer: ▲ **Tumor-specific T cells**

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.

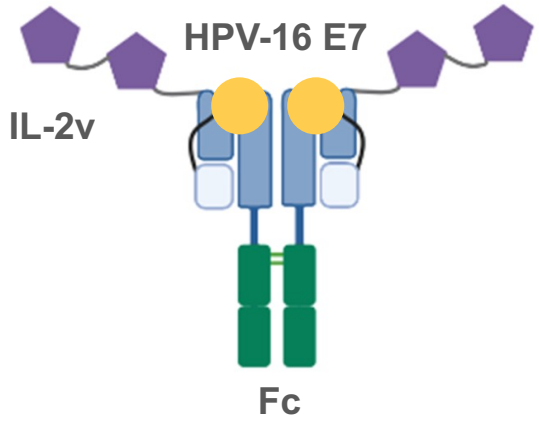
AUTOIMMUNITY

- **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


CUE-101

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

CUE-101



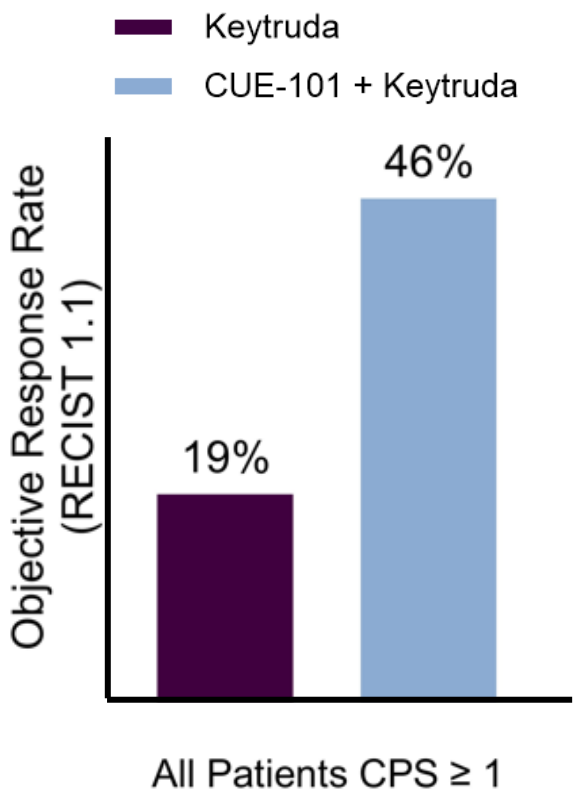
	CUE-101	CUE-101 + KEYTRUDA	Neoadjuvant	Adjuvant
Status	**Phase IA/IB** Fully Enrolled Doubled mOS vs. SOC	**Phase IA/IB** Fully enrolled Doubled ORR and mPFS vs. SOC	**IST** Ongoing	**IST** Planned
Market Opportunity	**~$400M**	**~$900M**	**~$1.5-2.0B**	

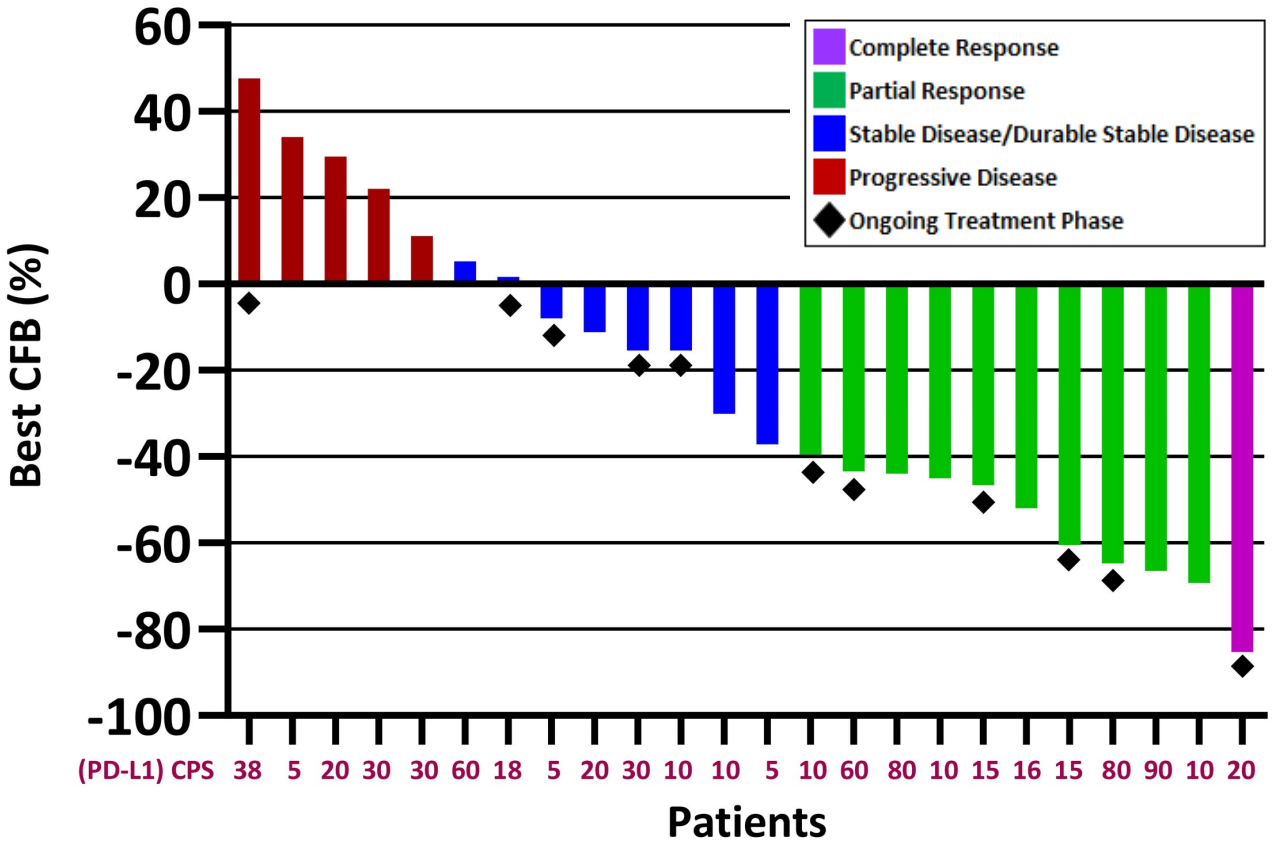
Abbreviations:
mOS = Median Overall Survival
SOC = Standard of Care
ORR = Overall Response Rate
mPFS = Median Progression Free Survival
IST = Investigator Sponsored Study

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%)



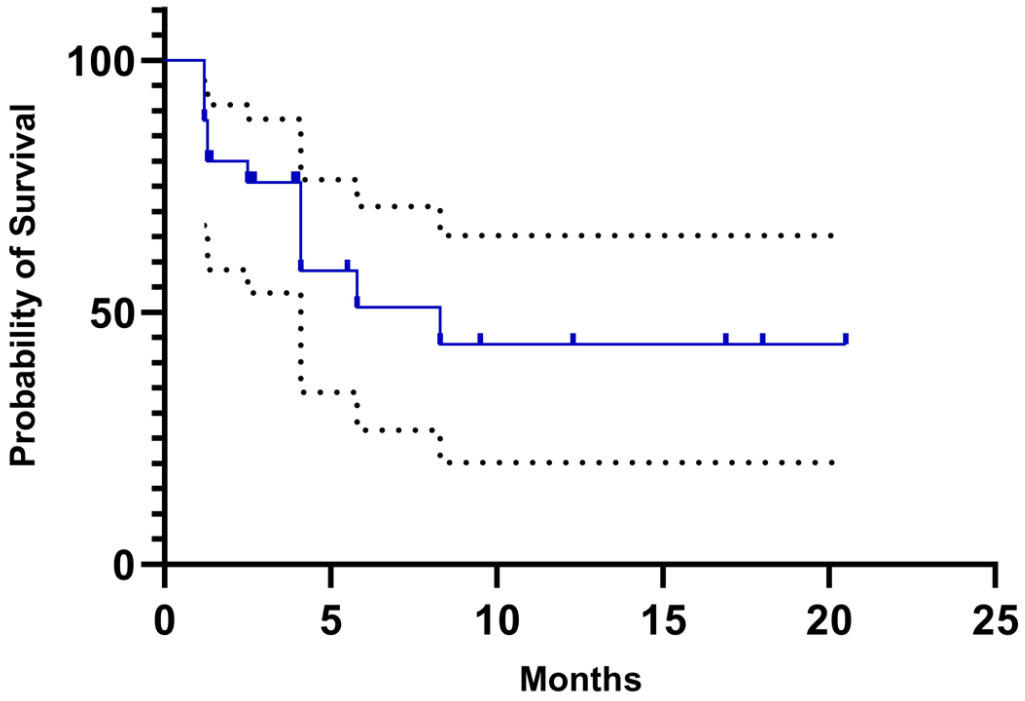


(1) KEYNOTE 048 Study; Burtness B et al, Lancet 2019; (2) Harrington et al, J Clin Oncol 2022.
1L = First line; CPS = Combined Positive Score

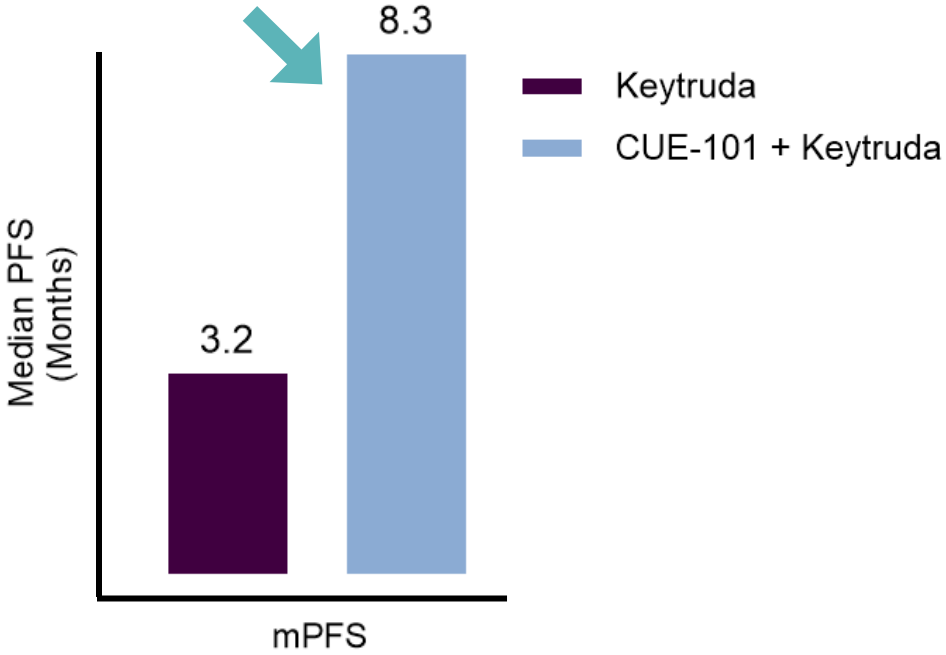
Data Extract: 06-Feb-2024. Includes 24/25 patients in Response Evaluable Population

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*



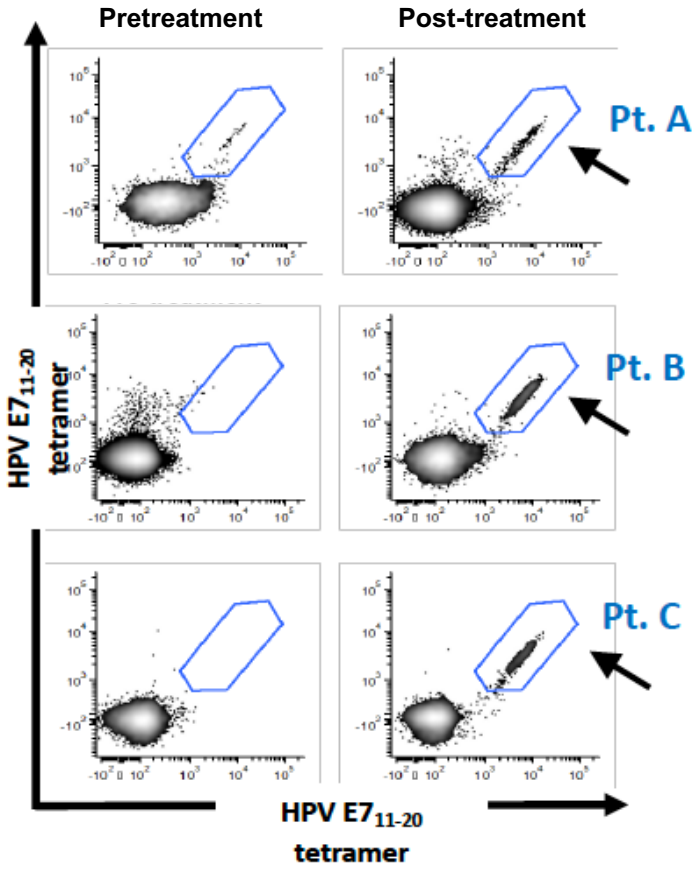
Kaplan-Meier estimate of median PFS 8.3 months [95% CI; 5.0, NA] in the 25 patients treated with CUE-101 (4 mg/kg) + Keytruda combination therapy.

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

Data Extract: 06-Feb-2024.

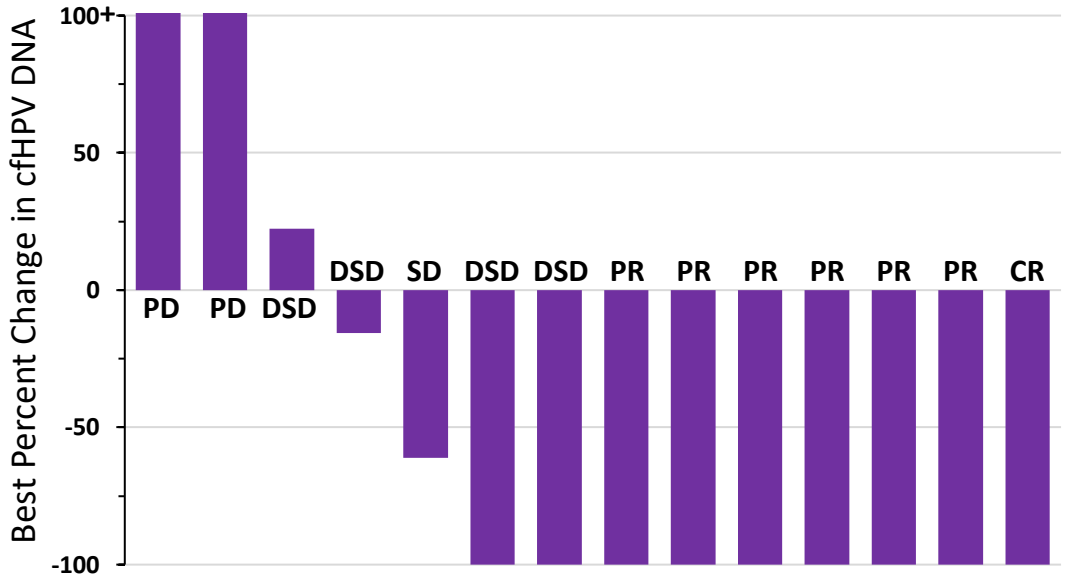
CUE-101 MoA: Tumor-Specific T Cell Expansion and Biomarker/Response

Tumor-specific T cell Expansions



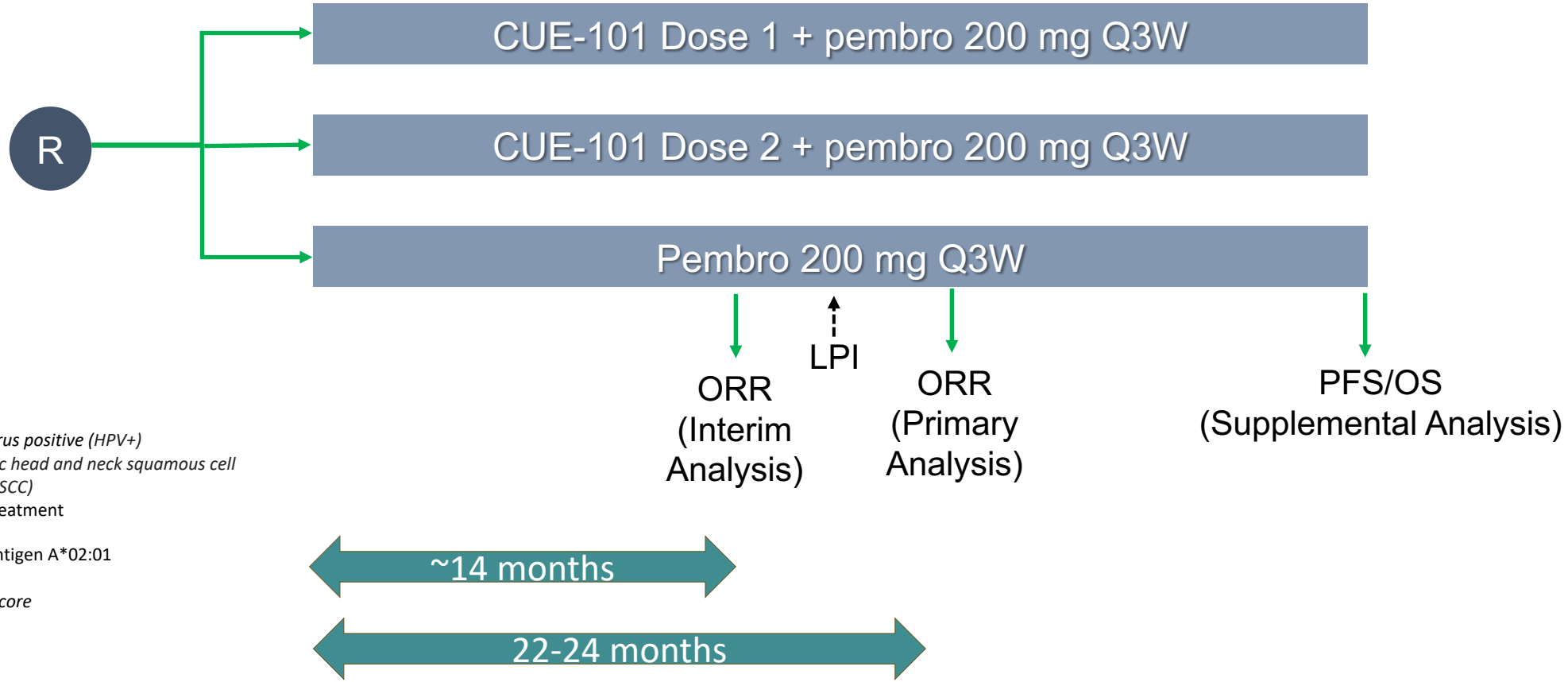
Examples of E7-specific T cell expansions in blood at different time-points from 3 subjects treated with CUE-101 at the RP2D dose of 4mg/kg

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

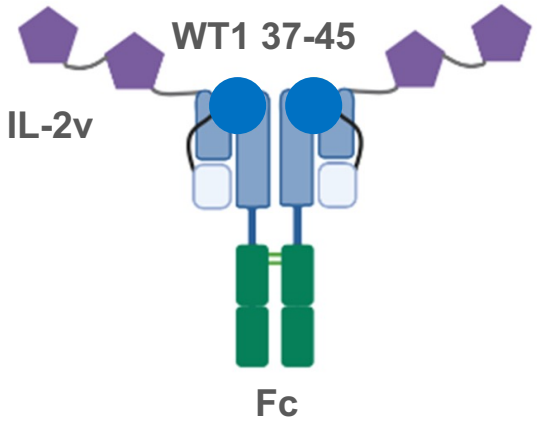
- **CUE-101-01 combination data compelling compared to historical, published metrics of clinical benefit**
- **Randomized Phase 2 study of CUE-101 +/- pembrolizumab provides:**
  - Confirmation of CUE-101 dose for Phase 3 study
  - Estimation of treatment effect (ORR and PFS) to inform Phase 3 study 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 BIOPHARMA

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

1L R/M

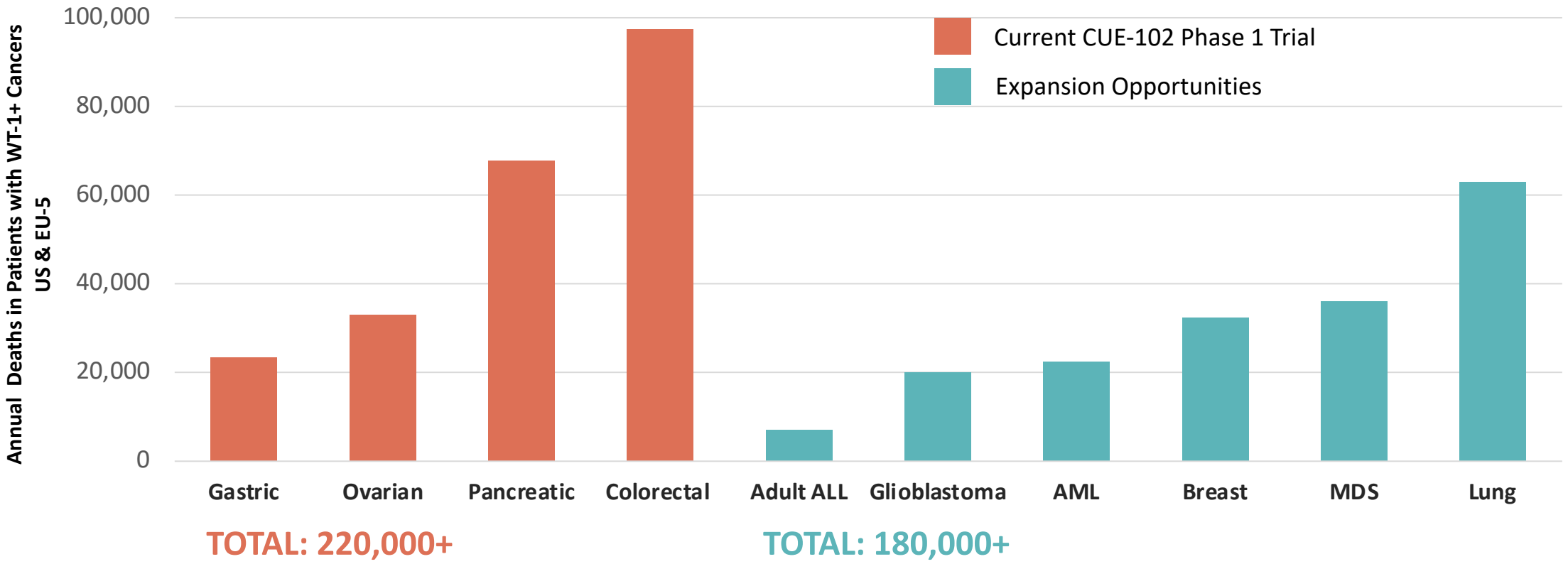
WT1-Positive R/M Locally Advanced

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

Regimen	**CUE-102**	**CUE-102 +/- SoC**
Status	**Phase IA/IB**	

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

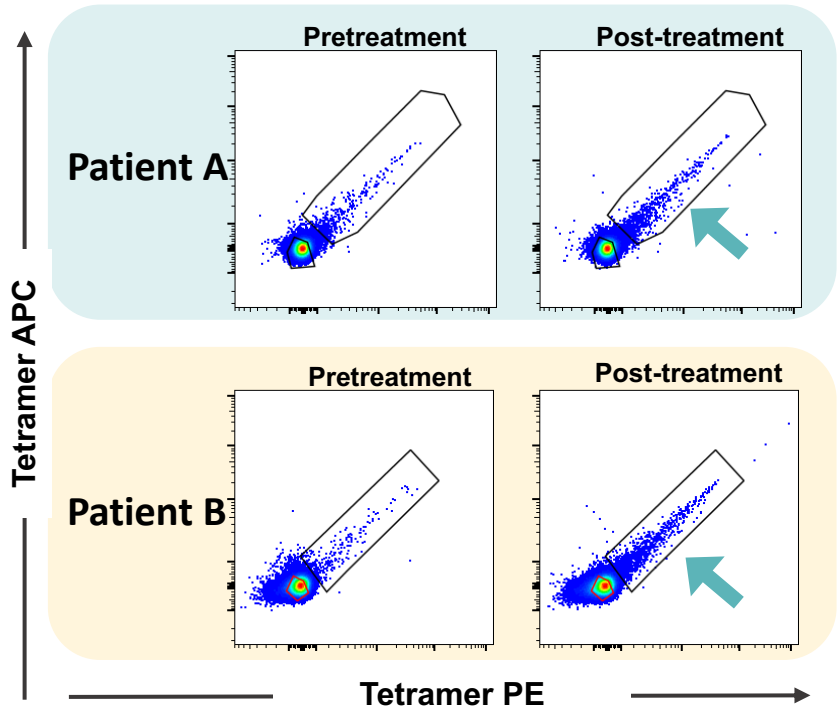
Significant Unmet Need in Patients with WT1-Positive Cancers



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

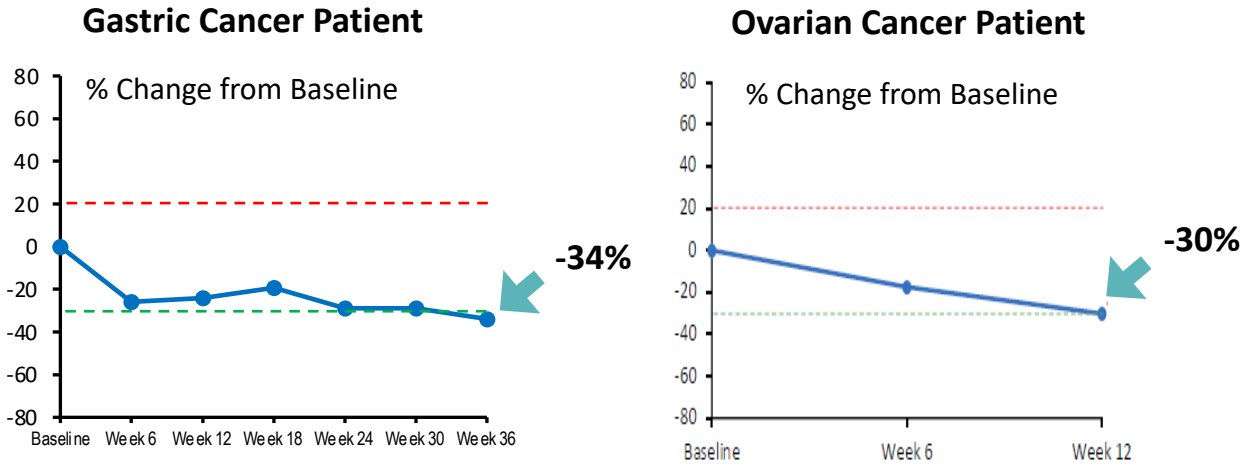
CUE-102 Treatment: Selective T cell Expansion and Tumor Reductions

Selective Expansion of WT-1-specific T cells



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

Examples of Tumor Reductions in CUE-102-treated Patients

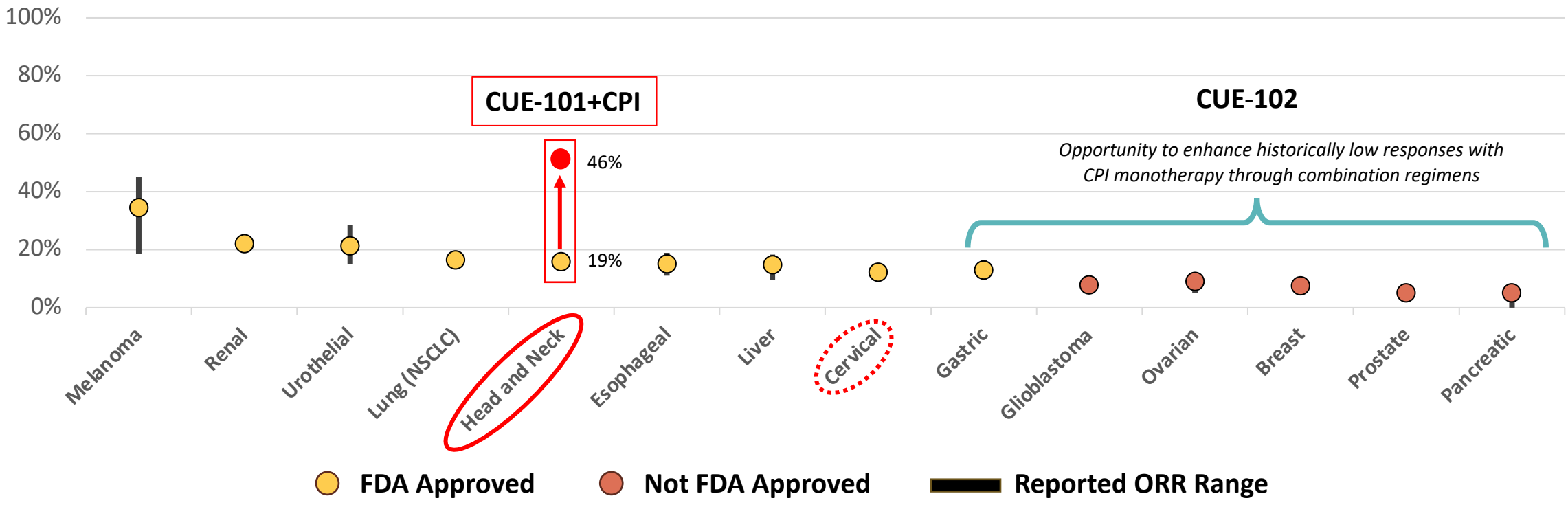


- Disease Control Rate (DCR) of 38% (9/24) across all patients with advanced colon, pancreatic, gastric and ovarian cancer during dose escalation (Part A)
- Clinical activity supports expansion into all 4 tumor types (Part B)

Data Extract: 06-Feb-2024.

CUE-100 Series: 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.

Autoimmune Diseases

CUE-401 – Conversion and Expansion of NEW Tregs

CUE-401: Designed for Conversion and Expansion of Tregs

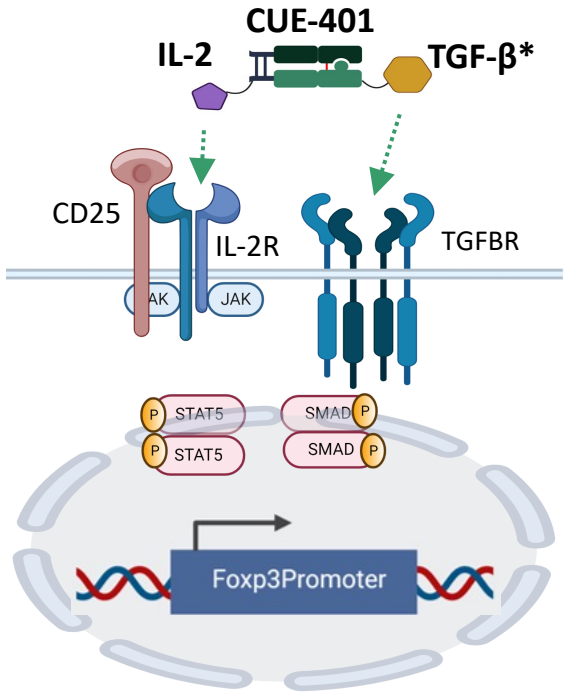
CUE-401 MOA can be broadly developed for many different autoimmune diseases

IL-2 Variant → *Same as in CUE-100 series*

Fc Backbone → *Allows for simultaneous delivery of both IL-2 and TGF-β, along with ease of manufacturability*

TGF-β Variant → *Improved safety and manufacturability*

CUE-401 results in induction of FOXP3+ Tregs

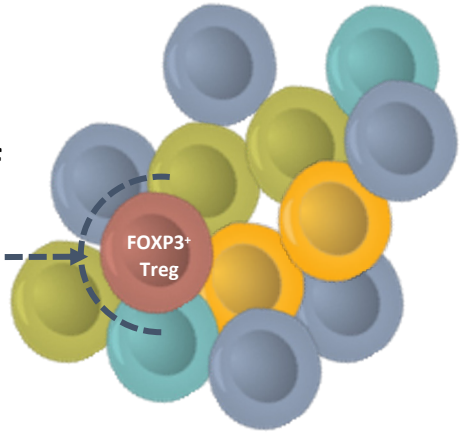


Ono Pharmaceutical funding ongoing research activities through preclinical option period
Cue retains a 50% co-development and co-commercialization right in the US market

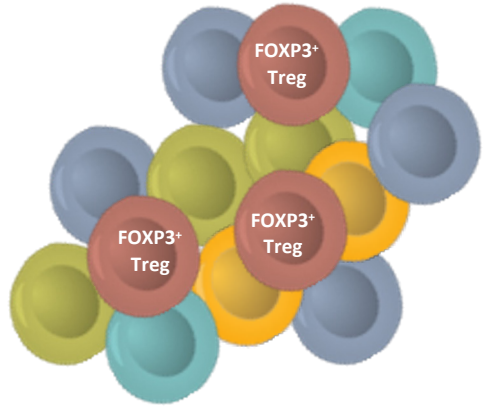
CUE-401 MoA: Quantitatively & Qualitatively Superior to IL-2 Muteins

CD25-biased IL-2 muteins

Focus on a minor population of pre-existing nTregs

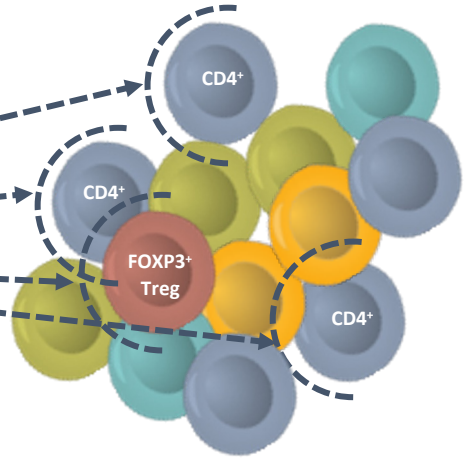


Limited Treg Expansion

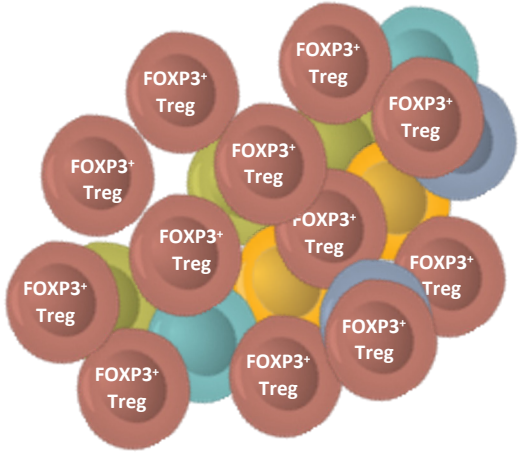


Two Key MOAs:
1) Convert non-Tregs → iTregs
2) Expand pre-existing nTregs

CUE-401

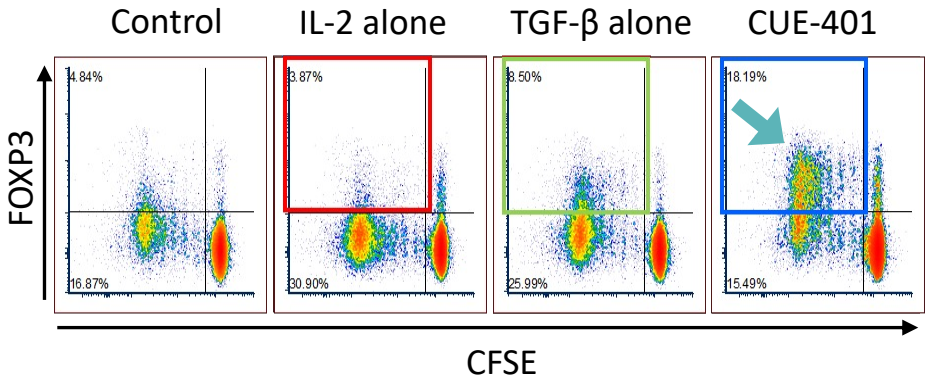


Greater Treg Frequency

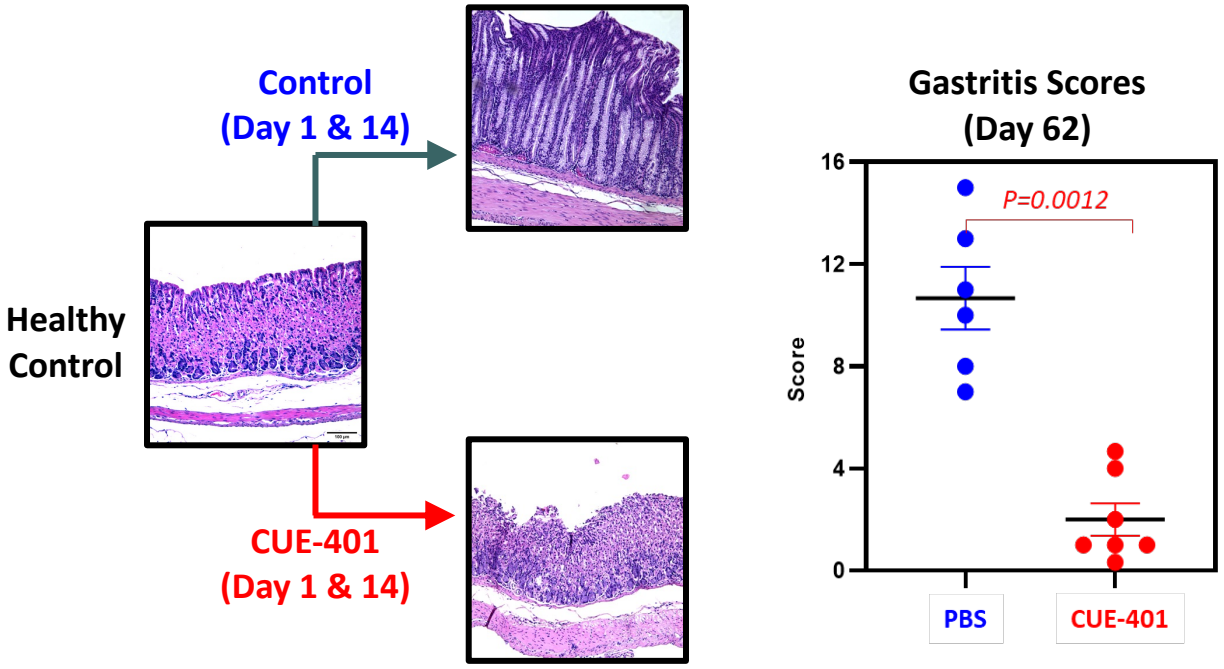


CUE-401: Mechanism of Action and In Vivo Efficacy

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

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

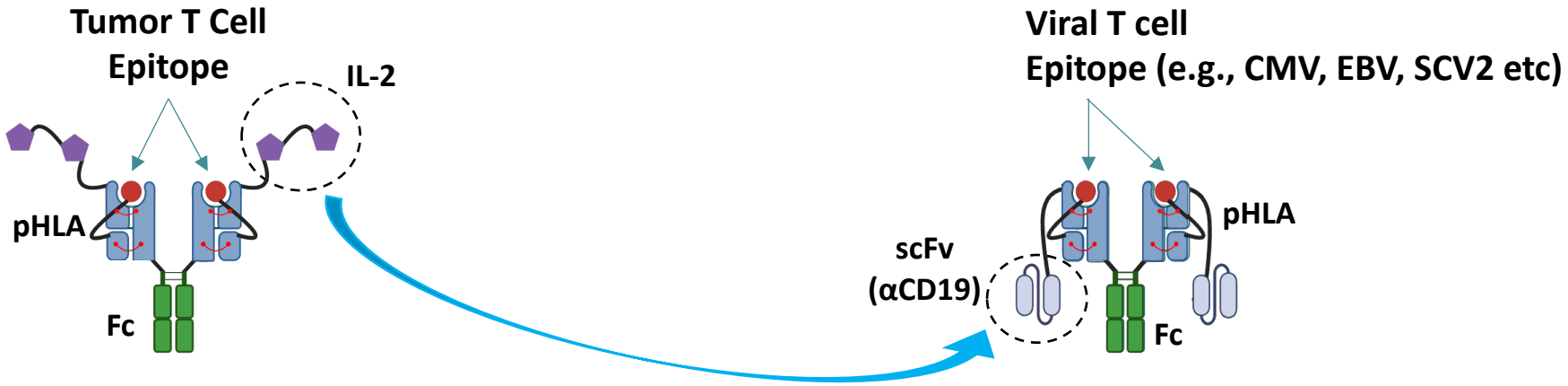
CAR-Ts Targeting B Cells in Autoimmunity

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

Source 1: EvaluatePharma

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



CUE-100 series (Oncology)

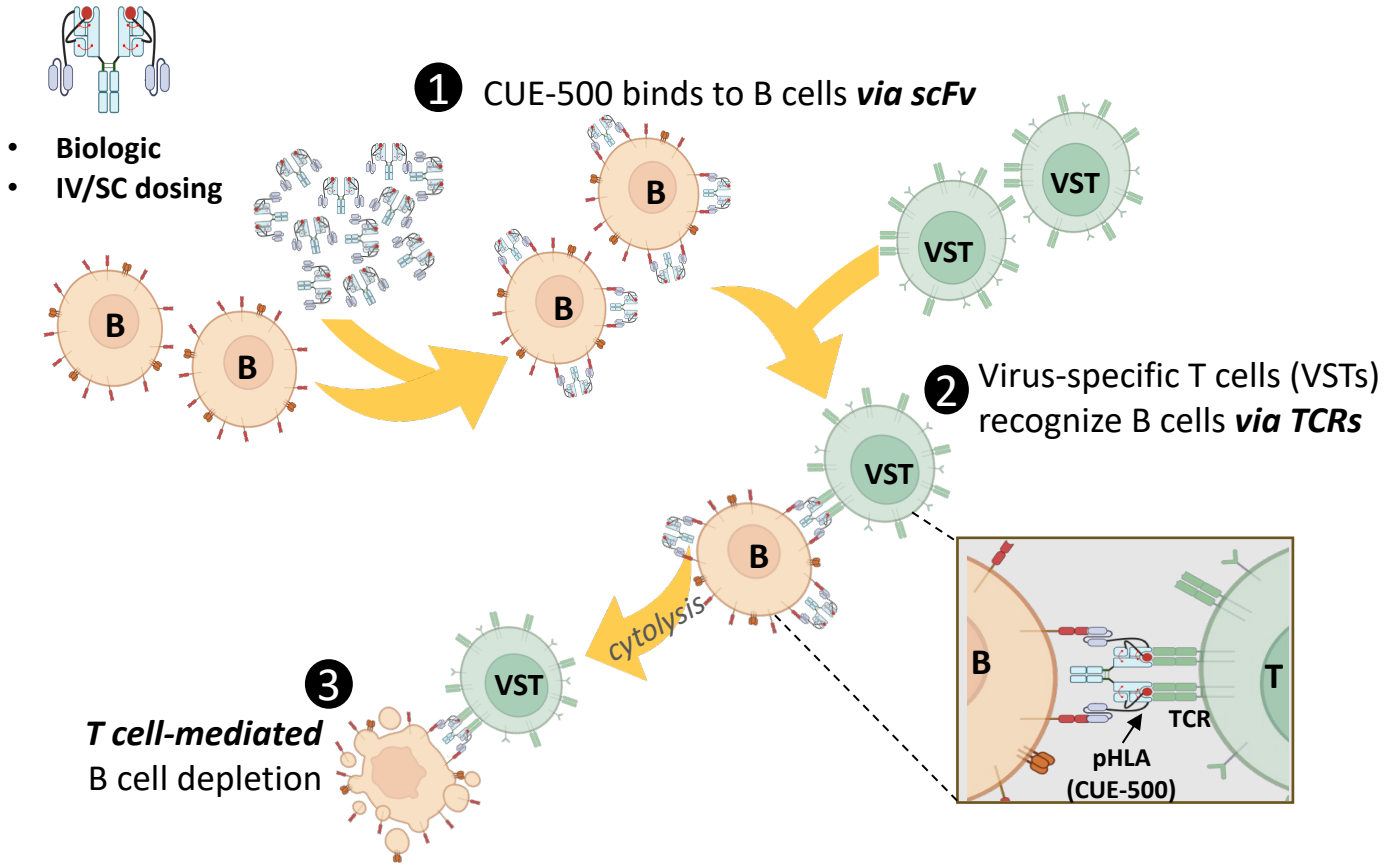
Selective Targeting of IL-2 to Tumor-Specific T cells

CUE-500 series

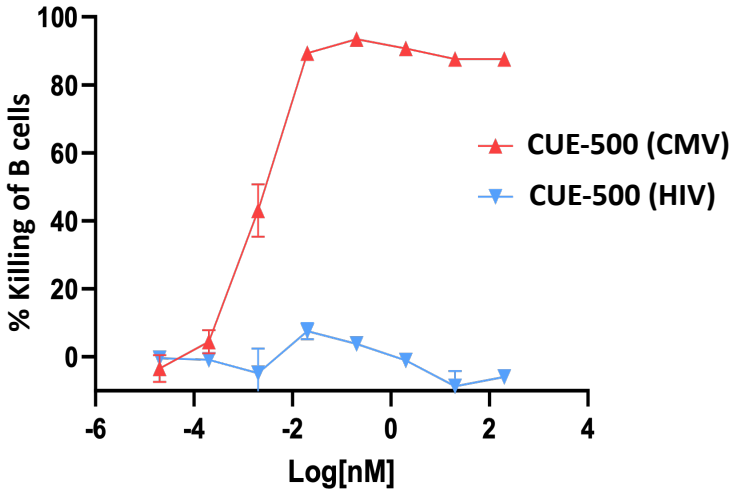
Engaging Virus-Specific T Cells (VSTs) to Deplete B Cells

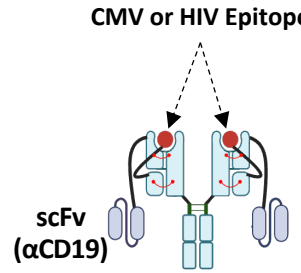
- ✓ Clinical Validation and Platform De-risking
  - ✓ MonoTx Efficacy (> doubling of mOS)
  - ✓ CPI Combo Efficacy (> doubling ORR and mPFS)
  - ✓ Alignment with FDA on a registration path
- ✓ Highly manufacturable with attractive COGS
- ✓ Favorable tolerability (Over 100 patients dosed; no MTD)
- ✓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

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



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

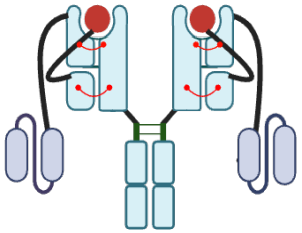




CUE-500

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.)

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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	• Autoimmunity: Clinical efficacy with limited durability	• Autoimmunity: Early data demonstrates robust efficacy and durability	• Autoimmunity: Limited experience
Challenges	• Limited durability • Variable efficacy • Reliant on Fc function and polymorphisms (low vs high responders) • Potential for broad immune activation	• Autologous with complex manufacturing process/supply chain • Requires pre-conditioning regimens and in-patient administration • Toxicity Risks: CRS and neurotoxicity	• 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

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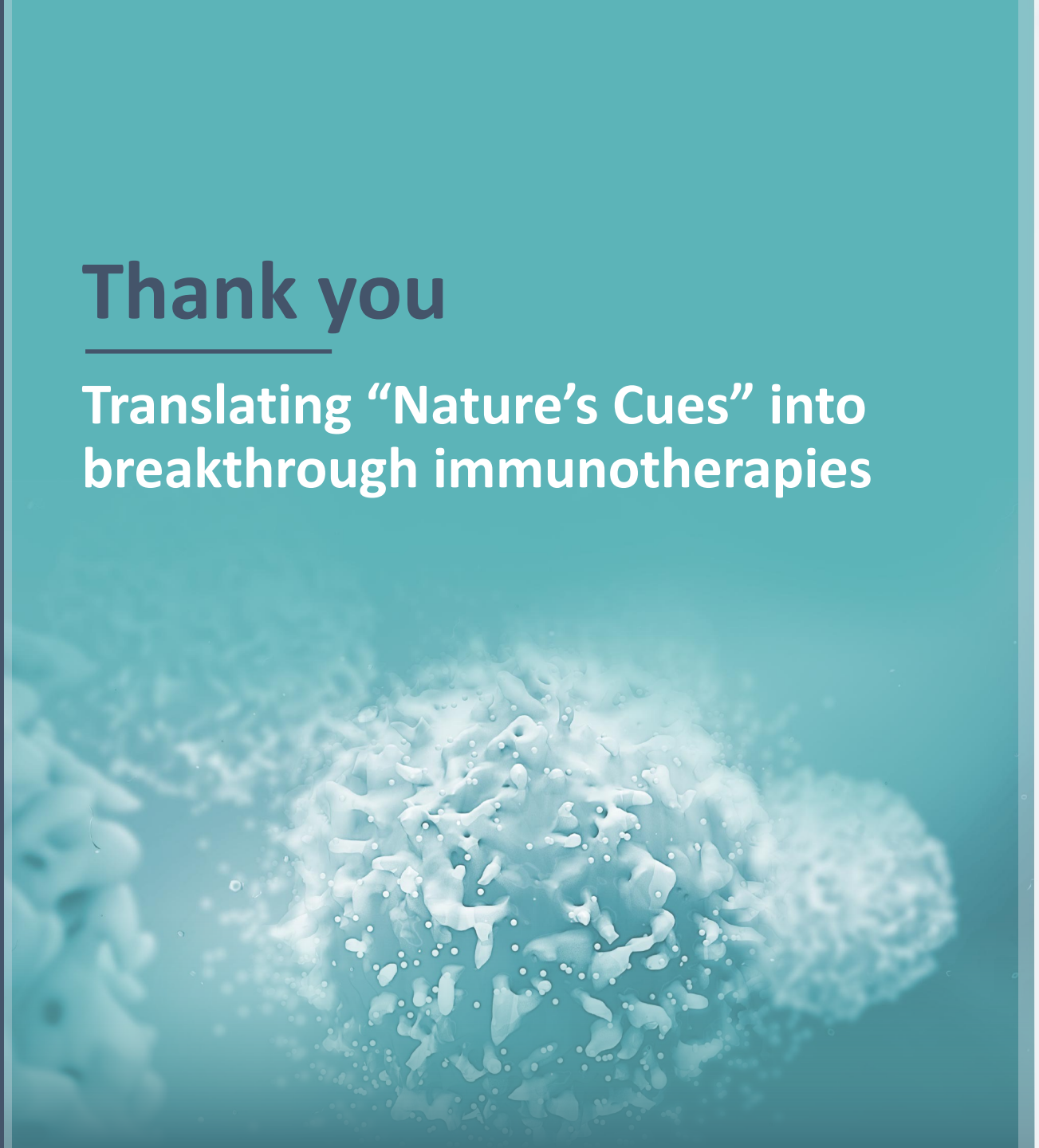
Thank you

Translating “Nature’s Cues” into breakthrough immunotherapies



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